The Schrödinger KNIME extensions

Computational Chemistry and Cheminformatics in a workflow environment

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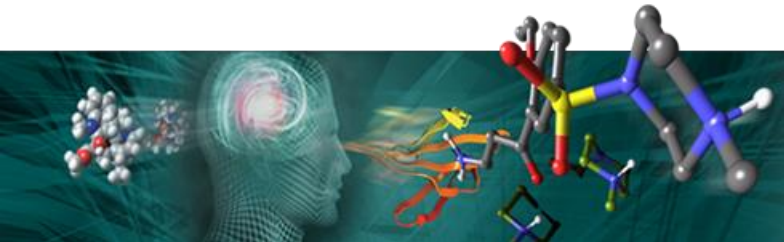
Volker Eyrich

KNIME UGM, Berlin, February 2015



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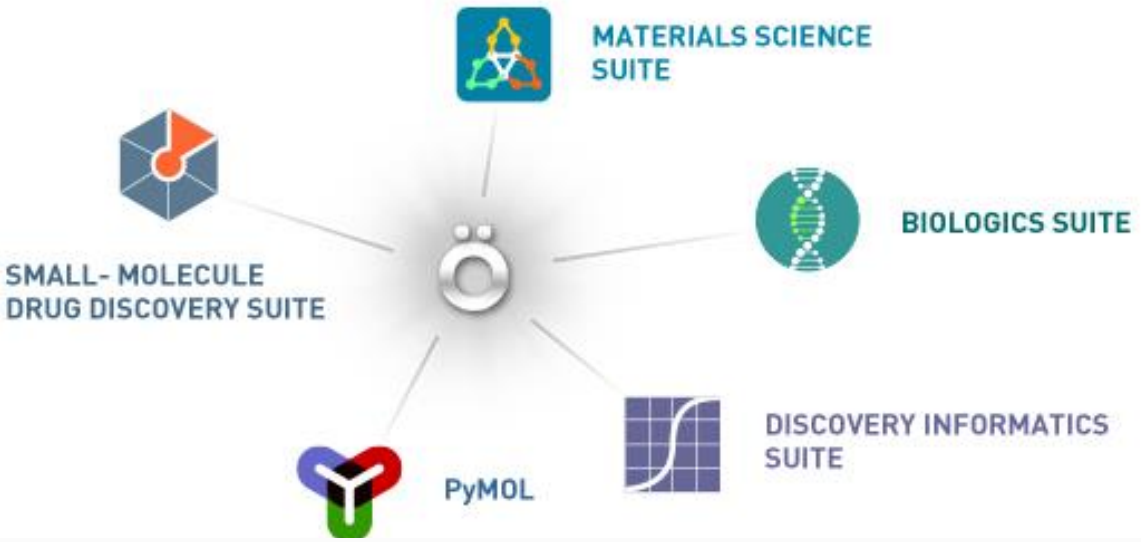
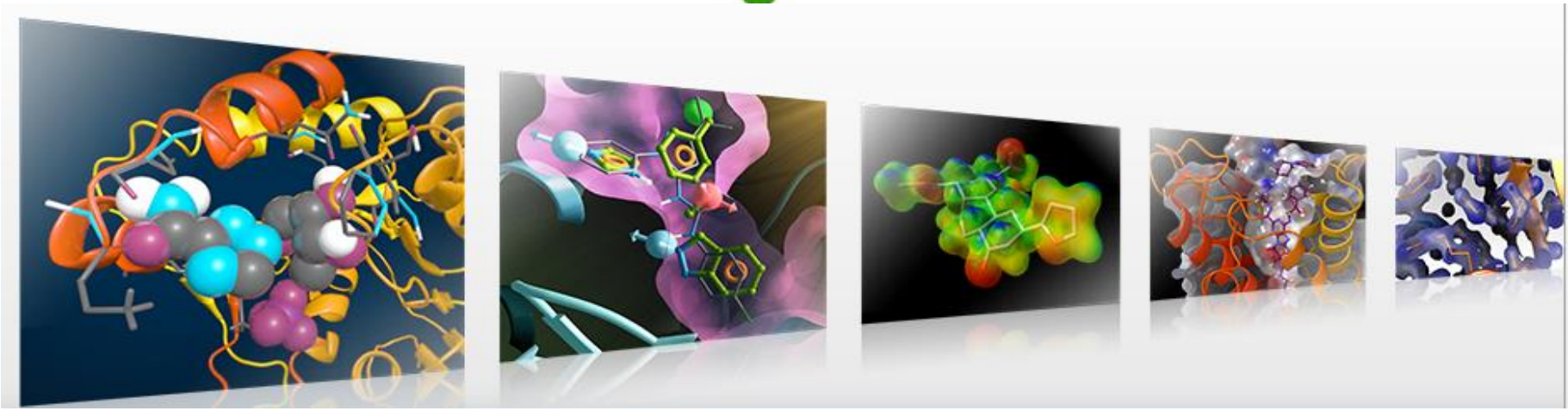
The Schrödinger Extensions

- **Computational chemistry and drug design**
- **150+ nodes**





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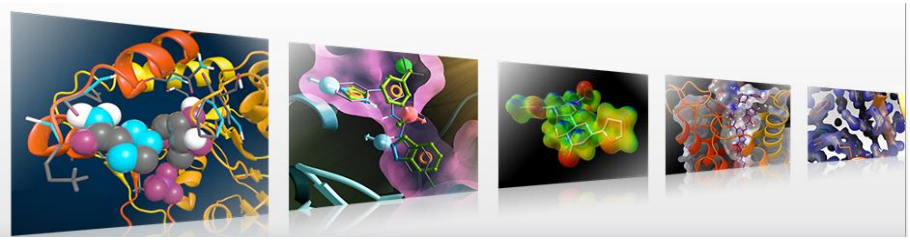
The Schrödinger Extensions

- **Computational chemistry and drug design**
- **150+ nodes**
  Linux, Mac, Windows 32 and 64 bit



- **Maestro integration**
  - Workflow execution
  - Structure exchange
- **Infrastructure**
  - Simpler batch execution
    Integration in Seurat and Live Design
  - Plugin installation automation

Molecular Mechanics – Macromodel
Molecular Dynamics – Desmond
Quantum Mechanics – Jaguar

Cheminformatics – Canvas
Pharmacophore modeling – Phase
Combinatorial Libraries – Combiglide

Docking – Glide
Protein Structure Prediction – Prime, IFD

Protein preparation – PPrep wizard
Ligand preparation – LigPrep, Epik
Property generation – Qikprop ...
Filtering

Data and structure manipulation
Scripting – shell, Python
Reporting – Run Maestro, Run PyMOL…

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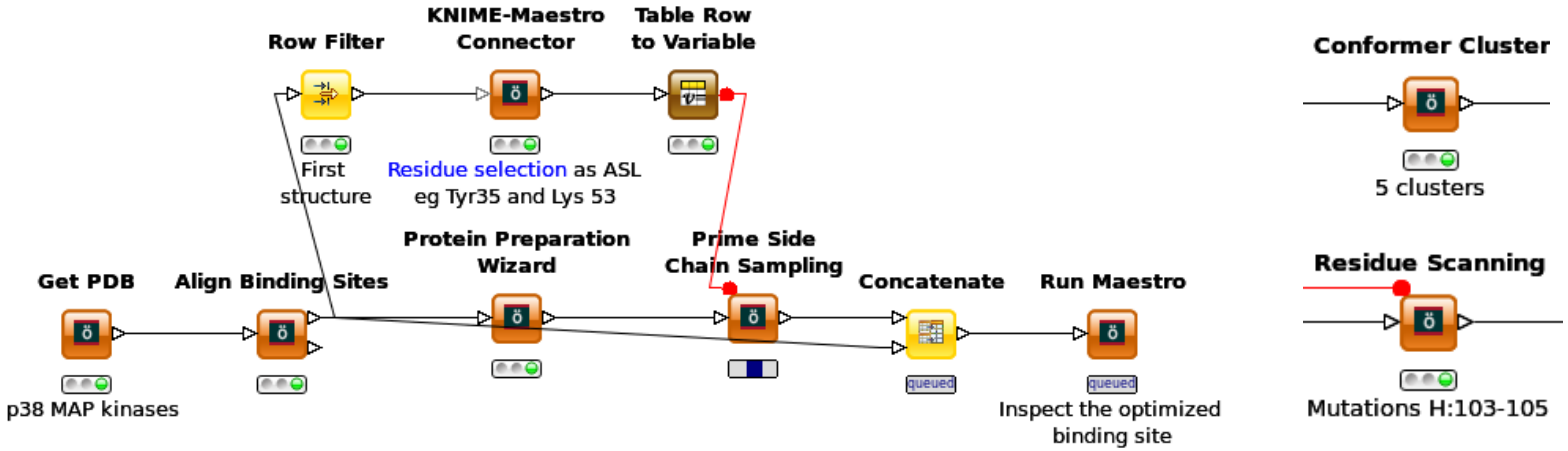
New Features and Free Nodes

- Free nodes
  - Will be part of the community contributions soon
    http://www.schrodinger.com/SchrodingerKNIMEFreeNodes
  - Free Maestro (all academic users) http://www.schrodinger.com/freemaestro
- New features:

  http://www.schrodinger.com/knimeworkflows/KNIME_newfeatures.pdf



- 50+ workflow examples on the Workflow page:

  http://www.schrodinger.com/knimeworkflows

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KNIME Workflow Page

Cheminformatics

- Substructure Search
- Clustering, diversity selection, similarity search
- Database analysis, MCS

Docking and post-processing

- Binding site (SiteMap, grid generation)
- Docking, Virtual screening, Ensemble docking
- Loop over docking parameters
- Validate docking parameters (using the Maestro connector node) ◄

Pharmacophore modeling

- Phase Shape screening , hypothesis identification and database screening

Molecular Mechanics

- Compare conformational search methods
- Conformational search ◄

Quantum mechanics

- ESP charges, Jaguar pKa, QM properties, Semiempirical
- Conformational search and QM refinement (using the Report designer)

Molecular Dynamics:

- Desmond simulation

Library design:

- Library enumeration

Protein design

- Split and align multimers
- Model building and refinement
- Induced Fit Docking
- Bioluminate

Real World Examples

- Vendor database preparation
- SiteMap and docking
- Binding site shape clustering
- Protein model building
- Co-crystallized ligand docking

Labs: Parameter flow variables

General tools

- Python script, Chemistry external tool, Run maestro command node use-cases…
- Run PyMOL
- Workflows/nodes in the current workspace
- KNIME-Maestro connector ◄
- Installation update/creation
- Batch execution

KNIME desktop: GroupBy, loop examples …

Simple examples: Epik, conformer cluster

Simplest, most exciting, new and improved◄ workflows

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Workshop on Friday

- Co-crystallized ligand redocking

  Derived from the work published by Paulette Greenidge from Novartis:

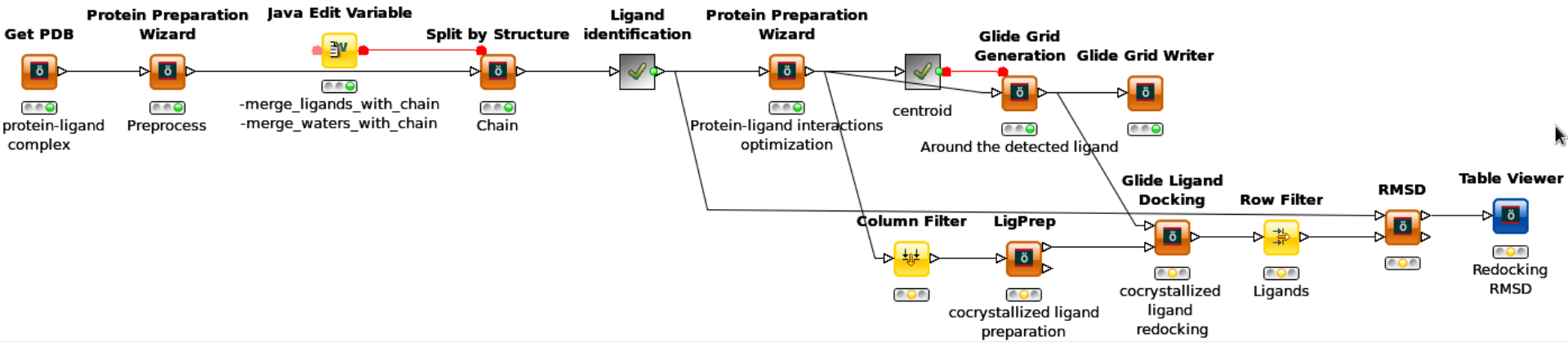
  Improving Docking Results via Reranking of Ensembles of Ligand Poses in Multiple X-ray Protein Conformations with MM-GBSA. PA Greenidge, C Kramer, JC Mozziconacci, W Sherman J Chem Inf Model. 2014, 54 (10), 2697-717

  MM/GBSA binding energy prediction on the PDBbind data set: Successes, failures, and directions for further improvement . PA Greenidge, C Kramer, JC Mozziconacci, RM Wolf J Chem Inf Model. 2013, 53 (1), 201-9

- New features: KNIME-Maestro connector node, Conformer cluster...

ftp://ftp.schrodinger.com/support/hidden/jcmozzic/BerlinUGM.zip

ftp://ftp.schrodinger.com/support/hidden/jcmozzic/BerlinUGMnoData.zip



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Schrodinger KNIME extensions

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Ravikiran Kuppuraj	Main developer
Matt Wirtala, Simon Foucher	QA
Daniel Schafer,	Technical support
Jeff Saunders and Pavel Golubkov	
Jarred Yacob	Marketing
Schrödinger Developers	

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Schrödinger nodes

- **150+ nodes covering the whole Schrodinger Suite**
- **Run on Linux, Mac and Windows 32 and 64 bit versions**

Molecular Mechanics
- MacroModel Single Point Energy, Minimization, Coordinate Scan
- ConfGen
- Conformational Search
- Premin, Impref, Uffmin

Quantum Mechanics
- Jaguar Single Point Energy, Minimization
- NMR Shielding Constants
- Jaguar Charges

Molecular Dynamics
- Desmond System builder
- Desmond Molecular Dynamics
- Trajectory extract frames and manipulation
- Trajectory reader, CMS reader

Cheminformatics

Fingerprint Based Tools
- Fingerprint Generation
- Generate Pairwise Matrix
- Similarity Matrix
- Dissimilarity Selection
- Build Report and Hierarchical Clustering

Filters and Mining Tools
- MCS
- Substructure Search
- Structure, REOS Filters

Utilities and Converters
- PCA, MDS
- Combine Fingerprints, Concatenate Bitvectors, Convert Fingerprint to Bitvector, etc

Modeling
- Bayes Model Building, prediction
- PLS Model Building, Prediction

Pharmacophore Modeling
- Phase Shape
- Phase DB Query, File Query
- Phase DB Creation
- Phase Hypothesis Identification

Combinatorial Libraries
- CombiGlide Reagent Preparation and Library Enumeration
- Fragments from Molecules and joiner

Docking and Scoring
- Glide Grid Generation
- Glide Ligand Docking, Ensemble Docking
- XP Visualizer

Post-processing
- Prime MM-GBSA
- Embrace Minimization
- Strain Rescore, Pose Entropy
- Pose Filter, Glide Merge, Sort Results
- Glide Ensemble Merge

Protein Structure Prediction
- BLAST
- Prime Energy
- Prime Build Homology Model
- Prime Side Chain Sampling, Minimization
- IFD and individual steps

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Schrödinger nodes

Protein Preparation
- Protein Preparation Wizard
- Protein Assignment

Ligand Preparation
- LigPrep and the individual steps
- Epik

Property Generation
- QikProp, Molecular Descriptors
- Canvas descriptors

Filtering
- Ligfilter, Ligparse, Propfilter

Scripting
- Run Maestro Command
- Chemistry External tool node
- Python Script nodes

Reporting
- Run Maestro, Run PyMOL, Run Canvas
- KNIME-Maestro connector
- Table viewer, Spreadsheet viewer

Tools
- SiteMap
- **Residue scanning/affinity maturation**
- **Conformer cluster**
- Workflow list
- Setup diagnosis

Data Manipulation
- Compare Ligands
- Lookup and Add Columns
- Group and Ungroup MAE

Structure Manipulation
- Add Hydrogens
- Delete Atoms
- Split by Structure
- MAE atom/bond property Parser
- Extract, Set and Delete MAE Properties
- Set Molecule Title, MAE Index

Utilities
- Get PDB
- Align Binding Sites
- Protein Structure Alignment
- RMSD
- Assign Bond Orders
- Unique Title Check
- Check PDB Name
- SD Format Checker
- Generate Smarts, Unique Smiles
- RRHO Entropy
- Boltzmann Population
- Volume Overlap Matrix

Readers/Writers
- CSV Reader (several inputs)
- Molecule Reader and Writer
- SD, PDB, Mol2 Reader nodes
- Sequence, Alignment Readers and Writers
- Fingerprint Reader and Writer
- Hypothesis Reader and Writer
- Glide Grid Reader and Writer
- Variable Based Glide Grid Reader

Converters
- String-to-Type
- Molecule-to-MAE, MAE-to-Pdb, to-SD, to-Smiles and to-Mol2, SD-to-Smiles
- PoseViewer-to-Complexes and Complexes-to-PoseViewers
- Hartree-to-kcal/mol and kJ-to-kcal

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