

DOUZIEMES ENTRETIENS
DE L'IBPC

CONFERENCE
Edmond de Rothschild

Jeudi 7 Juin - Vendredi 8 juin 2018

Journées organisées avec le soutien de :





DOUZIEMES ENTRETIENS DE L'IBPC

Les entretiens de l'IBPC ponctuent régulièrement la vie scientifique de l'institut. Ils représentent l'occasion pour l'ensemble des personnels statutaires et non statutaires de se retrouver pour découvrir la richesse et la diversité des recherches conduites au sein de l'IBPC. Les douzièmes entretiens de l'IBPC vont se dérouler sur deux jours, du jeudi 7 au vendredi 8 juin 2018. Ces journées seront clôturées par la Conférence Edmond de Rothschild.

Cet événement important dans la vie de l'institut placé sous la direction de Francis-André Wollman, directeur de l'IBPC a été organisé par :

Le comité d'organisation :

- Soumaya LAALAMI (UMR 8261)
- Christel LE BON (UMR 7099)
- Stefania VIOLA (UMR 7141)

Le comité scientifique composé de représentants statutaires et non statutaires de chaque unité :

- Laetitia CAVELLINI (UMR 8226)
- Sébastien CHAMOIS (UMR 8226)
- Olivier CASPARI (UMR 7141)
- Anna LIPONSKA (UMR 8261)
- Yvette NTSOGO (UMR 7099)
- Hubert SANTUZ (UPR 9080)
- Stepan TIMR (UPR 9080)
- Carine TISNE (UMR 8261)
- Katia WOSTRIKOFF (UMR 7141)
- Manuela ZOONENS (UMR 7099)

Les membres de la FRC 550, tout particulièrement :

- Yasmine ABDELJALIL
- Yves DAPRA
- Catherine LARGET
- Hélène VIRLOUVET-ALMEIDA

Un grand merci à Danielle BASCLE, Isabelle KREMPHOLTZ, Laurence GAUTHIER, Edith GODARD et Victoria TERZIYAN (gestionnaires des unités de l'IBPC), aux doctorants et post-doctorants pour leur contribution à la réussite de cet événement.

Jeudi 7 Juin 2018

9:00-9:20 Message de bienvenue par les délégués du personnel et le directeur de l'IBPC

9:20-10:20 Présentation des Unités

FRC 550 : Yasmine ABDELJALIL

Laboratoire de Physiologie Membranaire et Moléculaire du Chloroplaste UMR 7141 : Ingrid LAFONTAINE

Laboratoire de Biologie Physico-Chimique des Protéines Membranaires UMR 7099 : Fabrice GIUSTI

Laboratoire de l'Expression Génétique Microbienne UMR 8261 : Emmeline HUVELLE & Assia MOUHAND

Laboratoire de Biochimie Théorique UPR 9080 : Jérôme HENIN

Laboratoire de Biologie Moléculaire et Cellulaire des Eucaryotes UMR 8226 : Héloïse COUTELIER

10:20-10:50 Pause café

Biotic & abiotic interactions

Modérateur : Stéphane LEMAIRE

10:50-11:00 Présentation de la session

11:00-11:20 **Alexey KOREPANOV**

Bacterial small RNAs and iron acquisition

11:20-11:40 **Oliver D. CASPARI**

Testing for an antimicrobial origin of chloroplast transit peptides

11:40-12:00 **Felix DE CARPENTIER**

Stress-induced social behavior in *Chlamydomonas reinhardtii*

12:00-12:20 **Alexandra PELTEKIS**

Allelopathic interactions between phytoplankton species

12:20-14:00 **Apéritif de bienvenue**

Pause déjeuner libre

Membrane proteins and dynamics

Modérateur : Bruno MIROUX

14:00-14:10 Présentation de la session

14:10-14:30 **Anne-Elisabeth MOLZA**

In silico investigation of the Ryanodine Receptor Structure and Dynamics using an integrative methodology

14:30-14:50 **Dhenesh PUVANENDRAN**

Reconstitution of the activity of RND efflux pumps into proteoliposomes : a quantitative approach

14:50-15:10 **Justin FINDINIER**

Chlamydomonas FzI Is Required For Photosynthesis During High Light Stress

15:10-15:30 **Jordi ROYES MIR**

Looking at membrane proteins from a different perspective: bioproduction of functional thermo-responsive nanocapsules

15:30-16:00 Pause café

RNA metabolism

Modérateur : Harald PUTZER

16:00-16:10 Présentation de la session

16:10-16:30 **Lina HAMOUCHE**

News and Views: dynamics of the key ribonuclease initiating mRNA degradation in *Bacillus subtilis*

16:30-16:50 **Sébastien CHAMOIS**

Aberrant mRNA decay analysis in *Saccharomyces cerevisiae*

16:50-17:10 **Aude TRINQUIER**

Characterisation of the quality control link between tRNA maturation and ribosome assembly in *Bacillus subtilis*

17:10-17:30 **Domitille JARRIGE**

A mutagenesis study of specific mRNA/protein interactions in the chloroplast of *Chlamydomonas reinhardtii*

Vendredi 8 juin 2018

Présentation des plateformes

Modérateur : Francis-André WOLLMAN

9:00-9:10 Présentation de la session

9:10-10:10

Cristallographie : **Franck BRACHET**

Spectrométrie de masse : **Marion HAMON**

RMN : **Christel LE BON**

Bio-informatique : **Benoist LAURENT**

Visualisation : **Hubert SANTUZ**

10:20-11:00 Pause café

Structure, what else?

Modérateur : Marc BAADEN

11:00-11:10 Présentation de la session

11:10-11:30

Stephanie OERUM

Structural characterisation of RNase M5: insights into 5S rRNA binding

11:30-11:50

Stepan TIMR

Multi-scale modeling of protein diffusion and stability in crowded environments

11:50-12:10

Mathilde PIEL

Molecular bases of mitochondrial uncoupling protein 1 induced thermogenesis

12:10-12:30

Xavier MARTINEZ

UnityMol X, a software framework for intuitive and immersive molecular visualization

12:30-15:00 Pause déjeuner libre

Conférence Edmond de Rothschild

Modérateur : Francis-André WOLLMAN

15:00-15:10 Présentation de la session

15:10-16:40

Conférence Edmond de Rothschild

Professor Jeff Errington

Director of the Centre for Bacterial Cell Biology (CBCB)

Newcastle University



16:40-20:00

Cocktail

Biotic & abiotic interactions

- **Alexey KOREPANOV**
Bacterial small RNAs and iron acquisition
- **Oliver D. CASPARI**
Testing for an antimicrobial origin of chloroplast transit peptides
- **Felix DE CARPENTIER**
Stress-induced social behavior in *Chlamydomonas reinhardtii*
- **Alexandra PELTEKIS**
Allelopathic interactions between phytoplankton species

Bacterial small RNAs and iron acquisition

Alexey Korepanov, Jonathan Jagodnik, Claude Chiaruttini, Maude Guillier*

Groupe de Contrôle de l'expression génétique par les ARN, Laboratoire de l'Expression Génétique Microbienne, CNRS UMR 8261, Institut de Biologie Physico-Chimique, Paris, France
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Bacteria are extremely versatile organisms that can adapt to ever-changing conditions. This relies in part on their ability to extensively regulate their gene expression in response to their environment. Transcriptional regulation was initially described by the pioneering work of Jacob and Monod, and it was later established that expression of bacterial genes can also be subject to post-transcriptional regulation. Our view of post-transcriptional control has been recently challenged with the identification of a large number of small regulatory RNAs (sRNAs), many of which act by pairing to target mRNAs, thereby regulating their translation and/or stability.

The *Escherichia coli* *fepA* gene is an example of a gene controlled both at the transcriptional and the post-transcriptional level; it encodes the receptor for the iron-enterobactin complex. As enterobactin is the most potent siderophore, *fepA* is essential for bacterial survival under iron limitation, a condition that is frequently encountered by enterobacteria. Consistent with this, *fepA* transcription is under the control of the Fur regulator, allowing maximal expression of *fepA* under low iron.

In addition, we report here that *fepA* expression also responds to at least four different sRNAs. Interestingly, these sRNAs target different regions of the *fepA* mRNA and act according diverse mechanisms. Furthermore, they are expressed under different conditions, which considerably expands our knowledge of the signals leading to the *fepA* control. This work illustrates the great diversity of regulatory mechanisms involving sRNAs and highlights the complementarity of transcriptional and post-transcriptional controls in shaping bacterial gene expression in response to the environmental stimuli.

Keywords: Post-transcriptional control of gene expression, small RNAs, iron acquisition, *fepA*

Testing for an antimicrobial origin of chloroplast transit peptides

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Abstract

Chloroplast transit peptides (cTPs) are cleavable N-terminal extensions involved in the subcellular targeting of most nuclear encoded but plastid localized proteins. Different cTPs are very divergent in primary sequence, but share a propensity to form amphiphilic alpha-helix stretches when in contact with a membrane¹. In this respect they are very similar to a certain antimicrobial peptides (AMPs), which are used by most eukaryotes as well as some bacteria to kill microbial antagonists². In a neat analogy to post-import cleavage and proteolytic degradation of cTPs, certain bacterial defense mechanisms against AMPs involve uptake and intracellular destruction of the attacking peptide³. Might cTPs be the result of an arms-race involving AMPs between the cyanobacterial chloroplast ancestor and the protist host during the early phases of endosymbiosis⁴? To test this hypothesis, we have developed a fluorescent reporter system that allows candidate peptides to be screened for their ability to direct protein cargo into the chloroplast of the model green alga *Chlamydomonas reinhardtii*.

Keywords: organelle evolution, protein targeting, Venus fluorescent protein, bicistronic expression,

References

1. Krimm, I., Gans, P., Hernandez, J. F., Arlaud, G. J. & Lancelin, J. M. A coil-helix instead of a helix-coil motif can be induced in a chloroplast transit peptide from *Chlamydomonas reinhardtii*. *Eur. J. Biochem.* **265**, 171–180 (1999).
2. Nguyen, L. T., Haney, E. F. & Vogel, H. J. The expanding scope of antimicrobial peptide structures and their modes of action. *Trends Biotechnol.* **29**, 464–472 (2011).
3. Shelton, C. L., Raffel, F. K., Beatty, W. L., Johnson, S. M. & Mason, K. M. Sap transporter mediated import and subsequent degradation of antimicrobial peptides in *Haemophilus*. *PLoS Pathog.* **7**, (2011).
4. Wollman, F.-A. An antimicrobial origin of transit peptides accounts for early endosymbiotic events. *Traffic* (2016). doi:10.1111/tra.12446

Stress-induced social behavior in *Chlamydomonas reinhardtii*

Félix de Carpentier*, Christophe Marchand, Pierre Crozet et Antoine Danon

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Abstract

The alga *Chlamydomonas reinhardtii* is a model organism for research in plant biology, mostly because of the power and speed of genetic approaches that can be developed. We use *Chlamydomonas* to try to understand how a unicellular organism adapts to survive in a hostile environment. Indeed, we have shown that facing a moderate stress, the cells aggregate forming a multicellular structure in which they can be protected from the toxic environment. We created and screened a library of insertional mutants in *Chlamydomonas* that allowed us to identify original mutants deregulated in the process leading to the aggregation. A multidisciplinary approach combining genetics, molecular biology, cell biology and proteomics is used to characterize the most promising mutants. In particular, the affected genes have been identified, the proteins involved have been quantified by the mass spectrometry tools we have developed in the lab. We have interesting candidates of genes involved in the aggregation in response to stress. Thereby we have a better understanding of the dialogue between unicellular organisms and the adaptation in a hostile environment. Aggregates could be intermediate between unicellular and multicellular states, we therefore acquire a some insight in the evolution of multicellularity.

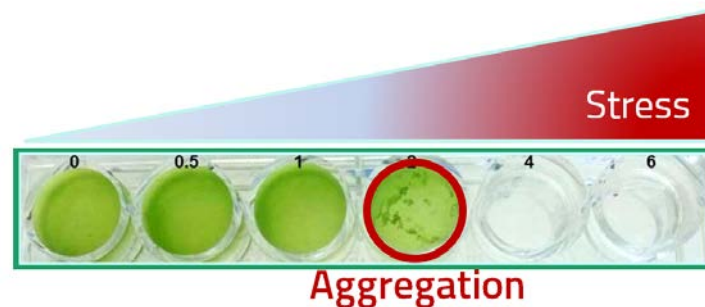


Fig.1 : In moderate stress conditions *Chlamydomonas reinhardtii* forms agregats

Keywords: Stress, Agregation, Multicellularity, Chlamydomonas, Alga

Allelopathic interactions between phytoplankton species

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Abstract

Phytoplankton are aquatic unicellular organisms (eukaryotic or prokaryotic) responsible for 50% of terrestrial photosynthesis [1]. Despite the importance of phytoplankton in water ecosystems, the level of understanding of the dynamics and the structure of phytoplankton communities is still limited. Different parameters could contribute to the structure of phytoplankton communities, like the competition for nutrients, predator-prey interactions and allelopathy. My PhD focuses on the latter: species are able to release secondary metabolites into the medium that have harmful (inhibitory) effects on target species, these interactions are known as allelopathy [2]. One of the main targets of these secondary metabolites is the photosynthetic apparatus of competitors, making photosynthesis an ideal probe to study allelopathy. Little is known about allelopathy in marine microalgae, in spite of the competitive advantage that these interactions could provide to invasive species. This is mainly due to a number of methodological difficulties [3], including lack of information on the relative physiologies of two microalgae in mixture.

We chose a new approach to explore these interactions based on a physical phenomenon, the electro-chromic shift (ECS) of photosynthetic pigments, when subjected to the electric field generated across the thylakoid by photosynthesis. On the one hand the ECS shows a different spectral signature in each photosynthetic clade of microalgae, allowing the extraction of the photosynthetic responses of each species in an assembly. We can therefore measure the photosynthetic activity of a species A alone or in a mixture with species B, and highlight an allelopathic interaction targeting photosynthesis. On the other hand all complexes involved in photosynthesis contribute to the generation of a trans-thylakoidal electric field (PSII, PSI, cytochrome *b6f*) or to its consumption (ATP-synthase) [4]. This allows to define the exact target of the released secondary metabolites on the photosynthetic apparatus. With this innovative method we are able to screen allelopathic interactions that affect photosynthesis between different clade of phytoplankton, which could help to understand better the role of allelopathy on the structure of the phytoplankton community.

We observed that the photosynthetic activity of some diatoms (*Thalassiosira pseudonana*, *Phaeodactylum trichornutum*) and prasinophytes (*Bathycoccus prasinos*, *Nephroselmis pyriformis*) was almost fully inhibited when mixed with the dinoflagellate *Ampidinium carterae*. We were further able to identify the target of the unknown secondary metabolites on the photosynthetic apparatus of the diatom *T.pseudonana*. The mechanism of inhibition seems to be the same for the others species and appears to affect the electrochemical gradient of H⁺ that will lead to the production of ATP by the ATP-synthase during photosynthesis.

Keywords: Allelopathy, Phytoplankton, Photosynthesis ,ECS

References

1. Field, C. B., Behrenfeld, M. J., Randerson, J. T. & Falkowski, P. G. Primary production of the biosphere: integrating terrestrial and oceanic components. *Science* 281, 237–240 (1998).
2. Molish, H. (1937). Die Einfluss seiner Pflanze auf die andere-Allelopathie. Jena, DE: VDM Verlag Dr. Müller.
3. Anderson, D. M., Kulis, D. M., Sullivan, J. J., Hall, S., & Lee, C. (1990). Dynamics and physiology of saxitoxin production by the dinoflagellates *Alexandrium* spp. *Marine biology*, 104(3), 511-524.
4. Bailleuil, B., Cardol, P., Breyton, C., & Finazzi, G. (2010). Electrochromism: a useful probe to study algal photosynthesis. *Photosynthesis research*, 106(1-2), 179-189.

Membrane proteins and dynamics

- **Anne-Elisabeth MOLZA**
In silico investigation of the Ryanodine Receptor Structure and Dynamics using an integrative methodology
- **Dhenesh PUVANENDRAN**
Reconstitution of the activity of RND efflux pumps: a bottom-up approach
- **Justin FINDINIER**
Involvement of Dynamin Related Protein in the dynamics of photosynthetic membranes of *Chlamydomonas reinhardtii*
- **Jordi ROYES MIR**
Looking at membrane proteins from a different perspective: bioproduction of functional thermo-responsive nanocapsules

In silico investigation of the Ryanodine Receptor Structure and Dynamics using an integrative methodology

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Abstract

The Ryanodine Receptor (RyR) is a homotetrameric intracellular calcium channel, with each subunit containing more than 5000 residues (~ 2.2MDa). In skeletal muscle the predominant isoform—RyR1— plays a main role on the calcium release from sarcoplasmic reticulum to cytosolic compartment which is essential for excitation–contraction coupling^{1,2}. Recent advances in electron microscopy field allow 3D structural determination of membrane proteins among these, the giant RyR with a high-resolution up to 3.6Å. Thanks to these data, near- atomic cryo-EM-based structures of RyR1 and RyR2 in open and closed conformation have been obtained³. Nevertheless, these structures are still incomplete and have numerous unknown and missing residues. Moreover, the allosteric modulation of RyR is still unclear. Here, we are studying the RyR1 structure and its conformational changes based on molecular modeling and normal modes methods to propose transition pathway to the opening-closing mechanism.

Thanks to this integrative methodology we can obtain full-length models of RyR, analyze protein motions and propose transition pathways between open and closed conformations. **Next steps will consist** in assessing the presence of transient pockets that probably will provide some clues about ligand interactions to this protein. Moreover, we will investigate the conformation of the unstructured region between the cytoplasmic and transmembrane domains combining protein sequence analyses and an interactive and flexible molecular dynamics method.

Further analyses using coarse grained and atomistic molecular dynamics simulations with the RyR embedded into the membrane bilayer could provide detailed structural information about protein stability, ligand binding effects and functional motions.

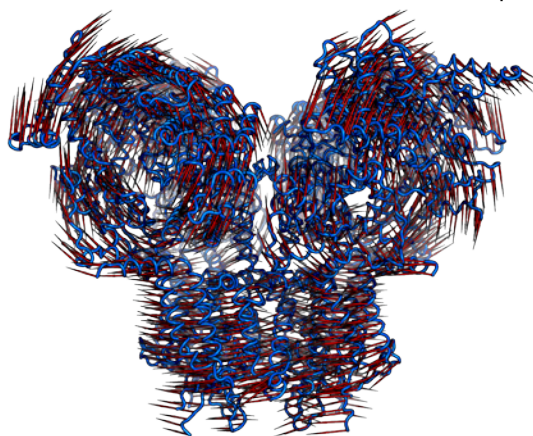


Figure 1: Carbon alpha atoms displacement prediction through low-frequency normal modes.

Keywords: Membrane protein, Allosteric motions, Molecular Modeling, Molecular dynamics, Integrative method

Acknowledgments

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References

- ¹Nature. 2015 Jan 1; 517(7532): 44–49
²Protein Sci. 2017 Jan;26(1):52-68 ³Cell. 2016 Sep 22;167(1):145-157.e17

Reconstitution of the activity of RND efflux pumps into proteoliposomes : a quantitative approach

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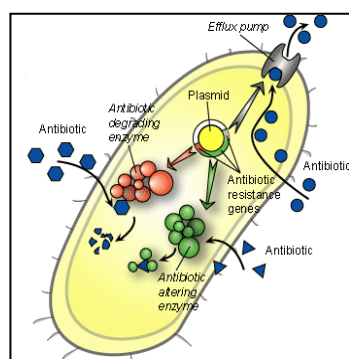
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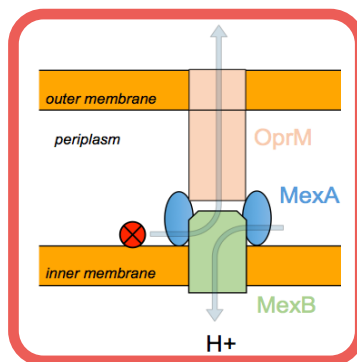
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Efflux pumps are the major systems in bacterial resistance against antibiotics. They are classified by the energy needed to be active (ATP hydrolysis or ion counter-transport). Efflux pumps from the RND (Resistance, Nodulation, and cell Division) family use a proton gradient to be active and are composed of three proteins: the Outer Membrane Factor (OMF), a channel localized in the outer membrane, the RND transporter in the inner membrane, and the Membrane Fusion Protein (MFP) which connects the latter proteins. We focus on the MexA-MexB-OprM efflux pump from *Pseudomonas aeruginosa*.

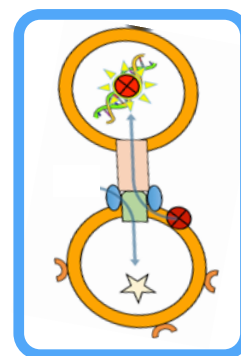
My research relies on the incorporation of efflux pumps into proteoliposomes. By the use of this technique, we reconstitute the RND and MFP proteins into one population of liposome, and the OMF in another, allowing reconstitution of the whole tripartite pump by associating the respective populations of liposomes. The proof of concept of this method has already been described and we now work at defining a better reconstitution procedure, liable to make our system quantitative. To do so we have to master the efficiency of protein reconstitution, control the remaining quantity of detergent upon protein reconstitution and the quantity of lipids component into the liposomes. I will present the roadmap towards the rational, step-by-step, reconstitution of the MexA-MexB-OprM efflux pump as well as the methodologies that will be undertaken for the quantification of the catalytic parameters of transport as well as possible perspectives regarding the screening of efflux pump inhibitors.



Pseudomonas aeruginosa



Efflux pumps



in vitro assay

References

Rigaud J-L, Lévy D (2003) Reconstitution of membrane proteins into liposomes. *Meth Enzymol* 372:65–86.

Verchère A, Dezi M, Adrien V, Broutin I, Picard M (2015) In vitro transport activity of the fully assembled MexAB-OprM efflux pump from *Pseudomonas aeruginosa*. *Nature Communications* 6(1). doi:10.1038/ncomms7890.

Puvanendran D, Cece Q, Picard M (2017) Reconstitution of the activity of RND efflux pumps: a “bottom-up” approach. *Research in Microbiology*. doi:10.1016/j.resmic.2017.11.004.

Keywords: proteoliposomes, efflux pump, antibiotic resistance, catalytic parameters

Chlamydomonas Fzl Is Required For Photosynthesis During High Light Stress.

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Abstract

Dynamamin-Related-Proteins (DRPs) are large GTPases widespread in the kingdoms of life from fungi and bacteria to higher eukaryotic organisms like mammals and plants. They are involved in membrane fission and, to a lower extent, fusion processes thanks to their particular ability to shape lipid bilayers. Growing evidences have placed DRPs as key actors for division and proliferation of energy transducing membranes organelles including mitochondria and plastids such as chloroplasts. In fact, DRPs have themselves, like chloroplasts and mitochondria, a prokaryotic origin and one could expect that the dynamics of respiratory and photosynthetic membranes is intricately linked to the remodeling properties of DRPs.

In this regard, mitochondria are organized as a tubular network regulated by fission and fusion events mediated by no less than three different DRPs. In yeast, Dnm1 promotes the division of mitochondrial tubules through the formation of a constriction ring whereas the mitofusin Fzo1 tethers outer membranes and triggers their fusion followed straight after by inner membrane fusion mediated by Mgm1¹. Then, while the role of DRPs in respiration has been fully demonstrated, their involvement in dynamics of photosynthetic membranes still needs to be more deeply investigated.

Despite the highly structured architecture of thylakoids, involvement of DRPs in shaping those sub-organelles has been barely studied. Six families of DRPs have been identified in plant genomes and only two of them have a function related to plastid membrane dynamics. The role of DRP5B in chloroplast division has been studied in many organisms and is reminiscent of Dnm1 function in mitochondrial fission^{2,3}. Another DRP called Fzl (Fuzzy Onion Like) for its resemblance to the yeast mitofusin Fzo1 has been associated to envelope and thylakoid membranes in *Arabidopsis thaliana*⁴. Fzl knock out leads to disruption of the chloroplast structure and increased H₂O₂ production, autophagy and cell death pathways activation. However, causality between these phenotypes is not established and, surprisingly, no photosynthesis impairment was shown⁴⁻⁶.

Here, we show that *Chlamydomonas reinhardtii* encodes a putative Fzl ortholog. CrFzl is constitutively expressed in *Chlamydomonas* and we confirmed its chloroplast localization. In order to study its function, the emerging CRISPR/Cas9 technology⁷ was employed to generate multiple CrFzl knock out strains. Phenotypic analyzes indicate the requirement of CrFzl for survival upon light stress as growth of CrFzl mutants is normal in the dark but increasingly affected with stronger light irradiance. Consistent with this, chlorophyll fluorescence measurements revealed specific impairment of photosynthesis upon high light treatment of the mutant cells. Fluorescence and electron microscopy approaches in stressful conditions revealed that mutant cells accumulate cytosolic structures corresponding to degradative vacuoles feeding on chloroplast, further illustrating the damage caused by excess light. Additional analyses are ongoing to evaluate the involvement of CrFzl in the fusion of thylakoid membranes but this work already demonstrates the contribution of CrFzl to light stress acclimation in the chloroplast.

Keywords: *Chlamydomonas*, dynamamin, chloroplast, light, stress.

¹ Westermann, B. *Nat Rev Mol Cell Biol* (2010) 11, 872-884.

² Gao, H. *et al. Proc Natl Acad Sci U S A* (2003) 100, 4328-4333.

³ Sakaguchi, E. *et al. Plant Sci* (2011) 180, 789-795.

⁴ Gao, H. *et al. Proc Natl Acad Sci U S A* (2006) 103, 6759-6764.

⁵ Landoni, M. *et al. J Exp Bot* (2013) 64, 4313-4328.

⁶ Tremblay, A. *et al. Sci Rep* (2016) 6, 37797.

⁷ Shin, S. E. *et al. Sci Rep* (2016) 6, 27810.

Looking at membrane proteins from a different perspective: bioproduction of functional thermo-responsive nanocapsules

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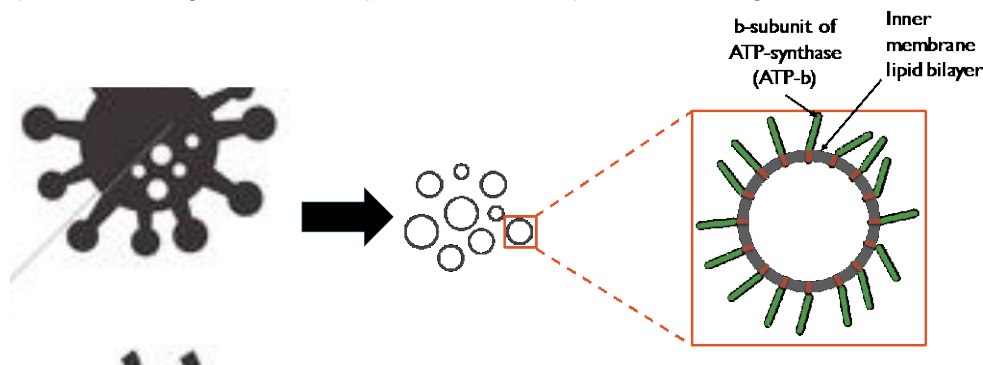
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Abstract

Advances in metabolic engineering and synthetic biology in the last 20 years have markedly facilitated the use of microorganisms as "cell factories"^[1] inspiring eco-friendly alternatives to chemical synthesis. Nowadays, "Microbial synthesis" becomes a promising tool in material and polymer science, mostly to produce biopoly(esters),^[2] or functional peptides such as temperature-responsive elastin-like polymers (ELP)^[3]. To go beyond the present molecular bio-engineerings, we propose to reroute cell machineries to also integrate formulation and assemblies of functional objects inside bacteria.

Here we will show how to replace "*in glassware*" formulation of nanocapsules for "*in vivo*" production. We will illustrate the design of genetically-encoded, custom polypeptide-coated nanocapsules, with a void volume in its interior susceptible of encapsulate active molecules. As a starting point, we used inner membrane proliferation induced by overexpression of a membrane protein (b subunit of ATP synthase) in C43(DE3) *E.coli*^[4] to produce lipid nanocapsules, which can be spontaneously decorated with artificial fusion polypeptides (Scheme 1). Optimization of mild extraction procedures (aqueous enzymolysis, low mechanical shear) yields homogenous population of capsules (size distribution and composition were characterized by particle tracking, DLS, fluorescence). Finally, coating our nanocapsules with a genetically encoded synthetic ELP moiety has granted access to stimulus-responsive nanocapsules, capable of undergo a reversible phase transition upon mild heating (<45 °C)



Scheme 1. "*In vivo*" production and isolation of thermo-responsive nanocapsules

Keywords: nanocapsules, bioproduction, stimulus-responsive, cell factory, encapsulation

References

[1] Clomburg, J.M., Crumbley, A.M., Gonzalez, R., Science, 2017, 355, aag0804.

[2] Thomson, N., Summers D., Sivaniah, E., Soft Matter, 2010, 6, 4045

[3] Yousefpour P., Chikolti A., Biotechnol. and Bioeng. 2014, 111 (9), 1699, & Bataille L., Dieryck W, Hocquellet A., Cabanne C., Bathany K., Lecommandoux S., Garbay B.; Garanger E., Prot. Expression & Purif. 2016, 121, 81.

[4] Arechaga I., Miroux, B., Karrasch S., Huijbregts R., Kruijff B., Runswick, M.J., Waker, J.E. FEBS letters, 2000,482, 215.

RNA metabolism

- **Lina HAMOUCHE**
News and Views: dynamics of the key ribonuclease initiating mRNA degradation in *Bacillus subtilis*
- **Sébastien CHAMOIS**
Aberrant mRNA decay analysis in *Saccharomyces cerevisiae*
- **Aude TRINQUIER**
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News and Views: dynamics of the key ribonuclease initiating mRNA degradation in *Bacillus subtilis*

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The metabolic instability of mRNA is crucial to the control of gene expression in all organisms. A very efficient way to control gene expression is the modulation of mRNA decay. Studies of prototypical gram-negative and gram-positive bacteria have highlighted the principal enzymes involved in the initiation of mRNA degradation, i.e. *E. coli* RNase E and *B. subtilis* RNase Y¹. Both endoribonucleases are tethered to the cell membrane^{2,3}. Being anchored at the membrane is not intuitive but apparently important for the function of these nucleases. We used total internal reflection fluorescence microscopy (TIRFm) and single particle tracking (SPT) to visualize RNase Y, and analyse its localization and dynamics in live cells. We find that RNase Y rapidly diffuses at the membrane in the form of very dynamic short-lived foci. The dynamic behaviour of RNase Y foci at the membrane can be categorized into three classes of movement. The formation of foci is not dependent on the transcription of RNA substrates. However, following transcription arrest, the kinetic parameters of RNase Y foci are altered. Foci become more intense, move faster and are more abundant, suggesting that they do not constitute the active form of the nuclease. Our results are in contrast with those obtained with *E. coli* RNase E where inhibition of transcription caused a reduction in foci formation and a uniform diffusion of the enzyme in the membrane⁴. The distinct localization and dynamic behaviour observed for RNase Y compared to RNase E foci might reflect differences in how the two nucleases are anchored at the membrane and in which form they are active. Recently, a complex of three small proteins, YaaT, YlbF and YmcA, has been shown to bind and alter RNase Y activity *in vivo*⁵. We have confirmed this observation by showing that two known RNase Y substrates, the *yitJ* riboswitch and the *thrS* leader mRNA, are less cleaved *in vivo* in *yaaT*, *ylbF* and *ymcA* mutants. However, while localisation of RNase Y foci is not changed, each of these mutations appear to influence the dynamics of the RNase. Using TIRFm and SPT, we observe changes in the motion and other kinetic parameters of RNase Y foci in the mutant strains compared to the wild-type strain. We will now use super resolution microscopy techniques to study RNase Y foci formation and its potential regulation by the regulatory proteins YaaT, YlbF and YmcA *in vivo* and analyse their role on RNase Y activity *in vitro*.

Keywords: Endoribonucleases, dynamics, TIRF microscopy, localization, membrane.

References

1. Initiation of mRNA decay in bacteria. Laalami S., L. Zig & H. Putzer. Cell Mol Life Sci. 2014 May; 71(10):1799-828.
2. Functional analysis of 11 putative essential genes in *Bacillus subtilis*. Hunt A., J.P. Rawlins, H.B. Thomaidis & J. Errington. Microbiology. 2006 Oct; 152(Pt 10):2895-907.
3. The RNase E of *Escherichia coli* is a membrane-binding protein. Khemici V., L. Poljak, B.F. Luisi, A.J. Carpousis. Mol Microbiol. 2008 Nov; 70(4):799-813
4. Membrane recognition and dynamics of the RNA degradosome. Strahl H., C. Turlan, S. Khalid, P.J. Bond, J.M. Kebalo, P. Peyron, L. Poljak, M. Bouvier, L. Hamoen, B.F. Luisi, A.J. Carpousis. PLoS Genet. 2015 Feb 3; 11(2):e1004961.
5. Biofilm formation by *Bacillus subtilis* requires an endoribonuclease-containing multisubunit complex that controls mRNA levels for the matrix gene repressor SinR. DeLoughery A., V. Dengler, Y. Chai & R. Losick. Mol Microbiol. 2016 Jan; 99(2):425-37.

Aberrant mRNA decay analysis in *Saccharomyces cerevisiae*

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Abstract

Messenger RNAs are susceptible to chemically induced defects such as reactive oxygen species (ROS), ultraviolet light or alkylating agents. For instance, it has been known that oxidation of RNAs can be promoted by mitochondrial dysfunction and recent studies in humans have suggested a correlation between high levels of RNA oxidation and age-related neurodegenerative disorders¹.

Oxidation can result in mRNA strand breaks, abasic sites or modified nucleobases. All forms of damaged RNAs can stall the translational machinery, which is detrimental to cell viability. A ribosome-based-quality-control process, called NO-GO decay, ensures that aberrant transcripts, such as truncated mRNAs or mRNAs having abasic sites, are quickly targeted for degradation in order to prevent another round of translation². Dissociation of ribosomes, nascent peptide degradation and mRNA degradation have been shown to contribute to this surveillance, but full comprehension of this regulation is far from being complete. For example, despite the fact that factors involved in the 5'-3' or 3'-5' mRNA degradation pathway are known to function in this process, an unknown endonucleolytic activity remains to be characterized³.

Our first aim is to fully characterize the factors involved in the degradation of these aberrant mRNAs and then to analyze their importance under cellular insults, such as oxidative damage by ROS upon mitochondrial dysfunction. The characterization of the factors cleaving these mRNAs has been an unresolved mystery for these last ten years, but we have recently developed new tools that we hope will allow us to go further towards an understanding of the sequence of events that lead to the destruction of damaged mRNAs. Using *S. cerevisiae* as a model organism, we will employ different genetic approaches or biochemical specific tools such as promiscuous biotinylation of neighbouring proteins to identify specific transient factors acting in the vicinity of stalled ribosomes

Keywords: RNA, RNA degradation, No-Go Decay, *Saccharomyces cerevisiae*.

References

1. Qiongman K., Chien-liang G.L. (2010) - Oxidative damage to RNA : mechanisms, consequences and diseases. *Cell Mol Life Sci.* ; 67(11): 1817–1829
2. Simms C, Hudson B, Mosior J, Rangwala A, Zaher S. (2014) - An Active Role for the Ribosome in Determining the Fate of Oxidized Mrna - *Cell Reports* 9, 1256–1264
3. Tsuboi T, Kuroha K, Kudo K, Makino S, Inoue E, Kashima I, Inada T.(2012) - Dom34:hbs1 plays a general role in quality-control systems by dissociation of a stalled ribosome at the 3' end of aberrant mRNA. *Mol Cell.* 25;46(4):518-29.

Characterisation of the quality control link between tRNA maturation and ribosome assembly in

Bacillus subtilis.

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Abstract

Ribosomes are large essential RNA and protein complexes in charge of protein synthesis in the cell. In rapidly growing cells, the biosynthesis of ribosomes accounts for most of cellular transcription and consumes a major portion of the cell's energy. Mistakes in ribosome assembly are therefore not tolerated and cells have active surveillance methods to rapidly degrade misassembled ribosomes.

Our team has identified a very intriguing link between transfer RNA (tRNA) processing by RNase P and ribosome biogenesis in the Gram-positive model organism *Bacillus subtilis*.

RNase P is an essential ribonucleoprotein – conserved through the three kingdoms of life – responsible for 5' tRNA processing. Surprisingly, depletion of RNase P leads to a defect in the 3' processing of 16S rRNA and to a strong 30S assembly defect that affects particularly the late steps of ribosome assembly. 16S rRNA maturation is believed to occur at the very last step of ribosome assembly and to act as a quality control check of assembled particles. Indeed, our experiments indicate that RNase P is not directly involved in 16S rRNA processing and that the 16S rRNA maturation defect is rather the consequence of the 30S ribosome assembly defect.

In order to characterize the mechanism involved we looked by northern blot at the expression of different ribosome assembly cofactors in cells depleted for RNase P. We observed that depletion of RNase P reduces sharply the amount of mRNAs of the RimM ribosome maturation factor and leads to a stabilization of transcripts encoding GTPases Era and YqeH. Late results suggest that reduction of RimM expression alone cannot explain the ribosome assembly defect. We are currently testing if overexpression of GTPases could poison 30S ribosomal assembly.

Additionally, we discovered that depletion of RNase Z (one of the tRNA 3' maturation enzymes) leads to a similar defect in late ribosomal assembly of the 30S. Therefore, observed defects seem to be a consequence of immature tRNA accumulation. These results made us consider the possible involvement of stringent response in the observed defect. Indeed, uncharged tRNAs present at the A site of the ribosome are known to trigger (p)ppGpp production by RelA¹, however the effect of immature tRNA on stringent response induction is still unknown. Moreover, (p)ppGpp has been shown recently to inhibit GTPases². Late results suggest that RNase Z or RNase P depletion could trigger stringent response, so we are now investigating the amount of (p)ppGpp produced and its role in the observed defects.

Keywords: tRNA maturation, ribosome assembly, rRNA maturation, stringent response.

References

¹ Potrykus, K., & Cashel, M. (2008). (p) ppGpp: still magical?. *Annual review of microbiology*, 62.

² Corrigan, R. M., Bellows, L. E., Wood, A., & Gründling, A. (2016). ppGpp negatively impacts ribosome assembly affecting growth and antimicrobial tolerance in Gram-positive bacteria. *Proceedings of the National Academy of Sciences*, 113(12), E1710-E1719.

A mutagenesis study of specific mRNA/protein interactions in the chloroplast of *Chlamydomonas reinhardtii*.

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Abstract

The chloroplast has evolved from a cyanobacterium which was absorbed by an ancestral eukaryotic cell. During this endosymbiotic evolution, many redundant plastidial genes were lost and others were transferred to the nucleus. But the chloroplast of *Chlamydomonas reinhardtii* still retains roughly 100 genes. The various sub-units of photosynthetic complexes are encoded in part in the nucleus, in part in the plastidial genome. To achieve their correct assembly, the expression of the two genomes needs to be coordinated. Organellar trans-acting factors (OTAF), encoded in the nucleus, are proteins which can bind specifically to an organellar mRNA and act upon it. Among those OTAF, the octotricopeptide repeat (OPR) family is abundant in green algae. The OPR is a degenerate motif of 38 amino-acids, folding into a tandem of antiparallel α -helices which can bind to RNA. An individual OPR is predicted to interact with one specific nucleotide thanks to specificity-conferring residues at defined positions within the repeat.

The aim of my project is to study this recognition mechanism, called the "OPR code". A first version of this "OPR code" was first theorised in our laboratory, using known OPR protein/mRNA couples. To confirm and build on it, I proceed in vivo, by mutating the chloroplastic targets of OPR factors to disrupt the binding, and then try to restore the OPR protein/mRNA interaction by mutating the specific residues in the corresponding OPR. A reliable code would enable the study of the many OPR factors of unknown target; help to better understand their role, in particular at the translational level. It could also be potentially used to design and build proteins able to interact with specific RNA.

Keywords: protein/mRNA interactions, chloroplast, *Chlamydomonas reinhardtii*, mRNA stability.

Structure, what else?

- **Stephanie OERUM**
Structural characterisation of RNase M5: insights into 5S rRNA binding
- **Stepan TIMR**
Multi-scale modeling of protein diffusion and stability in crowded environments
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UnityMol X, a software framework for intuitive and immersive molecular visualization

Structural characterisation of RNase M5: insights into 5S rRNA binding

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Abstract

In *E. coli*, the immediate precursor (pre) of 5S ribosomal RNA (rRNA) is cleaved by RNase E to yield the mature 5S rRNA. In many low G+C gram-positive bacteria, this cleavage is instead performed by RNase M5^{1,2}. The activity of RNase M5 is dependent on the small, ribosomal protein L18 that binds to the pre-5S rRNA prior to cleavage by RNase M5^{1,3}. The role of L18 in this reaction is yet unknown, but it is thought to induce conformational changes in the RNA to allow cleavage by RNase M5⁴. Structures are available for L18 alone or in complex with 5S rRNA, but no structural data are available for RNase M5 and little is known about its interaction with 5S rRNA. Here, we present a 1.3 Å and 1.5 Å resolution X-ray crystal structures of the N- and C-terminal domains of RNase M5, respectively, and model a full-length structure guided by low resolution Small-Angle X-ray Scattering (SAXS) data. Interestingly, the C-terminal domain resembles a known protein-protein interaction domain, but in RNase M5 this domain functions as a protein-RNA interaction domain. Guided by the crystal structures and NMR data, we map the interaction with the 5S rRNA, which involves both of the protein domains. We further investigate the role of L18 in this binding and find an increased affinity of RNase M5 full-length and fragments towards 5S rRNA in the presence of L18. We are currently running crystallisation trials for the full complex of RNase M5:L18:5S rRNA, to gain further insights into the role of L18 and the mechanism utilised by RNase M5 in the cleavage of 5S rRNA.

Keywords: RNase M5, 5S rRNA, X-ray crystallography, SAXS, protein-RNA.

References

¹Sogin, M. L. & Pace, N. R. *Nature* **252**, 598–600 (1974).

²Condon, C., Brechemier-Baey, D., Beltchev, B., Grunberg-Manago, M. & Putzer, H. *RNA* **7**, 242–53 (2001).

³Stahl, D. A., Pace, B., Marsh, T. & Pace, N. R. *J. Biol. Chem.* **259**, 11448–11453 (1984).

⁴Pace, B., Stahl, D. A. & Pace, N. R. *J. Biol. Chem.* **259**, 11454–11458 (1984).

Multi-scale modeling of protein diffusion and stability in crowded environments

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Abstract

In living cells, proteins operate in a highly crowded environment where up to 30% of the volume is filled by macromolecules. Despite intensive research, the effect of macromolecular crowding on protein mobility, stability, and ultimately function is far from clear.¹ The lack of understanding calls for detailed insights from computer simulations; however, current simulation approaches are seriously challenged by the wide spread of time- and length scales involved in crowding. Our novel multi-scale scheme, combining lattice Boltzmann molecular dynamics² with all-atom replica exchange simulations,³ bridges the gap between the existing simulation techniques and opens the way for large-scale simulations of the cellular interior.

To give a concrete example illustrating our computational approach, we will first focus on the unfolding of superoxide dismutase 1 (SOD1). This process has been implicated in amyotrophic lateral sclerosis, a lethal disease affecting motor neurons.⁴ We will present atomistic insights into how the thermal stability of SOD1 and its conformational states are affected by a crowded environment mimicking the crowding state of the cytoplasm. As a second example, we will report on one of the first detailed computational models of a biological nanoreactor, represented by a lipid vesicle filled with enzymes (α -chymotrypsin), substrates, and crowding agents. This large-scale model allows us to explore the combined effect of crowding and confinement on enzyme diffusion and enzyme–substrate encounter rates, marking an important step toward molecular simulation of whole cellular organelles.

Keywords: macromolecular crowding, diffusion, protein thermal stability, confinement, multi-scale simulations

References

- ¹ Gershenson A, Gierasch L M (2011) Protein Folding in the Cell: Challenges and Progress. *Curr Opin Struct Biol* 21: 32–41
- ² Sterpone F, Derreumaux P, Melchionna S (2015) Protein Simulations in Fluids: Coupling the OPEP Coarse-Grained Force Field with Hydrodynamics. *J Chem Theory Comput* 11: 1843-1853
- ³ Stirnemann G, Sterpone F (2015) Recovering Protein Thermal Stability Using All-Atom Hamiltonian Replica-Exchange Simulations in Explicit Solvent. *J Chem Theory Comput* 11: 5573-5577
- ⁴ Redler RL, Dokholyan NV. (2012) The Complex Molecular Biology of Amyotrophic Lateral Sclerosis (ALS). In *Molecular Biology of Neurodegenerative Diseases*, Teplow DB (ed) pp 215-262.

Molecular bases of mitochondrial uncoupling protein 1 induced thermogenesis.

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Uncoupling protein 1 (UCP1) is found in the inner mitochondrial membrane of brown adipocyte and belongs to the mitochondrial carrier family (SLC25). In the presence of long-chain fatty acids (LCFA), UCP1 increases the H⁺ conductance to 'short-circuit' the proton-motive force, which, in turn, increases fatty acid oxidation and energy release as heat. The precise location of the LCFA binding site(s) and proton conductance pathway in UCP1 have not been determined. Different models of UCP1 and UCP2 have been obtained by NMR in dodecylphosphocholine (DPC) and Zhao *et al.* proposed that K56 and K269 are crucial for LCFA binding and UCP1 activation in proteoliposomes [1]. However DPC has been shown to inactivate UCP1 [2]. Therefore we revisited those mutants in a mitochondrial environment using a robust expression system previously validated for UCP1 function. Wild type UCP1 and four mutants (R54S, K56S, K269S and K56S/K269S) were expressed in *S. cerevisiae* and mitochondrial respiration was assayed on permeabilized spheroplast. In contrast to Zhao *et al.*, all four mutants could be activated by lauric acid and inhibited by ATP similarly to the wild type protein. To address the identification of the fatty acid binding site in UCP1, we have synthesized LCFA based ligands functionalized with active probes and tested their ability to activate UCP1 in yeast mitochondria. We used β -lactoglobulin as a template to optimize crosslinking conditions either in solution or in crystals. Crosslinking experiments on UCP1 are under progress.

Keywords: Uncoupling proteins / Mitochondrial Respiration / Mutagenesis / Fatty Acid Crosslinking

1. L. Zhao, S. Wang, Q. Zhu, B. Wu, Z. Liu, B. OuYang, J.J. Chou, **Specific Interaction of the Human Mitochondrial Uncoupling Protein 1 with Free Long-Chain Fatty Acid**, *Structure* 25 (2017) 1–9

2. M. Zoonens, J. Comer, S. Masscheleyn, E. Pebay-Peyroula, C. Chipot, B. Miroux, F. Dehez, **Dangerous Liaisons between Detergents and Membrane Proteins. The Case of Mitochondrial Uncoupling Protein 2**, *J. Am. Chem. Soc.* 135 (2013) 15174–15182

UnityMol X, a software platform for immersive molecular visualization

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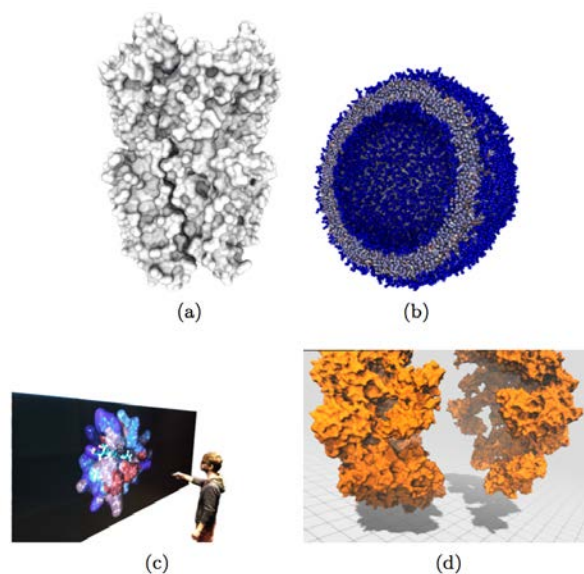
Abstract

Macromolecules have complex and dynamical three-dimensional structures tightly related to their biological function. Thus, the visual exploration of these structures plays a central role in biology and chemistry.

UnityMol provides a software framework to efficiently display structural molecular information and easily add new types of visual representations. Several examples of novel molecular representations can now be found in UnityMol, such as specific sugar representations², HiRE-RNA¹, OPEP or Martini coarse grain model representations for various molecule classes such as lipids and proteins used in molecular dynamics simulations.

UnityMol is based on a popular game engine named Unity3D, offering advanced rendering effects (like ambient occlusion, high-quality dynamic shadows,...) and easing the integration of advanced features like guided navigation. This software is also used to perform scientific research in human-computer interaction, or to design educational tools to teach biochemistry. Specific developments for the IBPC wall-sized display were also carried out.

Recent developments opened the way to immersive exploration of molecular data with virtual reality (VR) and augmented reality (AR) headsets, allowing to experience interactive molecular dynamics simulations with a rich interaction experience. Indeed, the innovative side of the UnityMol software lead to international collaborations both in public laboratories (Stanford University, Utrecht University) and companies (UCB BioPharma). We are currently working on a re-implementation using modern programming paradigms and benefiting from recent advances in visualization. In the near future, we hope UnityMol will provide a unique platform to explore and analyze molecular systems in a multi-user context.



Keywords: Molecular visualization, Virtual Reality, software framework, immersive exploration, 3D interaction

References

¹ Sébastien Doutreligne, Tristan Cragnolini, Samuela Pasquali, Philippe Derreumaux, and Marc Baaden. Unitymol: Interactive scientific visualization for integrative biology. In Large Data Analysis and Visualization (LDAV), 2014 IEEE 4th Symposium on, pages 109–110. IEEE, 2014.

² Serge Pérez, Thibault Tubiana, Anne Imbert, and Marc Baaden. Three-dimensional representations of complex carbohydrates and polysaccharides, sweetunitymol: A video game-based computer graphic software. *Glycobiology*, 25(5):483–491, 2014.

Conférence Edmond de Rothschild

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