M-1

Emission from the working and counter electrodes under co-reactant electrochemiluminescence conditions

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Electrogenerated chemiluminescence (ECL) is the emission of light from electron-transfer reactions between species which have been electrochemically generated at an electrode surface.[1] The emission in ECL systems is generally thought to occur at the working electrode, with emission at the counter electrode previously being dismissed as unwanted interference.[2] However, continued advancements in ECL have led to the introduction of multi-coloured ECL systems,[3-5] and thus has brought new importance to emission at the counter electrode.

Herein, we present a new approach to explore the potential-dependent multi-colour co-reactant ECL from multiple luminophores. We monitored the potentials at both the working and counter electrodes simultaneously, as well as the current and emission using cyclic voltammetry (CV) in systems containing tris(2-phenylpyridinato)iridium(III) ($Ir(ppy)_3$) and either tris(2,2'-bipyridine)ruthenium(II) ($[Ru(bpy)_3]^{2+}$) or bis[3,5-difluoro-2-(2-pyridinyl-κN)phenyl-κC][2-[1-(phenylmethyl)-1H-1,2,3-triazol-4-yl-κN3]pyridine-κN]iridium(III) $[Ir(df\text{-}ppy)_2(ptb)]^+$, with tri-*n*-propylamine (TPrA) as the co-reactant. Photographs were then obtained of the electrodes to confirm the source of the emissions (counter or working electrode, or both).

When $Ir(ppy)_3$ was combined with $[Ru(bpy)_3]^{2+}$ with TPrA as the co-reactant, the ECL profile (CV and ECL data) consisted of the combined characteristics of the two complexes, as well as additional features due to their interaction. This was also visualised with photographs, where at increasing positive potentials, the green emission from $Ir(ppy)_3$ is first seen, followed by the red emission of $[Ru(bpy)_3]^{2+}$.

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M-2

A novel approach for the determination of homogeneous kinetics using FT-ACV

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Electrochemical techniques are an effective tool for measuring the rates of reactions associated with charge transfers. Comparing experimental responses with simulated data is a common approach to determine homogeneous kinetics (, but the process is complex and time consuming. Looking at the variation in peak parameters of cyclic voltammograms (CV) as a function of timescale, which are then compared to a standard working curve is another method to determine which was pioneered by Nicholson and Shain in the 1960's. This way is a much faster but tends to lack accuracy due to subjectivity in determining baseline for a CV, especially for the reverse peak.

Here, we describe a novel methodology to determine the value of the homogeneous rate constant , associated with an EC process, in a single forward scan rather than comparing the forward and reverse scans. This approach uses Fourier transform alternating current voltammetry (FT-ACV), and focuses on the harmonics, which have dramatically diminished capacitive background, thus removing the uncertainty associated with the baseline. Because only a single scan is needed to determine the value of , the approach is faster and there is less chance of the data being compromised by electrode passivation, which often occurs on the reverse scan. The accuracy of the methodology was tested by comparison with simulated responses and real data for the oxidation of dopamine.

M-3

An efficient electrochemical pathway for a carbon-neutral and sustainable future

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Industrial decarbonisation is an important step in addressing climate change and creating a sustainable future. However, reducing carbon emissions while maintaining quality of life, is a global challenge for manufacturing processes requiring significant investment and a coordinated effort in process innovation. Electrochemical processing is poised to play a critical role in this decarbonisation effort by utilising renewable energy in manufacturing and processing industries. While extensive efforts have focused on the transportation and grid sectors, there has been considerably less focus on the electrification of the chemical and mining industry. Opportunities exist for the development and integration of novel electrochemical processes that offer carbon-neutral synthetic routes to important products by exploiting alternative pathways that overcome molecular transformations. However, electrochemical processing has yet to be optimised and its uptake is commercially limited because effective mixing remains a persistent problem. Accordingly, electrochemical processing is often performed in batch mode which is time consuming as it requires significant downtime between batches. CSIRO has developed a novel axial flow electrochemical reactor to address these issues by employing computational fluid dynamics (CFD) modelling to design and additively manufacture high surface area static mixers which act as central working electrodes. Evaluation of the CSIRO flow electrochemical cell shows that it performs best where mass transport plays a significant role in the reaction rate. Under this condition, CSIRO's flow electrochemical cell can enhance the electrochemical reaction rate up to thirty times compared to a traditional tubular flow cell reactor. Furthermore, the cell performance can be enhanced further by coating the static mixer electrodes with electrocatalysts suited to the application. This flow cell has application in a wide range of fields because of its flexibility in design such as water purification, water disinfection, material electrosynthesis, energy conversion and storage.

M-4

Bioelectrochemical nitrogen fixation using an engineered *E. coli*

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The use of microbes to carry out the reduction of N_2 to NH_3 avoids the challenges associated with anaerobic protein purification and allows both the enzyme and ATP to be regenerated *in vivo*. Nitrogen fixation however requires 8 electrons for every molecule of dinitrogen reduced. Supply of electrons to nitrogenase can be the limiting step in microbial systems. The use of redox mediators to supply electrons could be an avenue to address this bottleneck.

Here, we test microbial electrosynthesis, with a range of mediators, to determine if the rate of nitrogenase activity could be enhanced using a heterologous expression system for nitrogenase from *Klebsiella oxytoca* in *E. coli*, based on a natural promoter system.

M-5

Affinity-based interfacial sensing for detecting HOTAIR lncRNA in cancer plasma samples

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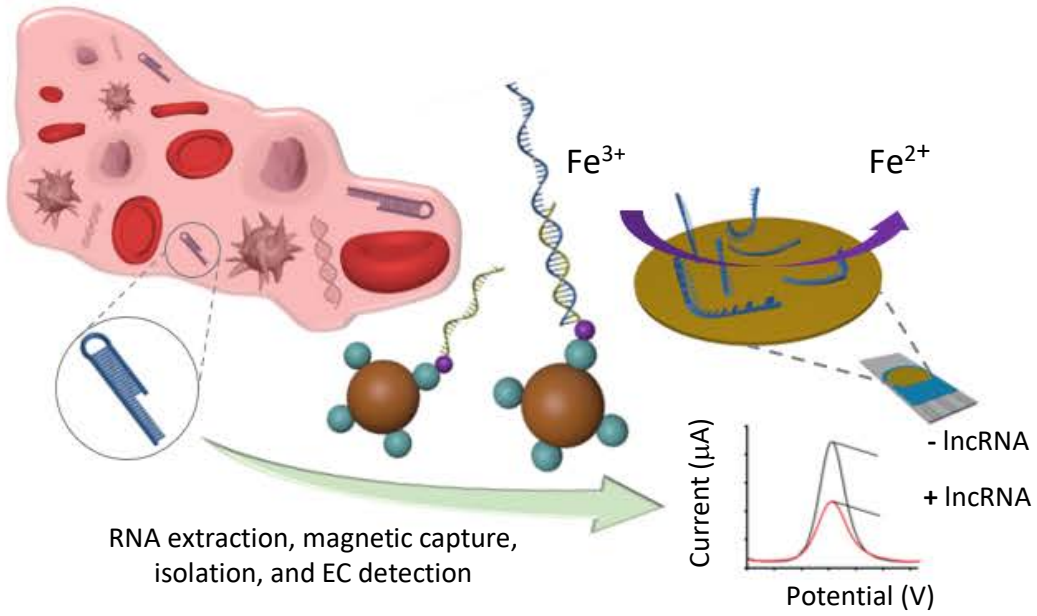
Long non-coding RNA Homeobox transcript antisense intergenic RNA (HOTAIR) has been shown to participate in different processes of normal cell development. Aberrant overexpression of HOTAIR contributes to the initiation, growth, and invasiveness of ovarian cancer. Using the affinity interaction of target HOTAIR sequences towards a screen-printed gold electrode (SPE-Au), herein we report on a novel, rapid and simple method to detect HOTAIR sequences. HOTAIR lncRNA sequences were first extracted from ovarian cancer cell lines and patient plasma samples and were magnetically captured and purified by complimentary capture probe-functionalized magnetic beads. Isolated target lncRNAs were directly adsorbed onto unmodified screen printed gold electrodes (SPE-Au) for direct quantification with $[Fe(CN)_6]^{3-/4-}$ redox couple. Our assay achieved a linear dynamic range of 100 nM and 1pM for detecting pre-clinical model HOTAIR lncRNA samples (%RSD = < 5%, for n = 3) and was highly specific, showing clear distinction between HOTAIR lncRNA targets and non-specific miR-891 and miR-486 (100 nM) (%RSD = < 5%, for n = 3). The method was also tested using clinical samples from ovarian cancer patients and the resulting differential pulse voltammetry signals (DPV) show clear distinction between the ovarian carcinoma samples and benign samples. The analytical performance of our method was validated using RT-qPCR.



M-6

Effect of electrochemical technique on reproducibility with screen-printed carbon electrodes

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Screen-printed carbon electrodes (SPCEs) have been emerging as an alternative to conventional carbon electrode materials such as glassy carbon (GC) for several decades.[1] SPCEs offer several advantages for real-world sensing applications. In particular, the individual cost per SPCE can be sufficiently low such that single-use disposable sensors can be developed, which circumvents many issues such as electrode fouling. Electrode printing methods are now sufficiently well-developed that the geometric area of the active electrode can be reproduced with high precision.

While engaged in a sensor development project using SPCEs, we realised that the reproducibility of the electrochemical response with such electrodes is often governed by factors other than the tolerance of the conductive area. Surprisingly, we have found that the reproducibility varies strongly depending on the electrochemical technique used to interrogate the sensor. We have investigated this phenomenon by evaluating the relative standard deviation (%RSD) for the voltammetric responses of GC and various SPCEs with the electrochemical probe, ferrocene carboxylic acid (FcCOOH). We compared the %RSD among 1st Harmonic Fourier Transform Alternating Current voltammetry (1H FTACV), 2nd Harmonic FTACV, square-wave voltammetry (SWV) and cyclic voltammetry (CV). Our results show that the RSD increases in the order CV < SWV < 1H FTACV < 2HFTACV; and that the RSD with GC is generally lower than that with SPCEs. We suspect that the occurrence of this phenomena is due to variability in capacitance between SPCEs, as the available microscopic area of each working electrode of SPCE may differ from one to another.[2, 3]

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M-7

Growing solids at liquid-liquid interfaces

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Interfacial crystal nucleation is a substantial phenomenon that plays an important role in many environmental, biological, and industrial processes. Manufacture of medicines is an example of the beneficial impact of crystallization, while reduced productivity due to the total or partial obstruction of pipes in oil and gas production processes would be detrimental[1-3]. Crystal growth control can involve changing physical parameters such as temperature, concentration, pH and pressure, but the use of electrochemistry is rare[4]. Electrochemistry at an aqueous-organic interface is a well-established branch of electrochemistry which is based on the junction between the two liquids, including solvents with low mutual solubilities and dissolved electrolytes[5]. In this investigation, however, the possibility of ion transfer across the interface between two immiscible solutions is used to investigate crystallization at an interface, which possibly opens new ways to study or apply interfacial crystallisation processes. In an effort to obtain information on crystallization at the aqueous-organic interfaces, nucleation and growth of barium sulfate was studied as a model crystallization system. To achieve this aim, Ba^{2+} has been placed in either the aqueous or organic phases so that it could undergo an interfacial interaction with SO_4^{2-} in the adjoining phase. Characterisation of precipitated solids formed at the aqueous-organic interfaces was performed by several techniques such as Raman spectroscopy, SEM, EDX and TEM. This confirmed that the contact of barium and sulfate ions due to the transfer of these ions across two immiscible solutions causes the interfacial crystallization of $BaSO_4$. It is also investigated what would happen when ionophore was present with an aim to see whether the crystallization could be controlled. The latest results of this study will be presented and discussed.

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M-8

A tuneable material platform for diabetes detection and monitoring

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Nanostructured electrode surfaces are proving to be critical tools for the development of highly sensitive electrochemical biosensors. Here, gold nanoislands (Au NIs) are directly self-assembled on screen printed carbon electrodes using a scalable gas phase deposition technology. It is demonstrated that by tuning the Au NIs deposition parameters, electrode surfaces with different surface coverage can be engineered with different linear ranges for the detection of glycated albumin (GA), a biomarker for diabetes.[1] This tuneable material platform showed the ability to detect GA concentrations as low as attomolar levels, using a DNA aptamer as a bioreceptor and differential pulse voltammetry as the electroanalytical tool, while at the same time the ability to detect clinically relevant concentrations of GA (10 to 250 µM).[2] Together with the high sensitivities, the developed sensor also showed superior selectivity for the detection of GA over other common molecules present in human serum such as human serum albumin, ampicillin, glycine, and glucose. This tuneability opens up a facile and rapid way to nanoengineer electrode surfaces for biosensors that require both an upper limit as well as a lower limit for the detection of biomarkers.

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M-9

Development of an Artificial Intelligence Platform for Voltammetric Mechanistic Studies

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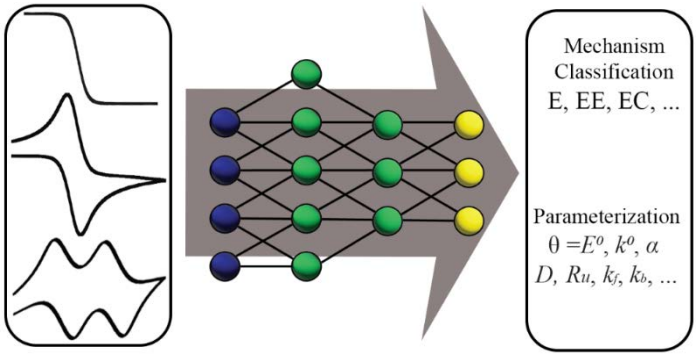
In recent years, significant progress has been made in applying Artificial intelligence approaches, such as Machine learning and Bayesian inference, to obtain mechanistic information in voltammetric studies[1,2,3,4]. Many methods developed have been applied satisfactorily to noisy synthetic data, but with limited success in analysing experimental data. The experimental data is often difficult to fit due to non-uniqueness of the fitted simulations or deviations of the experimental data from the theoretical model.

So far, the most widely used data analysis algorithms used in voltammetry employ general optimisation methods and Bayesian Inference[1]. However, it is difficult to use these approaches to automatically identify probable mechanisms and quantify all parameters involved. Recent research by the Monash Electrochemistry Group, has found that the weakness of each individual algorithm could be compensated by using a chain of algorithms. Consequently, the recently developed Artificial intelligence platform offers more accurate identification of experimental data than an individual algorithm. In particular, it has been found that a combination of these algorithms with a multivariate Deep neural network for general classification, an unsupervised clustering algorithm for feature extraction of training data, a Deep neural network for classifying the featured data and a Greedy algorithm for parameter selection has led to a more robust method for qualitative and quantitative analysis of experimental data. In this talk, this Artificial intelligence platform will be presented and possible implications for voltammetric data analysis using Artificial intelligence will be described.



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M-10

Investigating the influence of water on the oxidation mechanism of a catechol nitroxide

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Employing a material that is inherently capable of transferring numerous electrons per molecule can potentially boost the energy density of a flow battery system in cases where the molecular weight is kept low[1] and all charged states remain soluble and stable within the electrolyte. Unfortunately, satisfying these conditions with existing multi-redox centred organic materials remains rare.[2,3] This results in the need for not only the identification of multi-redox centred organic materials exhibiting good stability and solubility in their charged states, but the specific conditions that provide and enhance that stability and ability to remain soluble.

A promising redox active substituted isoindoline shown in Figure 1, in principle exhibits three redox centres on the molecule, with an exceptional theoretical capacity of 361.76 mAh g^{-1}. With an electrochemically reversible nitroxide moiety and two oxidisable hydroxyl groups, a catechol nitroxide appears to be a potential multi-redox candidate for use in a flow battery system. Initial cyclic voltammograms however, found that the electrochemical behaviour is complex, even more so when exposed to a proton source, even at trace amounts. Results indicate that proton availability and perhaps pK_a values of the different oxidised states of the molecule play a key role in determining the mechanistic process by which electrons are transferred between substrates. Investigating both environments was essential to gain insights into using nonaqueous and anhydrous conditions which are conducive to battery operation.

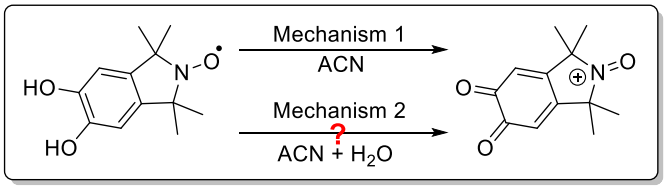

Figure 1: Structures of the catechol nitroxide and the oxidized form with the two different mechanisms differing in the presence of water.

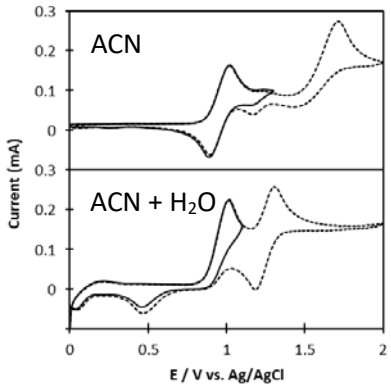

Figure 2: Voltammetric curves of a 10 mM solution of catechol nitroxide at 50 mV/s in anhydrous ACN (top panel) and wet ACN (bottom panel).

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M-11

Hydroxamate adsorption at copper and iron surfaces; by *in situ* neutron reflectometry

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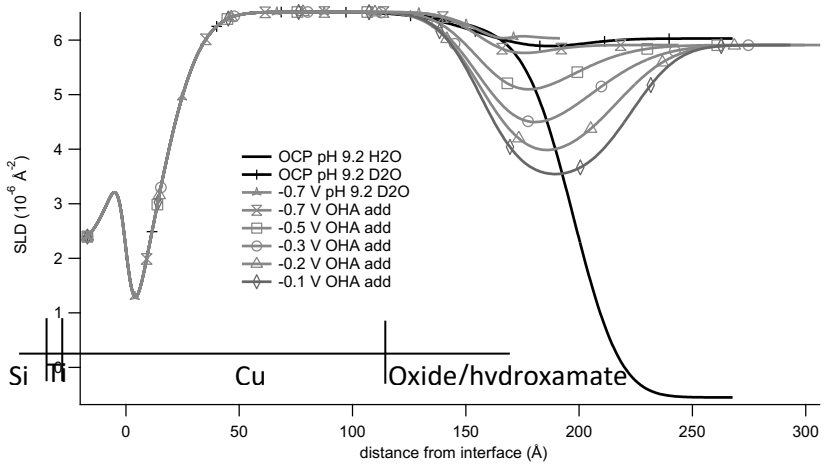
Metal complexes with hydroxamic acids play an important role in a number of areas of biological and industrial chemistry.[1] Hydroxamic acids are siderophores for some microbes, facilitating transport of iron and copper into the cell, they are applied as collectors in froth flotation for the recovery of valuable components from oxidized ores, including those of copper, iron and rare earth oxide minerals.[2,3] It is critical to identify the mechanisms by which hydroxamates interact with iron and copper in aqueous environments in order to optimise hydroxamate applications but, as yet, such studies are few. In flotation, for example, hydroxamates are ineffective for some iron oxides but sometimes collect non-target iron sulfide minerals.[4] The reasons for such equivocal responses have not been identified. Our spectroscopic studies have shown great differences in hydroxamate interactions with surfaces of iron oxide minerals, oxides on sulfide minerals and the native oxide on iron under ambient conditions: the usefulness of these techniques is restricted due to detection limits and instrumental environments. Neutron reflectometry enables the study of light elements against metal films to follow the initial stages of hydroxamate interaction with copper and iron thin films under solution conditions with temperature and or potential control. This has revealed the water content and likely bilayer structure of the initial surface layers, see below, under open circuit conditions and then rearrangement as the metal film is held under potential control. The fits below reveal an initial layer 8 nm thick with a volume fraction of 0.84. The layer thickness increased to 15 nm at -0.3 V at a similar volume fraction.[5]



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M-12

Low-cost Electrochemical Paper-based Device for Exosome Detection

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Exosomes are vesicles released by both healthy and cancer cells into the extracellular matrix and bodily fluid. Cancer cell-derived exosomes have attracted much attention in early-stage diagnostics and prognostics. Thus, detecting exosomes is of great interest to biology and medicine. However, many conventional detection methods require high-cost equipment and centralised laboratory facilities, making diagnostics inaccessible in limited-resource settings. In this study, we report a proof-of-concept low-cost electrochemical paper-based analytical device to quantify both the total bulk and cancer cell-derived exosomes in cell culture media. The device employs a sandwich immune assay design, where exosomes are initially captured using the electrode-bound generic antibodies (i.e. CD9) and subsequently detected via ovarian cancer-specific CA125 antibodies. Our proposed device quantifies the total exosome concentration with a detection limit of 9.3×10^7 exosomes/mL and ovarian cancer cell-derived exosomes with a detection limit of 7.1×10^8 exosomes/mL, with relative standard deviation of <10% (n=3). We suggest that this low-cost and simple electrochemical paper-based device could be an alternative tool for detecting disease-specific exosomes in biological samples with the potential to be further developed for point-of-care diagnosis.

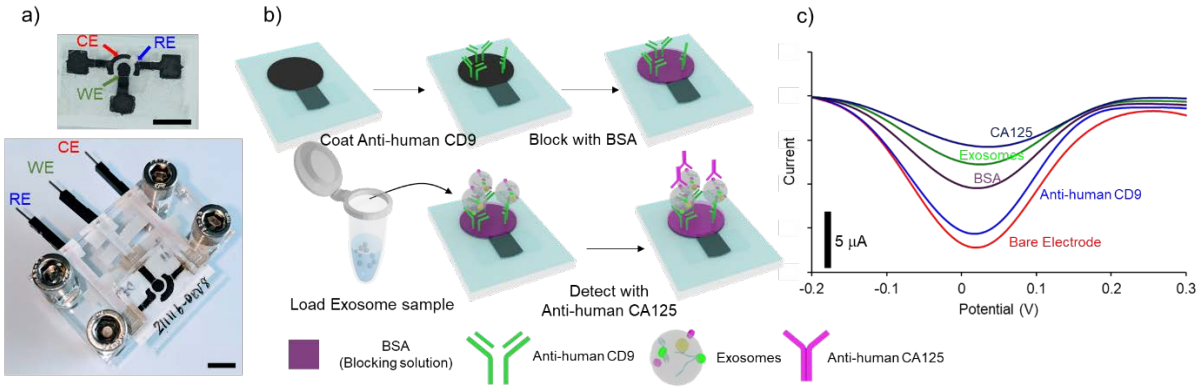

Figure 1 a) The paper-based carbon electrodes (PCEs) were fabricated using parafilm hot pressing and inserted into custom-made connectors for working, reference and counter electrodes, which is interfaced with the potentiostat to perform the electrochemical assay. b) The exosomes were extracted from the cell culture media and spiked in PBS buffer. CD9 antibodies were immobilised on PCEs by protein adsorption on the paper matrix. Total exosome populations were captured via their immune interaction with surface-bound CD9 antibodies. Ovarian cancer cell-derived exosomes were sub-populated by using CA-125 antibodies. c) DPV signal depicting the stepwise attachment of each layer on the PCEs surface. The scale bar represents 1 cm.

M-13

Hydrothermally-grown and Electrodeposited Cobalt Sulfide for Electrochemical Oxygen Evolution and Electrochemical Sensing

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A wide range of electrocatalysts have been developed and implemented for electrochemical water splitting and electrochemical sensing over the last decades[1, 2]. Yet, researchers typically use either a conventional synthesis method[3] (followed by drop-casting or spray-coating onto the electrode), or directly electrodepositing the catalyst[4]. However, a clear comparison of different synthesis techniques, and how this affects the electrochemical applications is less reported.

In this presentation, I will show a systematic comparison of cobalt sulfide (CoS) nanostructure-based electrodes prepared by one-pot hydrothermal (HT) and electrodeposition (ED) methods towards two applications: (a) electrochemical water splitting and (b) electrochemical glucose sensing. Systematic characterizations are performed using X-ray diffraction (XRD), scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDX), and X-ray photoelectron spectroscopy (XPS). It is observed that the CoS-ED electrode demonstrated enhanced oxygen evolution reaction (OER) performance with lower overpotential (~166 mV at 10 $mAcm^{-2}$), lower charge transfer resistance (~372 Ω), smaller Tafel slope (86 mV/dec), and better stability compared to the CoS-HT electrode. Moreover, the CoS-ED electrode-based sensor also exhibited better performance, higher sensitivity, better selectivity, and good stability for electrochemical glucose detection in comparison to the CoS-HT sensor. It is noteworthy that the advancement of deposition methods is of great importance for the fabrication of cost-effective, reproducible and efficient electrode systems in the future.

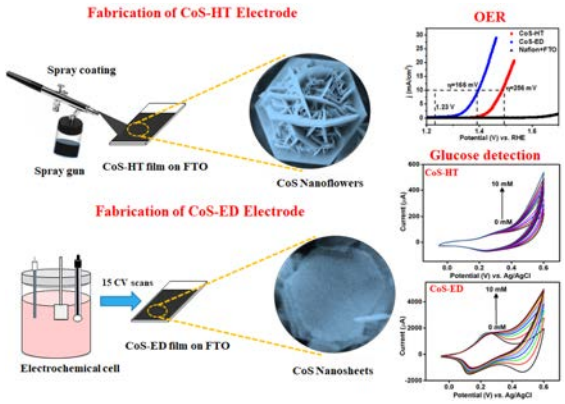

Figure 1. Graphical illustration of the preparation method for hydrothermal (HT) CoS coated electrodes and electrodeposited (ED) CoS electrodes. The linear sweep voltammetry and cyclic voltammetry scans to the right show the different performance of these electrodes towards the oxygen evolution reaction (OER) and glucose sensing from 0 to 10 mM (both in KOH electrolyte).

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M-14

Operando Investigation of the Performance and Stability of Fe-N-C Oxygen Reduction Reaction Catalysts in Proton Exchange Membrane Fuel Cell

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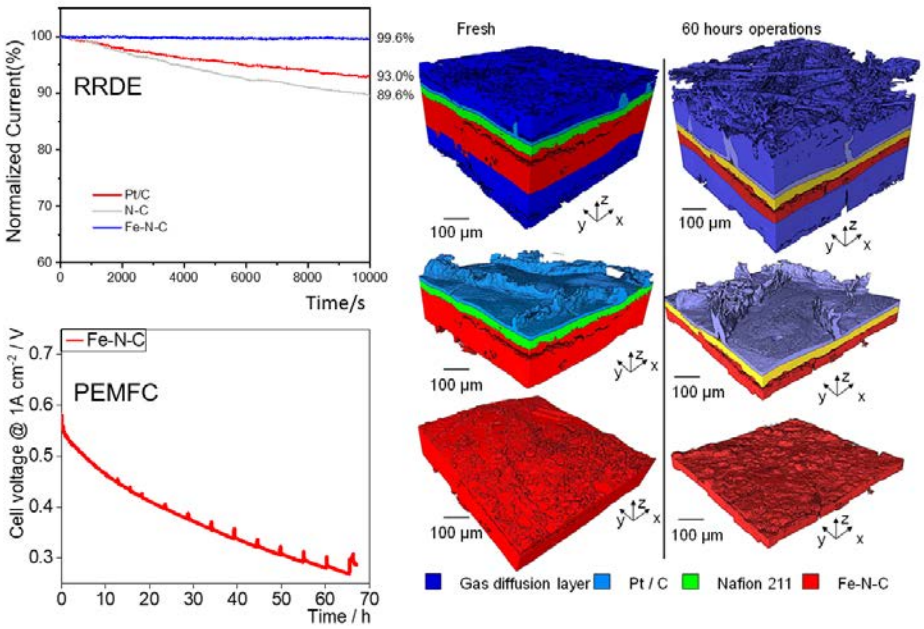
Abstract

Proton exchange membrane fuel cells (PEMFCs) using H_2 and O_2 to produce electricity with high energy conversion efficiency and energy density, zero CO_2 emission, and quick refueling are considered one of the most promising next-generation energy conversion devices.[1] Platinum (Pt) has the highest activity in catalysing the oxygen reduction reaction (ORR) and is currently used in commercial fuel cells. However, the high cost of Pt hinders the widespread application of PEMFC technology, requiring the replacement of Pt-based materials with low-cost, highly active and stable Pt group metal-free ORR catalysts. Although the ORR activity of Fe-N-C catalysts is recently approaching the performance of Pt/C, their stability is a huge challenge in real-world applications.

In this work, a series of novel Fe–N–C catalysts were prepared by heating a Fe-doped pre-carbonised ZIF-8 framework. The as-prepared catalyst with optimised Fe doping (Fe–N–C-300) containing both FeN_x active sites and Fe nanoparticles (NPs), demonstrates a high activity towards the ORR in acidic media with a half wave potential of 0.81 V vs. RHE and a peak power density of 1.08 W cm^2 in a PEMFC. Overall, the excellent ORR activity is attributed to *(i)* strong interaction between FeN_x and Fe NPs, optimising the binding energy that benefits the adsorption/ desorption of the ORR products and intermediates; *(ii)* Fe NPs assisting the exposure of otherwise inaccessible FeN_x active sites enhancing mass transport. In addition, we also investigate the degradations of a single-atom dominant catalyst (Fe-N-C-100) using *in situ* techniques such as electrochemical impedance spectroscopy and cyclic voltammetry and *ex situ* characterisations such X-ray computed tomography and HR-TEM.[2] These reveal that Fe demetallation combined with carbon corrosion would be the major reasons for undesirable stability during fuel cell operation.



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M-15

Ionic liquid mixtures: effects on redox kinetics and electrical double layer structure

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The application of ionic liquids as electrolytes has steadily increased over the last two decades thanks to their high thermal and electrochemical stability, low volatility, wide electrochemical windows, and intrinsic conductivity.[1] However, investigation of binary (two component) mixtures of ionic liquids for electrochemical applications has been rather unexplored. Ionic liquid mixtures allow for the manipulation of the physical and electrochemical properties of electrolytes without the need to synthesise new ionic liquids with different molecular structures.[2–5] The influence of bulk composition of ionic liquid mixtures on the redox kinetics of the oxygen/superoxide ($O_2/O_2^{\bullet-}$) redox couple was investigated for three mixtures of bis(trifluoromethyl)sulfonylimide-based ionic liquids on platinum and gold electrodes. Namely, 1-butyl-3-methylimidazolium bis(trifluoromethyl)sulfonylimide ($[C_4mim][NTf_2]$) mixed with diethymethylsulfonium bis(trifluoromethyl)sulfonylimide ($[S_{221}][NTf_2]$), 1-butyl-1-methylpyrrolidinium bis(trifluoromethyl)sulfonylimide ($[C_4mpyrr][NTf_2]$), and trihexyltetradecylphosphonium bis(trifluoromethyl)sulfonylimide ($[P_{14666}][NTf_2]$). These cations were chosen to reflect mixtures of ions with delocalised charges and point charges, differences in molar volume, and different capacities for forming nanostructures. Peak-to-peak separations and cathodic reduction potentials for the $O_2/O_2^{\bullet-}$ redox couple changed mostly linearly with respect to bulk composition of the mixtures, especially on platinum electrodes. Changes to the kinetics of the oxygen reduction reaction were then compared to the differences in the structure of the electrical double layer, which was probed using atomic force microscopy. The findings will be used to develop task-specific ionic liquid mixtures for amperometric oxygen sensors and inform the enhancement of electrical double layer capacitors derived from similar ionic liquids.

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M-16

Role Of Green Solvents in Rice Husk Treatment for Sustainable Battery Material

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Global demand of rechargeable Li-ion batteries has risen steeply due of it versatile potential and have ultimately increased the extraction of minerals. Battery components such as cathode and anode materials are mainly extracted by mining process and has its own limitation such as restricted geographical availability, impact environment as it releases toxic greenhouse gases, and non-sustainable resource, hence an alternative source for the battery material is necessary[1]. The use of alternative energy sources such as biomass has become a major focus for the energy storage market as a renewable source due to its carbon neutrality and abundance on the planet[2]. In terms of silicon-based anode materials for rechargeable batteries, silica-rich rice husk is an abundant and sustainable agricultural waste, which can be an attractive alternative to produce silicon/carbon (Si@C) materials[3]. Several million tons of rice husk wastes is generated in Australia each year, where it is either (a) left in the field, (b) disposed of directly into landfill or (c) used as low-value agricultural items, such as fertilizer additives, stockbreeding rugs, and bed soil[4]. Hence, utilising such waste biomass as a precursor for silicon/carbon preparation will not only reduce Australia's carbon footprint but also has definite potential for Australian primary producers to value-add and sell into the future high growth batteries anode market. This research aims to develop sustainable, low-cost rice-husk-derived silicon/carbon composite anodes using scalable techniques for next generation batteries. The objectives will be achieved by exploring novel green pre-treatment and processing methods as well as modification of electrode and electrolytes. The outcomes will provide an alternative market for the biomass and help to address energy security and climate change issues that currently challenge the global community.

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M-17

Hybrid ionic liquid electrolyte for long life practical Li metal battery

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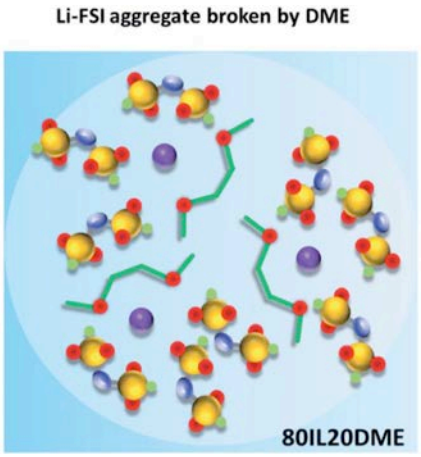
The application of ionic liquid electrolytes in room temperature high current rate cycling of lithium batteries are limited by the high viscosity and low ion transport properties despite their advantages in low vapor pressure, non-flammability and higher electrochemical stability. We explored a novel ether aided superconcentrated ionic liquid electrolyte: a mixture of ionic liquid, *N*-propyl-*N*-methylpyrrolidinium bis(fluorosulfonyl)imide (C3mpyrFSI) and ether solvent, *1,2* dimethoxy ethane (DME) with 3.2 mol/kg LiFSI salt. The hybrid ether aided IL electrolyte offered an alternative ion-transport mechanism and improved the overall fluidity of the electrolyte. Their speciation and solvation environment were investigated by Pulsed Field Gradient (PFG) NMR spectroscopy along with FTIR study. An optimum composition of 80IL20DME showed the best performing electrolytes among the series of hybrid mixtures. Further the molecular dynamics (MD) study on the electrolyte revealed that the coordination environment of lithium in the ether aided ionic liquid system offered a coexistence of both the ether DME and FSI^- anion simultaneously and the absence of 'free', uncoordinated DME solvent. According to MD simulations the fast exchange environment of these structures led to very fast kinetics for lithium plating/stripping process in which is consistent with the cyclic voltammetry experiments. Finally, the ether aided IL electrolyte was applied in making a practical lithium metal battery against a high mass loading (12 mg/cm^2) LFP cathode and cycled at a high current rate of 1 mA/cm^2 for 350 cycles without capacity fading. It offered a very stable cycling with an overall coulombic efficiency of >99.8%. The rate capability test showed that this electrolyte can pass current density as high as 7 mA/cm^2 with superior capacity retention and without any electrolytic decomposition. This ether aided IL was also able to demonstrate an 'anode free' LFP–Cu cell which was cycled over 50 cycles and achieved an average coulombic efficiency of 98.36%.[1] We believe the coordination chemistry and the excellent cycling stability collectively leads toward a breakthrough in realizing the practical applicability of this ether aided ionic liquid electrolyte in lithium metal battery applications, while delivering high energy density in a prototype cell.



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M-18

Natural graphite/silicon anode: Obstacles and opportunities

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Lithium-ion batteries (LIBs) are the future of low carbon-emission transportation. However, LIBs currently rely on synthetic graphite for their anode. This synthetic graphite consumes a lot of energy during its production which directly affects the cost as well as emitting a considerable amount of greenhouse gas. This counteracts the main advantage of LIB electric vehicles.

Natural graphite ore is a readily available material for incorporation into LIBs, with significantly less greenhouse emissions from production. Taking advantage of natural graphite sources can significantly reduce the production costs. However, different types of graphite can be obtained on different geological strata, refining the output to meet battery standards is a major obstacle for researchers. Furthermore, graphite-based anodes meet their limit in theoretical capacity at 372 mAh g^{-1}.[1] For this reason, the addition of materials to increase capacity and remain competitive in price is a direction that needs to be considered.

Silicon is a widely used material in the semiconductor industry and in terms of (LIBs), silicon is the material with the highest theoretical capacity (4200 mAh g-1 for $Li_{22}Si_5$)[2] which is 10 times higher compared with the current commercially available graphite. Although promising, pure silicon anodes have a major problem due to their large volumetric expansion during lithiation, leading to faster degradation mechanisms in LIBs. This is caused by the alloying reaction with lithium, causing an anisotropic expansion and electrical isolation.[3]

This work focuses on making use of the natural graphite sources and various Si particle sizes for fabricating Li-ion anode materials. We aim to increase the influence and innovative competitiveness of natural graphite anodes in the world battery market and the reduction of environmental emissions by reducing the cost disparity between fossil fuel vehicles and electric vehicles.

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M-19

Waterborne anticorrosive coatings with a coumarate based corrosion inhibitor and phosphate functionalization

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One of the most widely applied methods for the mitigation of corrosion is to cover metallic surfaces with organic coatings [1]. However, physical barrier properties may not be enough to prevent corrosion, mainly due to the heterogeneities and defects inherent in the film formation process [2], and to those that may be produced during the life of the coating. Active protection can be provided to the coating by incorporation of corrosion inhibitors [3]. Among organic molecules, the p-coumaric acid (p-CA) has been found to be promising for corrosion protection [4]. Therefore, in this work the anticorrosive properties of methoxy p-coumaric acid (H1), a derivative of the p-coumaric acid, were investigated by Electrochemical Impedance Spectroscopy (EIS) and Potentiodynamic Polarization (PP). Then, H1 was incorporated into an environmentally friendly poly(MMA/BA) latex by batch miniemulsion polymerization. A control latex wihout inhibitor was also produced for comparison purposes. The corrosion protection of the coatings was investigated by electrochemical analysis of the intact and scratched coated steel substrates. The intact coating with H1 incorporated presented significantly higher impedances when compared to the control, showing an improvement of the barrier protection. In the tests with the scratched coatings, H1 was able to mildly retard the drop of impedance with time, exhibiting some level of active protection.

Recently, promising corrosion resistance was found in waterborne (meth)acrylic films with phosphate functionality, achieved by using a phosphate reactive surfactant, SIPOMER PAM 200. When dried under controlled conditions of temperature and relative humidity (23 °C, RH = 60 %), the phosphate groups interact with the hydroxyl groups of the surface of the steel, producing a passive iron phosphate layer, covalently bonded to the polymeric film [5]. In an attempt to improve the corrosion protection properties of the coating with H1 incorporated, SIPOMER PAM 200 was fed to such latex by semibatch emulsion polymerization. A control phosphated latex was also produced without H1 inhibitor. Electrochemical analysis of both systems was carried out, with the SIPOMER addition leading to an improvement in performance for both systems.

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M-20

Electrochemical Sensors for Water Quality Monitoring of Inorganic Nitrogen

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There remains a high demand for real-time, accurate analysis of nitrogen contaminants in release waters. Current surface waters monitoring for sites near the Great Barrier Reef involves collection and transportation of samples for off-site analysis, which is time and labour intensive, and can risk sample integrity. A new generation of research in nanomaterial and electrochemical sensor fabrication has potential to tackle these shortcomings with enhanced, cost-effective sensors. In addition, improvements in data acquisition and relay imbedded within portable potentiostats have progressed to allow convenient on-site operability. The challenge remains in extending these advantages to the field setting.

Ion selective electrodes, such as membranes containing nitrate ionophore, and electrodes modified with nanocomposites, like nickel oxide-gold-reduced graphene oxide, have shown excellent electroanalytical performances under laboratory conditions. As few of these promising studies have transferred from the lab to on-site applications, this research project focuses on implementing the use of novel electrochemical devices to the existing monitoring sites near the Great Barrier Reef. Statistical analysis of results will allow direct comparison of data with the ongoing laboratory based spectrophotometric analysis.

Partnering with the Mackay/Whitsunday Regional Councils and the Queensland State Government via the Queensland Water Regional Alliance Program (QWRAP), Central Queensland University is investigating the application of these developments in electrochemical research on monitoring inorganic nitrogen in the Mackay/Whitsunday regions.

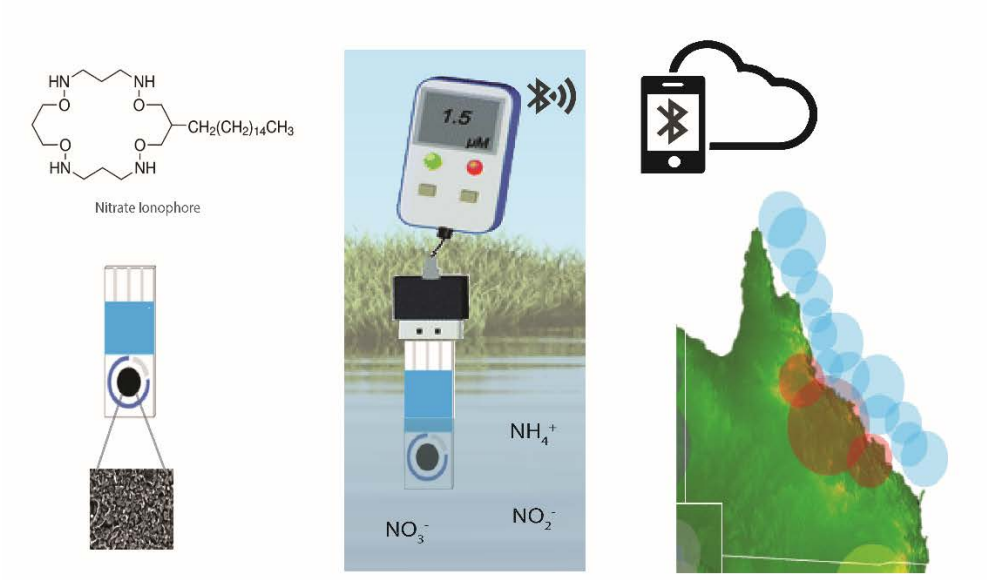

Figure 1: Example of a nitrate selective electrode and portable potentiostat device with data relay capabilities.

M-21

Super-exchange effect induced by metal-doping on $NiFe_2O_4(001)$ surface for oxygen evolution reaction

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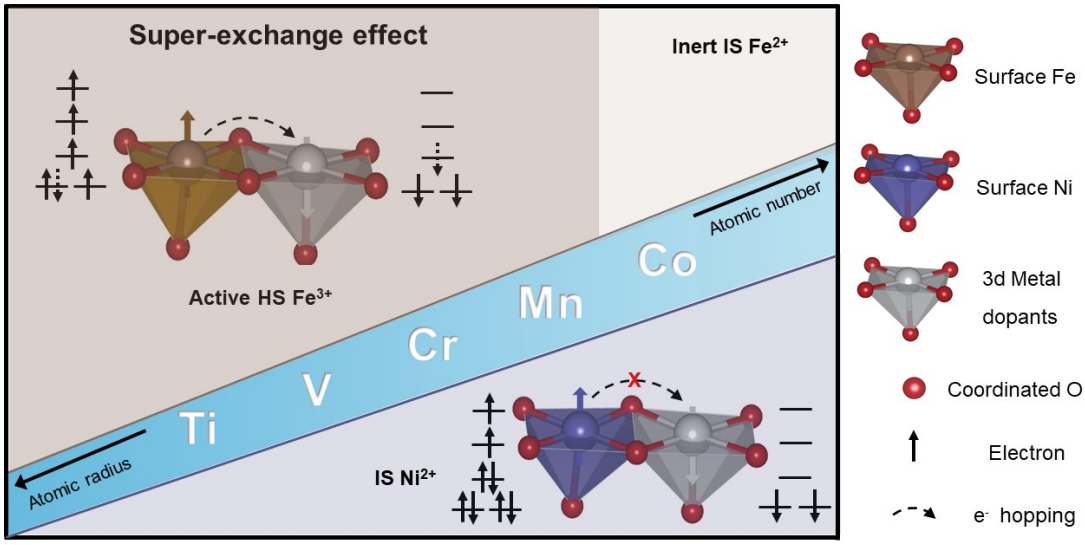
Development of electrocatalysts with highly intrinsic activity is necessary for commercial implementation of water electrolysis bypassing physical loading limitations. Earth-abundant electrocatalysts such as NiFe-based compounds including their oxides and hydroxides are good candidates for bottleneck oxygen evolution reaction (OER) in water splitting, thus necessary for studying underlaying activity enhancement mechanisms. Here, using density functional theory (DFT) and Hubbard U term (+U) calculations, the electronic structure of transition metal doped $NiFe_2O_4(001)$ surface is scrutinized for OER intrinsic activity. Results of spin-polarized DFT showed a strong super-exchange effect on the B-layer of $NiFe_2O_4(001)$ surface induced by early 3d metal doping. Intermediate spin Fe^{2+} ($3d^6$) sites transfer to high spin Fe^{3+} ($3d^5$) sites via charge transfer induced by super-exchange effect. The modulated electronic structure of Fe sites at B-layer, confirmed by Bader charge analyses, mediates the affinity of HS Fe^{3+} sites with OER intermediates and lowers the OER overpotential compared to IS Fe^{2+} sites at pristine spinel surface. This illustrates that strategically doping transition metal atoms in NiFe-based oxides is a promising avenue to promote super-exchange effect, which leads to the improving intrinsic activity of OER performance.[1]



Reference

[1] S. Wang, C. Zhao, "Super-exchange effect induced by metal-doping on $NiFe_2O_4(001)$ surface for oxygen evolution reaction." (To be submitted)

M-22

Corrosion engineering of ternary nonprecious metal hydroxides for oxygen evolution reaction

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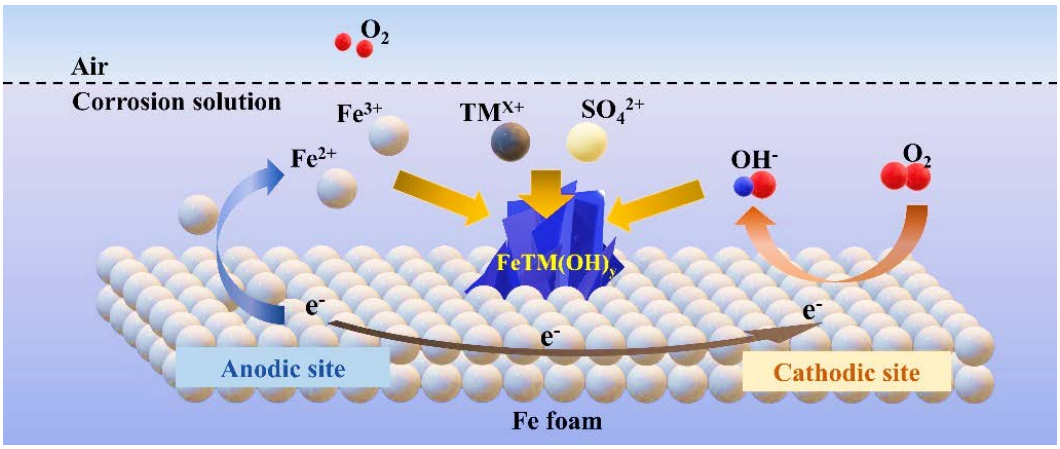
Hydrogen energy has become one of the trendiest energy sources due to its cleanness and environmental friendly nature and has become the subject of solving the energy and environmental crisis. Electrochemical water splitting has gained attention as a promising method to produce clean hydrogen. In contrast to hydrogen evolution reaction (HER), oxygen evolution reaction (OER) consumes more energy due to the multiple complex electron conversion steps, thus limiting the whole efficiency of electrochemical water splitting. This makes the advancement of electrocatalysts with negligible energy consumption is desired. Meanwhile, scaling up of the catalysts in terms of preparation and testing is another challenge in the field.

Here we demonstrate for the first time the fabrication of ternary metal hydroxides by corrosion using spontaneous corrosion electrochemistry for OER in alkaline media. The incorporation and partial leaching of Cr during oxygen evolution accelerate the conversion of the in-situ phase to the oxidation-active phase, providing activity beyond that of the baseline non-precious metal FeNi and FeCo hydroxide catalysts. The incorporation of Cr into binary FeNi and FeCo via corrosion reactions provides enhanced electrocatalytic intrinsic activity, interfacial charge transfer, and stability for electrochemical water oxidation. The corrosion strategy is non-energy consuming, simple to operate, and has the potential for large-scale preparation for industry.[1]



Reference

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M-23

Electrode-immobilized Human Sulfite Oxidase (HSO) as sulfite biosensors

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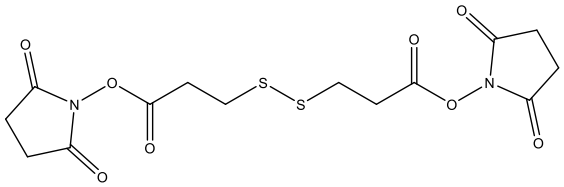
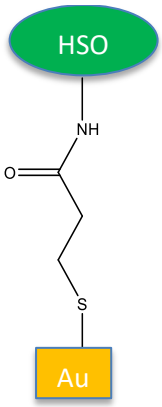
Human sulfite oxidase (HSO) is a molybdoenzyme which catalyses the oxidation of toxic sulfite into sulfate in the final step of cysteine catabolism. An HSO-based biosensor able to detect sulfite in wine and beer samples was developed with the enzyme immobilized on a glassy carbon (GC) electrode and entrapped under a dialysis membrane.[1] Presented herein are HSO biosensors *sans* membrane for more efficient mass transport of substrate to the enzyme. HSO was immobilized on GC using the protein crosslinker glutaraldehyde. HSO was also immobilized on gold electrodes modified with self-assembled monolayers formed from DSP (dithiobis(succinimidyl propionate), see Figure 1) and DSU (dithiobis(succinimidyl undecanoate)). Cyclic voltammograms at these electrodes in the presence of $[Fe(tacn)_2]^{3+}$ as mediator showed an increase in current with the addition of sulfite, consistent with catalytic oxidation of the substrate.

(A)



DSP = dithiobis(succinimidyl) propionate

(B)



(C)

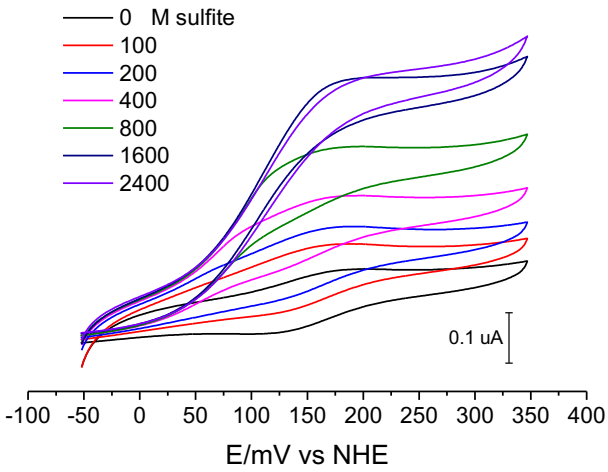


Figure 1. *(A)* Structure of DSP, *(B)* cartoon representation of HSO on Au electrode modified with SAMs formed from DSP, and *(C)* cyclic voltammograms of 25 µM $[Fe(tacn)_2]^{3+}$ at the Au/DSP/HSO electrode with increasing sulfite concentration.

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M-24

Textile-based electrofluidic platform for cell culture analysis

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Thread-based microfluidics have gained considerable attention as alternative for expensive and complicated microfluidics in biomedical applications. In contrast to passive methods, electrofluidics, electrically driven microfluidics, have a great potential to control and analyse fluids in these devices. Capillary electrophoresis is employed to analyse cell culture. However, real-time analysis of cell culture is a challenge, as most of the analyses are being done based on end-point measurement or discrete sample measurements. These measurements provide poor real-time results. In this study, 3D textile-based electrofluidic platform was integrated with 3D cell culture to perform real-time analysis of cellular metabolites. Human dermal fibroblast cells in GelMA were cultured on 3D core-shell textile structures and cell proliferation results proved that textile structures facilitated cell culture. Poor cell viability was observed when cells were in electrofluidic buffer solution, and when electric field was directly applied on the cells. Thus, a textile geometry was identified to improve the cell viability and satisfy electrofluidic requirements. In this geometry, cells were in culture medium, and latter was dragged towards the electrophoresis analysing zone by the electroosmotic flow. This novel application aims to enable the separation and analysis of cellular metabolites from a cell culture in one platform. This approach will build upon the advantages afforded by the open capillary system provided by the textile platform, where both delivery to the cellular platform and metabolite detection is possible at any given point.

M-25

Separation and in-line pseudophase microextraction with TDMAC admicelles in open-tubular capillary-based separations

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Chromatographic separation and in-line sample concentration of small molecules using an open-tubular (OT) capillary with a stationary chromatographic pseudophase coating of tridodecylmethylammonium chloride (TDMAC) aggregates are presented. The capillary was coated with 0.5 mM TDMAC (> critical surface aggregation concentration) to form a TDMAC bilayer at the solid surface-liquid interface. The coating was studied by capillary electrophoresis (CE) and OT liquid chromatography (OT-LC) using increasing concentrations of TDMAC in (pH 9.2) buffer. Reversed-phase OT-LC retention was shown by the inverse relationship of retention factor (*k*) of analytes and % organic solvent (i.e., methanol). Interestingly, using mobile phases with low and high pH in OT-LC, small organic cations were unretained and retained, respectively. This allowed us to develop pseudophase microextraction (PPME) of the cations at high pH followed by CE separation at low pH in the same column. For PPME, the cationic analytes (i.e., dextromethorphan, trimethoprim, propranolol, verapamil, clomipramine and amitriptyline) in 50 mM Na_2HPO_4 buffer (pH 11.9) were pressure loaded into a TDMAC coated capillary. The CE background solution of 2 mM 2-hydroxypropyl-β-cyclodextrin in 50 mM phosphoric acid (pH 2.0) was then introduced by pressure from the outlet, which eluted and concentrated the retained analytes to the inlet end of the column. The PPME-CE showed a 98-177x improvement in peaks heights for a 10x capillary volume load compared to a typical injection. The analytical figures of merit for the tested cations were LOD = 0.02-0.1 µg/mL, linearity R^2 > 0.99 and intraday and interday repeatability %RSD < 5% (n = 12). Application to real samples was tested using fortified river and urine samples with recovery values of 86 -110% and 94-108%, respectively.

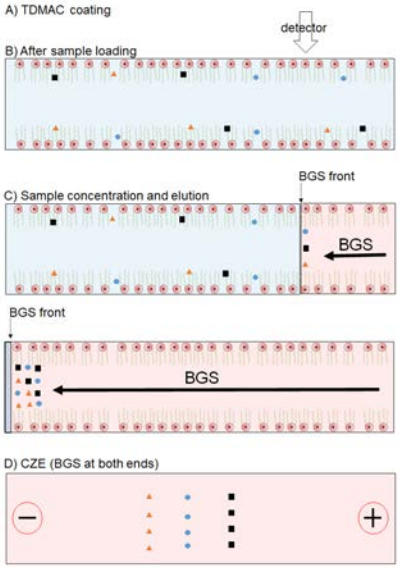

Figure 1. PPME-CZE scheme. A) The capillary was conditioned with 0.5 mM TDMAC solution. B) After sample loading in the basic solvent, the analytes (red, blue and green shapes) were trapped inside the capillary due to their interaction with the TDMAC admicelles. C) Acidic BGS was introduced from the column's outlet at 50 mbar. This was until the BGS front almost reached the tip of the capillary (~2 mm from the inlet). The analytes were released from the inner capillary walls and concentrated at the BGS front. D) The BGS vials were placed at both ends of the capillary and voltage was applied to separate the analytes by CZE.

M-26

Innovative Strategies to Protect Livestock and Native Animals from Introduced Species

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Introduced predators, such as foxes, are responsible for the extinction and endangerment of many native animals in Australia and globally, resulting in a decline in biodiversity. These predators also prey upon livestock causing substantial economic losses to the agricultural industry. Poison baiting has been effective at reducing the immediate threat of foxes, however, it often results in a rapid incursion of new foxes and off target poisoning. Additionally, poison baits do not directly deter foxes from attacking livestock or native animals. Conditioned-taste aversion is a promising, non-lethal alternative to poison baiting that can potentially be used for deterring foxes from preying upon livestock and native animals. Conditioned-taste aversion is a form of classical conditioning whereby a predator experiences non-lethal illness following the consumption of food that mimics the smell of a particular animal, conditioning the predator to avoid that animal.[1-2] The goal of this project is to develop a novel bait formulation that offers a controlled release of odours specific to prey species (e.g., sheep) and is palatable to foxes.

The volatile organic profile that contributes to the characteristic odour of sheep was determined using gas chromatography mass spectrometric analysis of various grades of Australian wool grease and lanolin. Subsequently, baits incorporating wool grease components and a conditioned-taste aversion taste agent were developed to mimic the odour profile of sheep.

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M-27

High Shear Mediated Fluoro-Surfactant Extraction of PFOA

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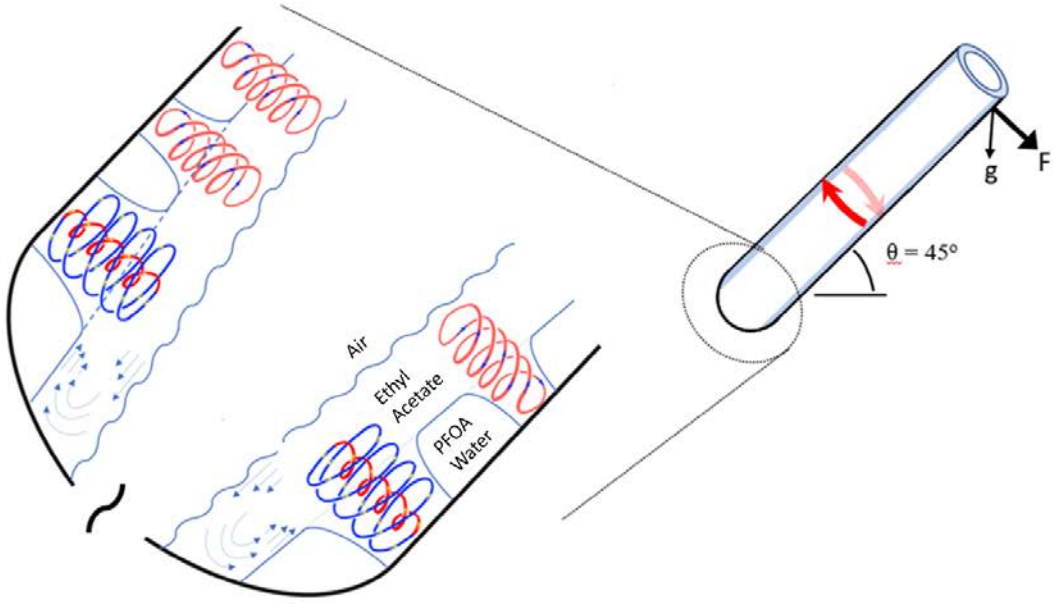
An innovative and rapid method is reported in extracting perfluorooctanoic acid (PFOA) under high shear. It involves using a fluoro-surfactant to detect anionic surfactants (AS), PFOA in this case, under intense micro-mixing and high-shear in the titled vortex fluidic device (VFD). The hydrophobic ion-pair of dye (ethyl violet)-AS is extracted to an organic phase (ethyl acetate) via liquid-phase extraction[1]. The VFD has been discovered to improve the mixing of immiscible fluids by centrifugally holding the biphasic system against the surface of a rapidly rotating tube, producing thin films[2]. In these thin films, topological flow regimes of micron to submicron scale promote substantial interphase mass transfer. Auxiliary materials, such as complex polymers, microgels, phase transfer catalysts, etc., are frequently used to mix immiscible liquids. However, our green chemistry solution of centrifugally separating immiscible liquids of different densities has implications for avoiding the use of these auxiliary materials and the creation of emulsions. It is a novel way for extraction and separation processing, overcoming mass transfer restrictions at liquid interfaces.



Fluid flows in the ethyl acetate layer impacting through the water layer onto the surface of the tube tilted at 45°, where there is no distinction in the double helical flow for the two immiscible layers.

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M-28

Lead isotope ratios of Fitzroy Basin river sediment, preliminary values.

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Freshwater river sediments were sampled from eight sites within the Comet, Nogoa and Mackenzie Rivers, Fitzroy Basin, Central Queensland, an area broadly associated with grazing, cropping and coal mining. Following ICP-MS measurement of total recoverable metal content (in the <60 µm size fraction), stable Pb isotope ratios (Pb^{207}/Pb^{206} = 0.838-0.886 and Pb^{208}/Pb^{206} = 2.08-2.18) were opportunistically determined and may help to better understand natural and anthropogenic inputs within this river system. The intra-assay (n = 10) relative standard deviation of ratios determined from CRM-016, a freshwater sediment from a stream in the Western United States, were 1.4 % and 1.2 % for Pb^{207}/Pb^{206} and Pb^{208}/Pb^{206}, respectively. Inter-assay (3 x n = 5) relative standard deviation for the same ratios were 0.78 % and 1.1 %, respectively. Various data visualisation techniques (e.g. two-ratio scatter plots) were used to investigate how the samples and CRM ratios compared with literature values including, the NIST SRM981 common Pb isotopic standard, sediment results from a coal mining area in India [1], and the Pb composition of various terrestrial materials compiled in a recent IUPAC Technical Report[2]. Aspects of a review of Pb isotopes in environmental sciences[3] and an estimate of Pb isotope composition of the Upper Continental Crust[4] are among the various other literature that will be considered when speculating on the potential sources of Pb in Fitzroy Basin sediments and when further evaluating the suitability of the sample preparation and analytical methods for retrospective stable Pb isotope analysis.

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M-29

Simplifying estimation of entropy and Gibbs energy from action for environmental systems

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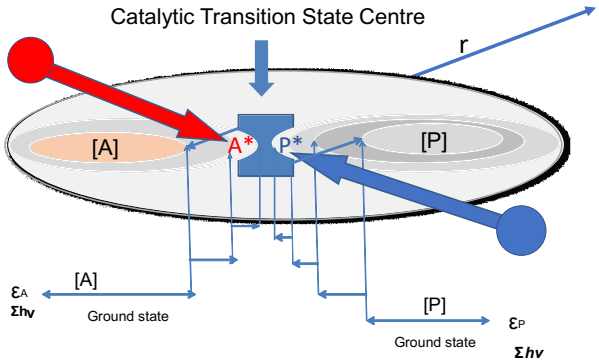
Our recent innovative articles (Kennedy et al., 2019; Kennedy and Hodzic, 2021, a,b) have shown how the entropy and Gibbs energy of gaseous systems can be estimated from molecular action – vibrational, rotational, translational and vortical. Action is a scalar property of periodic molecular motion with physical dimensions apparently the same as angular momentum ($mr^2\omega$), but including variation in phase angle ($mr^2\omega.\delta\varphi$). These estimates of action and entropy are based on a novel reinterpretation of statistical mechanics as initiated by Gibbs, using simple molecular and environmental properties. We refer to the method as action mechanics. These accurate methods of action mechanics provide a novel, highly useful approach to analysing thermodynamic properties of chemical systems, appropriate for both equilibrium and non-equilibrium systems. The values of entropy and Gibbs energy or chemical potential calculated are absolute in their nature. To illustrate the research and teaching value of action mechanics possible we will apply them to the following issues as quantum theory: (i) transition state reaction rate theory (ii) hydrogen as a source of renewable energy (iii) the action mechanics of wind power (iv) the power of tropical cyclones, and (v) the release of heat stored as vortical work by turbulence in flows of fluids.



Radial action transition states on a Brownian catalyst, proposed to generate activation energy for reversible reactions $A \Leftrightarrow P$ by forceful (δmvr) inertial collisions. At constant temperature, the difference in ground state energy $\varepsilon_{Po} - \varepsilon_{Ao}$ represents the enthalpy and chemical potential changes for the reaction.

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M-30

Electrochemical study of Per- and Polyfluoroalkyl Substances using a liquid-liquid interface

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Per-and polyfluoroalkyl substances (PFAS) are man-made chemical compounds that are highly persistent and are frequently used in various domestic and industrial applications. PFAS are distributed everywhere in the environment due to their remarkable stability. Different reports of PFAS have shown several health issues in human beings.[1] A variety of techniques are available for the investigation and characterisation of PFAS.[2,3] However, these techniques are often sophisticated, lab-based, and costly. Electrochemistry at the interface between two immiscible electrolyte solutions (ITIES) attracts much attention from many researchers due to its varied applications. In this electrochemical measurement set-up, species are detected on the basis of their ion transfer between the aqueous and organic electrolyte solutions. Accordingly, electrochemical measurements using the ITIES may be useful for the detection of ionised PFAS present in various environmental samples.

Picomolar concentrations of perfluorooctane sulfonate (PFOS) in aqueous solutions was detected by voltammetry at the ITIES,[4] which is lower than the benchmark figures for PFOS in drinking water mandated by the USA Environmental Protection Agency (EPA)[5] and the Department of Health, Australia.[6] In this presentation, voltammetric techniques (like cyclic voltammetry and differential pulse voltammetry) at the ITIES were used for the electrochemical study of perfluorooctanoic acid (PFOA) and the capability to detect the lower concentration of PFOA using the ITIES will be presented and discussed.

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M-31

Light and fast – high-throughput UV-Visible method for assessing antimicrobial activity

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Antimicrobial resistance is a global health issue which is projected to cause 10 million deaths a year by 2050 [1]. The current suite of laboratory techniques used to understand antimicrobial activity and the development of antimicrobial resistance are often labour and time intensive, sometimes requiring many days of preparation and analysis and therefore diagnosis. Here, we present a novel high-throughput technique for the assessment of both activity and resistance development using an automated UV-Vis spectrophotometer and chemometric analysis [2]. The technique was developed using existing classical antimicrobial agents such as tetracycline and amoxicillin, and novel agents such as inorganic nanoparticles. An automated spectrophotometer allows testing of many samples over a specified time period, while chemometrics gives in-depth chemical information on the system and insight into the biochemical changes occurring in the cells and liquid media [3]. This work has focused on a range of Gram-positive and Gram-negative bacteria but may be expanded to the study of fungi and other organisms in the future. The outcomes of this work will allow for the rapid testing of novel antimicrobial agents with minimal input from the researcher and insight into the biochemical interactions in the systems.

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M-32

The *in vivo* metabolism of Jungle Warfare in greyhounds

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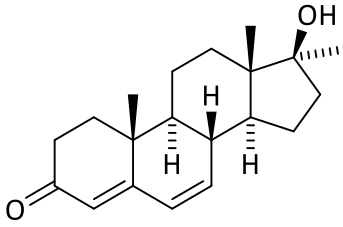
Δ6-Methyltestosterone was reported as the main active ingredient of the purported "dietary supplement" Jungle Warfare. This compound is structurally similar to 17α-methyltestosterone, containing an additional Δ6 double bond, and possesses notable anabolic-androgenic activity, raising concerns over the potential for abuse of Jungle Warfare in sport. Adopting the methodological workflow published in a recent study of Furazadrol metabolism in greyhounds,[1] the *in vivo* metabolism of Δ6-methyltestosterone in greyhounds was investigated. Urinary phase I (unconjugated) and phase II (glucuronide) metabolites were detected following oral administration using liquid chromatography-mass spectrometry. The major phase I metabolite was confirmed as 16α,17β-dihydroxy-17α-methylandrosta-4,6-dien-3-one by comparison with a synthetically-derived reference material. Minor amounts of the parent drug were also confirmed. Glucuronide conjugated metabolites were also observed, but were found to be resistant to hydrolysis using the *Escherichia coli* β-glucuronidase enzyme. Qualitative excretion profiles, limits of detection, and extraction recoveries were determined for the parent drug and the major metabolite. These results provide a method for the detection of Jungle Warfare abuse in greyhounds following oral administration suitable for incorporation into routine screening methods conducted by anti-doping laboratories.



Δ6-methyltestosterone

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M-33

Structural Analysis of Commercially Available Agrochemicals by Ion Mobility - Mass Spectrometry

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Agrochemicals are chemicals used in agriculture and can be classified into pesticides, herbicides, and fertilizers. The application of agrochemicals dates to the early Sumerian civilisation when elemental sulphur was used as a pesticide.[1] Modern chemistry has advanced agriculture by allowing the synthesis of more potent agrochemicals. However, agrochemicals come with drawbacks, negatively impacting the environment and non-target biological systems including humans. For example, Glyphosate, is the most used herbicide globally and is claimed to be safe, yet recent studies have found it to be a probable carcinogen.[2,3] Imidacloprid, a popular neonicotinoid insecticide considered harmless to mammals, is now linked as the leading cause of honeybee colony collapse disorder.[4] Some pesticides have also been known to curb soil fertility by binding with free metal ions in the environment.[5] Therefore, a technique to reliably determine agrochemical-metal structures is crucial to better understand unforeseen agrochemical interactions.

This study focuses on using ion mobility-mass spectrometry techniques to elucidate structures and investigate interactions of commonly used agrochemicals, mainly pesticides and herbicides, with other biorelevant metals (list some). Combined with density functional theory (DFT), comparison of experimental and theoretical collisional cross section (Ω) values can be exploited to elucidate structures. We have successfully elucidated multiple metal complex structures of glyphosate, aminomethylphosphonic acid, imidacloprid and chlorpyrifos. We are also able to better understand the binding affinities of different metal ions. The findings of the study form the basis of understanding interactions and molecular characteristics of these chemicals which allows manipulations of solutions conditions to achieve desirable outcomes.

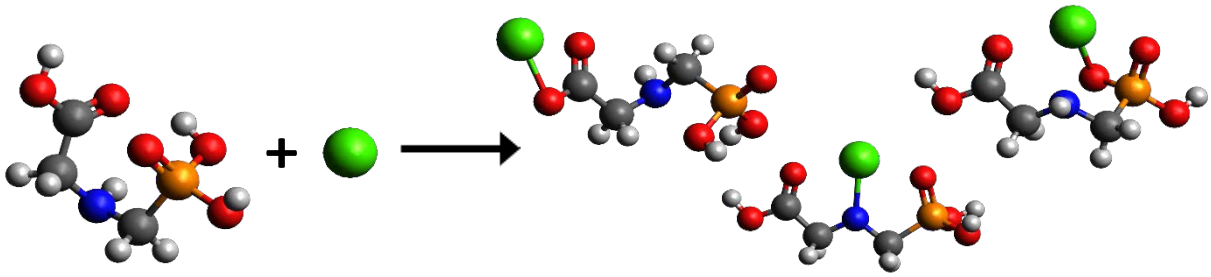

Figure 1. Reaction of glyphosate with calcium ion and a few of its possible resulting complex structures.

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M-34

Investigating vanadium sorption to reactive particulates in the marine environment using XANES spectroscopy

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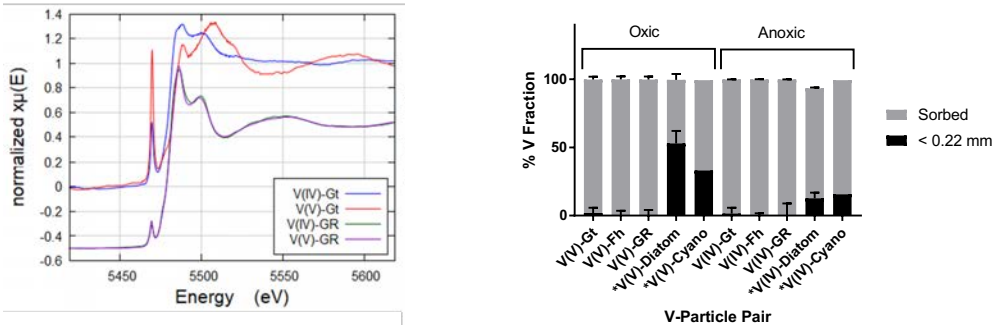
Vanadium (V) is a conservative, redox-sensitive transition metal ubiquitous in the Earth's oceans and its biogeochemical cycling is an expanding research area. In paleo-geochemistry, it is increasingly used as a paleo-redox tracer to provide information on the history of oxygen evolution in Earth's oceans and atmosphere [1]. For example, V geochemical data from ancient sediments played a key role in the recent revision of atmospheric oxygen concentrations prior to the Cambrian Explosion, some 540 million years ago [2]. In the modern environment, there is a growing concern over the cumulative anthropogenic release of V into the environment, due to the highly toxic nature of V [3].

There is some evidence that interaction of V with various particulate minerals and organic matter strongly affects its deposition in marine sediments. To investigate this mechanism, a range of marine particulate minerals were synthesised and reacted with V^{V} (as vanadate, $V^{V}O_4^{3-}$) and V^{IV} (as vanadyl $V^{IV}O^{2+}$), which were analysed using X-ray Absorption Spectroscopy at ANSTO Melbourne. The set of results are interpreted on the basis of the V oxidation state, possible changes during the sorption process, and the phase distribution of V between the sorbed and dissolved components. Significant sorption (>98%) of both V^{V} and V^{IV} were observed on iron oxide minerals in particular and were coupled with evidence of V reduction in selected cases. These results shed more light on the role of V-particulate interactions in the marine environment and their potential importance in deposition.



(Left) V K-edge XANES spectra of V-particulate sorption products; (Right) Sorbed and dissolved (<0.22 μm) V distributions in the tested systems. (Gt = goethite, Fh = ferrihydrite, GR = sulfate green rust)

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M-35

Spectrometric approaches towards onsite sample analysis

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The biggest challenge with the current onsite drug testing devices is that they result in a high percentage of false negatives and false positives and require a confirmatory test (Liquid Chromatography-Mass spectrometry or Gas Chromatography-Mass spectrometry) before prosecution. In a study done at the University of Sydney in New South Wales, Australia, it was found that the two most popular drug testing devices in Australia, the Draeger Drugtest 5000 (DT5000) and the Securetec DrugWipe 5s (DW5s) showed false positives of 10% and 5% respectively and false negative of 9% and 16% respectively [1]. It is crucial that these devices accurately differentiate between the presence and absence of drugs to avoid unfair cancellation of licence or compromising the safety of road users. This issue also extends to the mining industry where mandatory drug and alcohol testing is done before a shift. Recently, the Australian Mines and Metals Association reported that synthetic drugs are evolving rapidly and as a consequence, current technologies cannot detect them [2]. With the consideration that these devices cost about $40 (AUD) each, it is crucial that it accurately detects a range of drugs. Unfortunately, the detection mechanisms of DT5000 and DW5s are specific to only a few groups of drugs (cannabis, opiates, cocaine, amphetamines, methamphetamines, benzodiazepines and ketamine) [3], which leaves synthetic and new psychoactive drugs undetected. Therefore, using a non-selective detection device, like the mass spectrometer (MS), allows the quantification of drugs present in oral fluid without needing an additional preliminary test. Currently, with extensive sample preparation, these confirmatory tests are conducted in laboratories. Some groups have attempted to use ambient techniques with the MS, like paper spray ionisation (PSI-MS) which require little or no sample preparation before testing [4]. However, paper has a few disadvantages, such as, hydroxyl groups that can interact with the drugs and also it is difficult to fine-tune its chemistry, porosity and pore size. This study explores the use of free radical polymerisation concepts to create a more reliable material where the sample interaction, chemistry, porosity, and pore size can be fine- tuned to effectively detect and quantify different classes of drugs onsite within minutes, and without needing an additional laboratory confirmatory test.

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M-36

Developing a protocol for microplastic detection using micro-reflectance FTIR spectroscopy

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Microplastics present a serious environmental threat to marine and aquatic ecosystems, potentially harming organisms through ingestion and exposure to adsorbed persistent organic pollutants (POPs) [1]. Continued monitoring is crucial in assessing the hazards and provenance of plastics. Unfortunately, no techniques currently meet all analytical requirements for microplastic detection and quantification, and the lack of cost-effective, standardized protocols limits capability for routine monitoring.

Reflectance micro-FTIR spectroscopic imaging may present an ideal alternative to current microplastic analytical methods, as it provides spatially resolved chemical specificity (allowing determination of particle size, abundance and polymer identity) in a non-contact method (allowing high throughput of samples). It also eliminates the problems of complete infrared absorption by larger particles and requirement for expensive infrared-transparent filter papers/windows encountered with transmission mode measurements. However, the irregular morphology and inhomogeneous refractive indices of microplastics cause distortions which make reflectance-FTIR spectra difficult to manually interpret [1].

This study coupled reflectance micro-FTIR spectroscopic imaging with multivariate statistics (chemometrics) to develop a protocol for microplastic detection and a semi-automated data processing pipeline, allowing cost-effective and high-throughput analysis of microplastics in environmental samples. Investigation of the technique using standards produced a successful qualitative assessment of particle abundance and polymer identity (Figure 1). A chemometric model calibrated with standards was not directly applicable to environmental samples due to factors such as particle morphology and weathering. However, a calibration library of reflectance-FTIR spectra (alongside ATR-FTIR spectra for polymer confirmation) collected from the environmental sample itself was able to detect 91 – 100 % of particles.

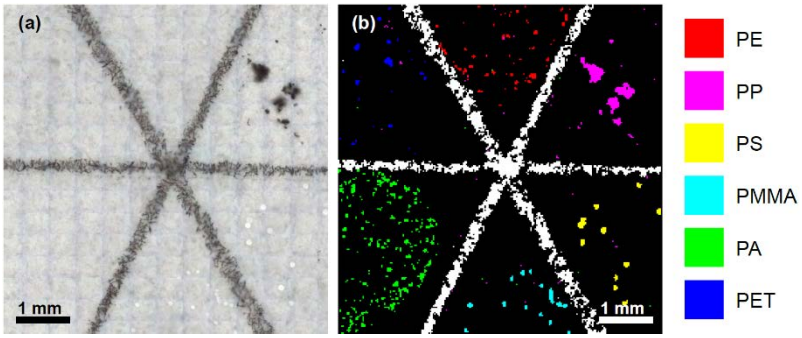

Figure 1: (a) Optical image of a filter paper spiked with six polymers in known locations and (b) false colour map showing the prediction of polymer identity using a chemometric model

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M-36.1

Towards the Development of Novel Intelligent Antibacterial Coatings

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Hospital-acquired infections pose a serious issue for the global healthcare system.[1] Such infections are mainly associated with sensitive medical implants including pacemakers, catheters, contact lenses, prosthetic joints, manifesting as high morbidity or even mortality.[2, 3] These infections arise from the accumulation of pathogenic microorganisms on the surface of the medical device or cutaneous tissues known as biofilms. Biofilms are intransigent and colonize any surface, medical device or implant which is not sterilized. The biofilm is then irreversibly attached and therefore difficult to eradicate from the surface.[4] In particular, significant efforts have been made to develop new strategies for antimicrobial materials or coatings but, due to the formation of the complex colonized biofilm and excessive use of antibiotics, most of the pathogens have developed either strong resistivity against any antibacterial action or resistance to the very drugs designed to kill the microorganism in question.[5] Therefore, the purpose of this study is to design a novel kill strategies including antimicrobial or antifouling agents to destroy and limit biofilm formation entirely without any microbial resistance.

Currently, metal-based nanomaterials are designated as the most promising antimicrobial agents as they show impressive biocidal properties and less cytotoxicity for microorganisms. Thus, for this reason, graphene and graphene-based nanocomposites have been used extensively for bacterial detection and antibacterial applications owing to their unique physical and chemical abilities to interact with microorganisms.[6, 7] In addition, silver nanoparticles have been widely applied due to their bactericidal efficiency and biocompatibility.[8] Additionally, researchers have begun to exploit targeted and precision-based medicine, therefore, stimuli-responsive magnetic nanoparticles have attracted great attention owing to exhibit brilliant superparamagnetic properties, biocompatibility, antimicrobial activity, and recyclability.[9]

From this perspective, our work centres on generating recyclable and synergistic graphene (Gr), iron (Fe), and silver (Ag) nanocomposite by spreading both iron oxide nanoparticles (MNPs) and silver nanoparticles (AgNPs) on the surface of graphene oxide (GO) sheets to obtain GO-MNPS-PNIPAM-Ag as a novel multifunctional and highly effective antibacterial material and confirm its application as a novel antimicrobial surface when screened against Gram negative and Gram positive microorgnisms.

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M-37

One chelator for imaging and therapeutic nuclides

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Since the approval of the radiotherapeutic Lutathera® (^{177}Lu-DOTA-TATE, TATE = Tyr^3-octreotate) by the FDA and EMA, the medicinal relevance of radiometal based pharmaceuticals remains essential.[1] However, the need for stable and inert complexes formed under mild condition with possibly thermolabile vectors for bioconjugation still is challenging. Bispidine (3,7-diazabicyclo[3.3.1]nonane) derived ligands have proven themselves as ideal chelating agents for metal ions, with fast complexation kinetics and high in-vitro and in-vivo stabilities.[2] Studies with nuclides of interest for radiotherapy, 177Lu and 225Ac were promising but with potential for improvement.[3,4] Here, we report a nonadentate bispidine ligand,[5] which shows radio-stabilities similar to DOTA but with much milder labeling conditions (5 min, 40 °C). The corresponding ^{111}In, ^{177}Lu and ^{225}Ac complexes are exceptionally stable with high molar activities. The radiochemical properties of the bioconjugated ligand (Fig. 1) are the basis for excellent radioimaging qualities with thermolabile bioconjugates.

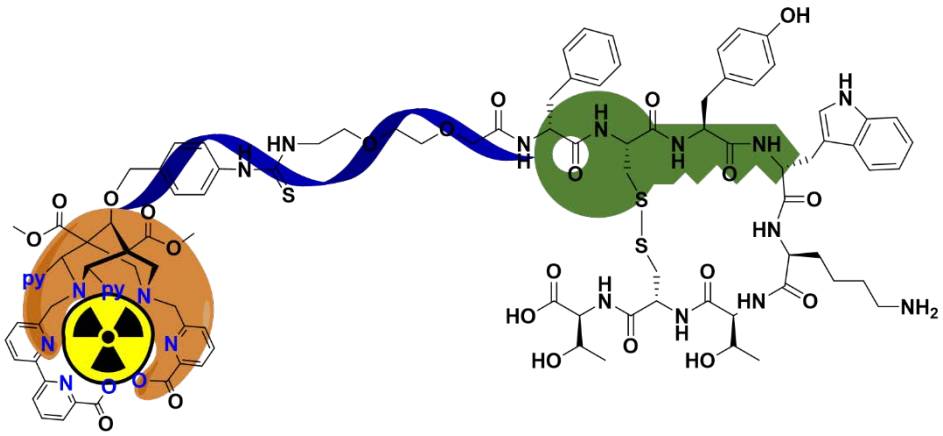

Figure 1. Conceptional Design of the radiolabeled bispidine-TATE conjugate.

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M-38

Challenges and Considerations of Clinical Radiochemistry

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Clinical radiochemistry laboratories provide highly specialised radiopharmaceuticals routinely for the purposes of Positron Emission Tomography (PET) diagnostic imaging and radiotherapies. These laboratories require unique conditions, standards, workforces, and equipment to fulfill this task. This poster aims to communicate the process, challenges, and how academic laboratories could benefit from translational research as well as procedural elements. This poster will provide introductory information of how radio nuclides are isolated, the synthesis performed, and quality controlled in a Good Manufacturing Practice (GMP). Furthermore, address the unique difficulties translating prospective radiopharmaceuticals to these clinical spaces.

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M-39

Novel Bis(thiosemicarbazonato) Technetium-99m Nitrido Complexes for Prostate Cancer Imaging

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Prostate cancer is the second most commonly diagnosed cancer in men and the fifth highest cause of death, worldwide.[1] Recently, nuclear imaging has been investigated to improve the diagnostic accuracy and to allow for earlier detection of prostate cancer.[2] This can be achieved by attachment of a radionuclide to a molecule that targets a receptor overexpressed in prostate cancer cells, known as the prostate specific membrane antigen (PSMA).[3] In this work, a series of bis(thiosemicarbazone) (BTSC) chelators were synthesised and attached to PSMA binding motifs using both solution-phase and solid-phase chemistry. The linker was altered to explore the hydrophilic/lipophilic balance of the chelators and the addition of amino acids to increase binding of the radiopharmaceuticals to the PSMA channel. The chelators were radiolabelled with the technetium-99m nitrido core, $[^{99m}Tc][TcN]^{2+}$, which has previously shown promising results with BTSC chelators.[4] The radiolabelling occurred in a simple one-pot synthesis at 85°C for 10 min and all chelators achieved a high radiochemical purity (> 99%). The hydrophilic/lipophilic balance was explored by reverse-phase HPLC and distribution coefficient (log*D*) that showed all complexes were hydrophilic with negative log*D* values. Preliminary *in vitro* stability studies, undertaken in the presence of a competing ligand (cysteine) and in human serum at 37°C, were very promising indicating that the complex was kinetically inert under both conditions over 24 h. This suggests the potential for these radiopharmaceuticals to be used as imaging agents for prostate cancer and further *in vivo* and *in vitro* studies will be undertaken to explore this.

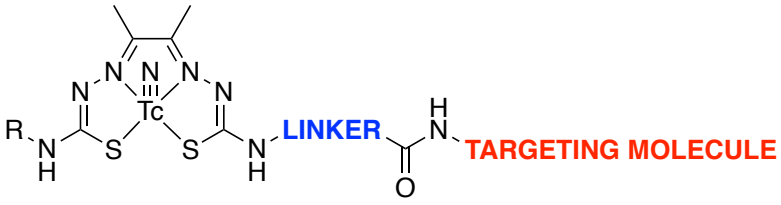

Figure: General structure of $[^{99m}Tc][TcN(BTSC)]$ for prostate cancer imaging.

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M-40

Synthesis and evaluation of desferoxamine-based ligands designed to improve ^{89}Zr-immunoPET performance

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Immunological positron emission tomography (immunoPET) imaging extends the capacity of traditional PET using immunological agents, such as monoclonal antibodies (mAbs) as targeting vectors. This improves the tumour-to-background ratio of the image compared to traditional PET. Radiometal-based immunoPET imaging agents consist of a radionuclide, a ligand to coordinate the radiometal, and the targeting vector. ^{89}Zr is an attractive choice as a radionuclide for immunoPET applications since its half-life ($t_{½}$ = 78 h) closely matches the circulation time of mAbs.[1]

Desferoxamine B (DFOB) is a hexadentate bacterial siderophore used for ^{89}Zr-immunoPET applications. DFOB is ideal as an Fe(III) chelator for secondary iron overload disease, but is less ideal as a ^{89}Zr(IV) ligand, since Zr(IV) has a preferred coordination number of 8. A previous study showed that introducing a fourth hydroxamic acid moiety to DFOB improves the stability of the metal-ligand complex,[2] with subsequent work designing strategies to improve water solubility.[3,4]

This work aims to generate suitable ligands that incorporate a fourth hydroxamic acid moiety group into the DFOB scaffold with any modification designed to maintain or improve water solubility and other properties. A polyethylene glycol group introduced into one target compound is predicted to improve water solubility. Further, the efficiency of mAb conjugation could improve upon extending the antibody-conjugation point further from the metal-ligand complex.

This work will describe the synthesis towards two DFOB-based ligands as the foundation towards evaluating performance as ^{89}Zr(IV) immunoPET ligands following mAb conjugation and radiolabelling.

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M-41

Developing flexible and switchable metallo-supramolecular architectures

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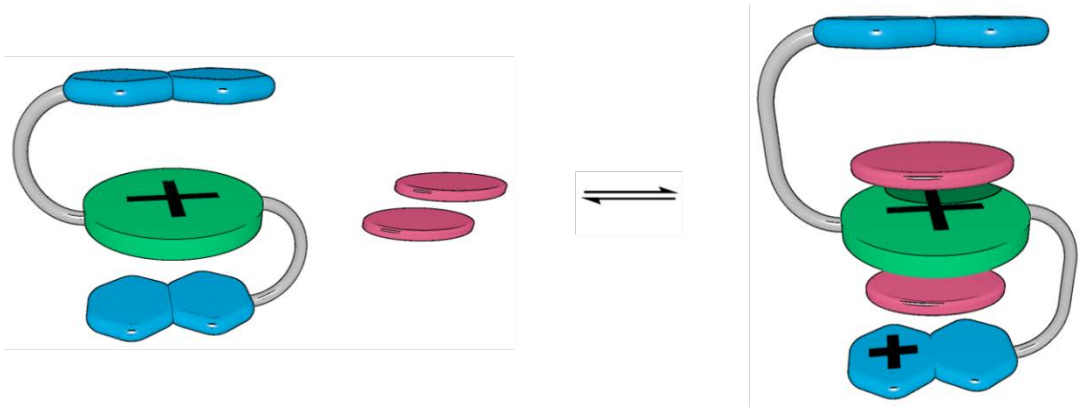
The capacity for self-assembled metallo-supramolecular architectures to interact with guests or substrates drives much of the interest in supramolecular systems. The ability to turn the binding event 'on' or 'off' is even more desirable as it would allow for greater control in self-assembly. Concentration and temperature have frequently been employed as a way to switch between self-assembled structures but have limited practical applications due to the sheer magnitude of systemic perturbation required for switching.[1,2,3]

Instead, we look to incorporate switchable functional groups into flexible systems to access biomimetic, stimuli-responsive molecular switches. To establish a practical method to do so, we are developing a flexible, self-assembled system capable of switchable molecular recognition of guests. Under standard conditions, π- π interactions exist between the aromatic tethers (Figure, blue) and the cationic panel (Figure, green) where the metal ion coordinates to each ligand. This results in self-recognition which occludes the cationic panel from the bulk solvent, and impairs the recognition of guests. By incorporating a charge-alterable group into the aromatic tether, a positive charge can be induced by various stimuli. In the presence of these stimuli, the acquired charge repulsion will separate the aromatic tether and cationic panel such that self-recognition is disrupted, allowing instead for the molecular recognition of a range of guests. This methodology could later be applied to incorporate greater control in more complex metallo-supramolecular systems such as interlocked architectures and foldamers.



Cartoon representation of a generalised system capable of switchable molecular recognition of guests

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M-42

Hydroxy groups enhance [2]rotaxane anion binding selectivity

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Hydrogen bonds have been used to great effect throughout supramolecular chemistry, especially in host-guest recognition[1] and self-assembly.[2] However, implementation of hydroxy hydrogen bonds in host-guest chemistry has significantly lagged behind other hydrogen bonding motifs.[3] Recent investigations into the ability of simple acyclic hydroxy containing anion receptors demonstrated that even within a competitive CD_3CN:D_2O 90:10 system, strong binding could be achieved, as well as binding of hydrated anions.[4]

In this work, hydroxy containing anion-templated [2]rotaxanes were synthesised. The anion recognition potential of these compounds was investigated by anion ^{1}H NMR titration studies, which revealed that the receptors bound a range of anions within a CD_3OD:$CDCl_3$ 1:1 solvent system. The crystal structure obtained confirmed the ability of the hydroxy containing [2]rotaxane to encapsulate chloride (Figure 1). Computational semi-empirical studies indicated that secondary intermolecular interactions between the axle hydroxy groups and the [2]rotaxane macrocycle contributed to the preorganization of the binding pocket, resulting in enhanced selectivity for chloride.

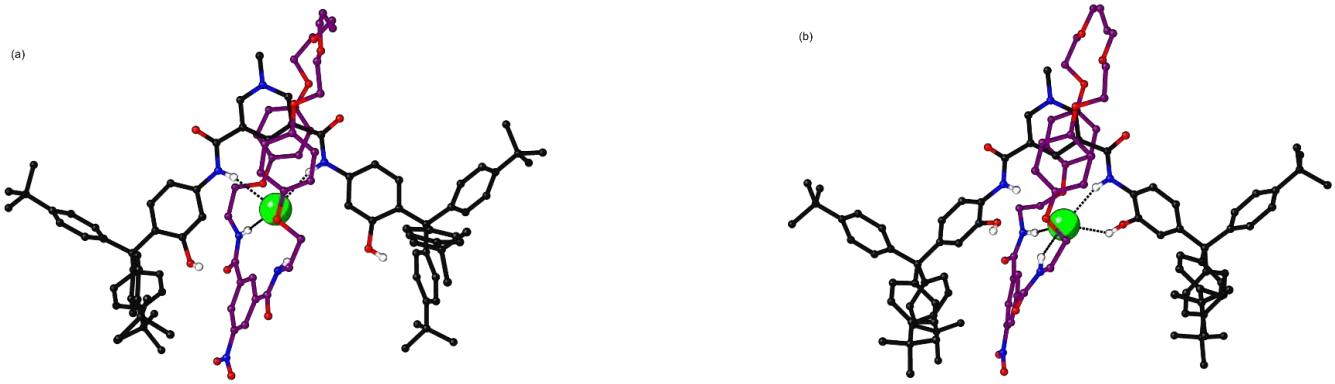

Figure 1. X-ray crystal structure of new [2]rotaxane. Intermolecular hydrogen bonds are shown as dashed lines. Most hydrogen atoms and solvent molecules are omitted for clarity.

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M-43

Emergent electronic properties from stacked molecules

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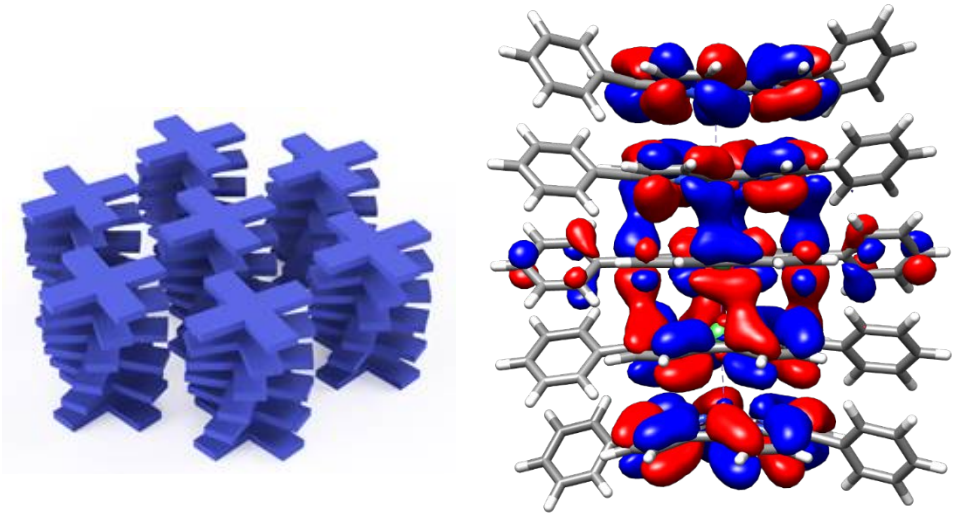
Electronic delocalisation in organic molecules has typically been approached using a conjugated π-bond framework to provide a pathway for electron movement. While this through-bond design has many applications, through-space conjugation is an emerging area of interest as it can allow electronic communication across non-covalently linked molecules,[1] and even give rise to 3D aromaticity.[2] A supramolecular semiconductor could demonstrate a dynamic response to environmental conditions and be able to self-heal defects in the conjugation pathway. We will present our computational and synthetic results towards evaluating through-space electronic delocalisation in liquid crystals with an aromatic or antiaromatic porphyrinoid core. Our computational results show that there is significant through-space electronic interaction, and effects consistent with 3D aromaticity between the stacked antiaromatic chromophores.

Figure 1: (*Left*) A graphical representation of columnar liquid crystals (*Right*) The HOMO isosurface for a stacked oligomer of π-conjugated molecules with no covalent links between subunits.



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M-44

Spin crossover in chalcogen-containing heterocyclic metal–organic frameworks.

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Metal–Organic Frameworks (MOFs) are an exciting class of materials that are capable of a multitude of properties owing to their synthetic flexibility. One such property is spin crossover (SCO), whereby the spin state of a metal centre can be switched from a paramagnetic high spin (HS, S = 2) state to a diamagnetic low spin (LS, S = 0) state through external stimuli such as temperature, light, pressure, or even guest inclusion. To date, a great array of spin crossover complexes and MOFs have been synthesised largely incorporating linear bidentate bipyridyl ligands and cyanidometallate coligands. Here, we present a family of iso-structural SCO MOFs containing non-linear bipyridyl chalcogen-containing heterocycles which exhibit a variety of SCO dependent on the central heteroatom, O, S, Se, and Te. The abrupt, single-step transition was shown to differ quite considerably, with both the temperature and hysteresis width varying with each heteroatom replacement. Furthermore, inclusion of several guest species was observed to induce multi-step transitions in several of the frameworks when compared to the as-synthesised materials. This broad display of behaviours highlights the sensitivity of the electronic switching behaviour to such small changes in structure, presenting an avenue towards further tuning of SCO materials as a whole.

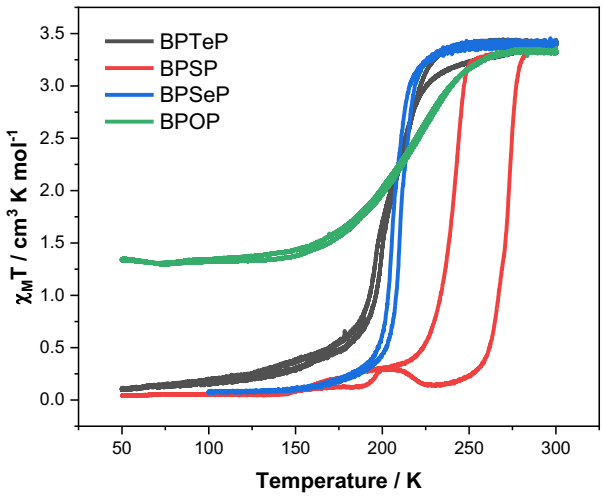

Figure 1: Magnetic susceptibility of each Hofmann-like framework in with varying heteroatoms in ethanol.

M-45

Metal Organic Framework Catalysis: An Organic Approach

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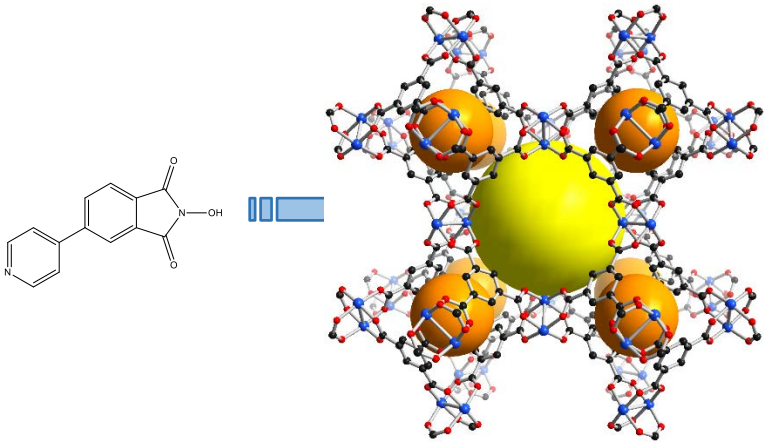
Efficient and cyclable catalysis is paramount to reducing waste in our chemistry driven economy. At the heart of the issue is a strong focus on heterogeneous catalysis. Solid catalyst can be easily isolated from their liquid substrates and reused; however, conditions necessitate the catalyst having a high surface area for efficient conversion. These converging needs make metal organic frameworks (MOFs) ideal candidates for such catalysts. MOFs have pore channels that provide adequate reaction environments, and open metal sites (OMS) for catalysis.[1] Much work has already been done to demonstrate the viability of MOFs as metal mediated catalysts, however ligand based organo-catalysts are yet to be fully realised.[2] Modification of prevalent ligands with desirable topologies has proved limiting - grafting pendant functionalisations may interfere with topicity, while additions must still allow enough space in the pores for sufficient catalyst-substrate interaction. N-hydroxy phthalimide is a good candidate for this role – NHPI has thoroughly demonstrated to be an efficient and broadly selective organo-catalyst for hydrogen abstraction reactions, having a simple work up for adding onto centred benzene ligand back bones. Thus far it been incorporated into one robust framework topology, and crucially, passing its first test with flying colours.[3]To circumvent the obstacles presented by grafting of catalytic functionalities onto structural ligands (cost, synthesis, yield, cyclability) NHPI may be introduced as a functional guest through coordination to open metal sites. This allows us to better tailor the pore space confinement effects and study the effect of different metal sites with respects to conversion by selection of the host framework.

Here we exhibit the catalytic faculties of MOFs structures doped with novel NHPI guests, as well as the electronic and spectral properties resulting for this exciting union.



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M-46

Investigating negative thermal expansion in metal–organic frameworks

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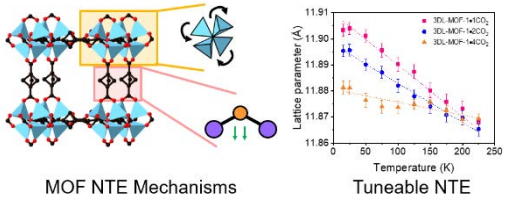
Metal–organic frameworks (MOFs) are an attractive class of nanoporous materials with potential interests in sustainable energy solutions, including applications in gas storage and separation, catalysis, sensors, and electronic devices. Understanding thermal expansion behaviour remains an important engineering consideration when designing for applications that are sensitive to expansion and stress. Our detailed investigation on the fundamental mechanisms of thermal expansion in MOFs endeavours to facilitate the process of engineering MOF materials to address sustainability challenges.

Negative thermal expansion (NTE), material contraction upon heating, is a desirable feature in the prospective design of zero thermal expansion materials. The discovery of anomalous properties in MOFs, such as NTE, sparks our curiosity to rationalise the mechanism of this unexpected behaviour. Our research aims to contribute knowledge to the following two pillars:

1. Understanding structure-property relationships – how does the framework structure alter the mechanisms leading to negative thermal expansion?
2. Understanding host guest interactions – how do guest interactions affect thermal expansion?

To instigate the structure-property relationship, we explored the thermal expansion properties of an isoreticular MOF series based on the archetypal MOF-5 ($[Zn_4O(1,4\text{-bdc})_3]$ bdc = benzene-1,4-dicarboxylate). Its thermal expansion was compared to its aliphatic analogues consisting of cubane-1,4-dicarboxylate (1,4-cdc) in CUB-5 ($[Zn_4O(1,4\text{-cdc})_3]$) and bicyclo[1.1.1]pentane-1,3-dicarboxylate (1,3-pdc) in 3DL-MOF-1 ($[Zn_4O(1,3\text{-pdc})_3]$).[1] In extension, we sought to exploit host-guest interactions to attain tuneable NTE, by charging 3DL-MOF-1 with CO_2 guest molecules and investigating the MOF properties using neutron powder diffraction. We demonstrated successful NTE quenching by increasing the CO_2 loading into the framework. To extend our understanding, we investigate a series of topologically complex moisture-stable quaternary MOFs that consist of three distinct linkers and one metal cluster. The holistic comprehension of structure-property relationships and host-guest interactions highlight the versatility of this class of materials to become the next generation of tuneable functional materials.



MOF NTE Mechanisms Tuneable NTE

(Left) Proposed NTE mechanisms in the aliphatic framework 3DL-MOF-1 consists of zinc tetrahedral Rigid Unit Modes (RUMs) and transverse molecular linker vibrations; (Right) neutron powder diffraction exploring host-guest interactions to accomplish tuneable thermal expansion.

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M-47

Anilate Sandwiches: A Recipe for Mixed Valency in Tetraoxolene-based Coordination Polymers

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Mixed valence coordination polymers display many notable properties, including their potential to exhibit electronic conductivity.[1] A popular strategy to achieve mixed valency is the combination of components with easily accessible oxidation states, such as redox active ligands and metal ions. Deprotonated 2,5-dihydroxybenzoquinone derivatives (anilic acids) can exist in three readily available redox states as a quinoidal dianion, a radial trianion or a tetraanion. Their incorporation into coordination polymers, along with Fe, have successfully resulted in the generation of mixed valence materials.[2-5] Our work aims to address the significant absence of neutral Fe-anilate coordination polymers that exhibit mixed valency through the employment of various co-ligands.

This work describes the structure and synthesis of a series of novel 1-D Fe-chloranilate based coordination polymers incorporating triaryl phosphine oxides as co-ligands. Single crystal X-ray diffraction was used to investigate the mixed valency exhibited by these compounds and the interesting intra-structure interactions between the bridging tetraoxolene ligands and the aromatic groups on the phosphine oxide co-ligands which induce these properties. Variable temperature structural studies show the temperature dependence of this mixed valency while conductivity measurements indicate that the crystalline solids are semi-conductors. We propose the implementation of these interactions as a strategy to achieve not only mixed valence anilate-based coordination polymers but to also generate tetraoxolene ligands with reduced oxidation states within materials.

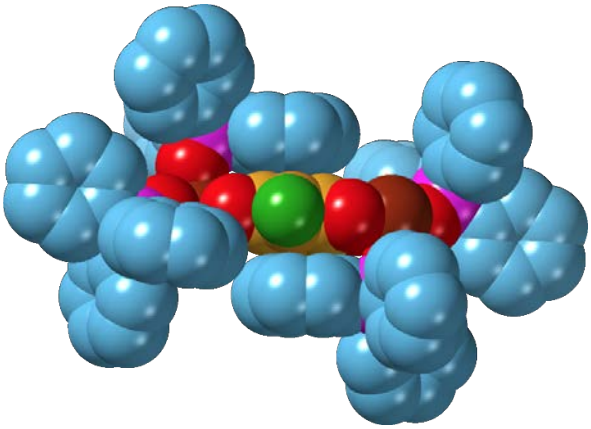

Figure 1: Representation of close face-to-face interactions between a bridging chloranilate ligand and triphenylphosphine oxide co-ligands within a Fe-tetraoxolene based mixed valence coordination polymer.

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M-48

Giant macrocycles from fused polynorbornane frameworks

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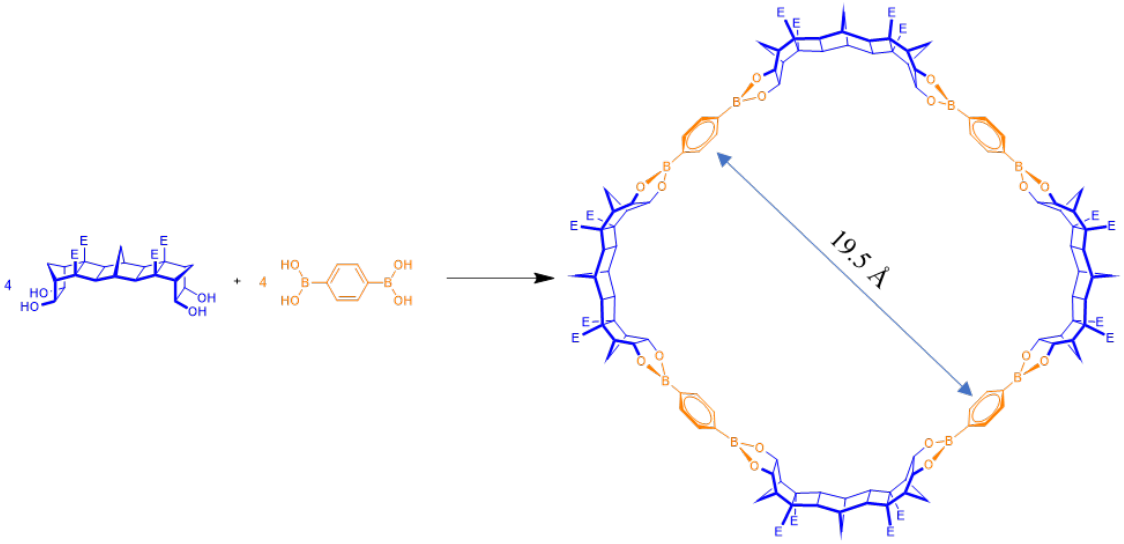
The development of new macrocycles is of interest in fields such as drug delivery, anion and cation sensing, energy storage, gas and liquid separations, and the catalysis of reactions. As such, the development of new macrocycles using novel synthetic approaches is an active research area.

Building block approaches that use boronic acids and catechols have been successful in accessing a wide range of macrocycles (1), however the use of fused polynorbornane diols in the self-assembly of macrocycles has not yet been reported, despite evidence that norbornane diols react far more effectively than catechols with boronic acids (2). Due to the high rigidity of fused polynorbornanes frameworks, macrocycles made with them would be especially robust, and highly preorganised. These characteristics, in particular the preorganisation, could lead to macrocycles with exceptional binding affinities (3).

This research project is focused on the development of a new series of covalent organic macrocycles based on fused polynorbornane frameworks. The reaction of a series of fused polynorbornane tetraols with benzene-1,4-diboronic acid to form large, highly rigid macrocycles will be presented, as well as strategies for the functionalisation of the surfaces and cavities of the macrocycles.



[4+4] Macrocycle

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M-49

Novel organogelators

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Gels have varying properties, which makes them hard to define but simultaneously provides numerous applications, such as thickening agents, drug delivery, regenerative medicine, sensors, and are common in the food industry. The commonly accepted definition for a gel is a substance with semi-solid properties, comprised of a solid and a fluid. Further classifications can be determined from the fluid a substance gels, or whether the gel formation is physical or chemical in nature. The gelators presented in this work are supramolecular organogelators. The synthesis and characterisation, using techniques such as nuclear magnetic resonance spectroscopy and atomic force microscopy, of novel gelators, including those based on calix[4]arenes, will be presented here. One calix[4]arene has been previously reported in the literature (Figure 1)[1], however the gelation properties were not described.

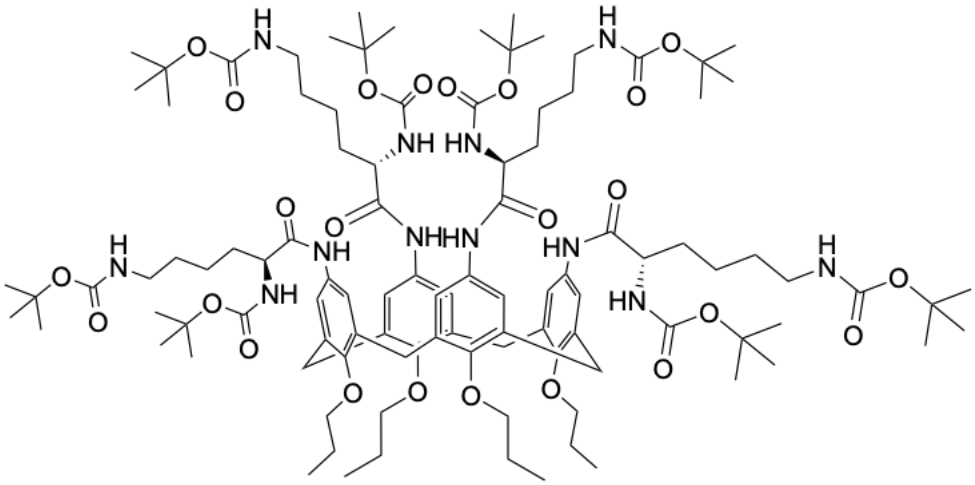

Figure 1: Structure of a previously synthesised calix[4]arene gelator.

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M-50

Probing topology, selectivity, and reactivity of complex mixtures of metallo supramolecular assemblies

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Metallo-supramolecular cages have unique structures which have applications in gas capture[1], drug delivery[2], catalysis[3] and antibacterial work.[4] In the past, the majority of research has explored symmetrical cages, subsequently limiting potential structures and applications. It is only recently that asymmetric structures have been investigated, with most structures minimising complexity by focusing on the formation of a single product. This reticence to study complex mixtures of cages could be attributed to limitations in characterisation techniques, where NMR and MS often provide insufficient data resolution to confidently and efficiently analyse these mixtures. Ion mobility mass spectrometry (IM-MS) is a specific type of MS which allows the clear resolution of different species based on their mass, shape and charge[5]. This project investigates the synthesis of complex mixtures of discrete metallo-supramolecular cages and their characterisation using IM-MS.

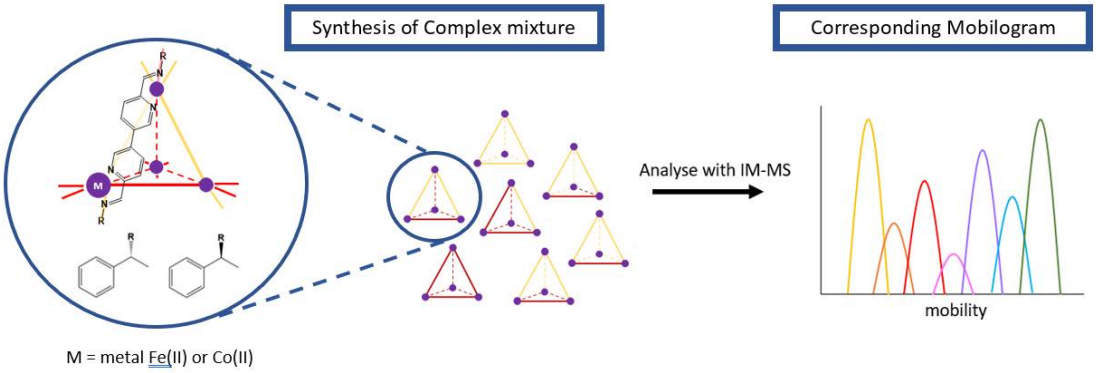

Figure 1: The complex mixture will be based on a cage within the literature[6], where the two different ligands synthesised using the two chiral amines (represented by the red and yellow lines) will be combined in the presence of a metal (the purple circles). This mixture will be analysed using IM-MS, where the mobilogram will resolve peaks of similar species based on their mass, shape and charge.

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M-51

Fluorinated Tetrapodal Anion Transporters

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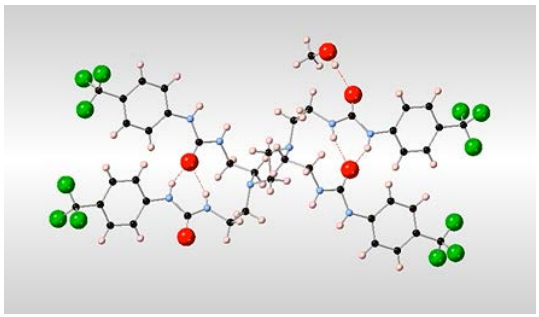
Synthetic transmembrane anion transporters have attracted significant research effort due to their potential applications as therapeutic agents for diseases like cystic fibrosis and cancer. While selective anion transport is desired for the treatment of diseases like cystic fibrosis, many synthetic transporters can facilitate proton transport via self-deprotonation or fatty acid aided transport.[1] Non-selective proton transport can dissipate the intra- and extracellular pH gradient with cytotoxicity side effects lending potential to possible anti-cancer therapies.[1-2]

Our previous work has shown that the fluorination of the tris-(thio)urea anion transporters showed enhanced anion-binding strength through increased hydrogen-bonding acidity while also increasing the overall lipophilicity of the transporters compared to the non-fluorinated analogues.[2]

Building from our previously reported non-fluorinated tetrapodal receptors, which could selectively bind and transport chloride anions across a lipid bilayer, here we report on the successful synthesis, anion-binding, transport activity, and transport selectivity properties of eight new fluorinated tetraphenyl(thio)urea transporters.[3]

Two of the transporters demonstrated a higher chloride binding affinity than the non-fluorinated analogues.



Single crystal X-ray structure of the Tetra-(trifluoromethyl)phenylurea transporter.

Across the series, the fluorinated transporters displayed the ability to efficiently self-deprotonation to undergo H^+/Cl^- co-transport even when membrane-bound fatty acids were sequestered from the vesicle membranes. All fluorinated tetraureas displayed a higher activity than the non-fluorinated analogue while two of the tetrathioureas displayed a > 3-fold increase in transport activity.

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M-52

Self-assembled M_3L_3 Metallocycles as Inorganic Crown ether Analogues

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Coordination-driven self-assembly emerges as an efficient tool in the construction of supramolecular systems. It involves reversible processes such as dissociation, association and recognition of molecules from interesting frameworks, preferably small polygons due to entropy effects. Metallocycles[1] are widely explored in guest binding, catalysis[1] and gas adsorption/separation applications. Here, we report an array of triangular metallocycles formed by copper (II) and a shorter bis-β-diketone ligand. Employment of shorter organic ligand kept the paramagnetic copper metal centres in the minimum distance possible. Furthermore, incorporating lanthanide guests in the cavity of the macrocycles induced a magnetic behaviour that makes them promising candidates for single molecular magnets. Single crystal studies revealed the triangular-shaped metallocycles with hexafluorophosphate as counter ions. The magnetic measurements were performed using VSM-3, and the powder-Xray diffraction confirms the phase purity. Recently, ammonium cation was incorporated in the binding site, resembling the crown ethers[2].

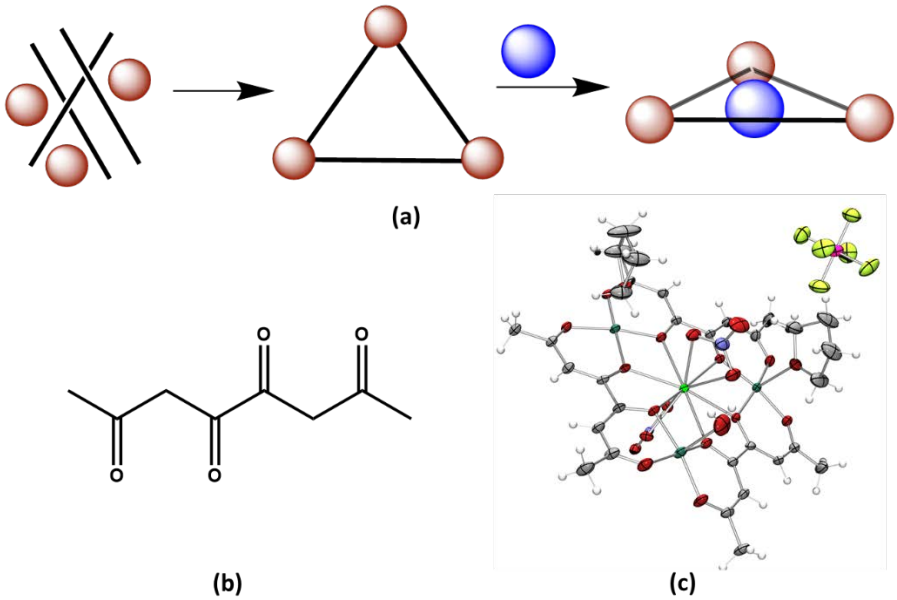

Figure 1. (a) Schematic representation of metallocycle formation; (b) bis-β-diketone ligand employed in the reaction; (c) Crystal structure of metallocycle with dysprosium ion occupying the binding cavity.

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M-53

Modulating the performance of an asymmetric organocatalyst in aliphatic multicomponent MOFs

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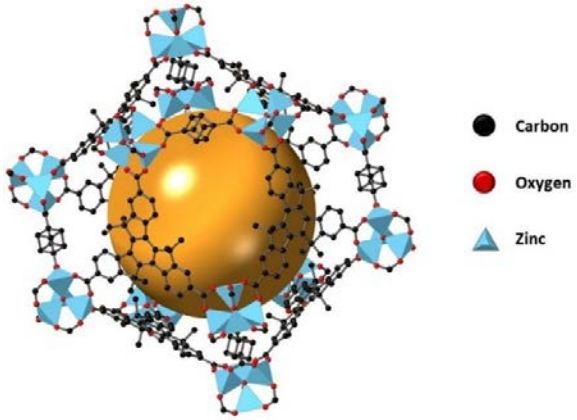
Metal-organic frameworks (MOFs) have become one of the most attractive classes of solid supports currently under investigation in heterogeneous catalysis.[1] However, methodically tuning the spatial environment around the active sites of heterogeneous catalysts remains a difficult challenge. A solution to this challenge can be approached through embedding a catalytic unit in a linker of a MOF, and then tuning its environment by modular control over the resultant pore space. Multicomponent MOFs provide ideal opportunities for modulating catalysis through introducing different functional groups to the surrounding linkers.[2] Studies of embedding prolinyl group (Pro) in a pore of MUF-77 [$Zn_4O(hmtt)_{4/3}(bpdc)_{1/2}(bdc)_{1/2}$] (hmtt = truxene, bpdc = 4,4'-biphenyldicarboxylate, bdc = benzene-1,4-dicarboxylate) frameworks have been previously investigated, where asymmetric aldol reactions were observed however the yield and enantioselectivity were not ideal.[2] Thus, the aim of this study is to employ a new strategy to modulate MOF catalytic activity using bulky, aliphatic linkers which can offer greater interaction sites to substrates.[3]

Using CUB-30-Pro [$Zn_4O(hmtt)_{4/3}(bpdc\text{-}Pro)_{1/2}(cub)_{1/2}$] (cub = cubane-1,4-dicarboxylate) as a platform aliphatic MOF, other aliphatic derivatives have been synthesised through exchanging the cubane for bicyclo[1.1.1]pentane-1,3-dicarboxylate (pdc) and cyclohexane-1,4-dicarboxylate (chyx). It is expected the catalytic performance of these modified MOFs will be improved by changing the bdc aromatic linker to aliphatic linkers to create an aliphatic environment adjacent to the active site. The structures were elucidated using single crystal X-ray diffraction and ^1H NMR spectroscopy, while the catalytic behavior will be analysed using HPLC.



Crystal structure view of a dodecahedral pore of CUB-30.

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M-54

C_4 Symmetric chiral cage from resorcin[4]arene derivatives

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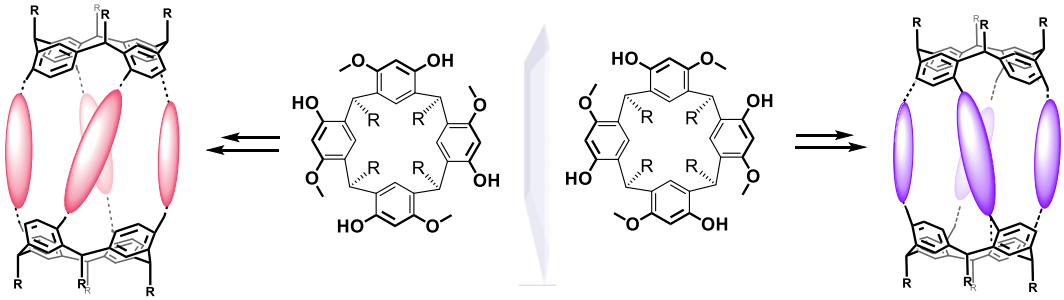
Cage architectures with a discrete inner cavity have been of long-standing interest.[1] The development of chiral cage molecule synthesis facilitates their potential application in chiral recognition, chiral catalytic vessel, and host-guest chemistry. The incorporation of chirality into the cage can be achieved either by employing chiral linkers (ligands) or chiral capping ends.

The macrocycle resorcin[4]arene is well known for its concave cyclic array, facile synthesis from resorcinol and a aldehyde, and in the application of host-guest chemistry. *m*-Cresol as a replacement of resorcinol gave birth to racemic tetramethoxy-tetrahydroxy resorcin[4]arene.[2] Further modification or extension on the upper rim of the cyclic array allows more space for guest binding by tuning the depth of the cavity and acting as a capping end of the cage skeleton. Herein, we explore the synthesis and properties of the C_4 symmetric chiral cage constructed from a chiral derivative of resorcin[4]arene via covalent bond formation, including the copper(I)-catalysed azide–alkyne cycloaddition (CuAAC) reaction.



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M-55

Amphiphilic Copolymers for the Extraction of Membrane Proteins

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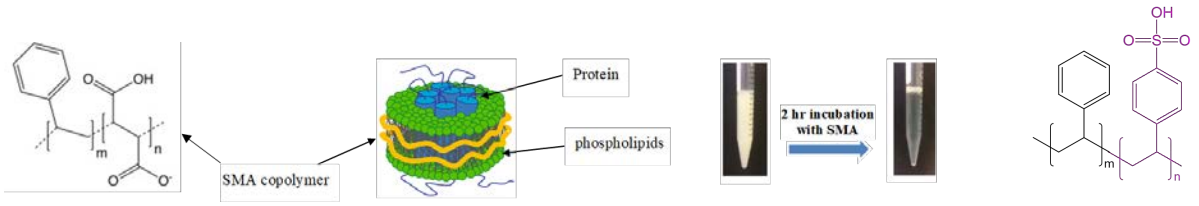
The conventional technique for extraction and solubilising membrane proteins is by using surface-active agents to form self-assembled spherical micelles. This method, however, could not fully maintain the native environment of membrane proteins and often lead to their destabilisation. Membrane proteins can be extracted, sans surfactants, using amphiphilic copolymers of acrylic acid, in particular, poly(styrene-co-maleic acid) (SMA) copolymers, forming stable nanodiscs known as SMA-lipid particles (SMALPs, Figure 1).[1] While superior to surfactant-based methods, the formation and stability of SMALPs are affected by pH and the presence of salts. A number of copolymer variants which could form SMALP-like particles have also been studied to overcome these limitations but with variable level of success.[1]



(a) (b) (c) (d)

(a) SMA copolymer; (b) Cartoon representation of SMALPs[2]; (c) Cloudy suspension of SMA and membrane protein turning clear when SMALPs formed[5]; (d) SSSA copolymer – this work.

This work represents our effort to design novel SMA-like amphiphilic copolymers that can operate at extended pH range and more salt tolerant than the current SMALP forming versions. By substituting maleic acid with the more acidic styrene sulfonic acid (SSA) and varying the SSA content in the copolymers, we managed to access lipid solubilisation at lower pH particularly at higher SSA content. FTIR confirmed the capture of the lipids by the SSA copolymers although the formation of lipid particles is yet to be verified.

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M-56

Delivering anion transporters to lipid bilayers in water

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The current method employed to deliver small molecule transporters to liposomal or cellular studies involves dissolution of transporters in DMSO.[1] This work involved the formation of inclusion complexes between 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) and a novel series of adamantyl-appended anionophores (**Figure 1**). The adamantyl group is an ideal size to fit in the cyclodextrin cavity.[2] It was intended that inclusion would greatly enhance the aqueous solubility of the transporter molecules, meaning they could be delivered to vesicle studies in pure water.[3] The inclusion of the transporter molecules within the cyclodextrin cavity was confirmed using numerous analytical techniques, and transport activity when delivered in DMSO or an aliquot of water was compared.

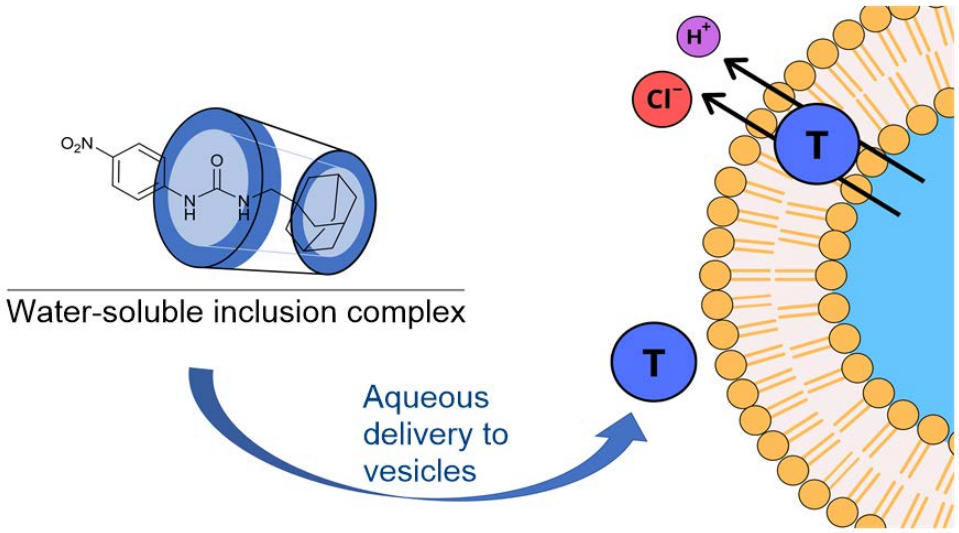

Figure 1. Schematic depicting the transporter-cyclodextrin inclusion complex formed to permit the delivery of the anionophores to model vesicles in water.

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M-57

Peptide-RNA binding from a Supramolecular Chemistry Perspecitve

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RNA's role in the body is largely dictated by its ability to interact with a variety of other biomolecules, namely proteins, lipids, and sugars. These four classes of molecules constitute the four major macromolecules responsible for life.[1] It has been well established that non-covalent interactions between RNA molecules and proteins are responsible for a variety of cellular functions by biologists, such as the regulation of protein synthesis and formation of liquid-liquid phase separated structures (membraneless organelles)[2]. Chemists have investigated the supramolecular behaviour of individual nucleobases and modified nucleobase structures. Nucleobases interact primarily by hydrogen bonding and pi stacking with other species[3]. However, these studies fail to investigate how entire nucleotides or oligonucleotides behave. The sugar-phosphate backbone of oligonucleotides is ignored in these studies, where the potential electrostatic and dipole interactions are not investigated. Furthermore, single nucleotides rarely exist in biology, so the exploration of how oligonucleotides interact on the supramolecular level would provide a link between the two disciplines.

This investigation designed and synthesised a library of seven hexamer peptides based on the -RGG motif found in RNA-binding proteins, and four pentamer, adenosine rich oligonucleotides, loosely based on the sequence of a codon. The peptide and RNA libraries were designed with the intent to investigate the sequence selectivity of these molecules and better understand the mechanisms which determine RNA-peptide binding. Preliminary aggregation studies using UV-Visible spectroscopy determined that these libraries of peptides and RNA when combined do not undergo significant liquid-liquid phase separation.

The project then evolved to use NMR binding studies to determine if binding was occurring, using the GGRRGG peptide due to its slight observed aggregation and two oligonucleotides, AAAAA and AAUAA. Preliminary NMR titrations were performed, which determined that AAAAA and AAUAA both bind to GGRRGG with a binding constant of ~1000 M-1, which suggests little selectivity between the two oligonucleotides. However, this technique for determining binding constants provides a jumping off point to further investigate RNA supramolecular interactions.

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M-58

Use of modulators and light to control crystallization of hydrogen bonded frameworks

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Crystallization of hydrogen bonded frameworks in aqueous environments can be challenging as it often leads to the formation of small crystallites/amorphous powders which cannot be characterised using single crystal X-ray diffraction techniques. In this work, we explored the effect of concentration, organic co-solvent and modulators on the formation of charge-assisted frameworks comprised of a tetraamidinium cation and diazobenzene based dicarboxylate anions.[1] Photo-switching ability of the azo-compound also allowed us to control crystallization via a light-induced cis/trans switching mechanism.

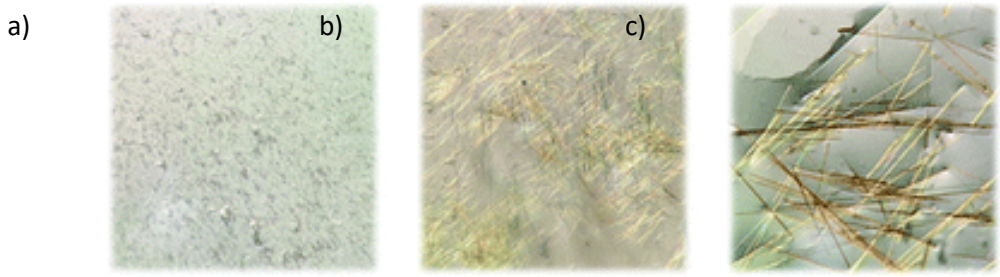

Figure 1. Crystallization of tetraamidinium with diazo compound using a) 10 equivalents of $NaSO_4$, b) 100 equivalents of $NaSO_4$ and c) UV-light in 1:1 EtOH:H_2O.

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M-59

Fused [n]Polynorbornanes for Metallosupramolecular Assemblies

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MOFs are continuous molecular architectures of organic ligands coordinated around metal ions or clusters. A key feature of 2D and 3D MOFs is their distinctive porosity; Each framework has uniform pores, the shapes, sizes and chemical environments of which are determined by the metal ions and ligands that make up the framework. This porosity gives MOFs remarkable properties including the ability selectively "take in" various chemical species, allowing these networks to "sort" gases. MOFs have one key weakness—the potential for the network architecture to collapse. Structural collapse can pose a hinderance as this causes the network to drastically lose both pore volume and surface area.

Two methods used to improve the stability of MOFs are increased hydrophobicity and heightened ligand rigidity. Fused [n]polynorbornane frameworks are rigid, aliphatic molecules that have been used previously for supramolecular applications, including the formation of discrete coordination cages. While fused [n]polynorbornane would seemingly be an ideal material for the synthesis of ligands for MOF formation, no instance of [n]polynorbornane being used in this way has been reported to date.

In this project, a collection of fused [n]polynorbornane ligands are synthesized and their use in the synthesis of MOFs is investigated.

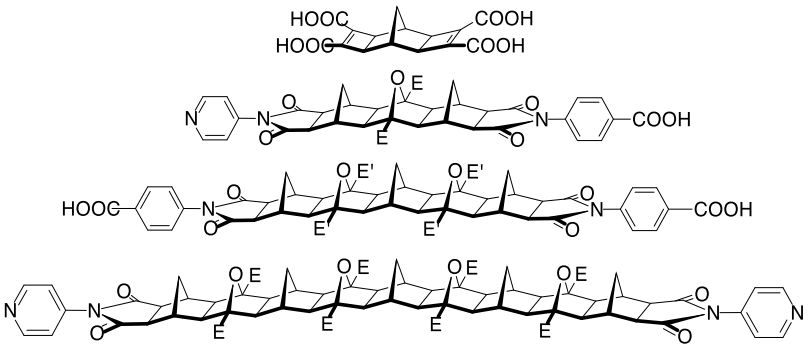

Figure 1. A sampling of ligands to be synthesized in this project

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M-60

Spin Crossover Behaviour of Metal Complexes Encapsulated in Halogen-Bonded Networks

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The ability to modify and fine-tune the properties of a crystalline material underpins the field of crystal engineering. Modification of crystal packing can result in a change or amplification of the properties of the crystal, such as the optical, magnetic, redox, electrical conductivity, catalytic and the spin crossover (SCO) properties.[1] This project aims to investigate the effect and methods in which SCO-active metal complexes of an iron(III) *bis*-Schiff base type can be incorporated into halogen-bonded frameworks. Encapsulation of complexes in these frameworks provides an avenue to modify the molecular arrangement of components within the crystal, whereby simultaneously modulating the SCO behaviour, without the need to change or functionalise the cationic species itself. Two distinct approaches were employed to modulate and fine-tune the SCO properties of $[Fe(qsal\text{-}OMe)_2][(1,3,5\text{-}TITFB)(NCS)]\cdot MeOH/H_2O$. The first approach involves the exploitation of a three-way solvatomorphic and magnetic hysteresis via a single-crystal-to-single-crystal transformation (Figure 1 (a)), through the reversible exchange of MeOH and water via a desolvated/dehydrated analogue, with a $\Delta T_{1/2}$ = 95 K. The second approach involves the combination of two different anions (NCS^- and I^-) in several different proportions. This enabled for tuning of the crystal structure and the SCO behaviour. Tuning the anion fractions provides an avenue to directly control the spin transition temperature of a particular co-crystal, where in this case the increase in I^- fraction (and the subsequent decrease in NCS^- fraction) results in marked changes in $T_{1/2}$ (Figure 1 (b)), shifting the profile to higher temperatures while maintaining a sharp spin transition curve and relatively high degree of cooperativity between cations.

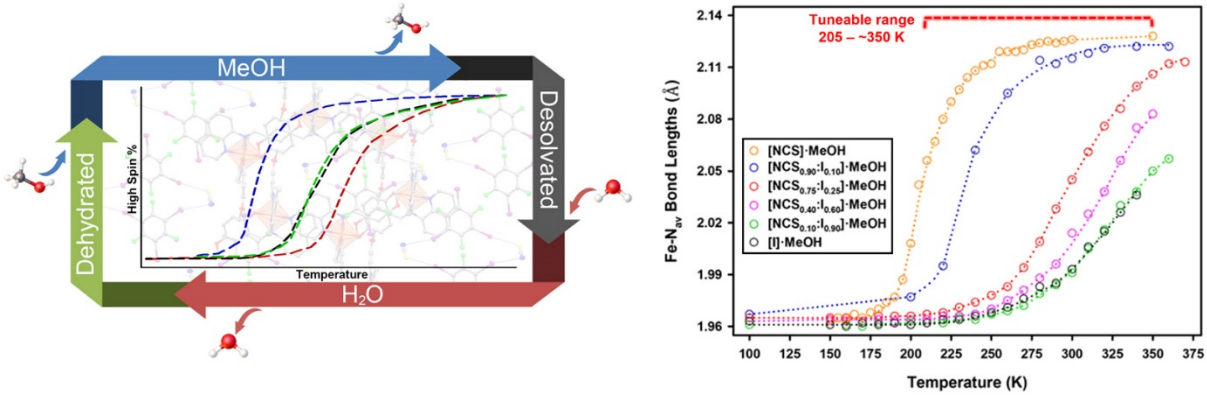

Figure 1: (a) Three-way solvatomorphic cycle of $[Fe(qsal\text{-}OMe)_2][(1,3,5\text{-}TITFB)(NCS)]$. (b) Overlayed plot of $Fe\text{-}N_{av}$ bond lengths vs temperature of the NCS^-/I^- mixed anion $([Fe(qsal\text{-}OMe)_2][(1,3,5\text{-}TITFB)(NCS_x{:}I_{1-x})]\cdot MeOH)$ series of co-crystals.

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M-61

Furazan-centred bis-ureas as transmembrane anion transporters

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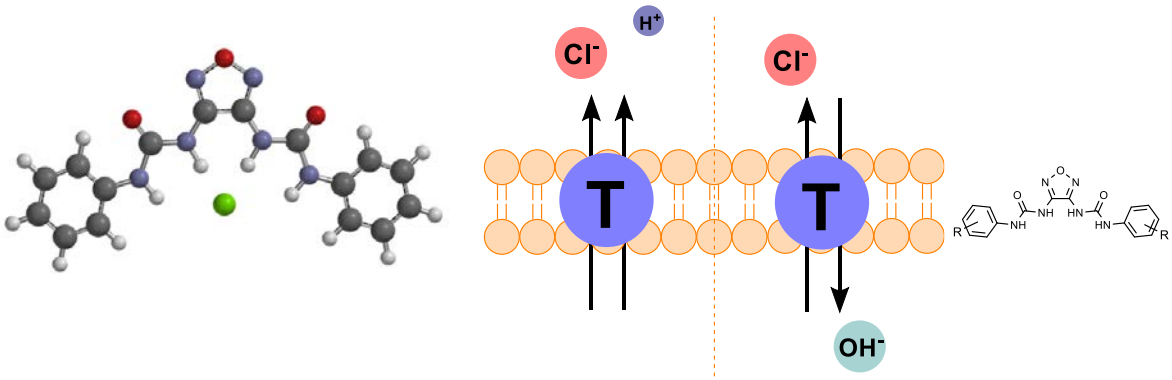
The transport of biologically relevant anions through membranes has been studied extensively over the past decade, and there have been a variety of anion transporter classes developed with potential therapeutic applications in the treatment of cancer and channelopathies.[1, 2] Furazans are a class of highly inductive heterocycles that possess interesting pharmacological activity.[3] Herein, we report the implementation of the furzan moiety into the design of a library of anionophores generating the first examples of a central 5-membered ring scaffold in anion transport. ^{1}H NMR titrations were used to determine the binding affinities to chloride, and anion transport assays were used to determine the anionophoric activity across phospholipid bilayers and to investigate the mechanism of chloride transport.



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M-62

Substituted cucurbituril conjugates with nanoparticles for drug delivery

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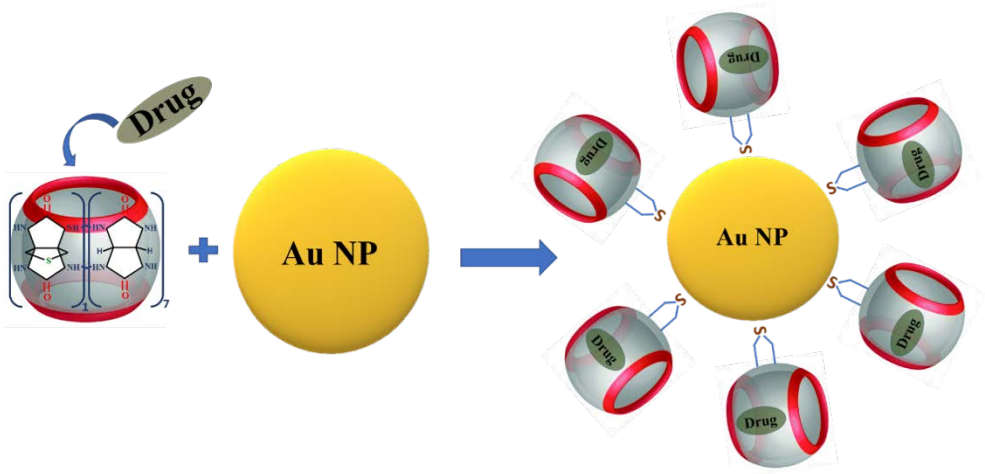
The emergence of macrocyclic structures like cucurbiturils, crown ethers, cryptands, etc., has brought supramolecular chemistry to the forefront of scientific development and progress in host-guest chemistry. The unique structural, chemical and guest binding properties of cucurbit[*n*]uril (Q[*n*]) have made them the topic of extensive research in the last few decades[1]. In addition, substituted cucurbit[*n*]uril has widened the range of applications of Q[*n*] including drug delivery, by modifying their properties[2,3]. One such modified cucurbit[*n*]uril involves equatorial substitution as a cyclopentano ring with a sulphur atom, i.e. tetrahydrothiophene (THT) Q[*n*]. This Q[*n*] can be used to synthesize and stabilize nanoparticles(NPs), like those of gold. Gold offers excellent biocompatibility and has the potential to deliver high concentration of drugs. Guest encapsulation of drugs is favored inside the cavity of THTQ[7 or 8].
The work presented here describes the synthesis of equatorially substituted THTQ[*n*]. The homologues of THTQ[7 and 8] were separated and purified. The THTQ[*n*] were used for the synthesis of gold nanoparticles, acting as a stabilizing agent to prevent aggregation of NPs, and were subsequently loaded with drugs.



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M-63

Synthesis of MOFs using Bulky Ligands for Gas Separation

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Metal-Organic Frameworks (MOFs) have gained increased attention as synthetic approaches for target applications such as gas separation and storage. The use of pillar ligands to construct these materials is an interesting aspect of MOF design as they can vary the level of interpenetration and provide a scaffold for interactions with guest molecules such as gases.

Our work has focused on the formation of new MOFs synthesised using bulky ligands both by themselves and as a pillar ligand. The pillar ligands have terminal nitrogen donors and contain additional functionality. This functionality and bulkiness play a pivotal role in MOF assembly as well as providing sites of interaction for the adsorbing molecules.

One of the synthesised MOFs, $[Zn_3(bdc)_3(L)]$, is composed of 2D sheets stacked together by pillar ligands forming a 3D framework, Figure 1. These sheets are made up of zinc(II) nodes coordinated via the carboxylate groups of 1,4-dicarboxylic acid. The 3D framework is then formed via the nitrogen donor ligands, acting as pillars between the sheets. Gas adsorption techniques were used to uncover the surface area and potential for selective CO_2 adsorption.

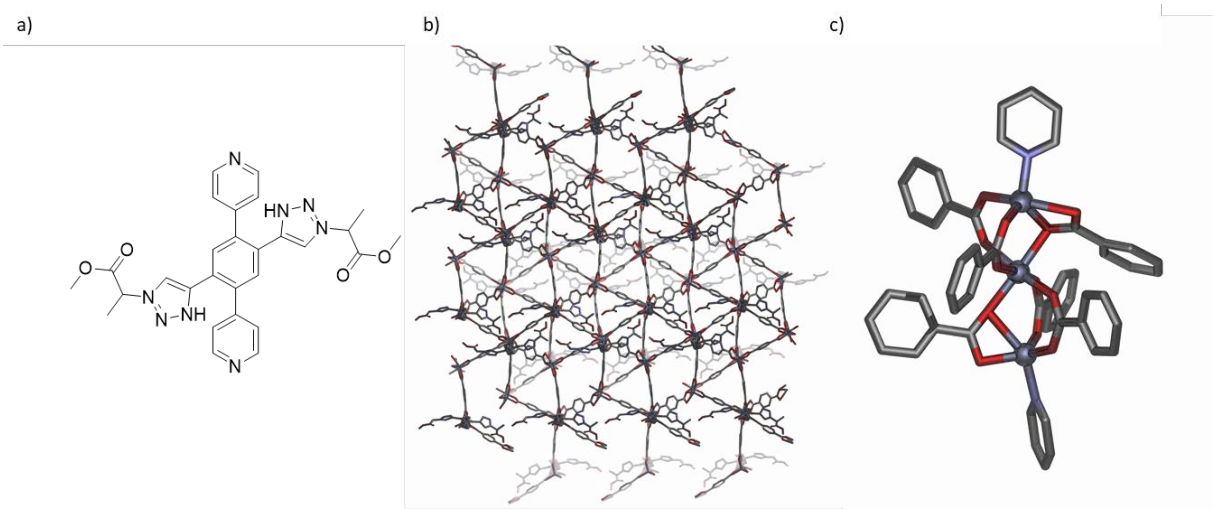

Figure 1: a) Pillar ligand b) MOF and c) zinc(II) node.

M-64

Employing a Chiral Auxiliary Strategy Towards Enantiopure Metal Organic Cages

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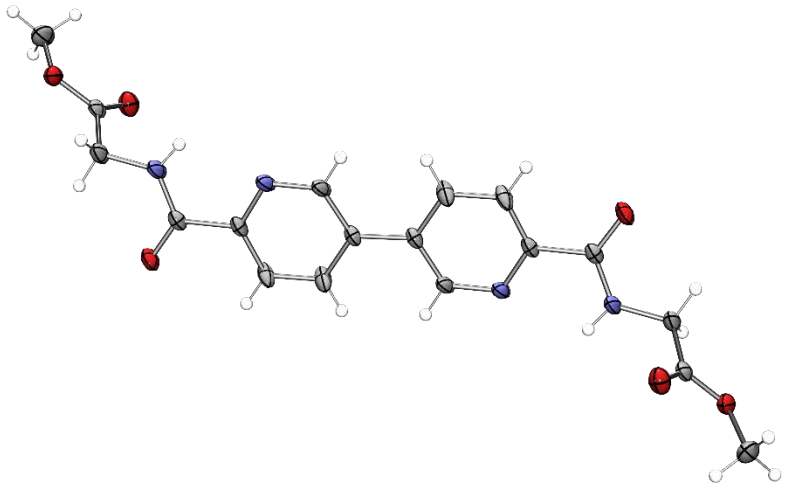
Metal organic cages are a promising class of discrete molecular containers that exhibit highly selective guest encapsulation for applications in molecular separations,[1] catalysis,[2] and the stabilisation of reactive species.[3] The rational design of organic ligand binding modes and corresponding metal coordination geometries leads to the predictable self-assembly of complex architectures such as tetrahedra, cubes,[4] and even a remarkable $M_{48}L_{96}$ Goldberg polyhedron.[5] Strongly directional metal-ligand interactions represent an integral component of cage design strategies. Here, we have designed M_4L_6 edge-linked tetrahedral cages with planar, C_2-symmetric bis(bidentate) 3,3'-bipyridine ligand backbones to provide the rigidity necessary for structure predictability. Together with octahedral transition metal nodes that define the vertices of the tetrahedron, these components self-assemble to enclose a central cavity that defines a distinct microenvironment. This microenvironment can encapsulate a range of different guest molecules based on its unique size, shape, and chemical properties. Enantiopure cage assemblies are a challenge to achieve. The popular approach is to produce chiral metal centres in-situ through the self-assembly of achiral components. However, this often leads to a mixture of diastereomers due to the lability of metal-ligand interactions. In this case, chiral amino acid auxiliaries are employed to impart permanent chirality onto the cage using enantiopure ligands. Although synthetically more challenging, this strategy guarantees lasting chirality acquired from the carbon stereocentres. A chiral metal organic cage would successfully define a chiral space for the enantioselective encapsulation of guest molecules.

Figure 1: Ortep structure of 3,3'-bipyridine ligand with glycine auxiliary. Atoms shown as 50% probability thermal ellipsoids.



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M-65

Squaramide Appended Polymers for Fluorescent Anion Sensing

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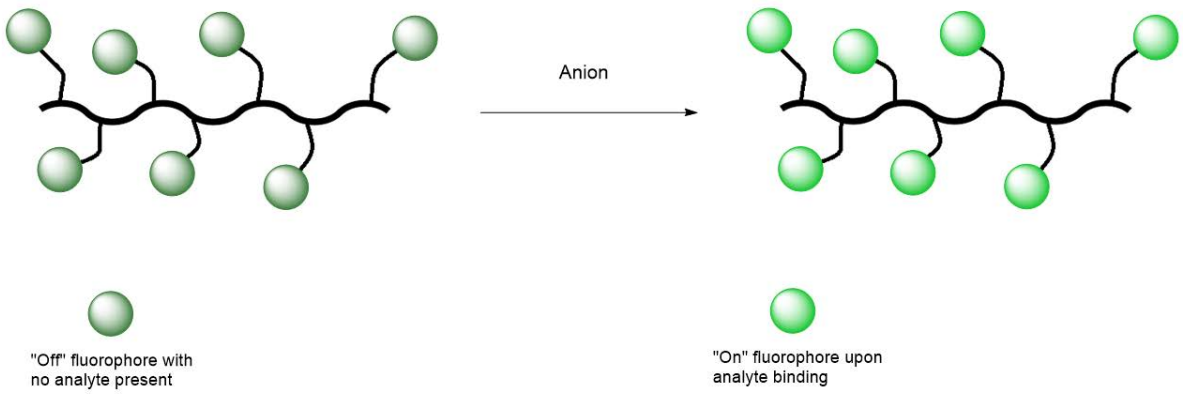
Anions such as sulfate and chloride are crucial to both biological and environmental processes, with variations in concentrations potentially linked to arthritis[1] and eutrophication.[2] Previous methods of detection require extensive sample preparation,[3] and are inefficient in comparison to optical based sensors. However, traditional optical sensors often bind weakly due to difficulties in forming multiple bonds to one analyte, leading to a lack of sensors for anions such as sulfate. There is a need to design receptors which can be readily synthesised and freely conjugated with a variety of anion binding motifs.

This study employs a readily synthesised copolymer of DEGMA ((diethylene glycol) methyl ether methacrylate) and Boc-AEMA (a boc-containing methacrylate derivative), which can be functionalised with squaramide binding units to increase the binding sites available on a single molecule. The ratio of DEGMA to Boc-AEMA was varied to investigate the influence of this on anion binding. We develop a method for the synthesis of these polymers, while also appending UV active squaramides for ease of detection. Anion screening was performed in acetonitrile, with the responses compared to a monomeric form of the squaramide binding motifs.



Fluorescent turn on of fluorophore conjugated polymer backbone upon analyte addition.

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M-66

Controlling the construction of chiral copper(II)-containing coordination cages

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The integral components of natural systems like the human body are often chiral, as evident in the helical nature of DNA strands and the right-handed bias of glucose and related sugars. However, the same is not always true in the field of supramolecular chemistry. Though the spontaneous resolution of chirality is possible, it is more often the case that chirality is imparted on a supramolecular assembly through deliberate design. Coordination cage complexes – which consist of metal ions bridged by bent organic ligands into an enclosed cage-like structure – can form helical structures serendipitously, but only in racemic mixtures. Obtaining homochiral coordination cages comes as a result of carefully selecting enantiopure bridging ligands.

Numerous design strategies have been developed in recent years to control the self-assembly of coordination cages, such as manipulating the induction of chirality in helical structures,[1] and the use of steric interactions to influence the self-sorting of multi-component cages.[2] These approaches allow the tailoring of coordination cages towards desired architectures or applications. Specifically, our group has focused on the design and combination of diphthalimide-derived ligands, which can be conveniently appended by amino acids to add coordinating groups and sources of chirality to the system. The core substituents in the diphthalimide backbone and the amino acids side chains can then both be altered to tune the properties of resulting cages.

This poster presentation will illustrate new chiral lantern-type coordination cages constructed using the synthetic strategies mentioned above. The rationale behind the design of these cages will be discussed, with an emphasis on the philosophies used to obtain predictable coordination geometries and cage configurations.

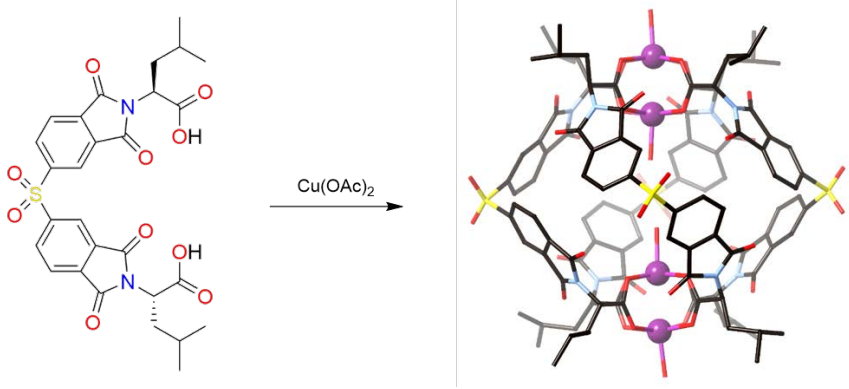

Figure 1. An example of a chiral Cu(II)-containing lantern-type coordination cage designed by Boer *et al*. using diphthalimide-derived ligands functionalised with enantiopure amino acid residues.[1]

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M-67

Improving hydrogen storage in Prussian Blue Analogues

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A prime opportunity currently exists to utilise hydrogen to decarbonise a range of industries including power generation and transportation. To decrease the cost and increase the capacity of hydrogen able to be stored, new alternative solid absorbent hydrogen storage technologies are required to be developed. Metal-Organic Frameworks (MOFs) are considered the leading solid-state hydrogen absorbent material as they can be designed to reversibly capture and release hydrogen gas on demand with a low energy penalty. Another promising set of hydrogen storage materials are Prussian Blue Analogues (PBAs), which whilst known for many years for their various optical, electronic, and magnetic properties, have only been investigated for hydrogen storage in the last 15 years.[1,2] Despite possessing a relatively lower gravimetric surface area and enthalpy of hydrogen absorption than the benchmark sorbent MOF-5, PBAs offer a number of distinct advantages including their low cost, environmentally friendly syntheses, moisture stability, coordinatively unsaturated metal sites for hydrogen adsorption, as well as potentially higher volumetric hydrogen absorption.

A series of PBAs have been prepared and their capabilities to store hydrogen at competitively low pressures determined using high pressure hydrogen adsorption studies. The scalability of these materials was investigated through screening synthetic conditions (reaction time, modulating agents, concentration, and doped incipient salt concentrations) and investigation of the resulting crystallinity and gas adsorption of PBAs. These results may lead to the development of optimal solid-state adsorbents that can cater to a range of different industrial applications.

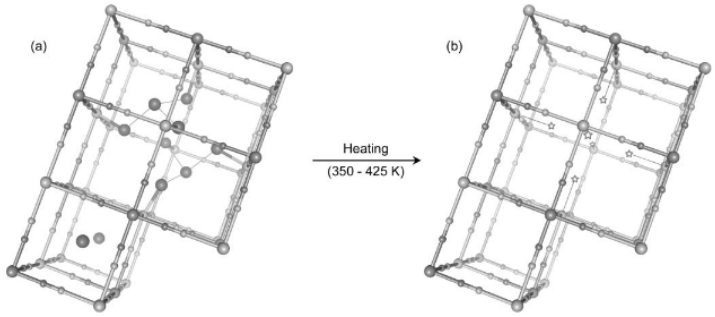

Fig 1. General cubic framework of PBAs of the form $T[M(CN)_6]$, where T = Fe, Co, Ni, Mn, Cu, etc.; M = Fe, Mn, Co, etc.) in the hydrated phase (a), showing coordinated and hydrogen bonding guest water molecules and the dehydrated phase (b) showing coordinatively unsaturated metal sites (stars) surrounding the lattice vacancies. Reproduced from Ref 2 with permission.

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M-68

A ratiometric probe for phosphatidylserine

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Phospholipids are the main components of cell membranes and play a crucial role in providing structural barriers, cell signalling processes and vesicular trafficking.[1] Additionally, many diseases are associated with lipid metabolic disorders, such as asthma, diabetes and Alzheimer's diease.[2] A peptide-based probe containing zinc(II) dipicolylamine and coumarin catechol moieties has previously been developed as a selective sensor for phosphatidylserine (PS) in cell membranes.[3] In this previous study, the probe used an intramolecular indicator displacement sensing mechanism to achieve the "turn-on" fluorescence response, which exhibited good selectivity to phosphatidylserine. However, this probe can only analyse the phosphatidylserine qualitatively, so we want to improve the probe to achieve quantitative analysis.

We are now investigating transforming the probe into a ratiometric probe for PS through the attachment of an additional fluorophore on the peptide backbone, which provides an "always-on" fluorescence. We envisage that once the zinc(II) dipicolylamine group binds to the phospholipid's head group, we would be able to see a turn on response from the coumarin fluorescence, which would lead to a change in the ratio of the fluorescence emission intensities of the fluorophores attached to the probe. In this way, we can quantify the phosphatidylserine in cell membranes.

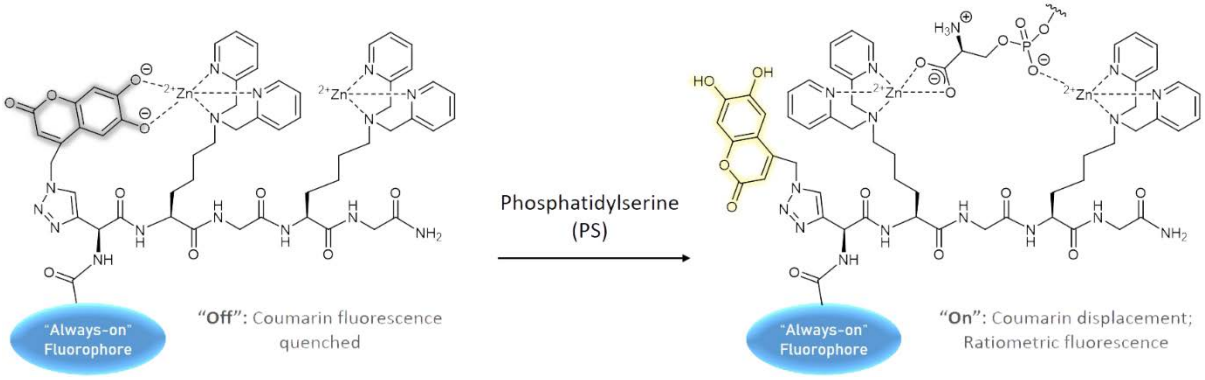

Figure 1: Peptide-based ratiometric probe containing two different fluorophore

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T-69

Waste-derived hole transport materials for future devices

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Low-cost flexible organic light-emitting diodes (OLEDs) incorporating nano-emitter[1] and charge transporting materials derived from waste open new opportunities for sustainable and cleaner production technologies. However, the materials developed from waste in general do not have good optical or electronic properties that are essential for their applications in electronic devices.

Herein, we have developed fluorescent carbon dots (CDs) as an emitter from the cheap staring precursor p-Toluene sulfonic acid (PTSA) and water-soluble hole transporting material with ultra-high charge mobility from the waste clothes to demonstrate the most sustainable light emitting diode devices. The OLED devices exhibit more than 2000 cd/m^2 of luminescence, which is one of highest efficiency reported for green CDs based OLEDs.

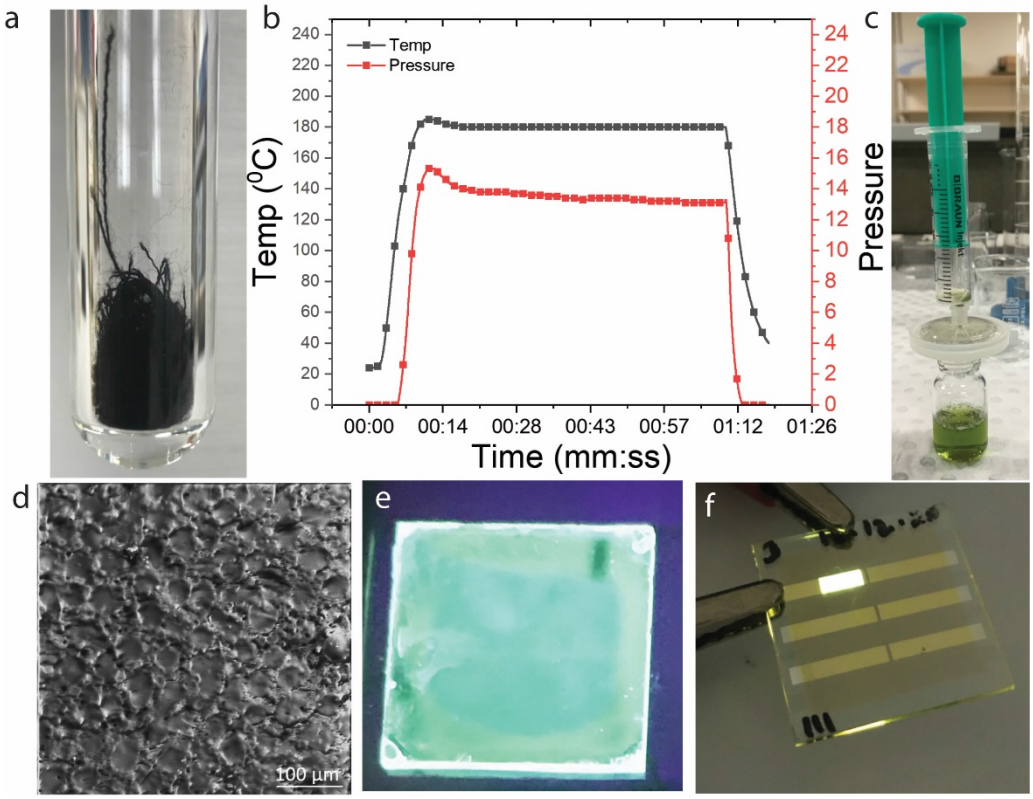

Figure (a) The waste cloth shredded in the reactor vessel. (b) Microwave assisted advanced oxidation process to dissolve all the amorphous contents of the precursor under constant pressure. (c) Filtration of the reaction products with 0.22-micron filter. (d) SEM of crystalline carbon as a hole transporting material. (e) Solid state thin film coating of hole transporting material and the green emitting carbon dots over UV lamp. (f) Demonstration of organic light emitting diode on a glass substrate.

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T-70

Development of Mesoporous Cu-Functionalised Carbon Nitride for the Detection of Important Metabolites

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Carbon-based materials including carbon nanotubes, graphene, fullerenes, carbon quantum dots and carbon nitrides are used in several applications including electronics, energy, sensing, catalysis, and biomedicine. Among these, carbon nitride has been widely used because of its significant enzyme mimetic activity. Introduction of unique textural features in these materials can significantly influence their properties. For example, mesoporous carbon nitrides with pore sizes between 2 to 50 nm demonstrate high surface area, large pore volume and uniform pore diameter that are useful in energy storage, gas adsorption, metal-free catalysis, photocatalytic water splitting, separation and sensing applications. Additionally, surface functionalization of porous carbon nitride with heteroatoms is a viable strategy to improve its efficacy in various applications. In this study, we have functionalised copper metal on higher nitrogen containing mesoporous carbon nitride (mp-C_3N_5) to impart peroxidase enzyme mimetic activity to carbon nitride and demonstrate its application in glucose and glutathione sensing. Copper doped mp-C_3N_5 (Cu-C_3N_5) was prepared by using a hard templating route where SBA-15 was used as silica template while, 3-amino 1,2,4 triazole (3-AT) and copper nitrate hemi-penta hydrate were used as carbon-nitrogen and copper precursors, respectively. Textural and structural analysis confirmed that the ordered 2D hexagonal porous structure of SBA-15 template was successfully transferred to mp-C_3N_5 though, the structural order decreased with increasing of copper concentration. The high nitrogen content of C_3N_5 enabled a high retention of copper in the mp-C_3N_5 matrix. Copper loading imparted the mp-C3N5 with exceptional peroxidase mimetic activity demonstrated by the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB) dye (generation of blue colour), in presence of H_2O_2. Exceptional peroxidase mimetic activity was applied for the detection of glutathione, a well-known antioxidant, and glucose, an important metabolite, within the relevant physiological concentration. The assay developed using mp-Cu-C_3N_5 could detect as low as 2 ppm of glutathione and detect glucose in a physiologically relevant concentration range of 0.1 – 4 mM.

T-71

The Effect of Organic ligands on MnO_x as H_2O oxidation Catalyst

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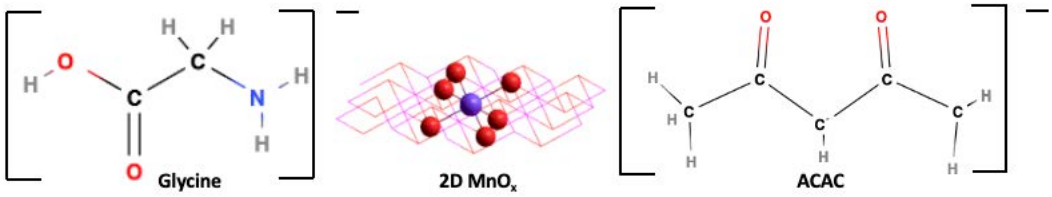
Water oxidation catalysts made from earth abundant materials are considered a key enabling technology for making a number of commodity products electrochemically. In recent years, it has been noted that several materials beyond metal oxides, particularly some metal-organic framework materials, are effective at water oxidation. This raises questions as to how inorganic/organic interfaces may change catalyst efficiency. In this study, we examined how the water oxidation efficiency changes when manganese oxide water oxidation catalysts were in the presence of organic ligands of acetylacetone (ACAC) and glycine.



The zeta potential measurements revealed the addition of organic ligands resulted in a better physical colloidal stability between the particles. Therefore, a mechanistic effect on the stability of the particles is exhibited. In parallel, the effect of organic ligands on the activity of MnO_x is studied by examining the effects on the decomposition of H_2O_2. The obtained results showed that at neutral pH both ligands are advantaging the decomposition rate. However, in the alkaline condition, the decomposition rate is insignificantly affected by the organic ligands compared to MnO_x. The two experiments divulged both ligands have a mechanistic effect on the stability and activity of MnO_x. Consequently, further studies are going to be conducted to better understand these interfaces and the effects on water oxidation.

T-72

Phosphorescent Complexes of Iridium, Ruthenium and Rhenium for Specialised Biological Applications

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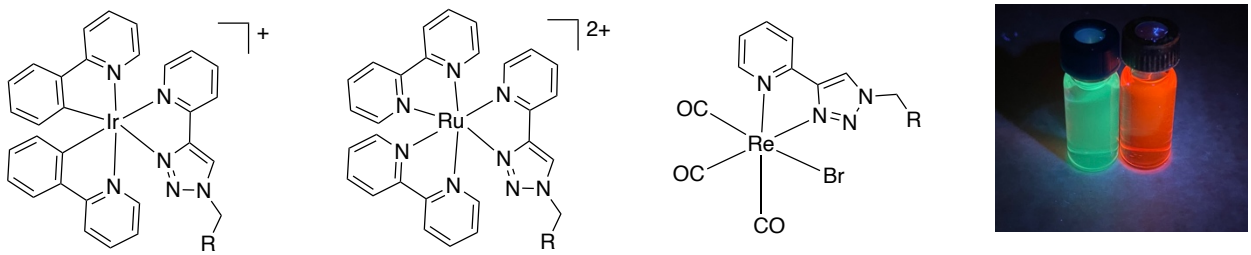
Phosphorescent d^6 metal complexes can be used as an alternative to organic fluorophores, quantum dots or fluorescent proteins. Their photostability, large Stokes shifts and long-lived excited states make them excellent candidates to be used as fluorophores for specialised biological imaging applications such as fluorescent guided surgery or live cell imaging.[1]

Bidentate 1,2,3-triazole ligands can be easily synthesised by copper catalysed azide-alkyne cycloaddition reactions, which allows for straightforward incorporation of various functional groups into the ligands. These triazole ligands can be incorporated into polypyridyl complexes of iridium, ruthenium and rhenium to provide a handle for bioconjugation.

A family of iridium, ruthenium and rhenium complexes, incorporating substituted triazole ligands, was synthesised and their electronic properties were investigated by cyclic voltammetry and electronic spectroscopy. Their emission properties were tuned by variation of the polypyridyl ligands and the triazole ligand.

Water-soluble iridium complexes were also prepared by incorporation of polyethylene glycol functionalised triazole ligands. Reactive functional groups such as maleimides were also installed on the water-soluble complexes, which allowed for conjugation to proteins such as bovine serum albumin and girentuximab, an antibody that selectively binds to carbonic anhydrase IX.



Left: heteroleptic phosphorescent metal complexes of iridium, ruthenium and rhenium incorporating a 1,2,3-bidentate triazole ligand. Right: two of the prepared complexes under UV irradiation.

Acknowledgements

We acknowledge the Australian Research Council, Australian Cancer Research Foundation, National Health and Medical Research Council, the Victorian Cancer Council, the Innovative Manufacturing Cooperative Research Centre, and Telix Pharmaceuticals for supporting this research

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T-73

In situ synthesis of metal fluorides with controlled chemistry

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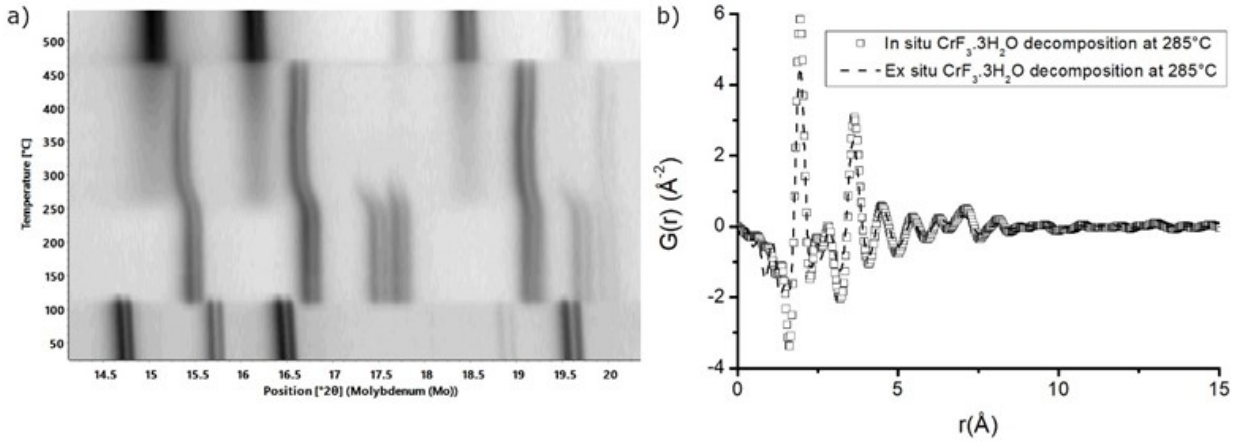
Iron fluoride ($FeF_3.nH2O$) shows high capacity as cathode material for lithium-ion batteries combined to low toxicity and low cost. The water content of iron fluoride has been shown to be of prime importance in the performances of the cathode[1,2]. So far, the various synthesis routes do not allow for a precise water content control, especially on the low amount regime which is the most interesting range of composition. In addition, CrF_3 has been shown to significantly increase the conductivity of LiF film[3]. Consequently, it is of interest to look for the in-situ formation of the various $MF_{3-x}(OH)_x\,nH_2O$ phases (M = Cr, Fe).

We aimed to investigate in-situ the formation of $MF_{3-x}(OH)_xnH_2O$ (M = Fe, Cr) phases to control the precise crystal chemistry using a controlled atmosphere environment and look for new phases not reported so far. To reach our goals, we investigated $MF_3.3H_2O$ (M = Fe, Cr) powder using in-situ high temperature X-ray diffraction (XRD) and Pair Distribution Function (PDF) analysis taking advantage of the transmission geometry. The use of capillaries enables us to control the generated atmosphere upon heating and thus assessing a rich chemistry. Some of the results are presented in Figure below for the $FeF_{3-x}(OH)_xnH_2O$ phases (a) and for $CrF_{3-x}(OH)_xnH_2O$ (b). Precise control of the water content of the $FeF_{3-x}(OH)_xnH_2O$ phase could be reached with n ranging from 1/3 to 0 with about 10 new pure phases. The controlled in-situ decomposition of $CrF_3.3H_2O$ led to the formation of a new $CrF_{3-x}(OH)_x$ pyrochlore which was characterized structurally and magnetically.



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T-74

UV induced hierarchical magnetic gold nanostructure moulding under high shear topological fluid flow

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UV irradiation of aqueous solutions of auric acid ($H[AuCl_4]$) under high shear in a vortex fluidic device (VFD), Figure 1, affords ultra-thin sheets of gold, prisms of gold, and a hierarchical structure comprised of gold prisms encapsulated within ultra-thin sheets of gold. The nature of the product formed depends on the rotational speed (ω) of the quartz tube in the microfluidic platform, concentration of auric acid, pH, and processing time, for the tube rotating at a fixed tilt angle fixed of $\theta = 45^{o}$. This processing occurs without the need for adding a reducing agent or surfactants, both of which can control the nucleation and directional growth of gold particles. Remarkably the gold nanostructures generated in the VFD are magnetic. The formation of thin sheets of gold encapsulating nanoparticles of gold as well-defined prisms is effectively a mould of a component of topological fluid flow in the VFD.[1] The length of these structures can be greater than the thickness of the film of liquid in the VFD, as hollow tubes, and we propose that they form in a 'spinning wheel' (typhoon like) topological fluid flow generated by the Coriolis from the hemispherical base of the tube, Figure 1(c).

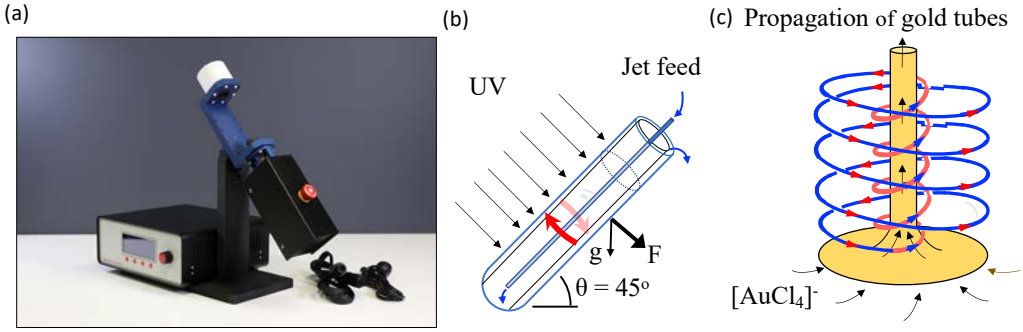

Figure 1: (a) Photograph of a Vortex Fluidic Device (VFD), (b) schematic of the set up for producing gold nano-structures under continuous flow, and (c) cartoon of the formation of hollow tubes of ultrathin thin gold, generated within the spinning top high shear topological fluid flow.

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T-75

Nitrogen Fixation by Highly Structured Phosphine Containing Transition Metal Complexes

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Ammonia production is one of the largest industrial processes on the planet accounting for nearly 1% of global energy usage.[1] The current method, developed in the early 20th century, is quite inefficient requiring high temperature and pressure as well as producing several unwanted biproducts such as CO_2. As such, investigations into a more efficient and environmentally sustainable method for NH_3 production are of vital importance.

Plants and microorganisms are able to convert atmospheric nitrogen (N_2) into NH_3 at ambient temperature and pressure using the enzyme nitrogenase. The exact mechanism for this process is unknown but it is clear that N_2 binding to a metal centre is a key step.

Since the first dinitrogen complex was reported in 1965[2] there have been many complexes explored as potential catalysts for NH_3 production. Initially a major focus was placed on molybdenum containing complexes as this was believed to be the metal necessary for biological nitrogen fixation. However, when it was discovered that iron was actually the common metal in the different forms of nitrogenase interest was renewed in the group 8 metal complexes.

This project focusses on group 8 and 9 phosphine containing metal complexes that can bind dinitrogen and activate it towards NH_3 production. These complexes will be treated with acid in order to produce ammonia (and hyrdrazine). An example of the reaction with acid can be seen in figure 1.

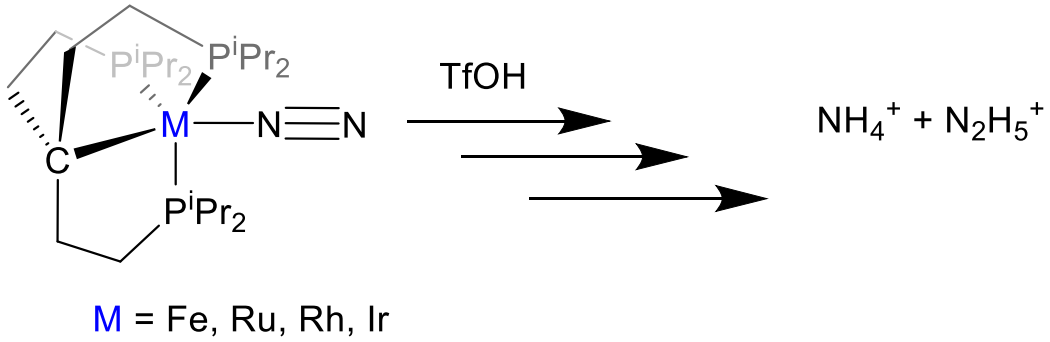

Figure 1: Reaction scheme for reduction of N_2 to NH_4^+ and $N_2H_5^+$

The amount NH_3 as well as N_2H_4 produced will be quantified using GCMS. Development of the GCMS method has also been a major step in this project as it allows hydrazine and ammonia to be quantified effectively using the same analytical technique.

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T-76

Structural, Redox, and Kinetic Investigations of Multifunctional Metal–Organic Frameworks Containing Tetrathiafulvalene

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Multifunctional metal–organic frameworks (MOFs), whose properties can be manipulated by controlled application of external stimuli, are of significant scientific interest due to their potential use in sensing, energy storage, photonic, and gas separation applications. This poster details investigations of the light-mediated [2+2] photocyclisation reaction between cofacial pairs of tetrathiafulvalene (TTF) units in a MOF.[1] The reaction is reversible upon heating, allowing the properties of the MOF to be varied as desired. The redox activity of TTF units is also exploited through chemical oxidation, yielding significant changes in the optical properties of the MOF, exhibited by the formation of two Intervalence Charge Transfer (IVCT) processes. Additionally, the solid state kinetics of a series of related frameworks are investigated over a range of temperatures. In all cases the reaction rates of the photocyclisation show a non-linear dependence on temperature. Each MOF exhibits a different maximum rate of reaction (which occur at different temperatures), facilitating insight into how subtle structural parameters influence [2+2] photocyclisations in MOFs.

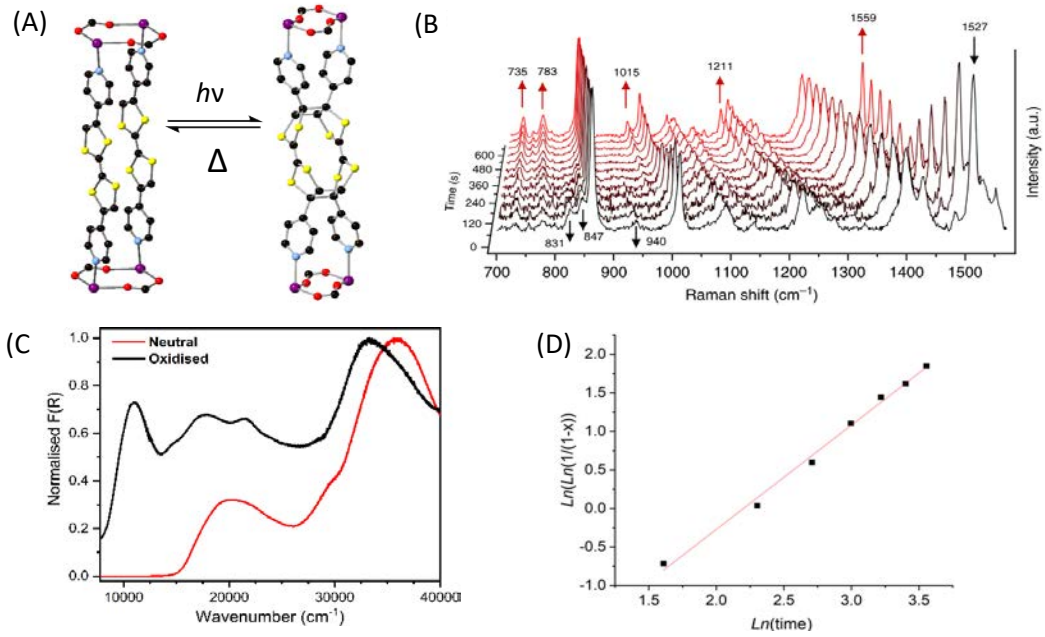

Figure 1. A. The [2+2] photocyclisation between cofacial TTF units. B. Light irradiated Raman spectra for monitoring the cyclisation reaction. C. Solid state UV-vis-NIR spectra showing IVCT bands in the oxidised framework. D. Johnson-Mehl-Avrami-Kolmogorov (JMAK) kinetic analysis of the photocyclisation.

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T-77

Explorations of electron-transfer within multi-site molecular frameworks

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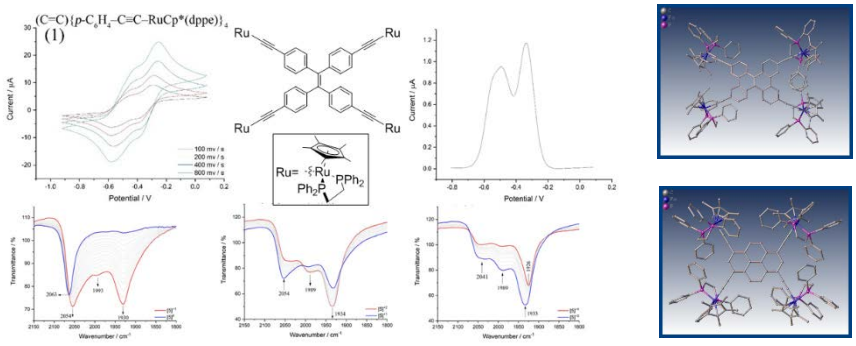
Electron transfer (ET) processes are ubiquitous in chemistry, governing the most elementary of bond-forming steps, and harnessed in events as complex as the photosynthetic cascade and respiration.[1a] The most common model systems to investigate these types of processes are mixed-valence (MV) complexes [{L_nM}-(μ-bridge)-{ML_n}$^+$], in which a bridging ligand connects two redox centres {ML_n} that are identical except in their oxidation forms.

Since the first fundamental and generally accepted quantitative description of ET in solution developed by Marcus in the 1950s, theoretical treatments have evolved in complexity, leading to various models of MV systems including two dimensional model Marcus-Hush and Generalized Mulliken-Hush (GMH) theories.[2b] As theory has developed, attention has been focused on the synthesis and study of a wide range of inorganic, organometallic and organic 'linear' MV systems.[2] However, beyond electron-transfer processes in linear bridged systems, a clear indication of the structure-property relationships that govern electron transfer processes and pathways in multi-metallic MV complexes is elusive.

In this presentation, we describe our efforts to move beyond the conventional linear mixed-valence complexes by using 1,3,6,8-tetraethynylpyrene, 1,1,2,2-tetrakis(4-ethynylphenyl)ethene and 2,7,10,15-tetraethynyldibenzo[g,p]chrysene bridging ligands and descriptions of these compounds using the Marcus-Hush 'two-state' model, to more complex molecular frameworks where electron exchange takes place between four sites.[3] These systems have potential to serve as molecular models for more complex intra-electron transfer effects such as quantum interference[4] and provide deeper insight into these fundamental processes.



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T-78

Fluorescent metal complexes for use in image-guided surgery of prostate cancer

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It is possible to provide improved treatments of Prostate Cancer (PCa) by early detection and resection of the carcinoma. Incomplete resection can result in metastasis into both bone and lymph nodes. The development of fluorescent techniques for the intraoperative detection of the marginal boundaries of the tumour have recently been investigated.[1] Of particular interest is the use of fluorescent metal complexes, such as those based on Ir(III), Ru(II) and Re(I), as they possess beneficial photophysical properties such as large stokes shifts, high quantum yields and long luminescent lifetimes.[2] Additionally, functionalisation of the metal complex with ligands such as 2,2-bipyridine-4,4-dicarboxylic acid provides sites for bioconjugation of a targeting peptide or peptidomimetic. Prostate Specific Membrane Antigen (PSMA), also known as glutamate carboxypeptidase II, has been identified as an efficient vector for PCa targeting due to its overexpression in PCa cells as well as having a close correlation to the cancers Gleason score.[3] Ureido based low molecular weight dipeptides of the structure lysine-ureido-glutamate have been shown to be efficient inhibitors of PSMA with many radiotracers developed utilizing this moiety. Further investigation has identified that bivalent PSMA inhibitors perform better than their monomeric counterparts, displaying longer tumour retention and increased cellular internalization of the tracers, resulting in superior tumour to background ratios.[4] This research aims to synthesize and characterise bivalently functionalised fluorescent metal complexes for intraoperative identification of PCa marginal boundaries.

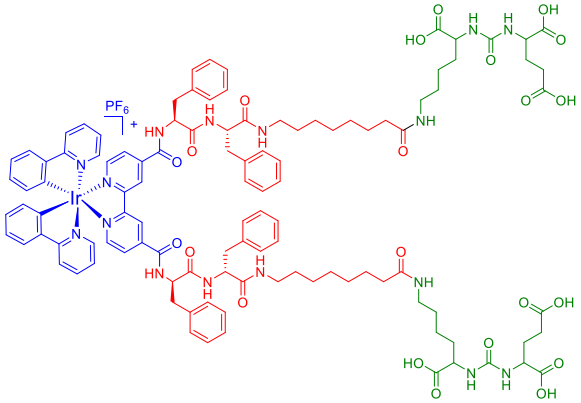

Figure 1::Structure of a bivalent fluorescent Iridium(III) complex for intraoperative PCa identification

We acknowledge the Australian Research Council, Australian Cancer Research Foundation, National Health and Medical Research Council, and the Victorian Cancer Council for supporting this research

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T-79

Cellular fates of the mitochondrial calcium uniporter inhibitors Ru360 and Ru265

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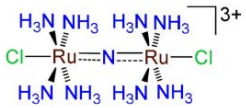
Ruthenium-265 (Ru265) is a μ-nitrido bridged binuclear ruthenium complex that is a potent and selective inhibitor of the mitochondrial calcium uniporter (MCU), an ion channel protein across the inner mitochondrial membrane responsible for regulating cytosolic Ca^{2+} concentration. Ru265 is a structural analogue of the μ-oxo bridged species Ru360, which was first discovered to have MCU inhibiting properties as an impurity in crude formulations of the trinuclear species ruthenium red. While Ru360 selectively inhibits the MCU with minimal off-target effects, cells must first be treated with a permeabilising agent to facilitate the cellular uptake of Ru360.[1,2] In contrast, the remarkably similar Ru265 is taken up readily by non-permeabilised cells.

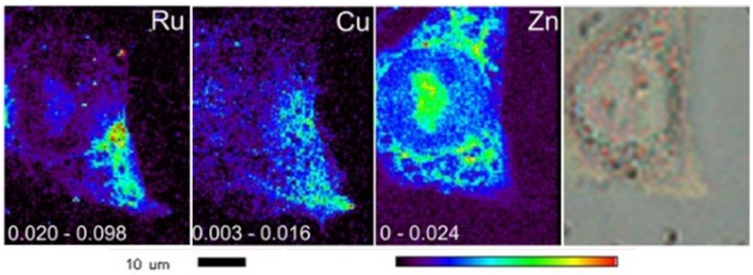
Extended X-ray absorption fine structure (EXAFS) spectroscopy and X-ray fluorescence microscopy (XFM) have been used to investigate the differing cellular fates of Ru265 and Ru360. We have used XFM on the 2-ID-D beamline at the Advanced Photon Source to observe the subcellular localisation of ruthenium in HeLa cells treated with either Ru265 or Ru360, as previously reported.[1] Further to this, we have recently collected EXAFS data on diruthenium complexes in human blood models at the Australian Synchrotron in an attempt to elucidate the differing structure-activity relationships in these two remarkably similar compounds.

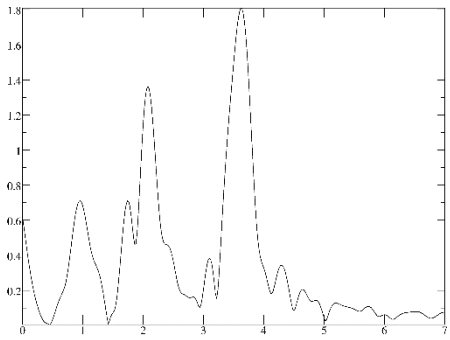
Clockwise from right: chemical structures of Ru360 and Ru265; EXAFS Fourier transform of Ru360 (5 mM) in MOPS buffer; XFM elemental maps and optical micrograph of a HeLa cell treated with Ru265 (50 µM).

Ru360



Ru265





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T-80

Accurately locating transition metal influenced hydrogen atoms with solution NMR spectroscopy

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Accurately locating hydrogen atoms continues to be a difficult task for most spectroscopic and X-ray diffraction techniques, especially when in proximity to transition metals, and, consequently, hinders investigations that aim to understand the properties of hydrides when they are bound to transition metals.

To accurately locate hydrogen atoms that are bonded to transition metals, solution NMR spectroscopy can be used to exploit the distance dependent interactions nuclei (^{1}H-X; X = ^{13}C, ^{2}H and ^{1}H···^{1}H) have with each other. Upon excitation, relaxation occurs between spin active nuclei, termed T_1 relaxation, and the T_1 relaxation efficiency depends on the bond length between nuclei.[1] The difference in relaxation ability of ^{12}C and ^{13}C nuclei is detected through the T_1 relaxation times of bound ^{1}H nuclei by inversion recovery experiments. Inversion recovery experiments can be modified to specifically select the ^{1}H-^{13}C resonance or the ^{1}H-^{12}C resonance and comparison of the two allows subsequent calculation of ^{1}H-^{13}C bond lengths.

The above nuclear interaction will be measured to obtain accurate atomic hydrogen positions on the transition metal agostic complex; [η^5-Cp*RhC$_{10}$H$_{13}$][PF$_6$]. This complex has an agostic methylene group where one ^{1}H-^{13}C unit is in a 3-center 2-electron bond with the rhodium center, while the other ^{1}H-^{13}C unit is free from the rhodium center. The contrast between the lengthened ^{1}H-^{13}C agostic bond and the unperturbed ^{1}H-^{13}C bond is expected to be reflected in the T_1 relaxation times of the two ^{1}H nuclei.

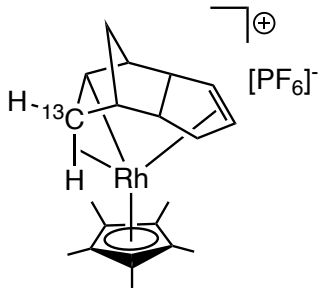

Figure 1: The structure of [η^5-Cp*RhC$_{10}$H$_{13}$][PF$_6$], and the relationship between T_1 relaxation times and the bond length of a ^{1}H-^{13}C group.

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T-81

Improving the bioavailability of copper *bis*(thiosemicarbazonato) complexes with enzyme-cleavable solubility modifiers

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Neurodegenerative diseases, such as Motor Neuron Disease (MND), are presently incurable and of increasing concern to the aging population. MND often leads to paralysis within 2-5 years of diagnosis and is characterised by oxidative tissue damage and motor neuron degeneration.[1] There is no clear understanding of the disease's mechanisms which makes it difficult to find treatments.

A bis(thiosemicarbazonato) copper(II) complex, called Cu(atsm) (Figure 1), is under investigation as a potential therapeutic for MND and Parkinson's disease.[2] Cu(atsm) is stable, lipophilic, charge-neutral, membrane permeable and capable of crossing the blood-brain barrier.[3] A major challenge to the clinical development of Cu(atsm) is its high insolubility in water which compromises administration of the complex and overall bioavailability. The proposed mechanisms of action of Cu(atsm) include its ability to reduce oxidative damage through selective delivery of copper to metal-deficient superoxide dismutase as well as the ability of the complex to inhibit lipid peroxidation and ferroptosis.[2,4]

Our aim is to develop second-generation derivatives of Cu(atsm) that have improved solubility but retain the stability, $Cu^{II/I}$ reduction potential and ability to cross the blood-brain barrier that is essential for biological activity. The synthesis of new prodrug variants will be presented where functional groups that improve water solubility can be enzymatically cleaved in the body to produce a biologically active molecule (Figure 1).

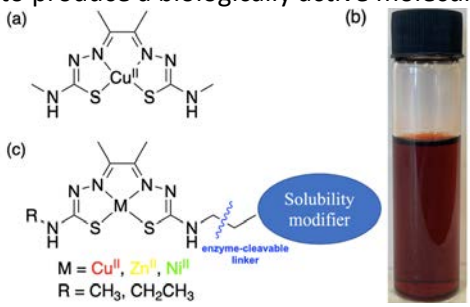

Figure 1. (a) Structure of Cu(atsm). (b) Cu(atsm) in solution. (c) Structure of Cu(atsm) prodrug.

We acknowledge the Australian Research Council, Australian Cancer Research Foundation, National Health and Medical Research Council, and the Victorian Cancer Council for supporting this research.

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T-82

Metal-to-metal communication through strongly conjugated frameworks in ruthenium complexes

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Despite heavy interest in the conductivity of quinones and their potential applications in molecular electronics, metallaquinones, which are complexes where at least one of the oxygen atoms of a quinone is replaced by a metal centre, are extremely under-researched and not yet been exploited. The chemistry which will be developed in this project will allow us to explore the aromatic/quinoidal dichotomy and compare the two linear conjugation pathways.[1]

This project draws inspiration from earlier work of Milstein *et al.* who reported two stable metallaquinones,[2, 3] which have not yet been studied electrochemically. Modification of the bridging system, number of metal centre(s) or length of organometallic complexes can significantly impact electronic and structural properties. We aim to reproduce and further characterise Milstein's compound *I*, synthesise and characterise di-ruthenaquinone *II* and *para*-ruthenaquinonoid oligomers *III* (*Figure 1*), and investigate electronic communication in the said compounds using spectro-electrochemistry and computational chemistry. DFT calculations using the latter will be performed to confirm properties including geometries and electronic structure (*Figure 2*). A clear classification of the target compounds based on their electronic delocalisation and results from spectro-electrochemical analysis will enable a detailed comparison of the effectiveness of benzenoids and quinoids as components in molecular electronics.[1]

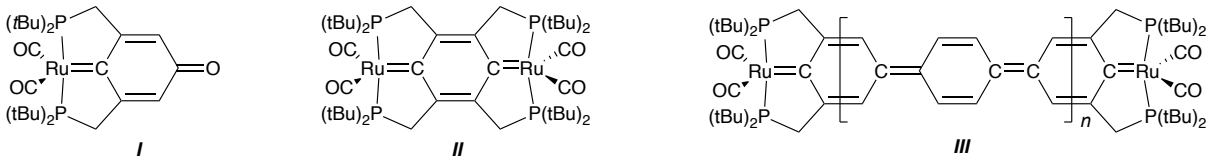

Figure 1. Target compounds.

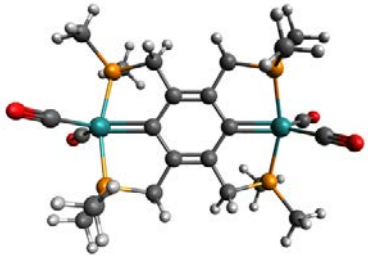

Figure 2. Preliminary geometry calculation with Orca for neutral gas-state complex II using the ωB97X-D3 functional and def2-SVP basis set.

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T-99

A new expression and purification system using SQ-affinity chromatography

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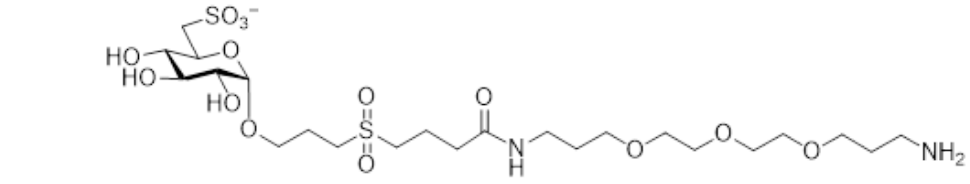
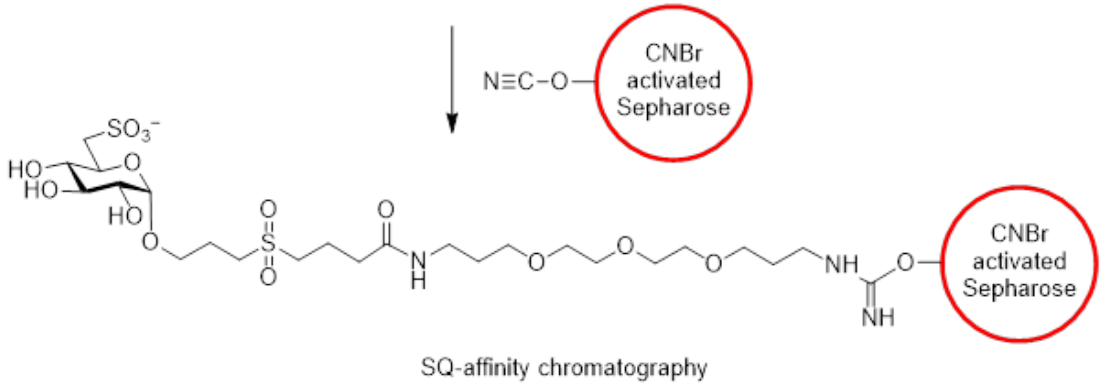
Heterologous protein expression is extensively used for production of proteins. Modern recombinant protein expression biotechnology often uses maltose binding protein (MBP) as an affinity tag partner. The gene encoding MBP is fused to the gene of interest; upon expression the MBP-fusion protein in *E. coli*, the protein can be purified by chromatography over cross-linked amylose, with elution using maltose. However, constitutively-expressed amylase from *E. coli* degrades the amylose column, limiting its reuse.

Sulfoquinovose (SQ) undergoes catabolism through the pathways of sulfoglycolysis. Our laboratory has discovered a sulfoglycolytic SQ monooxygenase pathway that contains an SQ binding protein (SQBP).[1] SQBP performs an analogous function to MBP. In this project we are exploring the use of SQBP as an alternative to MBP as a fusion partner for the affinity purification of recombinant proteins. This requires the synthesis of an SQ-modified agarose chromatographic support, with elution by SQ or other alkylsulfonates. Here we report the successful synthesis of an ethylene glycol-based SQ linker in our laboratory.



ethylene-glycol ether based SQ linker



SQ-affinity chromatography

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T-100

Gold catalysed counteranion directed chemoselective asymmetric synthesis of pyrroles and 1,8-dihydroindeno[2,1-b]pyrroles

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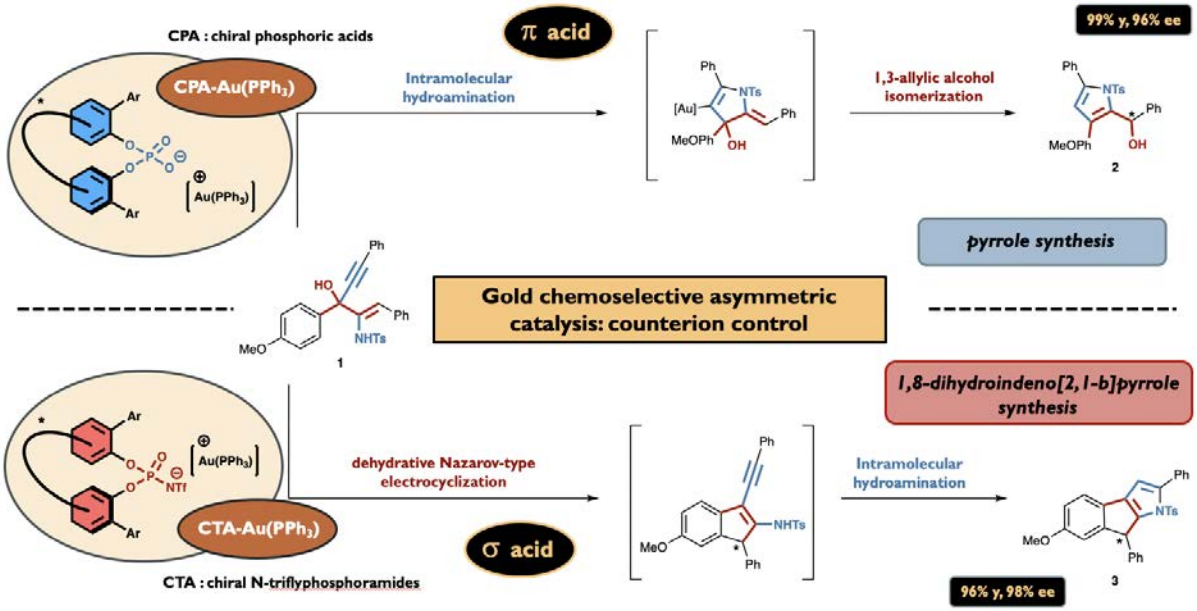
Pyrroles and indanes are present in a myriad of natural and synthetic compounds of interest ranging from naturally occurring porphyrins and alkaloids, to synthetic pharmaceuticals or polyaromatic frameworks investigated in material science and supramolecular chemistry.[1,2] Although the non-asymmetric synthesis of structures containing either motif is arguably one of the first milestones in the field of organic chemistry, the many currently reported enantioselective synthetic procedures still only partially meet the demand for reliable methods to construct optically pure pyrroles and indenyl containing structures. Here, we present a convenient gold(I)-catalysed methodology to convert propargyl alcohols of the type **1** to either pyrroles **2** or condensed indanes **3** while also uncovering a ground-breaking counteranion operated tuning of catalytical reactivity. In the presence of a chiral phosphoric acid counteranion we found compound **1** can be selectively converted into pyrrole **2** in quantitative yields and up to 96% ee, on the other hand, the use of a chiral triflimide counterion was found to give 1,8-dihydroindeno[2,1-b]pyrroles **3** in up to 96% yield and 98% ee.



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T-101

Glycine Receptor Modulators for Chronic Pain Therapeutics

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Chronic pain has deprived almost one in five individuals worldwide of their physical, social, and mental wellbeing, resulting in the inevitable abolishment of ones quality of life.[1] Current therapeutic interventions aren't ideal as they often mask the underlying issues or even manifest a host of undesirable side effects. [2,3]
The aim of this project is to explore the key chemotypes required for optimal glycinergic activity. 4-fluorobenzene sulfonamide (**Figure 1**) as the lead and the best substituents from the compounds identified by AMGEN will be utilised to create a library of hybrid molecules.[4] Three key pharmacophores will be studied in-depth to extensively investigate the interactions of each group required for the ideal modulation of activity. The preliminary *in vitro* studies completed on a functional glycine receptor with sulfonamides containing 4-fluorobenzene, benzoxazolone, and benzofuran positively modulated activity over 200%. These results indicate potential progression towards further understanding the binding requirements of the target site. In turn, it will elucidate our understanding of the ideal properties required for optimal glycinergic activity.

Figure 1: The lead compound to the proposed breakdown of the three key structural components utilising studies completed by Pfizer and AMGEN.

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T-102

A synthetic tigliane skeleton: structure activity relationship investigation using cancer cell lines

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Phorbol (**1**), a tigliane diterpene, was first isolated from *Croton tiglium* in 1935 but its structure took over three decades to elucidate. Due to their binding and activation ability to the isozymes of the protein kinase C (PKC) family, the phorbol esters have high potency as tumour promoters.[1] While in pursuit of synthesizing stereoisomers of phorbol esters utilising rhodium-catalysed [4+3] cycloaddition methodology,[2] the intermediates and a number of the inverted D-ring tiglianes were evaluated against a range of cancer cell lines. Although the natural phorbol, TPA (**2**), was the most potent in the MCF7 cancer cell line, the non-natural tiglianes (**3** and **4**) surpassed the activity of TPA in two other cancer cell lines. The results suggested the mode of action could possibly not involve the activation of PKC, but rather thiol addition based on NF-kB reporter activity.[3]

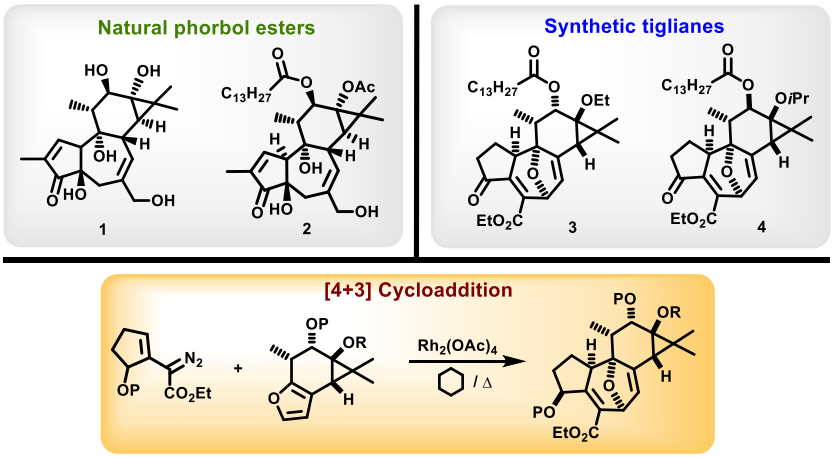

Figure 1. Natural tiglianes and non-natural synthetic skeletons.

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T-103

Synthesis of cholesterol-derived drug hybrids for treatment of *M. tuberculosis*

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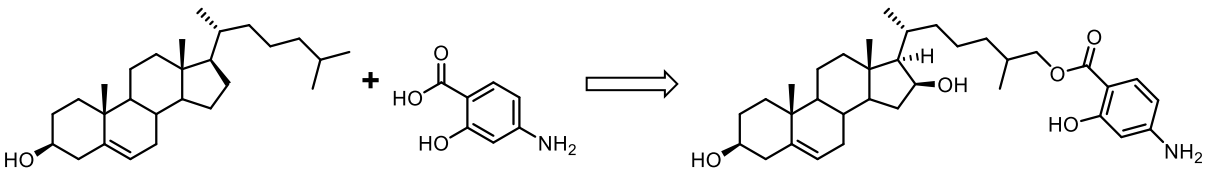
Tuberculosis is a communicable disease spread by the bacillus *Mycobacterium tuberculosis (Mtb).* Cholesterol is not synthesised in *Mtb* but its incorporation is important for the infection and virulence of the pathogen. 16,26-dihydroxycholesterol inhibits the growth of *Mtb* by preventing degradation of the sterol side chain by the organism by Cytochrome P450 enzymes.

A significant contributor to the antibiotic resistant nature, and perhaps the defining characteristic feature of *Mtb* is the uniquely waxy cell wall structure. This coating presents a significant challenge in the quest for new drugs with a robust approach to development and mechanism of action. Cholesterol-drug conjugates attempt to overcome these challenges by utilising the cholesterol import systems present naturally to activate drugs previously rendered ineffective by the formidable cell wall. A hybrid co-drug design may furthermore function as a means to circumvent rampant drug resistance.

This poster describes the synthesis of C-26 substituted cholesterols that contain a C-16 hydroxy group. A range of drug-like moieties were installed in the steroidal side chain to explore the inhibitory effects of functionalities at this position. Furthermore, novel methodology was developed to prepare co-drugs of 16-hydroxycholesterol and fragments with proven anti-tubercular activity. Compounds went on to be tested in a resazurin reduction microplate assay with wild type *Mtb* (H37Rv) in a SAR study to generate improved drug candidates in an iterative process.



Cholesterol scaffold | Drug conjugate | Improved anti-tubercular agent?

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T-104

Structure and Synthesis of Atropisomeric N-heterocycles

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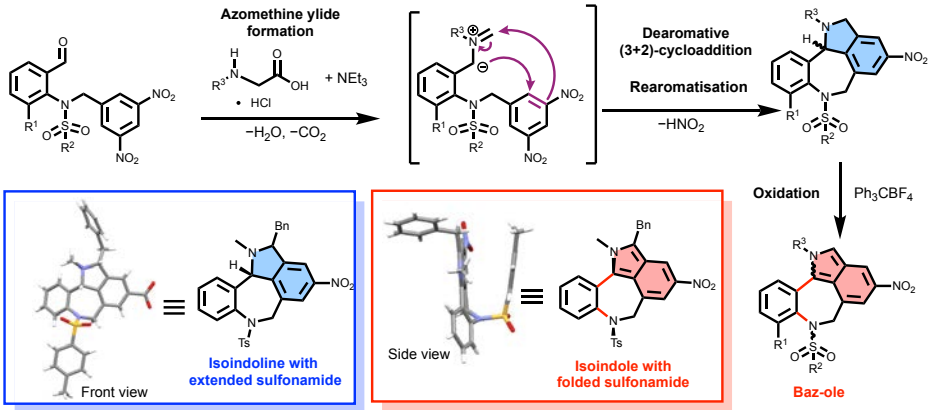
Atropisomeric heterocycles are an important but underrepresented class of pharmaceutically relevant chiral molecules. A dynamic chirality, atropisomerism arises from restricted rotation around the axis of at least one bond, with the rate of rotation mediated by the relative contribution of steric, electronic, and bonding forces to the Gibbs free energy of the transition state. With these relative contributions differing between systems, the scarcity of atropisomeric pharmaceuticals stems partly from the difficulty of predicting the chiral stability of atropisomers. By developing a greater understanding of the patterns of energetic contribution that structural and environmental components have on different types of atropisomeric systems, it becomes possible to tune the dynamic chirality of atropisomers to suit the needs of the researcher.[1] This work utilises a combination of synthetic and computational means to investigate and exploit the atropisomerism of a novel benzazepine-fused isoindole skeleton, dubbed 'Baz-ole', which was developed by the Hyland group (Scheme 1).[2] The synthesis involves a dearomative (3+2) cycloaddition between an azomethine ylide and pendant dinitrobenzyl group, followed by rearomatization, with the resulting isoindoline then oxidized to an isoindole. This oxidation induces a conformational change whereby folding of the sulfonamide group over the main structure of the system impedes inversion of the 7-membered ring, rendering the system atropisomeric. This poster will detail the synthesis of Baz-ole, the defining parameters of atropisomeric stability, and an exploration of how the chiral conformation can be exploited to direct facially selective Diels–Alder cycloadditions.

Scheme 1: Overview of Baz-ole synthesis with X-ray crystal structures illustrating the conformational difference between the isoindoline and isoindole skeletons.



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T-105

Studies towards a biomimetic synthesis of (±)-atrachinenins A-C.

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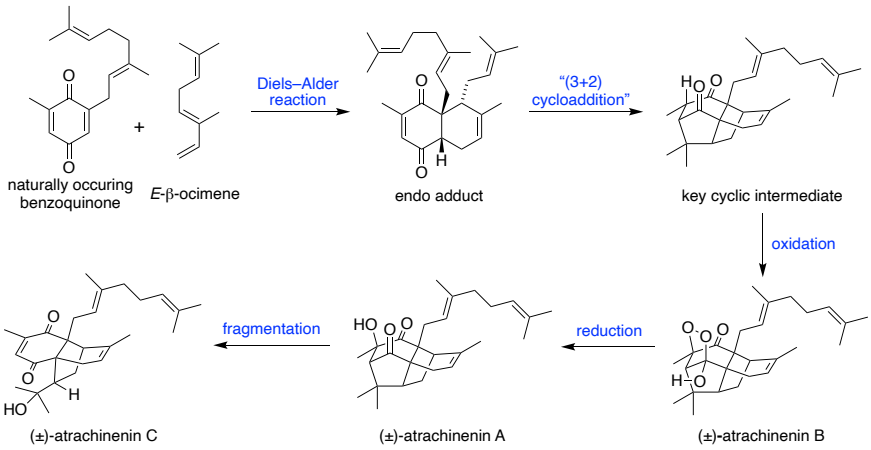
Stereochemically complex atrachinenins A-C (**1**-**3**) were recently isolated as racemates from the rhizomes of *Atractylodes chinensis*.[1] The rhizomes have been well described for their use in traditional medicinal practices, treating a variety of diseases, leading to an interest in the isolation of their natural products. Unlike the previously reported natural products, the atrachinenin meroterpenoids all feature a uniquely dense, cage-like framework, making them an intriguing synthetic target. Atrachinenin A exhibits a 6/6/5/5 fused system with a hemiperoxyketal bridge, which under reducing conditions could provide atrachinenin B. With a biosynthetic approach we envision the synthesis of these molecules could be achieved through an endo Diels-Alder cycloaddition between an unsymmetrical naturally occurring benzoquinone and *E*-β-ocimene. The endo adduct could then undergo an unusual intramolecular (3+2) cycloaddition followed by aerobic oxidation and intramolecular cyclisation to provide atrachinenin B. Finally, reduction of the endoperoxide to atrachinenin A and fragmentation to atrachinenin C, allows a concise synthesis of the natural product family. Initial experiments on a model system indicate that our proposed biomimetic cascade is viable and efforts are being made to complete the synthesis.



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T-106

Electronic and optical properties of [3]radialenes and related molecules

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[3]Radialene is the smallest omni-conjugated[1] molecule – so-called because all of its exocyclic substituents are linearly conjugated to one another, allowing for electronic communication along three different pathways. [3]Radialenes can be used as three-way conjugated linkers to build topologically interesting circuits. They have been employed in metallosupramolecular coordination chemistry[2] and in molecular electronics, and they feature heavily in patent literature as organic superconductors for OLED[3] devices. Despite these exciting advances, the fundamental nature of electron delocalization across the [3]radialene core is not well understood. This research explores the electronic and photophysical properties of [3]radialene and π-extended analogues, including triquino[3]radialenes,[4,5] which exhibit strong transitions in the visible part of the spectrum owing to their extreme conjugation (Figure 1).

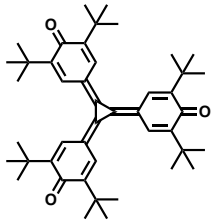

Figure 1: UV-visible absorption spectrum of triquino[3]radialene

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T-107

C(sp²) –H methylation of N-heterocycles using Corey-Chaycovsky reagents

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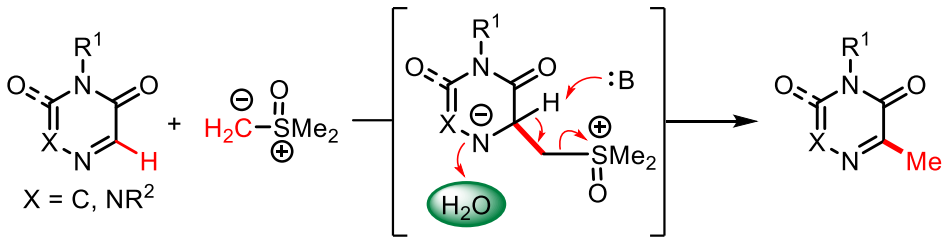
Methylation is one of the vital process in biological systems because DNA and histone methylation is responsible for gene expression without affecting the gene sequence. The direct methylation of *N*-heterocycles is an important transformation for the advancement of pharmaceuticals, agrochemicals, functional materials, and other chemical entities. Trimethylsulfoxonium salt that known as the Corey-Chaykovsky Reagent is a valuable precursor to sulfoxonium ylide and has been used to form cyclopropanation, aziridination or epoxidation reaction. Herein, we describe the direct C(sp²)–H methylation of iminoamido heterocycles as nucleoside base analogues with trimethyl sulfoxonium salts. Notably, Corey-Chaycovsky reagents were employed as alkylating agents in aqueous solution. A range of substrate scope and excellent level of functional group tolerance were attained. Moreover, this method can be readily applied to the C–H methylation of azauracil nucleosides. The gram-scale experiments and various synthetic transformations of the products highlight the synthetic importance of the developed method. Combined deuterium-labeling experiments aided the elucidation of a plausible reaction mechanism.



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T-108

Minisci-type Alkylation Mediated by EDA Complex and Blue LED Light

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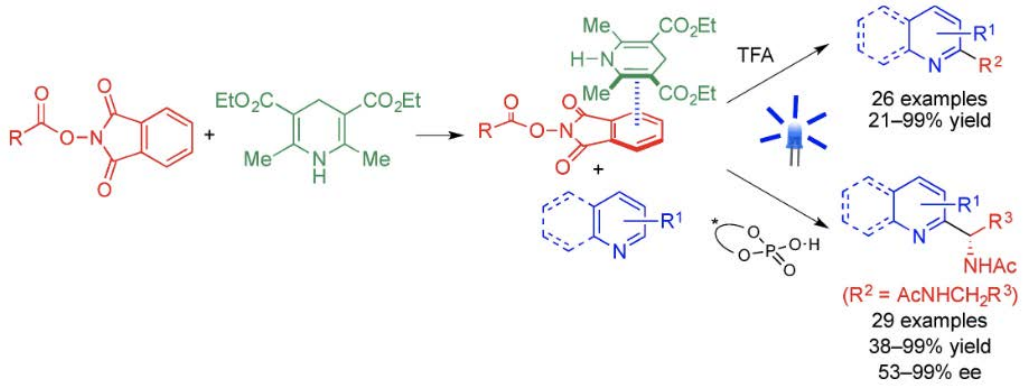
A synthetic method that enables the Hantzsch ester-mediated Minisci-type C2-alkylation of quinolines, isoquinolines and pyridines by *N*-(acyloxy)phthalimide esters (NHPI) under blue LED (light emitting diode) light (456 nm) is described. Achieved under mild reaction conditions at room temperature, the metal-free synthetic protocol was shown to be applicable to primary, secondary and tertiary NHPIs to give the alkylated *N*-heterocyclic products in yields of 27–99%. On introducing a chiral phosphoric acid, an asymmetric version of the reaction was also realised and provided product enantiomeric excess (ee) values of 53–99%. The reaction mechanism was delineated to involve excitation of an electron-donor acceptor (EDA) complex, formed from weak electrostatic interactions between the Hantzsch ester and NHPI, that generates the posited radical species of the redox active ester that undergoes addition to the *N*-heterocycle.



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T-109

Isolation and chemistry of diterpenes from *Dodonaea* species

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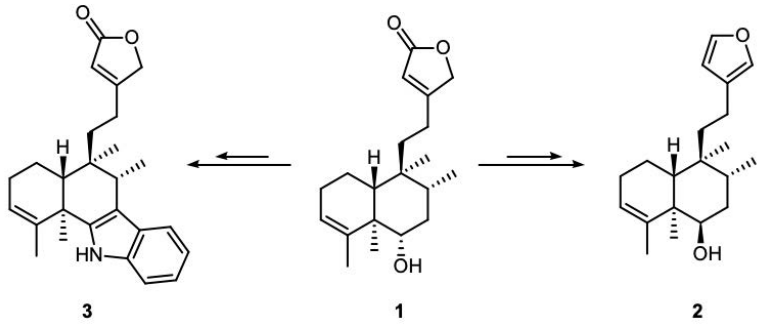
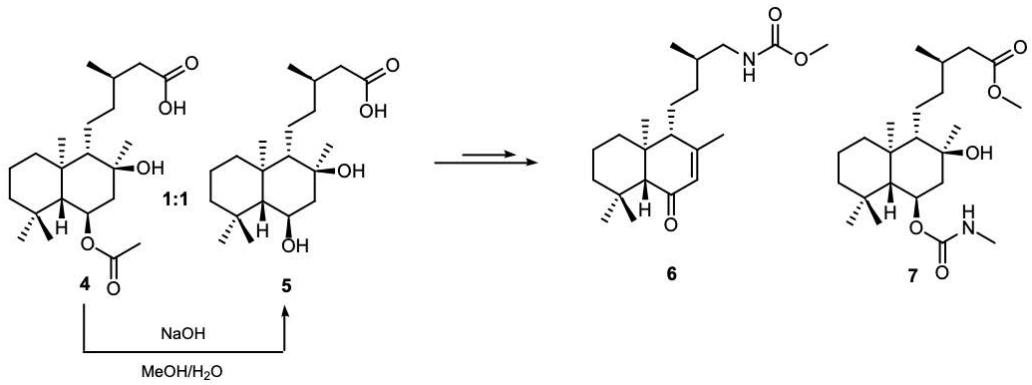
Using abundant natural products as starting materials provides viable access to otherwise inaccessible compounds. The work presented explores the chemistry of functionalised scaffolds from abundant sources of *Dodonaea* species increasing their 'drug-likeness'. The *Dodonaea* genus is a predominantly native genus to Australia and is an abundant source of complex diterpenes. Its leaves have a resinous exterior, which is reported to contain bicyclic diterpenes, in amounts of 4 – 6% (w/w) of dry plant.[1] Two *Dodonaea* species were investigated, *D. ceratocarpa* and *D. larreoides*. The clerodane **1** was isolated from *D. ceratocarpa* in 0.5% yield (w/w)[2] and has an interesting scaffold allowing transformations to the furan **2** and indole **3**.



D. larreoides afforded the labdanes, **4** and **5**, in a 1:1 mixture in 10% w/w of plant. Following hydrolysis of the acetate **4**, the diol acid **5** provides a diverse scaffold for chemical modifications to carbamates **6** and **7**. The chemistry employed focusses on enhancing the medicinal profile of synthesised compounds.



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T-110

Rhodium Catalysed Cycloisomerisation/6π Electrocyclisation of 5-(Ethynylamino)pent-2-yn-1-yl Esters to Partially Hydrogenated benzo[*f*]indoles

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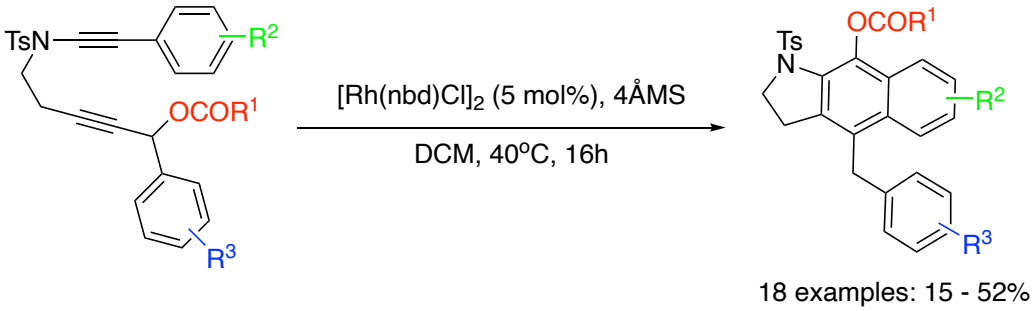
Rhodium-catalysed cycloisomerisations of propargylic esters is a very powerful and efficient strategy to construct molecular complexity from easily accessible starting materials. The reactions begin with coordination of the rhodium catalyst to the triple bond of the propargyl ester, consequently activating the ester group and resulting in a [2,3]- or [3,3]-sigmatropic rearrangement. A tethered functional group or a second substrate gives further reaction of the organorhodium species.[1] Diynes are another commonly used substrate in rhodium catalysis due to their relative predictability of the reaction, which typically sees the rhodium to the two triple bonds to trigger an oxidative cycloaddition to form a rhodacyclopentadiene intermediate.[2] Herein we present the synthesis of 2,3-dihydrobenzo[*f*]indole derivatives that proceed through a rhodium-catalysed cycloisomerisation/6π electrocyclisation of 5-(ethynylamino)pent-2-yn-1-yl esters. Our studies suggest that the reaction mechanism involves the formation of a rhodacyclopentadiene intermediate followed by de-esterification to generate a rhodium carbenoid species. Re-esterification at the carbenoid carbon centre of the organorhodium complex triggers a reductive elimination of the rhodium, forming an allene-ene which undergoes 6p electrocyclisation to give the 2,3-dihydrobenzo[*f*]indole product.



18 examples: 15 - 52%

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T-111

Ring Opening Reactions of Aziridines for Multi-Functionalised Products

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Aziridines have been of interest in organic synthesis, natural product chemistry, and medicinal chemistry because of their unusual structure and high reactivity.[1] The reactivity of the strained ring allows for potent biological activity, the aziridine being the key functional group for Mitomycins to exhibit anti-tumour and antibiotic activity.[2,3] Aziridine ring opening has been shown to readily occur under acidic conditions and is influenced by the *C*- and *N*- substituents on the aziridine ring.[4,5] For this reason, aziridines can undergo stereoselective ring opening reactions, making the functional group of great value in organic synthesis.

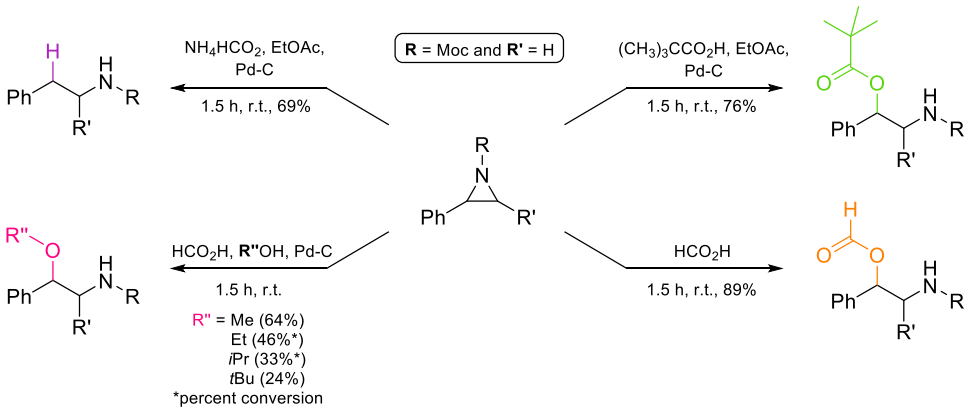

Figure 1. *Multi-functionalised products synthesised by acid-mediated ring-opening of aziridines.*

In this project, when the aziridine was subject to transfer hydrogenation conditions, using formic acid as a hydrogen donor, competing nucleophilic reactions initially dominated over hydrogenation reactions. Nevertheless, careful selection of reagents and conditions allows control over the outcome of the reaction and a range of interesting multi-functionalised products to be accessed (Figure 1).

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T-112

Annulative cyclization between *N*-arylindazolols and maleimides under rhodium(III) catalysis: Synthesis of spirosuccinimides

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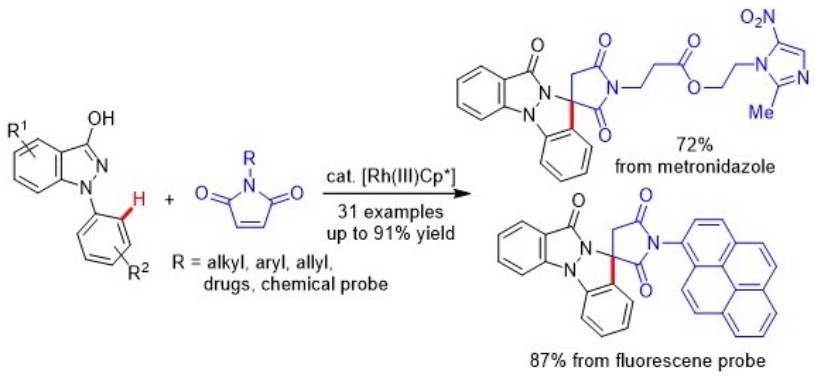
A Succinimide derivatives have attracted great attention due to their diverse biological activities such as anticonvulsant, anti-inflammatory, antitumor, and antimicrobial. Particularly, spirosuccinimides have been realized as valuable scaffolds in medicinal chemistry and drug discovery. Thus, the ability to synthesize substituted (spiro)succinimides is of importance from the perspective of furthering medicines, materials, and other chemical entities. To address these issues, maleimides have been recently utilized as synthetic precursor of (spiro)succinimides in the transition-metal-catalyzed C–H functionalization.
An indazole scaffold has emerged as a valuable framework of a number of fused and functionalized derivatives with interesting biological activities. With great progress on the transition-metal-catalyzed C–H functionalization, N-aryl indazol-3-ols as structural tautomers of N-aryl indazol-3-ones have been recently utilized for the construction of fused indazolones via C–C/C–N bond forming strategies. Driven by our ongoing interest in the catalytic C−H functionalization and annulative cyclization, we herein describe the rhodium(III)-catalyzed spiroannulation reaction between N-aryl indazol-3-ols and maleimides for the formation of a range of spirosuccinimide-containing N-aryl indazolones. This transformation is characterized by the scale-up compatibility, mild reaction conditions, and excellent functional group tolerance. The developed method is showcased by the construction of spirosuccinimides using bioactive molecule-linked and chemical probe-linked maleimides.[1]



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T-113

Synthesis of novel reversible, redox-responsive cyanine nitroxide-containing dyes.

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Mitochondria are very important organelles that display a broad range of cellular processes; however, their chemical biology remains limited[1]. Over the last decade, significant discoveries around mitochondrial function have been made through advancements in optical instruments and fluorescent-based detectors, permitting observation at high temporal and spatial resolutions. While several well-established dyes have been utilised, current approaches in fluorescence-based mitochondrial imaging studies encounter a significant issue: once the response is activated, it cannot be reversed to respond to subsequent changes occurring over time and thus does not provide real-time responses[2].

Nitroxides are remarkably stable, they are kinetically persistent free radicals that have been widely applied in biomedical treatments and diagnostics thanks to their radical scavenging ability[3]. By introducing a nitroxide into established dyes, their redox activity can be exploited to provide controlled reversibility to the fluorescent response.

This poster will provide some early outcomes of the synthesis of key aryl nitroxide benzoxazole and *3H*-indole intermediates for incorporation into commercially available cyanine dyes.

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T-114

Optimisation and target identification of a novel class of trypanosomacides

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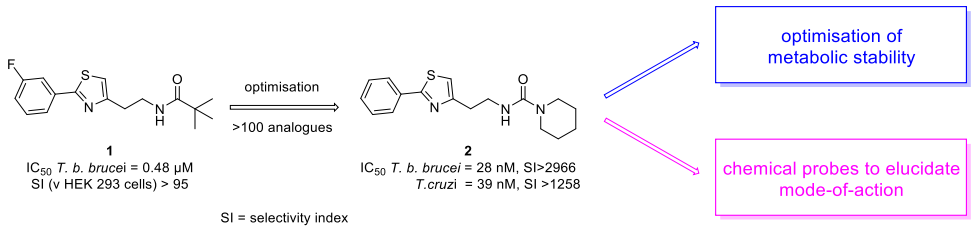
Trypanosomes are protist parasites that cause neglected diseases affecting millions of people, and considerable morbidity and mortality in the developing world. African sleeping sickness (human African trypanosomiasis, HAT) is caused by *Trypanosoma brucei* and *T. cruzi* is responsible for Chagas disease (American trypanosomiasis). The World Health Organization (WHO) has revealed that less than 1.1% of worldwide medical research and development funding has been dedicated to Neglected Tropical Diseases NTDs.[1]

While vector control programs have dramatically decreased the incidence and burden of HAT, Chagas disease is still of serious concern. Chagas is endemic in 21 Latin American countries and has become a global health problem due to migration of infected people to non-endemic areas.[2] There are 6–7 million active infections and more than 25 million people are at risk of the disease.[3] Nifurtimox and benznidazole are the only drugs available for the treatment of Chagas disease, and neither is effective against chronic infection, which can be lethal. Serious side-effects and growing resistance point to an urgent need to investigate and develop new therapeutic alternatives.[4]

Previous research in the Piggott group on the optimisation of high-throughput screening hit **1** resulted in the discovery of lead urea **2**, which has potent cidal activity against *T. cruzi* and *T. brucei*, while being comparatively non-toxic to mammalian cells.[5-7] An analogue of **2** cleared mice of *T. cruzi* infection, but only when xenobiotic metabolism was inhibited.



The overarching aims of this project are to continue lead optimisation providing compounds with greater metabolic stability, while maintaining selective potency. In addition, photoaffinity probes will be designed and synthesised, then used to reveal the protein target of this class of trypanosomacides.

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T-115

Catechol and crown ether 1,8-naphthalimide fluorescent probes

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Several fluorescent probes containing the versatile 4-hydroxy-1,8-naphthalimide scaffold have been developed in the past two decades, including those used as intracellular imaging agents[1], enzyme activity reporters[2], and sensors for the detection of ions[3], metals[4], and reactive oxygen species[5]. We recently reported a robust method for the synthesis of 3,4- disubstituted 1,8-naphthalimides containing hydroxy- and alkoxy- substituents[6].

Following on from this work, a methodology for the synthesis of a 3,4-dihydroxy- "catechol" 1,8-naphthalimide (1) has been established. Using this key compound, a "crown ether" substituted 1,8-naphthalimide (2) was successfully synthesised, and preliminary photophysical studies conducted.

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T-116

Characterizing the structure, bioactivity and bioavailability of active compounds from *Cymbopogon procerus*

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Herbal and natural medicines have long been a critical part of medical practice. Medicinal plants are a rich source of bioactive phytochemicals. *Cymbopogon procerus* (native lemon grass) is a native Australian species belonging to the family Poaceae. The essential oils of the plant consist of phenylpropanoids and volatile aromatic terpenes. Phenolic compounds, considered to be natural antioxidants and representing an important group of bioactive compounds, are also present in the plant.[1] In our project, we investigate the phytochemistry of *C. procerus* via extraction of plant material, fractionation of crude extract through Solid Phase Extraction (SPE) and purification of compounds using Reverse Phase High Performance Liquid Chromatography (RP-HPLC). Compounds are then identified using analytical techniques including one and two-dimensional nuclear magnetic resonance (NMR) and Liquid Chromatography Mass Spectrometry (LCMS). To date we have isolated a series of 17 phenylpropanoids compounds, terpenes and cis-3-hexenyl-β-D-xylose. The methanolic extract of stem and grass parts of this plants displayed highest antimicrobial activity against *Burkholderia humptydooensis* and *Staphylococcus aureus*.

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T-117

Mechanistic Insights into the Glycosylations of L-Idose Thioglycosides

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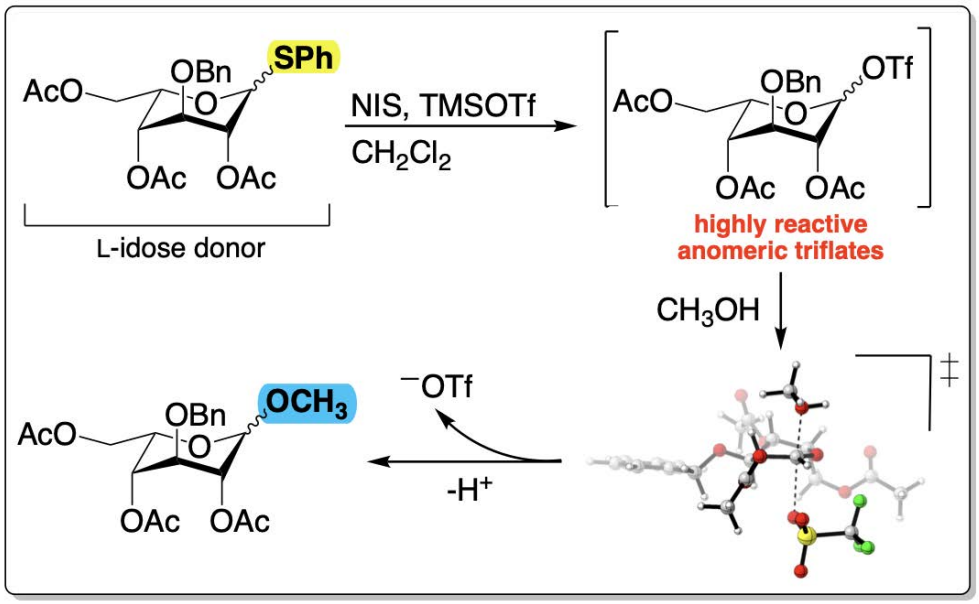
To construct a glycosidic bond with high stereoselectivity, both careful design of the donor substrate (the glycosyl donor) and consideration of the influence of all reaction conditions (alcohol acceptor, promotor, solvent, temperature) are necessary. For glycosylations of D-hexoses, installing a participating (acyl) group at C-2 is a widely adopted strategy which typically results in the exclusive formation of the 1,2-*trans* glycoside. However, for the analogous reactions of L-hexose donors, incomplete stereoselectivity is often achieved with simple acceptors – even in the presence of a C-2 participating group.[1] Given the profound biological and medicinal significance of L-idose glycosides[2] and encouraged by recent advances in the modelling of glycosylation reactions,[3] we sought to explain this unusual phenomenon with density functional theory (DFT) calculations. In what represents the first complete DFT study of an L-sugar glycosylation, the relationships between highly reactive intermediates along multiple reaction pathways are probed to unveil a valuable set of mechanistic insights.



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T-118

Towards Azabioisostere Design – seco-azahomocubanes

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Recent investigations into the potential and efficacy of the bioisosteric replacement of aromatic rings with hydrocarbon cages have been carried out to provide novel and more efficient structures for drug development and optimization.[1] For example, cubane has been validated by the Williams group as a benzene bioisostere in some drug and agrochemical templates.[2,3] Tertiary nitrogen-containing caged hydrocarbons are less common,[4] but have potential to act as heterocyclic isosteres in a similar way to that of cubane or bicyclo[1.1.1]pentane for benzene.

A range of *N*-substituted 2-azetines have been explored to further develop an understanding of the nature of this highly reactive system. Efforts in the deployment of azetines towards seco-azahomocubanes will be presented.

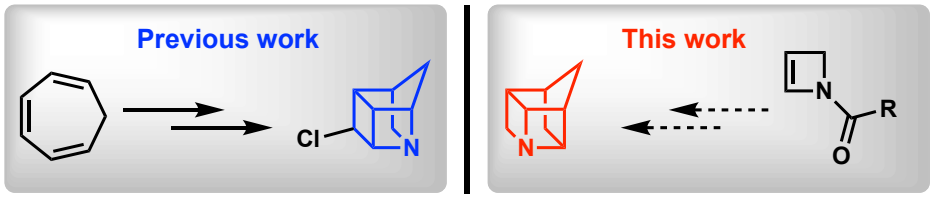

Figure 1. Previous and current work on strained aza-polycyclic systems.

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T-119

Towards the total synthesis of alpkinidine

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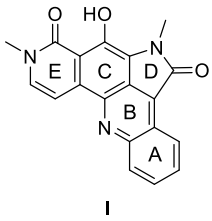
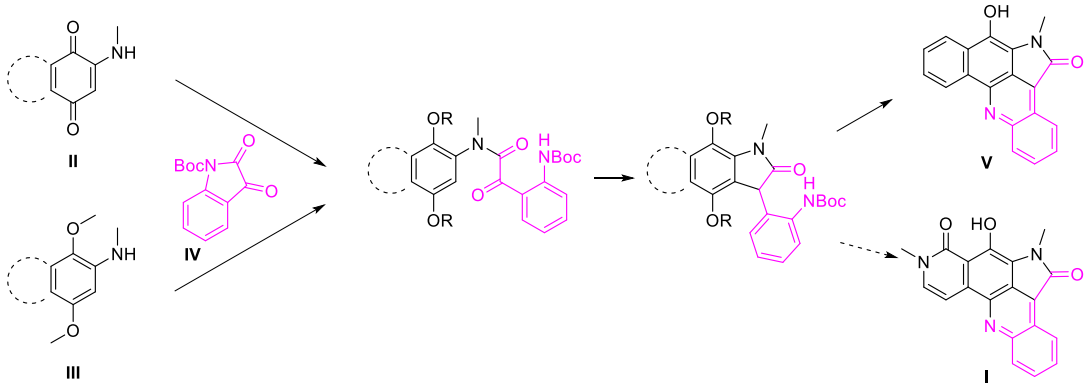
Alpkinidine (1) is a marine alkaloid from the sponge *Xestospongia carbonaria* (Figure 1).[1] The unique, highly condensed structure of this bisannulated pyrroloacridine, and its cytotoxicity, have attracted several synthetic efforts, but so far without success.[2-4] Synthesis is essential for comprehensive characterisation of both the structure and biological activity of the natural product.



I

Figure 1. Marine sponge *Xestospongia carbonaria* and its metabolite alpkinidine (I).[5]

This poster will report on the reactivity of methylamino-quinones II and -anilines III with N-Boc-isatin IV to rapidly assemble the B and D rings of alpkinidine (I) and related model compounds (e.g. VII).



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T-120

Rh(I)-Catalyzed Denitrogenative Transformations of 4-Vinyl-1,2,3-thiadiazoles

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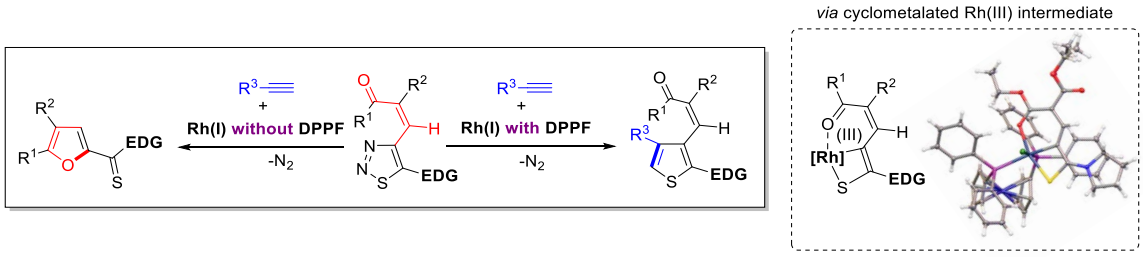
One of the most synthetically attractive routes to preparing a variety of heterocycles from a common intermediate is the inter- and intramolecular reaction of metal carbenes, which are traditionally prepared by denitrogenative decomposition of diazo compounds. In contrast to the *α*-diazo-carbonyl compounds and 1,2,3-triazoles widely used as precursors to metal carbenes, the synthetic potential of 1,2,3-thiadiazoles is relatively unexplored. Recently reported Rh(I)-catalyzed denitrogenative transformations of 1,2,3-thiadiazole derivatives demonstrated that they are useful precursors in the synthesis of sulphur-containing heterocycles.[1-3] To further explore the potential of 1,2,3-thiadiazoles in heterocycle synthesis, here we report new ligand-controlled Rh(I)-catalyzed denitrogenative transformations of 4-vinyl-1,2,3-thiadiazoles[4] into substituted furans and thiophenes. Experimental and computational mechanistic studies were performed to gain insight into the Rh(I)-catalyzed intramolecular transannulation of vinylic 1,2,3-thiadiazoles, with a focus on understanding the influence of the C5-substituent on reactivity and the role of the phosphine ligand. In addition, the true structure of the organorhodium intermediate involved in Rh(I)-catalyzed denitrogenative reactions of 1,2,3-thiadiazoles was revealed.[5]



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T-121

An efficient protocol for the synthesis of glycosyl fluorides

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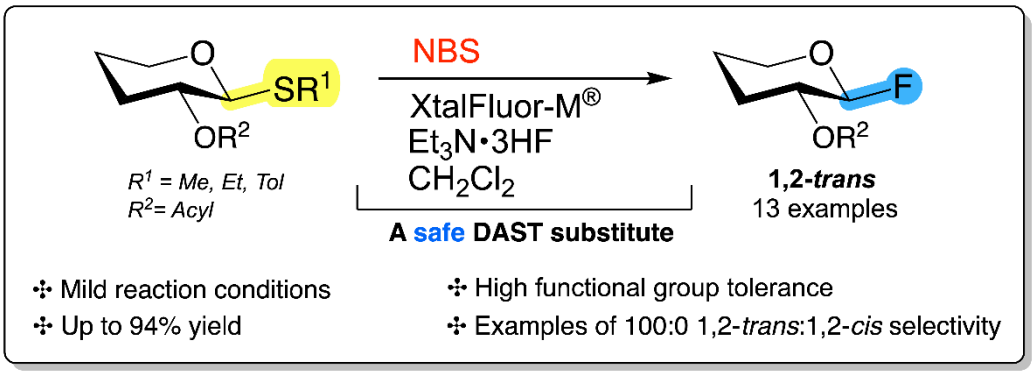
Glycosyl fluorides carry high utility as glycosyl donors, enzyme inhibitors and synthons for the construction of rare L-hexoses. However, the reagents currently available to prepare them are toxic, promote unwanted side reactions and can effect poor 1,2-*trans* stereoselectivity; these drawbacks are particularly pertinent to fluorinations with diethylaminosulfur trifluoride (DAST). Desiring a safer and more efficient avenue for the conversion of readily available thioglycosides to 1,2-*trans* glycosyl fluorides, we explored the efficacy of XtalFluor salts as alternatives to DAST. We reveal that a combination of XtalFluor-M®, *N*-bromosuccinimide (NBS) and $Et_3N{\cdot}3HF$ can mediate facile, high-yielding and stereoselective syntheses of 1,2-*trans* glycosyl fluorides. Optimisation and mechanistic studies suggest that a highly reactive XtalFluor-M®-bromide adduct plays an instrumental role in the fluorination process, and scoping studies show that routinely exploited protecting groups, including those which are acid-labile, are tolerant of the reaction conditions.



T-122

Chiral Gold Catalysed Cycloisomerisation/Regio- and Enantioselective Nitroso-Diels Alder Reaction

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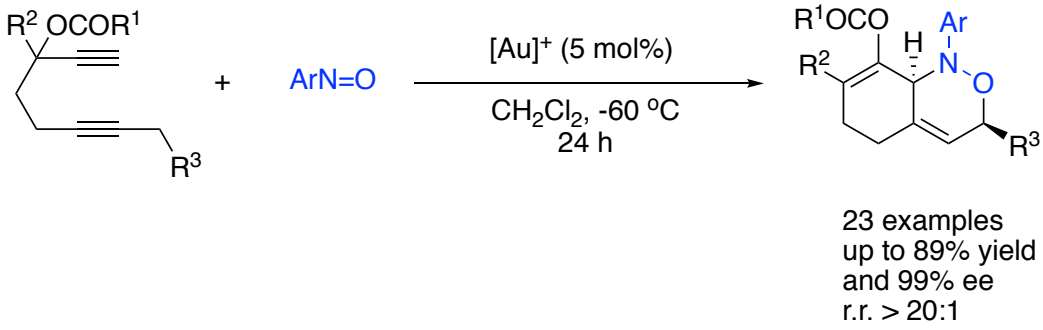
The nitroso-Diels Alder (NDA) reaction of 1,3-dienes with nitroso compounds is among one of the most powerful and efficient methods for the synthesis of 3,6-dihydro-1,2-oxazine derivatives.[1] Here we described an efficient chiral gold(I)-catalysed synthetic method that enables the cycloisomerisation/regio- and enantioselective nitroso-Diels Alder reaction of 1,6-diyne esters with nitrosobenzenes. The sequential ring formation protocol offers access to a wide variety of 3,5,6,8a-tetrahydro-1*H*-benzo[*c*][1,2]oxazines as a single regioisomer in yields up to 99% and enantiomeric excess values of up to 99%. This contrasts with the analogous NDA reactions of cycloisomerised 1,6-diyne esters with nitrosoarenes in the absence of the chiral gold(I) catalytic system, which gave the *N*,*O*-heterocyclic product with the opposite regiochemistry. Experimental and computational studies based on a postulated chiral dinuclear gold species containing two coordinated nitrosoarene molecules that undergoes an asynchronous concerted NDA reaction with the cycloisomerised 1,6-diyne ester provides insight into the observed product regio- and enantioselectivities.



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T-123

Small Molecule Probes for Visualising Aβ42 Monomer Sequestration by Macrocycle Conjugates

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Alzheimer's disease presents a growing problem worldwide due to the economic and social burden it imposes. Amyloid beta (Aβ) peptides are fragments of varying lengths derived from the amyloid precursor protein. The aggregation of the 42-residue fragment (Aβ42) into fibrils or oligomers has been implicated in the progression of Alzheimer's disease. Inhibiting this aggregation remains an important target in the search for effective treatments of the disease.[1]

The aggregation of Aβ42 follows a pathway that is analogous to crystal growth, comprising of an initial primary nucleation phase which generates seeds followed by elongation of the fibrils, or secondary nucleation to generate new seeds.[2] Previously reported aggregation inhibitors function by preventing primary or secondary nucleation processes, but are not able to suppress aggregation in the presence of seeds.[3]

We have synthesised a series of perphenazine-cyclam conjugates that redirect Aβ to form non-toxic aggregates, reduce amyloid formation and ameliorate the associated toxicity in neuronal cells. Kinetic studies demonstrate that these conjugates interact specifically with monomeric Aβ peptide and sequester it, suppressing the growth of fibrils and intermediate oligomers even in the presence of seeds.[4] This is an unusual and promising mode of small molecule interaction with Aβ which we are exploring further.

In order to elucidate the mechanism behind this behaviour, a series of protein NMR experiments utilising paramagnetic relaxation enhancement (PRE) have been devised. These experiments require modified probes, derived from cyclen and chelated with a series of lanthanide ions. The synthesis of these probes will be described. The results of these experiments can direct further research into the development of more potent inhibitors and resolve discrepancies in our understanding of the role that Aβ plays in the progression of Alzheimer's disease.

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T-124

Ratiometric Fluorescent Nanoprobe for ROS Detection Using Coumarin-3-Carboxylic Acid as a Detector

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Reactive oxygen species (ROS) are widely investigated for their features as they are highly reactive with biological materials, such as proteins, DNA, and RNA allowing them to produce oxidative stress (1). Hydroxyl radicals, one form of ROS, involve in some modifications that may cause clinical diseases, such as Alzheimer's disease, cancer, and cardiovascular diseases. Since the quantification of hydroxyl radicals has been the aim of researchers to develop nanoprobes combined with a delivery system that has a potential for treatment, yet there are some challenges affect designing nanoparticles with high selectivity and sensitivity toward hydroxyl radicals (2).

In this study, a ratiometric fluorescent nanoprobe was designed and prepared to detect hydroxyl radical by using coumarin 3-carboxylic acid (CCA) as the main detector and sulforhodamine B (SRB) loaded layered double hydroxide (LDH) as a fluorescent reference component. The coupling of CCA to bovine serum albumin (BSA) and the loading of BSA-CCA on the surface of LDH allowed the nanoprobe for ratiometric fluorescence detection of hydroxyl radical with high sensitivity and minimal interference from other biomolecules, ions, and ROS. As shown in Figure 1A, the prepared BSA-CCA@SRB-LDH exhibited intense emission at 580 nm. In the presence of increased concentration of hydroxyl radical, a new emission peak at 444 nm was emerged and the intensity was increased according to the concentrations of hydroxyl radical, while the emission at 580 nm was maintained, allowing the nanoprobe for ratiometric fluorescence (*I444/580 nm*) detection of hydroxyl radical. Moreover, as the loading of the BSA protein on LDH surface, the biocompatibility and colloidal stability of fluorescent LDH nanoprobe were further improved, allowing the future biological investigations of hydroxyl radical's evolution in vitro and in vivo.

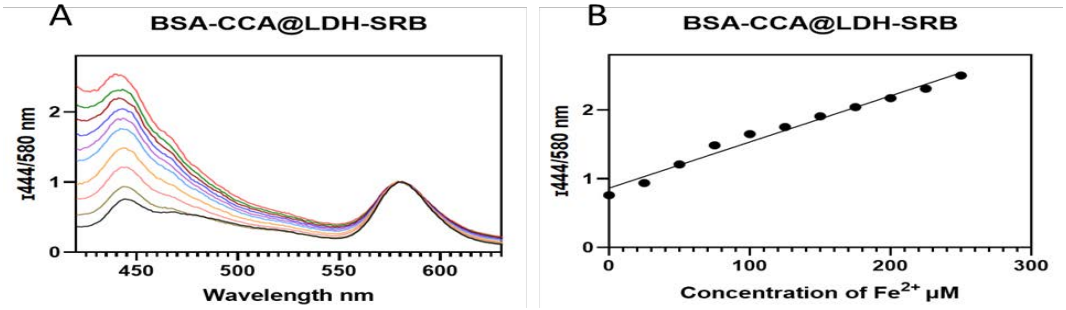

Figure 1: The fluorescence intensity of the ratiometric probe BSA-CCA@LDH-SRB. A: emission wavelength of BSA-CCA@LDH-SRB, B: I444/580 nm ratio of BSA-CCA@LDH-SRB.

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T-125

Synthesis and Characterization of Fluorescent Mn:ZnS/BSA Nanoparticles for Biosensing and Bioimaging Applications

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Fluorescent biosensing and imaging are contributing significantly in biomedical and clinical research (1). The development of fluorescent materials that can respond to the variations of various biomolecules and ions plays key roles in fluorescence biosensing and imaging, promoting better understanding the roles of these target analytes in biological processes (2). In contrast to other sensing and imaging technology, fluorescent biosensing and bioimaging have been one of the most promising approaches in biological and clinical investigations due to their unique properties, such as high sensitivity and selectivity, fast fluorescence response, and low cost (3). As a result, a series of fluorescent materials, including fluorescent nanomaterials and molecules have been recently developed for biosensing and imaging (2), while the development of new biocompatible nanomaterials with high fluorescence intensity and good biocompatibility remains challenging. In this work, a family of manganese-doped zinc sulphide (Mn:ZnS)-based fluorescence quantum dots (QDs) have been successfully prepared. The morphology and structure of the Mn:ZnS QDs were characterized by DLS, TEM, FTIR, UV-Vis and Fluorescence spectroscopy. Through coating of the Mn:ZnS with bovine serum albumin (BSA) during the synthesis, biocompatible Mn:ZnS@BSA was also prepared in situ. In comparison with Mn:ZnS, the new Mn:ZnS@BSA nanoparticle exhibited higher fluorescence intensity and excellent colloidal stability (Figure 1), which allow it to be further explored as the fluorescent nanomaterial for biosensing and imaging applications.

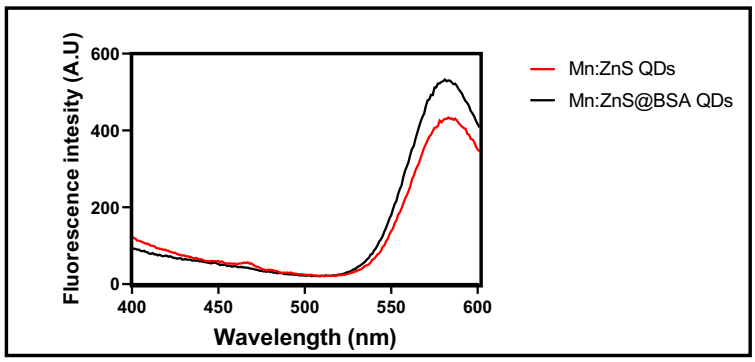

Figure 1. Fluorescence spectra of Mn:ZnS and Mn:ZnS@BSA in MES buffer of pH 5.5

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T-126

Examining the reactivity and speciation of selenoneine *in vitro* via synchrotron radiation

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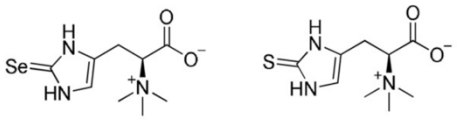
Selenium is a micronutrient essential for human health, with twenty-five human proteins confirmed to contain a selenocysteine (SeCys) group at their active site. Many of these proteins are enzymes involved in cellular redox reactions such as glutathione peroxidase (GPx) and thioredoxin reductase (TrxR).[1] The publishing of optimal dose guidelines for dietary selenium is complicated by the different bioactive properties exhibited by different forms of dietary and non-dietary selenium.[2]



A compound which has been a focal point of this research is the naturally occurring selenoimidazole compound selenoneine (Fig. 1) which can accumulate inside persons with a high seafood diet.[3] Selenoneine is the selenium isolog of the naturally occurring amino acid ergothioneine (above) and has shown to provide protection against oxidative insult *in vitro* with relatively low toxicity compared to other selenocompounds. The chemistry of the selenium-carbon double-bond is also unique amongst selenocompounds present in the diet, further indicating the importance of characterizing its metabolic pathway.

Total synthesis of selenoneine was recently reported by our collaborators in Switzerland[3] allowing *in vitro* tests to be undertaken. Using synchrotron radiation (X-Ray Fluorescence Microscopy and X-ray Absorption Spectroscopy) we have been able to analyse intact samples with minimal preparation and interference, ensuring the results are more reflective of the actual biological pathways occurring *in vivo*.

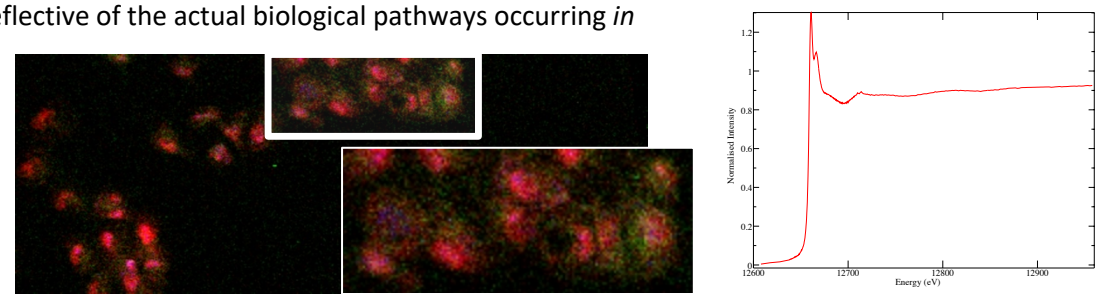


Figure. Left: XFM images of A549 cells treated with selenoneine, demonstrating cytoplasmic internalisation; and Right: X-ray absorption spectra of A549 cell pellet treated with selenoneine.

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T-128

Computational design, synthesis and activity of novel KDM4 inhibitors

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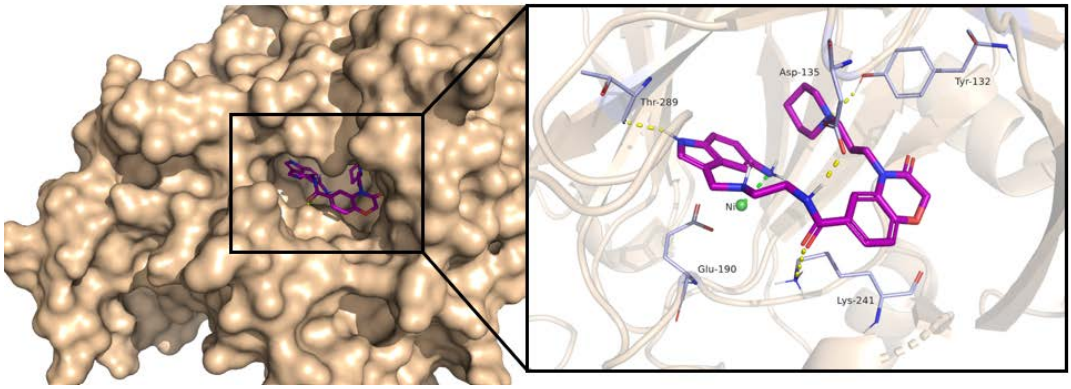
Epigenetics focuses on the modification of gene expression without a change in the DNA sequence, thereby inducing a change in *phenotype* without a change in *genotype*. A common epigenetic mechanism is the methylation of histone *N*-terminal tails above the DNA, which changes DNA's access to the transcriptional machinery. The canonical methylation sites are found on histone H3 at lysine 4 (H3K4), lysine 9 (H3K9), lysine 27 (H3K27) and lysine 36 (H3K36). These lysines can be monomethylated (me1), dimethylated (me2) or trimethylated (me3). The addition of methyl groups by histone lysine methyltransferases (KMTs), and their removal by histone lysine demethylases (KDMs), can either activate or repress genes, depending on the targeted lysine.[1,2] KMTs and KDMs have been associated with cancers, including melanoma, glioblastoma, kidney and prostate cancer.[3]

The KDM4 subfamily has 5 members (KDM4A-E; also known as JMJD2A-E) that demethylate histone H3 tails at di- and trimethylated lysine 9 (H3K9me3/me2) and lysine 36 (H3K36me3/me2). Physiological functions have been identified for KDM4s only in embryonic development, whereas many pathological roles for KDM4A/B/C have been found in various cancers.[4] However, there is a lack of high-quality probes to delineate the role of KDM4 in cancer and to rationalise development of drugs targeting these epigenetic enzymes. In this work we describe the computational design, synthesis and biochemical testing of small molecules targeting KDM4. Novel inhibitors show sub-micromolar potency and thus represent promising leads for development of probes, and potentially anti-cancer drugs, targeting KDM4.



Example of a designed analogue in the KDM4 binding site.

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T-129

Structure-based design of INTS3-hSSB1 Protein-Protein interaction inhibitors for cancer therapy

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Characterization of molecular mechanisms of protein-protein interactions (PPIs) involved in multiple complex biomolecular pathways has enabled identifying them as a new class potential drug target for a wide range of diseases, including oncology [1]. However, these PPI targets offer multiple challenges during the drug discovery process due to the absence of well-defined binding pockets, large hydrophobic interfaces with complex interaction patterns. In recent years, PPIs involved in DNA damage response and repair pathways have been widely investigated for the discovery of cancer therapeutics [2,3]. Inhibition of homologous recombination (HR) mediated DNA repair proteins have been exploited as potential chemotherapeutic strategies. The current study involves the design and identification of small molecule inhibitors of novel PPI target, human single-stranded DNA binding protein 1 (hSSB1)-integrator complex subunit 3 (INTS3) complex. This PPI plays a crucial role in the recognition and repair of cytotoxic DNA double-strand breaks via HR pathway [4]. We have utilized a structure-based design protocol to identify binding pockets at the PPI interface and virtual screening of ligand libraries against the INTS3 binding pocket. The virtual screening involves *in silico* docking of PPI libraries from Enamine into the INTS3-hSSB1 binding interface using Parallelised Open Babel and Autodock suite Pipeline (POAP), followed by molecular dynamics simulation studies and free energy calculations to narrow down the possible drug-like compounds and identification of hit molecules. We validated our *in silico* findings by employing *in vitro* biochemical, biophysical, and cell-based approaches to screen the top-scoring compounds and evaluate disrupting the PPI between INTS3 and hSSB1. Three of the tested compounds were capable of completely disrupting the interactions between both proteins. The structural information from these compounds can be utilized to design a series of compounds and generate the structure-activity relationships.

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T-130

Developing FtsZ inhibitors as Gram-negative antibacterial agents

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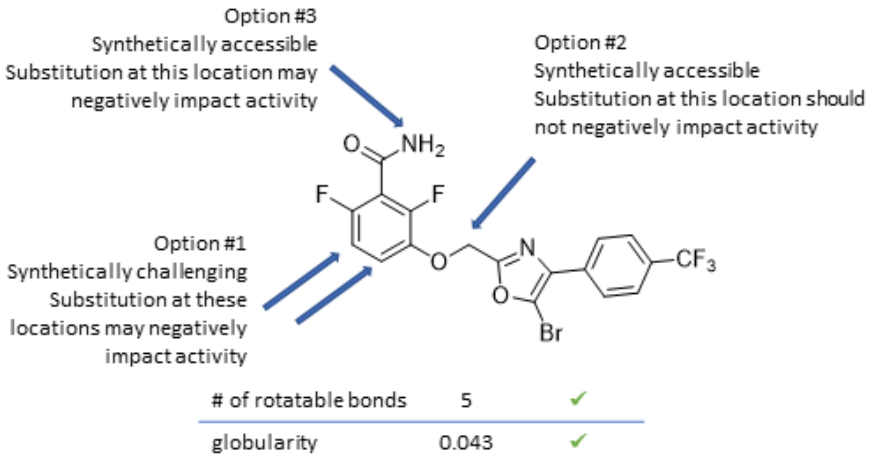
FtsZ is a highly conserved protein that is essential for bacterial cell division. Despite its potential as a drug target, only one drug targeting FtsZ has made it into clinical trials. TXA709's activity is limited to the Gram-positive species S. aureus.[1] Expanding the spectrum of activity to include Gram-negative pathogens is therefore highly desirable. Given its essentiality, a pan-species FtsZ inhibitor is theoretically possible, yet no such inhibitor has been developed, leading us to wonder why.

The outer membrane of Gram-negative bacteria represents an impenetrable barrier that prevents many antibiotics from reaching their intracellular target, largely due to efflux. This phenomenon has significantly hampered efforts to discover new Gram-negative antibiotics, prompting the development of empirical models to guide compound design. One such set of guidelines are the eNTRy rules, which predict the likelihood of a compound accumulating in E. coli (i.e., avoiding efflux) based on a set of design criteria.[2] In this manner, Gram-positive specific compounds can be converted to broad spectrum Gram-negative agents through judicious structural modification.[3] The observation that TXY436 (a TXA709 derivative) activity can be restored in Gram-negative bacteria by chemical attenuation of efflux suggests that appropriate modification of its structure might lead to a broad spectrum FtsZ inhibitor.[4] Based on these observations, I will describe our efforts to convert small molecule FtsZ inhibitors into novel broad-spectrum agents capable of targeting Gram-negative pathogens.



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T-131

Norbornane-based Antibacterial Agents with Substituted Guanidines

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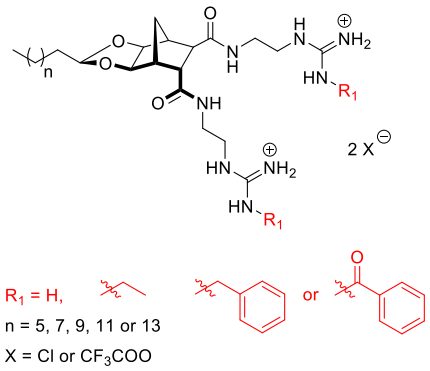
In order to combat the emergence of antibiotic resistant bacteria new drugs need to be developed to replace older, ineffective treatments. Naturally occurring cationic antimicrobial peptides form part of the innate immune defense systems of many organisms and generally exhibit broad-spectrum antibacterial activity. There are several limitations that prevent cationic antimicrobial peptides being commonly used in a clinical setting (i) poor in vivo stability[1] (ii) they can be haemolytic[2] and (iii) their structural complexity makes large scale synthesis economically unfeasible.[3] Due to these limitations attention has focused on developing synthetic antibacterial agents that mimic the biological activity of antimicrobial peptides without the aforementioned shortcomings.

A norbornane-based compound with benzyl substituted guanidines that was reported previously[4] displayed a minimum inhibitory concentration (MIC) against methicillin resistant *S. aureus* (MRSA) of 2 µg/mL, a significant improvement over its unsubstituted analogue (MIC_{MRSA} = 32 µg/mL). Following on from this intriguing result a series of 14 compounds with either benzyl, benzoyl, or ethyl substituted guanidines and two compounds with unsubstituted guanidines have been synthesized and evaluated for antibacterial activity against a range of Gram-positive and Gram-negative pathogens and cytotoxicity against human embryonic kidney cells.



Norbornane-based antibacterial agents.

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T-132

Modelling ligand docking to RNA in the design of oxazolidinone antibiotics

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Oxazolidinones are a broad-spectrum class of synthetic antibiotics with a chemical structure characterized by a basic nucleus of 2-oxazolidone, that bind to the 50S ribosomal subunit of both gram-positive and gram-negative bacteria. They are active against a wide spectrum of multidrug-resistant Gram-positive bacteria, such as vancomycin-resistant *Enterococcus*, *Mycobacterium tuberculosis*, and Methicillin-resistant *Staphylococcus aureus* (MRSA).[1] The class stops the growth and reproduction of bacteria by preventing the combination of mRNA and tRNA with the 50S and 30S ribosomal subunits to form a 70S initiation complex.[2] There have been various studies on oxazolidinone targets with RNA, such as linezolid, ranbezolid, and tedizolid. However there has been no rigorous benchmarking studying addressing the docking of large oxazolidinone molecule libraries, such as Zhao et al.'s 285 oxazolidinone derivative dataset,[3] against the 50S ribosome. We examined the performance of 5 docking programs (AutoDock 4, AutoDock Vina, DOCK 6, rDock, and RLDock) for their ability to model ribosomal-ligand interactions with oxazolidinones. 11 ribosomal crystal structures with oxazolidinones as the ligands were docked, with the accuracy being evaluated by calculating the root-mean-square deviation (RMSD) of the docked complexes and the programs internal scoring function. DOCK6 was found to be the best in reproducing the experimental pose and the highest average performing scoring function. The 285 derivatives were docked with DOCK6 to determine whether the program could predict the ligand binding poses, and to find potential interactions with *S. aureus* and MRSA ribosomes. It was found that DOCK6 did not show bias towards structural factors and performance of the derivative. General limitations of the scoring function are examined by using molecular fingerprints. Our results show that the ligand binding could be predicted in all derivatives using the existing software. The best and worst performing derivatives, with their differing structures, give insight to important molecular interactions and binding affinities in the active site of the crystal structures, in addition to deepen the understanding of ribosomal-ligand binding mechanisms. By using already established and well documented techniques on this previously untested oxazolidinone dataset, we are able predict promising or adverse interactions in the binding site of the ribosomes of *S. aureus* and MRSA.

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T-133

Real-time collaboration using GitHub as an open-access electronic laboratory notebook

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Electronic laboratory notebooks offer many advantages for researchers working in both industry and academia, including increased accessibility, version-control and improved data-sharing capacity. These features make them particularly useful for collaborative projects in which researchers may be geographically distant but working closely with others.[1] Open Source Malaria (OSM) is an example of such a project,[2] and has successfully used various ELNs including LabArchives and the open source platform LabTrove since its inception in 2009.[3] Together with sister open source drug discovery projects (e.g. Open Source Mycetoma), OSM has also used the open source, web-based program GitHub to facilitate open discussion and collaboration.

We now report our experiences using GitHub as both an electronic laboratory notebook and discussion platform, with case study examples from both synthetic and social science projects in open source drug discovery. We describe the advantages of using an open access, free and centralised platform that enables real-time discussion and data-sharing for collaborative projects, and explore the benefits of additional functionalities like metadata curation, attribution of provenance and project management tools. We suggest that making use of such properties facilitates better knowledge sharing and thus improves the transparency, reproducibility, and integrity of research.

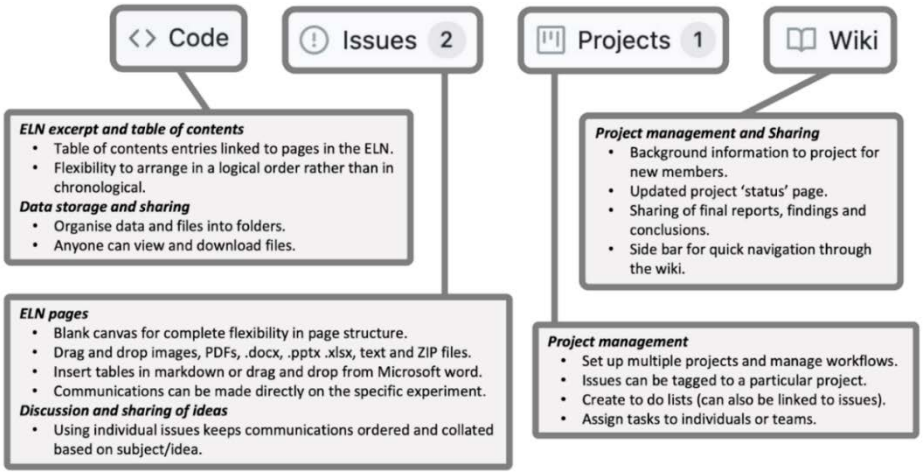

Figure 1. Overview of the structure and utility of GitHub

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T-134

Potent *Plasmodium falciparum* M1 & M17 Aminopeptidase Inhibitors with Novel S1' Moieties

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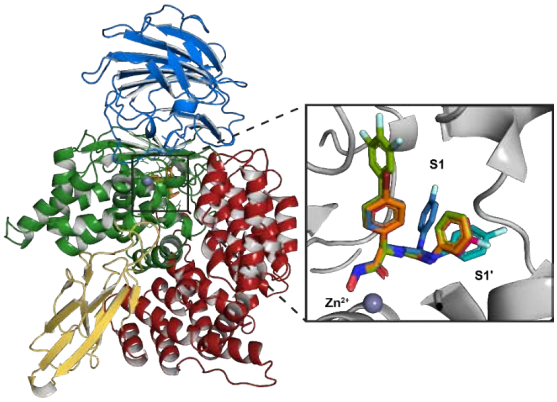
Malaria remains a global health burden, with an estimated 241 million infections occurring in 2020.[1] As resistance to frontline therapies grows, the development of therapeutic agents with novel mechanisms of action is required for elimination.[2] The plasmodial M1 and M17 metalloaminopeptidases (MAPs) have been identified as promising potential drug targets, as inhibition of these enzymes has been previously shown to result in antiplasmodial activity against both drug-sensitive and -resistant *Plasmodium falciparum*.[3] Previous SAR studies identified a range of inhibitors which possess the hydroxamate moiety that display moderately potent activity against MAPs. These compounds typically have non-polar functionalities in the S1'-region of the active site and structural biology studies have revealed that these inhibitors do not make strong intermolecular interactions with the S1' site of *Pf*A-M1 or -M17. Efforts to increase the polarity of these compounds via the introduction of hydrogen-bonding capable moieties has led to the identification of potent selective and dual *Pf*A-M1 and -M17 inhibitors, which also display moderate activity against *Pf*-3D7 parasites. Notably, the unsubstituted aniline moiety resulted in potent dual inhibition of *Pf*A-M1 and -M17 (*Pf*A-M1 K_i = 66 ± 2 nM, *Pf*A-M17 K_i = 57 ± 6 nM). Further derivatisation of this lead resulted in reduced inhibitory activity in both enzymes however bioisosteric replacement of the S1 3,4,5-trifluorophenyl moiety with a bromine atom saw a return of selective M1 potency. The combination of S1 bromine and S1' 3,5-difluoroaniline resulted in one of the most potent *Pf*A-M1 inhibitors to date (*Pf*A-M1 K_i = 16 ± 2 nM), whilst other S1' substituted anilines resulted in similar potencies.



X-ray crystal structure of novel hydroxamates bound to *Pf*A-M1.

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T-135

DECR1 inhibition: a novel prostate cancer therapeutic strategy

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Prostate cancer (PCa) is the fifth-leading cause of cancer-related deaths amongst males globally. Androgen suppression remains the most common treatment for androgen dependent localised disease and is achieved by radical prostatectomy, radiotherapy and androgen deprivation therapy (ADT). Despite initial responses to ADT, patients ultimately relapse into castration-resistant prostate cancer (CRPC), triggering an androgen independent disease state which remains resistant to androgen suppressive treatments. CRPC relies on fatty acid (FA) metabolism to fulfil energy requirements for metastatic cancer growth. β-oxidation is the principal step in FA metabolism and is responsible for the oxidation of all classes of FAs (saturated, monounsaturated and polyunsaturated). Conventional therapeutic strategies have focused on inhibiting carnitine palmitoyltransferase 1, the rate-limiting step in FA β-oxidation, as a means to starve the PCa cells. Although CPT1 inhibitors have demonstrated clinical potential, these therapies suffer from limitations pertaining to off-target effects and toxicity. Polyunsaturated fatty acids (PUFAs) are another lipid source but require derivatisation prior to β-oxidation being performed; a process which is controlled by three enzymes (dienoyl-CoA isomerase, 4-dienoyl-CoA reductase (DECR1) and enoyl-CoA isomerase). Of these three, DECR1 is the rate limiting enzyme in PUFA oxidation and has been observed to be upregulated in CRPC. As such, this project seeks to inhibit DECR1 as a strategy to limit lipid metabolism in PCa and prevent the formation of CRPC.

This project will utilise the diazaborine scaffold for the development of small molecule inhibitors of DECR1. Diazaborine scaffolds are an underexplored class of compound which have demonstrated use as antibacterial, antifungal and eczema agents. Diazaborines have previously demonstrated a high-affinity for the bacterial homologue of DECR1, offering a potential starting point for the development of DECR1 inhibitors in humans. Binding of diazaborines in the DECR1 binding pocket occurs only in the presence of NAD. Therefore, the ability for diazaborines to form a fourth strong dative bond with NAD, through the empty p-orbital of the boron atom, renders these molecules attractive for this project. At present, a diazaborine lead compound has been computationally validated in the human DECR1 binding pocket and biologically tested where the diazaborine inhibited cancer cell viability at high doses. A library of derivatives have been designed to probe the structure activity relationship of this class of compound and this presentation will discuss our synthetic efforts towards these first generation diazaborine targets.

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T-137

Development of Bruton's tyrosine kinase inhibitors for the treatment of neuroinflammatory disorders

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Chronic and uncontrolled inflammation is the underlying driver of many diseases in our society, including diabetes, cancer, and neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Central to the inflammatory response is the NLRP3 inflammasome, and its role in inflammation and disease has attracted much interest as a potential therapeutic target for mitigating inflammatory and neurodegenerative diseases.

Activation of the NLRP3 inflammasome is tightly regulated by a selection of kinases, ubiquitinases, and phosphatases. Research has demonstrated that inhibition of Bruton's tyrosine kinase (BTK) abrogates the NLRP3-dependent inflammatory response.[1] Therefore, inhibiting BTK shows promise as a new therapeutic target towards NLRP3-dependent diseases. Current inhibitors of BTK show undesirable side effects, and require further improvement towards treating chronic diseases. This present study aims to design and develop novel and safe BTK inhibitors with a particular focus on brain penetrance for the treatment of neurodegenerative diseases. I describe the design of BTK inhibitors using *in silico* drug design tools, which revealed new classes of potential inhibitors. This presentation will provide an overview of the chemical reactions used towards the synthesis of novel fused pyrimido kinase inhibitors. We anticipate that the discovery of new BTK inhibitors will enable the development of safe and effective medicine for NLRP3-related neuroinflammatory disorders.

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T-138

Alkaloids of *Acacia auriculiformis*

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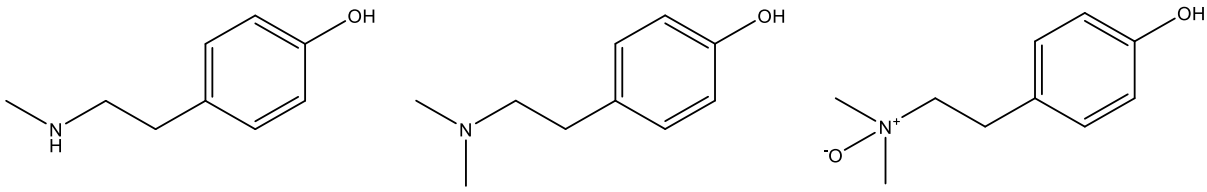
Natural products from a range of sources continue to play a key role in new drug development. Ethnomedicinal knowledge offers a curated library of traditionally used and medicinally active plants. Our group is exploring the phytochemical profile of a range of native Australian plants used in traditional Aboriginal medicine. *Acacia auriculiformis* from the family *Fabaceae/Leguminosae* is small to medium-sized tree native to northern regions of Australia, Papua New Guinea and Indonesia. More commonly known as the 'ear-pod wattle', the pods and leaves have been used traditionally by Aboriginal communities to prepare an antiseptic skin wash and to produce a soapy lather to relieve itching of the skin.[1,2] The plant has also been used to poison fish by crushing leaves and throwing them into watering holes.[2] The leaves and seed pods are known to be rich in triterpenoid saponins,[3-7] responsible for the plant's soap-like properties. Numerous flavonoid compounds have also been reported isolated from the heartwood[8], aerial parts[9] and bark.[10] Our preliminary *A. auriculiformis* leaf extracts (voucher no. Leach4878) indicated the presence of a wide variety of alkaloids not previously reported. We report the structure elucidation of a number of alkaloids using high resolution mass spectrometry and 1D and 2D ^{1}H, ^{13}C and ^{15}N NMR techniques. These compounds have been isolated from *A. auriculiformis* for the first time, including several previously unreported compounds.



N-methyl tyramine | Hordenine | Hordenine *N*-oxide

Alkaloids newly isolated from *A. auriculiformis*.

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T-139

Synthesis of phenazine-2,8-dicarboxylates for use as DNA intercalating agents

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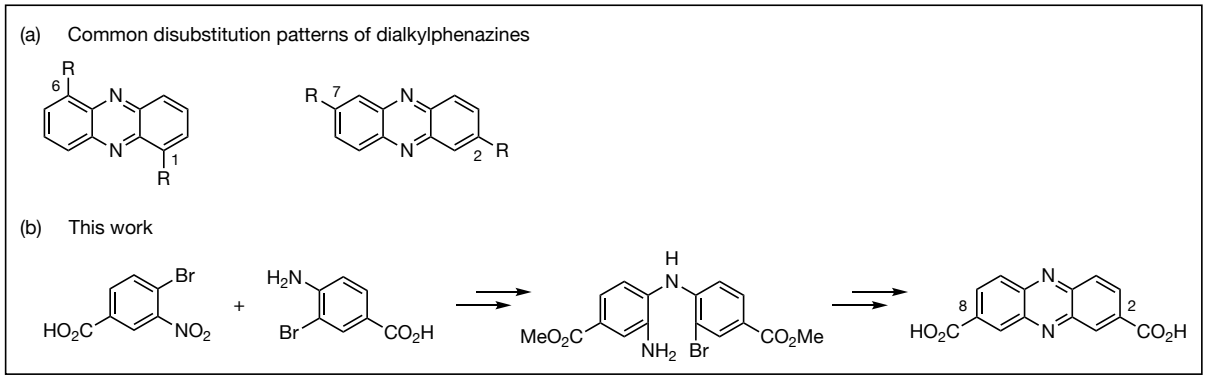
Phenazines constitute an important class of polycyclic aromatic heterocycles with applications as bioactive agents, organic dyes, organic conductors and molecular switches. Of interest to our group is phenazines' ability to intercalate between the base pairs of DNA to elicit biological responses, such as antitumour activity.[1]

Phenazines are both naturally and synthetically derived and can typically be synthesized through the construction of the central pyrazine ring from substituted benzenes via concurrent or sequential C–N bond formations.[1] When applied to the synthesis of disubstituted phenazines in which a single substituent resides on each benzannulated ring, these methods typically furnish rotationally symmetric 1,6- or 2,7-disubstituted phenazines (a), or else lack regioselectivity. More recently, sequential Buchwald-Hartwig N-arylations have been utilised to selectively furnish phenazines with further substitution patterns.[3] Despite this, 2,8-disubstituted phenazines (b) remain conspicuously rare, particularly bearing acyl substituents. Furthermore, this substitution pattern is even rarer than a cursory literature search might suggest, as a lack of conclusive characterisation data has led to a suspicion that 2,7-disubstituted phenazines might previously have been misassigned as 2,8-isomers.

In this work,[4] dimethyl phenazine-2,8-dicarboxylate and its corresponding diacid are synthesised following a route involving inter- and intramolecular Buchwald-Hartwig N-arylations (b). We describe a simple NMR-based experiment to unambiguously assign the 2,8-disubstitution patterns in phenazines, and the carboxylic acid synthetic handles have allowed us to expand this phenazine centre into novel DNA intercalating agents. This ability to position substituents specifically around the phenazine core paves the way for the development of new antitumour drug candidates.



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T-140

Prioritising Hits of Dengue Polymerase for Elaboration into High Affinity Leads

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Dengue virus is a mosquito born flavivirus that causes 390 million infections each year. 40 % the worlds population live in at risk areas and there are no known small molecule treatments. There are four serotypes of Dengue and the viral RNA dependant RNA Polymerase is the most conserved of the non-structural viral proteins. This makes Dengue polymerase an attractive target for the development of pan-serotype Dengue virus inhibitors. A pocket on dengue polymerase, known as the p-pocket, was discovered by the Novartis Institute of Tropical diseases and small molecules bound to this pocket were found to inhibit viral replication.[1] Currently known p-pocket inhibitors have poor solubility and permeability.[2] Hence there is a need for novel inhibitor chemotypes for Dengue Polymerase with improved properties.

In the current work we describe our fragment screening and development pathway. A primary fragment screen was conducted by ligand detect NMR and then hits were further validated by multiple ligand detect NMR experiments in competition with a known p-pocket binder. In order to rank the hits and asses their developability we developed a quantitative SPR assay with the aid of protein stability characterisation via thermal shift. We then employed a novel cheminformatic workflow to aid commercial analogue selection to quickly generate series of compounds to asses SAR and developability of a given series. 7 chemical series gave analogues with LE > 0.28 $kcal.mol^{-1}.HAC^{-1}$ providing multiple possible starting points for development of higher affinity lead like compounds. The most promising fragments are currently being explored through the use of off-rate-screening[3] by SPR to rapidly explore vectors of these compounds and preliminary results will be presented.

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T-141

Novel Chemoreactive Probes of ATF936 for the Treatment of Autosomal Dominant Hypocalcemia

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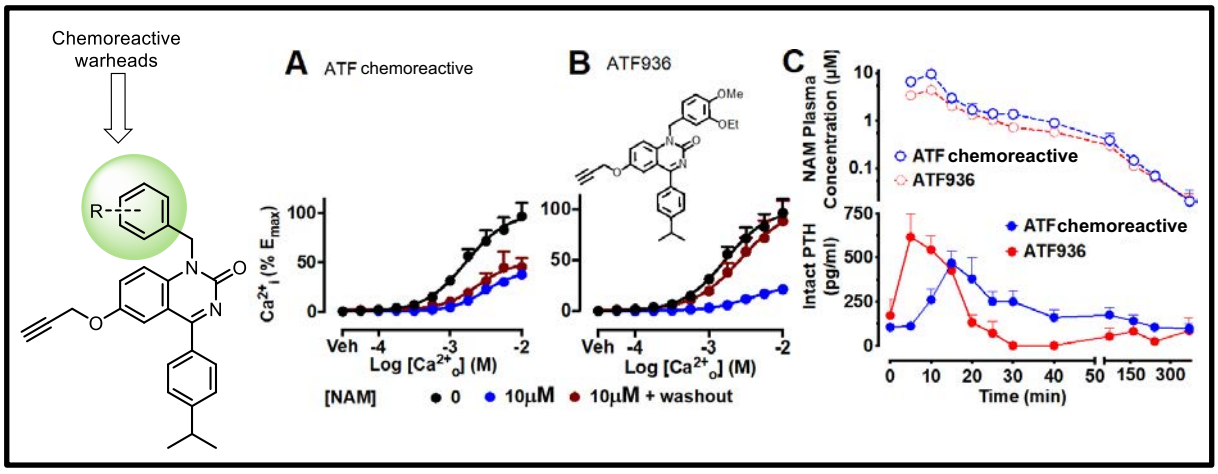
The CaSR is a class C GPCR that responds to elevated Ca^{2+} via $G\alpha_{11}$ by inhibiting parathyroid hormone (PTH) secretion and promoting renal excretion of Ca^{2+} and other salts to restore physiologically normal Ca^{2+} concentrations. Autosomal dominant hypocalcemia (ADH) type 1 and 2 are disorders of calcium homeostasis caused by gain of function mutations in the CaSR. A lifelong disease, ADH symptoms include paraesthesia, painful muscle spasms and recurrent childhood seizures. Current treatment options include Vitamin D analogues and calcium supplements which cause excessive activation of renal CaSR thereby aggravating hypercalciuria and predisposing ADH patients to nephrocalcinosis and renal failure. ATF936 is a negative allosteric modulator (NAM) of the CaSR originally developed for the treatment of osteoporosis, where it was designed to have a short duration of action to prevent bone resorption.(1) It has been shown that CaSR negative allosteric modulators (NAMs) transiently raise PTH levels in ADH1 patients restoring Ca^{2+} concentration to a physiological normal range (2), thus the need for the design of longer acting CaSR NAMs. Herein we disclose the discovery of a covalent chemoreactive NAM for the CaSR that (i) demonstrates irreversible binding to the receptor and (ii) stimulates prolonged PTH release *in vivo*. This 'first-in-class' chemical probe may provide invaluable insight towards the development of longer acting NAMs for the treatment of ADH.



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T-142

Identification of the Potent and Selective Anti-Cancer Agents: Metal Complexes of Di-2-Pyridyl Ketone 4-Ethyl-4-Methyl-3-Thiosemicarbazone

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The development of novel chemotherapeutics with a high therapeutic index is required to selectively target cancer without inducing deleterious side effects. Previously, met-haemoglobinemia and hypoxia were noted as side effects associated with the in vivo administration of the experimental anti-cancer agents, Triapine and di-2-pyridylketone 4-cyclohexyl-4-methyl-3-thiosemicarbazone (DpC), in humans and animal models. These detrimental effects are a major concern and are critical to overcome.

The novel thiosemicarbazone, di-2-pyridyl-ketone 4-ethyl-4-methyl-3-thiosemicarbazone (Dp4e4mT), demonstrated the greatest anti-proliferative activity of all agents tested, with the potency of the ligands being in the order: Dp4e4mT > di-2-pyridyl ketone 4,4-dimethyl-3-thiosemicarbazone (Dp44mT) > DpC >> desferrioxamine (DFO). In fact, Dp4e4mT was significantly ($p < 0.01$) more active than DpC and particularly DFO. The $Cu(Dp4e4mT)_2$, $Zn(Dp4e4mT)_2$ (**Fig. 1**), and $Ga(Dp4e4mT)_2$ complexes demonstrated similar or slightly greater anti-proliferative efficacy than the ligand alone.

Dp4e4mT and its complexes exhibited potent and selective anti-proliferative activity.

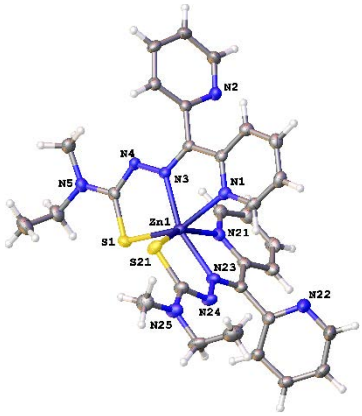

Fig. 1. ORTEP representation of $Zn(Dp4e4mT)_2$ complex at a 50% probability level.

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T-143

Development of AC265347-Inspired Calcium-sensing Receptor Ago-Positive Allosteric Modulators

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The calcium-sensing receptor (CaSR), a class C G-protein coupled receptor, is a clinical target in the treatment of hyperparathyroidism and related diseases. The CaSR, expressed ubiquitously in the body, plays an important role in the maintenance of extracellular calcium homeostasis via a negative feedback loop of parathyroid hormone (PTH) secretion.

Clinically approved cinacalcet acts as a positive allosteric modulator (PAM) at CaSR to supress the secretion and normalise serum PTH concentrations in hyperparathyroidism. However, the use of cinacalcet is limited due to adverse side effects including hypocalcaemia, nausea and vomiting, and in some instances, a lack of efficacy. The CaSR agonist and PAM (ago-PAM), AC265347, is chemically distinct from clinically approved phenylalkylamine CaSR PAMs. AC265347 potently suppressed PTH release in rats with a lower propensity to cause hypocalcaemia compared to cinacalcet.[1] Furthermore, AC265347 has shown to be more effective at restoring the signalling of several naturally occurring CaSR mutations compared to cinacalcet. The novel scaffold of AC265347 offers a potential for a more efficacious therapy over the current treatment.

Here we report a structure activity relationship (SAR) study seeking to optimise AC265347 as a drug candidate by employing synthetic strategies including exploration of small substituents, bioisosteric replacement and scaffold hopping approach. Alongside the use of the operational model of allostery, we were able to quantify affinity, cooperativity and agonism of the novel compounds synthesised in this work. Structural modifications on the AC265347, subtle or profound, resulted in varying pharmacological profiles. Herein, we disclose the discovery of AC265347-like compounds with diverse pharmacology and improved physicochemical and drug-like properties.

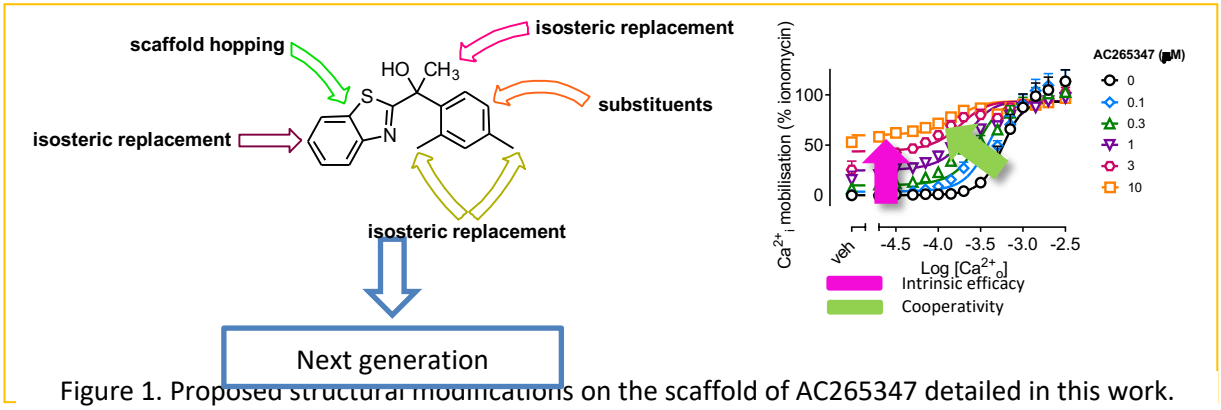

Figure 1. Proposed structural modifications on the scaffold of AC265347 detailed in this work.

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T-144

[1,4]-Substituted Azepines: Optimising Access to Biologically Active Tricyclics

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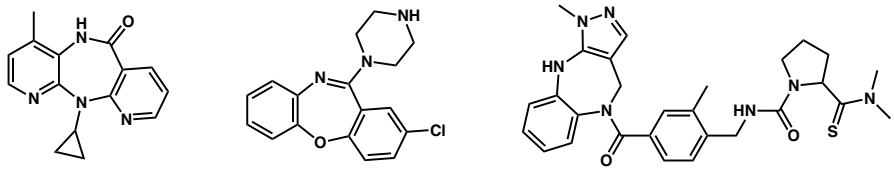
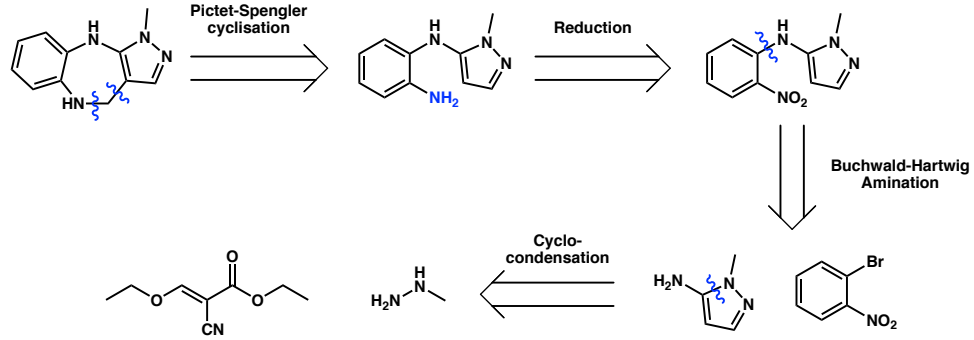
Heteroatom containing 1,4-azepines are an exciting structural motif in medicinal chemistry due to their biological activity over a broad range of ailments in mammalian systems. Current pharmaceutical examples include the HIV-1 non-nucleoside reverse transcriptase inhibitor nevirapine (1) and tricyclic antidepressant amoxapine (2).[1,2] More recently, drug discovery programs have also identified LIT-001 (3) as a non-peptide agonist for the oxytocin receptor to treat depression and anxiety.[3]



1 2 3

A key feature of these molecules is the benzodiazepine motif, of which a five-step syntheses for pyrazolo[3,4]benzodiazepine has previously been reported.[4] Optimisation of the synthetic route to obtain this chemically diversifiable handle is of high interest and herein we report a new method of access to this interesting structural motif.



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T-145

Development of MALDI immunoassays for sensitive detection of amyloid-β aggregation

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Alzheimer's Disease (AD) is neurodegenerative disorder known to affect approximately 50 million individuals worldwide, yet methods of early diagnosis are still severely limited. AD has long been associated with fibrillar aggregates of the protein amyloid-β in the brain and hence, being able to detect and observe early aggregates or associated biomarkers would have major significance in diagnosis and disease monitoring. Immunoassays are frequently used as a method of detecting biomarkers and make use of the highly specific interactions between antibodies and antigens. While immunoassays typically rely on spectroscopic methods, instead incorporating mass spectrometry may provide opportunities to significantly improve sensitivity and efficiency of detection. This can be achieved by the implementation of a "mass tag" – a compound conjugated to an antibody which is designed to cleave under whatever conditions might be present in a mass spectrometer. With this approach, the detection of a particular m/z value can report on the presence of a particular biomarker.

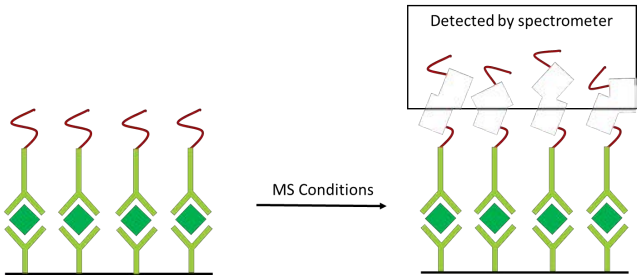

Figure 1: Dissociated mass tag indicates the presence of biomarker

Here we present development of a highly sensitive MS-based immunoassay for detection of oligomeric amyloid-β, designed for matrix assisted laser desorption ionisation mass spectrometry (MALDI-MS). For use in this assay, an appropriate mass tag has been synthesised, incorporating the photocleavable *ortho*-nitrobenzyl ether group, which has been well characterised to cleave under the conditions of MALDI-MS. In this approach, sensitivity is enhanced by coupling streptavidin coated gold nanoparticles with biotinylated antibodies and mass tags such that many mass tags are able to be conjugated to a single antibody. While in this case, the assay has been used for the detection of amyloid-β aggregates, this approach may easily be adapted for the multiplexed detection of alternative biomarkers and the improved sensitivity and throughput offers an example of the advantages MS may bring to biomolecule detection.

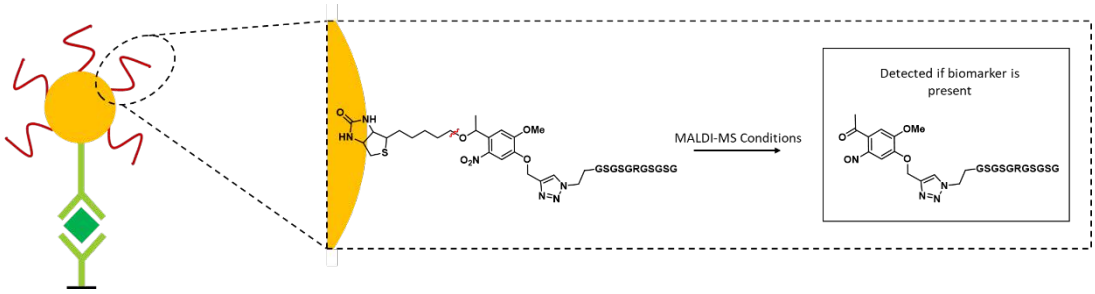

Figure 2: Mass tag design allows binding of multiple tags and cleavage under MALDI-MS conditions

T-146

From friend to foe: strategies for evolving with pathogenic microbes

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Due to overuse and misuse, less than a century since the discovery of the first antibiotic, we now face the looming threat of a post-antibiotic era with antimicrobial resistance (AMR) on the rise[1]. The WHO has predicted that the death toll due to AMR will rise to 10 million annually by 2050 if no action is taken[2,3]. With no new classes of antibiotics discovered since 1984, the discovery of novel antimicrobial agents is of paramount importance[3].

The Community for Open Antimicrobial Drug Discovery (CO-ADD) provides a free screening service for researchers to test the activity of compounds against ESKAPE pathogens[4]. To date, CO-ADD has screened over 310,000 compounds from 310 research groups in 48 countries resulting in 2798 hits that are effective antimicrobials at concentrations non-toxic to human cells *in vitro*. Analysing the entire CO-ADD library (310,000 compounds) based on potency, synthetic tractability, and novelty I found that 206 of the compounds in the database were organoselenium compounds displaying antimicrobial activity against gram-positive bacteria and fungi. Of these compounds, 77 qualified as active with an MIC $\leq$ 16 μg mL^{-1} against at least one out of the 7 CO-ADD microbes, representing a 37% hit rate, significantly higher than the over-all hit rate of 1.6% across the whole CO-ADD library.

These organoselenium compounds also display reduced cytotoxicity and haemolytic activity against human embryonic kidney cells (HEK 293) and human red blood cells in comparison with the rest of the library (34% vs 65% of compounds showing HEK293 $CC_{50} \leq 32$ μg mL^{-1} and haemolytic $HC_{10} \leq 32$ μg mL^{-1}). Furthermore, preliminary observations also indicated that the substitution of sulfur for selenium within a chemotype produced enhanced antimicrobial potency. It was also observed selenium-containing species consistently displayed antifungal activity, suggesting the inclusion of selenium within organic scaffolds introduces a novel antifungal modality. Current literature supports this claim, with organoselenium compounds recognised as having access to unique modes of action: ROS generation, targeting critical thiol residues in enzymes, or disrupting the transmembrane protein Pma1p responsible for regulating the intracellular pH and proton gradient in fungi.

Overall, these results warranted a closer inspection of the organoselenium compounds in CO-ADD. This data analysis highlights the potential of organoselenium compounds as novel antimicrobial agents. This talk will focus on the synthesis, activity, and efficacy of organoselenium compounds and selenium containing peptides as non-conventional antimicrobial agents.
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T-148

Design and Synthesis of $P2X_7$ Receptor Antagonists for the Treatment of Neurodegenerative Diseases

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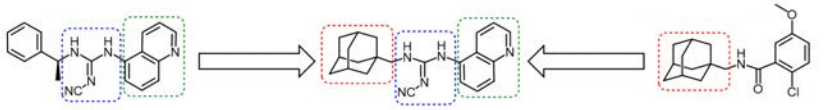
The $P2X_7$ receptor ($P2X_7R$) is an ATP-mediated ligand-gated ion channel upregulated on activated immune cells (*i.e.*, microglia) within the central nervous system (CNS).[1] Activation of the $P2X_7R$ triggers a myriad of downstream signaling events that results in the release of interleukin-1β, cell death and proliferation. This is seen in pathological signalling states consistent with neurodegenerative disorders; Alzheimer's Disease and Parkinson's Disease.[2,3]

High-throughput screening campaigns have facilitated the discovery of a multitude of potent $P2X_7R$ antagonists.[4,5] However, there is no clinically approved $P2X_7R$ antagonist currently on the market, with CNS permeability a common issue throughout the drug discovery process. Previous work developed a hybrid pharmacophore model that displayed potent inhibition at the $P2X_7R$ which has since been refined following several structure-activity relationship studies. These studies identified a highly potent adamantly cyanoguanidine framework, exemplified by lead compound **1** (IC_{50} = 18 ± 2.0 nM).[6]

The current study aims to probe interactions between novel ligands and the $P2X_7R$ binding site to improve the pharmacophore framework of **1**. This will be achieved by bioisosteric replacement of the cyanoguanidine linker to explore the influence of electrostatic distribution and positioning of hydrogen bond donors (HBD) and hydrogen bond acceptors (HBA). Furthermore, the project aims to reduce the lipophilicity and increase potency of lead compound **1** to afford optimal *in vitro* activity.

This research has seen the synthesis and initial *in vitro* evaluation of a small compound library. While improved potency was not achieved, a critical HBD necessary for nanomolar potency was identified within the linker framework. Ongoing *in vitro* evaluation of these $P2X_7R$ antagonists will influence the direction of future research in this field. Ultimately, this knowledge may lead to the development of a CNS-permeable ligand that reduces IL-1β secretion and restores microglial phagocytosis. This will be the first innovation to combat neuronal degeneration for the treatment of



Abbott Laboratories
Competitive Antagonist
logP = 4.4
IC_{50} = 93 ± 2.0 nM

Kassiou Group
Slowly Reversible NAM
logP = 4.7
IC_{50} = 18 ± 2.0 nM

AstraZeneca
Reversible NAM
logP = 4.1
IC_{50} = 11 ± 3.1 nM

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T-152

Harness Nature's strategy to develop safer and more effective leads for thrombosis

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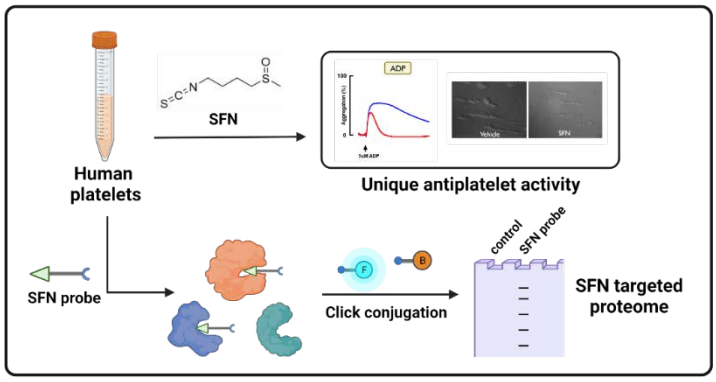
Thrombosis is the leading cause of death and disability in Australia and globally. However, all approved antithrombotic drugs (including anticoagulants and antiplatelet agents) have the potential risk to cause uncontrollable bleeding during accidental overdose. Bleeding risk is also the paramount consideration when evaluating the performance of antithrombotic leads in modern (pre)clinical trials; we thereby focus on studying the protein targets modulated by natural antiplatelet agents found in healthy diets with a view to identify safer protein targets for future antithrombotic discovery campaign.[1,2] Here we demonstrated that sulforaphane (SFN) – a predominant electrophilic lipid isolated from cruciferous vegetables – exhibits a novel mode of covalent inhibition of human platelet aggregation under thrombotic conditions, without disturbing the normal clotting function of platelets in wound healing. SFN is known to covalently engage with protein cysteine residues;[3] therefore, activity-based protein profiling (ABPP) was employed to map the modified proteome in platelets using a respective proteomic probe (IGP). Our preliminary results based on multiple donor samples indicate that protein disulfide isomerase is a kinetically privileged sensor that is able to react rapidly and quantitatively with SFN. In addition, we also demonstrated that a PDI inhibitor, PACMA-31, can recapitulate the phenotype triggered by SFN. Taken together, our research can potentially provide a new pathway to identify safer antiplatelet targets leveraging the unique biological activity and safety feature of dietary natural products, and sheds a new light on rationalising the cardiovascular-protective roles of healthy diets at the molecular level.



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T-153

Solid phase synthesis as a rapid and efficient methodology for PROTAC synthesis

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Targeted protein degradation utilising PROTACs is a field of ever-increasing interest within the drug discovery space. Numerous clinical candidates now exist which exhibit this modality.[1] An often-forgotten aspect of PROTACs is their developmental history rooted in peptides. The first published PROTAC was peptide-based, and one of the most commonly used E3 ligase recruiting ligands (VH032) is a peptidomimetic.[2] Consequently, well-established peptide synthesis strategies are suited to application in PROTAC discovery.

Our goal is to employ the efficient and adaptable methodology of solid phase synthesis (SPS) in the context of PROTAC development. Key to this approach is the ability to rapidly synthesise derivatives due to high rates of conversion and minimal purification, especially when compared to traditional solution phase methods. Furthermore, solid phase methodology lends itself well to parallel synthesis- particularly attractive for PROTAC optimisation given the importance of linker diversification. The utility of this strategy will be illustrated through the synthesis of VHL-recruiting PROTACs where we are exploring multiple possible avenues of polymer attachment and different solid phase reactions. We have successfully prepared the BET bromodomain targeting PROTAC MZ1 by SPS, along with known and novel analogues. The approach will then be applied to development campaigns targeting other proteins of biological interest.

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T-154

Exploring Tricyclic Indoles as Potential Cannabinoid Type 2 Receptor Ligands

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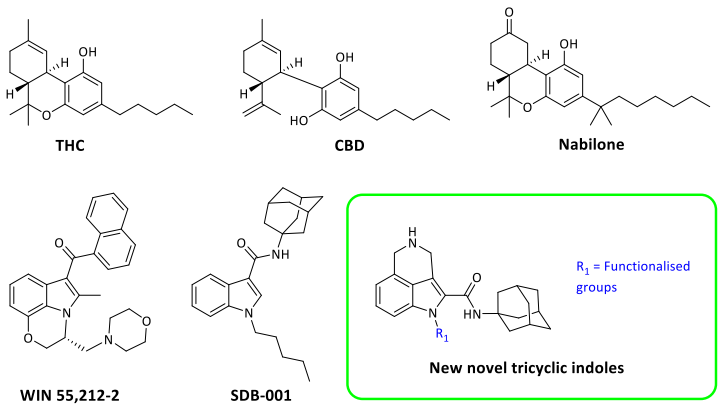
(-)-*trans*-Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the two main active constituents found in *Cannabis.* The undesirable psychoactive side effects of *Cannabis* stem from THC, whereas CBD is believed to be responsible for the valuable anti-inflammatory properties and has therapeutic potential. THC is a partial agonist at Cannabinoid Type 1 Receptor (CB_1R), which is primarily located in the central nervous system, and Cannabinoid Type 2 Receptor (CB_2R), predominantly situated in the peripheral immune system. CBD has been found to be a negative allosteric modulator at CB_1R and a partial agonist at CB_2R. Treatment and management of neuroinflammatory diseases such as multiple sclerosis, epilepsy and Alzheimer's, has potential to be improved by CB_2R agonists, via a reduction in microglia activation. Sativex (a 2.7 mg/2.5 mg mixture of THC/CBD) has been used for the treatment of multiple sclerosis, although some patients are reported to suffer from nausea. Other drugs like Dronabinol and Nabilone, are used to increase appetite in cancer or AIDS patients and as a treatment for chronic pain, respectively. Among the reported synthetic cannabinoids to date, the indole compounds have been shown to have potential to be incredibly potent CB ligands. WIN 55,212-2 is a potent agonist at both receptors, producing a similar effect to THC with a higher affinity. THC and WIN55,212-2 have also been shown to have antineoplastic activity in several cancer models *in vitro* and *in vivo*[1]. SBD-001 is an illicit non-selective full agonist at both receptors, similar to WIN 55,212-2. Our group has shown by altering the carboxamide at C-3 of SBD-001, to C-2, yields CB_2R selectivity over CB_1R[2]. The research to be presented consists for 6 novel tricyclic indoles with the C-2 carboxamide motif, synthesised over 9 steps, and purified by preparative-HPLC to >95%. Some of these compounds were found to be non-selective antagonists at CB receptors and one compound was found to reduce the viability and proliferation of glioblastoma KNS42 cells, which overexpress CB_1R.



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T-155

Molecular modelling-led design of hydrazides as KDM4 inhibitors

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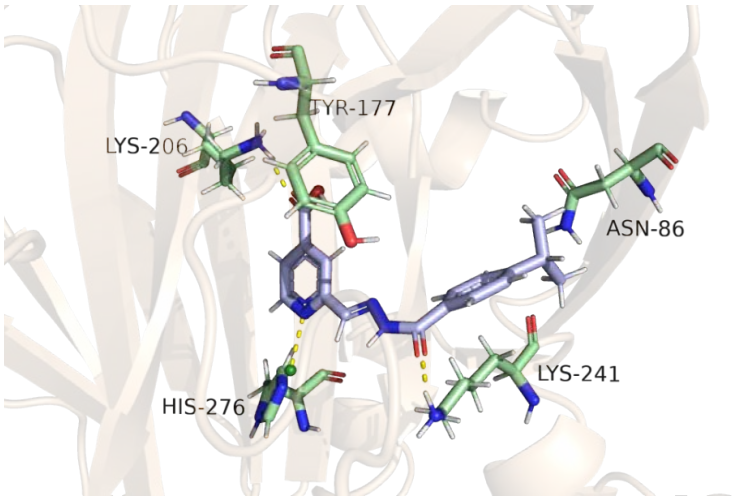
Modern epigenetics focuses on the modification of gene expression, without a change in the DNA sequence (i.e., a change in *phenotype* without a change in *genotype*). The three primary epigenetic tools include enzymes that can introduce changes to DNA and histones (writers), the proteins that read these changes and interpret the modifications (readers), and the enzymes that remove these chemical tags (erasers).[1,2] One of these erasers is the histone lysine demethylase enzyme (KDM). KDM's primary role is in the demethylating of lysine residues, primarily in proteins and nucleic acids. The KDM family consists of, at present, 30 discovered members from eight families (KDM1-8), and their action has been associated with cancer, neurological diseases, as well as inflammation and metabolic disorders.[3,4]

The KDM family has at least 30 distinct members: our research focusses on KDM4. The KDM4 variants are regarded as oncoproteins, and are overexpressed in various human cancers including pancreatic, lung, prostate, gastric and breast, to name a few.[3] In this work we describe the computational design and subsequent synthesis of a range of small molecules as KDM4 inhibitors, and thus represent promising anti-cancer therapeutics.



The interactions observed by one of the newly designed analogues in the KDM4 binding site

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T-156

Interrupting the Conversation: *In Silico* Design of Dual Acting Quorum Quenching Agents

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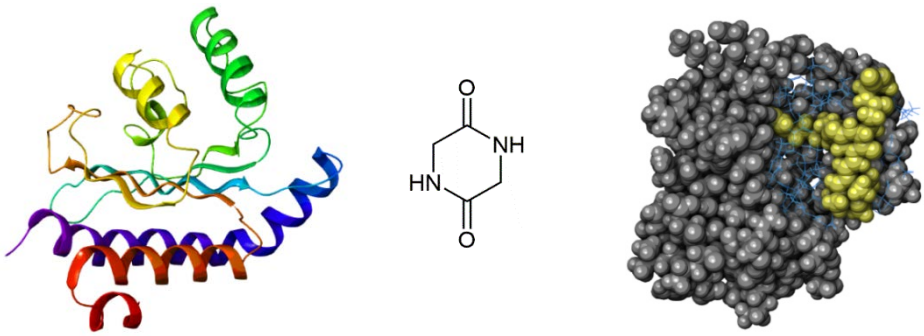
Bacteria communicate via a process known as Quorum Sensing (QS). This phenomenon allows bacteria to adapt to their surrounding environment and survive harsh conditions such as pH changes, nutrient deficiencies and antimicrobials such an antibiotics.[1] One of the ways in which bacteria can survive these conditions is by forming a biofilm. Biofilms are an aggregation of planktonic cells coated in an Extracellular Polymeric Substance (EPS) which form on surfaces and interfaces and are resistant to antibiotics.

Previously, our group has shown that a class of stable free-radical compounds called nitroxides are able to disperse biofilms back into planktonic cells, which are more susceptible to antibiotics.[2] Additionally, there has been much work in the literature around synthetic quorum quenching agents being used to control the quorum sensing systems of bacteria. In this work, we used *in silico* modelling to design dual-action anti-biofilm compounds, based on the highly modifiable diketopiperazine scaffold. These compounds, containing both a nitroxide moiety and common motifs from known QS molecules, were designed to dock into the LasR protein. This protein sits at the top of the quorum sensing hierarchy of *Pseudomonas aeruginosa* and as such, presents an important therapeutic target.[3]



Left: Ribbon representation of LasR protein; Middle: DKP core scaffold; Right: LasR protein (grey) showing docking of ligand (yellow) with surrounding binding sites (light blue)

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T-157

Development of fluorescent probes to explore the chemistry of living cells

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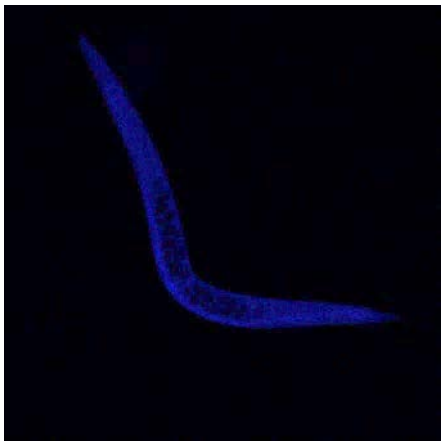
Having access to a range of chemical tools is essential for exploring the chemistry of living cells at a molecular level. Small molecule fluorescent sensors which are highly sensitive and can be functionalised in a variety of ways offer a powerful approach to probe many molecular species and study their effect in cells. We have developed probes capable of sensing a range of biologically relevant stimuli such as oxidative stress, pH and the concentration of metal ions. These have been successfully applied in mammalian cells and the use of approaches such as organelle targeting groups and ratiometric responses have enabled greater insights to be gained into these cellular environments.[1,2] There is, however, a need to expand the current set of fluorescent probes available to allow for sensing of cellular environments in non-mammalian systems. These have relevance in a number of settings; as model systems for the study of human disease, as instigators of pathogenic disease or as organisms widely used in industry. Here we will report on our efforts to determine the suitability of our current probes for use in non-mammalian systems and to develop new fluorescent sensors for use detecting analytes relevant in these cellular environments.[3]



Confocal microscope image of *C. elegans* treated with FCR1

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T-158

Anthelmintic sesterterpenes from *Phyllospongia bergquistae*, and structure revision of phyllolactones A–D

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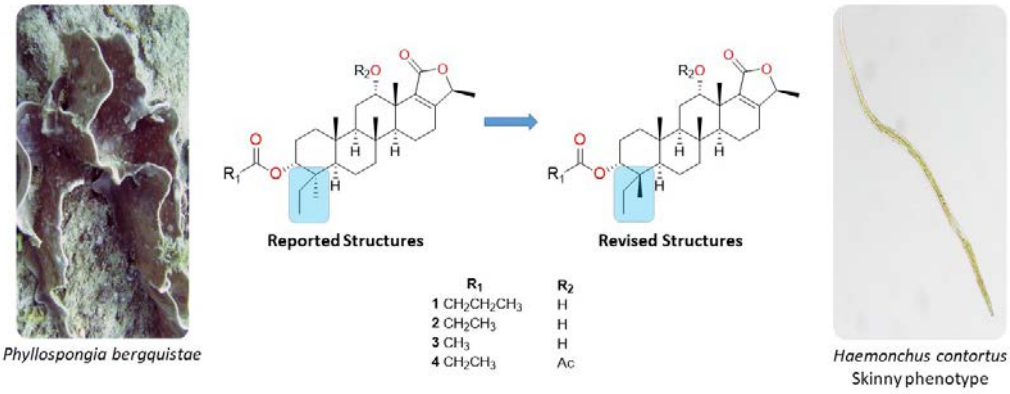
High-throughput screening of the NatureBank marine extract library (7,616 samples) identified an extract derived from the Australian marine sponge *Phyllospongia bergquistae* with activity against *Haemonchus contortus* (barber's pole worm) – an economically important parasitic nematode. Bioassay-guided fractionation of the CH_2Cl_2/MeOH extract from *P. bergquistae* led to the purification of four known bishomoscalarane sesterterpenes, phyllolactones A–D (**1**–**4**). The absolute configurations of phyllolactones B (**2**) and C (**3**) were determined by single-crystal X-ray diffraction analysis; literature and data analyses revealed the need for these chemical structures to be revised. All four compounds induced a lethal, "skinny" (*Skn*) phenotype in larvae of *H. contortus* at concentrations of between 5.3 µM and 10.1 µM. Phyllolactone C (**3**) was shown to be the most potent metabolite, inducing the *Skn* phenotype in 89.5% of larvae. These data indicate that the bishomoscalarane sesterterpene structural class warrants further investigation for nematocidal or nematostatic activity.



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T-161

Determination of the bioactive potential of sesame seeds from Australia

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The therapeutic and medicinal properties of sesame and its products may be attributed to the high levels of health-promoting compounds found in this crop. The key classes of bioactive compounds in sesame seeds are phenolics and lignans; however, there is limited information available about the level of these compounds in Australian-grown sesame. Twelve black sesame varieties were grown in controlled field trials under irrigated (I) and drought (D) conditions at Alton Downs (Central QLD) during spring season (middle November 2019) and harvested during autumn season (middle March 2020). Polar compounds were extracted from the sesame seeds using 90% methanol prior to determining the antioxidant activity of each extract using the ferric reducing antioxidant power (FRAP) assay. The total phenolic content (TPC) of the methanolic extracts was also determined. HPLC-DAD was used to profile sesame lignans present in the sesame neat extracts. The most prominent peaks found in the HPLC-DAD analysis were identified as sesamolin and sesamin. The TPC, FRAP, lignan contents obtained showed statistically significant difference between the varieties and between varieties grown in I and D conditions ($p<0.05$). Moreover, varieties 5 and 3 grown in D conditions showed the highest TPC and FRAP values. Whereas variety 2 grown in D conditions showed the highest sesamin and sesamolin content. Overall, there was a weak correlation evident between the FRAP and TPC values obtained ($R^2= 0.5434$) for the samples analysed. The data obtained in this study is also comparable with those reported in literature. Thus, there is great potential for the investment and expansion of Australian-grown sesame as health benefitting compound in the Australian market.

T-162

Developing fragment-bearing peptidomimetics as inhibitors of ALT-positive osteosarcomas

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Osteosarcoma is the most common type of primary bone malignancy that arises during the adolescent growth spurt. With no targeted therapies available, a third of adolescent osteosarcoma patients succumb within five years and the burden of disease on survivors is significant.[1] A potential strategy for treating osteosarcoma is to target the cellular mechanism known as Alternative Lengthening of Telomeres (ALT),[2] which is required by >60% of osteosarcomas for continued growth.[3] There is no evidence that ALT activity occurs in healthy cells, offering a significant window for therapeutic intervention.

The ALT pathway is mediated by two interacting protein partners: FANCM and RMI1/2. Genetic disruption of FANCM-RMI leads to ALT-specific telomere dysfunction and cell death.[4] The FANCM-binding pocket on RMI1/2 presents an ideal target for a medicinal chemistry approach: the interaction is driven a 12-mer peptide from the FANCM MM2 domain,[5] providing a site for competitive targeting that is structurally defined and ready for novel inhibitor design.

In this presentation, I will report our latest investigations into developing peptide-based inhibitors against the FAMCM-RMI interaction. We have validated two fragment binders to the RMI1/2 subcomplex from a 1200-member library screen and two cyclic-peptide binders from an mRNA display screen.[6] We have then systematically designed over 50 fragment analogues to obtain structure-activity relationships, analysing binding by SPR in combination with computational molecular docking.[7] Current efforts focused on combining these approaches to ultimately develop novel lead compounds with translational potential for osteosarcoma treatment.

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T-163

Trehalulose formation in Australian stingless bees: an intermolecular isomerization of sucrose

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Trehalulose, a rare sucrose isomer, is the dominant bioactive sugar in stingless bee honey (Meliponini). We have previously reported on animal experiments in which sugar solutions were fed to confined *Tetragonula carbonaria* stingless bees and determined that the trehalulose in honey was produced by isomerization of sucrose by these stingless bees (Hungerford, 2021). However, the details of this formation were still unknown, particularly whether the process related to a microbial transformation, or a bee produced enzyme. In this study, we investigate formation of trehalulose from sucrose by different stingless bee parts: head, thorax and abdomen. In addition, we utilised ^{13}C- labelled sucrose to trace the monosaccharide moieties throughout the process.

The experiments were conducted by incubating sugar solutions with macerated worker *Tetragonula carbonaria* body parts (head, thorax and abdomen). For the incubated sugar solutions, sucrose solution (50:50 sucrose/water w/w) and 1:1 glucose/fructose solution (25:25:50 glucose/fructose/water w/w/w) were used for comparing relative proficiency of each bee part. Further a 1:1 mixed ^{13}C-labelled/unlabelled sucrose solution (37.5:37.5:25 $^{13}C_{12}$-sucrose/$^{12}C_{12}$-sucrose/water w/w/w) was incubated with macerated bee heads to reveal the isomerization mechanism. The sugar composition of solutions after bee part incubation was quantified through ion chromatography.

The desired sucrose isomerization occurred predominately in head samples, with trehalulose constituting 76.2-80.0% of total detected sugar and with co-formation of the trisaccharide erlose as a minor product. By contrast, sucrose hydrolysis occurred in abdomen samples, with glucose and fructose observed as 49.4-51.7% and 48.3-50.6% respectively of total detected sugar. Incubating 1:1 glucose/fructose solution with bee parts did not result in trehalulose formation. By tracing the ^{13}C labelled monosaccharide moieties through the isomerization from sucrose to trehalulose and the formation of erlose, for the first time, the mechanism was established as an enzymatic intermolecular displacement reaction. Sucrose acts as glucose donor giving a β-D-glucosyl enzyme intermediate with fructose release (Figure 1) as demonstrated by mixed isotope products. Glucosylation of fructose or sucrose forms trehalulose (favourable) or erlose (less favourable), respectively. This study provided insight into the molecular mechanism of converting sucrose to trehalulose by stingless bees. It promotes further research on the trehalulose catalytic enzyme in stingless bees and highlights the potential biosynthetic capacity of this enzyme.

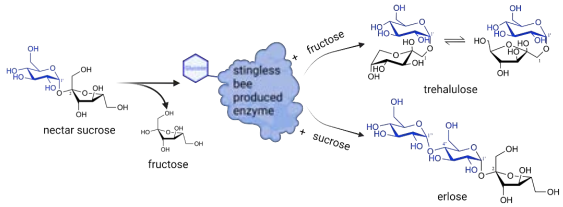

Figure 1: The proposed trehalulose formation mechanism by stingless bees

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T-164

Investigating the chemistry of Australian ginger

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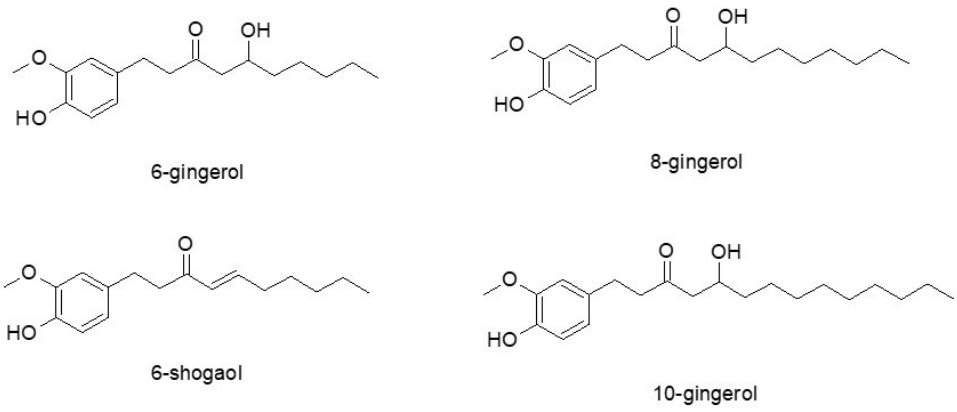
Ginger (*Zingiber officinale*) is best known for its pungent, aromatic flavour; however, it also provides numerous health benefits. It is currently a niche crop in Australia, with an annual farmgate value of AUD $32 million. Consequently, there has been limited research performed on the chemistry of Australian ginger to date. This study aimed to provide more insight into the quality of Australian-grown ginger and its changes during storage and processing.

Firstly, a sample of fresh ginger was subjected to oven drying and the changes in pungent constituents (gingerols and shogaols) and volatile compounds quantified through HPLC-DAD and GC-MS, respectively. This confirmed that 6-shogaol was virtually absent in fresh ginger, but was produced through the dehydration of 6-gingerol under moderately high temperatures (60°C). The major pungent compounds in the dried ginger were isolated using semi-preparative HPLC. The 6-gingerol fraction showing the highest antioxidant activity, suggesting that this compound is the major contributor to the antioxidant properties of ginger.

Subsequent work was performed on dried, processing-grade ginger from a commercial supplier (dried under more mild conditions; ~35-40°C). An in-depth investigation into volatile composition was conducted on three ginger samples stored for varying periods (1, 2 or 3 years), with a total of 100 volatile compounds identified. Additionally, the pungent constituents were quantified in 100 ginger samples from 2 seasons and 6 different growers. This revealed a significant level of variation by both season and grower. However, the 6-gingerol to 6-shogaol ratio was relatively consistent between different conditions, suggesting that zeroth-order reaction kinetics could potentially govern the gingerol-to-shogaol conversion reaction under mild dehydration conditions. This remains an area of ongoing investigation.

Finally, the prediction of the concentrations of pungent compounds was investigated using several rapid analytical techniques, including near-infrared spectroscopy, mid-infrared spectroscopy and hyperspectral imaging. Several of these techniques showed potential for estimating the gingerol and shogaol contents, as well as predicting the ratio of gingerol-to-shogaol in the dried ginger samples. This could aid in quality assurance of ginger processing industries.



The structures of the four main pungent compounds present in dried ginger

T-165

Cubane as a Scaffold for Fragment Library Construction

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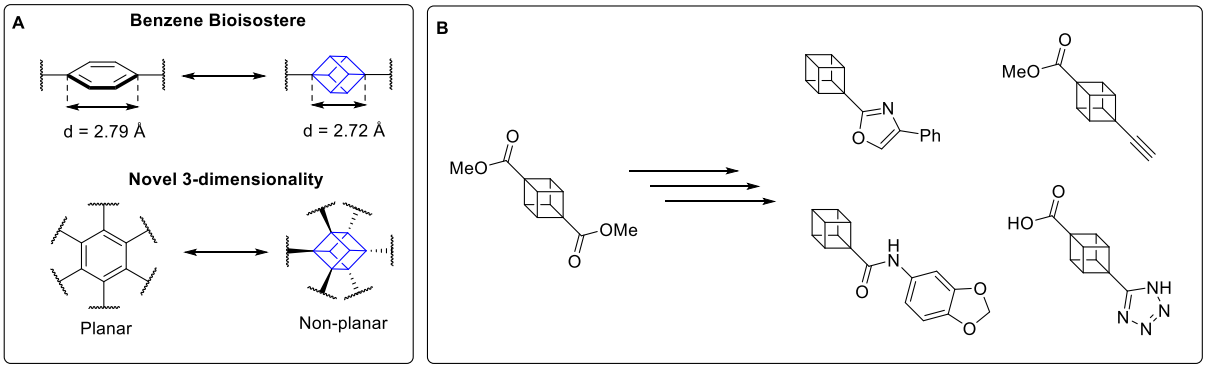
Much innovation in drug discovery has been built on improved synthetic manipulation of an increasing number of hydrocarbon scaffolds that has provided a large source of structurally-diverse molecules with unique chemical and physical properties.[1] Furthermore, a recent push in pharmaceutical sciences to escape from the "flatland" of planar aromatic molecules has assisted the privileged structure status of caged hydrocarbons for their novel three-dimensionality.[2] One such hydrocarbon, cubane, has gained much contemporary research interest due to its remarkable stability, low toxicity and its validation as a bioisostere of benzene.[3] More importantly, the potential to functionalise cubane at each carbon atom provides an opportunity to generate complex three-dimensional molecules with unique biological activities.[4]

Fragment-based drug discovery methodology allows the identification of low molecular weight ligands that can be elaborated into potent, drug-like molecules.[5] Compared to high-throughput screening, even modestly-sized compound libraries can be used to develop leads provided that broad structural and chemical space is represented. To accelerate the incorporation of the cubane scaffold into the drug discovery pipeline, a library of mono-/poly-substituted fragment-like compounds bearing the cubane moiety is to be constructed. The syntheses of several novel cubane fragments will be described.



(A) Geometric comparison of cubane and benzene highlighting bioisosteric relationship and three-dimensionality. (B) Condensed scheme for the synthesis of several novel cubane fragments

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T-166

Characterisation of 6-deoxy-6-sulfofructose-1-phosphate aldolase

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Sulfoquinovose (SQ) is sulfonated sugar analogous to glucose with a sulfonate group at C6. SQ is one of the most abundant organosulfur species in environment and is produced by photosynthetic organisms.[1] The breakdown of SQ is achieved by bacteria through the pathways of sulfoglycolysis. Degradation of SQ by sulfoglycolysis in *E. coli* involves series of enzymes for conversion of SQ via SFP to dihydroxyacetone phosphate (DHAP) and dihydroxypropane sulfonate (DHPS). In *E. coli*, scission of the 6-carbon chain of SFP into DHAP and DHPS is catalysed by the class I aldolase YihT, The characterisation of this class I aldolase enzyme showed that it involves a Schiff base mechanism.[2]

Bioinformatics analysis has identified a putative class II aldolase (which are typically characterised as metalloenzymes) in *Yersinia aldovae* and *Hafnia paralvei*. This presentation will focus on the kinetics and structural characterisation of these class II aldolases.

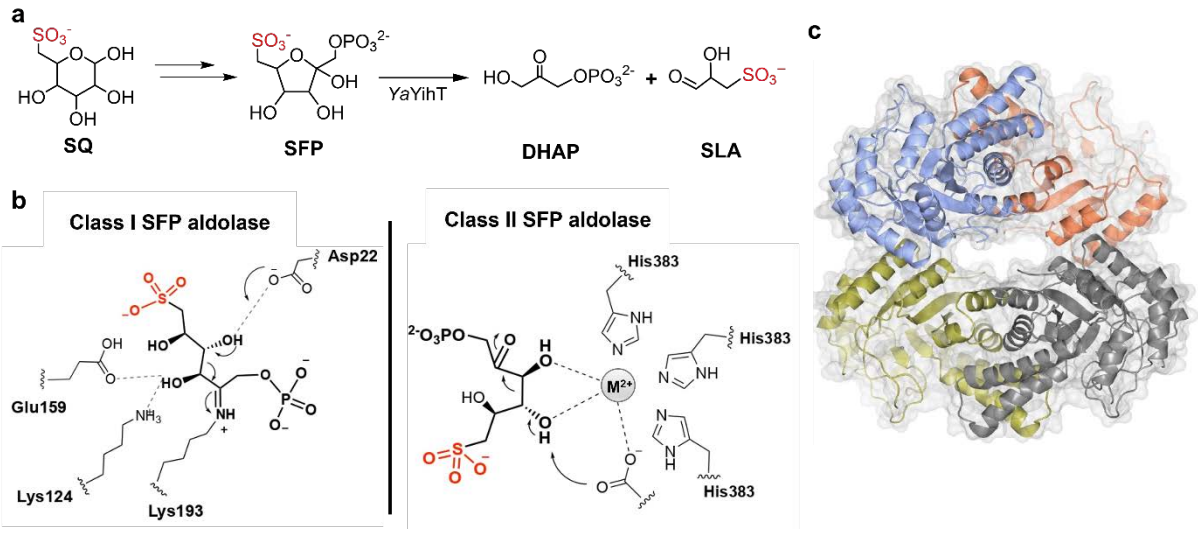

Figure 1. a) Conversion of SQ to SFP, the aldolase catalysed conversion of SFP to DHAP and SLA. b) mechanism for class I and class II aldolases c) crystal structure of class II aldolase from *Yersinia aldovae*.

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T-167

Development of Fluorescent Tools for the Study of Amyloids

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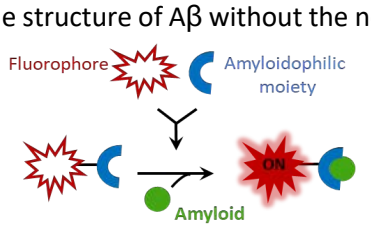
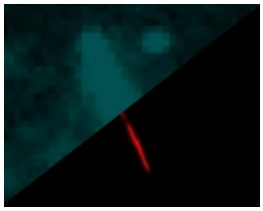
Amyloids are protein aggregates that form fibrils displaying a characteristic cross-β structure. [1] Amyloids can be comprised of various different proteins or fragments of proteins, and are implicated in a wide range of neurodegenerative conditions, most notably Alzheimer's and Parkinson's diseases. [2-4] While the appearance of amyloid fibrils is commonly used as a diagnostic marker, it is not yet entirely clear what their role is in the progression of disease. To better improve our understanding of amyloids, and to enable early diagnosis and treatment it is important to understand these structures at the nanoscale.

The challenges associated with studying amyloid are many. Structurally, amyloids and their pre-fibrillar oligomers can be heterogeneous in structure and size. [5] In addition, suitable techniques for studying amyloids are limited. Techniques such as fluorescence microscopy, PET and SPECT [6] do not give the resolution necessary for structural studies. On the other hand, methods which can give adequate structural information, such as AFM, TEM or X-ray crystallography cannot be performed in living cells and often require cumbersome sample preparation. The limitations inherent in these techniques can be avoided by developing fluorescent amyloid sensors that are compatible with super-resolution microscopy techniques – specifically dSTORM (**d**irect **s**tochastic **o**ptical **r**econstruction **m**icroscopy). In this presentation, I will discuss our recent work on the design and development of fluorescent amyloid sensors. The fluorescence turn-on feature of the probes offers direct visualisation of specific amyloids such as amyloid-beta (Aβ) against a range of aggregation-prone proteins including tau, insulin and RIPK3 (receptor interacting protein kinase) fibrils. Our sensor exhibits specificity towards amyloid-beta (Aβ) against a range of amyloids including tau, insulin and RIPK3 (receptor interacting protein kinase) fibrils. In addition, the sensor exhibits photoswitching properties facilitating its use in super-resolution imaging of amyloid fibrils, allowing the visualisation of the nanoscale structure of Aβ without the need for extensive sample preparation.





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T-168

Synthesis and evaluation of sialyltransferase inhibitors

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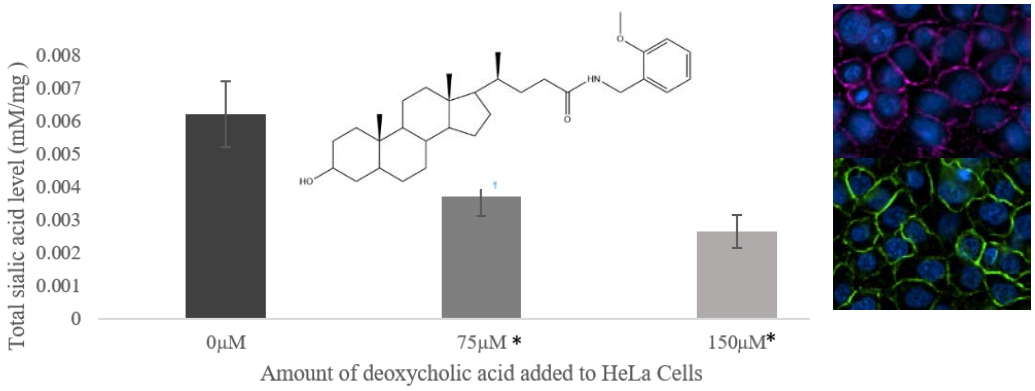
Sialyltransferases catalyse the transfer of sialic acids to the cell surface and hence participate in key biophysiological processes in human health and diseases, such as cancer. Enhanced tumour progression due to the overexpression of cell surface sialic acids in various cancers underlines the importance of sialyltransferases as a potent therapeutic target in anti-cancer drug development. This research aims to design and synthesise potent sialyltransferase inhibitors and evaluate the extent of sialylation caused by the proposed compounds.

Lithocholic acids are known to inhibit sialyltransferase activity, hence potent screening compounds were pharmacokinetically designed. A library of lithocholic acid derivatives were designed and synthesised. Multiple approaches were attempted to evaluate the extent of sialyltransferase inhibition activity of proposed compounds. These approaches include 1) direct quantification of the total sialic acids with high performance liquid chromatography (HPLC), 2) detection and visualisation of sialic acids via flow cytometry and 3) fluorometric analysis with commercial assay kits.

An efficient method was developed using a reverse-phase ion-pairing HPLC-UV using triisopropanolamine as the ion-pairing reagent with a C18 column.[1] By applying the proposed method, a statistically significant decrease was observed for both HeLa and HuCCT1 cell lines with the application of deoxycholic acid – a known sialyltransferase inhibitor. Hence, the proposed method seems promisingly applicable to evaluate the effectiveness of proposed compounds. Furthermore, the compounds were evaluated via flowcytometry. Maakia amurensis lectin was used to detect α2,3-sialyltransfersae activity and sambucus nigra lectin was used to detect α2,6-sialyltransfersae activity.

The HPLC method would be used as the 1st screen to observe a decrease in overall sialylation, followed by flowcytometry analysis to tell us which specific linkage is being affected. Finally, the assay kit will confirm if the inhibition is specifically due to the specific subtype of the investigated sialyltransferase enzyme. This research may allow a new way to explore sialylation of cancer cells and provide positive insight into drug development for cancer treatment.



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T-169

Flavonoid-Nitroxide Hybrid Antioxidants

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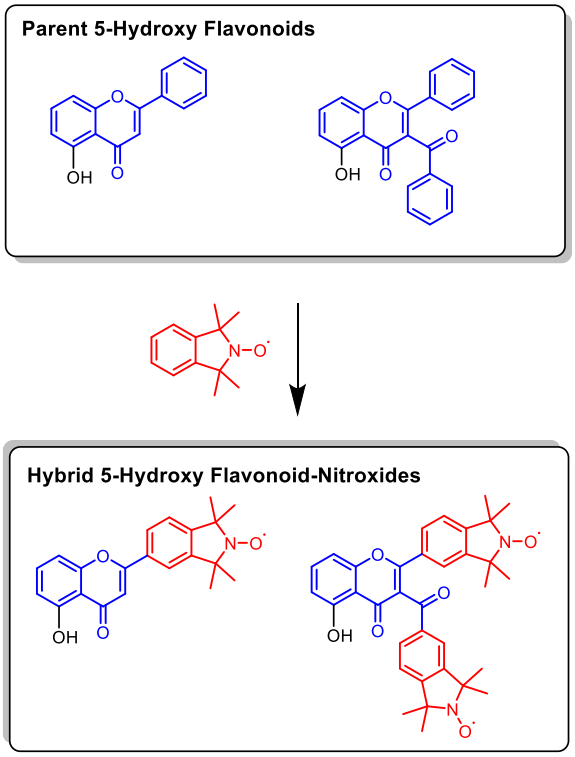
Within all cells, the redox system operates as the backbone of all cellular processes. The balance of cell life and cell death is mediated by the production and elimination of reactive oxygen species (ROS). Various diseases, such as neurodegenerative diseases, have been linked to a high concentration of ROS, known as a state of oxidative stress. Various antioxidant molecules have been investigated to alleviate oxidative stress. Yet, the discovery of more potent antioxidant molecules is still necessary. It is hypothesised that a single molecule with the ability to undergo multiple antioxidant reaction pathways may provide additional potency. Flavonoids, a well-known class of plant derived antioxidant molecules, as well as nitroxides, a stable free radical functionality, are explored as novel antioxidant therapeutics through the synthetic strategy of molecular hybridisation. Preliminary antioxidant assays of cyclic voltammetry and peroxyl radical scavenging show the effect of the hybridisation strategy on the antioxidant potential.



T-170

Sulfolactaldehyde dehydrogenase (GabD) of *Rhizobium leguminosarum:* Kinetic and structural analysis

Jinling Li,[a] Mahima Sharma,[b] Amani Alhifthi,[a] Gideon J. Davies,[b] Spencer J. Williams[a]
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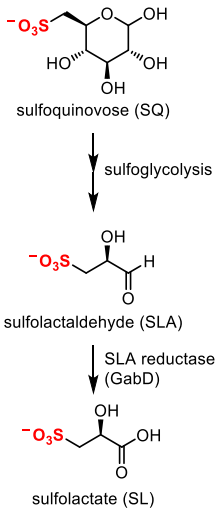
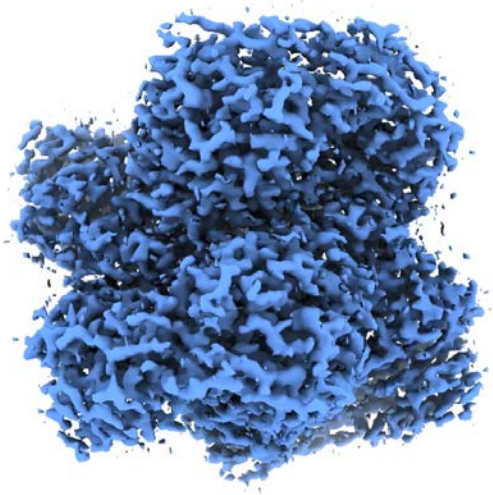
Sulfolactate (SL) is a product of sulfoquinovose (SQ) degradation through the pathways of sulfoglycolysis. It functions as a metabolic 'currency' of sulfur, supporting cross-feeding of diverse bacterial communities. SQ is produced by phototrophic organisms on a grand scale, estimated at 10 gigatons per year, meaning that as a degradation product of SQ, SL is also likely to be of major significance in the global biogeochemical sulfur cycle.

Rhizobium leguminosarum bv. trifolii SRDI565 (*Rl*-SRDI565) encodes within its genome a putative sulfoglycolytic Entner-Douderoff (sulfo-ED) gene cluster that includes a gene annotated as sulfolactaldehyde (SLA) dehydrogenase (*Rl*GabD) that putatively reduces SLA to SL.[1]

In this study, we report a kinetic and structural study of *Rl*GabD showing it to be an SLA dehydrogenase. We measure Michaelis-Menten kinetics and show its ability to use both NAD^+/$NADP^+$ as cofactors, as well as its sensitivity to inhibition by modified NADH analogues. We determine its kinetic reaction order and show that it follows an equilibrium random mechanism in the forward direction. Surprisingly, we show that *Rl*GabD possesses weak but measurable activity on the structurally related cellular metabolite, glyceraldehyde 3-phosphate (GAP). Finally, we report the 3D structure of SLA dehydrogenase using CryoEM and define its quaternary structure. These structures provide a basis for understanding the dual NAD^+/$NADP^+$ activity of this enzyme.





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T-171

Family Amaryllidaceae plants for the source of Amaryllidaceae alkaloids

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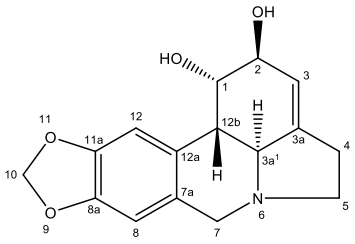
Over 600 Amaryllidaceae alkaloids have been isolated almost exclusively from family Amaryllidaceae, and hence the given name. The significance of the Amaryllidacea alkaloids as the important heterocyclic alkaloid class is demonstrated by galanthamine (or galantamine), which was one of early drugs used clinically to treat mild to moderate severity of Alzheimer's disease and is still being used today, under the brand names of Reminyl™ (2001) and Razadyne™ (2004) approved by FDA.

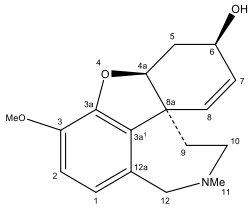
The Amaryllidaceae family has over 1191 species in 81 genera based on the National Centre for Biotechnology Information (NCBI) Taxonomy Brower. The family consists of three subfamilies of Agapanthoideae (1 genus, 5 species), Allioideae (12 genera, 617 species) and Amaryllidoideae (68 genera, 569 species). We used a combination of key words search in the Chemical Abstract Service (CAS) SciFinder-n platform for the occurrence of Amaryllidaceous alkaloids, with a focus on the isolation and detection in the subfamilies, genera and species searched.

Results show that lycorine was a ubiquitous Amaryllidaceae alkaloid and galanthamine has been isolated from the genera *Cyrtanthus, Galanthus, Leucojum, Lycoris, Narcissus, Ungernia, Chlidanthus, Crinum, Eucharis, Eustephia, Pancratium* and *Phaedranassa*. 37 genera contain Amaryllidaceae alkaloids that have been isolated and reported in literature and they are from 68 genera of subfamily Amaryllidoideae. Among the 68 genera, 6 genera are reported to have detected the Amaryllidaeae alkaloids and 25 genera have not been reported. Further studies from the Amaryllidaceae family as the source of for the Amaryllidaceae alkaloids are warranted.

Drug discovery from the Amaryllidaceae alkaloids is discussed and appreciated, for example as anti-inflammatory agents[1].



Lycorine



Galanthamine

Acknowledgment

The authors are grateful for accessing the repository and collection of over 700 Amaryllidaceae alkaloid samples provided by Dr Henry M. Fales, NHLBI Laboratory of Applied MS, NIH, Bethesda, to Professor Martin G. Banwell at the Research School of Chemistry, Australian National University, Canberra.

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T-172

Developing cyclooctatetraene (COT) as a biomotif in vitamin K antagonists

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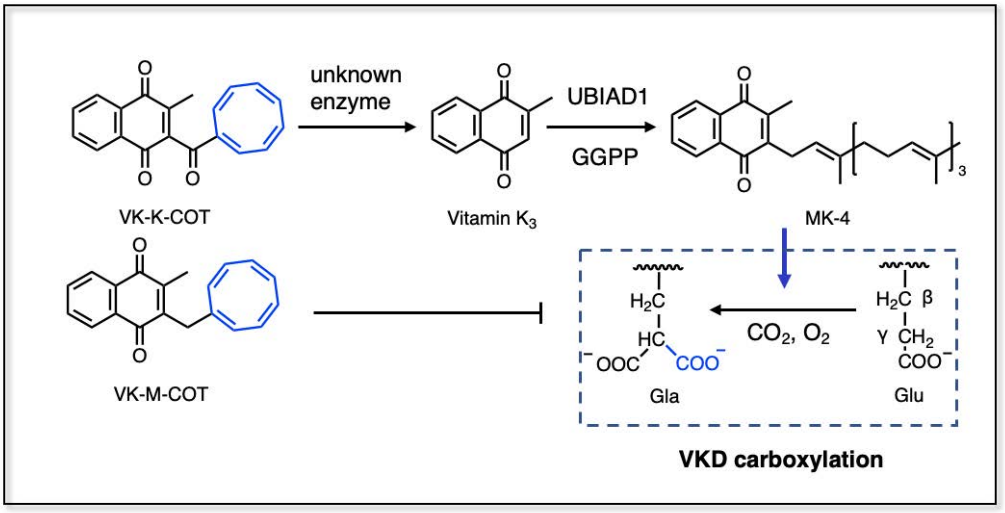
Coumarin-derived vitamin K antagonists (VKAs, e.g., warfarin), which target vitamin K epoxide reductase (VKOR), are clinically used for anticoagulation therapy. However, the dose requirement of VKAs is susceptible to the genetic variations of VKOR which lead to a limited therapeutic index. Recently, we reported that replacing a phenyl group with cyclooctatetraene (COT) in warfarin significantly increased its tolerance to naturally occurring VKOR mutations, but it still had a 25-fold difference in activity. To achieve the desirable anticoagulation effects with fixed doses of VAKs, COT-Vitamin K_3 was further explored. It was discovered that COT-Vitamin K_3 inhibited both VKOR and gamma-glutamyl carboxylase (GGCX) in the vitamin K redox cycle and it was tolerant of genetic variations of VKOR whose warfarin resistance varied over 400-fold. Interestingly, replacing the methylene group with carbonyl group at 3-positon of sidechain reversed the anticoagulation effect of COT-Vitamin K_3. This reverse resulted from the cleavage of sidechain and conversion to menaquinone-4 (MK-4) by the prenyltransferase UBIAD 1.



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T-173

Development of Selective p38γ activators for the treatment of Alzheimer's Disease

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Dementia represents one of the greatest medical challenges of the 21st century with an estimated financial burden of over $1 trillion USD globally.[1] Alzheimer's disease (AD) accounts for approximately 70% of all cases of dementia, with cases of AD having more than doubled in the past 7 years.[1] Symptoms include memory loss, an inability to process questions and instructions and a deterioration of social skills. Current therapeutic strategies for AD are limited to providing temporary relief from symptoms, however no disease-modifying treatments exist. AD is characterised by the presence of amyloid β (Aβ) plaques and neurofibrillary tangles (NFTs) of tau protein. Due to several failed clinical trials targeting Aβ, research into tau pathology has accelerated in recent years.[2] When tau is hyperphosphorylated it becomes prone to aggregation, resulting in the formation of tau oligomers and NFTs, eventually leading to neuronal cell death.[3,4] It was recently discovered that site specific phosphorylation of tau by mitogen activated protein kinase p38γ is neuroprotective in mouse models of AD.[5] Work by Cappelli et al. has suggested that exchanging substituents of the 2- and 3- positions of 5-membered heterocycles may be able to convert p38 inhibitors into activators.[6] In order to investigate this hypothesis further, a small library of poly-substituted pyrroles based on existing p38 inhibitors has been synthesised in an effort to synthesise selective p38γ activators.

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T-174

Bioassay-guided fractionation protocol for determining novel bioactive compounds in selected Australian flora

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A large variety of unique and distinct flora of Australia have developed exceptional survival methods and phytochemicals and hence may provide a significant avenue for new drug discovery. Several literatures have identified some native Australian plants as having high therapeutic potential. Despite this, the bioactive compounds of some of these species are yet to be discovered. In the current study methanolic extracts of plants namely *Pittosporum angustifolium* (Gumbi gumbi), *Terminalia ferdinandiana* (Kakadu plum), *Cupaniopsis anacardioides* (Tuckeroo) and *Syzygium australe* (Bush cherry) exhibited high phenolic content and antioxidant capacity and hence were selected for the bioassay guided fractionation protocol. The protocol developed is outlined in Figure 1.

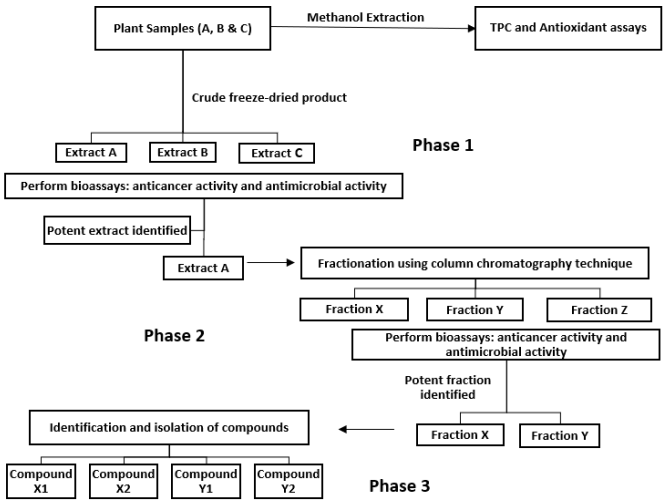

Figure 1: The developed bioassay guided fractionation protocol.

Upon completing Phase 1 of the protocol, *P. angustifolium* and *T. ferdinandiana* were identified as most promising plants with potentially novel bioactive compound(s). Although *P. angustifolium* was found to have the highest apoptotic effect against HeLa and HT29 cancer cell lines, no antibacterial activity against common human pathogens: *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhimurium* were observed. On the contrary *T. ferdinandiana* extracts have displayed some antibacterial activity against the tested pathogens and only its seed extracts have shown some apoptotic activity against the cancer lines tested. We are currently in phase 2 of the protocol and have successfully fractionated freeze dried methanolic extracts of *P. angustifolium* using a G1364F 1260 Infinity II Analytical Fraction Collector and have obtained five fractions. The five fractions were selected based on the chemical activity regions on the phenolic profile chromatogram obtained using High-Performance Liquid Chromatography (HPLC). We postulate that the bioassay screening of the five fractions will enable further separation of the most bioactive fraction and ultimately phase 3 of the protocol will lead to the isolation and identification of a novel bioactive compound in *P. aungustifolium*. Thus far the developed protocol has shown to be robust and effective in screening plants with high phenolic and antioxidant capacity and hence can set precedence for future screening of native Australian plants for novel bioactive compound(s).

T-176

Boron-based fluorophores for bio-imaging applications

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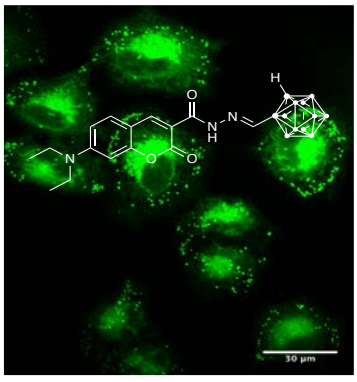
Recent advances in fluorescence imaging involving near-infrared (NIR) light have enabled greater tissue penetration depth, high spatial resolution, reduced photon scattering, and minimal interference from tissue autofluorescence.[1] The high sensitivity, selectivity and non-invasive nature of NIR imaging has provided visualisation of tissues and organs, as well as unique insights into complex biological processes.[2] Hence, NIR fluorophores are viable candidates for biological imaging and sensing applications. A family of novel boronated coumarin fluorophores, containing a terminal boronate ester, boronic acid, and *closo*-carboranyl moieties, were successfully synthesised and characterised in this work.[3] All compounds displayed a significant bathochromic shift in the excitation and emission maxima when compared to the parent coumarin. Confocal microscopy studies using lung cancer cells demonstrated distinctive intra-cellular distributions of selected fluorophores. In particular, the apparent selectivity of the *closo*-carborane dyes towards lipid droplets was prevalent, and hence these fluorescent molecules may be adapted for use as an alternative to the commonly used lipid stain Nile Red. Furthermore, a change in the nature of the boron moiety leads to dramatic changes in the intra-cellular distribution of the fluorophores, *e.g.* the boronic acid derivatives show excellent localisation within the endoplasmic reticulum (ER). A rational design strategy for developing idealised photophysical and photochemical properties of a new class of xanthene-based amino-functionalised NIR fluorophores has also been implemented through extensive consideration of structure-photophysical property relationships. The key results of this work will be presented, showcasing the versatility of boron in new fluorescent molecules.



Confocal microscope image of A549 cells treated with *closo*-1,2-carboranyl-coumarin, showing coumarin fluorescence (λ_{ex} = 458 nm, λ_{em} = 468-568 nm).

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T-177

Defining steric requirements of cannabinoid receptor activation using synthetic cannabinoid receptor agonists

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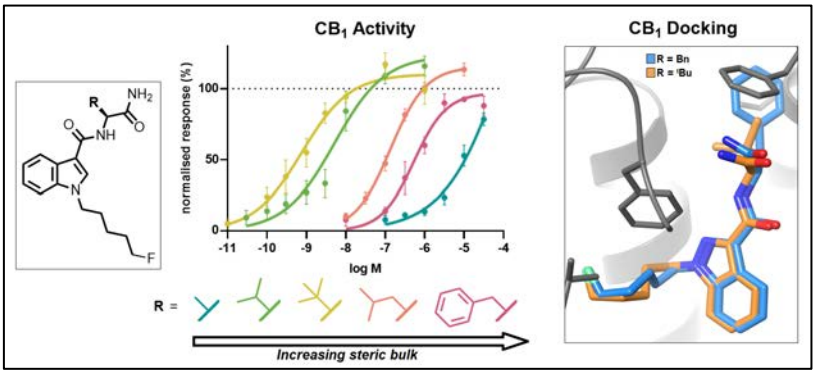
Synthetic cannabinoid receptor agonists (SCRAs) are a diverse class of new psychoactive substances (NPS). Recently detected SCRAs commonly comprise of an N-alkylated indole, indazole or 7-azaindole scaffold bearing amide-linked pendant amino acid groups, inspired by a historical Pfizer patent.[1] To explore the contribution of the amino acid side-chain to the cannabinoid pharmacology of SCRA NPS, a systematic library of side-chain modified SCRAs was prepared based on the detections of amino acid derivatives such as 5F-AB-PINACA, PX-1, PX-2, and NNL-1.[2] *In vitro* binding affinities and functional activities at cannabinoid type 1 and 2 receptors (CB_1 and CB_2) were determined for all library members.

While some were minimally active (**9**, **10**, **20**), most compounds studied showed high to moderate affinity and potency (Ki = 0.32–5129 nM, EC50 = 0.24–529 nM), with clear structure-activity relationships emerging. Affinity and potency at CB_1 changed as a function of both the heterocyclic core and the pendant amino acid side-chain. Ensemble docking at CB_1 revealed a clear steric basis for observed SAR trends. *In vivo* radiobiotelemetry studies found that, despite both having been detected in recreational drug markets, both PX-1 and PX-2 fail to induce centrally CB_1-mediated effects (e.g. hypothermia) in mice. Together, these data provide valuable insights regarding structural contributions to the cannabimimetic profiles of the compounds studied and other SCRA NPS.



Summary of structure-activity relationship.

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T-178

Kinetic Modelling of Coacervation for Proto-Ribosome Peptide Synthesis

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The most fundamental biochemical reaction, necessary for all life, is the synthesis of proteins. Biological protein synthesis is catalysed by the ribosome, a cellular machine consisting of RNA and proteins. Coacervation is a ubiquitous cellular process and has been shown to occur when non-coding RNA in the cell interacts with intrinsically disordered proteins to undergo liquid-liquid phase separation[1]. The primary benefit of liquid-liquid phase separation is the ability of chemical species to condense into supramolecular compartments, while maintaining the benefits of solvent interactions in the liquid phase. Recent developments in liquid-liquid phase separation research, has led to the discovery of active coacervates[2], capable of non-enzymatic catalysis which can potentially be harnessed to induce non-enzymatic synthesis of proteins as a model proto-ribosome system.

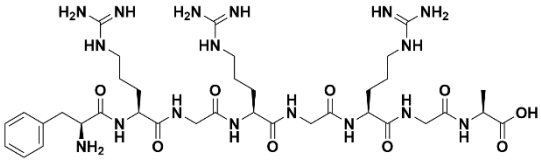

Figure 1: phe-arg-gly-arg-gly-arg-gly-ala

The initial step of this project is to improve the stability of the coacervates as monitored through kinetic studies. The RNA and peptides were designed to include more spaced out charged species resulting in the synthesis of phe-arg-gly-arg-gly-arg-gly-ala (FRGRGRGA, Figure 1). Experiments were performed with poly-uracil polymeric RNA as a control, with current work being undertaken with two different RNA strands: GUCAAGCCA (G = guanine, U = uracil, C =cytosine and A = adenine) as a mixed strand, and decameric-uracil (10-U). Initial kinetic modelling (Figure 2) showed the stability of coacervate formation and decay was dependent on a combination of pH, addition order and mixing ratio. In general, the systems saw greater initial turbidity with the addition of RNA first. With a lower pH, there was an overall improvement in stability. The mixing ratio played a key role in determining the formation of coacervates, as turbidity great enough to indicate liquid-liquid phase separation was not observed until equal parts of peptide and RNA were mixed (irrespective of mixing order) and was only sustained as the addition of peptide exceeded the quantity of RNA. The only observed exception to this observation was at pH 4, when the RNA was five times the amount of peptide, the coacervation exceeded the coacervation observed in other systems. However, compared to the first order decay exhibited in the other coacervation decay systems, the 5(R):1(P) – pH 4 system underwent a two-stage decay process and reached the dissolution point more rapidly than the other coacervate systems, suggesting pH is important in driving the kinetics of the system

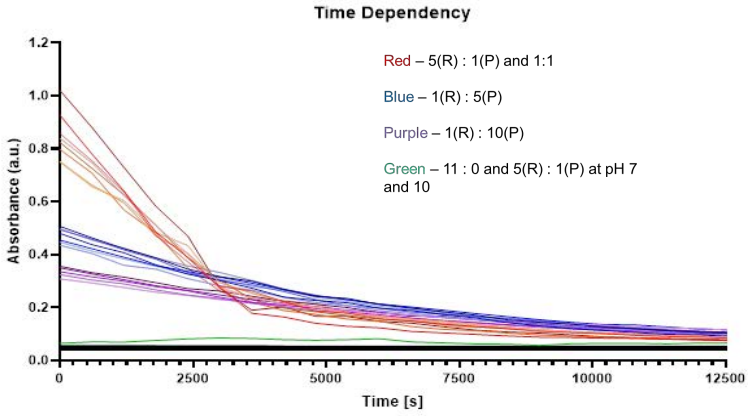

Figure 2: Turbidity measurements performed on a TECAN plate reader, monitoring the long-term coalescence of coacervate microdroplets in solution. Samples of poly-U and FRGRGRGA were mixed together: 11:0, 1:10, 1:5, 1:1, 5:1, 10:1, 11:0; at pH's 4,7 and 10. The system was monitored for four hours.

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T-179

In-depth characterisation of *Naja nivea* venom using a multifaceted mass spectrometry approach

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Snakes possess extremely complex venoms consisting of a mixture of bioactive proteins and peptides. This complex mixture has evolved to allow snakes to efficiently immobilise, kill, and digest prey, and has been of interest to scientists for decades due to both the potential pharmacological significance and the envenomation of humans. In 2017, the World Health Organisation added snakebite envenomation to their list of neglected tropical diseases, highlighting the importance of research in this area. While antivenom treatment is readily available in developed countries, individuals in developing countries do not experience this luxury. Snakebite envenomation is responsible for more deaths per annum than any other neglected tropical disease due to the expense and instability of current antivenoms.

Our work utilised a traditional bottom-up proteomics approach to characterise the proteome of *Naja nivea*, a snake from South Africa classed as medically important due to the lethality of its venom and its tendency to enter human settlement. We have found that the venom proteome of *Naja nivea* contains proteins belonging to ten toxin families, the most abundant being three-finger toxins. In addition to this fundamental proteomic characterisation, we have investigated the presence of quaternary structures in *Naja nivea* venom using complimentary native, reduced, and denatured mass spectrometry experiments. We have reported the first evidence of both covalent and non-covalent quaternary structures in *Naja nivea* venom. This work will provide a starting point for new antivenom development, specifically targeting quaternary structures within venom that have been shown to exhibit greater toxicity than their tertiary counterparts.[1]

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T-181

Optimization of side activity of a clinical cancer drug towards dynamin

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Cancer is a disease caused by the uncontrolled proliferation of cells and has been identified as the cause of 9.9 million deaths in 2020, with 18 million new cases globally and is estimated to double by 2040.[1,2] In 2019, cancer was the leading cause of death in Australia – with almost 50,000 deaths and accounts for 7% of direct health system costs.[3,4] Despite this, the survival rates and quality of life of cancer patients have shown no significant progress over the past 5-decades. New targets and new approaches are required to address this growing burden.

Here we report the targeting of dynamin – a large multidomain GTPase enzyme and one of the two key proteins involved in endocytosis – towards developing anti-cancer drugs.[5,6] Through the careful use of synthesized compounds, it has been revealed how dynamin have non-endocytic roles in cancer, roles that can be harnessed for future development of anti-cancer therapies. In cancer, the two key roles of dynamin that can be targeted as shown by known dynamin inhibitors are the ability to cluster target receptors at the cell surface for antibody-dependent cellular cytotoxicity and the ability to inhibit cytokinesis at the mitosis phase which leads to apoptosis.[7,8]

Aside from developing wholly new strategies towards cancer treatment, this work also involves repurposing a current drug in the clinic. Given the high attrition rates, substantial costs and time requirements needed in drug discovery and development, drug repurposing has become an attractive and pragmatic approach for drug development because it involves the use of de-risked compounds and the potential of rapid clinical impact at a lower cost than *de novo* drug development.[9,10] The clinical drug and lead compound of this work – DC-01 – is a compound currently in the clinic as an ALK inhibitor and has shown to inhibit dynamin as well. By exploring the structure activity relationship and focusing towards increasing the off-targets effects towards dynamin by compound design and synthesis, we have produced a number of synthetic analogues of DC-01 that are predicted to impart selectivity and or specificity in their inhibition of dynamin and can be harnessed towards developing future cancer treatments.

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T-182

Optimization of phenylsulfonyl piperazines as antimalarials that block erythrocytic invasion

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Emerging resistance of the malaria parasite *P. falciparum* to gold standard artemisinin therapies has forced an urgent need to identify new antimalarials with novel mechanisms of action. The invasion of red blood cells by *Plasmodium* merozoites is key to the proliferation and survival of the malaria parasite therefore providing an attractive target for developing novel therapies.

A screen of the Medicines for Malaria Venture Pathogen Box employing transgenic *P. falciparum* parasites identified the phenylsulfonyl piperazine MMV020291 as a specific inhibitor of erythrocyte invasion.

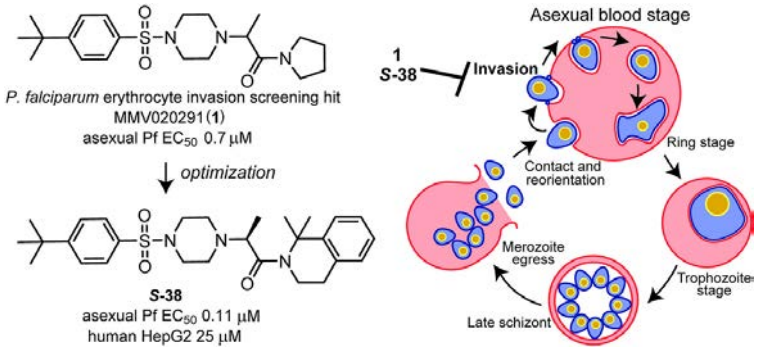
Our medicinal chemistry efforts to define the SAR of this racemic hit, not only resulted in optimised compounds with improved *P. falciparum* asexual stage potency, but also the discovery that the alpha-carbonyl *S*-methyl isomer is over 30 times more potent than the *R*-methyl isomer, indicating that the *S*-isomer is predominantly responsible for the antimalarial activity observed.[1]

The optimized compounds also possessed comparable activity against multidrug resistant strains of *P. falciparum* and blocks erythrocyte invasion consistent with the asexual activity observed.

MMV020291 *P. falciparum* resistant clones were generated and genome sequenced, with key mutations identified on the binding interface of *Pf* Actin. This protein has crucial roles in the motility of plasmodium parasites, erythrocyte cell entry and the parasites cell division (cytokinesis).

Cell imaging studies of parasites treated with MMV020291 analogues show the disruption of cell division in a similar manner to *Pf* Actin knockout parasites, providing strong evidence that MMV020291 prevents red blood cell invasion through interference with actin-1 dynamics in the malaria parasite.

This chemical optimization of MMV020291 and characterisation of its mechanism of action provides a potential new therapeutic target for the treatment of malaria.



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T-183

Identification of Potential Chemical Probes for Parkinson's Disease from Traditional Herbal Medicine

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Traditional Chinese medicine (TCM) has been around for thousands of years and is increasingly gaining popularity in the Western world as the alternative treatment for various complex disorders including the incurable neurodegenerative condition Parkinson's Disease (PD). One of many directions in recent studies of PD is utilizing phenotypic assay, or cytological profiling, to evaluate the phenotypic changes of PD-implicated cellular components in patient-derived olfactory neuroepithelial (hONS) cells, upon treating the cells with extracts or pure compounds. To obtain the small molecules for PD phenotypic study, *Ligusticum chuanxiong* Hort, a popular Chinese herbal medicine ingredient known to treat PD-like symptoms in TCM practices, was selected for chemical analysis. Fifty-three secondary metabolites, including six new compounds, were isolated from the ethanolic extract of *L. chuanxiong*; their structures were elucidated based on several spectroscopic techniques such as NMR, MS, FT-IR, and UV, as well as theoretical DFT calculations. Cytological profiling of the isolates against PD hONS cells revealed thirty-two compounds significantly perturbated the staining of several cellular organelles, with more than 1.5-fold change compared to the DMSO control, especially for that of early endosome, lysosome and LC3b. Given these biological compartments are closely related to PD pathogenesis, the results helped explain the traditional medicinal use of *L. chuanxiong* in the treatment of PD and suggested the hit compounds can be used as potential chemical probes to map the molecular mechanisms underlying PD, potentially leading to discovery of new therapeutic targets for PD.

T-186

Nonenzymatic DNA ligation within liposomes facilitated by surface acoustic waves

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Deoxyribose nucleic acid (DNA) is a molecule that contains all the genetic information required for an organism to function, and therefore has high applicability in biomedicine. With increasing interest in gene therapy and over 100 clinical trials being undertaken every year,[1] there are increasing numbers of new gene therapy drugs being approved.[2] However, synthesis of DNA becomes increasingly difficult as its length increases. Long oligonucleotides have reduced solubility[3] and increased potential replication error[4] resulting in very low yields. Current methods involve the synthesis of shorter oligonucleotide fragments which are then ligated to achieve the desired final sequence. This is a time and resource intensive process resulting in a final product that is highly expensive.[5]

Here, we aim to develop a new method to synthesise long strand DNA molecules via imidazolium based non-enzymatic ligation reactions, confined within a liposome. Imidazolium-functionalised nucleotides are actively loaded into the liposome throughout the reaction via surface acoustic waves. This ensured the reaction runs to completion, taking advantage of the increased kinetics due to confinement[6] without limiting the reaction due to poor passive loading. The reaction was monitored by measuring the fluorescence with intercalating dyes, as well as through polyacrylamide gel electrophoresis. The bioactivity of the completed product was then evaluated using the polynucleotide product in a polymerase chain reaction.

Current findings of this research confirmed that small molecules can be loaded into liposomes post-formation with the use of surface acoustic waves without releasing the previously encapsulated material. This is vital to maintain the confinement conditions of the reaction. While further research into optimising the reaction conditions is required, the results obtained show promise for a more efficient method for synthesising DNA. Our method will decrease production costs of biomedicine associated with the currently extremely low yield of long strand DNA molecules.

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T-187

Role of FG-nucleoporin hydrophobicity in nucleocytoplasmic transport: A Langevin dynamics simulation study

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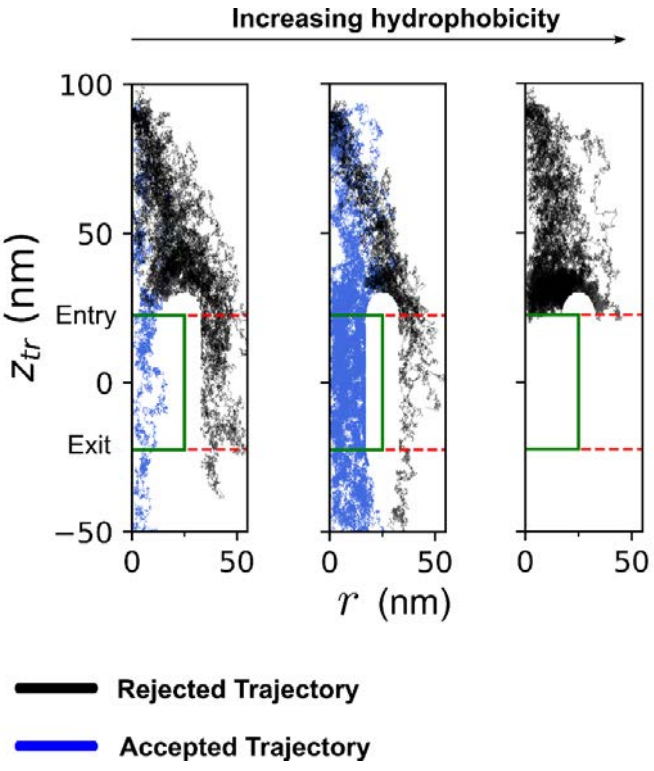
Bidirectional transport of proteins and mRNA across the nuclear envelope in eukaryotes occurs through the nuclear pore complex (NPC). NPC transport is characterised by both specificity and selectivity toward the cargo. These unique features of NPC transport are often ascribed to the presence of phenylalanine-glycine (FG) repeats in the intrinsically disordered FG-nucleoporins (FG-Nups) that line the central channel of NPC. FG repeats are hydrophobic in nature and are solely responsible for recognition of cargoes assigned for NPC transport. However, the role of FG-Nup hydrophobicity in determining the selectivity of the NPC is not properly understood. We used Langevin dynamics simulations and a coarse-grained polymer-based minimalistic model of the NPC to simulate protein transport through the NPC. Specifically, transport of both inert (no FG binding sites) and patchy (containing FG binding sites) spherical tracers was simulated for NPCs containing varying hydrophobic fractions of FG-Nups. Whereas, transport probabilities of inert tracers were nearly zero for any hydrophobic fraction, patchy tracers showed significant transport probability depending on the FG-Nup hydrophobicity. Specifically, our simulations showed that transport probabilities of patchy tracers were non-zero only in a certain range of hydrophobic fractions. Significantly, the relevant range of FG-fractions observed in the simulations matched very well with FG-fractions present in FG-Nups across diverse eukaryotic species, including *Saccharomyces cerevisiae* and *Homo Sapiens*. Thus, using a simple polymer-based model, our simulations were able to capture both specificity and selectivity of the NPC.



T-188

Targeted Protein Degradation in the context of Antimicrobial Discovery

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Antimicrobial resistance (AMR) is recognized as one of the top 10 global public health threats currently facing humanity**,** with the lack of novel antimicrobial agents in clinical development failing to combat rapidly emerging strains of multidrug resistant bacteria.[1] Targeted protein degradation is gaining traction as an innovative therapeutic strategy. The therapeutic utility of TPD is exemplified by PROteolysis TArgeting Chimeras (PROTACs), bifunctional molecules with dual affinity for a target protein and ubiquitin-proteasome (UPS) regulating E3 ubiquitin ligases. PROTAC's exhibit event-driven pharmacology, with ternary complex formation between protein components driving activity. This distinguishes TPD agents from inhibition-based agents, providing them with sustained activity against resistant disease pathologies, potent catalytic activity, and heightened target specificity. Currently, PROTAC agents treating resistant forms of cancer have exemplified these characteristics, leading to their successful advancement through Phase I and II clinical trials.[2]

A therapeutically viable strategy for achieving TPD in the context of antimicrobial drug discovery is yet to be conceived, however given their sustained activity against resistance mutations, applying TPD to design an antimicrobial agent could provide an effective response to the AMR crisis. Prokaryotic protein quality control is regulated by conserved families of protease complexes. Activity varies between families, providing each with unique core functions and regulation mechanisms. Generally, substrate selection is maintained via a hierarchical network utilizing degradation tags to signal misfolded substrates for proteolysis, using adaptor proteins to spatially align the substrate with the proteolytic complex and induce the conformational change necessary for proteolytic activation.[3]

This talk will present a developmental framework for new antimicrobial TPD agents. A variety of potential strategies for achieving targeted protein degradation in bacterial systems will be discussed, and particular focus will be given towards potential issues faced in validating each strategy.

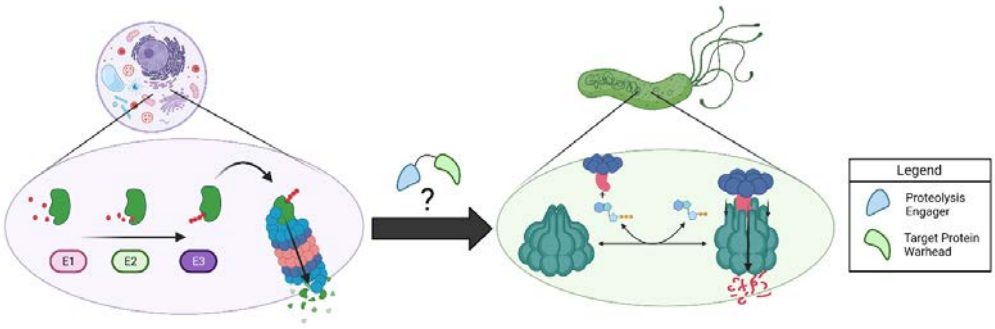

Figure: Adapting TPD strategies to bacterial proteolytic systems may produce novel antimicrobial agents to overcome the AMR crisis.

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T-189

Role of α-helices in β-sheet Rich Aggregate Formation in Amphibian Antimicrobial Peptide

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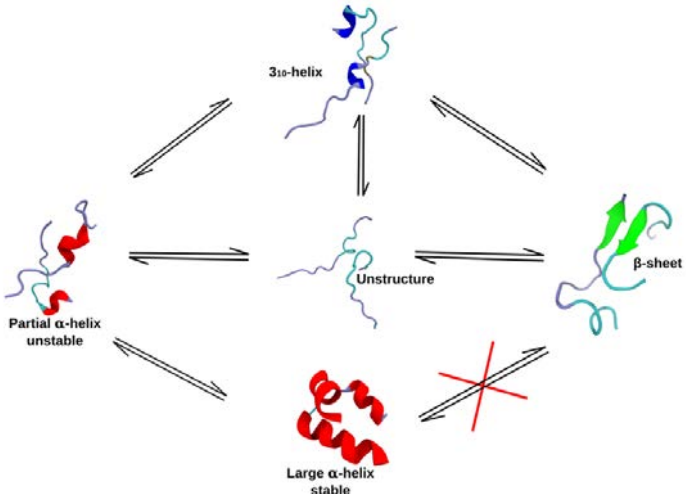

Figure 1: α-helix to β-sheet secondary structure transition pathway

Amyloid linked diseases, such as Alzheimer's, Parkinson's diseases remain devastating for patients and their families. However recent researchers and biopharmaceutical industries have become increasingly interested and turned their attention to understanding the origin of protein/peptide aggregation and amyloid formation mechanism. Here, we have used an amphibian-origin uperin peptide, that is both antimicrobial and amyloidogenic, to investigate the structural changes that lead to amyloid formation. These uperin peptides acquire a variety of secondary structural changes leading to self-assembly and aggregation into amyloid-rich fibrils under physiological conditions. Microsecond time-scale molecular dynamics (MD) simulations reveal an important role of the helical intermediates leading to beta-sheet rich aggregates. We show that unstable partial alpha-helical peptides play a key role in beta-sheet rich aggregation processes. Uperin peptides, with partial helical structures, aggregate to form small clusters via hydrophobic interactions in the initial stages of aggregation. This leads to an increase in the local concentration which triggers an alpha-helix to beta-sheet transition in these aggregates. Whereas, electrostatic interactions between aspartic acid (4th position) and arginine (7th position) are responsible for the initial helix formation, helix to beta-sheet transitions occur via 310-helix or random coil structures. However, in some cases beta-sheet formation occurs directly from a random coil structure without undergoing helical structure. These beta-sheet rich aggregates can be inhibited by prevention of a partial helix formation. Thus, the alpha-helix could be targeted in order to inhibit beta-sheet formation and peptide/protein aggregation for therapeutic applications.

T-191

Reactivity of usnic acid and evaluation of derivatives for antiproliferative activity

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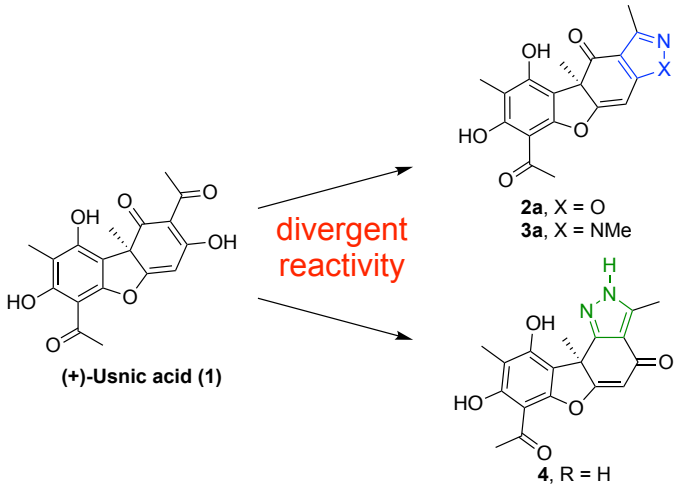
Natural products continue to be an inspiration for new drugs to treat debilitating diseases such as cancer. Usnic acid is a secondary metabolite isolated predominately from lichen species and has shown to exhibit antiproliferative properties, however its application is limited by poor drug-like properties and low specificity. We report our work on investigating the reactivity of usnic acid for incorporating heterocyclic rings and the divergent reactivity that can be obtained. The synthesised derivatives were then tested against HeLa cancer cells for their antiproliferative properties. A number of promising compounds were obtained with IC_{50} values as low as 50 nM against HeLa cancer cells after 48 hours.

The molecular mechanisms underlying activity and efficacy in vivo were also tested.[1,2] We found that these compounds induced massive vacuolization which originated from the endoplasmic reticulum (ER). ER stress led to cell death with features of apoptosis and paraptosis. When applied to nude mice with xenografted breast cancer cells, tumour growth was stopped. In treated mice, vacuolization was observed in tumour cells, but not in other organs. This study shows that the antiproliferative activity relates to the induction of ER stress in cancer, not in healthy, cells and it leads to breast cancer cell death in vitro and *in vivo*.



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T-192

Exploring panobinostat analogues with hydrogen-bonding capacity engineered into the distal binding pocket.

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Histone deacetylase (HDAC) enzymes are crucial structural modulators of chromatin, which affect differentiation, cell proliferation and homeostasis of eukaryotic cells[1]. Overexpression of HDACs has been implicated in cancer, neurological diseases, infection, and inflammation[1]. HDAC inhibitors have been approved for use in non-solid cancers, but their therapeutic benefit is coupled with serious adverse effects. The low specificity of inhibitors to the HDAC isoforms and other Zn(II) containing metalloproteins is proposed to precipitate these adverse effects[2]. This has prompted a search for optimised inhibitors to reduce these adverse effects.

Molecular modelling studies have identified acidic amino acid residues at the surface of HDAC2 isoform capable of forming hydrogen bonds to the cap group and linker regions of an HDAC inhibitor[3-4]. This project aimed to develop a library of cinnamyl-hydroxamate compounds that incorporate a hydrogen bonding group (carboxamide) to probe these acidic amino acid residues.

The use of the naturally occurring amino acid tryptophan, allowed easy addition of the carboxamide group into two regions of the inhibitor and provided structural diversity. Three sets of compounds were prepared by coupling *N*-hydroxycinnamate and tryptophanamide analogues to form a methyl ester intermediate which was subsequently converted to a hydroxamic acid. The carboxamide group was installed in alternative stereochemical configurations (from stereopure L- or D-tryptophan starting materials) to explore enantioselective effects.

The structural diversity of the presently synthesised compound library will inform the future design of HDAC targeting drugs, by highlighting the cost or benefit of a carboxamide group in differing regions of a HDAC inhibitor.

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T-193

Synthesis and evaluation of delocalised lipophilic cations/ionic liquids as mitochondrial-targeted anticancer agents

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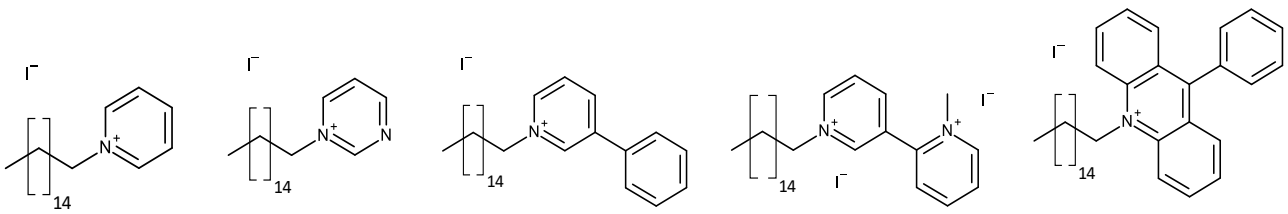
Traditional chemotherapies for metastatic breast cancers target DNA replication in rapidly dividing cells, and have achieved limited success due to a variety of dose-limiting toxicities and the lack of specificity for cancer cells. There is a critical need to develop novel anticancer agents that selectively target tumour cells and reduce the adverse toxicities associated with existing chemotherapy. Cancer cell mitochondria have shown to be structurally and functionally different from those in non-cancerous cells, presenting an opportunity to develop mitochondrial-targeted anticancer agents.[1]

Delocalised lipophilic cations (DLCs) are membrane-permeable ionic molecules that accumulate in mitochondria in response to the mitochondrial membrane potential ($\Delta\Psi_m$).[2,3] Hyperpolarised mitochondria and greater $\Delta\Psi_m$ are universal features of cancer cells relative to non-cancerous cells, which allows for the selective accumulation of DLCs in mitochondria of cancerous cells.[1-3] It is therefore viable to develop novel DLCs that target tumour cell mitochondria and exhibit targeted cytoxicity, using the basis of selective uptake.

In this work, I synthesised a library of DLCs with amphiphilic ionic liquid-like structures. The size, hydrophobicity and number of cationic charges were varied (see Figure 1), and the analogues were screened against human MDA-MB-231 breast cancer cells using the MTS assay. A well-defined structure-activity relationship emerged that revealed larger and more lipophilic head-groups improved activity, while increased number of cationic charges decreased cytotoxicity. DLC **5** emerged as a potent anticancer agent (IC_{50}: 0.76 µM, see Figure 1). The capacity of the DLCs to permeabilise tethered bilayer lipid membranes correlated with MTS anticancer activity, which suggested that DLC-mediated decreases in cell viability were linked with membrane disruption. Finally, JC-1 assays indicated that **5** efficiently depolarised mitochondria in MDA-MB-231 cells relative to other DLCs. These results show that cationic head-group structure has a large impact on anticancer activity, and that DLCs disrupt mitochondrial membranes to reduce cell viability.



1 IC_{50}: 7.7 | **2** IC_{50}: 24 | **3** IC_{50}: 1.6 | **4** IC_{50}: 8.3 µM | **5** IC_{50}: 0.76

Figure 1. Some examples of DLCs that were synthesised and screened against MDA-MB-231 cells.

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T-194

The conformational control and chameleonic polarity of Fluoro-siphonarienal

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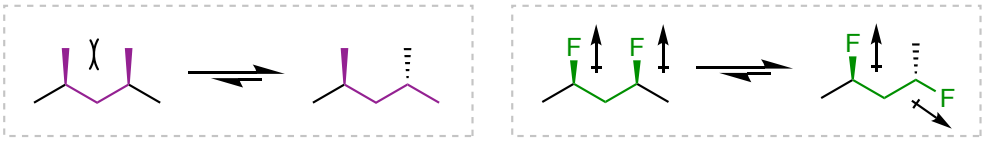
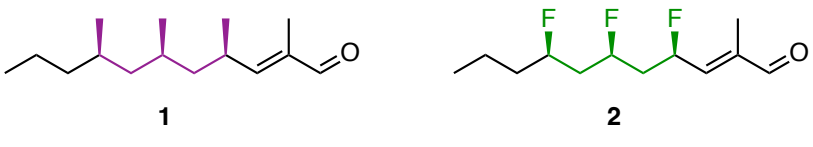
Fluorine's ability to control the conformations of molecules is an underutilised tool in medicinal chemistry. One aspect of this shape-control is the dipolar repulsion of the polyvinyl fluoride motif (Figure 1a), which mimics the steric repulsion of *syn*-pentane.[1] We sought to exploit this conformational mimicry within the context of the deoxypolypropionate natural product Siphonarienal (**1**, Figure 1b). We synthesised an all-*syn* fluorinated analogue (**2**) *via* an iterative sequence of enantioselective fluorinations and 2C homologations.[2] A comprehensive DFT-based investigation of **1** and **2** revealed that the alkyl chains of both molecules adopt similar low-energy conformations (Figure 1b). Intriguingly however, the fluorinated analogue (**2**) accesses a broader range of dipole moments across its different conformations, thereby exhibiting the potential to display chameleonic polarity which could be beneficial to cell permeability. Furthermore, we found that the fluorinated analogue (**2**) is more stable towards liver microsomes compared to the natural product (**1**).[2] Overall, this work provides early proof-of-concept that the polyvinyl fluoride motif could be a valuable structure for applications in medicinal chemistry.

(a) Conformational influences in hydrocarbon vs. fluoroalkyl chains:



(b) The natural product siphonarienal (**1**) and a novel fluorinated analogue (**2**):



1 **2**

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T-195

Catalytic asymmetric transformations by the protein conjugated metallocorroles

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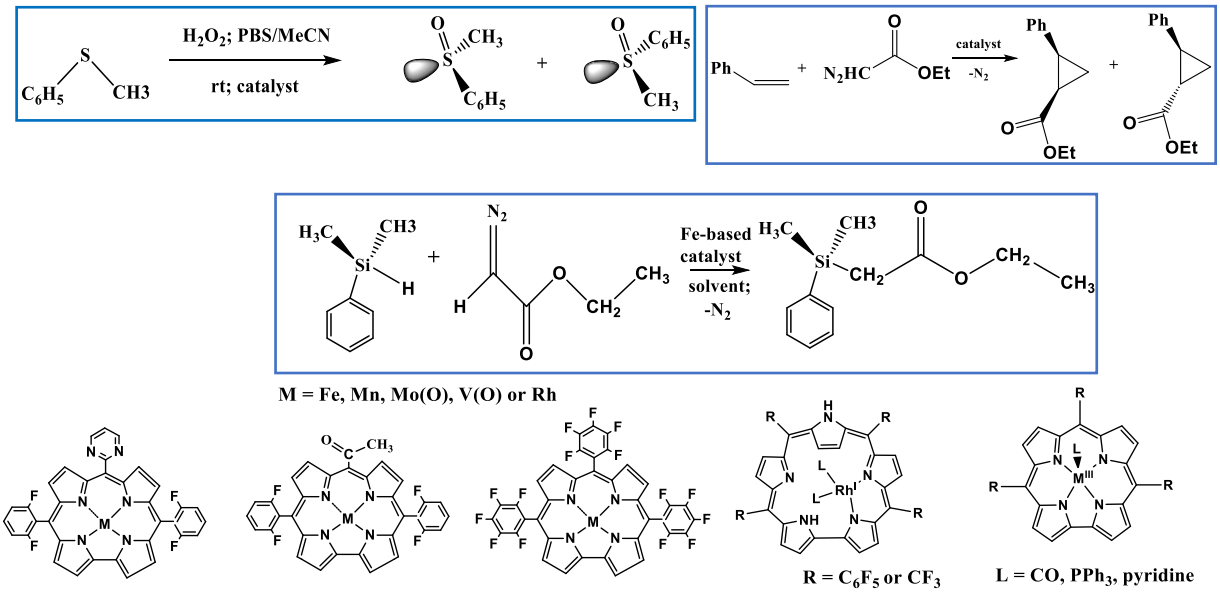
Metal-catalysed asymmetric synthesis remains as the forefront of modern research because of its far-reaching importance and the scientific challenges involved in the design of efficient systems. The discovery of stable corroles and their metal complexes has initiated extensive research on their fundamental physical and chemical properties, which was rapidly followed by advantageous utilization in many fields.[3] The investigated reactions include asymmetric oxidation of sulphides to the corresponding sulfoxides and cyclopropanation of styrene by carbenoids.[1,2] The extremely simple biomimetic oxidation system, consisting of mixing metal complexes of corroles with serum albumins and utilizing hydrogen peroxide, led to asymmetric sulfoxidation of thioanisoles with high chemical yields and good enantioselectivities.[2] The flexibility of the system allows for many other easily performed optimizations (pH, additives, solvents, *etc.*) which suggests that it might be of practical utility as well. We will now describe how metallocorroles catalyse the reaction of diazo compounds with silanes.



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T-197

Shifting paradigm: High relaxivity, Gadolinium & Manganese based Dual Modal Imaging/Theranostic Agents

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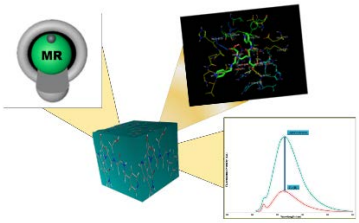
The individual imaging modalities such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Optical Imaging (OI) have shortcomings such as lack of specificity, lack of spatial resolution, quantifying difficulty respectively. A combination of multiple molecular imaging techniques has been suggested to overcome these difficulties. However, the problem could not be resolved by the simple addition of two types of imaging agents, unless they have identical pharmacodynamic properties. Therefore, the necessity for the introduction of dual-purpose contrast agents or multimodal imaging probes has been justified. Additionally, the toxicity of Gadolinium and Manganese in their own right invoked the need to have stable metal complexes as dual-modal Imaging agents. On contrary, despite the great wealth of information they provide, their synthesis is far from trivial. Herein we report the modular approach adapted for the synthesis of ligand systems based upon polyamino-polycarboxylates containing versatile auxiliary groups *via* an easy-to-make, one-pot synthesis.

Initially, we synthesized centrally and terminally functionalized chromophore bearing DTPA analogues *via* multistep synthesis and subsequently prepared gadolinium complexes. We reported highly reproducible, markedly higher relaxivity than other DTPA-based contrast agents for the centrally functionalized chromophore bearing DTPA analgoue for the first time. We also showed that the ligand-based fluorescence is not quenched upon complexation with Gd. However, complexes based on Gd, specifically, some extracellular gadolinium-based contrast agents could trigger the development of Nephrogenic Systemic Fibrosis (NSF), a fibrotic disorder generally observed in renal failure patients. This has led to regulatory actions by FDA and EMA. This has prompted the resurgence of research on non-gadolinium based analogues.

Inspired by the success of preparing dual-modal imaging agents based on DTPA analogues, we embarked on the preparation based on EDTA bisamides, targeting transition metal complexes. More specifically, we synthesized and characterized Manganese and Copper complexes with 4-(aminomethyl)pyridine and 2-aminoanthraquinone as fluorescent auxiliary groups. In particular, the manganese complex of EDTA bisamide of 4-(aminomethyl)pyridine (MnL^1) exhibited relatively higher relaxivities (3.52 $mM^{-1}s^{-1}$ (at 30 MHz, 37 °C) than commercial contrast agent Teslascan® and comparable relaxivities with performance comparable to the commercially available gadolinium-based contrast agents, Magnevist® and Dotarem®. Furthermore, the versatility of the respective ligand $\mathbf{L^1}$ to act as *on-off type*, fluorescent-based chemosensors for Cu (II) along with its potential for live-cell imaging via time-gated fluorescence spectroscopy also was well established. Moreover, structure-based virtual screening unveiled the potential anticancer activity of $\mathbf{L^1}$**.** Apart from acting as MRI/OI agent, given the momentous changes taking place towards the application of Mn^{55} isotope in PET imaging, the application of MnL^1 and CuL^1 as PET/OI imaging agents is also hereby envisaged.



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T-198

Computational design of oxazines as novel KDM4 inhibitors

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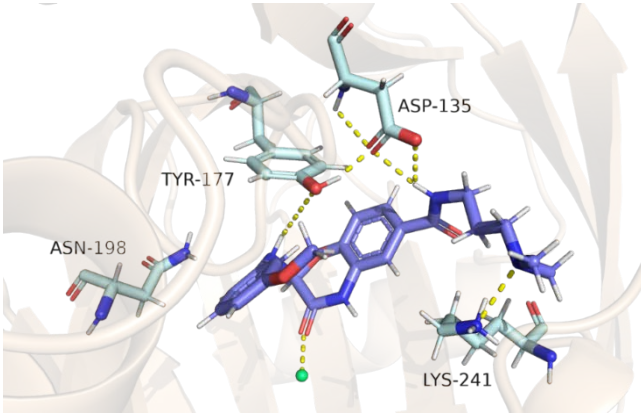
Post-translational alkylation of DNA and histone proteins in cell nuclei account for the majority of typical epigenetic modifications. In healthy cells, the rates of DNA and histone protein alkylation are mediated by a number of distinct dealkylase families.[1] The histone lysine demethylase (KDM) superfamily of proteins is responsible for the demethylation of the mono-, di- and/or tri-substituted H1K26, H3K4, H3K9, H3K27 and H3K36 lysine residues, accounting for a significant portion of regular histone modification. The KDM superfamily is regularly observed to be upregulated in a broad range of cancer cell lines and tissues, indicating its potential as a druggable epigenetic target.[2-4]

Histone lysine demethylases KDM2 through KDM8 catalyse the oxidative demethylation of histone lysine residues in a Jumonji C domain with Fe(II) and 2-oxopentanedioic acid as cofactors. The binding structure and enzymatic activity of other cofactors including but not limited to glycerol, Zn(II) and Ni(II) have also been observed using X-ray crystallography and biological assays respectively.[3,4] As a result, the development of novel histone lysine demethylase ligands has primarily focused on inhibitory 2-oxopentanedioic acid mimics and bidentate-chelating molecules.[2] In this work, we report the early development of a range of substituted benzoxazines through a molecular modelling led approach.



The interactions observed by one of the new analogues in the KDM4 binding site

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T-200

Deciphering the Binding of anionic glycosaminoglycans to the SARS-CoV-2 spike protein

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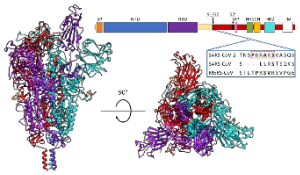
The SARS-CoV-2 rapidly spread through the world's population after its discovery in 2019. The virus infects cells via the glycosylated spike protein expressed on its surface. The protein uses glycosaminoglycans (GAGs) as cofactors to bind to the angiotensin-converting enzyme-2 (ACE2) receptor [1]. At the time of this research, the appearance of a mutation in the N-terminal domain warranted further investigation as the change to a positive residue may be indicative of increased binding to GAGs [2].

Using cosolvent molecular dynamics simulations we assessed the binding of heparin tetrasaccharides to the glycosylated spike trimer. Heparin and heparan sulfate molecules of dp 10 and dp 12 were comparatively docked using GlycoTorch Vina [3] to a glycosylated spike trimer with the introduced mutation S247R. Molecular dynamics and binding energetics were calculated for the d.p.12 molecules to understand the binding mechanism to the spike protomer.

The cosolvent simulations identified a new binding site on the NTD. Heparan sulfate bridged the gap between S247R and the furin cleavage site, while heparin was bound to the furin cleavage site and surrounding glycosylations. This site overlaps with the binding region of some neutralizing antibodies, and more recent strains of the virus have included mutations in those same regions.

This work demonstrates the preferential affinity for particular GAG sulfation patterns and lengths, as they link oligosaccharide binding sites of the protein. This bridging manipulates conformational changes in the protein and supports the proposed use of heparan sulfate mimetics in developing a treatment for COVID-19. This work has been published in the Computational and Structural Biotechnology Journal [4].



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T-201

Identification of a new anthelmintic chemotype using an advanced screening platform

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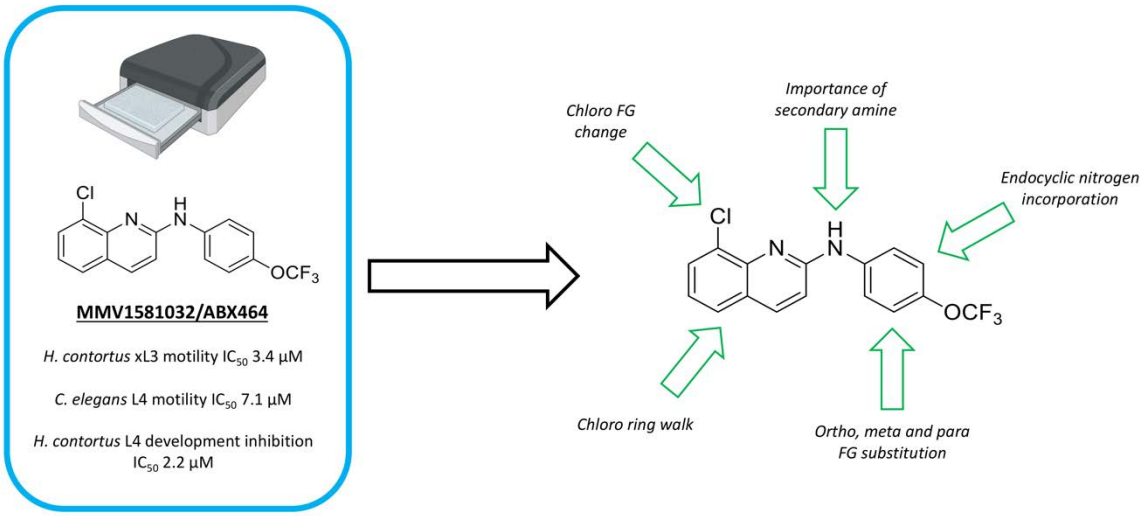
Parasitic roundworms (nematodes) cause infections and diseases (nematodiases) in humans and animals that have a major adverse socioeconomic impact worldwide. Human helminth infections disproportionately affect poverty-stricken communities, and global agricultural losses attributed to nematodiases are estimated at tens of billions of dollars. Nematodes of the order Strongylida, including *Haemonchus contortus*, are particularly important. The excessive use of anthelmintic compounds to treat infections and disease has led to widespread resistance to these drugs, such that there is a need for new anthelmintic chemotypes with distinctive mechanisms of action.

To discover such chemotypes, we screened the Medicines for Malaria Venture (MMV) *Pandemic Response Box* of compounds against *H. contortus* and its free-living relative, *Caenorhabditis elegans*—a model organism. This screen, conducted using an established phenotypic platform, identified MMV1581032, which significantly inhibited motility and the development of *H. contortus* and *C. elegans* adults in the low micromolar range[1]. As MMV1581032 has favourable physicochemical properties, it is a promising candidate for further investigation as a nematicide. This presentation will focus on our efforts to define the structure-activity relationship towards compounds with improved nematocidal potency and will discuss in-roads to uncover the mechanism of action of MMV1581032.



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T-202

Design and Synthesis of Novel Nitroxide-Corticosteroid Hybrids

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Corticosteroids are an extensive class of both naturally occurring and synthetic steroid hormones known widely for their potent anti-inflammatory effects. Consequently, they are used globally in medicine as a commonly prescribed treatment for many acute and chronic inflammation-mediated conditions such as diabetes, cancer, cardiovascular diseases, arthritis, hay fever and chronic obstructive pulmonary disease.[1] Whilst corticosteroids can combat the inflammation component of these diseases, they do not address the potential root cause of oxidative stress.[2] Furthermore, it has been shown that oxidative stress can significantly decrease the efficacy of corticosteroids.[3]

This research aims to address these issues by the design and synthesis of novel antioxidant-corticosteroid hybrid drugs which incorporate an antioxidant linker. Among the wide variety of effective synthetic antioxidants are a group of stable free radicals called nitroxides with ideal antioxidant properties such as low molecular weight, membrane-permeability and non-toxicity. Using the structure-activity relationship of corticosteroids (Figure 1a), several hybrid molecules featuring a variety of cleavable and non-cleavable nitroxide linkers attached to well-known corticosteroid prednisone have been designed and their synthesis in progress (Figure 1b). Investigation into the activity of all synthesized hybrids by generic antioxidant and competitive GR binding assays is ongoing and will evaluate the validity of this hybrid corticosteroid approach as a potential novel broad-spectrum treatment and guide future synthetic targets.

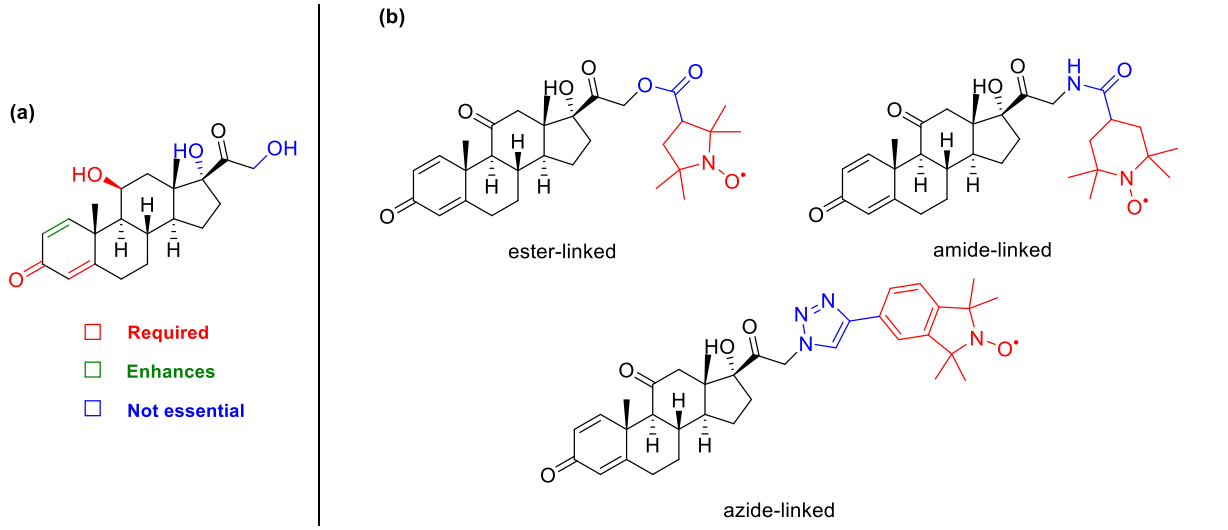

Figure 1: (a) Structure-activity relationship for the glucocorticoid (anti-inflammatory) action of prednisolone (active metabolite of prednisone). (b) Synthetic examples of prednisone-antioxidant hybrids comprising of various linkers (blue) and nitroxide ring classes (red).

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T-203

Characterising synthetic cannabinoid receptor agonists AB-4CN-BUTICA, MMB-4CN-BUTINACA, MDMB-4F-BUTICA, MDMB-4F-BUTINACA and analogues

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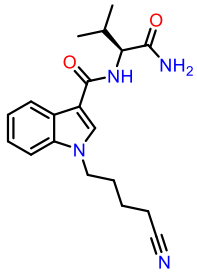
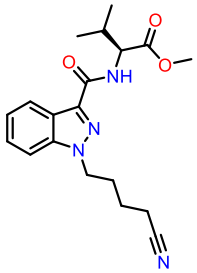
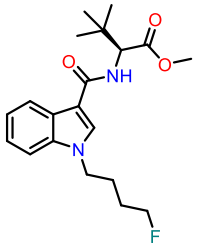
ES: espa0134@uni.sydney.edu.au, AA: adam.ametovski@sydney.edu.au, EAC: elizabeth.cairns@sydney.edu.au



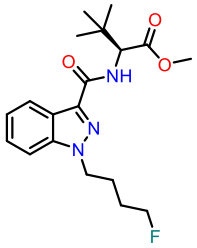
CB_1 K_i = 550 nM
CB_1 EC_{50} ($G_{i/o}$) = 370 nM
CB_1 E_{max} = 109%



CB_1 K_i = 17 nM
CB_1 EC_{50} ($G_{i/o}$) = 3.5 nM
CB_1 E_{max} = 117%



CB_1 K_i = 13 nM
CB_1 EC_{50} ($G_{i/o}$) = 3.2 nM
CB_1 E_{max} = 113%



CB_1 K_i = 4.1 nM
CB_1 EC_{50} ($G_{i/o}$) = 0.55 nM
CB_1 E_{max} = 108%

Synthetic cannabinoid receptor agonists (SCRAs) remain one of the most prevalent classes of new psychoactive substances, with often little to no spectral or pharmacological data available at the time of detection. To facilitate proactive screening of SCRAs as they emerge, recently detected SCRAs AB-4CN-BUTICA, MMB-4CN-BUTINACA, MDMB-4F-BUTICA, and MDMB-4F-BUTINACA, and a series of 32 analogues including indole-, indazole-, and 7-azaindole-3-carboxamides have been synthesised, characterised and pharmacologically evaluated *in vitro*. Compounds were synthesised *via* alkylation of suitable indole-, indazole-, and 7-azaindole precursors followed by trifluoroacetylation and/or hydrolysis. Finally, routine amide coupling provided the desired species, and chemical characterisation completed. Affinity for hCB_1 or hCB_2 was determined in HEK293 cell membranes using [^{3}H]-SR141716A (CB_1) or [^{3}H]-CP55,940 (CB_2). Functional activity was determined using AtT20-FlpIn cells stably transfected with hCB_1 or hCB_2, via a FLIPR Membrane Potential Assay kit (blue) and a FlexStation 3, using CP55,940 as reference. The detected compounds AB-4CN-BUTICA (-*p*Ki [hCB_1]= 6.26 M, -*p*EC_{50}[hCB_1] = 6.43 M, E_{max} = 109%), MMB-4CN-BUTINACA (-*p*Ki [hCB_1]= 7.76 M, -*p*EC_{50}[hCB_1] = 8.45 M, E_{max} = 117%), MDMB-4F-BUTICA (-*p*Ki [hCB_1]= 7.88 M, -*p*EC_{50}[hCB_1] = 8.50 M, E_{max} = 113%), and MDMB-4F-BUTINACA(-*p*Ki [hCB_1]= 8.39 M, -*p*EC_{50}[hCB_1] = 9.26 M, E_{max} = 108%) ranged from moderate to high affinity and potency at CB_1 while displaying high efficacy. Most compounds displayed similar activity at CB_1 and CB_2, ranging from subnanomolar to submicromolar affinity and potency. Structure-activity relationships observed were consistent with previous studies regarding head and core group activities at CB_1 and CB_2. Notably, the 4-fluoro derivatives displayed slightly increased potency at CB_1, whilst retaining similar activity at CB_2, compared with the 4-cyano analogues. Such information is critical for informing the relevant health and legislative bodies on the profile of these compounds, given the high potencies and efficacies observed.

T-204

Accessing a clinical metal chelator and analogues using synthetic and enzymatic approaches

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Desferrioxamine B (DFOB) is a hydroxamic acid-based bacterial metabolite essential in guaranteeing cellular iron supply. The exquisite affinity for Fe(III) has led to the clinical use of DFOB as a scavenger for excess iron in patients with transfusion-dependent haemoglobin disorders.[1] There is an increased potential in the utility of DFOB and analogues in medicine and bioimaging, which warrants further study into new methods to access these compounds.

The synthesis proposed in the current work recognises the trimeric structure of DFOB consisting of one type A monomeric unit linked to two type B monomeric units (Fig.1).[2] This work sought to prepare native DFOB, and analogues containing ether oxygen atoms in the backbone. The work considered that the siderophore synthetase enzyme DesD, which is involved in native DFOB biosynthesis, could be used in this molecular assembly, in the presence of type A and type B monomeric substrates. Native and ether-containing monomeric units A and B were prepared and incubated with recombinant DesD.[3] This predicted for the production of a suite of eight analogues of DFOB, including native DFOB, with ether subunits inserted into positions 1 and/or 2 and/or 3.

The proposed scheme is flexible and can be adapted to produce trimeric adducts and dimeric species and various structural analogues. This improved access to structural variety may reveal nuances in the relationship between DFOB structure and properties that may inspire further therapeutic use.

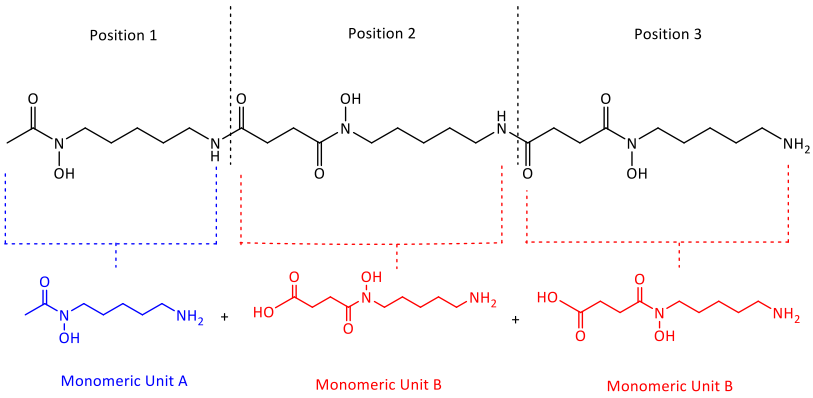

Figure 1. Structure of desferrioxamine B (DFOB) and type A (blue) and B (red) monomeric units.

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T-205

Rational design of selective sialyltransferase inhibitors

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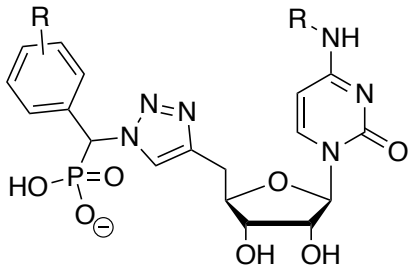
Sialic acids are one of the most important sugars in humans, after glucose. Normal sialylation, catalysed by one of 20 human sialyltransferase enzymes, is integral to physiological function. However, aberrant sialylation contributes to the increased immune evasion, treatment resistance and metastatic spread of a tumour.[1] Pan-sialyltransferase inhibitors reduce sialylation and have shown great potential as a treatment for metastatic and drug-resistant cancer.[2] The design of selective sialyltransferase inhibitors could improve these compounds' efficiency, while also reducing their off-target interactions. [3, 4]

This work investigates the design of a transition state-based sialyltransferase inhibitor selective for ST6Gal1 over ST3Gal1. Ligand design was guided by free energy perturbation experiments, which focused on utilising minor differences between the nucleotide-binding region of the two active sites to improve selectivity. Derivatives at the cytidine 4*N* position were found to enhance the compounds' potency and selectivity for ST6Gal1 over ST3Gal1 *in silico*. These molecules were subsequently synthesised and screened against ST6Gal1 and ST3Gal1 *in vitro*. Enzyme inhibition screening was performed using a UMP/CMP-GloTM glycosyltransferase activity assay developed by Promega. Compound structures and their biological evaluation will be presented at the conference.



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T-206

Chemical Investigation of *Clerodendrum polycephalum* for Antimalarial Compounds

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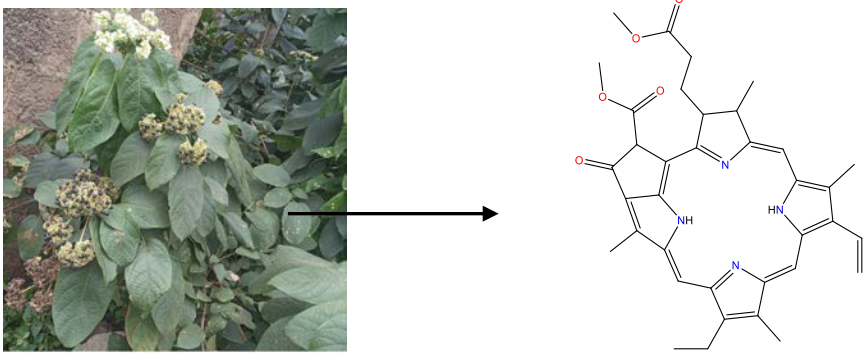
Clerodendrum from family Lamiaceae (Verbenaceae) is spread around the world and known for its ethnomedicinal properties. *Clerodendrum polycephalum* grown in Nigeria has been traditionally used for malaria treatment. Extract of the leaves tested for *in-vivo* antimalarial activity showed better chemo-suppressive, and prophylactic activity against standard drug chloroquine and pyrimethamine, respectively. Curative assay has also been good, and extract showed no toxic effects.[1]

However, no compounds have been reported for anti-plasmodial activity of the extract. So, isolation, purification, and structure elucidation of active compounds is the focus of this project. Chromatographic separation, HPLC purification, LC-MS, and 1D-/2D-NMR led to the isolation of ten pure compounds, including five known, namely, acacetin, loliolide, methyl-pheophorbide a, bis(2-ethylhexyl) phthalate and 12,16-Epoxy-6,11,14,17-tetrahydroxy-17(15→16)-abeo-5,8,11,13,15-abietapentaen-7-one, 4 new clerodane diterpenes and one abietane diterpene. Isolated compounds were tested against *Plasmodium falciparum* with methyl pheophorbide a showing an IC_{50} of 4.49 μM. Our results supported the traditional use of the plant as anti-malarial agent.



Methyl pheophorbide a

Fig: *Clerodendrum polycephalum* (Photo provided by collaborator Dr. Francis B. Adewoyin, Ile Ife, Nigeria)

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T-208

Secondary Structure Transitions for a Family of Amyloidogenic, Antimicrobial Uperin-3 Peptides

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Secondary structure changes are an inherent part of antimicrobial (AMP) and amyloidogenic peptide activity, especially in close proximity to membranes, and impact the peptides' function and dysfunction roles. The formation, and stability of α-helical components are regarded as essential 'intermediates' for both these functions. To illuminate the conformational transitions leading to amyloid formation we use short cationic AMPs, from an Australian toadlet, Uperoleia mjobergii, (Uperin 3 family, U3) and assess the impact on secondary structural elements in the presence of a membrane mimetic surfactants, sodium dodecyl sulfate (SDS) or dodecylphosphocholine (DPC). Specifically, Uperin 3.x, where x=4, 5, 6 wild-type peptides and position seven variants for each, R7A or K7A, were investigated using a combination of experimental and simulation approaches. In water, U3 peptides remain largely unstructured as random coils, with the addition of salts initiating structural transitions leading to assembly towards amyloid. Solution NMR data show that an unstructured U3.5 wt peptide transitions in the presence of SDS to a well-defined α-helical structure that spans nearly the entire sequence. Circular dichroism (CD) and ThT fluorescence studies show that all six U3 peptides aggregate in solution, albeit with vastly varying rates, and a dynamic equilibrium between soluble aggregates rich in either α-helices or β-sheets may exist in solution. However, the addition of SDS leads to a rapid disaggregation for all peptides and stabilisation of predominantly α-helical content in all the U3 peptides. Molecular dynamics (MD) simulations show that the adsorption of U3.5 wt/R7A peptides onto the SDS micelle is driven by Coulombic attraction between peptide cationic residues and the negatively charged sulfate head-groups on SDS. Simulating the interactions of various kinds of β-sheet dimers (of both U3.5 wt and its variant U3.5 R7A) with SDS micelles confirmed β-sheet content decreases in the dimers after their attachment to the SDS micelle. Adsorbed peptides interact favourably with the hydrophobic core of the micelle, promoting intramolecular hydrogen bonds leading to stabilisation of the α-helical structure in peptides, and resulting in a corresponding decrease in intermolecular hydrogen bonds responsible for β-sheets. Recent data using DPC micelles will be presented and conclusions discussed in light of the SDS data.

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T-209

Australian honey bee propolis: Quality and chemical diversity

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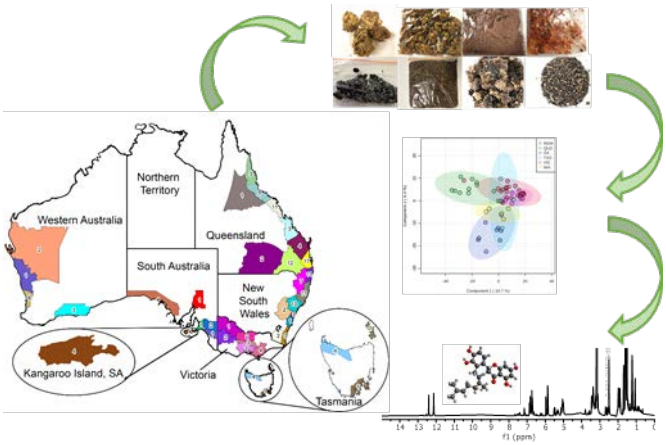
Propolis, which is a resinous mixture bees produce from saliva, beeswax and the exudate of tree buds, sap flows and other botanical sources, has been used in traditional medicines as a natural antibacterial agent. It was identified as one of the good sources of bioactive drug-like molecules to prevent various diseases such as microbial infections, cancer, diabetes, heart, inflammation, Alzheimer, Parkinson, early aging and atherosclerosis.[1] Over the last three decades, the interest in propolis chemistry and its pharmacological properties has noticeably grown in a world.[1] Although Australia possesses a well-renowned pristine environment mostly due to our vast stretches of unique and diverse native flora, Australian propolis is currently considered as a nuisance and regularly discarded by most Australian beekeepers.[2] As a result, the natural diversity of Australian propolis types as well as their biological properties from different regions of Australia are unknown. From a study of 158 propolis samples collected from different regions across six Australian states (New South Wales, Queensland, South Australia, Tasmania, Victoria and Western Australia), my presentation will show i) a comprehensive picture about the quality and chemical diversity of the Australian honey bee propolis; and ii) chemical composition and biological activities of the Queensland propolis, one of the high-grade Australian propolis types.



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T-211

Fluorescent stains for imaging hypoxia in cells and tumour models

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Fluorescence imaging has greatly advanced our knowledge of how chemicals and chemical reactions play a role in cellular function and dysfunction, but the number of ideal fluorescent probes is limited. An ideal responsive probe is one that contains a fluorophore tethered to a sensing group for selectivity of the analyte in question, and a targeting group for sub-cellular localisation. To date, probes that are both targeted and selective are relatively rare and most localised probes are discovered serendipitously rather than by design. A challenge in this field is therefore the identification of suitable fluorophore scaffolds that can be readily attached to both sensing and targeting groups.

Tissue hypoxia is a condition where an inadequate supply of oxygen is able to reach tissues. Due to the lack of oxygen, hypoxia can also lead to an increase in the reducing environment, therefore leading to many detrimental effects. Hypoxia is therefore a hallmark of many vascular and pulmonary diseases, such as cardiac ischemia[1] and strokes.[2] Hypoxic regions are also characteristic of solid, cancerous tumours that grow away from blood vessels and therefore lack a sufficient oxygen supply.[3] Although it has been established that hypoxia is a factor in the development of a myriad of human diseases, we are still unsure of the exact role it plays. Therefore, it is vital to be able to visualise hypoxic regions in order to understand the role that hypoxia plays in the progression of many diseases.

Hypoxia responsive fluorescent probes are therefore of great interest due to their non-invasive and highly sensitive nature. In this work, a library of fluorescent hypoxia sensors bearing nitroaromatic groups based on naphthalimide and coumarin fluorophores were synthesised. Their selectivity was determined through fluorescence titrations and cyclic voltammetry. Cell studies in monolayers and tumour spheroids further reveal the suitability of these probes for the imaging of hypoxia.[4]

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T-212

Inventing a privileged scaffold: Novel 4-arylbenzosuber-1-ones and their applications in drug discovery

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Expanding and diversifying the chemical repertoire of druggable space is an exciting prospect to investigate as it opens the opportunity for novel discoveries. The use of privileged scaffolds can accelerate the typical slow process in drug discovery programs. Privileged scaffolds, which have been described as structures with affinity for different drug targets, can assist in the generation of novel lead compounds. One such example for this work is the benzodiazepine scaffold, which is well-known for its anxiolytic and sedative activities. Its molecular skeleton was the inspiration for the identification of a novel isostere known as 4-arylbenzosuber-1-one.[1]

The synthetic route for this new compound class involves a regioselective intramolecular Friedel-Crafts acylation of 4,5-diarylpentanoic acids. The complete formation of the desired benzosuberone regioisomer over a competing product was dependent upon the ring activation and/or deactivation of the chosen substituents. The results demonstrated that the complete formation of either the tetralone or the benzosuberone regioisomer was possible under the same reaction conditions. Selected bromo or methoxy substituents could be used as auxiliaries, included in precursors to afford the desired regioisomer and then subsequently removed.

The establishment of the synthetic route to access this novel scaffold present opportunities to explore new areas in drug discovery. This novel scaffold can be further elaborated to introduce key binding moieties by using its structural likeness to benzodiazepines, flavonoids and a recently approved drug, known as rimegepant, as guides.

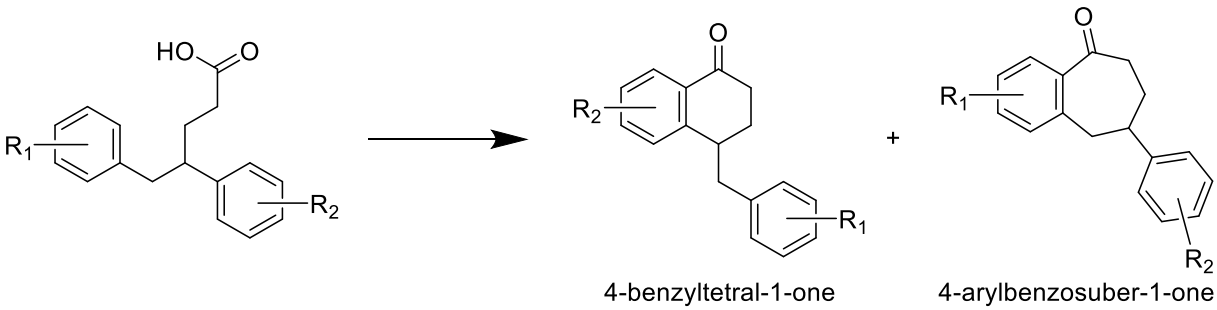

Figure 1. Synthesis of 4-benzyltetral-1-one and/or 4-arylbenzosuber-1-one.

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T-213

Synthesis and Biological Evaluation of Nitroxide Based Anti-Inflammatory Drugs and Fluorescent Agents

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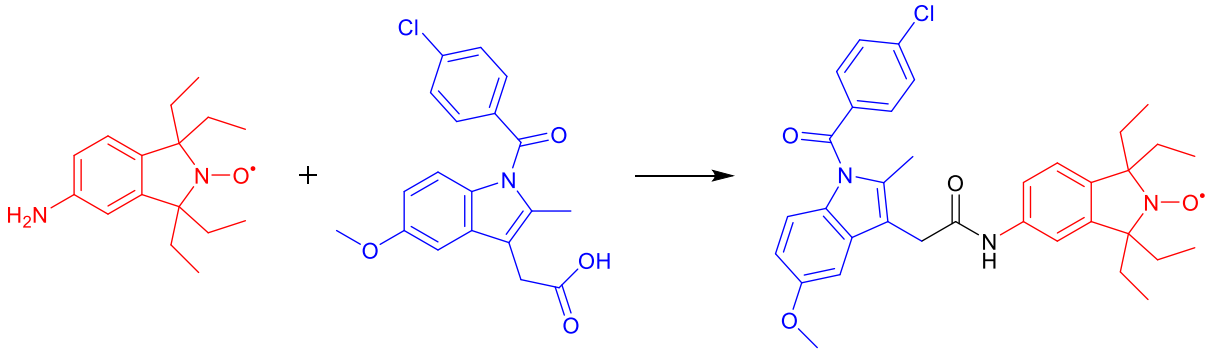
Oxidative stress has been identified as one of the major underlying causes of chronic-inflammatory disease. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are among the most common therapeutic approaches for the treatment of inflammation; however, they provide little benefit for modulating reactive oxygen species (ROS) and oxidative stress states. As such, a synergistic approach combining antioxidant and anti-inflammatory agents is necessary to combat chronic inflammatory diseases and the associated ROS induced pathogenesis. The antioxidant ability of isoindoline nitroxides has been known for decades and demonstrated by numerous research groups. Previously our group has used pharmacophore hybridisation to synthesise a range of dual-acting conjugates by combining nitroxides and NSAIDs, two of which showed improved efficacy compared to their parent templates[1]. This project continued this approach by linking the nitroxide 1,1,3,3-tetraethylisoindolin-2-yloxyl (TEIO) to commercially available NSAIDs and corticosteroids to synthesize a range of dual acting drugs. Novel nitroxide based fluorescent agents have also been synthesized for monitoring the efficacy of these new therapeutic agents.



Nitroxide | Anti-inflammatory | Enzymatically Cleavable Anti-inflammatory Antioxidant Conjugate

Figure: Dual Acting Indomethacin-TEIO conjugate

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T-214

Taking the Fight to Cancer: Polyoxazoline Nanocarriers of a Novel Aziridine Payload

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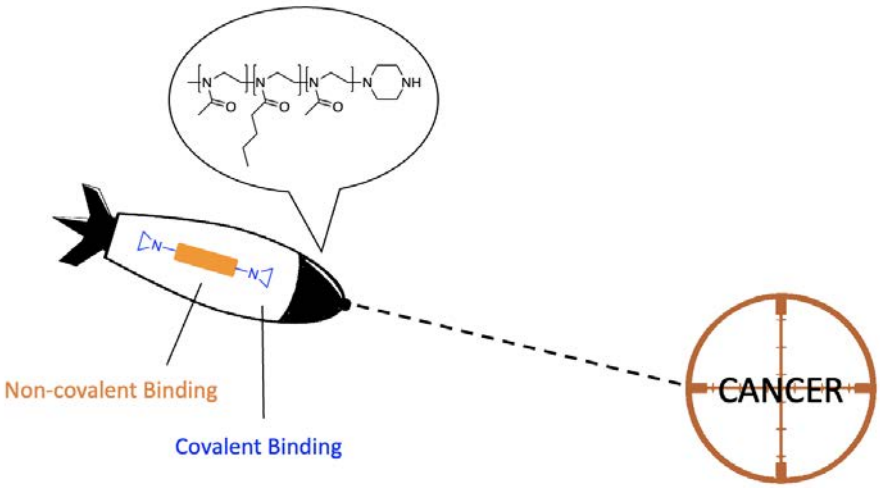
Historically, there has been reluctance from the research community to design covalent drugs due to their potential for increased toxicity. This is particularly relevant for cytotoxic chemotherapy, since many covalent cancer drugs such as cisplatin and bendamustine already make up the cancer armamentarium. However, covalent drugs have seen a resurgence of attention over the last two decades,[1] in the form of *targeted* covalent inhibitors. Targeted covalent inhibitors contain non-covalently-binding regions, along with covalently-binding moeities, such as aziridines, and are designed to have specificity for their targets. In tandem, the literature is focusing more and more on nanoparticles for use in drug delivery.[2,3] Of these, polyoxazoline micelles have shown great promise in solubilising and improving the toxicity of anti-cancer drugs towards cancer cells.[4] This work presents a potential drug candidate based on electrophilic aziridines that are directed towards the nucleophilic sites on DNA. A triblock co-polymer based on polyoxazolines, which contains a mixture of hydrophilic and hydrophobic blocks, was chosen as the nanoparticle scaffold to deliver the drug to cancer cells.



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T-215

Biologically active compounds from Australian marine invertebrates for the treatment of parasitic diseases

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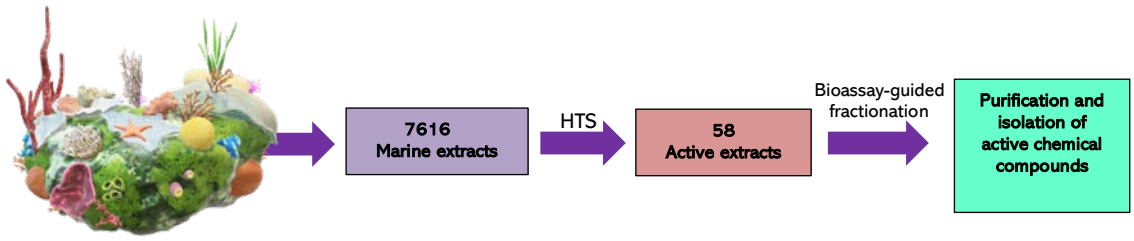
NatureBank is a unique drug discovery platform based on natural product extracts and fractions that have been derived from Australian plants, fungi, and marine invertebrates. In a recent study, we screened a collection of extracts (n = 7616) derived from marine invertebrates sampled from Australian waters in a high throughput bioassay for in vitro anti-parasitic activity against the *Haemonchus contortus,* a pathogenic nematode of livestock. From this high throughput screen (HTS), 58 extracts were identified to be active. Out of the active extracts, the majority originated from sponges (54) whereas 3 and 1 active extracts were obtained from chordates and a coral, respectively. This PhD project involves the bioassay-guided fractionation of purified marine extracts. An overview of the current progress will be given during this presentation. Our future works will include the purification and isolation of active chemical compounds in these extracts using mixed chromatographic methods and structural identification of the molecules using 1D/2D NMR and MS. Further *in vitro* anti-parasitic activity against the parasitic nematode *H. contortus* will be determined for the pure compounds.



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T-216

Modifying the core scaffold of noscapine in the search for anti-cancer agents

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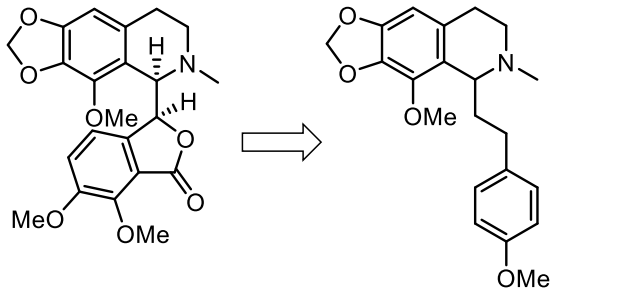
Cancer is the second leading cause of death worldwide, and was responsible for nearly 10 million deaths in 2020. Globally, nearly 1 in 6 deaths are attributed to the disease, a figure that is more than the combined death count from three other major public health problems: HIV/AIDS, tuberculosis, and malaria.[1] The limitations of current cancer therapeutics, such as toxic side effects, issues with administration, and the development of drug resistance, highlight the urgent need for alternative treatments. Noscapine is a naturally occurring phthalide tetrahydroisoquinoline alkaloid derived from the opium poppy and has long been used as an antitussive agent. Recently noscapine has been shown to possess weak anti-cancer properties by disrupting tubulin dynamics in the G2/M phase of mitosis, leading to apoptosis of cancerous cells.[2] Noscapine possesses an array of positive traits that make it an ideal candidate for development into a viable chemotherapy, including low toxicity in humans, oral bioavailability, and evasion of multidrug resistance. Many efforts have been made to design derivatives with increased potency, however almost all chemical modifications reported on the noscapine scaffold have been changes to existing, or introduction of new, substituents on the core ring structure.[3] Current work within our group has shown that the core scaffold of noscapine can be modified in a way that leads to an increase in anti-mitotic activity. A series of phenethyl substituted tetrahydroisoquinoline compounds were synthesised and assessed for their abilities to inhibit cell growth in breast cancer cell line, MCF-7. Several of our synthesized compounds demonstrated an increase in anti-cancer activity, with the 4-methoxyphenethyl derivative inhibiting cancer cell growth with an approximate 3-fold increase in potency compared to noscapine. Future work will focus on derivatisation of this new scaffold in an attempt to further increase potency, with the goal of safer and more effective chemotherapeutic cancer treatments.



Noscapine
MCF-7 EC_{50} = 61 µM

4-Methoxyphenethyl derivative
MCF-7 EC_{50} = 23 µM

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T-217

A next-generation label-free MALDI MS based HTS solution utilizing timsTOF technology

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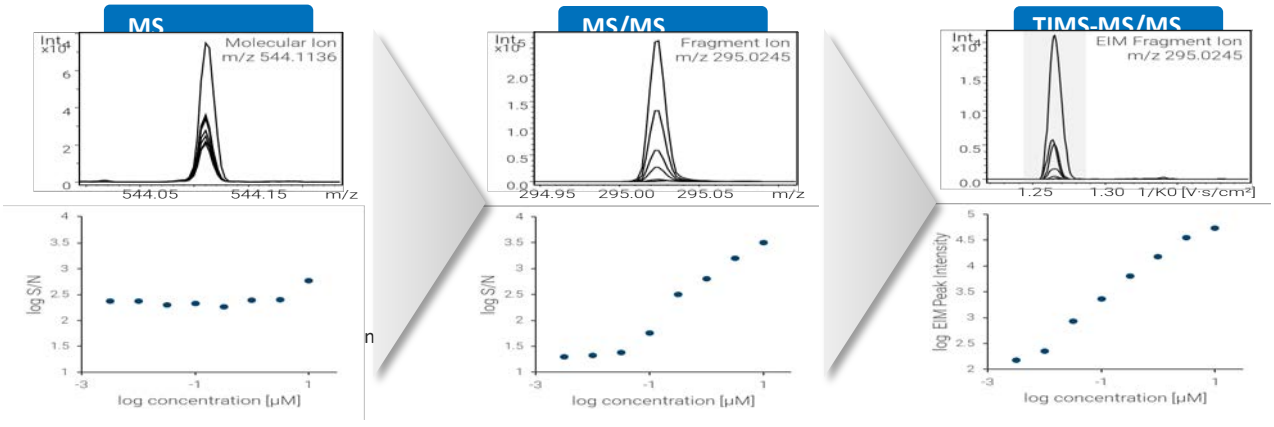
MALDI mass spectrometry (MALDI-MS) has evolved into an established, highly capable label-free HTS readout method accelerating drug discovery. MALDI-MS enables fast reading rates of up to multiple wells per second and has proven itself to feature an outstanding level of robustness. As a result of this, MALDI-MS has been successfully applied to full-deck screening of primary compound libraries comprising a million or even more compounds at unparalleled speed.

We introduce here timsTOF MALDI PharmaPulse (timsTOF MPP), a next-generation MALDI-MS based solution for label-free HTS taking advantage of new and innovative timsTOF technology. timsTOF relies on ultrahigh-resolution time of flight mass spectrometry (UHR-TOF) in combination with trapped ion mobility spectrometry (TIMS) as an upfront ultrafast dimension of separation orthogonal to MS.

In this poster contribution, we will address the following system key features illustrating the unique capabilities of the new HTS platform:

1. For the first time ever, ultrafast MALDI based HTS readout is available in combination with high-resolution Q-TOF mass spectrometry.
   1) Robust and reliable quantitative feature extraction from high-resolution MS data enhances the confidence level of HTS results for a wide spectrum of target compounds ranging from small molecules to larger sized peptides.
   2) Assay specificity is improved significantly by engaging advanced timsTOF MPP operation modes (e.g. MS/MS, TIMS) resulting in lowered FDR and expanded quantitation range.
   3) TIMS provides an additional dimension of separation in the gas phase being significantly faster than LC or SPE (≤ 1s per separation cycle, typically). TIMS is capable of separating isobars and isomers and allows, therefore, quantitation of target compounds indistinguishable by mass spectrometry alone.
   4) Beyond quantitative HTS assays, timsTOF MPP enables high-confidence near real-time verification of chemical synthesis products based on multiple physical properties, i.e. accurate molecular mass, isotope pattern, collisional cross-section (CCS) and, on demand, MS/MS fragmentation, thus reducing feedback time and chemical costs in high-throughput experimentation (HTE) chemistry.
   5) As part of the timsTOF MPP solution, tailored application software is available to support seamless campaign setup and execution in various HTS workflows, system integration in a fully automatized HTS environment via an integrated automation interface and data transfer to external software for further downstream analysis.



T-218

Probing the electron transfer mechanisms of mitochondria and their redox active constituents

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Mitochondrial dysfunction and reactive oxygen species (ROS) are implicated in theories of aging and disease.[1] A disequilibrium between the production and subsequent removal of ROS leads to a state of oxidative stress characterised by deleterious reactions in mitochondria and cells.[2] Despite this, current biochemical methods are limited in their ability to probe and quantify the roles individual enzymes and molecules play in ROS metabolism in the highly redox active environment of the mitochondrion.[3]

A novel method employing both direct current (dc) cyclic voltammetric and Fourier transformed alternating current voltammetric (FTacV) techniques was developed to assess the electron transfer mechanisms of surface confined mitochondria and their key redox active constituents; hemin, cytochrome c (cyt c) and coenzyme Q10 (coQ10).

Whilst both Vulcan XC-72 carbon black and highly-ordered multiwalled carbon nanotubes[4] provided effective materials to facilitate biological adsorption and electron transfer at the working electrode, the former was chosen as the most robust surface based on a study of hemin. After confirming cyt c and coQ10 were surface confined on carbon black-glassy carbon electrodes using dc cyclic voltammetry, the first FTacV studies of these molecules were obtained. Subsequent voltammetric simulations suggested a single electron, chemically reversible electron transfer process for cyt c, and qualitatively agreed with a proposed mechanism for a sequential two electron transfer process for coQ10.

The dc cyclic voltammetry and first FTacV studies of cumulus cell mitochondria were also successfully obtained and revealed a single, chemically reversible electron transfer process at 322 mV *vs* Standard Hydrogen Electrode. This could not be attributed to any of the anticipated mitochondrial constituents and thus further studies are required to identify the source of this mitochondrial process. Ultimately, this provided a proof of concept that FTacV can be successfully applied to small biomolecular constituents as well as more complex proteins and cellular organelles.

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T-219

Discovery of Novel B^0AT1 (SlC6A19) Inhibitors

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Transport of amino acids by epithelial cells of the intestine and kidney plays an important role in amino acid homeostasis of mammalian cells.[1] Furthermore, amino acids are important signaling molecules that regulate protein biosynthesis, autophagy, ribosome biogenesis, gluconeogenesis, neurotransmitters, release of hormones, and numerous other functions. As a result, amino acid transporters are increasingly investigated as potential drug targets.[2]

The protein B^0AT1 is a symporter of sodium and neutral amino acids that plays a major role in the transport of these nutrients by the epithelial cells of the intestine and kidneys. It is a viable target for treating amino acid metabolism disorders such as phenylketonuria. The aim of this project is to find and synthesise effective inhibitors of B^0AT1. A study conducted by Bröer *et al.* identified three potential inhibitor candidates based on the results of a preliminary high-throughput screen (**Figure 1**). Inhibitors E4 and CB3 were selected to be the foci of this project, since both candidates contained reasonable variations in both structure and functional group diversity for extensive exploration of structure activity relationships.

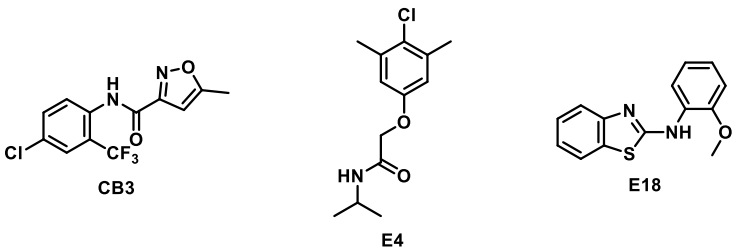

Figure 1: B^0AT1 inhibitor candidates with assigned codenames

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T-220

Design and Synthesis of Novel Polθ Inhibitors for Treatment of Cancers

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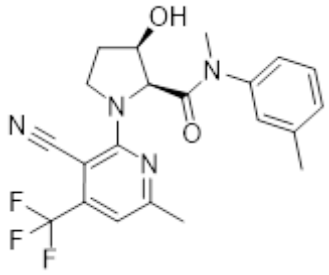
Polymerase Theta (Polθ) is a protein which is involved in DNA repair *via* the Theta-Mediated End Joining (TMEJ) pathway[1]. Polθ is known to be error-prone and is overexpressed in cancers with homologous recombination deficiency (HRD)[2]. An allosteric Polθ inhibitor named ART558 was recently reported, that induces synthetic lethality in HRD tumour cells and could be used to target PARP inhibitor resistance[3]. This project involves the design of novel Polθ inhibitors based on ART558 *via* bioisosteric replacement and pharmacophore investigation with biological screening, followed by their synthesis and biological evaluation. Molecular dynamics (MD) is also employed to investigate interactions between ART558 and the polymerase domain of Polθ. This project aims to compare the activities of ART558 with its bioisosteric analogues, to discover novel Polθ inhibitors with the pharmacophore of ART558 and to locate the binding site of ART558 on the polymerase domain of Polθ.



ART558

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T-221

Nanocarrier for biomolecules delivery to plants

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Biotechnology applying biomolecules to regulate the plant physiology and to promote crop production is critical in addressing the sustainable development of agriculture. However, the delivery of biomolecules to plant cells has been a longstanding problem due to the barriers in plants, such as cell wall. Nanotechnology provides a promising way of delivering the biomolecules to plants, while the lack of knowledge in plant-nanoparticles interactions hindered the development of nanocarriers for plants. To address this situation, this study focuses on reveling nanoparticle internalization, translocation, and delivery of biomolecules to plants and plant cells. Started with a cellular level organ, pollen, where it is demonstrated that layered double hydroxide (LDH) clay nanoparticles up to 50 nm in diameter can be readily internalized, particularly by early bicellular pollen, in an energy-dependent and energy-independent manner without physical or chemical aid. Then we progress towards leaves and demonstrate that 30-40 nm LDH nanoparticles can be rapidly taken up by intact Nicotiana benthamiana leaf cells, chloroplasts, and root after application. We also describe the distribution of the infiltrated clay nanoparticles in the leaves as well as demonstrate their translocation through the apoplast and vasculature system. And the nanoparticle internalization and translocation from root pathway was also investigated. Meanwhile, LDH nanoparticles can greatly enhance the internalization of nucleic acids to facilitate siRNA-mediated down-regulation of the targeted transgene mRNA in pollen, leaves and roots.

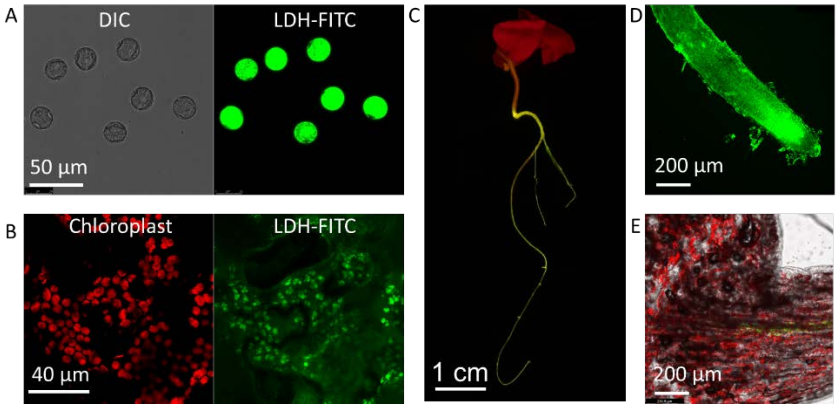

Figure 1. (A) LDH taken up by pollen, (B) LDH co-localize with intracellular chloroplasts in leaf cells, (C) LDH uptake by root and translocate to stem and leaves, (D) LDH taken up by root, (E) LDH translocate to leaf.

T-222

Incorporating alkylthioaryl linkage in macrocyclic peptidomimetic design: Discovery of novel melanocortin ligands

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Cyclic peptides and peptidomimetics have gained enormous attention as therapeutics during the past decade with many natural and non-natural macrocycles being identified with promising pharmacological activities. A tremendous amount of research has been concentrated on developing efficient synthetic strategies to access cyclopeptides and cyclopeptidomimetics.[1] Nucleophilic aromatic substitution (S_NAr) is an effective cyclisation method that is orthogonal to conventional peptide chemistries. Application of this strategy in the assembly of alkyl-aryl or biaryl ether bridged peptide macrocycles is well documented, but focus has been primarily on nitro-activated S_NArs.[2] The synthetic viability of S_NAr macrocyclisation involving other substituents has been neglected.

Aiming to further broaden the scope and utility of S_NAr macrocyclisation, we established a range of melanocortin receptor-targeting peptides bearing nitro-, cyano-, ethynyl-fluoroarenes and fluoroheteroarenes as substrates for S_NAr reaction mediated macrocyclisation with cysteine residues. The resultant alkylthioaryl-bridged macrocycles were susceptible to chemical modification, enabling the generation of structural variants. Libraries of 19- to 22-membered heterodectic macrocyclic peptides were prepared, and resulted in a diverse series of melanocortin agonists with high potency activity and selectivity for different receptor subtypes.

The successful extension of the domain of S_NAr reactivity to substrates containing cyano and ethynyl functionalities as well as heterocycles, and the feasibility of post-cyclisation functionalisation boost the utility of S_NAr reaction in macrocyclic peptidomimetic design, advancing access to diversity-oriented ligand libraries with enhanced properties.

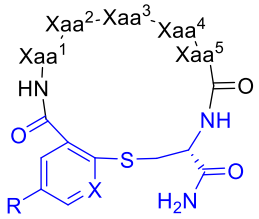

Figure 1. Design of alkylthioaryl-bridged macrocyclic peptidomimetics using S_NAr macrocyclisation.

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T-223

Design, synthesis and screening of a library based on *Eremophila*-derived serrulatane scaffold

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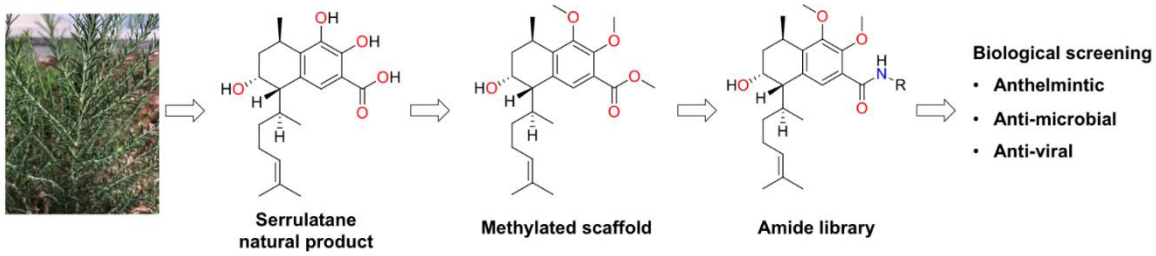
Chemical libraries generated from natural product scaffolds are important in drug discovery, particularly for optimising pharmacological properties and investigating structure-activity relationships of bioactive natural products. This approach allows rapid production of structurally diverse compounds with lead- or drug-like properties that can improve potency, toxicity, selectivity, lipophilicity, bioavailability, and other drug discovery parameters. Chemical studies on the aerial parts of the Australian desert plant *Eremophila microtheca* afforded the known bioactive diterpenoid scaffolds, 3,7,8-trihydroxyserrulat-14-en-19-oic acid and 3-acetoxy-7,8-dihydroxyserrulat-14-en-19-oic acid. The most abundant serrulatane scaffold was converted to the poly-methyl derivatives, 3-hydroxy-7,8-dimethoxyserrulat-14-en-19-oic acid methyl ester and 3,7,8-trimethoxyserrulat-14-en-19-oic acid methyl ester using simple and rapid methylation conditions consisting of DMSO, NaOH and MeI at room temperature. Subsequently, a 12-membered amide library was synthesised by reacting the methylated scaffolds with a diverse series of primary amines. The chemical structures of the 12 new semi-synthetic analogues were fully characterised following 1D/2D NMR, MS, UV, ECD and $[\alpha]_D$ data analyses. All compounds were evaluated for their anthelmintic, anti-microbial and anti-viral activities. This presentation will describe the chemistry and biological activities for this natural product biodiscovery project.



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T-224

Gallium nanodroplets for anti-inflammatory without interfering with iron homeostasis

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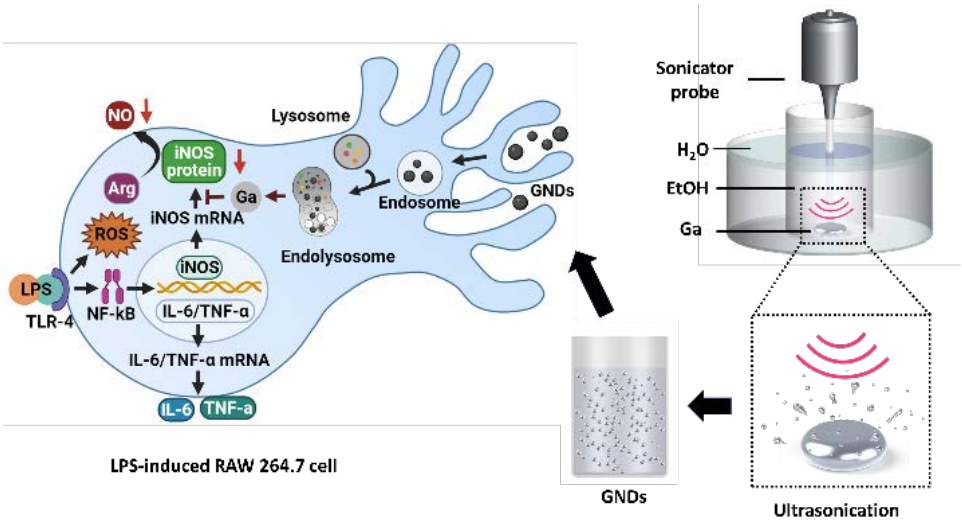
Gallium (Ga) compounds, as the source of Ga ions (Ga^{3+}), have historically used for anti-inflammatory[1]. Currently, the widely accepted mechanisms of the anti-inflammatory effects for Ga^{3+} are rationalized based on their similarities to ferric ions (Fe^{3+}), which permits Ga^{3+} to bind with Fe-binding proteins and subsequently disturbs the Fe homeostasis in the immune cells[2,3]. Here in contrast to the classic views, our study presents an unexpected mechanism of Ga for anti-inflammatory by delivering Ga nanodroplets (GNDs) into lipopolysaccharide-induced macrophages and exploring the processes. Surprisingly, the GNDs show a selective inhibition of nitric oxide (NO) production without affecting the accumulation of pro-inflammatory mediators. This is explained by GNDs disrupting the synthesis of inducible NO synthase in the induced macrophages, without interfering with the Fe homeostasis. The Fe^{3+} transferrin receptor-independent endocytosis of GNDs by the cells prompts a fundamentally different mechanism from that imparted by Ga^{3+}. This study reveals the fundamental molecular basis of GND-macrophage interactions, which offers a base for innovative use of Ga for anti-inflammatory, and future biomedical and pharmaceutical applications.



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T-225

Microwave assisted synthesis of fluorine containing curcuminoids using Nickel(II) bis(acetylacetonate)

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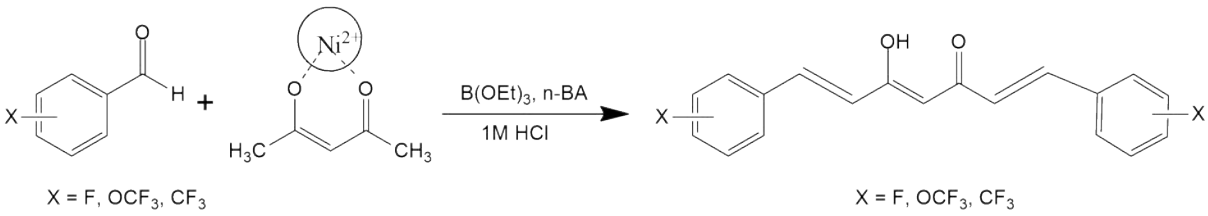
Curcuminoids have been recognized for over 50 years as potent anti-inflammatory and anti-cancer agents. Over the past two decades hundreds of curcumin derivatives have been synthesised and published, with a focus being on their potential in treating cancer and their role in inhibiting inflammatory mediators. More recently, a small number of publications have shown that halogenated curcuminoids have potential as antibacterial agents[1]. These results, although preliminary and limited, suggest that fluorine substituted curcuminoids are promising antibacterial agents with similar or equivalent potencies to clinically relevant fluoroquinolones[2].

The most utilised synthesis of curcuminoids was published by Pabon in 1964[3] and involves the use of a bidentate metal complex made from Boron trioxide (B_2O_3) and acetylacetone which undergoes symmetric aldol condensation with a suitable aromatic aldehyde (which in the case of curcumin is vanillin), in the presence of a dehydrating agent (trialkyl borate) and *n*-butylamine as a base catalyst. Pabon's method has been slightly adapted and used extensively over the past four decades to produce hundreds of symmetrical curcumin derivatives; however, the synthesis of fluorine containing curcuminoids using this method is overall poor yielding (<5%)[4]. This poor yield is in part due to the interaction between the boron bidentate ligand and the aromatic aldehyde containing fluorine(s) used in the reaction.

Work within our group to date has concentrated on optimizing the synthesis of fluorine containing curcuminoids using various non-boron bidentate acetylacetonates, bases and the use of microwave assisted synthesis methods. Using a nickel acetylacetonate and a microwave assisted synthesis protocol, we have reduced reaction times from 16 to 2 hours for the synthesis of many *mono-*, *di*-fluoro, trimethylfluoro- and trimethoxyfluoro-substituted curcuminoids and further increased yields as high above 90% in many instances.



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T-226

Biocompatible peptide bicyclisation using dicyanopyridine amino acids

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Bicyclic peptides are becoming an increasingly prominent class of potential next-generation therapeutics. Owing to their unique properties, they are capable of bridging the gap between small molecules and antibodies.[1, 2]
The most frequently used synthetic procedures to generate bicyclic peptides rely on the formation of disulfide or thioether bonds and often require special reagents or catalysts.[2, 3] We present a substantially different bicyclisation strategy, based on the catalyst-free, biocompatible 'click' reaction between cyanopyridine and 1,2-aminothiol, previously developed in the Nitsche group.[4, 5]
A novel reagent enables the synthesis of unnatural amino acids through its reaction with the nucleophilic side chains of cysteine and lysine-like amino acids. These dicyanopyridine-featured amino acids can be generated as Fmoc derivatives for incorporation into standard solid phase peptide synthesis (SPPS). Alternatively, dicyanopyridine amino acids can be synthesised on the solid support during SPPS *via* the use of inexpensive orthogonally protected amino acids. The bicyclic peptide is subsequently formed within minutes through a spontaneous intramolecular reaction in aqueous solution at physiological pH. The process is orthogonal to all canonical amino acids and fully amenable to automation.
To demonstrate the great potential for drug discovery, we generated a bicyclic inhibitor of the Zika virus protease NS2B-NS3, which is derived from the protease's recognition sequence. Bicycles can also be further modified post-synthetically, for example, to introduce labels or even generate tetracyclic peptides.
This methodology pushes the boundaries of bicyclic peptide synthesis, informs next-generation drug design and is likely to be compatible with genetically encoded peptide libraries.

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T-227

Synthesis of covalent peptide inhibitors for the Chikungunya virus non-structural protein-2 protease

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The Chikungunya virus (CHIKV) is an alphavirus transmitted to humans by the Aedes mosquitoes surrounding the tropical and subtropical regions of the world. Transmission was first detected in 1952, and there have been ongoing outbreaks in the Indian Ocean from 2007. The CHIKV disease is characterized by an abrupt onset of fevers, headaches, chronic and severe musculoskeletal pain. There are few data on the specific inhibition of CHIKV activity. Therefore, our research aims to inhibit the non-structural protein-2 protease (nsP2pro), which is mediated by a cysteine-histidine dyad[1]. Preliminary data on the inhibition of CHIKVnsP2pro have proven to be challenging. Through literature investigation and in silico modelling we designed covalent peptide inhibitors and aim to synthesise dipeptides incorporating reactive functional groups (warheads), including aldehyde, α-ketoamide, and nitrile substituents that irreversibly bind at the active site. Macrocyclic peptides cyclised via a thiazoline motif will also be explored as an alternative strategy to prepare peptidomimetic inhibitors for CHIKV nsP2pro. Our research will highlight the efforts towards synthesizing peptidomimetics to inhibit the challenging protease. The nsP2pro enzyme is also highly conserved among alphaviruses, providing opportunities for broad-spectrum inhibitors that may be active against other alphaviruses. The ongoing pandemic should bring awareness to the dangers of neglected viruses in third-world countries that could bring harm to our communities.

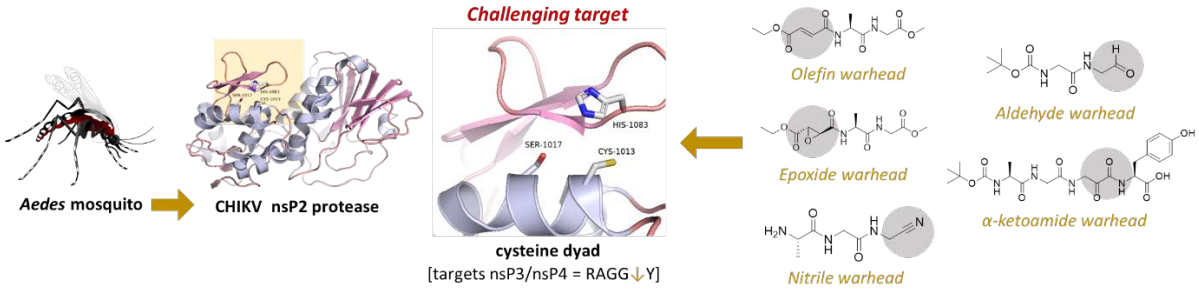

Figure 1. Examples of peptide-based inhibitors designed and synthesised to inhibit the cysteine dyad of CHIKV nsP2 protease (PDB: 3TRK) of the *Aedes* mosquito .

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W-228

Green dyeing process optimization of fibers using protic ionic liquids.

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Textile dyeing industry is the most chemically intensive and the second polluter of clean water (after agriculture)[1]. Usually, it uses non-eco-friendly traditional processes, with large amounts of water and chemicals as additives, which can have a huge environmental impact and could be harmful to human health[2]. Recently, papers have been published focusing in finding alternative sustainable process to reduce the amount of water and chemicals used, as well as improve the quality of the dyeing and keep the cost of the process low[3]. Protic Ionic Liquids (PIL) come into the light as new versatile media for many chemical syntheses, enzymatic catalysis and green engineering processes. PILs are made up of a pair of positive and negative ions, but they are liquid at room temperature unlike conventional molten salts. Also, PILs have low cost, most of them are biodegradable and they mostly have simple synthesis[4]. In this work, a reduced number of dyeing agents was used to optimize an alternative green procedure available in the open literature. Textile dyes, a cationizer pre-treatment fibre technique, and protic ionic liquids as additives in aqueous solution were analysed for the dyeing process of six different fabric types. The results with 30% m/m of PILs in aqueous solution shows colour strength up to 250 times higher than the alternative procedure available, and the cationization technique had a key role in colour fixation. In addition, cytotoxicology assays of the fabrics dyed in PILs aqueous solution were evaluated and they did not present any toxicology. Consequently, the alternative procedure proposed reduces its environmental impact, and on the other hand increased its dye quality, according to the dyeing agents results in terms of quality measurements such as absorption of colour and wash fastness standards of the dyed fibre. Moreover, this work innovates dyeing processing in using a reactive dye as an "universal dye", aiming for a more sustainable and safe profile for the textile industry.

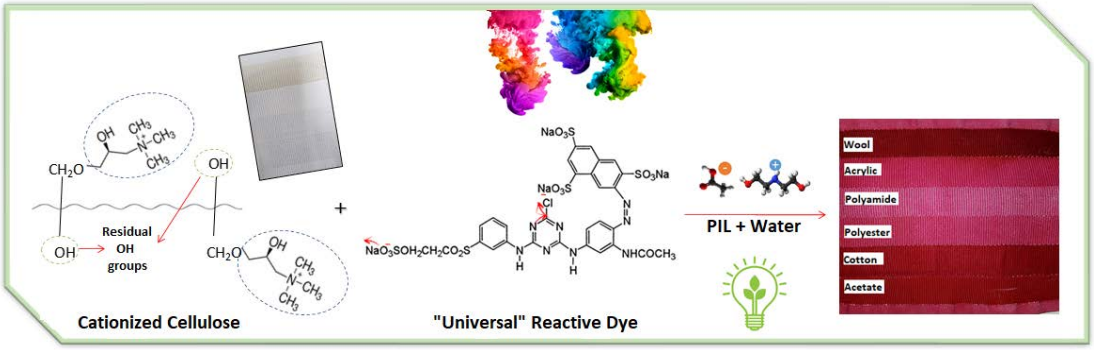

Figure 1. Multifiber Dyeing Process using Protic Ionic Liquids as only additive.

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W-229

Selective ring-opening of polycyclic naphthenic molecules over Ni-based catalysts

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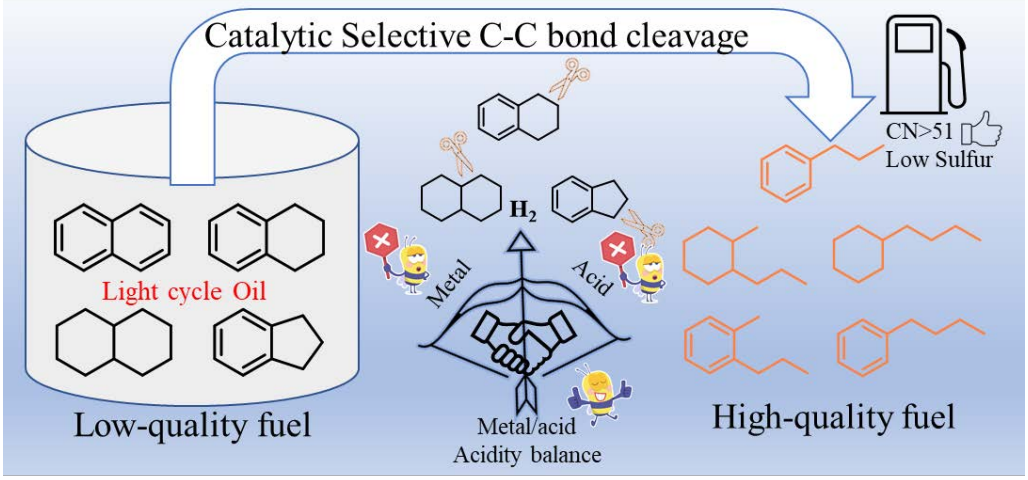
The selective C-C bond cleavage of mono- and bicyclic naphthenic molecules via catalytic ring opening plays a vital role in refining low-quality fossil oils and pyrolysis oils derived from municipal solid waste or waste biomass and tyres.[1] Recently, a new technology involving the complete saturation of the aromatic structures followed by the selective cleavage of endocyclic carbon-carbon bonds in polycyclic molecules (selective ring opening-SRO) is attracting attention to produce cleaner burning diesel (Figure 1).[1] Studies performed on metallic Ir, Pt, Ru, and Rh supported catalysts have determined that these noble metals are highly effective and selective toward ring opening products.[2] However, the high cost of these metals and poor activity towards opening C6 polycyclic molecules hinders their practical application. The choice of support greatly influences SRO activity and acidic supports can promote low temperature ring opening via an initial ring contraction step producing a strained C5 ring that is more susceptible to SRO. Here we report on a systematic study of the reactivity of low-cost Ni catalysts on different supports, including Al_2O_3, Al_2O_3 + zeolite mixtures, zeolites, and mesoporous Al-SBA-15, for the selective ring-opening polycyclic molecules such as decalin. All Ni-based catalysts were prepared by a wet-impregnation method and tested for ring-opening at high pressure (10 bar H_2) and moderate temperature (250 °C). The impact of Ni nanoparticle size, support acid strength and porosity and metal:solid-acid ratio on activity and selectivity in decalin



SRO will be discussed.

Figure 1. Selective ring-opening of polycyclic molecules over metal/solid-acid support catalysts

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W-230

NiFe/CeO_2 catalyst with good oxygen resistance for the NO reduction by CO

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Selective catalytic reduction (SCR) is an advanced active emissions control technology system that injects a liquid-reductant agent through a special catalyst into the exhaust stream of a diesel engine.(1) SCR has been widely used for the removal of NO in the industrial flue gas. The reduction agent NH_3 in many SCR systems, however, causes secondary pollution such as NH_3 slip and additional costs. As a result, using CO (CO-SCR) in the catalytic reduction of NO is a promising technology for industry where both CO and NO are present in the flue gas.

The oxygen present in the flue gas significantly inhibits the CO-SCR catalyst activity, which limits its industrial applications. One solution is to design high performance catalysts for the CO-SCR reaction in the presence of oxygen. In this study, the modified iron and cerium oxides (Fe/CeO_2) CO-SCR catalyst was obtained from a screen of different metals and metal oxides for this purpose. The results show that the Fe/CeO_2 catalyst achieves 99% NO conversion at 200°C without oxygen, which decreases dramatically to 42.7% when the oxygen is present (0.5 vol%). By contrast, the Ni-doped Fe/CeO_2 catalyst demonstrates significant enhanced oxygen resistance with 92% NO conversion at 150°C in the presence of 0.5 vol% oxygen. The new NiFe/CeO_2 catalyst was then characterised using techniques such as N_2 adsorption, XRD, SEM/TEM, XPS, H_2-TPR and in situ DRIFT, in order to investigate the mechanism and to further improve the catalyst. The results reveal when doped by Ni, the NiFe/CeO_2 catalyst improves the redox performance, since the Ni-Fe interactions increase the BET surface area of the catalyst, generate more surface oxygen vacancies (SOV) and surface synergetic oxygen vacancy (SSOV) in CO-SCR reaction. In situ DRIFT results confirm that better redox performance of the NiFe/CeO_2 catalyst is conducive to the conversion of adsorbed NOx species to the reactive intermediate NO_2^- species during the reaction. Meanwhile, the enhanced SOV/SSOV of the NiFe/CeO_2 catalyst remains active in the presence of oxygen. As a result, the NiFe/CeO_2 catalyst exhibits promising catalytic activities in CO-SCR reaction with presence of oxygen.

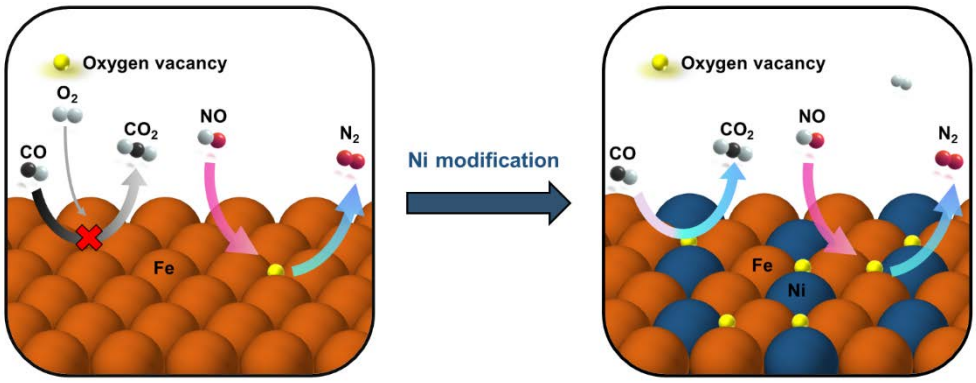

Figure: CO-SCR reaction over the Fe/CeO_2 catalyst (left) and the new Ni-modified NiFe/CeO_2 catalyst (right).

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W-231

Plasmonic silver nanoparticles enhanced immobilised Cr^{3+} catalysts for producing 5-hydroxymethylfurfural from sugars

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5-hydroxymethylfurfural (HMF) is a precursor to producing high-value biofuels, fine chemicals, and polymers. The conversion of naturally abundant six-carbon sugars to obtain HMF can increase the commercial value of the chemical by around 600-fold. The conversion has the potential to address environmental concerns, energy security and rural development. A variety of approaches have been developed to produce HMF from sugars. Cr^{3+} ions have been exploited as efficient Lewis acid catalysts for the isomerisation of glucose to fructose, the rate-limiting step for the generation of HMF from glucose. Here we report that visible-light irradiation promotes the catalytic performance of Cr^{3+} ions immobilised on a *γ*-alumina surface in the presence of silver nanoparticles (AgNPs). In one example, a 68 % yield of HMF for the conversion of *D*-glucose was achieved at 70°C under visible-light irradiation using the AgNPs-Cr^{3+} composite catalyst, where the turnover number is 13.4 times higher than in the absence of the AgNPs.

The principal mechanism of photocatalysis is that light-excited charges induce chemical reactions. Promoting chemical transformations by other mechanisms is of great interest. In the present study, the plasmonic AgNPs are not active catalytic sites but concentrate incident light to high intensities. Visible-light irradiation can excite the immobilised complex of Cr^{3+} ions and aldose molecules to high-energy electronic states. The excited states are active for the isomerisation from the aldose to the corresponding ketose. The concentrated light increases the population of the complexes at the excited states and, thus, accelerates the isomerisation process.

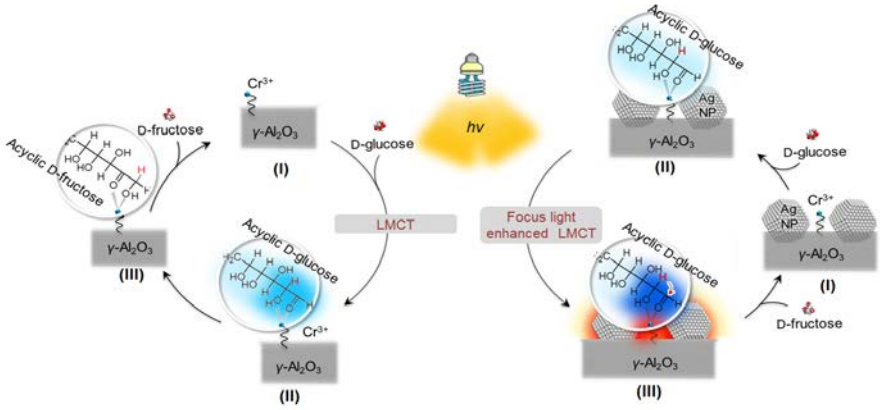

Figure Proposed mechanisms for the photocatalytic isomerisation of D-glucose. The left is the photocatalysis cycle with catalyst without AgNPs, and the right is that with AgNPs. The blue colour on the glucose molecule shows the electron distribution, and the red colour between the AgNPs indicates the intense EM field within the nanostructure.

The light irradiation also promotes hydrolysis of the Cr^{3+}ions. Protons released from the hydrolysis reaction are a Brønsted acid that catalyses the dehydration of ketose to HMF. Therefore, no additional Brønsted acid is required in the conversion. The new mechanism may substantially expand the potential applications of photocatalysis.

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TH-83

A photo-switchable molecular capsule: sequential photoinduced processes

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Photochromism is defined as the reversible conversion of two chemical species in response to light, with photochromic compounds being important due to their various real-world applications.[1] Among the different classes of photochromic compounds, diarylethenes (DAEs) offer thermal stability of the photogenerated isomers, fatigue resistance, and high quantum yields, proving them important for various applications.[2] The incorporation of DAEs in metal-organic frameworks, nanomaterials, and polymers has led to substances with novel properties.[3] Polyoxometalates (POMs) are inorganic discrete and nanosized metal-oxygen compounds of early transition metals commonly found in their highest oxidation with a range of structural and compositional diversity, making them suitable for various applications.[4] Functionalisation of POMs with organic species results in various organic-inorganic hybrid materials with tunable properties.[5] In 2018, we reported a POM-DAE complex that showed modified photochromic properties compared to the parent DAE.[6] Based on these earlier findings, we extended our study and have since succeeded in obtaining a photochromic molecular capsule with the generic formula $[(POM)_2(DAE)_3]^{x-}$ (1). The compound has been structurally characterized using single-crystal x-ray diffraction while also being studied extensively in solution using a suite of spectroscopic techniques.

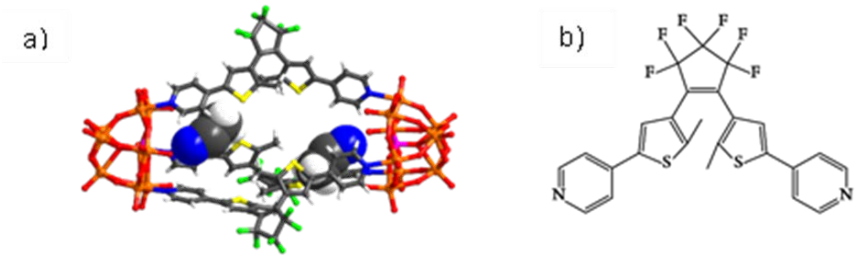

Figure 1: a) Graphical representation of the chiral molecular capsule (1) obtained from single-crystal X-ray diffraction structure determination b) Chemdraw representation of DAE ($C_{25}H_{16}N_2S_2F_6$).

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TH-84

Kinetics of thiosulfate oxidation using $TCNQF_n$ (n = 0, 2, 4) derivatives

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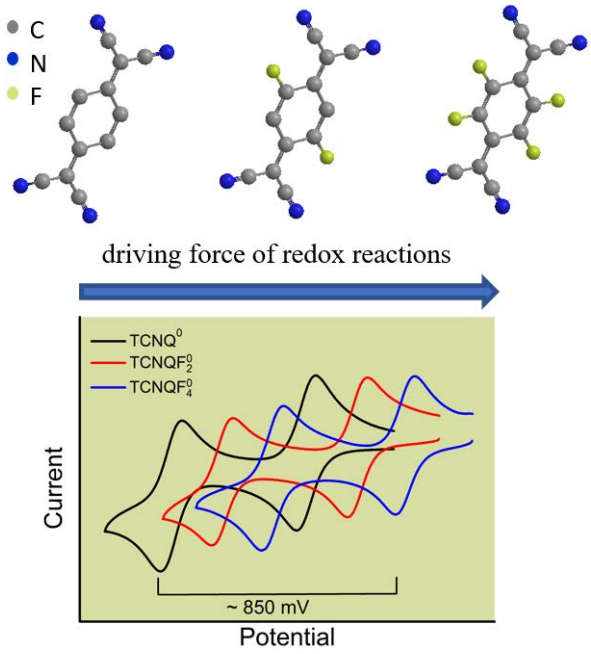
Abstract

Fluorine substituent effects on the and (n = 0, 2, 4) half-cell reactions where TCNQ = 7,7,8,8-tetracyanoquinodimethane provide access to an extensive range of reversible potentials (~850 mV) which are available to tune and exploit the driving force of redox reactions: in this case the oxidation of to by or . The - / redox reactions have been evaluated by steady-state or transient cyclic voltammetry and UV-visible spectroscopy in acetonitrile containing 5 % water. In this mixed solvent system, all the (n = 0, 2, 4) - / redox reactions are thermodynamically favorable, as are the reactions of (n = 2, 4) with . However, does not react with . These results enable a reversible potential for the / half-cell reaction to be estimated. Interestingly, in the investigation of the reaction of and in a 1:2 concentration ratio, the protonated intermediate () is detected, albeit transiently. In contrast, when the oxidant is (2,5-difluoro-7,7,8,8-tetracyanoquinodimethane) or (2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane), no protonated intermediate is detected. However, if equimolar mixtures of (n = 0, 2, 4) and are used, the protonated intermediate is detected in all cases. Mechanisms are provided to explain catalysis by the protonated intermediate and the role of the thermodynamic driving force in the oxidation of by .



TH-85

Towards antiaromatic supramolecules

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The recent advent of synthetically available antiaromatic compounds has challenged the notion that such compounds are inherently unstable. Nickel norcorrole, an antiaromatic porphyrinoid, is remarkably bench stable.[1] Metallonorcorroles should be able to coordinate axial ligands, a binding mode which has been extensively explored in other porphyrinoids. However, this chemistry has not yet been explored in the currently reported norcorroles. Supramolecular complexes of antiaromatic compounds are particularly desirable as they would allow the construction of multichromophoric arrays with unusual properties, such as increased single molecule conductance.[2] Unfortunately, pyridine ligands bind weakly to nickel porphyrinoids, generating paramagnetic complexes which are difficult to analyse by NMR. Here we show the synthesis of a novel norcorrole and demonstrate its ability to bind axial ligands.

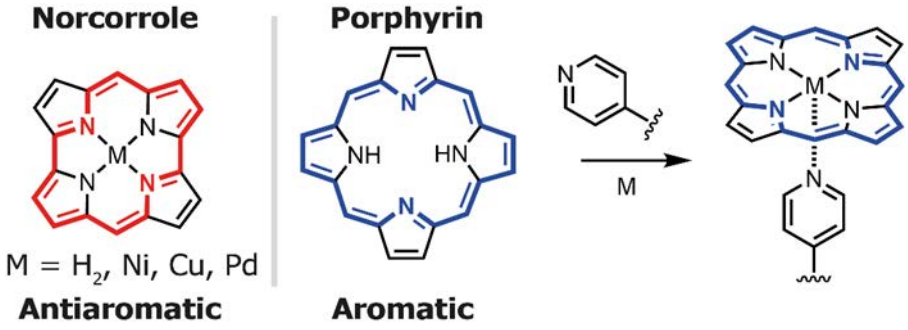

Figure 1. Antiaromatic metallonorcorrole (left) and aromatic metalloporphyrin showing axial binding of a pyridine ligand (right).

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TH-86

Midnight Blue: A vibrant family of phosphoniothioacyl complexes from phosphoniocarbynes and sulfur

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Many thousands of organometallic complexes bearing carbonyl (CO) and phosphine (PR_3) ligands are known, yet conspicuously combination of these ligands has never been observed. Phosphines can attack thiolato- or halocarbynes to give phosphoniocarbynes,[1] while addition of sulfur converts aryl-carbynes to thioaroyl or dithiocarboxalate complexes.[2] *Phosphino*-carbynes may present a competitive site (P) for sulfur addition.[3]

Here we report the serendipitous discovery of previously unknown phosphoniothioacyl complexes through the sulfurisation of phosphoniocarbynes with elemental sulfur. A family of brightly coloured complexes have been characterised, varying the phosphine component by electron donation and Tolman cone angle properties prior to preliminary reactivity and theoretical studies. So while $OCPR_3$ remains remain unknown, the viability of $SCPR_3$ has now been established.

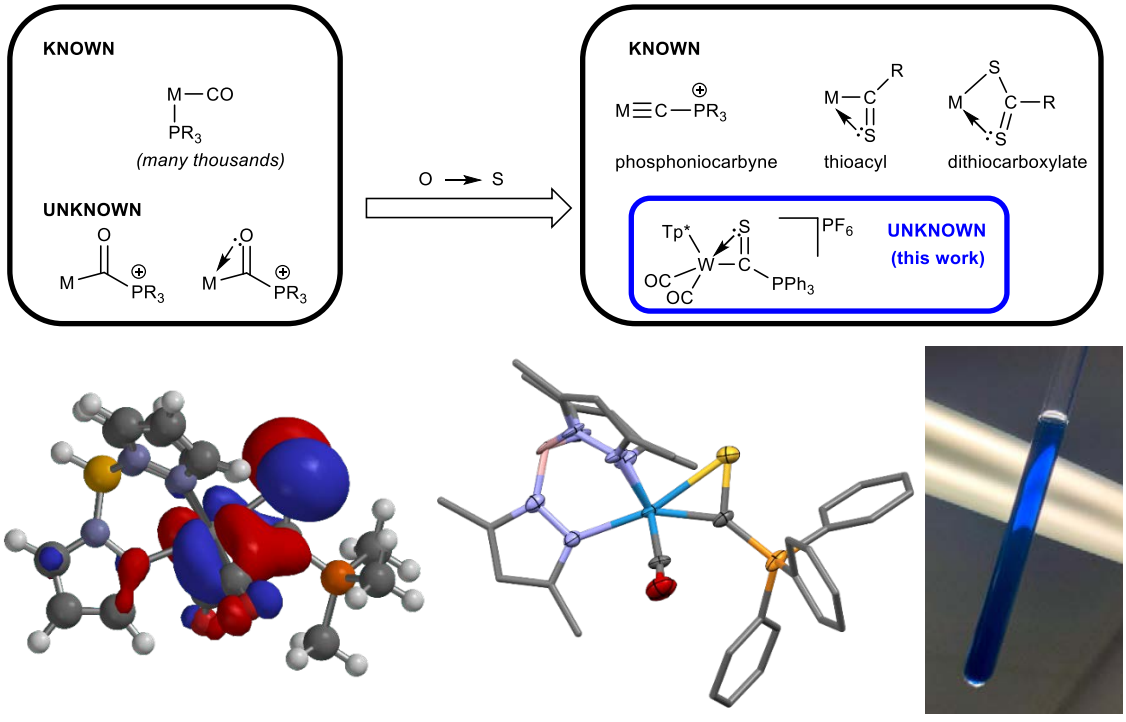

Figure 1: (a) HOMO diagram DFT:ωB97X-V{6-31G*};LANL2Dζ ; (b) molecular structure in a crystal; (c) dilute sample of compound in CH_2Cl_2.

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TH-87

A versatile bis(thiosemicarbazone) macrocyclic chelator for use in radiopharmaceuticals

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Developing radiopharmaceuticals for imaging and/or therapeutic applications using radiometals requires chelators that can generate stable and inert complexes. Chelators that can provide a suitable coordination environment for a range of radiometals with different applications are particularly useful.[1] Thiosemicarbazone functional groups are versatile N,S donors that can coordinate metal ions as neutral or anionic ligands, with the resulting complexes displaying diverse coordination chemistry. N-heterocyclic thiosemicarbazones have been investigated for their pharmacological properties, which have shown that the metal complexes can display bioactivities which differ from those of either the ligand or the metal ion.[2,3] A new bis(thiosemicarbazone) macrocyclic chelator has been synthesised that has versatile coordination chemistry, chelating a wide range of metal ions.[4] The versatility of the ligand results in both 6- and 8-coordinate complexes depending on the metal ion. The first-row transition metals Mn^{2+}, Co^{2+} and Zn^{2+} generate 6-coordinate complexes with distorted octahedral geometry in the solid state (Figure 1).[4] Density functional theory calculations indicated that the relative energies of the diastereomers are within 10 kJ mol^{-1}. Magnetic susceptibility of the complexes indicated that both the Mn^{2+} and Co^{2+} ions are high-spin. The In^{3+} ion generates complexes with both 6- and 8-coordination numbers under certain conditions as seen by ^{1}H NMR. The ligand was radiolabelled with the positron emitting isotope gallium-68 which produced a single species in high radiochemical purity (>95%) at 90 °C for 10 min. As a result, this chelator has demonstrated the potential for use in a variety of radiopharmaceutical applications.

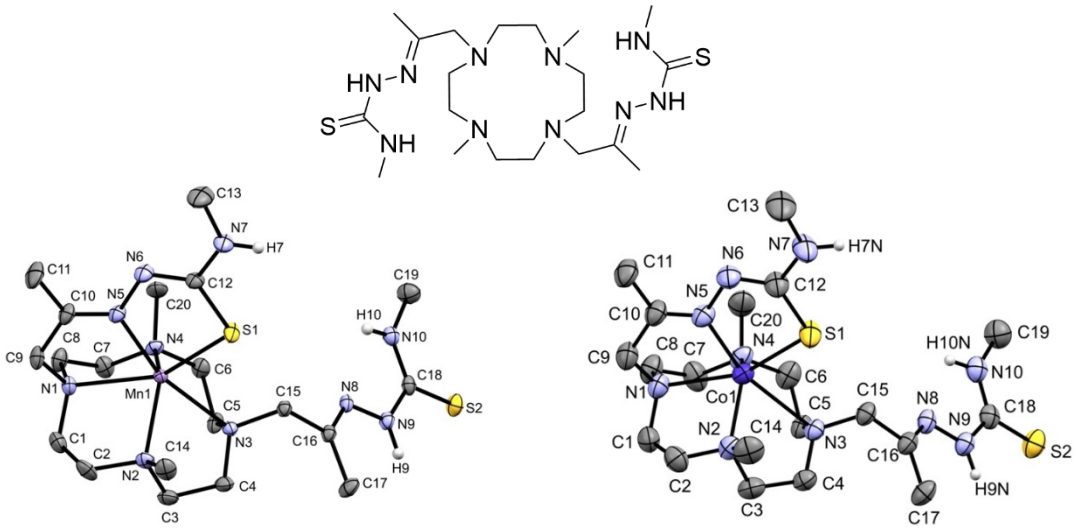

Figure: The structure of the bis(thiosemicarbazone) macrocyclic chelator (top), the x-ray crystallographic structure with Mn^{+2} (bottom left) and Co^{2+} (bottom right).

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TH-89

Sensitised Lanthanoid Luminescence using Bimetallic Cu(I)-Ln(III) Complexes

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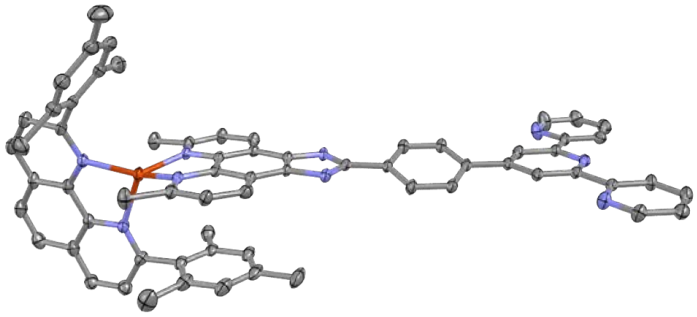
Trivalent lanthanoids typically possess sharp emission bands with long excited state lifetimes that have found a variety of applications in (bio)sensing, imaging, and telecommunications.[1] However, the direct photoexcitation of these 4*f** states is inefficient due to their intrinsically low extinction coefficients. Instead, a commonly used strategy to circumvent this limitation is the incorporation of a strongly absorbing organic and/or inorganic antenna ligand bound to the Ln(III) cation.

In particular, polypyridyl Ru(II) and cyclometalated Ir(III) complexes have been used with considerable success as chromophores for sensitised Ln(III) luminescence from Near Infra-Red (NIR) emitters such as Nd(III) and Yb(III).[2, 3] Owing to their relatively long-lived ^{3}MLCT excited state lifetimes, these antenna metalloligands demonstrate highly efficient lanthanoid sensitisation, and rapid rates of intramolecular energy transfer.

Nonetheless, in an effort to replace the use of precious metal based luminophores, we have begun investigating the use of more earth abundant sensitisers, such as Cu(I) polypyridyl complexes. Despite several challenges, mostly related to the rapid deactivation of their ^{3}MLCT excited state, this class of complexes may be promising candidates considering their otherwise similar excited state properties.

Herein, we report the synthesis and characterisation of a series of heterobimetallic *d-f* complexes, incorporating a sterically encumbered heteroleptic Cu(I) chromophore as an antennae, covalently linked to a 2,2':6',2''-terpyrdine group as a pendant Ln(III) chelator. Excitation via the visible absorbing Cu(I) MLCT band leads to intramolecular energy transfer, and subsequent characteristic sensitised emission from various NIR emitting lanthanides. To the best of our knowledge, this represents the first example of sensitised lanthanide luminescence using a Cu(I) based chromophore.



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TH-90

Nonlinear Optical Properties in Chiral Metal-Organic Frameworks for All-Optical Switching

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Continued technological innovation in the modern era has been as a result of global information infrastructure. Vast quantities of information can be transmitted using light (photons) which is enabled by optical fibre networks. Information is relayed by photons, but the signals are converted into an electronic form to be processed and stored. This results in enormous energy consumption and slower signal speed.

All-Optical devices are regarded as an enabling technology to manipulate photons such that there is no need for signals to pass into the electrical domain, thus leading to ultrafast speeds (> 500 GB s^{-1} /in terahertz range). To date, the major bottleneck in the materials that have been investigated is that energy barrier and response time is too slow to be meaningfully used. The lack of efficient photon-photon interactions has fuelled research into alternative methods.

Nonlinear optical materials[1] such as chiral Metal-Organic Frameworks (MOFs) are a new potential platform technology to bypass the electrical domain and achieve ultrafast and energy-efficient photon-photon interactions.

Post synthetic modification (PSM) of achiral MOFs provides a facile strategy to introduce chiral groups into frameworks, potentially rendering the overall solids chiral. The isostructural MOFs [M^{II}_2(μ-dobdc)] (also known as MOF-74 where $dobdc^{4-}$ = 4,6-dioxido-1,3-benzenedicarboxylate^{4-} and M = Zn, Co, Ni, Mg, Mn, Fe, Cu, Cd) will be post synthetically modified with chromophores to enhance nonlinear optical properties. The results of our initial investigations into the nonlinear optical phenomena will be presented here.

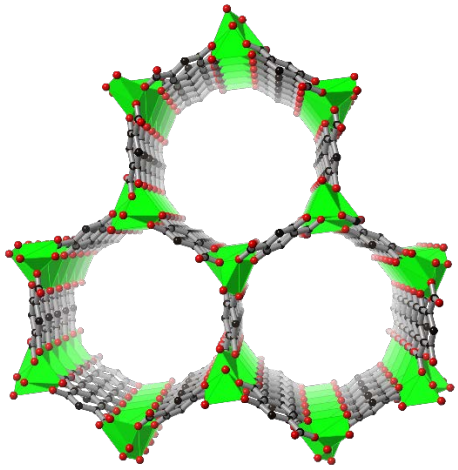

Figure 1: Mg-MOF-74 Crystallographic structure

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TH-91

Zirconia solid acid catalysts for sustainable chemical manufacturing

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Biomass conversion is of great importance for sustainable chemical manufacturing, whereby biofuels and specialty chemicals are generated from naturally produced biomass waste. Mesoporous solid acid catalysts are considered as one of the most viable solutions to be applied in biomass conversion reactions since they offer high surface area, large pore diameters and tunable acidity. Zirconia, a polymorphic white crystalline ceramic material, is a promising catalyst or catalyst support due to its hydrothermal stability, amphoteric character, and possibility to tune acidity with dopants.

However, the wider application of ZrO_2 catalysts requires rational design to unravel structure-activity relationships and maximize catalytic productivity. In this study, pure monoclinic and tetragonal zirconia families with surface area of ~90 m^2/g were synthesized and their physicochemical properties, such as porosity, microstructure, evolution of acid-base sites as a function of morphology, and hydrothermal stability determined. Sulphated ZrO_2 (SZ) families were also synthesized by doping zirconia with H_2SO_4 to enhance solid Brønsted acidity, while ZrO_2/SBA-15 families were synthesized using mesoporous SBA-15 frameworks to enhance ZrO_2 dispersion.

Levulinic acid is classified by the US DoE[1] as a valuable platform chemical which is readily obtained by the dehydration of glucose, and is a precursor to the renewable solvent γ-valerolactone (GVL) (Figure 1). The production of GVL from levulinic acid proceeds via the Meerwein–Ponndorf–Verley (MPV) reduction reaction using iso-propanol as a hydrogen donor. The activity of these zirconia catalysts will be reported in both batch and continuous flow systems for the conversion of levulinic acid to GVL. Dual bed configurations will be explored in continuous flow reactors employing SZ and ZrO_2/SBA-15 catalysts for the tandem esterification of levulinic acid and subsequent MPV reduction to enhance the continuous production of GVL.

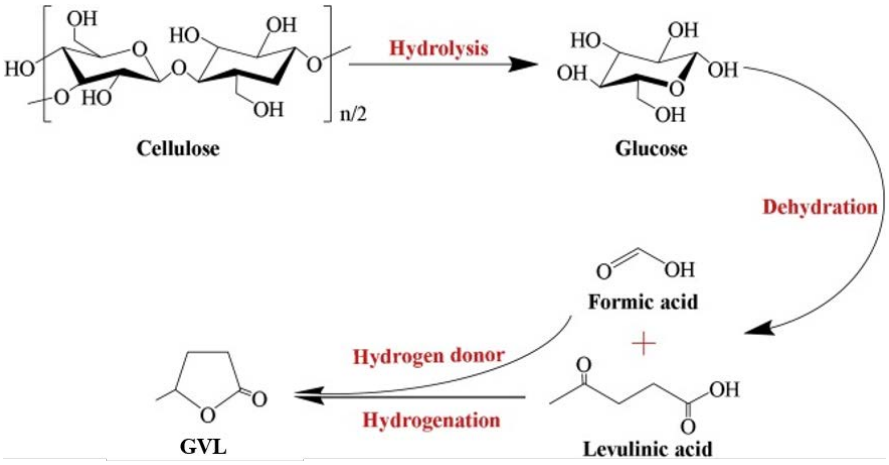

Figure 1. Proposed reaction pathways for the acid-catalysed hydrolysis of cellulose to GVL[2]

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TH-92

Solution and solid-state properties of environmentally sensitive organic fluorophores

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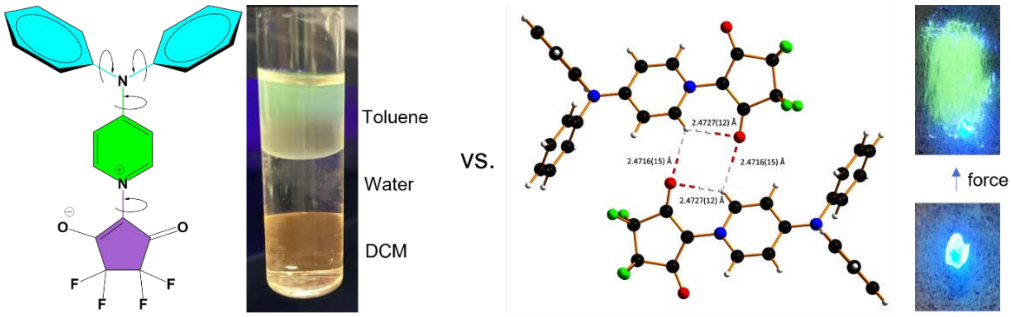
Luminescence is a key phenomenon exploited in biological studies and optical applications. The elimination of potentially toxic and expensive metals is an attractive idea for novel smart materials. This research investigates the synthesis, characterisation and application of organic solvato and mechanochromic fluorophores, based on the Ritchie group's recently published novel class of pyridinium betaines.[1] The potential applications for such bright and chromic materials are numerous, including as mechano/biosensors, optical components in luminescent solar concentrators and organic light-emitting diodes, and in anticounterfeiting materials.

The pyridinium betaines under study build upon the previously established species by showing distinct solution and solid-state properties. In solution, absorption and emission transition energies are affected significantly by solvent polarity, due in part to having large dipole moments, as well as multiple rings capable of rotation. In the solid-state, however, the transition energies are notably affected by application of force, such as anisotropic grinding, where blue-emitting crystals switch to green emission upon mechanical grinding. There are many ground and excited-state mechanisms that can lead to variation in luminescence behaviour, including pH sensitivity, excimers/exciplexes, twisted intramolecular charge transfer, excited-state intramolecular proton transfer and hybridized local and change-transfer states.[2,3] To that end, the origin of these solution and solid-state properties is probed via techniques including photophysical studies (fluorescence spectra, lifetimes and quantum yields), solid-state structural analysis (single-crystal structures and powder diffraction), in tandem with quantum chemical calculations to help explain the underlying mechanisms.



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TH-93

Post-synthetic Hydrophobic Modification of Metal-organic Frameworks for Improved Gas Separation

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The high porosities and internal surface areas of metal-organic frameworks (MOFs) makes them especially suitable for roles in gas sorption and separation. One issue with many MOFs for applications regarding gas sorption and separation is the competition between target molecules and water for sorption at pore sites, particularly in humid environments.[1] On potential strategy for improving the thermodynamic and kinetic properties for sorption of the target molecule over water involves increasing the hydrophobicity of a MOF. Within the current known library of MOFs, only around 100 exhibit intrinsic hydrophobic properties.[2] To overcome this limited selection of frameworks, investigation into strategies for introducing hydrophobicity through post-synthetic modification can help tailor MOFs for applications in gas sorption and separation. Using the robust and well-studied framework UiO-66-(NH_2) $[Zr_6O_4(OH)_4((C_6H_3(NH_2)(COO)_2)_6]_n$ a range of post-synthetic modifications can be used to increase the internal, and external hydrophobicity, allowing for greater selectivity for the target molecules over water.

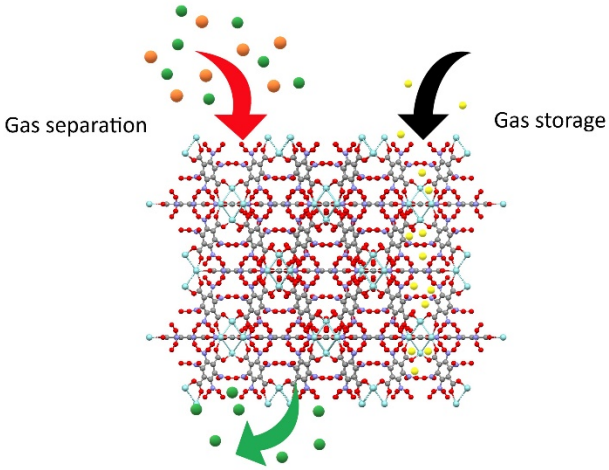

Figure 1: Framework UiO-66-NH_2 and applications for gas separation and storage.

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TH-94

Targeted Alpha Therapy with Actinium-225 Labelled Antibodies

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The emerging potential of radionuclide therapy with alpha (α^+) emitting actinium-225 has stimulated significant interest in developing chemistry to enable the selective delivery of actinium to tumours. Ac-225 ($t_{1/2}$ 9.9 days) decays to the long-lived isotope Bi-209 ($t_{1/2}$ 1.9 x 10^{19} y) *via* the release of a total of four α-particles, and two beta (β^-) particles. The high particle energy and linear energy transfer of α-emission delivers high doses of radioactivity, capable of causing double stranded breaks in DNA, across relatively short distances (40-90 µm). Therefore, there is significant interest in developing bifunctional chelators that form stable complexes with Ac^{3+} which are easily conjugated to antibodies for targeted alpha therapy of cancer. Carbonic anhydrase IX (CAIX) is a metalloenzyme which is overexpressed on the surface on clear cell Renal Cell Carcinoma.[1] The monoclonal antibody Girentuximab selectively binds CAIX with high affinity (Figure 1a) and has the potential to selectively deliver therapeutic radiation to tumours.

A crown ether macrocyclic ligand functionalised with two picolinic acid arms, H_2macropa (Figure 1b) forms stable complexes with actinium (III), the largest trivalent cation in the periodic table.[2,3] In this work a new bifunctional variant with a pendant diethyl squarate ester, H_2macropa-tzPEG$_3$Sq, that allows the conjugation of the macrocycle to antibodies will be presented (Figure 1c). The conjugation of H_2macropa-tzPEG$_3$Sq to Girentuximab (and other cancer targeting antibodies) and radiolabelling with Ac-225 will be discussed. An evaluation of the therapeutic efficacy of [^{225}Ac]Ac-macropa-tzPEG$_3$-Girentixumab in a mouse model of renal cancer will also be presented.

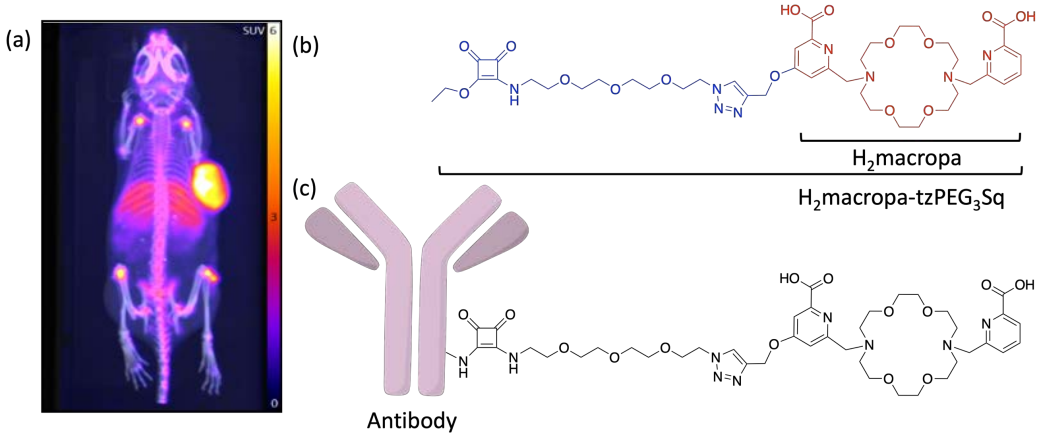

Figure 1. (a) Positron Emission Tomography image of [^{89}Zr]Zr-DFOsq-Girentuximab mice showing CAIX overexpression in a renal tumour model; (b) chemical structure of H_2macropa and H_2macropa-tzPEG$_3$Sq; (c) H_2macropa-tzPEG$_3$Sq conjugated to a monoclonal antibody.

We acknowledge the Australian Research Council, Australian Cancer Research Foundation, National Health and Medical Research Council, the Victorian Cancer Council and Telix Pharmaceuticals for supporting this research.

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TH-95

Incorporation of Ir(III) cyclometalated motifs into chiral heterometallic supramolecular assemblies

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The self-assembly of discrete multicomponent metal-organic coordination cages is an active area of research in supramolecular chemistry. The metal ions that are incorporated into these assemblies typically play a structural role, often being selected for their predictable coordination geometries, coordinative preferences and bond lability.[1] However, many transition metals such as Ir(III), and complexes thereof, often possess interesting electrochemical and/or photophysical properties which can be integrated into supramolecular systems.

Given its robust photoluminescent properties, predictable geometric orientation and kinetic stability, the fac-[Ir(ppy)$_3$] motif (ppy = 2-phenylpyridinato) is a suitable building block for the incorporation into photoactive supramolecular structures. To take advantage of the kinetic inertness of [Ir(ppy)$_3$], we have used a metalloligand approach whereby chelating moieties, which are attached to the inert core, can interact with labile metals and facilitate the self-assembly process.

We have prepared a racemic Ir(III)-containing metalloligand consisting of three 2,2':6',2''-terpyridine units appended to a fac-[Ir(ppy)$_3$] core via phenyl linkers. Metal-directed self-assembly with Cd(II) forms a $[Ir_2Cd_3]^{6+}$ helicate and mesocate pair, whereas reaction with Zn(II) leads to the formation of *T*, C_3 and S_4 diastereomeric $[Ir_4Zn_6]^{12+}$ tetrahedra. To eliminate the formation of mixed stereoisomers, we have developed a method to resolve the metalloligands into the enantiopure Δ/Λ isomers which involves modification of the [Ir(ppy)$_3$] core to incorporate a chiral pinene motif, enabling the construction of enantiopure tetrahedra.

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TH-96

FTIR spectroscopy: A powerful technique to study electronic structure of mixed-valent complexes

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Mixed-valent (MV) complexes $[L_xM^{n+}]\{\mu\text{-}B\}[M^{(n+1)+}L_x]$ have played a significant role in developing understanding of electron transfer processes.[1] Conventional methods of analysis are based on the band-shape of the optical Inter-Valence Charge Transfer (IVCT) transition, using the relationships developed by Hush and described within the general framework of Marcus-Hush theory.[2] However, the application of the 'two-state' Marcus-Hush theory to many systems is complicated by various factors, including the difficulties in identifying the IVCT band, the presence of multiple CT bands with similar character which often overlap with other low energy (e.g. dd) transitions, the convolution of the redox sites over the terminal and bridging moieties and the presence of different conformers in the solution. The degree of electronic (de)localization of these conformers can change upon changing the orbital overlaps between the terminal and bridging fragments, further convoluting the transitions within the NIR region.[3]

FTIR spectroscopy has proven to be a powerful tool in studying the conformational effects on the electronic structure of MV states because of being better-resolved than electronic spectroscopy, relatively fast time-scale and the characteristic shifts in ν(C≡C)[4] ν(CO)[5] ν(C≡N)[6] frequencies which provide structural information. Selection rules further help distinguish localized, delocalized and bridge-centred redox events. This experimental method is further complemented by advances in DFT-based computational methods, which seek to overcome the traditional problems of the correlation problem through appropriate balanced global, range-separated or local hybrid functionals.

In this presentation, we describe our efforts to employ a combination of FTIR spectroscopy - DFT calculations to study the role of different combinations of redox-active metal (M), supporting (L) and bridging (B) ligands in the electronic structure of MV complexes. The results will propose some strategies to impose a degree of control on the electronic communication between the redox centres (by inserting a metal fragment, changing the metals or the substituents on the bridge) with a computationally cheaper protocol.

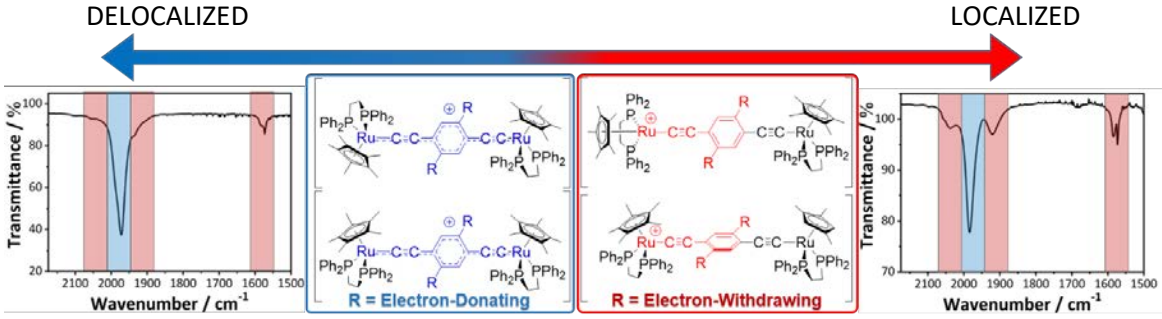

Figure. FTIR spectra provide evidence for conformer effects and electronic structure in MV complexes

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TH-97

Selective carbon-phosphorus bond cleavage for accessing superbulky divalent lanthanoid sandwich complexes

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The synthesis of divalent lanthanoid metallocene complexes bearing bulky polyaryl substituents has become a hot topic within organometallic chemistry, owing to the interesting physical properties, and limited reactivity of these complexes. Currently two major pathways have been employed to synthesise these poorly soluble complexes: either by protolysis utilising very reactive lanthanoid benzyl precursors,[1,2] or by redox transmetallation protolysis, utilising heavy metal reagents.[3,4] Herein, we describe a new synthetic route used to access these superbulky divalent metallocenes, by selective cleavage of a carbon-phosphorus bond, avoiding the use of reactive lanthanoid precursors, or heavy metal reagents, such as bis(pentafluorophenyl) mercury.

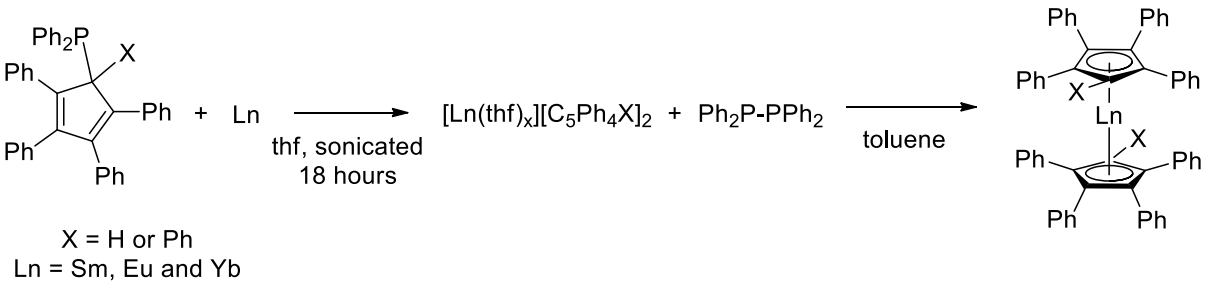

Figure 1 – Reaction scheme for the synthesis of superbulky lanthanocenes from polyarylcyclopentadienylphosphines

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TH-98

How far can bent ligands go in Spin Crossover Frameworks

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Spin crossover (SCO) complexes have attracted enormous attention in the past few decades due to their potential applications in nanotechnological devices, such as molecular switches, sensors, and memory storage. Such complexes show bistability which is attributed to their ability to be reversibly switched between two electronic states – high spin (HS) and low spin (LS) –by external stimuli (i.e., change in temperature or pressure, guest present or light irradiation).[1-2] Herein, we describe that inclusion an angular bridging ligand into a Hofmann-type framework produces an irregular 2-D network (Figure 1) in which six- and five-coordinate FeII species co-exist. The octahedral sites show thermally-induced spin-crossover and the rare five- coordinate FeII sites are high-spin and present a valuable new methodology for stabilizing and studying rare coordination environments in a biomimetic context.

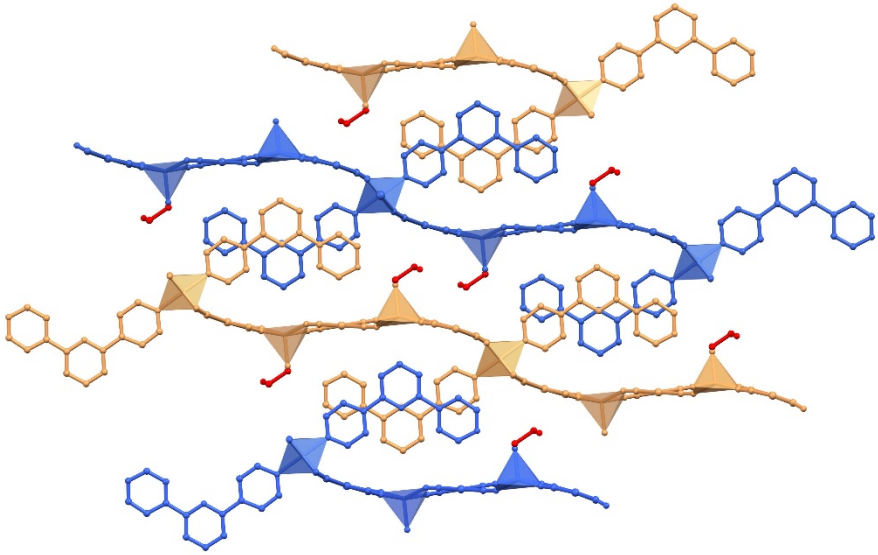

Figure 1. Irregular two-dimensional Hofmann structure using an angular ligand.

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TH-232

Liquid metal-based implants: a proof-of-concept

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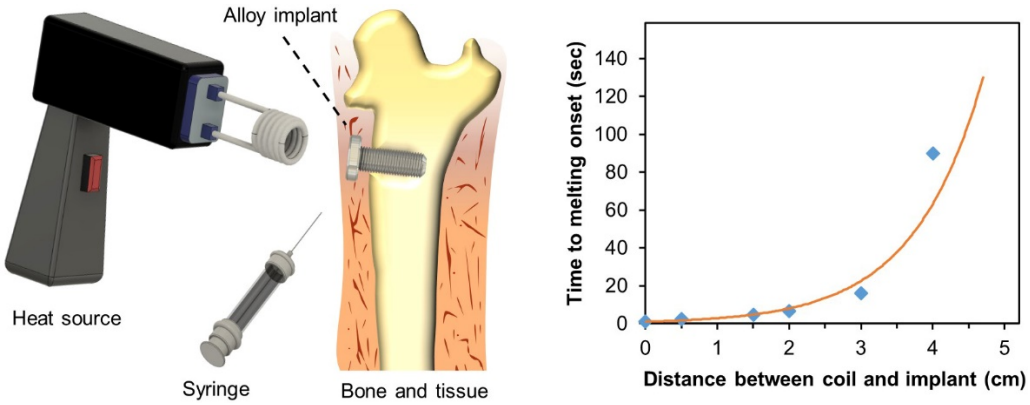
Low melting point eutectic alloys have been investigated for their unique properties such as single point melting temperature, homogenous structures, and uniform distribution of phases. In this work, we utilized a series of post-transition liquid metal alloys as low melting temperature materials for novel temporary implant design. In particular, Field's metal, a eutectic alloys of indium-tin-bismuth, and Field's metal-like alloy with traces of zinc (0.4 wt%) were investigated through a series of structural, thermal, microstructural, and mechanical tests.

In addition, the *in-vitro* biocompatibility of the alloys was assessed to investigate their potential application as bioimplants. Field's metal and the alloy with zinc presented low melting point (~62 °C and ~60 °C, respectively) and were investigated to address one of the major issues faced by the conventional use of bioimplants, which is the invasive surgery for the removal of the implant.

We provide a proof-of-concept utilizing remote heating for the melting and removal of the Field's metal-based alloys. This approach enabled a contactless melting and extraction for the non-invasive removal of the bioimplant. The implant removal was demonstrated when fixed in a polymer matrix, that can be potentially translated to the human body. This innovative approach will provide fundamental insights for future biomedical applications and the design of liquid metal-based implants for non-invasive surgical removal procedures.



Schematic representation of the melting and removal of the low melting point liquid metal implant and time to melting onset as a function of the heat source distance.

TH-233

High Shear Induced Covalently Assembled 2D Arrays of Fullerene C_{60}

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Fullerene C_{60} can be polymerised in the solid state at high temperature and pressure and in solution through cavitation. We have established the ability to covalently self-assemble C_{60} using a vortex fluidic device (VFD) where the 20 mm diameter quartz tube has a flat base rather than the conventional hemispherical base.[1,2] This increases the shear stress associated with the 'spinning top' (typhoon like) topological fluid flow in the thin film, inducing 'crystallisation' of C_{60} from a toluene solution below the saturation concentration, and depending on the rotational speed (ω) and the processing time for the tube tilted at 45°, rectangular faceted 2D sheets of covalently linked C_{60}, ca 5 nm thick, of uniform dimensions up to 10 - 20 μm in length and 3 to 5 μm in cross section are formed, Figure 1. Also, important is that the processing is without the need to use surfactants to control the nucleation and growth of the material, or the application of high pressure, although this may arise in localized regimes in the thin film of liquid, associated with the topological fluid flows.[1,2] The novel nano fullerene C_{60} material was studied using different characterisation techniques included SEM, AFM, XRD, STA and TEM. The results establish that C_{60} can be polymerised in a controlled way, forming 2D arrays of the fullerene linked by 2+2 addition reactions, rather than crystallising as a self-assembly process at the van der Waals limit.

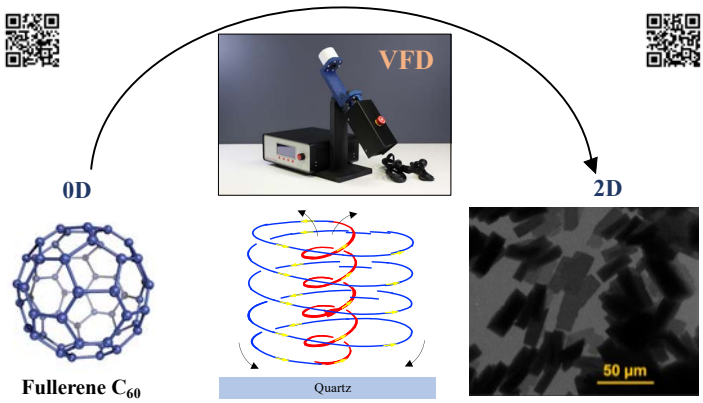

Figure 1: Formation of 2D C_{60} rectangles sheets at the surface of the VFD flat tube associated with high shear Coriolis force 'spinning top' flow.

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TH-234

Electrolytes based on hexamethylguanidinium organic ionic plastic crystal for Sodium Batteries

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Current battery storage relies on unsustainable mining of global reserves of lithium and cobalt that could potentially become constrained and expensive. In addition, battery technologies have safety issues, particularly at elevated temperatures. Sodium based batteries are emerging as a viable beyond Li-ion battery technology for future energy storage. Sodium has certain advantages such as greater abundance than lithium, better intrinsic safety and potentially a relatively high energy density. Currently, much research is focussed on the electrode materials (hard carbon anodes and new cathodes) however the electrolyte component is an important enabler of the technology. Ionic liquids and organic ionic plastic crystals (OIPCs) have been shown to be good electrolyte candidates for Na batteries, enabling Na metal anodes.[1]

Organic ionic plastic crystals (OIPCs) are purely ionic solid state electrolyte materials that are increasingly drawing attention due to their unique combination of properties such as negligible volatility, non-flammability and increased safety in contrast to electrolytes based on organic, flammable solvents that are typically used in electrochemical cells. Additionally, many of them are characterized by high thermal and electrochemical stability that makes them an attractive candidate for many electrochemical device applications. In order to enable use of OIPCs in sodium batteries a source of Na^+ needs to be added to the neat plastic crystal. Addition of sodium salt significantly changes their properties and understanding the effect of incorporation of a second component on the materials properties and battery performance is crucial for designing new electrolytes.

Based on a recently reported promising new OIPC - hexamethylguanidinium bis(fluorosulfonyl)imide ([HMG][FSI]) and prior work showing its favourable electrolyte properties after Li salt addition (good transport properties and reversible deposition and stripping of lithium),[2] this material was chosen to be studied for sodium battery applications. In this work we focus on [HMG][FSI] and the effect of doping with different concentrations of sodium salt (NaFSI) on the material properties.[3] All the electrolytes and the neat OIPC were evaluated in terms of thermal properties, solid state structures, ionic conductivities, ion diffusion and electrochemical properties. Interesting and usual conductivity behaviour was observed for [HMG][FSI] and low sodium salt concentrated mixtures. All compositions of OIPC with NaFSI resulted in promising solid-state electrolytes, and a phase diagram where the eutectic point was determined is proposed.

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TH-235

Analysis of gelatin methacryloyl bioinks using small-angle X-ray scattering[1]

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The current gold standard of soft materials used for tissue engineering is gelatin methacryloyl (GelMA), a semi-synthetic collagen-derived biomaterial that has found widespread utility as a bioink for 3D bioprinting. Although a fundamental understanding of controlling the mechanical properties of GelMA exists, the nano- and cell-scale network topology needs to be investigated to produce controlled structures. Here, for the first time, small-angle X-ray scattering (SAXS) is used to elucidate how structural changes on the network level dictate the final properties within a GelMA hydrogel. Scaffold nanostructure was observed pre- and post-crosslinking, with emphasis on assessing structural changes in response to changes in Degree of Functionalization (DoF) and polymer concentration. Samples were modelled regarding local-polymer conformation (mass fractal dimension), distance between entanglements (correlation length), and mesh size. Importantly, DoF is observed to alter crosslinked polymer conformation and nanoscale mesh size. These results inform future design of GelMA-based bioinks, allowing researchers to further leverage bio-printing technology for broad-spectrum applications such as cell/stem cell printing, organoid-based tissue structure, building cell/organ-on-a-chip, through to the hierarchical engineering of multicellular living systems.

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TH-236

Population Protecting Implants: Targeted Control of Invasive Predators to Mitigate Catastrophic Predation

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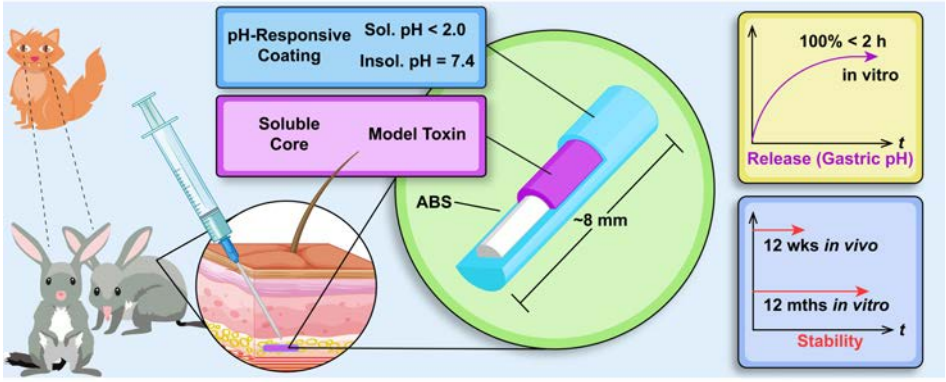
Feral cats (*Felis catus*) present a significant threat to endangered native mammals in Australia, killing 459 million mammals annually and leaving many species facing extinction.[1] Attempted reintroductions of threatened mammal species often fail due to the persistence of intractable feral cats, termed 'problem individuals' and the swift depredation of the reintroduced population.[2] Here, we report the development of the Population Protecting Implant, a subcutaneous implant for native mammals, designed to release a toxic payload in the gastric environment of a feral cat, to target these problem individuals. A novel reverse-enteric coating was developed that exhibited targeted solubility at gastric pH and was utilised to prepare large batches of implants manufactured *via* fluidised bed spray coating. Manufactured implants exhibited a uniform reverse enteric coating, low intra-batch variability, and compatibility with conventional syringe implanters. *In vitro*, implants bearing a 300 µm coating were afforded significant stability and retention of the payload at subcutaneous pH (12 months), and rapid release of the payload at gastric pH (< 2 h). In addition, implants exhibited favourable stability *in vivo* in rats (12 weeks) with no observed difference in biocompatibility compared to conventional radiofrequency identification microchips. This work demonstrates a proof-of-concept of the Population Protecting Implant and serves as the basis for its future development and translation into the field.



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TH-237

Phytochemistry of *Denhamia obscura* (A. Rich.) Meisn. Ex Walp.

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This research stems from a collaborative endeavour between UQ, Integria Healthcare®, Menzies School of Health and Traditional Homeland Enterprises. This work seeks to characterised the phytochemical composition of traditional medicines used by Aboriginal and Torres Strait islander communities of the Northern Territory.

The phytochemical profile of the endemic Australian plant Denhamia obscura has not previously been reported, despite its tradition use. Research into the chemical composition of different parts of the plant was carried out (leaves, seeds and root bark), since the leaves are used to treat respiratory ailments,(1) and the root bark is used as an oral anaesthetic.(2) In addition to the chemical characterisation, the crude extract and the four most abundant compounds from the root bark, were tested for antimicrobial, anti-inflammatory, and cytotoxic properties.

We report the isolation and characterisation of di and triterpenes, with two novel natural products, previously reported in synthetic papers.(3, 4)

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TH-238

Transition metal complexes as precursors for the synthesis of catalytic nanoparticles

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Nanoparticles are being used for diverse purposes due to their exceptional properties, including catalytic activity, high resistance to oxidation and high thermal conductivity.[1]
The distinct properties of nanoparticles arise mainly from their structural features, such as shape and size, and from their composition; thus, the design of nanoparticles and the control over these parameters is critical for their efficient use and application.[2] The choice of the right precursor is of utmost importance for this purpose. Though it might seem expensive to use an organometallic derivative, not always easy to prepare, in order to decompose them, two main advantages of the use of organometallics can be encountered. First, the milder conditions of decomposition allow better control of the material formation. Second, clean procedures, which avoid the presence of contaminants such as salts, halides and, main group oxides on the material surface, can be elaborated.[3] Moreover, the well-known composition of the precursor allows a better control on the composition and structure of the final nanoparticles.

In this contribution, we aim to synthesize readily achievable transition metal complexes, including Cobalt, displaying a variety of organic ligands. Mono and poly-dentate alkylamines and alkylphosphines, with different degrees of branching will be selected as ligands, and the final complex will be characterized through NMR, UV-Vis and FTIR Spectroscopy and X-Ray diffraction.
The complexes will then be applied as precursors for the synthesis of nanoparticles and the effect of the various type of ligands on the size, shape and composition of the nanoparticles will be observed. Also, the effect of the counterion will be investigated, varying the negative charged ion from halogens to bigger organic molecules, and observing the outcome on the structure and composition of the nanoparticles.

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TH-239

From plastic waste to fuels via Ru nanoparticles: computational mechanistic insights

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Catalytic upcycling of plastic waste has potential as a promising future technology for the achievement of a circular economy. A major current challenge in this field is to find a reliable system that could convert plastic waste to useful products such as fuels or High Value Liquid (HVL).[1]

Many systems have been investigated over the course of the last 20 years, ranging from zeolites[2] to the most recent photocatalytic active oxides.[3,4] There have been a few mechanisms proposed for these various catalytic systems, however, none have been properly understood. An understanding of the plastic upcycling mechanism would guide the synthesis of a more efficient and catalytically active class of substrate. Recently, ruthenium-based catalysts have emerged as promising systems for polyethylene upcycling, showing potential for improved efficiency of the process.[5,6] The most experimentally tested systems are ruthenium metal nanoparticles, which can be grown with control of the crystal's surface orientation, resulting in a catalyst which is highly tuneable.

In this contribution, we use periodic density functional theory (DFT) calculations to accurately predict the adsorption energies of relevant reactants, products, and intermediates, as well as the reaction free energies of all the mechanistic steps for the ruthenium-based experimental systems. We perform this investigation for both the (100) and (001) Ru surfaces, which are the most catalytically active according to previous reports.[4,5,6] These results allow us to establish important design principles for plastic upcycling catalysts, which can be used to improve the efficiency of existing catalysts as well as design new catalytic systems. As part of this study, we develop a suitable protocol for future first-principles studies in the field of plastic waste upcycling. This includes performing important tests to establish a good model for the polymeric chain of polyethylene based on short oligomeric species. We believe that our approach will lead to a good balance of both chemical accuracy and computational cost.

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TH-240

Employing Graphene Fluoride as a Conductive Agent in All-Solid-State Batteries

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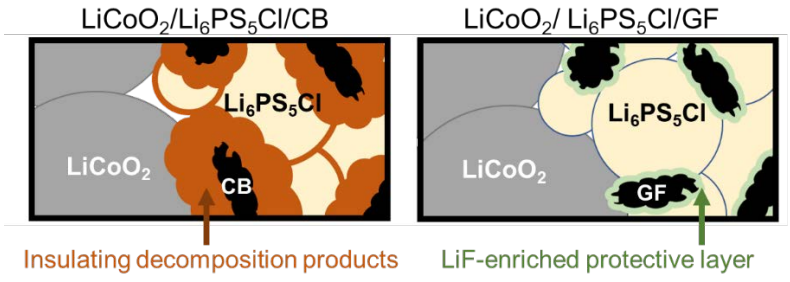
Using a solid-state electrolyte (SE), all-solid-state batteries could provide improved safety and higher energy density than conventional Li-ion batteries. In this regard, it is important to develop a SE with superior ionic conductivity and chemical compatibility with electrode materials. Li_6PS_5Cl is a promising SE that features high ionic conductivity up to 10^{-3} S cm^{-1} at room temperature, owing to the anion site disorder and high polarizability of sulfur.[1-2] However, the chemical instability of Li_6PS_5Cl during cycling limited the implementation in practical usages.

This study employed graphene fluoride (GF) as a conductive agent for the cathode composite to improve the phase stability of Li_6PS_5Cl. GF was fabricated using a facile microwave-induced exfoliation method.[3] By mixing Li_6PS_5Cl with GF rather than conventional Super P carbon black (CB), we observed significant improvements in the chemical stability of Li_6PS_5Cl. From X-ray photoelectron spectroscopy, it showed the diminished phase decomposition of Li_6PS_5Cl. In addition, LiF was detected, attributing to the interfacial reactions between GF and Li_6PS_5Cl. This LiF-enriched protective layer could be the reason for preventing the phase decomposition of Li_6PS_5Cl.

Furthermore, we conducted cyclic voltammetry and galvanostatic measurements by fabricating a $LiCoO_2$ composite containing GF/Li_6PS_5Cl composite. The cyclic voltammetry results revealed that GF contributes to a reversible redox profile with a low anodic current. During the galvanostatic measurements, GF containing cathode displayed an improved capacity and high Coulombic efficiency. Our results show that GF is a promising candidate for conductive agents in all-solid-state batteries, which function as the electron pathway and an interfacial stabilizer to improve the chemical stability of Li_6PS_5Cl, resulting in substantially improved electrochemical performance.



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TH-241

Understanding the interfacial region in organic ionic composite materials

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The study of interfaces and interfacial regions in solid-state composite electrolytes is relevant since they determine the morphology, thermal and ion transport properties [1]. The comprehension of these processes is crucial to design and tailor the properties of electrolytes used in energy storage devices like batteries, solar cells, etc. Electrolytes can be inorganic or organic such as organic ionic plastic crystals (OIPC), polymers, and composites of these. Composites between OIPCs and polymer particles have recently been of interest because they combine the non-flammability, non-volatility, plasticity, electrochemical, and thermal stability of OIPCs, while at the same time offering the mechanical stability provided by the polymer [2,3]. The thermal and ion transport properties of composites lie in structural changes in the bulk and local level and the formation of interfacial regions that serve as pathways for ions.

We have studied novel composite electrolytes formed between the OIPC and polymer nanoparticles. The composites were prepared following the solvent casting method [1]. Different characterization techniques were used to study and correlate bulk and local properties. For example, the morphology and thermal changes were observed using optical microscopy and differential scanning calorimetry (DSC). In addition, solid-state NMR is implemented to study the structural changes and ion dynamics and is correlated with electrochemical impedance spectroscopy (EIS) to determine the ionic conductivity in the composite. It is expected that the composites will take advantage of the intrinsic properties of the OIPC like plasticity, the mechanical strength of the polymer, and the formation of the interphase between them, which will improve ion transport properties.

This study will help us to understand the mechanisms that are taking place in the interfacial regions of the composite and how they modify properties like ion transport, thermal behaviour, and interfacial contact that will boost the design of solid-state electrolyte composites for the next generation of Li-ion batteries.

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TH-242

Vortex fluidic high shear fabrication of indium and gallium composite ultrathin sheets

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2D Nanomaterials are ubiquitous in contemporary advances in science[1]. Devising new methods that reduce the complexity of the processing while being scalable and high in green chemistry metrics is therefore important. We have developed a method for fabricating partially oxidized ultrathin gallium/indium sheets from a eutectic melt of the two metals[2]. This involves exfoliation of the planar/corrugated oxide skin of the melt[3] in *n*-propanol using the high shear vortex fluidic device (VFD) comprised of a hemispherical base 20 mm outer diameter (OD) quartz tube, tilted at 45° and rapidly rotating at 7000 rpm, Figure 1. The 2D sheets afforded a composition of 2-15% indium relative to gallium, range in thickness from 20 to 42 nm and have a lateral dimension of 10 to 30 µm. Unoxidized indium and gallium were observed to be sandwiched between gallium oxide layers, as determined using Auger depth profiling. This finding coupled with an understanding of the sub-micron topological fluid flow in the VFD[4] using n-propanol as a solvent provides an understanding of the mechanism of formation of the composite 2D sheets**.** From an application perspective, the gallium/indium 2D sheets is shown to reduce the contact resistance between metals such as Pt and Si as a semiconductor offering new opportunities for controlling Si surface properties at the nanoscale.

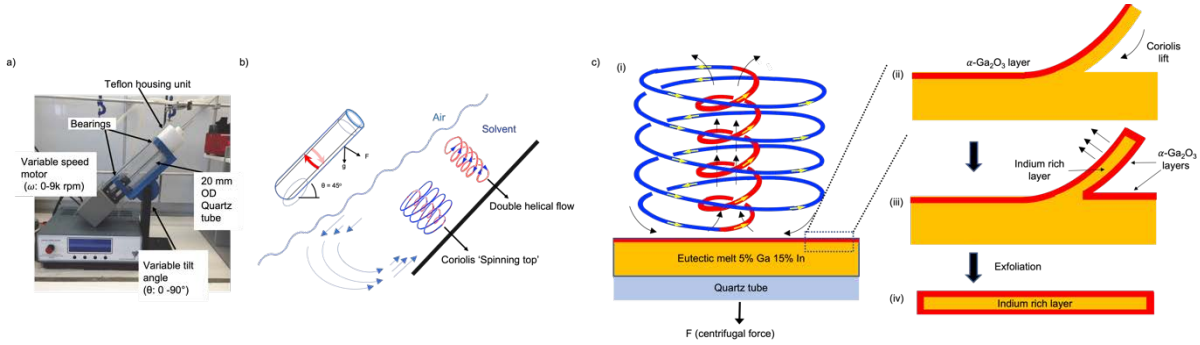

Figure 1: a) Labelled photo of the Vortex Fluidic Device (VFD), b) fluid flows occurring in the VFD: Double helical flow and Coriolis spinning top flow, and c) Proposed formation method: i) low pressure zone from the Coriolis fluid, ii) initial peeling of the α -gallium oxide layer, iii) oxidation of exposed oxygen at the surface of the eutectic melt, and iv) resulting layered sheet structure.

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TH-243

Efficient photothermal conversion triggered by near-infrared light in a dithiolene-based metal-organic framework

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Photothermal metal-organic frameworks (MOFs) are a particularly interesting group of materials capable of absorbing light and converting it into heat.[1, 2] We present a novel efficient photothermal MOF containing Ni-dithiolene ligands, denoted Zn1, which has intensive absorbance in the near infrared (NIR) region and is capable of heating rapidly by irradiation with NIR light at a relatively low power density. By further incorporating Zn1 into a self-healable polymer, the mechanical damage of the composite can be recovered using irradiation with NIR light. The reversible dynamic covalent bonds in the polymer enable the recovery to be thermodynamically driven and responsive to heat.[3, 4] Our results provide an opportunity to maneuver the point of repair and avoid shape changes in practical applications with the use of clean energy with lower power consumption, which can also be further developed for long-distance repair.

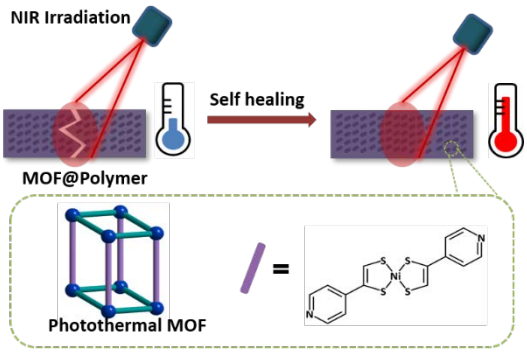

Figure 1. The self-healing process of Zn1@polymer composite under NIR irradiation.

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TH-244

Exploring diffusion mechanisms in solid-state electrolyte Li_3OCl using molecular dynamics simulations

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Solid-state batteries are currently at the centre of attention due to the possible improvement in energy capacity, density benefits, and it is safety aspect compared with liquid electrolytes. The lithium-rich antiperovskite solid state electrolyte Li_3OCl exhibits and ionic conductivity of about 10^{-3} S cm $^{-1}$ at room temperature. Computational simulations of lithium-ion migration is important for understanding the diffusion pathways over a vast temperature range. However, it is quite difficult to determine diffusion coefficients of smaller magnitude using equilibrium simulations so very high temperatures are required. Therefore, non equilibrium simulations (NEMD) was used to determine diffusion coefficients using appropriate colour field values. In this work, we also consider the main defects of Li_3OCl to further calculate the room temperature ionic conductivity via non equilibrium simulations (NEMD) method.

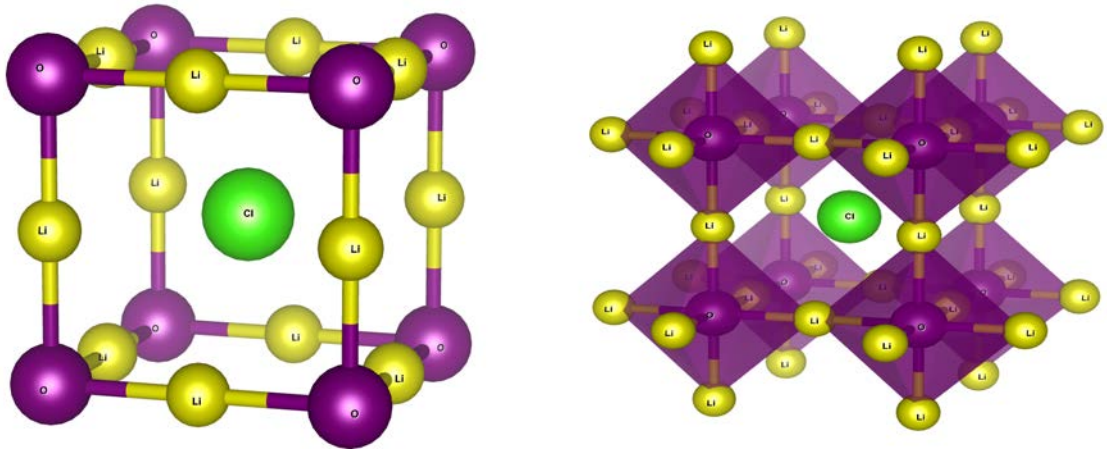

Figure 1: Schematic diagram of pure Li_3OCl crystal structure

TH-245

Suppressed phase segregation with 2D layerd perovskite for wide-bandgap perovsktie solar cells

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Mixed-halide perovskites have emerged as promising materials for tandem applications including perovskite-silicon and perovskite-perovskite tandems due to their tunable bandgap in the entire visible region. However, when mixed-halide perovskite film is placed under illumination, negative ions, such as I- and Br-, tend to move and compensate the positive space charge on the grain boundary. As a result, I-rich region will form, causing a drop of obtainable bandgap and an increase in trap density. A facile strategy is demonstrated in this study to achieve a photostable wide-bandgap perovskite layer. This involves incorporating a long-chain phenethylammonium (PEA+) cation into the mixed-halide perovskite layer. With the incorporation of PEA+ into the film, we can observe the formation of two-dimensional (2D) platelets, interspersed between three-dimensional (3D) perovskite grains, which could maintain the positive space charge along the grain boundary. Eventually, this significantly suppressed the phase segregation and reduced the density of trap states. The resultant mixed halide perovskite exhibits a wide bandgap of 1.82 eV, which is the optimal bandgap for all perovskite tandem application. It is observed that the incorporation of PEA+ can also passivate the traps along the perovskite grain boundary, hence effectively increasing device efficiency. Moreover, the long-term operational stability of the corresponding device is also remarkably enhanced, retaining nearly 70% of the original efficiency after 500 h under continuous light illumination.

TH-246

Synthesis of Multi-resonance Thermally Activated Delayed Fluorescence Emitters for Organic Electronics

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Interest in multi-resonance thermally activated delayed fluorescence (MR-TADF) emitters has increased in recent years owing to their ability to 'scavenge' triplet states formed during electronical pumping of organic devices. The majority of MR-TADF materials reported are insoluble carbon-rich materials, which require high-temperature vapour deposition for device fabrication. This work summarises the progress towards solution-processable MR-TADF compounds.

TH-247

Aminopropyl grafted silica catalysts for tributyrin transesterification: a molecular dynamics study

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Biodiesel fuels derived from renewable sources are an important resource in the global transition to net-zero CO_2 emissions due to suitability as drop-in alternatives to existing diesel supply chains and engines systems.[1] Heterogeneous base catalysts, such as amine functionalised silicas, are a potential replacement for liquid bases (alkali hydroxides), circumventing existing requirements for post-reaction processing steps and associated waste generation to neutralise corrosive by-products.[2-3]

The surface chemistry of amine functionalised silicas remains poorly understood due to limitations in experimental techniques which are poorly suited to elucidate local interactions between solvents/reactants and active sites in the liquid phase. Computational approaches such as molecular dynamics simulations enable in-silico studies of complex multiple-component systems, and interdependent interactions between surface species, as a function of time.[4-5] Here we demonstrate how hydrogen bonding between amine active sites and tributyrin and methanol reactants (solvent), and steric effects, influence the spatial distribution and proximity of molecules and hence the transesterification of triacyl glycerides (TAG) to biodiesel.

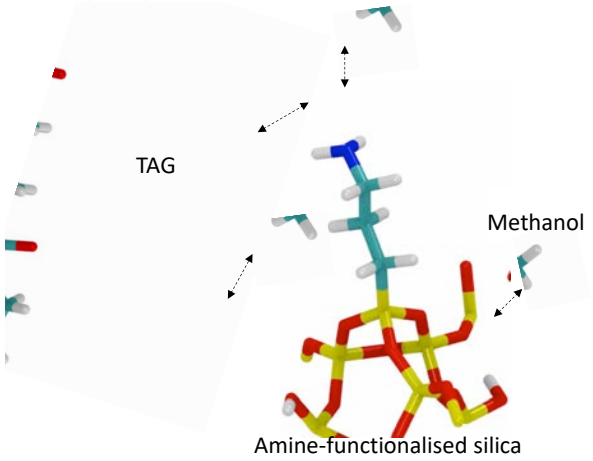

Figure 1. Complex interactions in the transesterification of triglycerides with methanol catalysed by amine-functionalised silica can be modelled using molecular dynamics.

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TH-248

Surface vs. Bulk Characteristics: Clarifying the Oxygen XPS Peaks in $BaSnO_3$ Perovskite

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Perovskite materials have been well researched over the past 70 years, as their general form (ABX_3) allows for a variety of elements to be accommodated into their structure, and thus the generation of a large range of structures and properties. However, in literature, there is a strong sense of ambiguity in their structure from analysis of the uncertain oxygen XPS spectra, making it difficult to investigate their aptitude for various applications, such as for dielectric materials in capacitors and semiconductors in solar cells.

The structural refinement and subsequent investigation of $BaSnO_3$ by X-ray Diffraction (XRD), X-ray Photoelectron Spectroscopy (XPS), Electron Spin Resonance (ESR) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS), shows that contrary to previous assumptions, these materials are consistent with a single-phase cubic perovskite structure. There is no chemical, structural, or spectrographic evidence for oxygen vacancies in the lattice, or additional oxygen, that was previously assigned to the secondary strong peak in the O1s XPS spectrum. Instead, this investigation showed a clear difference between the atomic arrangement on the surface of the material and the bulk lattice structure, clarifying the current misunderstanding of the identity of this peak.

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TH-249

Ionogel electrolyte based on *N*-ethyl-*N*-methylpyrrolidinium bis(fluorosulfonyl)imide and NaFSI mixtures for sodium batteries.

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The development of highly conductive and safe electrolytes for sodium-ion batteries is an emerging field beyond lithium battery technologies. In this work we have developed new iongel electrolytes consisting of binary salt mixture of organic ionic plastic crystal, OIPC *N*-ethyl-*N*-methylpyrrolidiniumbis(fluorosulfonyl)imide (C_2mpyrFSI), NaFSI salts supported by electrospun PVDF nanofibers. The binary mixture near to eutectic point was selected after detailed phase diagram analysis and then to prepare iongel electrolytes. The ionic conductivity of prepared iongel composite reaches to 2.6×10^{-3} S cm^{-1} at ambient temperature. This iongel membrane possessed a relatively high Na-ion transference number of 0.44 at 50 °C. We also demonstrate the performance of Na-ion batteries using $NaFePO_4$ cathode (1.75 -4.0 V). The assembled cells show a good capacity retention with close to 100 % columbic efficiency at various C rates between C/20, C/10 and C/5, achieving 120 $mAhg^{-1}$ at C/20. The long-term charge/discharge performance is also demonstrated. Our study provides a feasible method to prepare highly conductive iongel electrolytes for future Na-battery applications.

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TH-250

Magnetoelectric Polymer Composites for Wireless Electrochemistry

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The coupling between electric and magnetic fields in Magnetoelectric (ME) composite materials gives rise to an ME effect. Polymer-based ME composites are increasingly studied and typically consist of two types of materials, a piezoelectric polymer and magnetostrictive alloy. When a magnetic field is applied to the magnetostrictive material it induces strain in the magnetostrictive material which then transfers to the piezoelectric material via mechanical coupling of the two materials. The strain exerted on the piezoelectric material induces electrical polarization that generates an output voltage (or the ME effect) [1].

Polymer-based ME composites are envisaged for use in "wireless" or contactless stimulation involving electrode devices (e.g. implantable electrodes and neural prosthetic devices) in biomedical applications. For example, the use of a remote magnetic field to generate an output voltage for delivering electrical stimulation at the electrode-tissue interface negates the need for electrical connections and wires. Most studies of ME composites are done under ambient conditions (i.e. in air) however to our knowledge the ME effect is yet to be measured in liquid environments. Hence, our research aims to gain a better understanding of the ME properties and effects in liquid, which has potential for advances and new opportunities in wireless electrochemistry, sensors, and implantable electrode devices.

To study the ME response in liquids, ME measurements were performed on polymer-based PVDF/Metglas laminate composites which was placed in a solution filled tube. This setup was positioned (Figure A) inside the magnetoelectric setup (at DC Mag. Field 8 Oe and AC mag. Field 1 Oe) whilst measuring the ME output voltage using a lock-in amplifier at different frequencies. The effect of PVDF film thickness, insulation layers and electrode configuration on the ME response were investigated. Among the several insulation coatings that were tried (Wax, PDMS) parylene coating had the minimum effect on the output ME response compared to in air which enables the ME operation in liquids. More importantly PVDF/Metglas laminates only with one side insulation were explored further for the development and configuration of these ME devices as "Wireless" electrochemistry.

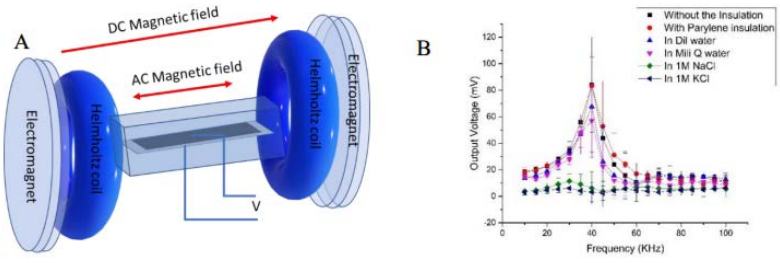

Figure (A) Schematic view of the bulk system for ME voltage measurement in liquids. (B) Magnetoelectric response of PVDF/Metglas fully covered in Parylene.

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TH-251

Hydrophobic milled recycled carbon fibre: An avenue for PFAS waste remediation

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Milled Recycled Carbon Fibre (mRCF) is one of a variety of commercially available forms of recycled carbon fibre, most commonly used as a filler material[1] or to enhance the conductivity of composites[2].

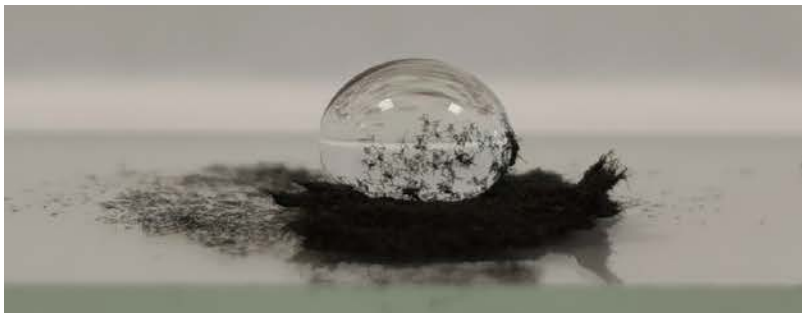
One significant problem of environmental concern are perfluoroalkyl and polyfluoroalkyl substances (PFAS) as these are persistent in the environment and are extraordinarily stable. The origin of these compounds come from many sources but are common in firefighting materials such as foams and can be by products of common items such as non-stick cookware, lubricants, and chemically resistant plastics. While PFAS are commonly removed by the application of activated carbonaceous materials, the regeneration of these sorbents poses a significant problem. Surprisingly, the use of carbon fibres – principally used to reinforce plastics for high performance composites, have not been assessed for their ability to adsorb PFAS.

This work examined the suitability of mRCF as a means of removing environmental PFAS, to then be incorporated into an epoxy resin composite material as a value-added filler material after its use in environmental PFAS remediation.

mRCF that boasted hydrophobic properties was able to be prepared through aryl radical attachment at the fibre surface through the use of aryl nitro diazonium salts in the presence of Fluorolink MD700, a highly fluorinated commercially available monomer featuring methacrylate groups which enable polymerisation to the surface through this method.

The impact of this hydrophobic surface on the moisture uptake of mRCF/epoxy composite samples was investigated through a two month water ingress study at 35° C, with samples being incrementally removed and weighed as the study progressed. Mechanical flexural data was obtained for each sample shortly after being weighted.

This approach provides a non-traditional value-added alternative application of reclaimed carbon fibres rather than send these materials to landfill.



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TH-252

Quantum and classical mechanics insights for the improvement of marble conservation treatments

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Marble artefacts situated outdoors are prone to deterioration by exposure to rain. The dissolution of marble is due to the aqueous solubility of its primary constituent, calcite ($CaCO_3$). Rainwater is naturally acidic, and with decreasing pH, calcite's dissolution rate increases. An innovative method of surface protection and consolidation relies on the in-situ formation of a stable calcium phosphate (CaP) layer through the reaction between an aqueous solution containing diammonium hydrogen phosphate ($(NH_4)_2HPO_4$) and the calcite surface.[1] Ideally, the CaP layer formed is comprised of hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), the most stable CaP phase at pH > 4.0 with reduced solubility and a slower rate of dissolution than calcite, in addition to an excellent match to crystal lattice parameters.

Coatings formed by this method have been shown to provide incomplete coverage and exhibit micro-cracks and pores, reducing their acid-resistance and protective ability for the calcitic substrate. Recently, experimental tests have shown that surface coverage and consolidative ability provided by the CaP coating has been improved by the addition of small organic molecules (ethanol, isopropanol[2] and acetone) to the to the aqueous reaction mixture. Based on biomedical literature, the improvement in surface coating is hypothesised to be partly due to their adsorption affinity to calcite, but the exact mechanism is unknown.

In this contribution, we use density functional theory with periodic boundary conditions to provide insights into adsorption geometries and binding energies of organic molecules important to the treatment (water, ethanol, isopropanol, and acetone) on the [10$\bar{1}$4] calcite surface. Furthermore, we expanded this study to include a range of similar small, organic, oxygen-containing molecules with the potential to inform the design of improved protective treatments.

Subsequently, we use classical mechanics to investigate how adsorption behaviour is affected when these molecules coexist in aqueous solutions of ethanol, isopropanol, and acetone, and improve the characterisation of the molecular layer forming on the [10$\bar{1}$4] calcite surface. Our results complement experimental observations and previous theoretical studies, providing insights into the mechanism of CaP formation and allowing for improvements to current marble conservation techniques.

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TH-253

Design and synthesis towards efficient molecular thermoelectric materials

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The loss of energy through waste heat has become an increasing concern in the current world climate. Interest has sparked into the development of viable waste heat recovery techniques and subsequently the field of thermoelectrics.[1] Waste heat conversion by thermoelectric materials is based upon the Seebeck effect which describes the production of an electrical voltage in response to an applied thermal gradient. The dimensionless figure of merit, *ZT*, describes thermoelectric material efficiency.[2]

G = electrical conductance *S = Seebeck coefficient*

T = absolute temperature *k = thermal conductance*

From *ZT*, it can be seen that efficient thermoelectric materials require both a high *electrical conductance* and high *Seebeck coefficient*, in addition to a low *thermal conductance*. Conventional materials display a relative dependence of *electrical* and *thermal conductance*, resulting in commercially unviable *ZT* values.[1] Molecular materials have shown potential in minimizing the interdependence of *electrical* and *thermal conductance*, while increasing the value of the *Seebeck coefficient*.[2-4] The design, synthesis, and characterization of candidate molecular materials is required to experimentally validate theoretically predicted values. Herein, we have synthesized anthraquinone, naphthalene diimide, and oligoyne series of compounds with varying anchor group functionalization to characterize their resulting thermoelectric properties.

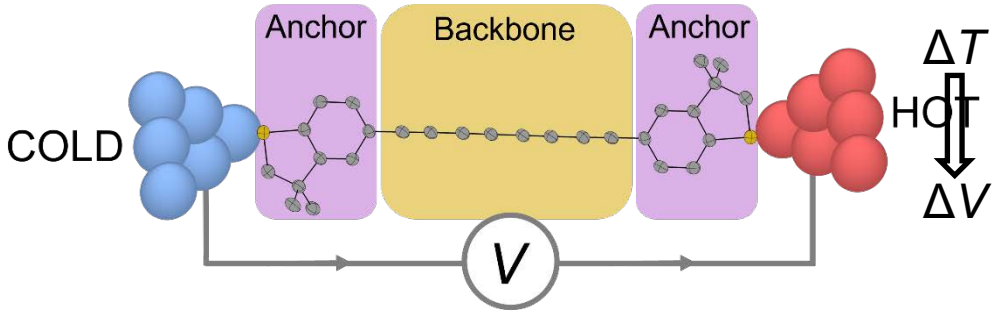

Figure 1: Schematic diagram of a molecular thermoelectric device.

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TH-254

Casting light on the mechanical properties of materials based on freeze-dried bigels

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Although water covers 71% of our planet, only 3% of the world's water consists of freshwater and two-thirds of that are unavailable for our use. Clean and accessible water resources are shrinking rapidly. According to the World Wildlife Fund (WWF), two-thirds of the world's population may experience water shortages by 2025 [1]. Moreover, water scarcity has been listed in Global Risks Report 2021 prepared by the World Economic Forum as one of the largest global threats in terms of potential impact and likelihood over the next decade [2]. Researchers are searching for innovative solutions for challenges posed by water scarcity, including wastewater treatment, water reuse and recovery or seawater desalination [3,4]; however, no one notices the potential in reducing water consumption during the preparation of daily care products. Bigels are formed by combining two immiscible gels at a high shear rate. Their many advantages over other semisolid formulations have drawn recent scientific attention [5]. Freeze-drying of bigels exhibits an unprecedented approach to formulating modern, functional materials.
This study aimed to prepare materials based on freeze-dried bigels. Bigels were obtained by mixing hydrogel (based on whey protein isolate) and oleogel (composed of sunflower oil, ethyl cellulose and emulsifier Span 80). The mechanical properties of prepared materials were analyzed using a mechanical testing machine (Shimadzu EZ-Test EZ-SX) and the three-dimensional structure on a scanning electron microscope (SEM).
Modifications in the composition of materials significantly influenced their appearance and structure, as well as mechanical properties. The obtained matrices can be the basis for obtaining a new class of ecological materials for dermatological and cosmetic purposes.

Acknowledgements
Support from PROM Project - International Scholarship Exchange of Doctoral Students and Academic Staff, contract number POWR.03.03.00-00-PN13/18, is gratefully acknowledged.

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TH-255

Nanocellulose-based Coating Materials for Face Mask

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As new variants of the coronavirus emerge and will continue to mutate infecting millions around the globe, the need for better personal protective equipment (PPE) is becoming vital, particularly face masks. The limitation of the current face masks is their inability to filter smaller particles such as viruses that range from 10–200 nm. [1,2] We are using nanocellulose (NC) found in abundance commonly derived from plants or bacteria to address the limitation by tuning the pore size of the current facemask to be able to filter smaller particles.[3, 4] The presence of the abundant hydroxyl groups on the surface of NC allows for surface functionalisation, introducing charges utilising the electrostatic interaction filtration mechanism to capture the virus particles. To achieve this, chemically modified NC materials shown in the Figure 1 below were coated onto the middle layer of commercially available nonwoven face mask with different morphologies, surface charges and hydrophobicity. Herein, we demonstrate the characterisation to investigate the interaction between chemically modified NC and the nonwoven. The bacterial and particles filtration efficiency was investigated to ensure compliance with the current face mask standard. It was found the positive charged NC showed higher filtration efficiency and coating properties in comparison with the other modified NC.

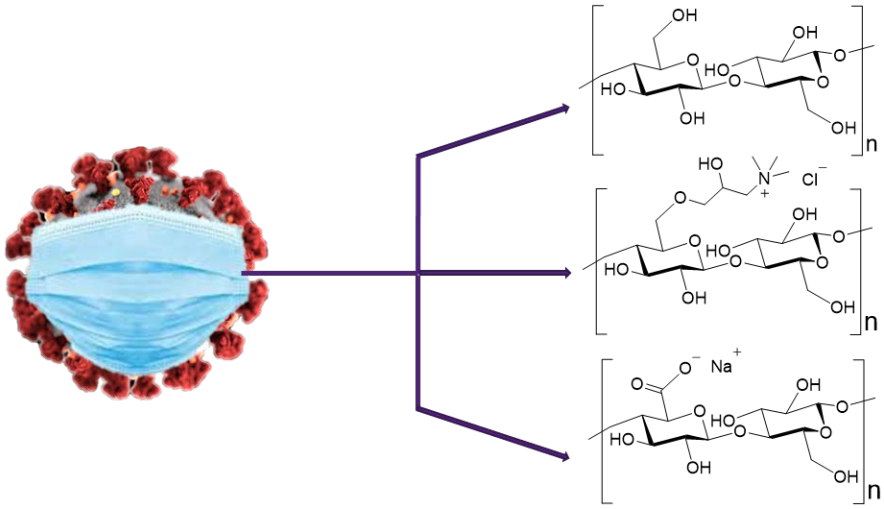

Figure 1: Chemicals structure of the nanocellulose and functionalised nanocellulose material.

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TH-256

TiO_2/CoAl-LDH nanocomposites for CO_2 photoreduction

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In 2017, 80% of global energy was produced by burning fossil fuels [1]. It is anticipated by 2040 that global energy demand will increase by 28%, with CO_2 levels reaching 750 ppm by 2050. This will increase average global temperatures by 2.7 °C with severe consequences for climate change [2]. Sunlight is the most abundant renewable energy source on Earth, providing 100000 TW per annum, exceeding annual global energy consumption [3], and hence offers a means to transitioning away from reliance on fossil fuels. Mimicking biological photosynthesis, inorganic semiconductors can harvest light energy to enable charge separation, and thereby drive the photocatalytic reduction of CO_2 and water to hydrocarbons [4].

Herein, cobalt aluminium layered double hydroxides (LDHs) were synthesized via coprecipitation and hydrothermal methods [5] to produce visible light photocatalysts with solid basicity. A modified alkali-free coprecipitation method produced pristine CoAl LDHs with 6 times greater surface area and CO_2 adsorption capacity than hydrothermal CoAl LDHs, reaching 120 m^2/g and 91 µmol/g respectively. Physicochemical and optical properties of CoAl LDHs were tuned by tailoring the Co:Al molar ratio. Increasing Co:Al ratio from 1.3 to 3.2 lowered the band gap from 1.5 eV to 0.7 eV. At Co:Al ratios >2.3, limited availability of Al^{3+} ions and an abundance of Co^{2+} ions increased the proportion of tetrahedrally coordinated Co^{2+} ions in the hydroxide sheets, and increased absorbance in the near infrared region. High Co loadings can also induce defects and vacancies in the hydroxide layer to promote CO_2 adsorption and act as charge trap sites. To improve separation of photoexcited charge carriers, UV light active P25 was introduced to form P25-CoAl LDH nanocomposites [6]. Initial CO_2 photoreduction in a liquid phase batch reactor evidence photocatalytic activity of P25-CoAl LDHs exceeding that of either component. Fine-tuning of CoAl LDH surface and optical properties through heterojunction formation with TiO_2 to increase the interfacial contact area and CO_2 adsorption capacity is a promising route to an effective CO_2 photoreduction system.

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TH-257

A New Class of Hydroxybenzotriazole Esters with Cannabinoid Receptor Activity

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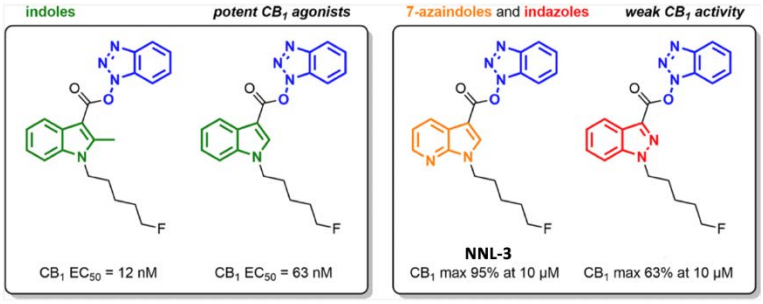

Synthetic cannabinoid receptor agonists (SCRAs) are an important class of new psychoactive substances (NPS) and their discovery continues to rapidly expand. A hydroxybenzotriazole (HOBt) containing SCRA (NNL-3), was recently detected[1] in a synthetic cannabis sample, however, there is currently no information regarding the pharmacological profile of this class of SCRAs and their interaction with human CB_1 and CB_2 receptors. This study[2] involved the synthesis and pharmacological evaluation of seven HOBt indole-, indazole-, and 7-azaindole-carboxylates bearing a range of N-alkyl substituents. All analogues except a 2-methyl-substituted derivative had a low affinity for CB_1 (K_i = 3.80−43.7 μM) and CB_2 (K_i = 2.75−18.2 μM) in competitive binding assays. A fluorometric functional assay showed that 2-methylindole- and indole-derived HOBt carboxylates were potent and efficacious agonists of CB_1 (EC_{50} = 12.0 and 63.7 nM; E_{max} = 118 and 120% respectively) and CB_2 (EC_{50} = 10.9 and 321 nM; E_{max} = 91 and 126% respectively). All other analogues containing exhibited low potency are had submaximal effect. A reporter assay monitoring β-arrestin 2 (βarr2) recruitment to the receptor was also performed, confirming that the 2-methylindole example was the most potent and efficacious at CB_1 (EC_{50} = 131 nM; E_{max} = 724%) and CB_2 (EC_{50} = 38.2 nM; E_{max} = 51%). These data suggest that NNL-3 is unlikely to be psychoactive in humans due to its lack of CB1 receptor activity.

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TH-259

Exploration and development of sulfur-based polymer composites

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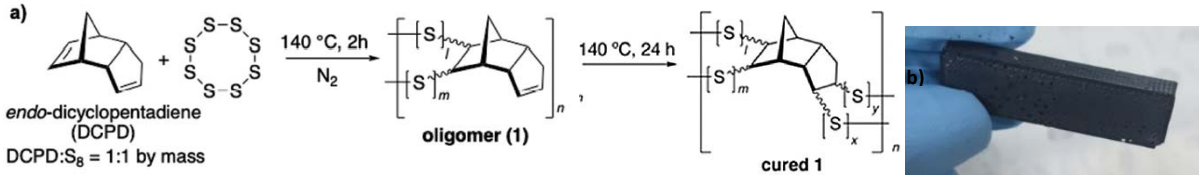
In its elemental form, sulfur remains a highly abundant and extremely low-cost element, that is commercially available in high purity. This is a consequence of hydrodesulfurization, a step in the petroleum refinery process used to extracted sulfur compounds from crude oil and gas. This process sources over 60 million tonnes of elemental sulfur annually and conventional uses of this sulfur, like manufacture of sulfuric acid, and sulfur-based fertilizers, use up only a fraction of this reserve that continues to lie in above ground deposits (figure 1). [1]

Figure 1. Elemental sulfur reserves.

The development of methods to synthesis novel materials using sulfur has recently increased in interest partly motivated by the sheer abundance of the element. One such polymeric material synthesized via the simple reaction between dicyclopentadiene (DCPD) and sulfur was used as a surface coating material. This S-DCPD polymer has provided solvent- and acid-resistant coatings that facilitate mercury removal from mixtures of water and diesel fuel, in addition to preventing corrosion of metals and concrete while being thermally repairable.[2] This work will investigate the synthesis and characterization of the S-DCPD polymer as a bulk material and as the matrix component of carbon fiber composites. The structural properties of both the polymer and the composite are to be established using standard test procedures including flexural strength, tensile strength, hardness, and compressive strength. Furthermore, the recyclability of the polymer and its composites are to be examined and developed upon to exploit the repairability and other unique properties of the polymer material. Furthermore, functionalization of carbon fiber surface would be explored to improve interfacial properties of the composite material.



Figures 2. a) Synthesis of S-DCPD polymer; b) S-DCPD polymer.

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TH-260

Molecular dynamic simulation of the interaction between phytochemicals and silver nanoparticle surfaces

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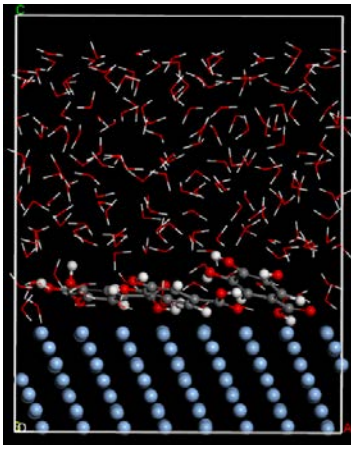
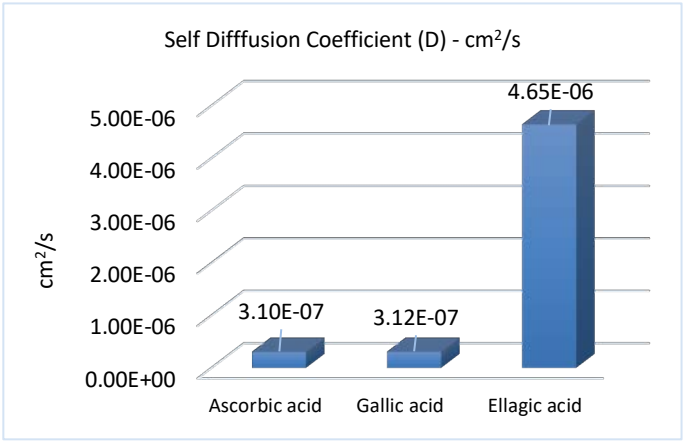
Silver nanoparticles encapsulated with plant phytochemicals have several biomedical applications. Formation and biomedical properties of silver nanoparticles depend mainly on the nature of the phytochemicals that adsorb on the Ag surface. We have synthesised Ag Nanoparticles using Kakadu plum extracts. However, it is difficult to experimentally determine the components in the plant extract that adhere to the Ag nanoparticle surface. Hence molecular dynamics (MD) simulations are used to study the interaction of phytochemicals with the Ag nanoparticle surface. Geometry optimisation of organic molecules is performed using Density Functional Theory (DFT) and MD simulations are performed using COMPASS II force field[1] and Forcite+ module of Materials Studio[2]. Interaction between the (111) surfaces of Ag nanoparticles and three different phytochemicals, ascorbic acid, gallic acid and ellagic acid present in the water extract of Kakadu plum is investigated.



Silver slab hydrated by water molecules and gallic acid molecules (after 1ns MD



Self-Diffusion Coefficient of ascorbic acid and Ag surface, gallic acid on Ag surface, ellagic acid and Ag surface

The interaction energy obtained from the MD simulations indicates that gallic acid-silver surface system has highest stability among the systems investigated. Based on the radial distribution function values, ascorbic acid has strong interaction with silver surface compared to other two phytochemicals studied. Also, ascorbic acid has the lowest self-diffusion co-efficient closely followed by gallic acid indicating strong interaction of both molecules with Ag surface. Since the synthesis of nanoparticles requires high alkaline conditions, based on pKa values, ionic form of these molecules is also being investigated. These simulation results will also provide a theoretical support for determination of different functional groups that preferentially adhere to silver nanoparticle surface.

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TH-261

Progress towards a Rapid-Scanning Time-Resolved THz Spectrometer for Singlet Fission

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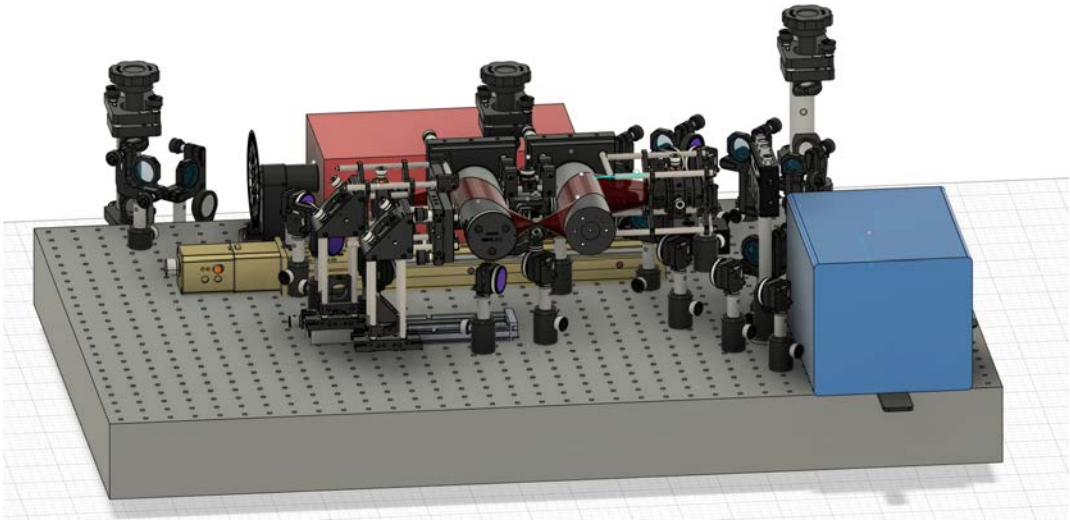
There has been recent interest in singlet fission materials due to their potential in surpassing the thermodynamic efficiency limit in single junction photovoltaic cells. Ultrafast spectroscopic techniques such as transient absorption (TAS) and time resolved photoluminescence (TRPL) have aided the study and development of singlet fission chromophores[1] by providing insight into singlet and triplet excited state dynamics. These techniques however do not allow direct observation of exciton dissociation into charges, and observation of the resulting carrier dynamics within chromophores and acceptor materials.

Ultrafast Time-Resolved Terahertz Spectroscopy (TRTS) provides a method of achieving this by providing a sub-ps resolved probe of photoconductivity in materials. TRTS has been used to investigate exciton and carrier dynamics in inorganic and organic semiconductors[2] but has not been used to date in singlet fission materials. This is due in-part to both the slow scanning speeds of conventional TRTS systems due to the need to scan two delay stages to obtain a 2D pump-probe spectrum.

To address this we have constructed a TRTS system with rapid-scanning delay stage. By modifying a commercial THz:TDS system driven by an 80MHz Ti:Sapphire oscillator, we have achieved >60dB dynamic range spectra with 10s acquisition times, improving upon 38dB after 50 minutes of acquisition. The next stage will be to build the capability to switch the optical pump and THz generation source to a 1kHz Ti:Sapphire amplifier to enable the high pump pulse fluences required for TRTS. It will be utilised to investigate a range of samples including tetracene/silicon heterojunctions and acene/TiO_2 ballistic transport based solar cells.



CAD rendering of TRTS. Some parts hidden to show the THz path (in red).

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TH-262

Effects of additives on the crystallisation of solids contributing to crystal arthritis

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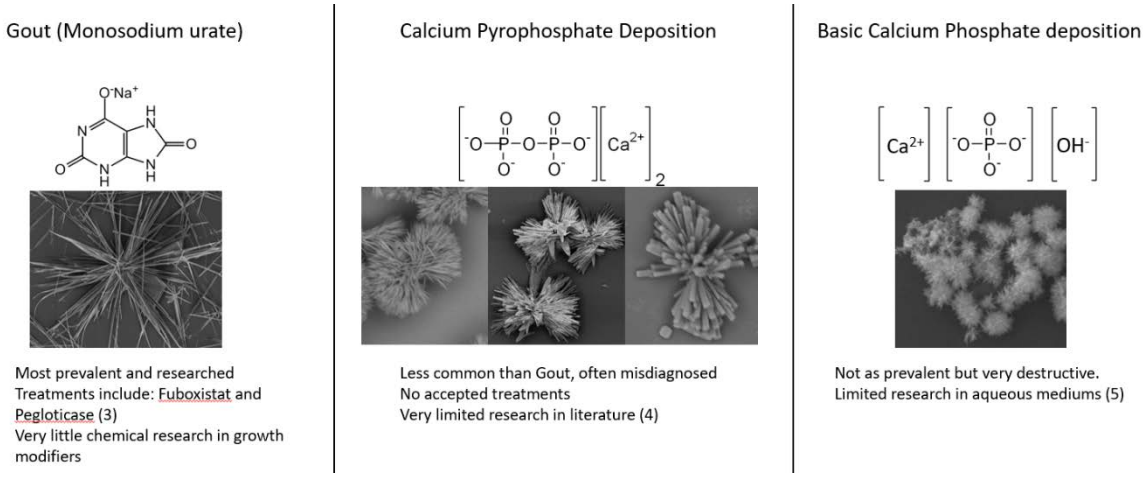
Pathological biomineralisation often occurs *in-vivo* and one example of this condition is crystal arthritis, the formation of crystals in the joints causing inflammation. (1) Many of these diseases are treated by prescribing painkillers or aspirating the joint to reduce pressure. (2) There is unfortunately little integration of growth modifying chemicals or using the understanding of growth modifiers to determine chemical interactions with the crystals. As this is often considered from a medical perspective very little is known on the actual chemical impact that certain molecules can have.



Crystal growth modifiers is a term for chemical additives that can alter some factor of the crystal development. (6) When a growth modifier is applied to a system, factors such as the nucleation, aggregation, growth and speciation can be controlled or altered. There are many well-known chemicals that can alter the formation of crystals, most of these are metal ions or carboxylic acid additives. (6)

We use methods such as X-ray diffraction, infrared and Raman spectroscopy as well as zeta potential to determine the impact that additives can have on the many variables of crystal growth. This will give context to the observed changes from the presence of the additives observed in scanning electron microscopy.

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TH-263

Tuneable Emission in Single-Molecule Dye Conjugates

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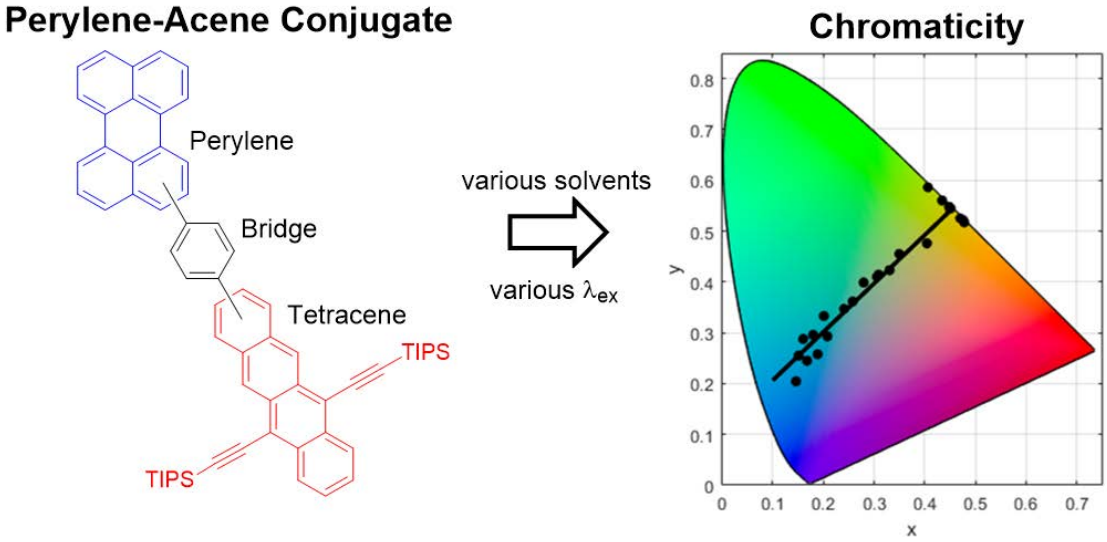
Single-molecule tuneable emission is a desirable property for applications in advanced displays and lighting, or for biological imaging.[1] Current examples of these molecular systems show excellent colour tuneability, but have poor emission efficiencies, limiting their application.[1] A novel perylene-acene system was designed which offers excellent solvent and excitation wavelength tuneability, in addition to moderate emission efficiencies. Ultrafast transient absorption spectroscopy has been used to explain the unique mechanism of colour tuneability.



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TH-264

DFT Guided Design of Selective Rare Earth Mineral Flotation Collectors

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Selective flotation of rare earth minerals is a challenging field that is of ever-growing importance with the ubiquity of rare elements in modern electronics and other technologies. The rare earth element (REE) containing deposit in Esperance, Western Australia is an example of a challenging ore deposit with complex gangue minerals that make flotation and enrichment of the REE difficult. The main phases present are kaolinite [$Al_2Si_2O_5(OH)_4$], K-feldspar ($KAlSi_3O_8$), ilmenite ($FeTiO_3$), quartz (SiO_2) and apatite ($Ca_5[PO_4]_3F$) with additionally detected phases of monazite [$(Ce, La, Th)PO_4$] as the primary REE bearing mineral.[1] This work seeks to aid in the design of novel polymer collector reagents for targeted flotation and recovery of the monazite mineral in this Esperance, WA deposit.

To effectively utilize DFT in this problem, the polymer design is reduced to components of i) coordination group design and ii) investigation of surface update of REE hydroxyl species and other cations hydroxyl species present due to gangue minerals. To address part i) a set of 12 candidate ligand groups were chosen after careful review of existing REM flotation collector, binding energy of these ligand complexes in solution with La^{3+}, Y^{3+}, Al^{3+}, Fe^{3+}, Fe^{2+} (HS & LS) cations and their various hydroxylated forms were screened. Subsequently the absolute affinity of a ligand candidate for La^{3+} (light REE representative) or Y^{3+} (proxy for heavy REE) can be calculated as well as the selectivity for REE species calculated vs. the gangue species. Phosphinate/Phosphinic Acid and Monoester Phosphoric Acid are predicted to be the best performed ligand candidates across the set of compounds modelled.

Part ii) of the problem is addressed by modelling the adsorption on mineral surfaces of monazite, fluoroapatite and kaolinite and the affinity of the various lanthanum, yttrium & calcium hydroxyl species for the different surfaces. These interactions are a critical feature to account for since REE are known to accumulate on kaolinite surfaces.[2] While the conclusions for this part of the study are more qualitative than the first based on the reliability of the model structures, the important La^{3+} cations provided by a potential $LaCl_3$ activator are predicted to be energetically more favourably adsorbed to monazite than kaolinite or fluoroapatite minerals.

This work highlights the utility of spitting the problem of computational modelling of mineral collectors up into workable parts and has provided direction and insight for experimental collaborators to build from.

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TH-265

Characterising the membrane-binding properties of peptides that potentiate the effect of the anti-fungal drugs amphotericin

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Invasive fungal infections cause severe clinical outcomes and have high mortality rates. Amphotericin B is one of the most effective antifungal drugs and is used to treat life-threatening fungal infections despite its dose-limiting toxicity causing severe side effects including vomiting, fever and chills, pain at the injection site, and chronic kidney damage. Nevertheless, AmB is still used because it remains effective against a wide range of pathogens, and resistance is rare. AmB interacts with ergosterol in the fungal cell membrane to form pores and sequester the sterol from the membrane. Cell death is induced by pores leading to leakage of ions, thus disrupting ion homeostasis and the lack of ergosterol that interferes with various cell-internal processes.

Lactoferrin (LF) is a protein derived from milk that has a synergistic effect with AmB. Lactofungin (LFG) is a peptide obtained by pepsin digestion of LF, that when used with AmB was found to increase the efficacy of AmB by a 4-16-fold in many clinically relevant fungal species such as *Candida albicans*, *Candida neoformans* and *Candida glabrata* (Fernandes, Payne, & Cartera, 2020).

Recent experiments with model membranes show that the synergy is lipid-dependent and specific to ergosterol (unpublished). It is hypothesized that the LFG binds AMB in solution or inside membranes and that the LFG-AMB complex then further interacts with ergosterol on fungal membranes to form pores that are more stable than AMB pores.

To address this hypothesis, we study the binding of LFG to AmB and AMB in ergosterol-containing membranes using Isothermal Titration Calorimetry (ITC). We found that when AmB is titrated into solutions of LFG, heat is released, indicating that LFG binds to AmB. Analysis shows that the binding is dominated by enthalpy, with a small entropic component.

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TH-266

A simple and efficient strategy to improve QM/MM models

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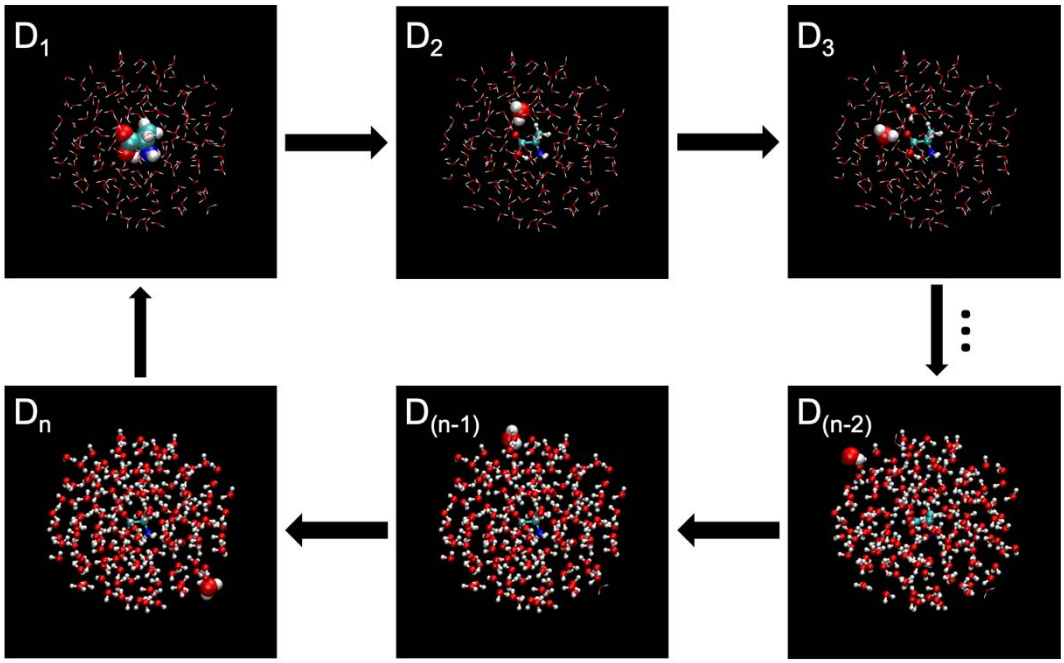
Modelling large and complex chemical systems cost-effectively has been a challenge even with the advances in computational power in the last few decades. And multi-scale QM/MM or QM/QM' approach has been proven a valuable tool to balance accuracy and cost in modelling such systems. In our earlier work, we have identified a few key ingredients in QM/MM and QM/QM' in QM region selection, which is one of the key factors contributing to reducing the computational cost.[1] Inspired by one of the most applied QM/MM with water clusters, we investigate how QM quality charges as the embedding charges (c.f. AMBER/TIP3P charges) in the QM/MM models could reduce the size of the QM region. Additionally, we apply a fragmentation approach in calculating the QM charges for large systems, significantly reducing the computational cost in obtaining the QM charges.[2] The findings in this work would pave the way to getting accurate chemical properties for large systems more steadily and feasibly.



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TH-267

Immobilised Metal-organic Catalysts for CO_2 Reduction: Substrate Effects on Reaction Energetics

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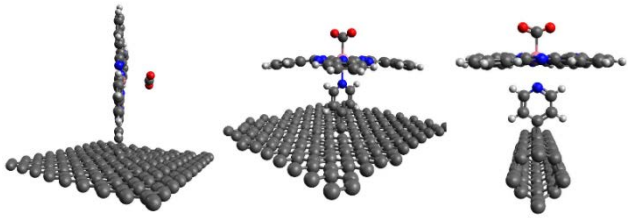
Recently, experimental studies of covalently immobilised CO_2 reduction metal-organic catalysts have reported remarkable activity [1,2]. However, a detailed understanding of the reaction mechanisms, and a consistency in methodology and comparison with similar systems is lacking. Extensive density functional theory (DFT) investigations of covalently immobilised cobalt-centred phthalocyanine (CoPc) and tetraphenylporphyrin (CoTPP), as used in CO_2 reduction reactions (CO_2RR) are reported for graphene and single-walled carbon nanotube (SWCNT) substrates, including the effects of immobilisation on defect sites and by linkers [3]. It is determined that benzene can be used to probe a surface and determine favourable immobilisation sites for CoPc and CoTPP, except in the case of immobilisation on a single vacancy (SV) defect which shows distinctly different immobilisation behaviours between benzene, CoPc and CoTPP. A charge analysis is conducted, and it is established that to achieve a charge state of Co^{I} on the cobalt center of immobilised CoPc and CoTPP, a total additional charge of -3*e* is required which is compared to the -1*e* additional charge for isolated (or homogeneous) CoPc and CoTPP. CoPc is found to have more electro-negative interactions with defective and non-defective graphene substrates unlike CoTPP. In studying the adsorption energies on graphene and SWCNT substrates for different defect sites and covalent immobilisation techniques, it is found defect sites have a stronger effect on weakly bound intermediates such CO and CO_2. Notable free energy reaction pathway differences are found for CoPc and CoTPP immobilised upright on chosen defect sites, while differences between graphene and SWCNT substrates were less significant even for linker-immobilised systems. CoPc immobilised via pyridine linker is found to have the most favourable reaction pathway due to strong exothermic behaviour and a weak endothermic final step, matching its excellent experimental performance, while defect sites only have a minor effect on the reaction pathway. A consistent and systematic comparison of calculated free-energy reaction pathways for experimentally known linker and multi-defect systems shows good and



consistent agreement with experimental performances.

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TH-268

X-Ray Constrained Wavefunction Based on Hirshfeld Atoms

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20 years ago, Grimwood and Jayatilaka[1] reported the first wavefunction reconstructed from a molecular oxalic acid dihydrate crystal using an X-ray diffraction experiment. This method has never been tested in its ability to produce reliable results. In this talk we describe a slightly new approach using Hirshfeld atoms and apply this new method to the original data as well as 13 other oxalic acid dihydrate data sets from Kaminski et al.[2]. We explore the reproducibility of the electron density and the feasibility of an experimental exchange correlation from these data.

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TH-269

A computational study investigating the polysulfide shuttle effect in lithium-sulfur batteries

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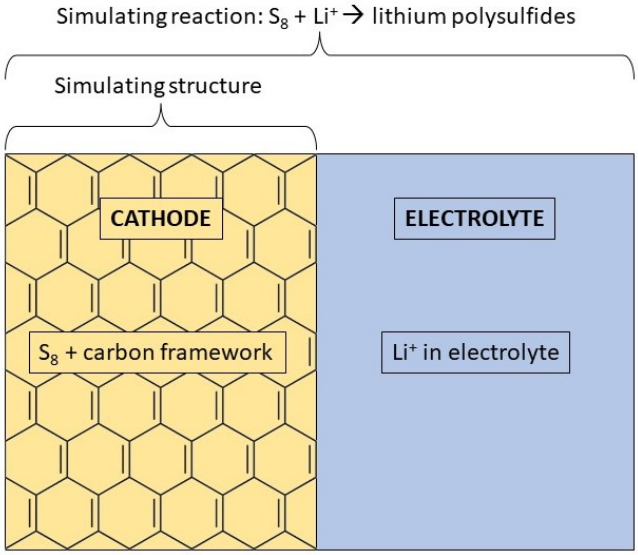
The design of new materials for energy storage devices is an active area of research, particularly in respect to finding alternatives to the conventional lithium ion battery. Lithium-sulfur (Li-S) batteries are a promising candidate due to their high theoretical specific capacity and energy density. However designing efficient Li-S batteries encounters a range of challenges, such as the insulating nature of sulfur, dendrite formation, and the polysulfide shuttle effect.[1] This presentation will focus on addressing the polysulfide shuttle effect, where polysulfide products formed at the cathode dissolve into the electrolyte solution and react at the anode without providing electrical current to the cell. One method of mitigating the loss of efficiency from this process is designing cathodes from carbon-sulfur composites with small pore sizes, which have been proposed to trap polysulfides in the cathode and prevent their dissolution. We will discuss how computational modelling of carbon and sulfur cathode materials with varying pore sizes gives insight into the mechanism of polysulfide retention or dissolution to help in advising future development of cathode materials in Li-S batteries.



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TH-270

Analysing photolysis pathways for formation of fluoroform using microwave and FTIR spectroscopy

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The previous generations of refrigerants, chlorofluorocarbons (CFC's) and hydrofluorocarbons (HFC's) have had a significant impact on both the ozone depletion rates and the greenhouse effect respectively (1). Hence, a new generation of refrigerants were required following the global phase out of hydrochlorofluorocarbons (HCFC's) (2). The solution was to utilise hydrofluoroolefins (HFOs), compounds with a theoretical lower greenhouse warming potential (GWP) and ozone depletion potential (ODP), as a result of their high reactivity with atmospheric radicals (3). Recent studies have argued that the decomposition of HFO-1234ze to trifluoroacetaldehyde (CF_3CHO) can go on to produce HFC-23 (CHF_3) (4,5). HFC-23 is a well-known powerful greenhouse gas (GHG) with a significant GWP of 11,700 (6). Previous studies were not conducted under atmospheric conditions.

This study will photolyse CF_3CHO under atmospheric conditions and quantify the products by combining Fourier transform infrared (FTIR) and Fourier transform microwave spectroscopy (FTMW). FTIR is routinely used to examine the reaction mixture, however, the reactants/products of interest have near identical functional groups and results in a convoluted spectrum (See Figure 1). The use of FTMW will account for this limitation studying the rotational spectrum of the compounds present following photolysis. This technique is more selective when analysing a group of compounds with similar functional groups and orientations over vibrational based spectroscopic methods.

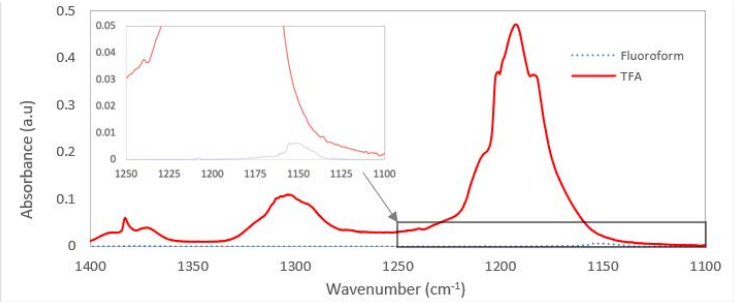

Figure 1. Synthetic FTIR spectrum of 1% Fluoroform and 99% Trifluoroacetaldehyde (TFA).

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TH-271

Triplet Exciton Control via Solid-state Interactions in Organic Light Emitters

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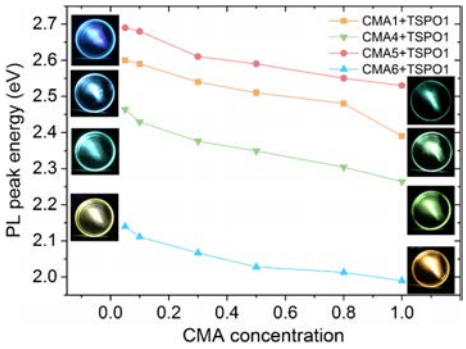
Thin-film organic light-emitting diodes (OLEDs) have developed into a flourishing commercial industry in the last few decades. However, efficient deep blue OLEDs remain one of the key challenges limiting their broader application due to low quantum efficiency and short operational lifetime. Carbene-metal-amides (CMAs) are a promising family of donor-bridge-acceptor molecular charge-transfer (CT) emitters for OLEDs. CMAs possess both small lowest-lying singlet-triplet energy splitting which is commonly seen in the thermally-activated delayed fluorescence (TADF)-type emitters and heavy atoms which are used in the phosphorescent-type emitters. CMAs exhibit high electroluminescence quantum efficiency and rapid harvesting of triplet states.[1,2] However, the photophysics of the emission mechanism is not fully understood. Here I demonstrate a universal approach to tune the energy of the CT emission in CMAs. A blueshift of up to 210 meV is achievable in solid state via dilution in a polar host matrix. The origin of this shift has two components: constraint of thermally-activated triplet diffusion, and electrostatic interactions between guest and polar host. These discoveries offer new insight into coupling between the singlet and triplet manifolds and the effect of heavy atom in CMA materials.[4] This approach is also realised in OLEDs devices, shifting the emission of sky-blue chromophores into the practical blue range.[5]



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TH-272

Theoretical investigation into the dehydrogenation of perhydro-N-ethylcarbazole and derivatives

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Perhydro-N-ethyl carbazole (12H-NEC) has been suggested as a potential liquid organic hydrogen carrier (LOHC) as it can store up to 5.8 wt% H_2 and can undergo catalytic dehydrogenation to of N-ethyl carbazole (NEC) at relatively low temperatures and subsequent hydrogenation back to 12H-NEC. [1]

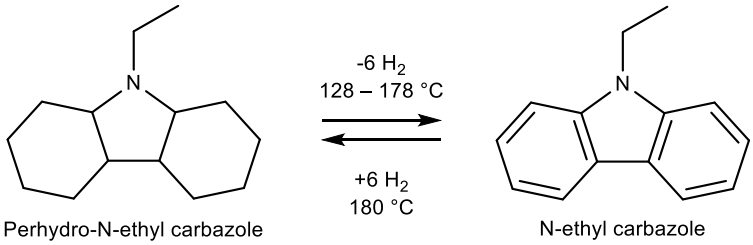

Figure 1: Dehydrogenation and hydrogenation reaction of Perhydro-N-ethyl carbazole and N-ethyl carbazole respectively [2]

It has been shown that in the presence of catalysts the possibility of dealkylation of NEC can occur at temperatures above a certain threshold (usually 350K), likely explained by the relatively weaker nitrogen-alkyl bond. [3] A possible solution to this problem could be by adding different substituents to the alkyl group.

I will explore the possible derivatives of NEC and their effect on the dehydrogenation energies as well as stability of the molecule. Additionally, studying the effect of such derivatives can give a better understanding of the dehydrogenation reaction not only for 12H-NEC but also other potential hydrogen carriers.

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TH-273

Comparative First-Principles Phonon Dispersion of Rutile and Anatase TiO_2

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The phonon frequencies are very sensitive to the applied exchange-correlational (XC) functionals and accuracy of the psedopotentials. Stable phonon dispersion had been reported previously for both rutile and anatase TiO_2 using local density approximation (LDA),[1-2] however soft phonon modes were reported for rutile TiO_2 using higher rungs of Jacob's ladder such as PBE generalized gradient approximation (GGA) and HSE06 hybrid functional.[3] Herein the structure and phonon dispersion of rutile and anatase TiO_2 are studied using PBEsol GGA, TPSS meta-GGA, PBE0 and HSE06 hybrid functionals. Comparison of predicted lattice parameters by these XC functionals show excellent experimental agreement and calculated phonon frequencies show stable phonon modes for both rutile TiO_2 (Figure 1a) and anatase TiO_2 (Figure 1b). The choice of XC-functionals show sensitivity to the propagation of phonon frequencies along the high symmetry Brillouin zone path. Nevertheless, the highest rungs of Jacob's ladder, PBE0 and HSE06 produce identical phonon dispersion curves for both rutile and anatase TiO_2.

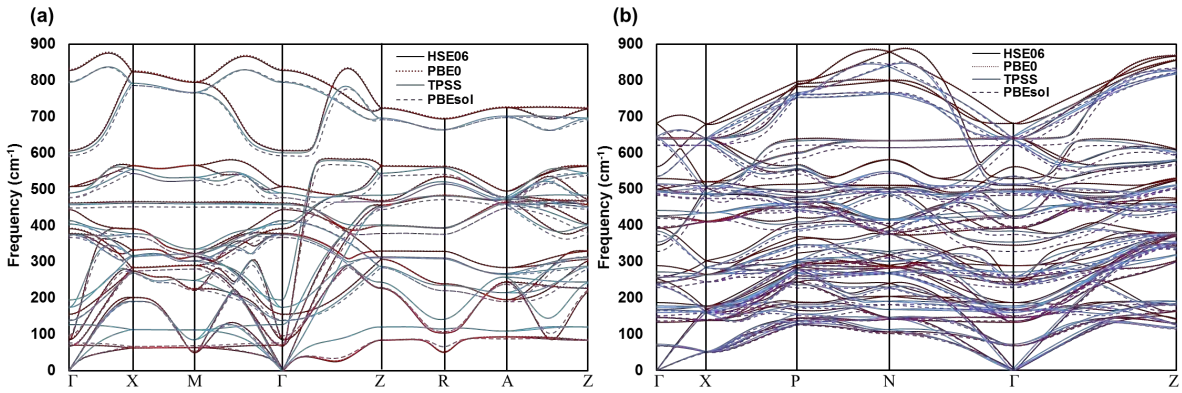

Figure 1. Calculated phonon dispersion curves of (a) rutile-TiO_2, and (b) anatose-TiO_2.

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TH-274

Hybrid Inorganic-Organic Luminophores for the Advancement of Luminescent Solar Concentrators

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Efficient solar harvesting technologies have the potential to alleviate climate change. However, their potential is limited by the fact that solar panels by themselves are large, bulky and costly in terms of installation. Devices known as luminescent solar concentrators (LSCs) can potentially be coupled to solar cells to improve versatility, aesthetic appearance, and efficiency.

LSCs (Figure 1.) are formed from simple transparent substrates with a light harvesting luminescent materials (luminophores) dispersed within them. The luminophore acts to absorb incoming sunlight, and via emission event redirects the light towards the edges - as the transparent substrate acts as a waveguide. Solar cells coupled to the edges can then collect the concentrated radiation.

LSCs are currently not commercially viable as a suitable luminophore has not yet been engineered that maximises solar concentration. In our work we seek to synthesise non-toxic hybrid inorganic-organic (quantum dot-dye antenna) luminophore materials built to maximise the light harvesting and concentration ability of LSCs.

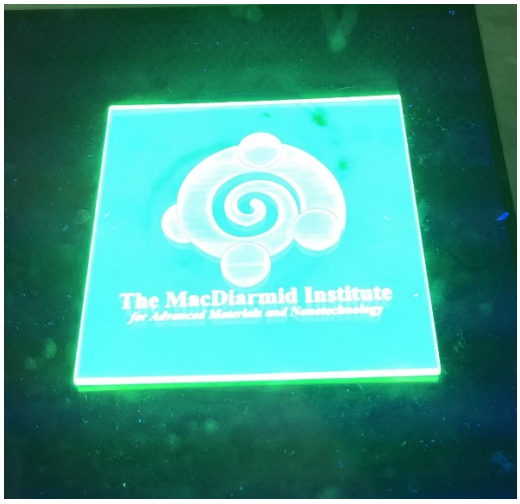

Figure 1. Luminescent Solar Concentrator. Note converted radiation is concentrated to the edges by total internal reflection, causing them to glow.

TH-275

The Bromide-Sulfur dioxide van der Waals Complex: A Peculiar Case of Photodetachment

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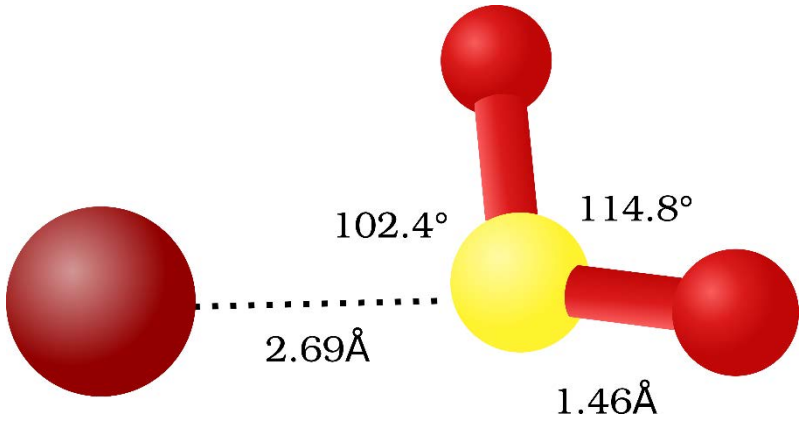
Van der Waals complexes formed between a bromide anion and a sulfur dioxide molecule have been investigated both computationally and experimentally using anion photoelectron spectroscopy. Contrary to the corresponding iodide complex; the bromide photoelectron spectrum exhibits spectral features that cannot be assigned under a conventional direct detachment PES framework. Spectral features associated with direct photodetachment have been computationally investigated utilising energies computed with the CCSD(T) method. However, in order to probe the origin of additional spectral features, multireference methods have been utilised to determine energetics associated with the excited states of the bound anion, and based on these calculations we attribute these features to autodetachment from an excited SO_2 molecule. These features express similar dynamics to those observed in a number of iodide-nucleobase complexes investigated by Neumark *et al.*[1]



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TH-276

Computational investigations of aluminium-ion species as intercalants in graphitic cathode structures

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Investigations into new and alternate battery chemistries are becoming increasingly relevant to commercial technology applications where heightened value is being placed in efficiency and ethical considerations. In particular, research into the use of aluminium-ion based batteries as an alternative to commercially prevalent lithium-ion batteries has been rejuvenated following pioneering research of Lin et al. in 2015.[1] While significant strides have been made in understanding the properties of aluminium-ions as cathode intercalants,[2] research has predominately focused on intercalant mechanisms in charge/discharge environments.

Investigation of aluminium-ion intercalant properties in intercalated cathode environments, including the diffusivity and mobility of aluminium-ions as influenced by the graphitic cathode interactions, is anticipated to provide further understandings of the core characteristics in modern aluminium-ion battery design. We investigate these properties via computational molecular dynamics simulations, with an aim to determine the qualities and challenges that intercalant density and stage positioning, and cathode composition and structural parameters, may present for system optimisation. This research is performed with intention of improving understanding of fundamental mechanics and force relationships in modern aluminium-ion battery design.

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TH-277

Do modern TD-DFT methods rise to the challenge of noncovalent excited-state binding?

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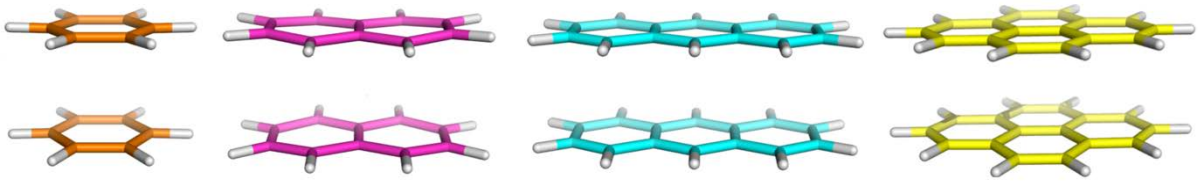
Excimers—excited dimers—are supramolecular systems whose binding strength is due to many components that are ongoing challenges for computational treatment of excited states, such as charge transfer, exciton coupling, and London dispersion interactions. As a perspective on the ability of current time-dependent density functional theory (TD-DFT) methods to capture these challenging interactions, we present a study of four model excimer systems with nine density functional approximations with and without the application of additive dispersion corrections against a reliable wavefunction reference.[1] This study shows some of our recently published range-separated double-hybrid density functionals[2] as the most promising candidates for future descriptions of excimer binding. Additionally, it further encourages the excited state-specific reparametrisation of dispersion corrections for a more accurate and efficient treatment of dispersion for TD-DFT methods.



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TH-278

Lactoferrin-derived peptides synergistically increase the membrane-disrupting activity of antifungal drug amphotericin B.

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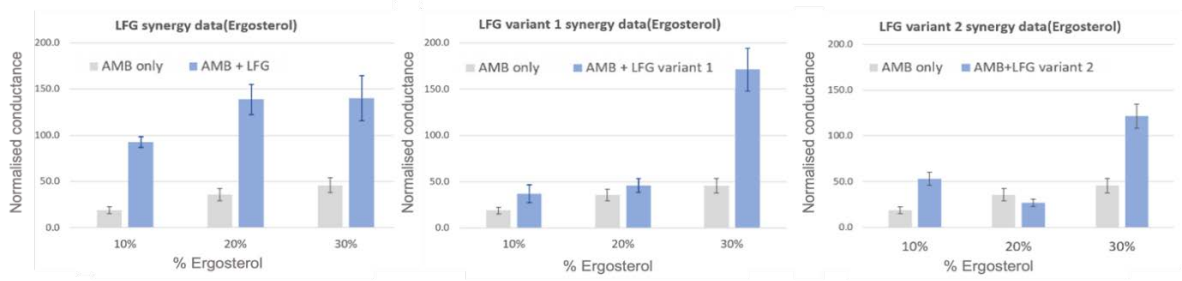
Invasive fungal infections (IFIs) are becoming more common and cause an estimated 1 million deaths per year globally. These infections are challenging to treat, with mortality rates between 10% and 50%, even in developing countries with good health care. Despite its high toxicity, amphotericin B (AMB) remains a clinically important anti-fungal drug particularly for treating multi-drug resistance IFIs. The concentration-dependent toxicity of AMB is related to the structural similarity of ergosterol and cholesterol, which are found in all mammalian cells. Developing an adjuvant drug to reduce the clinical dose of AMB has the potential to significantly improve the mortality of IFIs and improve patient outcomes.

Lactofungin (LFG) is a 30-residue peptide derived from the milk protein lactoferrin. LFG is synergic with AMB despite the peptide itself not showing any anti-fungal effect[1]. In addition, it is non-toxic to human cells. This study aims to investigate the sterol-dependent membrane-disrupting activity of AMB with LFG and LFG variants that show a range of synergy profiles on different fungal pathogens. To achieve this, we use tethered lipid bilayer membranes with electrochemical impendence spectroscopy (tBLM/EIS), in which membrane disruption is reported as an increase in the conductance of ions across the membrane. tBLMs were composed of the neutral phospholipid POPC and increasing concentrations of cholesterol and ergosterol.

The LFG and several tested variants show no membrane-disrupting activity on membranes with ergosterol or cholesterol, consistent with its lack of cytotoxic activity on mammalian and fungal cells. However, when combined with AMB, LFG and several variants significantly increase the membrane-disrupting activity of AMB on ergosterol-containing membranes (Figure below). The synergy profiles of the different variants from tBLM/EIS experiments are consistent with cell-based data, suggesting the synergy is lipid dependent and ergosterol-specific, and sterol-containing model membranes are good model systems to study the mechanism of ABM-LFG synergy.



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TH-279

Exploring local self-diffusion coefficients in confined carbon nanomaterials

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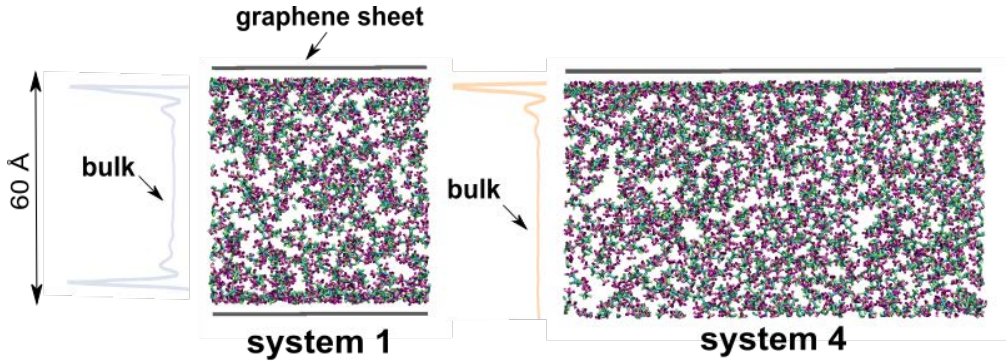
Understanding the position-dependent self-diffusion coefficient of chemical species is important for a variety of biological and nanoscale applications. For example, the behaviour of a species at a solid-liquid interface, such as at an electrode in battery system will be notably different to the behaviour in the bulk. Recently, we have defined a way to measure a local self-diffusion coefficient using a statistical mechanical approach and tested it by simulating a Lennard-Jones fluid.[1]

In this work, we apply our new method to a realistic system, by simulating all-atom butane in a series of carbon slit pores. We demonstrate for the first time that our method can be applied to molecular systems and demonstrate the convergence of the local self-diffusion coefficient to the bulk diffusion coefficient. We show that finite-size effects on measured local self-diffusion coefficients can be significantly enhanced compared to homogeneous systems. This demonstrates that even greater care should be taken when comparing results of simulations of different sizes and systems should be sufficiently large to achieve true bulk behaviour.



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TH-280

Understanding the solvent effect in acid catalyzed reactions of biorenewable platform chemicals

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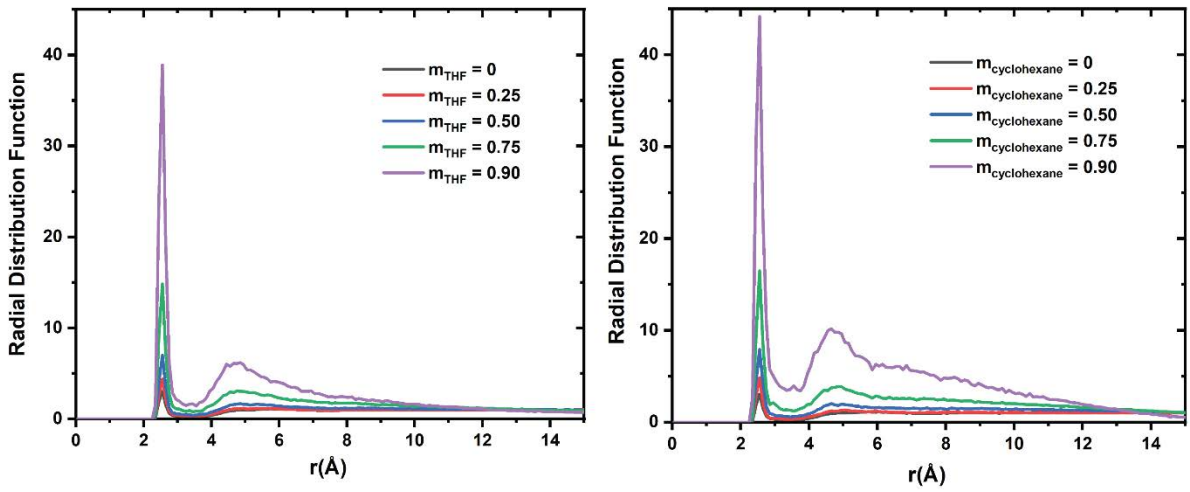
Valorizing biomass-derived lactones involve removal of oxygen-based functionalities to get a variety of high-value chemicals and liquid fuels. Under specific catalytic and solvent conditions, these reactions may exhibit marked differences in reaction kinetics and selectivity. To study the reactivity in different classes of solvents such as polar protic, polar aprotic and non-polar, the acid catalyzed dehydration of mevalonolactone (MVL) is carried out in water, tetrahydrofuran (THF) and cyclohexane environments using Car-Parrinello Molecular Dynamics (CPMD). In the preliminary analysis, we observe a higher protonation barrier on MVL in water at 15-20 kJ/mol in comparison to that in THF and cyclohexane environments. Further, to understand the solvation of reactant in mixed solvents, i.e., different ratios of THF-water and cyclohexane-water systems around MVL, the radial distribution function (rdf) plotted in figure below suggests that the local domain surrounding MVL is populated with water molecules, thus providing easy transfer of protons to MVL. This observation is also supported in our previous work involving dehydration of 4-hydroxy-6-methyl lactone (HML) [1]. This presents the need of machine learning (ML) model to predict solvent effect with simple descriptors derived from classical molecular dynamics (MD). Therefore, in this work, we build a robust ML model with the inclusion of features such as diffusion coefficient of proton, structural properties of reactant and a few physical properties of solvent viz. dielectric constant, viscosity, polarity index, etc.



Profiles presenting water distribution around MVL in different THF-water and cyclohexane-water mixtures.

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TH-281

Probing Ultrafast Hole Transfer in an Organic Donor/Acceptor System

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One of the highest performing materials for active layers in organic photovoltaics is a blend of the polymer PM6 electron donor and non-fullerene electron acceptor Y6.[1] In this talk, we will first discuss the preparation of blend nanoparticles of PM6 and Y6 in a 1:1 mass ratio by miniemulsion, using sodium dodecyl sulfate (SDS) or 2-(3-thienyl)ethyloxybutylsulfonate sodium salt (TEBS) as surfactant. The PM6:Y6 nanoparticles prepared with TEBS have an intermixed morphology, suitable for applications such as organic photovoltaics. We will then present ultrafast pump-probe spectroscopic data of the PM6:Y6 nanoparticles collected at 400 nm and 800 nm pump wavelength. Pumping at 400 nm results in excitation of primarily PM6 (electron donor) whereas a pump wavelength of 800 nm excites Y6 (electron acceptor) only. Excitation of PM6 is followed by electron transfer from PM6 to Y6, which leads to generation of long-lived hole and electron in PM6 and Y6, respectively. In contrast, excitation of Y6 initiates a hole transfer reaction, which involves a separate mechanism but results in the same outcome. Our work has led to further insight into the critical role played by hole transfer in charge generation in the high-performing photovoltaic materials PM6:Y6. Our latest results indicate that these mechanisms are also responsible for the photocatalytic ability of PM6:Y6 nanoparticles to undergo hydrogen evolution.

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TH-282

Exploration of cocamidopropyl betaine: a closer look at individual amidopropyl betaines' self-assembly

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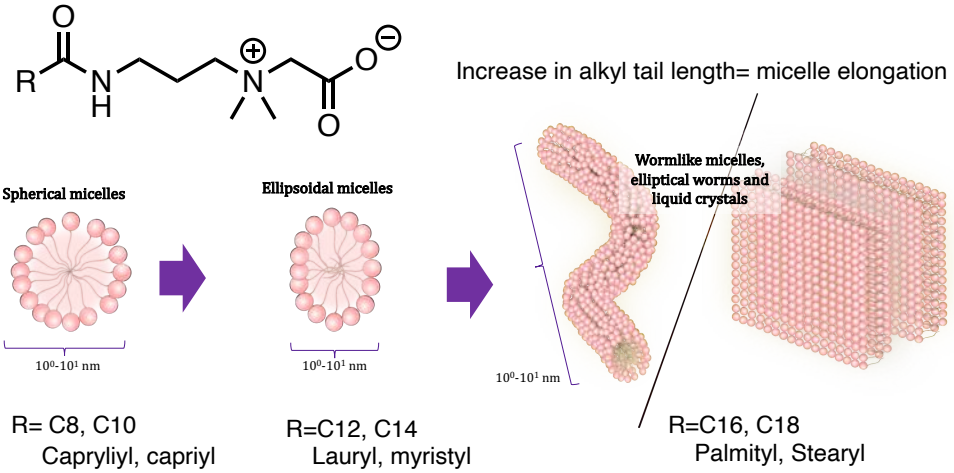
Cocamidopropyl betaine is a surfactant mixture that sees widespread utility in personal care and industry, due to its mildness and simple synthesis. Additionally, cocamidopropyl betaine exhibits synergism with other surfactants, leading to the formation of wormlike micelles and therefore resulting in viscoelastic solutions. The feedstock used to synthesise this surfactant mixture dictates the individual components and ultimate properties of cocamidopropyl betaine. Here, we investigate the surface-active properties and self-assembly a library of synthesised pure amidopropyl betaines, found within cocamidopropyl betaine. Small-angle neutron scattering, bubble pressure tensiometry, pendant drop tensiometry, foaming studies, optical and polarising light microscopy are employed in order to determine each individual component's behaviour and surface-active properties. It is evident that an increase in alkyl tail length modulates properties within this class of molecules, leading to the formation of different micelle geometries in solution and consequent physical behaviour, as well as widely varied surface activity, adsorption dynamics and foaming capabilities. These results indicate potential new approaches to tuning the properties of mixed surfactant systems, using carefully designed tail mixtures.



TH-283

Computational *de-novo* structural elucidation using mass spectrometry

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Mass Spectrometry (MS), coupled to either gas chromatography (GC) or high-performance liquid chromatography (LC), is commonly used in fields such as natural product chemistry, metabolomics and environmental chemistry. Its primary use is the identification of (i.e determine the molecular structure) chemical compounds within some mixture. Generally, information regarding elemental composition can often be systematically retrieved using MS. In addition, "library searching" can be used to identify commonly occurring compounds with the use of a mass spectral library (database). However, if the molecule is not found in the spectral library, then extraction of additional structural information from the data can, in the case of small molecules, only be achieved with the case-by-case interpretation of the mass spectrum by an expert. This severely limits the ability for GC-MS or LC-MS experiments to perform high-throughput screening of chemical mixtures for compounds of interest. Furthermore, though the advent of tandem mass spectrometry (MS^n) allows for additional fragmentation information to be extracted from a mass spectrometry experiment, much of this information cannot be readily used within a library search, and so can become under-utilised. Thus, it is desirable to implement computational methods which can systematically extract structural information from MS data, or be able to, given a list of "candidate" structures, decide which structure is the closest match to the data.

We believe that such a method should be divided into two components. The first component consists of converting MS data from a list of masses and abundances to an intermediary representation. By considering differences between the masses and using a network-based method, we can derive a representation of the data which explicitly encodes it as a set of topological constraints on the space of possible analyte structures, much like the network-based "fragmentation trees" derived from MS/MS data in [1]. Furthermore, the relative abundances can be converted to a probability reflecting the likelihood of an ion in the mass spectrum fragmenting (further) into a smaller ion. The outcome of this component is to, for some arbitrary candidate structure and some given MS data, propose a fictitious fragmentation mechanism which "best explains" how the structure may fragment in order to produce the data. The second component tests the fictitious fragmentation mechanisms generated by comparing the experimentally derived probabilities to the theoretical probability computed with a quantum chemical method, at specified "pinch points" in the mechanism. This may reduce both the computational cost and the accumulation of errors compared to a first principles simulation of the mass spectrum (e.g [2]). Ultimately, this allows the fictitious mechanism, and consequently the corresponding candidate structure, which most closely matches with the data, to be determined. We present preliminary findings on the development of this method.

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TH-284

The Ebola virus delta peptide is a cation selective viroporin

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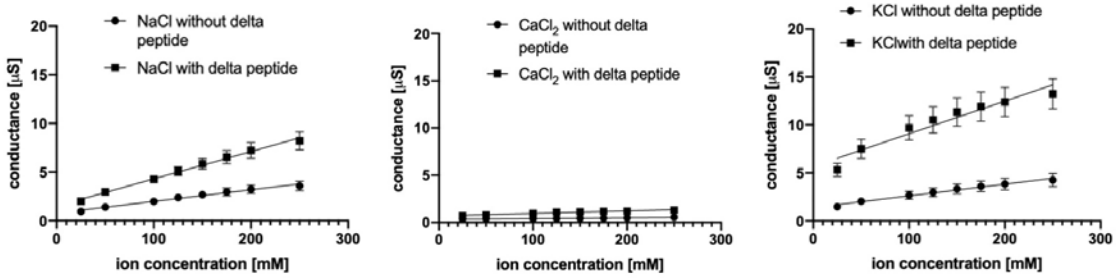
Ebola virus disease is a rare but severe infectious disease with an average mortality rate of 50% (WHO, 2020). There is a lack of effective countermeasures and no targeted treatment. The Ebola virus (EBOV) delta peptide is a partially conserved and non-structural protein encoded in the viral genome. The EBOV delta peptide functions as a viroporin. These pore-forming peptides are found in most viruses and form ion channels in membranes to disrupt ion homeostasis and related physiological processes in the host cells. Like other viroporins, the EBOV delta peptide plays a critical role in the life cycle of the virus and affects viral pathology. Like the inhibitors developed for the M2 viroporin in the influenza virus, the delta peptide viroporin has the potential to serve as a target for developing anti-viral treatments. To facilitate this, more information on the structure and function of the delta peptide pore is required.

The aim of this study is to characterize the ion selectivity of the EBOV delta peptide using tethered bilayer lipid membranes (tBLMs) and electrochemical impedance spectroscopy (EIS). We have recently used this method to characterise the ion selectivity and pore structure of the pore-forming peptide GALA [1]. To determine the ion selectivity of the EBOV delta peptide, we form peptide pores in tBLMs composed of the neutral phospholipid POPC and the negatively charged lipids POPG (50:50 mol%). Pores are titrated with increasing concentrations of the KCl, NaCl and $CaCl_2$ solutions. To control for background ion permeation, bilayers without peptide pore are used.

Up to now, we have found that EBOV delta peptides are cation-selective. The figure shows comparisons of the normalized conductance for cations in the absence and presence of EBOV delta peptide. The slopes of concentration-dependent membrane conductance represent the ion selectivity of EBOV delta peptide pores. A steeper slope suggested a higher ion permeability. The difference between KCl, NaCl and $CaCl_2$ slopes indicated that EBOV delta peptide selective Na^+ and K^+ to pass through easily (ion permeability for $K^+ > Na^+$), and few Ca^{2+} can pass through the pore. The results of our study can help researchers to understand the pathology of Ebola virus and develop more effective drugs and vaccines.



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TH-285

Surface dynamics and development of adsorbed films of pentane isomers on graphite[001]

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The diffusion of molecules in the adsorbed phase in gas-solid or liquid-solid systems contribute significantly to mass transfer in porous materials [1]. Within porous materials, surface diffusion can be classified into three diffusion regimes corresponding to the monolayer, multilayer and condensed regions of adsorption [2]. While the movement of the molecules are restricted to the plane parallel to the surface in the monolayer region, there is a possible distribution of diffusion coefficients within the multilayer region and in the condensate of a filled pore [3]. While the concept of different regimes of diffusion is recognised, the understanding of the surface diffusion is still lacking due to the difficulties in measurements and the various parameters affecting this process and there remains a lack in understanding how the diffusion coefficient changes as the adsorption transits through these regimes, especially for complex molecules. To fill this gap, we have performed computer simulation to study the diffusion of hydrocarbon isomers, namely of n-pentane and neo-pentane, in their bulk phases and in the adsorbed phase for a range of pressures and temperatures. Our study focused on how geometric constraints would affect the diffusion process and whether a reduction in dimensionality due to adsorption would affect the diffusion of these two isomers relative to their movement in the three-dimensional bulk phases.

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TH-286

Untangling quintet state dynamics of singlet fission with nutation ESR

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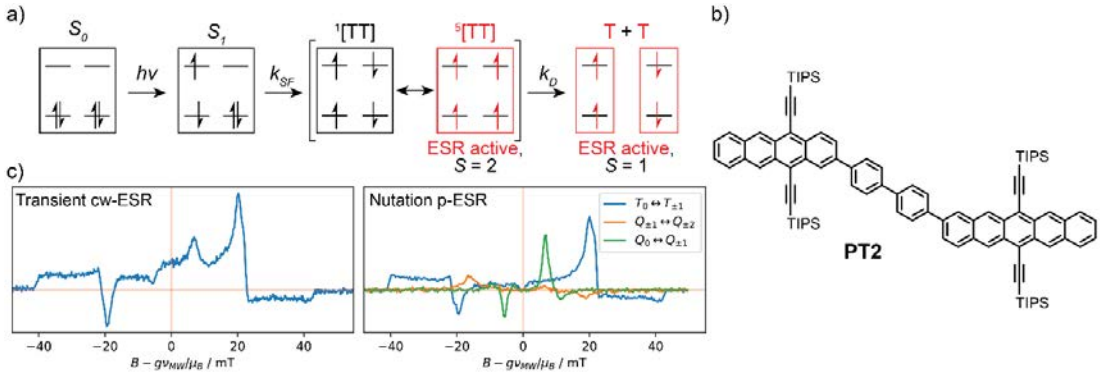
Singlet fission (SF) is a fast spin-conserving electronic process in which one high-energy singlet exciton splits into two lower-energy triplet excitons (Figure 1b). While the initial (S_1) and final ($T_1 + T_1$) states involved in singlet fission are unambiguous, the route between them remains far from clear. A key intermediate is the $4e^-$ coupled triplet-pair state, $^{2S+1}[TT]_m$, which initially forms as singlet $^1[TT]_0$ before subsequently dephasing to an unusual organic quintet $^5[TT]_m$ and/or disassociating into free triplets.[1] The $^5[TT]_m$ quintet has recently drawn interest as a five-level organic qudit that can be photoinitiated into a 'clean' spin state and used to execute quantum gate operations with a long coherence time.[2]



a) Singlet fission yields triplet and quintet excited states, suitable for transient ESR studies. b) Continuous-wave ESR of spin states following SF in c) pentacene-tetracene dyad PT2 show multiple peaks corresponding to overlapping transitions, which can be resolved by pulsed ESR nutation. Differences between these two experiments hint at multiple coexisting exciton pathways.

The excited states formed by SF possess rich spin dynamics ripe for magnetic resonance, and transient electron spin resonance (ESR; also called EPR) has emerged as a key tool for investigating this process. We have previously used continuous wave ESR to perform routine measurements, or alternatively nutation pulsed ESR to assign the (S, m_s) spin numbers of a transition (Figure 1b). We now extend these pESR nutation measurements into an extra dimension by acquiring a series of spectra while sweeping the magnetic field or time to obtain field- or time-dependent spectra, resolved by spin transition. These transition-resolved nutation spectra allow us to directly measure the dynamics of previously overlapping spin transitions as they evolve over time. Simultaneously, differences between the field-swept pESR and cw-ESR spectra have informed our understanding of the theory of $^5[TT]$ quintet formation by revealing the distinct quintet subpopulations accessed *via* different populating pathways.

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TH-287

Synthesis and reactivity of highly reduced metallosupramolecular complexes in the gas phase

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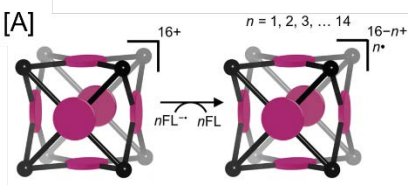
Transition metal complexes with accessible low oxidation states are central to modern catalysis. Investigating the intrinsic properties and reactivity of such complexes beyond their conventional oxidation state(s) is complicated by an inability to cleanly isolate a pure population, as well as their propensity to react with solvent or ambient air. Using an ion-trap mass spectrometer, gas-phase electrochemical reduction is deployed as a dual-function tool to synthesise and probe the reactivity of highly reduced metal complexes. The effect of precursor ion charge state, ligand structure, and guest encapsulation on the reaction products and rates is explored.

Face capped $Fe_8L_6.(OTf)_{16}$ cubic supramolecular cage [A] was synthesised via literature procedures.[1] Experiments were performed on an unmodified dual-source mass spectrometer (Orbitrap Elite, Thermo Scientific, San Jose). Positive cage ions were generated by electrospray ionisation (ESI) from MeCN solutions, whereas radical anions of fluoranthene ($FL^{-\bullet}$) were produced by chemical ionisation. Ions of opposing polarity were stored together in the ion trap for a defined period (1-200 ms), after which the ion trap was scanned out and the reaction products analysed at high mass resolution.

Electrospray ionisation of the cage produced multiply charged cations of the form $\{[A].(OTf)_{16-z}\}^{z+}$ (z = 5-16). Reaction of isolated $[A]^{16+}$ with $FL^{-\bullet}$ yielded $[A]^{(16-n)+}$, with products associated with up to 14 reduction steps (n) detected. Notably, no change in molecular mass was observed. Repeating the experiment with a fullerene guest inside the cube (i.e., $[C_{60}\subset A]$) similarly yielded ions assigned to $[C_{60}\subset A]^{(16-n)+}$, confirming that the structural integrity of the coordination complex was retained despite the significant exothermicity of the ion-ion reactions. In each case, the reaction kinetics could be modelled as a series of stepwise, single electron transfers under pseudo-first order conditions. Further, the reactivity of the reduced complexes was investigated by re-isolation of each product ion in the presence of adventitious O_2.

The selectivity of mass spectrometry enables the isolation and interrogation of transient species, including highly reduced complexes. This work opens an avenue to further investigations of these elusive species by interfacing the current method with gas-phase chemical or spectroscopic methods.



Up to 14 stepwise reduction reactions are observed for metallosupramolecular complex [A].

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TH-288

Actinic Wavelength Action Spectroscopy of Anionic Halogen Oxide Reaction Intermediates

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Halogen oxides (X_aO_b) are significant in our atmosphere due to their high reactivity with ozone and role in particle formation pathways[1]. The aim of the present study is to investigate the photodepletion of XO_b^- (where X=Br or I, and b = 1 or 2) within the visible range of 650 - 410 nm (15385 - 24390 cm^{-1}) *via* electron photodetachment and photodissociation action spectroscopy. Gas-phase spectra are obtained at room temperature by coupling a tuneable OPO laser with a linear ion-trap mass spectrometer. A bound excited-state is present in this visible range, in each case, which will either undergo autodetachment *via* electron loss ($XO^\bullet + e^-$) or undergo photodissociation. Depending on the vibrational energy level of the excited-state, either photodissociation or photodetachment is favoured. Investigation of the potential energy surface using the multireference configuration interaction (MRCI) method shows that, within the investigated energy range, the initially prepared excited-state are close to curve-crossings that mediate photodissociation and the EA for electron detachment. From this study XO_b^- has been shown to photodeplete at visible wavelengths and, with previous studies showing that XO_b^- will react with ozone to form higher order halogen oxide clusters, may together contribute to the low abundance of halogen oxides detected in the atmosphere and therefore why they have eluded detection.

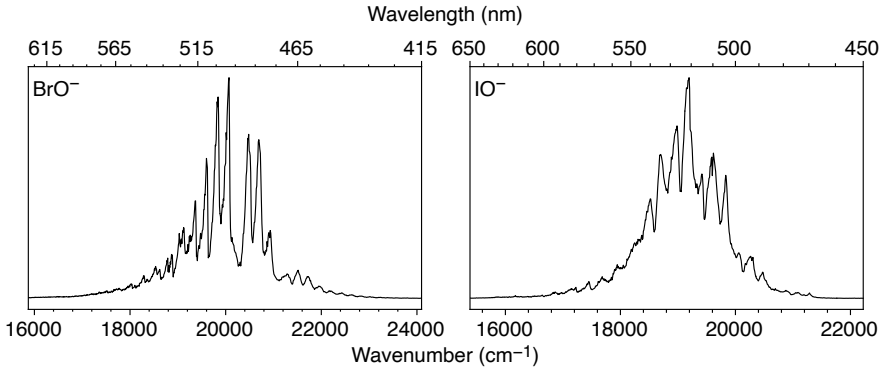

Figure 1: Photodissociation action spectra of BrO^- (left) and IO^- (right) within the actinic range.

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TH-289

Non-equilibrium molecular dynamics for optimising salt exclusion of multi-layer graphene oxide membranes

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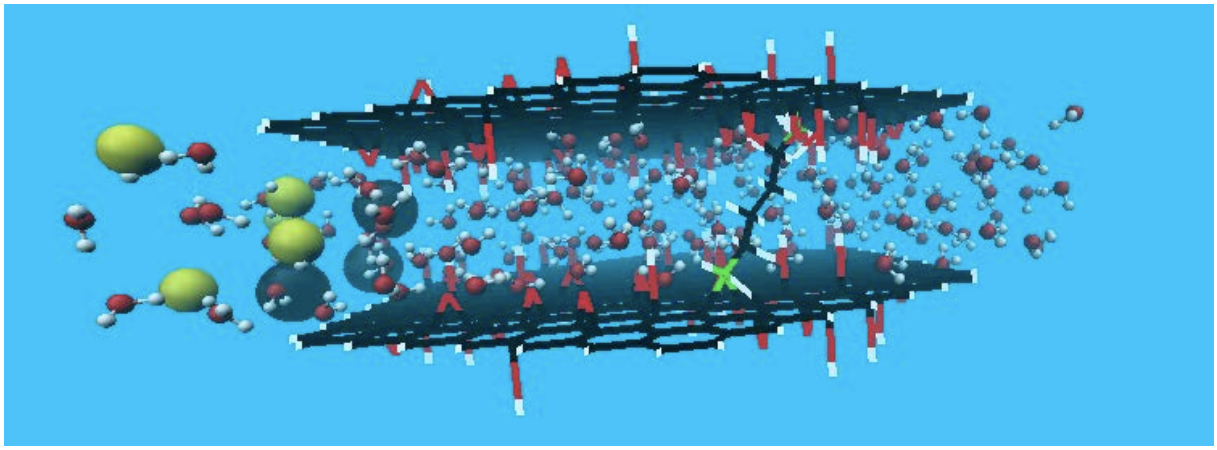
Optimising the process of removing salt from seawater to levels that are drinkable and agriculturally usable is of great importance for meeting the survival needs of our growing population. Currently, most commercialised desalination membranes are polymer-based, however graphene oxide (GO) demonstrates greater water flux and fouling resistance to chloride ions.[1] Experimental and molecular dynamics investigations are now focusing on optimising salt exclusion with GO membranes.[2]

Multilayer GO membranes self-assemble in water with potentially greater mechanical stability for a greater surface area.[3] However, the spacing between GO sheets swells due to the hydrophilicity of the hydroxide groups, limiting the size-based exclusion of salt ions. One way to control interlayer spacing is with linker groups covalently bonded to one or both GO sheets on either side of the space, that hold the layers together at a controlled spacing.

Experimental work has demonstrated the desalination capability of GO membranes cross-linked with cyclic[4] and amine[5] structures. We will present results of molecular dynamics simulations carried out to understand these experimental findings and investigate the viability of new linker species for improving salt exclusion and fouling resistance in GO desalination membranes.



The passage of hydrated Na^+ and Cl^- ions is blocked by the narrow interlayer spacing of the GO sheets while water flows as a bilayer, with spacing controlled by a 1,4-diaminobutane linker.

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TH-290

The Electrostatic Origins of Specific Ion Effects: Quantifying the Hofmeister Series for Anions

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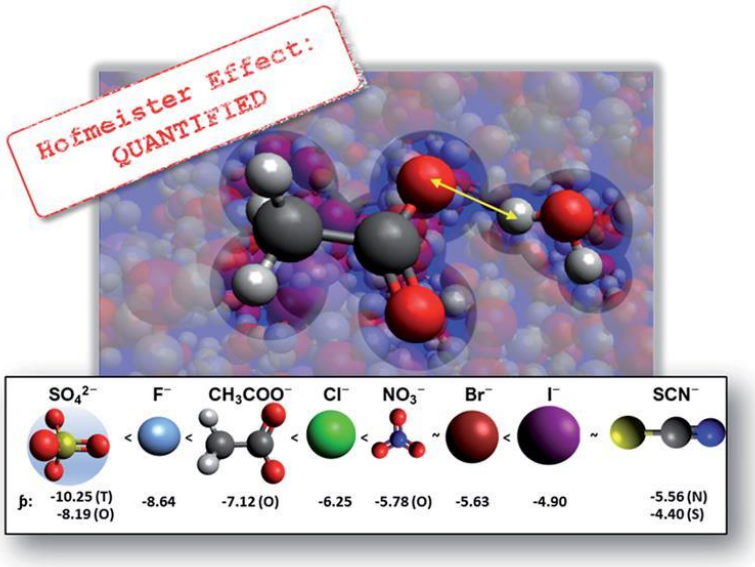
Specific-ion effects and the Hofmeister series have been known since the 1880s. They are ubiquitous throughout the chemical, biological and physical sciences. Despite intense research, our understanding of their origins remains poor. Here we reconsider the origins of specific ion effects through the lens of Coulomb interactions and establish a new foundation for anion effects in aqueous and non-aqueous environments [1]. We show that, for anions, the Hofmeister series can be explained and quantified by consideration of site-specific electrostatic interactions. This can simply be approximated by the radial charge density of the anion which we have calculated for commonly reported ions. This broadly quantifies previously unpredictable specific ion effects, including those regarding solvent properties, virus activities and reaction rates. Furthermore, in non-aqueous systems, the relative magnitude of the anion series is dependent on the Lewis Acidity of the solvent, as measured by the Gutmann Acceptor Number. Analogous SIEs for cations bear limited correlation with their radial charge density, highlighting a fundamental asymmetry in the origins of specific ion effects for anions and cations, due to competing non-Coulombic phenomena.



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TH-291

Anomalous polymerization rates of moderately hydrophilic monomer

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Many industrially important polymers are prepared by radical polymerisation of water-soluble monomer. In aqueous solutions, the polymerisation propagation rate, k_p, of a number of monomers have been found to have a strong dependence on concentration, having a greater k_p in dilute solutions. One proposed explanation is that during polymerisation in aqueous solution, replacing water by monomer increases the barrier to rotational motion in the transition state, due to the strong hydrogen bonding interactions between monomers.[1] While this explanation appears to have been generally accepted,[2-4] the barrier-increase mechanism implies that the more likely a monomer molecule is to form a hydrogen-bond with another molecule of monomer, the stronger the aqueous solution effect will be. However, N-vinyl pyrrolidone (NVP) and dimethyl acrylamide (DMA), which in their un-ionised forms cannot act as hydrogen-bond donors and hence are incapable of dimerisation, show concentration dependences as strong as monomers that form hydrogen bond dimers. An alternative explanation is that these systems partition into domains of increased local monomer concentration and medium-scale clusters of hydrogen-bonded liquid water with robust ice-like structure.[5]

To investigate the anomalous polymerization rates of NVP and DMA in aqueous systems, we probe the kinetics and local monomer environment utilizing experimental and computational techniques. We use Quasi-Elastic Neutron Scattering to characterize the translational and rotational diffusive motions of the monomers, Small-Angle Neutron Scattering to characterize the structure of the system over the range 1-100 nm, and Nuclear Magnetic Resonance to investigate the diffusion dynamics. Molecular dynamics simulations are paired with these experiments in order to validate the simulated systems investigate the properties on an atomistic scale. Initial results indicate that with increasing monomer concentration, there is a decrease in rate of monomer diffusion and an increasingly ice-like local water structure. In this paper we will present these results and those of further experiments.

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TH-292

Machine learning a steady-state fluctuation theorem

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Non-equilibrium processes are ubiquitous in nature and everyday life, yet our understanding of them from a thermodynamics perspective is limited. One of the few thermodynamic relations that is valid arbitrarily far from equilibrium is the fluctuation theorem (FT), which quantifies the probability of observing, over some period of time, events that violate the 2nd law of thermodynamics and result in a decrease in entropy.[1] The FT has been used to derive a number of useful relations, such as the dissipation theorem that allows for more accurate measurement of thermodynamic properties over shorter time periods. However, the FT is only an exact relation under certain conditions: when the thermodynamic distribution of the initial systems is an equilibrium one. Often, we are interested in non-equilibrium steady-state systems, which by definition do not begin at equilibrium, and for these the FT is only an approximate relation that is asymptotically valid as the duration of the measurement increases.

One interesting aspect of the FT is that in theory it can be used to predict whether a movie of a non-equilibrium physical process is being played forward or backward. Furthermore, it was recently shown that a neural network trained to predict the direction of such movies (beginning in an equilibrium distribution) recovered the FT without any prior knowledge of it.[2] In this work, we apply similar techniques to movies taken from non-equilibrium steady-states. We find that a simple neural network uncovers a relation of the same form as the FT which is significantly more accurate than the approximate relation that has been derived from theory, despite having access to only the same information. The uncovered relation is shown to be valid even for very short measurements, and for various non-equilibrium processes. In future, this work could allow the accurate measurement techniques derived from the FT to be extended to processes that do not begin in an equilibrium distribution, and help further the understanding of non-equilibrium thermodynamics.

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TH-293

Chemical color-diffusion nonequilibrium molecular dynamics for ionic conductivity with ion–ion correlation

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1. Introduction

All-solid-state batteries have attracted attention as safe next-generation power sources. A major challenge for the practical use is developing highly-conductive solid electrolytes (SEs). Molecular dynamics (MD) has been used for evaluating ionic conductivities towards promising SEs. Conventional MD studies have estimated conductivities with Nernst–Einstein (N–E) dilute approximation neglecting the contribution of ion–ion correlation effect for reducing computational cost. However, N–E approximation relies on the infinite dilution limit, which does not hold for SEs due to their high carrier density [1]. In this study, we developed a non-equilibrium MD (NEMD) method (Chemical color-diffusion NEMD (CCD-NEMD)) to calculate the ion conductivities with the effect of correlations between the ion carriers. CCD-NEMD imposes an external field, which promotes ion hopping, leading to low computational cost with sufficient accuracy. For validation, we calculated the conductivity of the representative SE, $Li_{10}GeP_2S_{12}$ (LGPS) [2].

2. Computational Details

We implemented the CCD-NEMD method in the CP2K software. The experimental crystallographic position [2] was used for the initial structures of the *ab-initio* MD simulations (Fig. 1). *NVT* simulations were performed at the level of PBE-D3/DZVP-MOLOPT-SR.

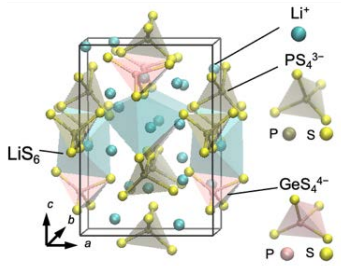

Fig. 1. The LGPS structure obtained at 1200 K.

3. Results & Discussion

We calculated the N–E approximated, non-approximated conductivities obtained by equilibrium molecular dynamics (EMD), and one of CCD-NEMD, denoted as σ_{dilute}, σ_{EMD}, and σ_{NEMD} at 1200 K, respectively. We show the cumulative averages of the conductivities as a function of time in FIG. 2. The lines and error bars in FIG. 2 denote the average and standard deviation of the five independent samples with different initial velocities, respectively. The σ_{NEMD} was in good agreement with the σ_{EMD}, which demonstrates that CCD-NEMD can include ion–ion correlation appropriately. The σ_{dilute} was smaller than σ_{EMD} and σ_{NEMD} because N–E approximated σ_{dilute} neglects the contribution of ion–ion correlation effects. The relative error of σ_{NEMD} (± 11%) is three times lower than that of σ_{EMD} (± 33%) and even lower than and N–E approximated σ_{dilute} (± 18%). The convergence time to a relative error of 30% was about 10 ps for σ_{NEMD}, while that for σ_{EMD} and σ_{dilute} was about 50 ps and 25 ps as shown in the arrows in FIG. 2. These results strongly support that CCD-NEMD can provide the conductivity with a small error using shorter computational time than conventional EMD.

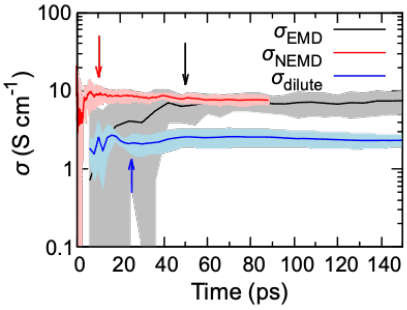

Fig. 2. Cumulative averaged σ_{dilute}, σ_{EMD}, and σ_{NEMD} along *c*-axis at 1200 K.

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TH-294

Determining Suitable Periodic DFT Methods for Modelling Titan-Relevant Molecular Minerals

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Saturn's largest moon, Titan, has geological features somewhat similar to those found on Earth, with seas, lakes and sweeping dunes. Unlike the Earth, however, the temperature hardly varies from around 92 K and the surface composition is dominated by molecular materials composed of H, C and N. The presence of liquid hydrocarbon seas and an active weather system on Titan could allow for deposited 'pure' compounds from the atmosphere to mix and form molecular co-crystals. No comprehensive computational chemical methods have been applied to all currently known Titan co-crystals. Determination of co-crystal structures could lead to more complete understandings of how geological processes affect and interact with minerals on the surface of Titan, as currently little is known of such phenomena.(1)

We completed a thorough periodic DFT study of the set of structurally determined, Titan-relevant molecular co-crystals and the single-component crystals of their respective co-formers. A range of different exchange-correlation functionals were tested along with various dispersion correction methods. This included a combination of post-hoc corrected and inherent van der Waals dispersion functionals. In order to ensure structures converged as accurately as possible, a multi-step geometry optimisation was performed on all systems. This method has been previously used by Taylor and Day(2) on a large set of molecular crystals whose structures were obtained from diffraction data. The more accurate DFT dispersion corrected methods calculated lattice parameters and cell volumes closer to experimental data. Many of the functionals consistently underestimated cell volumes, which has been observed in previous work.(3) Co-crystallisation was generally seen to be a thermodynamically unfavourable process. However, the magnitude of decrease in stability was usually relatively small. We will also present a preliminary study of the crystals under Titan-relevant pressures.

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TH-295

Can Computational Tools Accurately Predict Solvent Effects on Nucleophilic Reactions?

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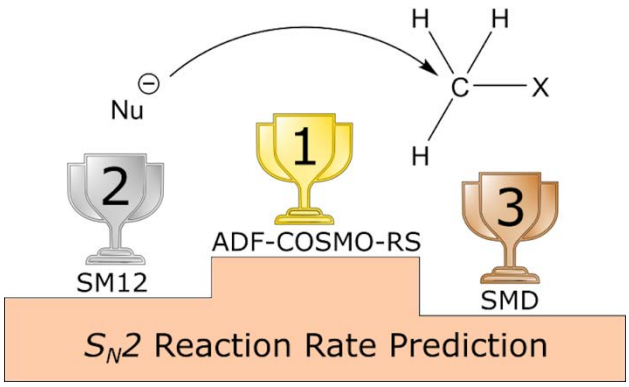
Solvents can play an important role in controlling the thermodynamics and kinetics of chemical reactions.[1, 2] In this talk, I will present a comparison of several computational modelling approaches when applied to three simple S_N2 nucleophilic reactions. Three continuum solvent models, SMD, SM12, and ADF-COSMO-RS, and an explicit solvent model using CGENFF were evaluated for their ability to reproduce experimental rate constants for three simple S_N2 reactions in 8 solvents.[3]

For the explicit solvent model, the use of different approaches for obtaining atomic charges was examined. This includes density functional theory (M062X/6-31+G(d)) calculations of restrained and unrestrained electrostatic potential (RESP and ESP) charges as well as atomic charges optimised to reproduce interaction energies of the solute monohydrate complexes. It was found that the monohydrate interaction energy-based charges gave the best agreement with experimental.

This study revealed that the continuum solvent models outperform the explicit solvent model for the prediction of absolute rate constants, with the best performing method, ADF-COSMO-RS, having an average error when compared to experimental values of 1.4 log units. However, for the prediction of relative rate constants, SM12 and the explicit solvent model outperformed both SMD and ADF-COSMO-RS. Significantly, none of the solvent models were able to reliably predict solvent effects on trends in nucleophilicity. These findings raise questions about the application of theory to elucidate solvent phase reaction mechanisms, and to understand reactivity.



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TH-296

Photodissociation Dynamics and Products of Fluorinated Carbonyls

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Refrigerant gases, foam-blowing agents, fire retardants, etc. have gone through four generations of different chemical classes with each being banned by the Montreal Protocol[2] and its proceeding amendments.[3] The first two generations were chlorofluorocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs) which were banned for the destructive affect they had on the ozone Layer. These were replaced by the third-generation hydrofluorocarbons (HFCs) that, despite having no ozone depletion potential, are powerful greenhouse gases. The most environmentally hazardous HFC is fluoroform (CHF_3 or HFC-23) with a global warming potential (GWP) of 12,400, meaning that one tonne of the compound (CHF_3), emitted today, has the equivalent effect of 12,400 tonnes of carbon dioxide on surface warming over a 100-year period. Hydrofluoroolefins (HFOs) are the most important fourth generation refrigerants and are HFCs that incorporate a carbon-carbon double bond, making them reactive in the troposphere. They have no ozone depletion potential, short atmospheric lifetimes, and very low global warming potentials (GWP ~1).

Fluorinated carbonyls are known atmospheric decomposition products of HFOs but, as Campbell *et al.* reported, it is likely that some of these then break down into HFCs as in the case of CF_3CHO which photodissociates into CHF_3.[4] This is significant as it changes the effective GWP of the initial HFO and therefore its classification under the Montreal Protocol, amongst other regulations, to a potentially restricted substance. The aim of this project is to first assess other fluorinated carbonyls which are likely decomposition products of HFOs to determine if this dissociation pathway is general, then to develop a model for fluorocarbonyl atmospheric photochemistry so that new potential chemicals can be designed with environmental risks that can be evaluated before large-scale emission.

This poster will present velocity map imaging studies, computational chemistry and atmospheric modelling for the photolysis of a range of fluorinated aldehydes that are likely products of the atmospheric decomposition of HFOs.

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TH-297

Neutral-Catalysed Tautomerization of *para*-Aminobenzoic Acid Protomers

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Intramolecular proton transfer in gas phase ions can be catalysed by neutral molecules with significant implications for the distributions of protonation site isomers formed during electrospray ionization (ESI) mass spectrometry experiments. *Para*-aminobenzoic acid (*p*ABA) has become the archetype molecule for studying the changing distribution of protonation isomers (protomers) under the influence of different solvent and ESI source conditions. Recent work from our laboratory has shown that proton transfer between the amine and benzoic acid groups in *p*ABA can be catalysed by a single methanol molecule under the reduced pressure conditions within an ion trap. A generalized scheme for neutral-catalysed intramolecular proton transfer in $[p\text{ABA+H}]^+$ is shown in **Figure 1** A.

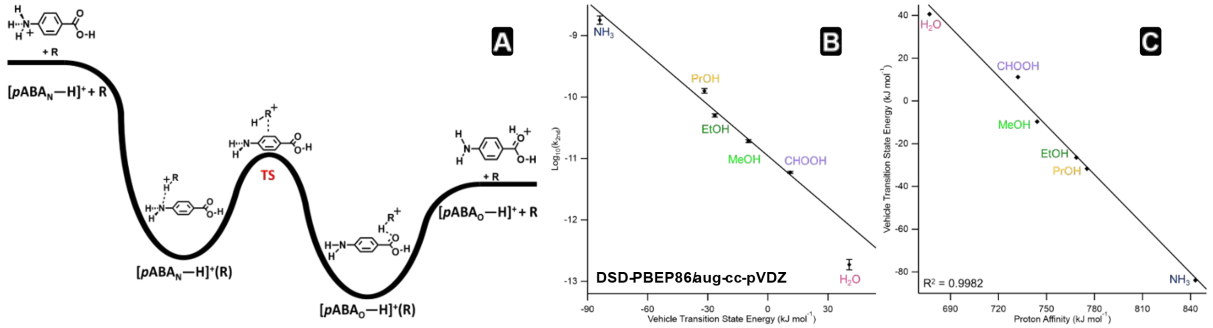

Figure 1. Panel A contains a schematic for neutral-catalysed tautomerism of $[p\text{ABA}_\text{N}\text{—H}]^+$ to $[p\text{ABA}_\text{O}\text{—H}]^+$. Predictive framework (panel B) for neutral-catalysed tautomerism of *p*ABA, calculated with DSD-PBEP86/aug-cc-pVDZ. Panel C shows the transition state energy is dictated by the proton affinity of the neutral catalyst.

Experiments were performed on a Thermo Fisher Scientific LTQ-XL mass spectrometer that was modified with a gas-handling manifold. $[p\text{ABA+H}]^+$ ions were generated through ESI, stored in an ion trap and allowed to react with the following neutrals entrained in helium buffer gas: water, formic acid, methanol, ethanol, propanol, ammonia and acetonitrile. $[p\text{ABA+H}]^+$ ions were subjected to collision induced dissociation (CID) to yield the time dependent protomer ratios and first-order-rate constants were extracted from fitting CID ions. The log of the second order rate constants were extracted from a series of catalyst concentrations and plotted against the calculated transition state barrier separating the protonation sites (**Figure 1** B) that show a linear response. The catalyst proton affinities were plotted against the same transition state energies to show a strongly correlated linear relationship (**Figure 1** C). This shows the transition state energy controls the reactivity for proton transfer catalysis and the transition state energy can be reduced by choosing a suitable neutral catalyst with a larger proton affinity.

The results from this study can be used to help control the placement of protons in polyfunctional molecules in mass spectrometry experiments and predict the mechanism for proton transfer reactions that can occur during electrospray ionization.

TH-298

One-dimensional van der Waals heterostructures: A computational benchmarking study

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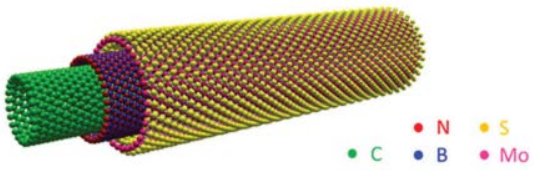
The field of one-dimensional van der Waals (1D vdW) heterostructures is less studied than its two-dimensional (2D) counterpart. The first successful experimental synthesis of a 1D vdW heterostructure[1] was reported only recently; a carbon nanotube (CNT) was encapsulated by three layers of boron-nitride nanotubes (BNNT) and a molybdenum disulfide nanotube (MoS_2NT). 1D vdW heterostructures open an avenue of unique combinations of crystals beyond conventional limits of 2D materials and display additional emergent property tuning possibilities. Structure, properties and mechanism of growth and nucleation may be explored using computational methods beyond the accessible regime of experiment.

This begs the question which is the central problem being addressed in this study: how do we model and study 1D vdW heterostructures using computational methods? Several key factors need to be considered. These heterostructures are made up of hundreds or even thousands of atoms which are affected by noncovalent interactions and strain. Compared to 2D materials, 1D vdW heterostructures have additional factors affecting structure and properties such as axial lattice mismatch, tube diameter, interlayer distance and the strain associated with small and highly curved tubes. Choosing a computational method that can calculate the structure and properties accurately using reasonable computational resources is important for future computational studies of 1D vdW heterostructures.

GFN2-xTB[1] is a tight-binding method suitable for calculations on systems with between one hundred and several thousand atoms and, for molecular benchmarks[1], affords remarkable accuracy at low computational cost. Here we investigate the performance of the GFN2-xTB method for studying these complex inorganic nanostructures, by comparing its performance in predicting ionic geometries, lattice parameters and structure-property relationships in 1D vdW heterostructures with density functional theory.



Example of a 1D vdW heterostructure with an inner CNT encapsulated by BNNT and MoS_2NT[1].

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TH-299

How Nano Confinement Effects Solvated Ion Properties: A Molecular Dynamics Study

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Nanoconfinement has been widely applied to different fields such as water desalination, DNA sequencing, electrochemical devices etc. due to the advantageous electronic and mechanical properties. [1] However, the application of nanoconfinement to electrocatalytic reactions is relatively new such as the development of nanozymes. [2] Importantly, there is still a lack of understanding of the mechanism of these electrocatalytic reactions in nanozymes.

In this poster, we present the results of molecular dynamics (MD) simulations investigating how the properties of ions under nanoconfinement conditions differ from their properties in bulk solution, such as energy penalty for entering the carbon nanotube which is used as a model of the actual channel. We also studied the impact of channel width, electrolyte concentration and charges on the mobility and transport of several monoatomic cations as well as the hydronium ion, which is of interest as the reactant of the oxygen reduction reaction (ORR). It is envisaged that these findings would assist in the experimental design of more effective and efficient nanozymes.

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TH-300

Benchmarking Density Functional Theory for reactions catalysed by metalloenzymes

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The field of computational enzymology is useful for both understanding and designing enzymes. Computational studies aid in the elucidation of structures and reaction mechanisms through comparison with experimental results and spectroscopic properties, and the insights gained can then be used to assist in the design of modified or completely artificial enzymes. These studies often involve treatment of the active site with quantum-chemical methods such as density functional theory (DFT), and lower level methods for the remaining enzyme. The accessibility and cost-effectiveness of density functionals make them ideal candidates for quantum-chemical treatments of enzyme active sites, however the choice of density functional is not trivial.

Benchmark studies that assess the performance of density functionals for main group chemistry are numerous, but transition metals are poorly represented due to difficulties in obtaining reference data. Of the studies that do cover transition metals, even fewer focus on organometallic reactions, open shell systems or larger complexes, and therefore there is little benchmark data that is truly relevant to metalloenzyme chemistry. We aim to fill this gap with the creation of a benchmark set for reaction energies of transition metal-containing metalloenzymes. The set contains active site models for 15 metalloenzyme reactions, representing eight different transition metals, open- and closed-shell species, and large systems.

Using high level theoretical reference data, we use this set to benchmark various DFT methods, and compare the effect of the DFT-D3(BJ) and DFT-D4 dispersion corrections on the tested functionals' performance. We also compare these results with our previous benchmark study of enzymatically catalysed reactions[1], and show how the inclusion of transition metals affects the benchmarking outcomes – notably, double hybrid DFT does not provide large improvements over hybrid DFT due to the poor performance of MP2 for transition metals.

We hope that this set can be used by both those needing to choose methods for metalloenzyme applications, and the theoreticians who develop them.

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TH-301

Gas-phase electronic spectra and photodissociation pathways of positively charged PAHs

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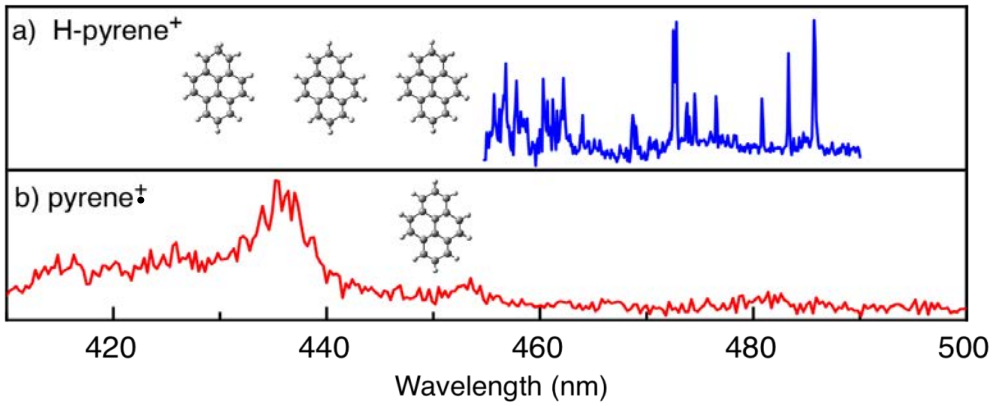
Polycyclic aromatic hydrocarbons (PAHs) are a series of compounds that are formed in hydrocarbon combustion and contribute to soot formation. They are also suspected to exist in interstellar space. It has been suggested that PAHs contribute to the diffuse interstellar bands (DIBs), a series of absorptions in the visible to NIR region of light presumed to arise from molecular electronic transitions. However, despite extensive studies no correspondence has been found between any DIB and measured transitions of neutral or ionized PAHs. Under high UV flux conditions, which prevail in certain regions of space, PAHs undergo ionization and hydrogen loss, leading to either dehydrogenated structures and/or rearrangement into different isomers.[1] To investigate these processes, we aim to measure electronic spectra of positively charged PAHs and their photofragments. Spectra are obtained using a custom-built ion mobility mass spectrometer coupled with a cryogenic quadrupole ion trap. PAH and fragment cations are generated through laser ablation of a solid disk composed of the target PAH and graphite. Ions are mobility- and mass-selected to isolate the target isomer population, which is guided into a quadrupole ion trap (QIT) where the ions are collisionally cooled with He gas and exposed to tunable light from an optical parametric oscillator. An electronic action spectrum is obtained by monitoring charged photofragments as a function of wavelength. As an example, Figure 1 shows electronic action spectra of a) the protonated pyrene cation and b) the pyrene radical cation, which are similar to previously recorded spectra. [2,3] In the future we aim to obtain electronic spectra of pyrene photofragments, that correspond to loss of one and two H atoms, and acetylene molecules.



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TH-302

Anion photoelectron spectroscopy of halide-alkene van der Waals complexes

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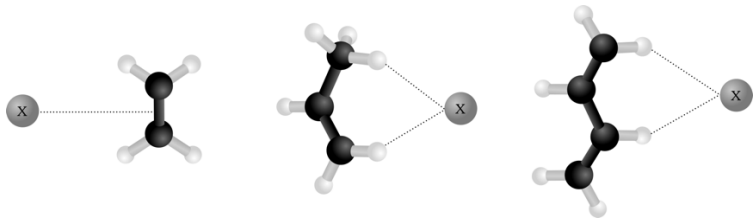
Unsaturated hydrocarbons represent attractive reactants for a wide range of industrial, atmospheric and extraterrestrial chemistry. The detection of propene in both the atmospheres of Titan and the ISM in the Taurus Molecular Cloud (TMC-1), place it as an important intermediate in a bottom-up approach to the formation of long-chain hydrocarbons in extraterrestrial environments.[1,2]

$$HC^{\bullet} + C_2H_6 \rightarrow C_3H_6 + H^{\bullet}$$

$$HC^{\bullet} + C_3H_6 \rightarrow 1,3 - C_4H_6 + H^{\bullet}$$

$$HC_2^{\bullet} + C_4H_6 \rightarrow C_6H_6 + H^{\bullet}$$

Combined anion photoelectron spectroscopy (PES) and computational studies of the simplest unsaturated hydrocarbon, ethylene, bound to bromide and iodide, have shown that two anion conformers are present.[3] These are similar in energy with a negligible barrier between them but represent distinct bonding motifs. Presented here are similar combined anion PES and calculations of halide-propene and halide-1,3-butadiene complexes and their implications for gas-phase solvation and reactivity are discussed.



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TH-303

Reactive scattering of clusters of transition-metal atoms with small molecules

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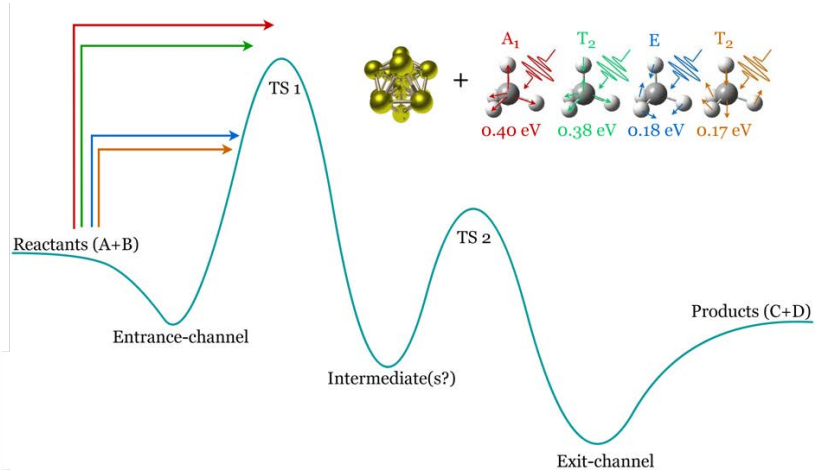
Metal complexes and clusters offer the opportunity for rich chemistry, be that metal-ligand binding, the mediation of ligand-ligand interactions and cluster size-reactivity effects. While mode-selectivity and its effects on reaction dynamics have been explored between gases and extended surfaces, the same has not occurred in the context of metal clusters.[1] This is of particular interest for the possibility of control of gas-phase reactivity via quantum selected vibrational states of reactions. Here we present the design and development of a new experiment that seeks to address this area.

Spectrometer development includes design of a new clustering source with capability for the formation of larger and bimetallic gas-phase metal clusters. This is then coupled to a new instrument to size-select these clusters and explore mode-selectivity in the metal cluster, ligands and reactant gas.



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TH-304

Model Chemistry Recommendations for Harmonic Frequency Calculations: A Benchmark Study

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While harmonic frequency calculations are widespread across chemistry[1] sparse benchmarking is available to guide users on appropriate model chemistry recommendations (i.e., a method and basis set pair). Instead, studies exploring the dependence of harmonic frequencies on model chemistry have focused on producing multiplicative scaling factors to match the calculated harmonic frequencies to experimental fundamental frequencies, by approximating anharmonicity in this property[2].

Along with the scaling factor, it is often common to calculate the root-mean-squared error (RMSE) between the scaled harmonic and experimental fundamental frequencies, and use this value as metric of model chemistry performance. We recently compiled a set of over 1,400 scaling factors[3] spanning hundreds of methods and basis sets from the literature, allowing approximate comparisons between different model chemistries[4]. However, initial recommendations from this analysis can only be preliminary, as the differences in the benchmark databases used means that the RMSE metrics cannot be fairly compared across different publications.

To overcome this limitation, we introduce a new benchmark database for vibrational frequency calculations (VIBFREQ1292) containing 1,292 experimental fundamental frequencies and CCSD(T)-F12c/cc-pVDZ-F12 harmonic frequencies for 141 molecules. Comparisons between our experimental and *ab initio* data demonstrate the overall improvement of using frequency-range-specific scaling factors over global scaling factors, allowing us to redefine the anharmonicty error (previously set at 24.9 cm^{-1})[4] as ranging between 3.1(3)-15(1) cm^{-1}, with a median value of 7.6(5) cm^{-1}.

Using VIBFREQ1292 as our reference set, we have rigorously assessed the performance of over 300 general-purpose model chemistry choices for harmonic frequency calculations. Model chemistry recommendations, as well as expected computational errors will be presented in this talk.

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TH-305

A new approach to calculating activity/osmotic coefficients for electrolyte solutions

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Electrolyte solutions are critically important components in many chemical processes, e.g., water treatment, fuel cells, battery systems and CO_2 capture. To improve the efficiency of these chemical processes, the properties of electrolyte solutions have widely been researched using both experiments and modelling methods. One of the most successful methods of modelling electrolytes is the Pitzer equations, first described more than 50 years ago[1], which are used to calculate the properties of aqueous electrolyte solutions, like activity and osmotic coefficients. However, these equations require many empirical parameters for each electrolyte that are quite difficult to determine, limiting their use to cases that have been experimentally well characterised. Recent advances in computational methods mean that it should soon be possible to move away from this reliance on empirical methods.

Here, we test and compare several methods for calculating the osmotic coefficients and activity coefficients of NaOH and NaCl over a wide concentration range from molecular simulation using statistical mechanical methods such as the modified Poisson-Boltzmann equation. We combine these methods with neural network potential molecular dynamics (NNP-MD) trained on short ab initio MD simulations to demonstrate good experimental agreement. Moreover, this method requires no empirically adjustable parameters, which is a significant improvement compared with the Pitzer equations and point charge based molecular dynamics methods. The agreement with osmotic coefficients also demonstrates the accuracy of the NNP-MD method.

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TH-306

Polyisocyanopeptide based nanoworms – cellular interaction and biodistribution profile

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The stereo-stability and the high degree of function displayed by biopolymers is attractive to mimic with synthetic polymers because of its potential application in materials and biomedical field. Polyisocyanopeptides (PICs) are particularly noteworthy among artificial polymers because of their stable helical backbones with a high helix inversion barrier. They have been demonstrated to assume a four repeats per turn (approximately) β-helical conformation that is stabilized by a β-sheet peptidic hydrogen bond network present between monomers n and n + 4 [1-3]. Further, the hydrophobic interaction of oligo(ethylene glycol) moieties incorporated along the polymer backbone makes PIC a thermoresponsive material. This extracellular matrix (ECM) mimicking, water-soluble, semi-stiff, rod-like polymer has been utilized for various applications from wound healing [4, 5], stem-cell activation [6] to immunotherapy [7, 8]. In this poster, I will present my preliminary work on understanding the usage of PIC nanoworms in nanomedicine field, in particular, as an immunostimulatory platform. I will mainly discuss the results of postpolymerization modification of PIC, cell association trend and molecular imaging data.

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TH-307

Radiation activated drug delivery for in vivo release

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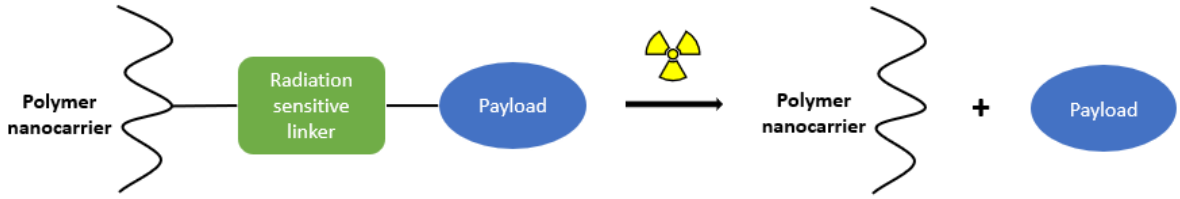
Stimuli responsive polymer nanocarriers aim to increase the efficacy and decrease the side effects of pharmaceuticals used in the treatment or for the detection of disease. Activating molecules within the body provides the ability to control where and when the drug or probe can interact with the intended tissue. Light activated drug delivery systems have shown high temporal-spatial control of drug release; however, light has limited penetration into tissue. This makes treatment of disease deep within the body difficult without the use of invasive light sources. By harnessing radiation produced by radionuclides and particle accelerators, polymer drug delivery systems can be activated within the body. Light and reactive oxygen species (ROS) produced by radiation was investigated as a stimulus to initiate cleavage chemistry, releasing a payload. Several model pro-drug molecules and polymer building blocks were synthesised and tested with different radiation sources to determine activation rates. The most efficient stimuli responsive chemistries will be discussed for use in a stimulus responsive polymer nanocarrier.



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TH-308

Uncovering the localised mechanochemistry of polymers using novel multiscale chemical analysis.

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Materials are rarely deployed in static environments, rather they are exposed to diverse and varying stresses within dynamic environments. Recent advances in mechanochemistry have revealed the prospect not only to enable a cleaner route to chemical transformations but also to offer previously unobtainable opportunities in the production and screening of materials [1]. To date this field of research has been constrained by the inability of current polymer characterisation techniques to provide essential localised multiscale chemically mapping information.

A 2021 Nature Review [2] concluded that "the unifying feature of mechanochemical phenomena may be the coupling between inertial motion at the microscale to macroscale and changes in chemical bonding". This study presents the recently developed Secondary Electron Hyperspectral Imaging (SEHI) as a multiscale material characterisation technique applied within a Scanning Electron Microscope (SEM). SEHI is based on the collection of secondary electron emission spectra at low primary beam energies allowing the chemical inspection of uncoated polymer and metal surfaces [3]. This presentation brings the use of a novel in-situ SEM holder together with the application of SEHI to provide enhanced material characterisation capabilities including; surface chemical spectroscopy and imaging methods at multiscale levels. All of which are considered essential to provide the fundamental analysis needed to evaluate the effects of mechanochemical interactions [4].

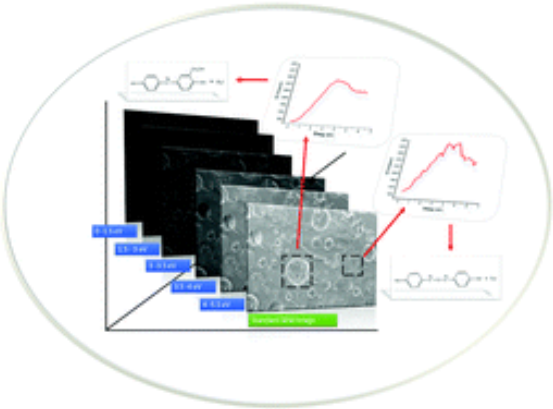

Figure 1: Application of Secondary Electron Hyperspectral Imaging (SEHI).

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TH-309

Cyclic poly(2-oxazoline)s and related compounds as biomaterials – challenges to scale-up

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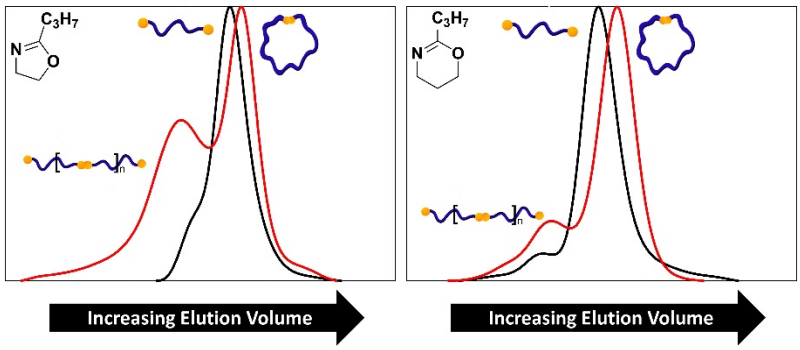
The unique material properties of cyclic polymers have made them attractive biomaterials, prompting the need for more efficient cyclization protocols. Due to their chemical versatility, poly(2-oxazoline)s (POz) and poly(2-oxazine)s (POzi) provide potent candidates in this field. However, little to no comprehensive data on the cyclization process of these materials is available, especially not for POzi. In this study, we investigate the impact of a number of reaction parameters (batch volume, catalyst equivalents, molecular weight, and polymer addition method) on the macrocyclization efficiency of POz and POzi using copper(I)-catalysed azide-alkyne cycloaddition (CuAAC). It was found that POzi show more efficient conversion to the desired monocyclic species compared to POz, possibly due to increased chain flexibility of POzi. Considering macrocyclization efficiency, up to 33× more cyclic POzi could be synthesized per volume of solvent, compared to previous protocols for related POz, indicating potential for the future scale-up of macrocyclic POzi.



TH-310

Rendering non-responsible micelles pH-responsive through the incorporation of oligoelectrolytes

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Polymeric micelles have been extensively studied for the delivery of hydrophobic drugs. A major challenge with traditional micelles is triggering the rapid intracellular release of their cargo to overwhelm efflux pumps and result in cytotoxic doses. To address this challenge, there have been various responsive micelle systems developed that can respond to triggers in the endosomal environment, resulting in cargo release. However, these polymers tend to be quite specialised and lack significant studies of their fate and safety profiles. As an alternative approach, we were interested in the possibility of rendering a typically non-responsive micelle with pH-responsibility. In this instance, it may be possible to take established non-responsive micelles that have been extensively studied and add a pH-trigger to allow more rapid cargo release in the endosome. Therefore, the aim of this study was to render poly(ethylene glycol-*b*-caprolactone) (PEG-b-PCL) micelles pH-responsive through the incorporation of oligo(vinyl pyridine) (OVP) in the core. At pH 7.4 the OVP is neutral and hydrophobic, whereas approaching its pKa value (~ pH 5), the OVP becomes protonated and hydrophilic, resulting in its expulsion into the aqueous phase. Well-defined PEG-b-PCL copolymers were prepared and used to prepared micelles in PBS via a solvent evaporation approach in the presence of OVP at different weight fractions (0.1, 0.2 and 0.3 weight fraction relative to the copolymer). Their physicochemical properties and pH responsiveness over the pH range from 7.4 to 3.5 was investigated via NMR spectroscopy, DLS, UV-vis spectrophotometry, fluorimetry and SAXS. The CMC of the copolymers remained unchanged following encapsulation of OVP in the core. DLS indicated the formation of well-defined micelles complete with encapsulated OVP, and NMR revealed changes in the protonation state of OVP with pH. Co-encapsulation of OVP and doxorubicin within the micelles provided for a pH-triggered burst release of doxorubicin with decreasing pH. Overall, this is a promising strategy for the pH triggered release of cargo from typically non-responsive micelles.

TH-311

Multi-input sensing using flexible poled fluoropolymers

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The dawn of information communication technologies and Internet of Things (IoT) has seen a rise in interest from stakeholders involved in remote sensor technologies and perpetually powered electronic devices.[1] Functional materials provide a pathway to harness ambient energy by converting vibrational energy (kinetic energy) and temperature changes to electrical energy by means of the piezoelectric and pyroelectric effects. However, in applications such as biomedical prosthetics, health monitoring systems, and soft robotics (mechanically compliant machines) - widely used ceramic transducers and rigid sensors pose challenges in device fabrication and energy harvesting. This scenario is compensated by the complexity of brittle ceramics and signal processing systems required to harvest the energy.[2]

In recent times, PVDF (polyvinylidene fluoride) has been tested and proved to be a highly flexible and reliable functional material. Although promising, the piezoelectric charge constant of PVDF (d_{33}) is orders of magnitude lower than other inorganics such as PZT (lead zirconate titanate) and BTO (barium titanate).[2] Therefore, energy harvesting from such fluoropolymers requires sophisticated electronic interfaces and strategically layered and patterned micro-electromechanical systems (MEMS). We address the compatibility issues associated with PVDF-trifluoroethylene (TrFE) and demonstrate its useability with modern electronic devices, through the use of optimised charge amplifiers and low power rectification processes.

We have previously shown that the introduction of co-monomers such as TrFE to form PVDF-TrFE together with additives such as SWCNTs (single walled carbon nanotubes) and MXene nanosheets has resulted in composite piezoelectric generators (PEGs) with enhanced piezoelectric charge coefficient d_{33} (over 38%) relative to pristine PVDF-TrFE.[3, 4] These results proved that PVDF-TrFE coupled with nano-additives were suitable for flexible PEGs which could be exploited for numerous applications. Therefore, in this work, with the aid of nano-additives, we have further investigated the compatibility of PVDF-TrFE for temperature sensing, pulse detection and strain detection, with a focus on developing accurate and integrated measurement electronics. The results showed that PVDF-TrFE produces a maximum peak to peak voltage of 2.65 V in response to a temperature change of 10 ^{0}C and a steady DC voltage level of 2 V was produced when stimulated through finger tapping at a rate between 1-3 Hz. These results indicate the potential for PVDF-TrFE to function as a multi-input sensor for temperature and pressure. The transparency and processability of our PVDF-TrFE inks demonstrate its versatility and suitability for sensing components in electronic skins.

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TH-312

Polyisocyanide polymer matrix for the study of cellular behaviour under microgravity condition

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Mechanical unloading under space microgravity highly influences the mechanosensitive cells in bone tissue causing reduction of bone density in Astronauts limiting long-term space missions.[1] These changes are not fully recoverable, and the mechanisms of gravity-dependant cytological changes are still not clear. This research mainly focuses on investigating the effects of microgravity on cells in a 3D biomimetic matrix and quantification of force-mediated changes in cellular behaviour mainly on bone cells. Application of a 3D biomimetic cell culture system is appreciated over 2D culture systems that tend to exhibit aberrant behaviours due to the flattened shape and abnormal polarization. In 3D culture systems, cells are likely to receive signals from all three dimensions as in the in vivo environment.[2] Among the hydrogel systems developed for 3D cell culture, polyisocyanide(PIC) polymer hydrogel gain more attention due to its thermo-responsive and stress stiffening properties similar to cytoskeletal proteins which are hardly found in other synthetic, polymeric hydrogels. [3-5] Functionalization of the polymer with peptides of interest using copper free strain-promoted alkyne–azide cycloaddition (SPAAC) click reaction improves the biocompatibility through mimicking certain integrin binding sites. [6] The influence of microgravity and 1g forces on the matrix-focal adhesion will be studied using a novel microgravity platform and cutting-edge force-mediated STED-confocal spectroscopy.

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TH-313

Nitroxide-functionalized phthalocyanine and porphyrazines as switchable photoacoustic molecular imaging agents

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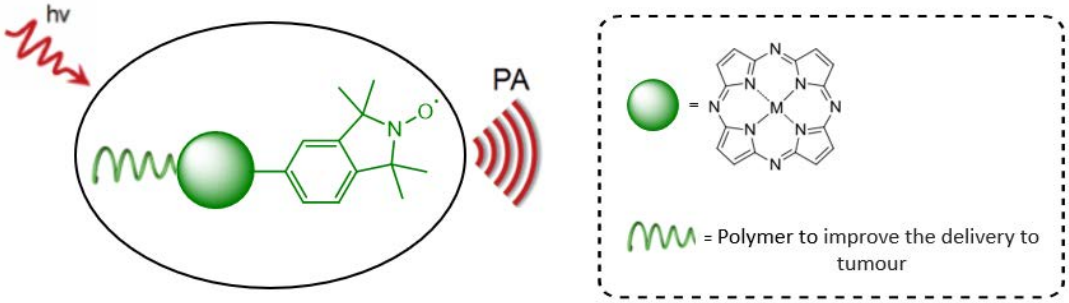
Within the field of molecular imaging, photoacoustic imaging (PAI) is a relatively new hybrid modality that applies near-infrared light excitation and acoustic detection aiming to achieve a unique specificity in addition to enhance tissue penetration.[1, 2] To date, many organic imaging agents have been explored and the class of tetraazaporphyrins has attracted considerable attention, however, there is still a challenge related to the poor targeting to tumors, bringing the need for the development of smart molecular probes, responsive to biochemical processes.[3, 4] In biological conditions, the unique structure of nitroxides allow them to participate in redox reactions, controlling reactive oxygen species (ROS) production, and regulating oxidative stress.
This project aims to investigate nitroxide-functionalized phthalocyanines (Pc) and porphyrazines (Pzs) hybrids as photoacoustic molecular imaging agents.[5] The synthetic incorporation of nitroxide functionalities quench the fluorescence of these compounds and it is hypothesized that the absorbed optical energy can be converted into heat and consequently modify the photoacoustic signal detected. Initially, nitroxides tethered Pcs/Pzs will be explored and through this investigation it is expected to understand how these compounds respond to PAI modality and better comprehend the mechanism of energy transfer from light to acoustic. After that, other strategies can be studied in the future, such as, the use of polymers to improve the targeting to tumors.



General nitroxides-functionalized tetraazaporphyrins hybrids investigated in this project.

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TH-314

Phase Stabilization of Pure Formamidinium Lead Iodide at Ambient conditions

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Increasing energy demand and unavoidable carbon foot prints due to the excessive use of fossil fuels require an alternative and environment friendly energy source. Photovoltaic (PV) technologies have been developed to harvest solar energy and generated green electricity to reduce carbon emission. While the commercial silicon-based solar cells dominate the PV market at present, the emerging perovskite solar cells (PSCs) have shown considerable advantages including low-temperature solution processes, high defect tolerance, and light weight. In last decade, the power conversion efficiency (PCE) of PSCs has been improved considerably from 3.8% to a certified 25.7%, which is now comparable to the commercial silicon solar cells and surpasses other thin-film PV technologies. However, long-term ambient stability remains a significant challenge for the practical application of PSCs, which can be mainly ascribed to the instability of perovskite thin-films under ambient conditions such as oxygen, temperature, light, and humidity. Due to its intriguing optoelectronic properties and relatively non-volatile organic cation, formamidinium lead iodide ($FAPbI_3$) perovskite material features promising photovoltaic performances and superior thermal stabilities. Not only its potential to achieve high efficiency due to its inherent narrow bandgap of 1.45 eV, but also it does not have phase segregation issue that is normally happened in mixed-halide mixed-cation perovskites. Currently, the greatest challenge is to stabilize the photoactive phase of $FAPbI_3$ at room temperature. The black α-phase is the only phase that is more photoactive at high temperatures (160 °C and above), while the black phase has great tendency to convert into yellow-phase which is a non-perovskite phase at the room temperature. Compositional engineering has been used to overcome difficulties in fabricating high-quality phase-pure $FAPbI_3$ perovskite films together with its ambient instability. However, this comes alongside an undesirable increase in bandgap that sacrifices the device photocurrent. Here we report a method to attain the pure black α-phase and long-term ambient stability of $FAPbI_3$ perovskite. The alkylamine ligands with different carbon chain lengths such as oleylammonium iodide (OLAI), butylammonium iodide (BAI), and phenylethylammonium iodide (PEAI) were used to treat the surface of $FAPbI_3$ perovskite thin films to stabilize its α-phase of over period of one year at ambient conditions. The optimized post-annealing process resulted in surface passivation by the formation of 2D/3D perovskite stacking architecture to suppress the undesirable non-radiative recombination with a reduced surface trap density, thus leading to an increased PCE of 20.1% and improved long-term ambient stability more than 1000 hours.

TH-315

Electrosynthesis of polypyrrole-coated α-MoO_3 for aqueous electrochemical Al^{3+}-ion storage

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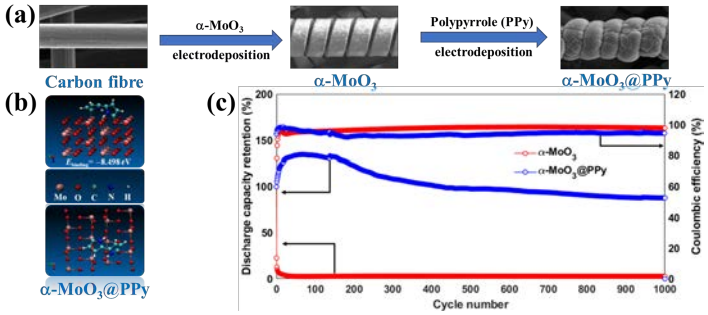
Orthorhombic molybdenum trioxide (α-MoO_3) is a promising electrode material for aqueous electrochemical metal-ion storage due to its unique layered structure. However, its poor electronic conductivity and instability in aqueous electrolytes hinder its applications in electrochemical energy storage. In this paper, we report on the synthesis and assessment of electrochemical properties of a polypyrrole-stabilised α-MoO_3 electrode for aqueous Al^{3+}-ion storage. This binder-free, PPy-coated α-MoO_3 electrode (α-MoO_3@PPy) synthesised using an electrodeposition method has a high mass loading (~16 mg/cm^2). The α-MoO_3@PPy electrode exhibits a high cycling stability in a 1 M aqueous $AlCl_3$ electrolyte with a capacity retention of 88% after 1000 cycles. A full electrochemical Al^{3+}-ion pseudocapacitor cell fabricated with the α-MoO_3@PPy as anode and copper hexacyanoferrate (CuHCF) as cathode delivers a high rate capability with energy densities of 0.33 and 0.20 mWh/cm^2 at current densities of 1 and 10 mA/cm^2, respectively. In addition, this cell is stable against cycling with a capacity retention of 70% after 1800 cycles. This work provides an approach to the synthesis of stable α-MoO_3-based electrode materials for aqueous electrochemical energy storage.



1. Electrochemical synthesis of polypyrrole-coated α-MoO_3 (α-MoO_3@PPy) on carbon fibres. (b) DFT-based geometry optimisation of a polypyrrole chain segment on α-MoO_3 along with the calculated binding energy ($E_{binding}$). (c) Cycling stability test of α-MoO_3 and α-MoO_3@PPy electrodes in 1 M $AlCl_3$ aqueous electrolyte.

TH-316

Development of Liquid Metal Catalysts for Carbon Dioxide Reduction to Carbonaceous Products

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Carbon dioxide is considered one of the most serious greenhouse gases due to its contribution to global warming, ocean acidification and ozone layer depletion [1]. Catalytic CO_2 reduction processes have the potential to reduce CO_2 emissions while producing valuable fuels and chemicals. Electrochemical and plasma CO_2 reduction are considered effective and economic technologies for CO_2 reduction due to renewable energy utilization [2]. However, the traditional solid based catalysts that have been developed for these processes suffer from various issues including poor product selectivity, high cost and low stability. Liquid metal catalysts present a promising alternative for CO_2 reduction. Here we report successful CO_2 reduction on Ga and Ga-Cu catalysts via electrochemical and dielectric barrier discharge (DBD) plasma processes at room temperature. Electrochemical CO_2 reduction resulted in C_3 products such as propanol and acetone. On the other hand, plasma-assisted CO_2 reduction converted CO_2 to graphitic carbon. Electrons generated at the Ga-Cu working electrode or via a plasma flux on liquid Ga are suggested to facilitate CO_2 activation where Ga is suggested to play a vital role in CO_2 dissociation, while Cu and Ga facilitates C-C bond formation.

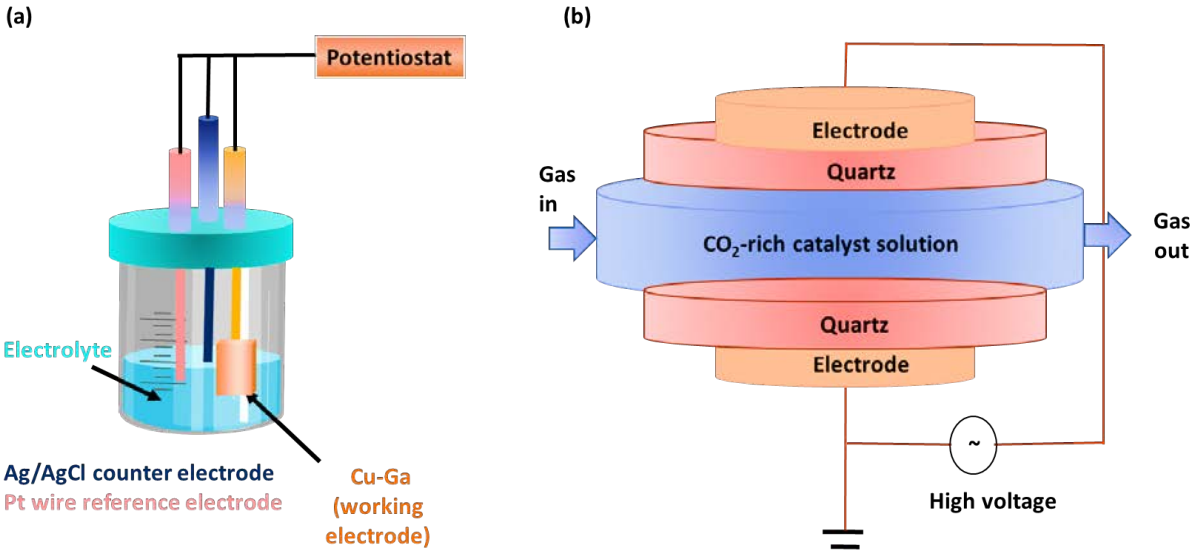

Figure 1. Electrochemical cell setup, (b) dielectric barrier discharge plasma set-up.

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TH-317

Exploring the potential for water-based upconversion to enhance hydrogen production by photolysis

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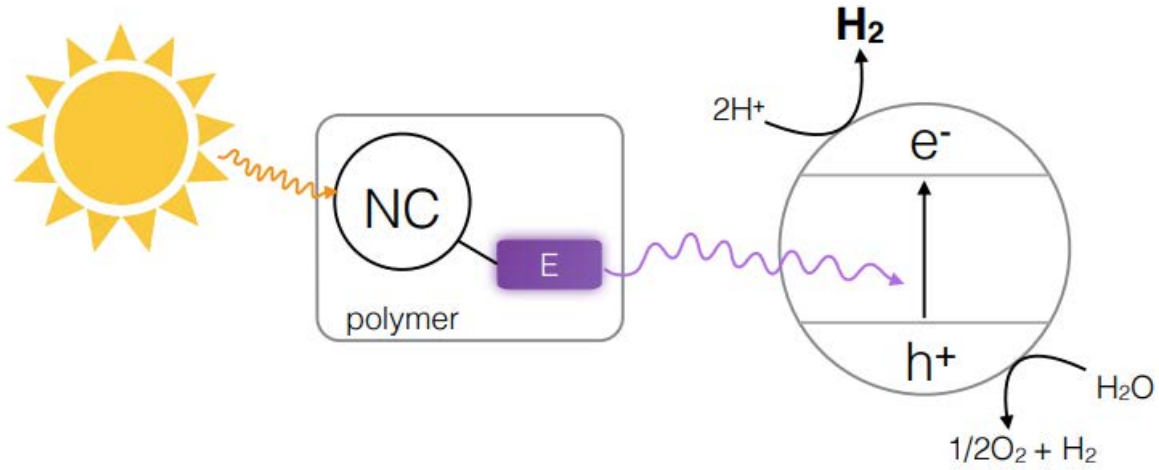
The response to the climate change crisis requires a radical shift from fossil fuels to achieve 'net zero' carbon emissions. Hydrogen (H_2) is an attractive alternative, however, production of "green" hydrogen fuel is limited by its high energy cost. The energy required to split water into hydrogen and oxygen via a photocatalytic system under standard conditions, is 4.915 eV. This is equivalent to the energy generated from one photon of ultraviolet light,[1] meaning that the amount of solar radiance that can be used to drive this reaction is greatly restricted. However, through the photon upconversion process of triplet-triplet annihilation (TTA), one visible light photon can be produced from two infrared photons, to yield the same energy output. Thereby allowing for a wider range of the solar spectrum to be utilised. It has been established that nanocrystal/organic sensitiser hybrid models are able to achieve efficient upconversion.[2] However, these systems are faced with two main challenges 1) for TTA to occur, all components must be in close proximity and 2) triplets are quenched by oxygen. This work aims to combat these challenges through the development of a polymer encapsulated nanocrystal/sensitiser conjugated system.



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TH-318

Techno-Economic Analysis of Liquid Hydrogen Carriers in Hydrogen Storage and Transportation

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Hydrogen will play an important role in future decarbonisation. Australia's National Hydrogen Strategy aims to position Australia as a major global player by 2030. As the most common substance in the universe, hydrogen can be produced from various resources, leading to environmental benefits. The life cycle of hydrogen energy includes production, storage, and transportation, which contributes to the techno-economic assessment (TEA) equation. Japan's Kawasaki Heavy Industries has already built the world's first ship to transport liquid hydrogen. The Suiso Frontier arrived in Australia on Jan 21st 2021 on its maiden voyage of 9,000 km from Japan, demonstrating the feasibility of a liquid hydrogen supply chain. However, this is only one form in which hydrogen can be utilised in an energy supply chain.

The most important component in the life cycle of hydrogen is storage which also impacts transportation. The current dominant approach for hydrogen storage is densified storage via compressed gas (CGH_2) and liquid hydrogen (LH_2) (1). Hydrogen carriers are hydrogen-rich liquid or solid-phase materials from which hydrogen can be liberated on demand. Liquid organic compounds have emerged as favourable hydrogen storage media because of their desirable properties, such as low cost and compatibility with existing fuel transport infrastructure. This project uses TEA techniques to assess a class of liquid hydrogen carriers (LHCs) such as ammonia, methanol and formic acid, which are decomposed completely after extraction of hydrogen, and LHCs that are reusable during the reversible (de)hydrogenation process without significant degradation with negligible emissions (2), such as toluene, dibenzyltoluene (DBT) and N-ethylcarbazole (NEC) (3). The figure below demonstrates a complete green hydrogen supply chain including production, storage, transportation, and application. The project uses techno-economic analysis to evaluate the economic feasibilities of the most promising LHCs in the storage and transportation phase of the hydrogen lifecycle. Preliminary results will be presented.

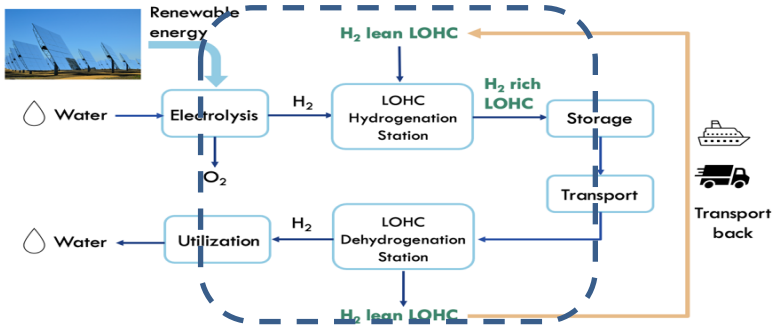

Figure. The green hydrogen supply chain and the dashed box indicates LOHCs in H_2 storage and transportation

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TH-319

Investigating the hybrid interface of transition metal dichalcogenides and organic semiconductors.

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Monolayer two-dimensional transition metal dichalcogenides, such as MoS_2, have a direct bandgap, large exciton binding energies and strong spin-orbit coupling. When coupled with organic semiconductors exciting possibilities can be realised in optoelectronics. These possibilities include field effect transistors, photodetectors, and sensitisers for photon management processes such as the up and down conversion of photons. To date, hybrid devices have shown improvements in field effect transistors and photodetectors.[1-2] However, little is known about the triplet exciton behaviour at the interface between these materials. Triplet excitons play a key role in the up and down conversion process.[3] Using femtosecond transient absorption and photoluminescent spectroscopy the hybrid interface is investigated. The dynamics of charge transfer and triplet states are uncovered, providing insight on the engineering of the interface for optoelectronic devices.

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TH-320

Molecular dynamics investigation of graphynes as a supercapacitor electrode material

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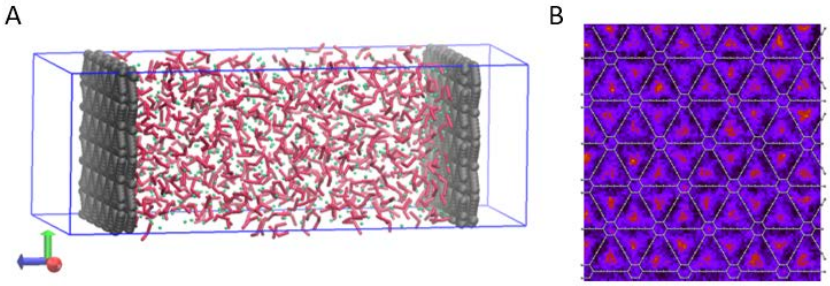
Electrochemical energy storage plays an important role in almost all aspects of life in a world of ever advancing technology. Coupled with the needed move away from fossil fuels, understanding and developing new greener and more efficient electrochemical energy storage devices is vitally important. Supercapacitors are a group of energy storage devices which store charge by non-faradaic interactions at the electrode-electrolyte surface. Characterised by their high power capabilities compared to batteries and high cyclability, they have become a popular area of research.[1]

In this work, we investigated two materials as candidates for supercapacitor electrodes, graphdiyne and graphtriyne, which are part of a group of 2D, sp and sp^2 hybridised carbon allotropes named graphynes.[2] We used molecular dynamics simulations to model supercapacitor systems of graphdiyne and graphtriyne electrodes with an ionic liquid electrolyte, BMIM PF_6. We investigated the interactions between the electrolyte and electrodes and their effect on the stacking arrangement of the carbon electrodes. Additionally, we determined the electric double layer capacitance of graphdiyne, finding a marked improvement in the specific capacitance compared to graphene. Through our analysis we demonstrated the potential for graphynes as supercapacitor electrodes due to their unique 2D porosity.



A) Example of graphdiyne supercapacitor system. B) 2D heat map of the ionic liquid density at the electrode surface

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TH-321

Active Learning in Bayesian Neural Networks for the Predictions of the Functional Properties of Millions of Novel Van der Waals Heterostructures

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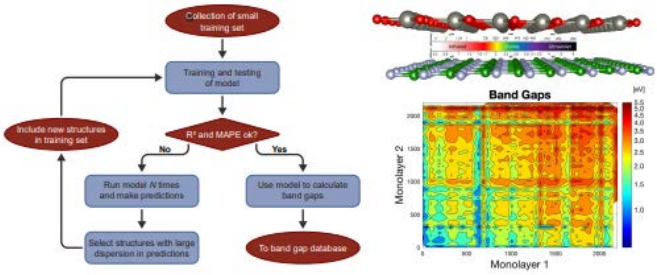
There are currently more than 6000 theoretically predicted 2-dimensional (2D) van der Waals materials with functional and structural properties that can be significantly different from their 3-dimensional counterparts. The combination of more than one monolayer to form heterostructures can potentially give rise to an extremely large set of structures with unique and exotic properties that will drive novel industrial applications. However, even combining only two different monolayers into bilayers, the number of possible heterostructures exceeds millions, making the analysis of the properties of this class of materials impractical from both an experimental perspective and using conventional ab-initio computational models. Here, a time and resource-efficient active machine learning approach has been used to create a database containing the functional and structural properties of millions of van der Waals layered structures. We predicted the interlayer energy, elastic constant, bandgap and piezoelectric constant of layered materials composed of two different 2D structures mainly in view of their application in energy conversion devices (e.g. photocatalysis). Our active machine learning models can predict results of computationally expansive approaches (i.e., density functional theory) with high accuracy.[1,2,3]



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TH-322

Nano-engineered electrocatalyst for Nitrogen Reduction Reaction

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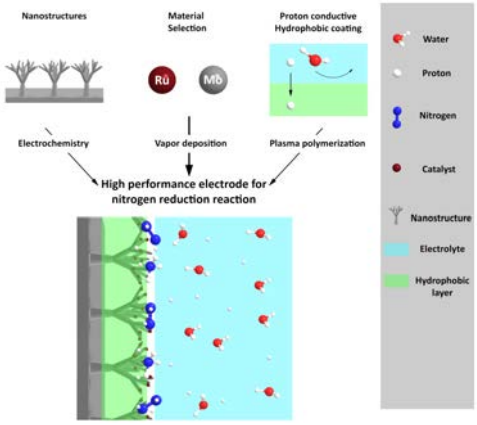
Ammonia is expected to be the next generation carbon-free energy carrier. It is 1.8 times more energy dense than liquid hydrogen and easier to liquify, store, and transport. A multi-billion tonne market is on the horizon. To realize the potential of ammonia, an efficient, reliable, and environmentally friendly production method is required to replace the energy demanding and CO_2 emitting Haber-Bosch process.[1] Central to realizing this is the development of a catalytic electrode to convert nitrogen-based chemicals into ammonia. It is the aim of this project to create a high faradaic efficiency (FE) and high yield electrode for nitrogen reduction reaction (NRR) to in water-based electrolyte.

The competing hydrogen evolution reaction (HER) and low nitrogen solubility in water are the major obstacles in NRR in water-based electrolyte. Literatures independently showed that (i) materials near the top of the Sabatier principle volcano plot[2], (ii) nano-structure[3], and (iii) surface hydrophobicity[4] would favor the nitrogen reduction reaction and suppress the hydrogen evolution reaction. However, the synergetic effect has not been studied and the faradaic efficiency and yield are far from practical usage.

In this project, an electrode composing of heterogeneous nanostructure and proton conductive hydrophobic thin film will be fabricated with a combination of electrochemistry, vapor deposition, and plasma polymerization. The theory and methods employed to design the electrode will be presented.



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TH-323

Mapping oxidation state and structural dynamics in thin film electrocatalysts

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First row transition metal oxides have shown potential as affordable catalysts for the oxygen evolution reaction (OER), while adding small amounts of costly elements such as gold offers significant improvements in catalytic activity while maintaining affordability [1]. Upon catalysis, these materials undergo changes in both oxidation state and crystallinity [2]. Agoston et al. suggested that these structural and chemical changes occur non-uniformly across the surface and some of the catalysts have amorphous parts that may play a significant role in the catalytic activity which need to be analysed [3]. We investigate the correlated oxidation state and crystallinity changes in cobalt oxide and cobalt oxide-gold electrocatalysts by developing a novel synchrotron based method to simultaneously collect spatially resolved XANES (X-ray Absorption Near Edge Spectroscopy) and 2D microdiffraction over relatively large areas. This method provides unprecedented insights to information related to crystallinity changes that may accompany these oxidation state changes on the micron scale. Thin films of $Co(OH)_2$ (CoAu0%) and $Co(OH)_2$-Au (CoAu10%) were electrochemically deposited and submitted to OER for 4 hours with the Co-Au system showing better catalytic performance. We investigated the films before and after OER with SEM and EDS revealing uneven dispersion of Au on the surface with small agglomerations that may act as additional active sites with increased surface area from the uneven scattering and formation of small clusters on the surface. NEXAFS (Near Edge X-ray Absorption Fine Structure) spectra collected at the SXR beamline in the Synchrotron facility in Melbourne, show reduced ligand to metal charge transfer in the CoAu10% system which may account for the increased performance. In addition, we present preliminary results on our novel method development from recent experiments at the Australian Synchrotron.

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TH-324

Improving the performance of the Li-mediated nitrogen reduction reaction

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Increasing energy demand around the world motivates intense research and development of the renewable energy sources, which most commonly are intermittent and harvested in the form of electricity, which is hard to store on a multidigit megawatt scale. One promising strategy to address this is to convert renewable electricity to ammonia, which can be potentially used as a highly convenient and safe energy carrier and fuel.[1] This requires the development of an electrochemical processes for the ammonia synthesis that occurs under mild conditions contrasting the high temperature and pressure conventional catalytic Haber-Bosch process.[2] The key challenge of the ammonia electrosynthesis is the electrochemical activation of dinitrogen at the cathode through a 3-electron 3-proton nitrogen reduction reaction, which is impossible to achieve in a regular electrocatalytic way under aqueous conditions. In fact, the only known genuine method to electrochemically reduce N_2 to NH_3 is the so-called lithium redox mediated NRR, which builds upon the inherent reactivity of Li^0 to N_2.[3] Notwithstanding its apparent simplicity, this Li-mediated reaction presents a host of challenges and many aspects of its mechanism and kinetics remain unknown. The aim of the present work is to advance the understanding of the lithium redox mediated ammonia electrosynthesis through systematic investigation of the effect of the operating parameters (N_2 pressure, electrode potential, water concentration, etc.) on the kinetics and faradaic efficiency of the process.[4] Through this understanding, we have achieved a stable operation of the system for 60 h, as well as have demonstrated a faradaic efficiency of the process up to 60 % at moderate N_2 pressure of 15 bar, which is a significant improvement over the previous work.

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Ferroelectric polarization modulated band bending in $BiFeO_3$ photoelectrode

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Ferroelectrics have attracted great interest in the PEC field due to the external electric field assisted switchable polarization and PEC performance. However, the role of ferroelectric property in a more complicated way in PEC process is not well understood. The PEC performance of $BiFeO_3$(BFO) were measured in 1 M NaOH electrolyte with 0.1 m H_2O_2 as hole scavenger. As shown in Fig 1a-b, the photocurrent shows dramatical increase with the negative polarisation bias increased from 0 to 40 V, while the photocurrent decreases moderately with the positive polarization bias increased from 0 to 40 V. Based on the above results, it is illustrated that ferroelectric polarization can affect the charge recombination instead of surface reaction kinetics, thereby resulting in the enhanced/reduced photocurrent density of BFO. The surface potential of the poled BFO sample is adjusted monotonically by the applied bias, where the BFO poled with negative bias shows more negative surface potential and the positive bias exhibits the opposite effect. It can be found that the Fermi level of the surface is gradually positive shift after the negative polarization as shown in Fig 1d, which induces stronger upward band bending and then enhances the anodic photocurrent density. As the magnitude of the applied bias is increased, the polarisation charge increases, resulting in more positive shift and stronger internal electric field. On the opposite, the positive polarization brings decreased work function and negative shift of Fermi level, unfavourable for the upward band bending. The anodic photocurrent density was dramatically decreased. Systematic studies reveal that adjusting the strength and direction of the external bias could induce the change of energy band structure of ferroelectric materials, thereby tunning the ability of charge transfer and separation. By taking the external effect into the PEC system, it is expected to generate cutting-edge knowledge in advanced photoelectrocatalyst design.

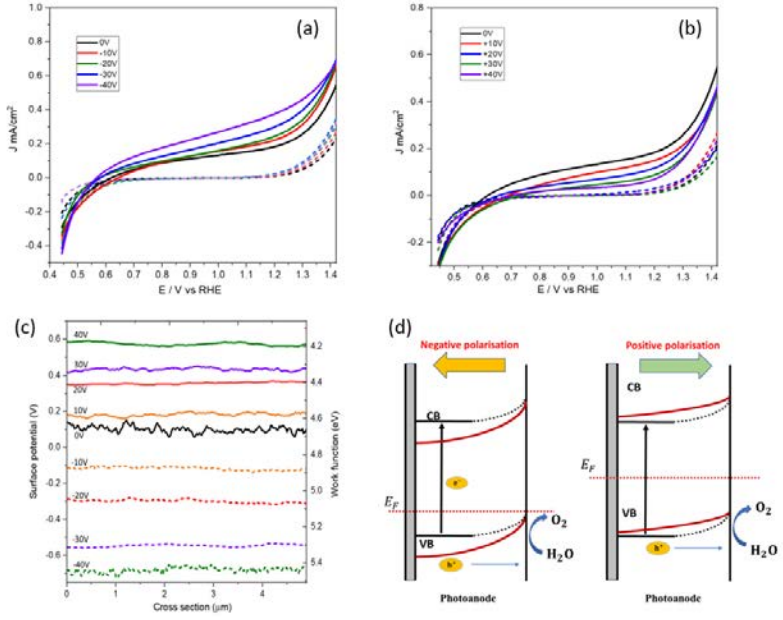

Figure 1. Photoresponse of $BiFeO_3$ photoanode before and after (a). Negative polarization, (b). Positive polarisation; (c). Cross section profiles of the surface potential distributions and work function of BFO photoanode before and after polarization; (d). Schematic energy band diagrams of the BFO film serving as a photoanode.

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Analysis of catalytic ink used for proton exchange membrane fuel cells (PEMFC'S)

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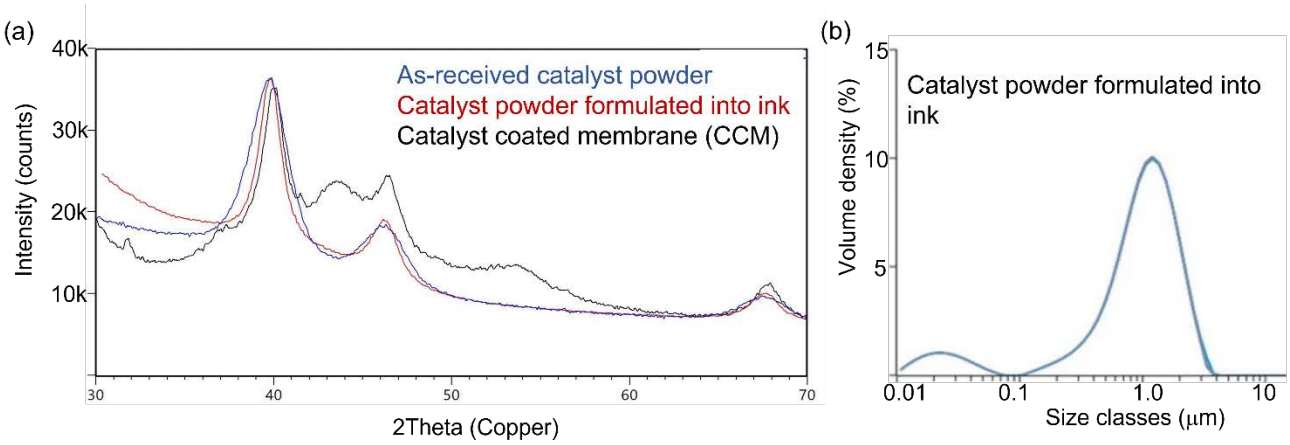
Pt-based catalytic inks are the key component when balancing cost, performance, and durability of proton exchange membrane fuel cells (PEMFC's). Particle size and dispersion of ink components define important parameters such as ink viscosity, ionomer distribution and morphology, catalyst utilization, interaction between the catalyst and ionomer, and the homogeneity and continuity of the electrode layer[1]. Particle size is crucial but difficult parameter to measure for catalytic inks due to their structural complexity and the large size scale range. Here we present the approach to the comprehensive characterization of catalytic ink components utilizing X-ray diffraction XRD), laser diffraction (LD) and dynamic light scattering (DLS) techniques on the example of the catalytic ink, made with 40% Pt on carbon support and Nafion ionomer dispersion. Some of the results are summarized in Figure below. (a) XRD data revealed the increase of Pt crystallite size in the ink and when printed as an electrode layer on the membrane. The coursing of the Pt catalyst may indicate ink overheating during processing steps and may adversely affect the catalytic performance. (b) LD detected the presence of the sub-100nm size population in the ink, which suggests that the ink was over-dispersed and Pt particles may have detached from the carbon support.



Additionally, we discuss the use of zeta potential measurements in the analysis of the interactions between the ionomer and the carbon-supported catalyst to predict the ink stability.

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Water purification using a green science approach

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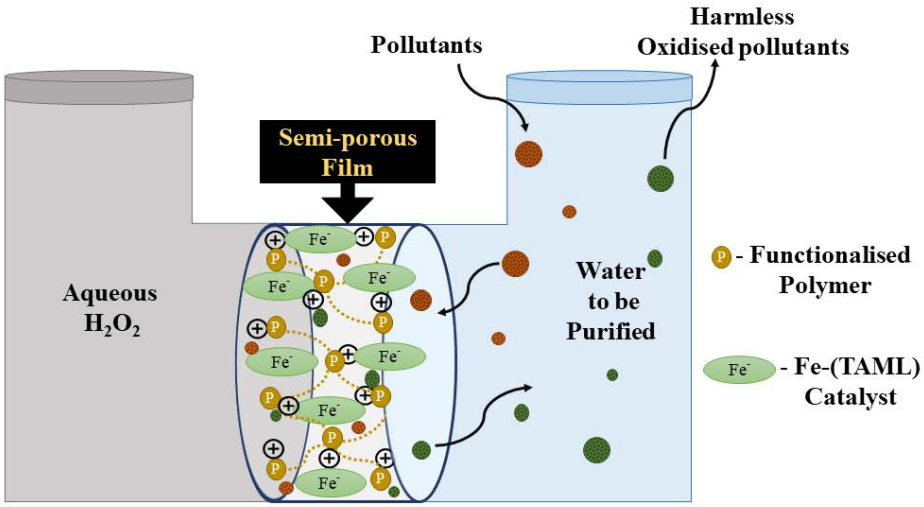
Globalization and urbanization along with increase in the world's population is intensifying the stress on water resources even in many first world countries. Scarcity in the availability of clean water globally has necessitated the adoption of water reuse and recycling. However, the elimination of trace contaminants such as pesticides, pharmaceutical residues, agricultural wastes, endocrine disruptors etc. is quite challenging.[1] Current purification techniques like chlorination, reverse osmosis, coagulation, charcoal adsorption, etc. all work to some extent, but none provide ideal solutions for the removal of many of these organic impurities.[2] Hence the development of a new purification system which is cost-effective, eco-friendly and efficient in eliminating all micro-pollutants from bulk water is an important goal.

In this research project, a novel purification system that is based on specially functionalized polymeric films, which can strongly adsorb oxidation catalysts like Fe-(TAML),[3] concentrate pollutants from water and oxidatively convert them into harmless products has been investigated. The hydrogen peroxide which activates the oxidation catalyst is separated from the bulk water by the semi-porous film, thus avoiding hydrogen peroxide wastage and further contamination of the water. The Fe-(TAML) catalyst immobilized within the polymer film operates as a heterogenous catalyst to oxidize impurities when activated by peroxide. The catalytic activity of the system was studied by the oxidative degradation of water-soluble dyes that act as easily monitored pollutant mimics. The system shows promising and consistent degradation activity over ten cycles of testing, thereby paving way for novel and efficient innovations in the engineering of economical and greener techniques for water purification. A 3-dimensional representation of the semi-porous film is illustrated below.



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TH-328

Development of New Organic Ionic Plastic Crystals

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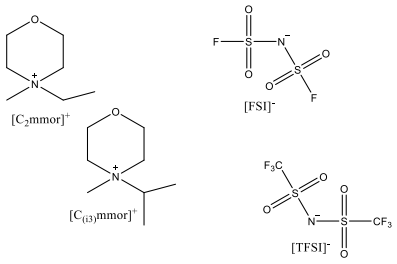
Organic ionic plastic crystals (OIPCs) are emerging candidates as solid-state ion conductors for various applications, especially batteries.[1] They can also be potential candidates for developing new gas separation membranes.[2] OIPCs are disordered solids at room temperature, which are made entirely of ions. They show a long-range ordered crystalline lattice, but short-range disorder that typically comes from the ions' translational and rotational motions. OIPCs show beneficial properties such as negligible volatility, which makes them suitable for long term device use, while the high thermal and electrochemical stability delivers the primary necessity to be used as solid-state electrolytes for many device applications.[3] Thus, this has encouraged many researchers to explore different cation and anion combinations to develop new OIPCs with good properties.

Here we report the synthesis and characterization of new OIPCs utilizing morpholinium cations. The morpholinium ring is substituted with linear ethyl and branched isopropyl substituents to form 4-ethyl-4-methyl morpholinium $[C_2mmor]^+$ and 4-(iso)-propyl-4-methyl morpholinium $[C_{(i3)}mmor]^+$ cations respectively. These cations were combined with the charge diffuse bis(fluorosulfonyl)imide $[FSI]^-$ or bis(trifluoromethanesulfonyl)imide $[TFSI]^-$ anions to produce four new OIPC salts. The thermal and transport properties were measured by Differential Scanning Calorimetry (DSC) and Electrochemical Impedance Spectroscopy (EIS) respectively. Solid-state NMR have also been carried out to investigate the ion dynamics in the materials. Of the new solid salts, the FSI-based OIPCs shows higher conductivity values compared to the TFSI-based OIPCs. $[C_{(i3)}mmor][FSI]$ has the highest conductivity of 1×10^{-6} S cm^{-1} at 30 °C. Furthermore the $[C_2mmor][FSI]$ OIPC shows the widest temperature range of the most conductive phase ('phase I') ranging from 11°C - 130 °C. These results are promising for further investigation of these materials, for example as electrolytes for lithium or sodium batteries.



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Molecular crowding electrolytes for stable proton batteries

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Aqueous batteries are promising for the storage of renewable yet intermittent energy sources due to high safety, low cost, fast kinetics and environmental benignity. Among all cations, proton is the smallest and lightest, therefore is favourable for transportation to reach complete occupancy of electrode lattice with minimum structural distortion. Also, in synergy with a unique displacive diffusion (Grotthuss mechanism), ultrafast rate-capability can be reached for proton (de)intercalation. However, proton is solvated by water molecules in aqueous electrolyte, and proton-insertion is demonstrated accompanied with desolvation process, which may deteriorate the electrode-electrolyte-interface and affect the electrode stability significantly.
Herein, we report a molecular crowding electrolyte with the usage of poly(ethylene glycol) (PEG) as crowding agent for fast and stable electrochemical proton storage, combining with expanded working potential window to 3.2 V. Spectral characterisations confirm the formation of hydrogen bond between water and PEG molecules, which is beneficial for confining the activity of water molecules. Dynamic structural evolution of MoO_3 anode is studied by *in-situ* X-ray diffraction (XRD) in molecular crowding electrolytes, revealing a reversibly step-by-step naked proton storage mechanism. Surficial adsorption of PEG molecules on MoO_3 anode works in synergy to alleviate the destructive effect of water co-intercalation into MoO_3 lattice, thereby achieving much-enhanced cycling stability. This strategy offers practical applications of proton electrochemistry thanks to the low-cost and environmentally friendly nature of PEG additives.

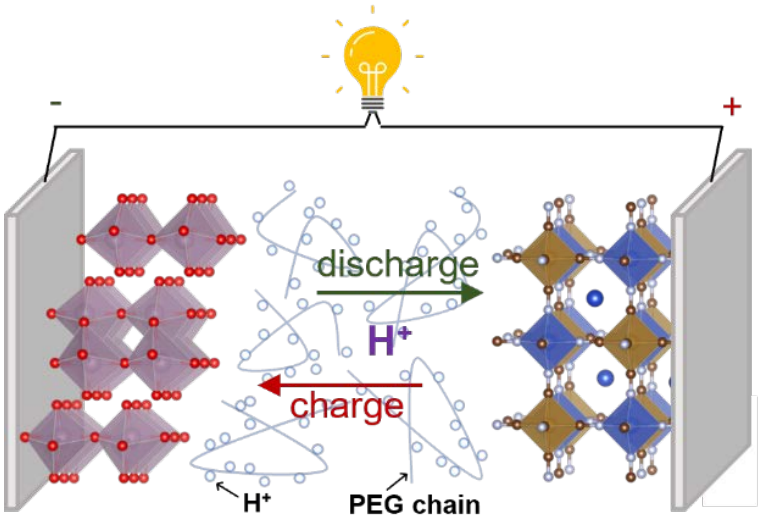

Figure. Schematic illustration for VHCF//MoO3 full cell using molecular crowding electrolyte.

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