

Welcome to the 20th edition of the BioSolveIT newsletter!

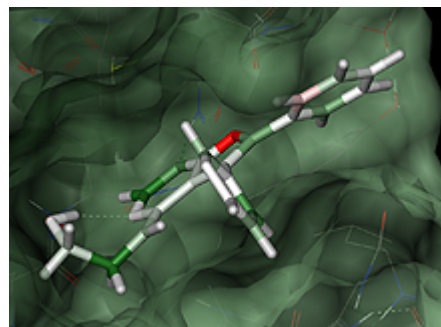
In our newsletter we publish information about new developments, events, milestones, and scientific facts on a quarterly basis.

[Mr. Screening and Dr. *Hyde*: the revolution in binding affinity assessment!](#)

With the advent of *LeadIT* 2.0 came a revolution in binding affinity prediction: *Hyde* Scoring. This radically new scoring function is based on pure physical principles: the hydrogen bond energy and the hydrophobic effect are both implemented in a consistent way via atomic *logP* increments.

The distinctly new approach in *Hyde* is the heavy penalization of unmet interactions: A hydrogen bond taken out of the solvent - and not having an ideal partner in the protein; or the phenyl ring that is dehydrated and put into a hydrophilic active site region. Thus, not by rewarding H-bonds but by penalizing unfavorable situations, false positives are effectively ruled out in an *in silico* screen.

A *Hyde* assessment provides the user with an estimated free energy of binding. Additionally, an intuitive color coding of the atoms reveals access points for molecular optimization: Red atoms convey unfavorable contributions to binding, green atoms correspond to favorable contributions. Thus, immediate remedy can be established by modifying the structure and re-assessing it.



Hyde aims at helping teams of MedChems and Comp-Chems to decide which molecules to further pursue in a synthesis; also you could rank a series of compounds regarding their score. More application fields could be the refinement of crystal structures, or checking the effects of molecular variations on antibiotics resistances.

Of course, *Hyde* is streamlined into the *LeadIT* GUI and can be accessed through *FlexX* and *ReCore*, respectively by a mouse-click.

Have examples, pictures, and more on the [Hyde website](#).

[KNIME® nodes revised and extended](#)

Visual programming environments become more and more popular in life sciences and in cheminformatics. As a [Partner of KNIME®](#) BioSolveIT supports this trend by providing interface nodes to all its major software tools.

We now have *KNIME®* nodes for the following scenarios:

- searching through compound libraries and Fragment Spaces with our fuzzy similarity engine *FTrees*
- docking with *FlexX*
- aligning molecules in 3D with *FlexS*

This suite of tools is completed by a few auxiliary tools like a very comfortable interactive table that visualizes *FTrees* mappings and allows interactive sorting and filtering, a 3D viewer to browse through sets of *FlexS* alignments, and a really fast engine to convert standard molecular and graphic formats.

The 2D drawing engine which can also be used as renderer within **KNIME**[®] is based on the latest 2D drawing technology from the [Center for Bioinformatics in Hamburg \(ZBH\)](#).



KNIME[®] nodes will soon get the certification stamp from **KNIME**[®]. Please obtain more details from our [KNIME](#)[®] website.

A final touch of usability rounds up the new generation of our **KNIME**[®] nodes:

There are new, separate installation packages for all binaries that install all required software out of the box. The easy update mechanism that was introduced into **KNIME**[®] with Version 2.3.0 is now supported. And finally, all functionality is also available on the **KNIME**[®] cluster and integrates seamlessly into **KNIME**[®]'s reporting facilities. These were the last preparative steps before the BioSolveIT

96% redocking success rate? No problem! _____

BioSolveIT visited this Spring's ACS Meeting in beautiful Anaheim, CA. The sky was wonderfully blue and there were several talks dedicated to the science around BioSolveIT's software portfolio. Nadine Schneider from the Rarey-group at the University of Hamburg contributed her work about **Hyde**'s revolutionary **visual binding** to the Docking and Scoring session organized by Greg Warren, Openeye, and Neysa Nevins, GSK.

Her [excellent slides](#) revealed that a re-docking of all structures from the provided dataset with **FlexX** followed by a re-scoring with **Hyde** brought 86% of the complexes under 2Å RMSD if only the top-ranking pose was considered. Taking the best out of the first 32 docked poses pushed that score even over the 96% line. In a remarkable 85% of those cases a solution under 1Å RMSD could even be found.

Carsten Detering talked about how the chemical universe can be conquered more efficiently by incorporating chemical synthesis into creating a giant combinatorial chemistry space. In this context, giant means traditionally intractable numbers of $>10^9$ molecules. Without ever enumerating the fragments to compounds, **FTrees-FS** can search directly in the fragment space for compounds similar to one or more given queries. Find the talk [here](#).

This possibility was also addressed in a talk co-authored by Warren Wade of BioBlocks and Christian Lemmen, CEO of BioSolveIT. "With this method, we can virtually search the Syntheverse. The user gets hits from an **FTrees-FS** search, and these hits can directly be synthesized according to BioBlocks' building blocks and reaction protocols", says Christian. "Everything possible from BioBlocks' pool of reactions is virtually accessible, and ultimately in reality as well." Even considering only two reactions, access is given to numbers of compounds in the millions. With the inclusion of more reactions, this number can easily be pushed into the billions or trillions. Please find the slides [here](#).

Carsten gave a second talk about **LeadIT/ReCore**'s ability to strengthen teams of MedChems and CompChems due to its interactivity and intuitive GUI design. Find out more about the software [here](#); the talk can be downloaded [here](#).

BioSolveIT participated again in the session "Challenges in Industrial Computational Methods". There was a wealth of interesting and stimulating talks, e.g. by Dominic Ryan, Terry Stouch, or Vijay Pande, followed by intensive discussions about various topics of scientific software applications in the industry and in academic institutions. In this session, Christian Lemmen talked further about the new **Hyde** ligand binding assessment: "[Hyde: Scoring for lead optimization](#)".

BioSolveIT's webinar series: sit back, relax, enjoy success _____

Since the first release of **LeadIT** by the beginning of 2010, BioSolveIT has successfully made use of a modern means of communication: webinars. A BioSolveIT webinar allows 14 people concurrent access to a high-quality presentation about BioSolveIT's state-of-the-art software

products. The webinars are usually separated into a short presentation (about 20-25 minutes) and a live demo, during which questions from the audience guarantee an interactive experience. After the webinars, each participant receives a demo license of the presented product. On this basis, the avid researcher can try out the examples of the webinar or select his/her own brain teasers to solve. Upcoming webinars will cover the new **Hyde** binding affinity assessment. Check our web site for dates or simply [send us specific requests](#).

tips & tricks: **Hyde** ligand affinity assessment

In this Newsletters' tips'n'tricks section we will showcase the novel ligand binding affinity assessment **Hyde**. [Read more!](#)

You can view previous topics of tips'n'tricks [here](#). If you have any questions or know of any tip-s'n'tricks yourself that you would like to share with the BioSolveIT user community, we would appreciate your input at support@BioSolveIT.de.

BioSolveIT news in brief

- During the last Fall ACS Meeting in Boston we tried something new - and hopefully of interest for you: We conducted an interview with Mr. Rule-of-Five, **Dr. Chris Lipinski**. The interview covers about 30 questions from current topics in the pharmaceutical industry, such as improving research through team building, outsourcing, virtual chemistry and other relevant topics to the industry. The reason for discovery of the Rule-of-Five was - as Chris claims - "scientific fooling around" with a novel statistical software package he had discovered. It was merely a matter of about two hours to get the data together, but he also claims he would have never discovered it if he hadn't had time in his office alone. Watch the full interview [here](#).
- PoseView** is a radically new 2D drawing engine for protein-ligand complexes. This great software facilitates grasping binding of a ligand to protein cavity and was developed by Katrin Stierand in the research group of Matthias Rarey in [Hamburg](#). The difference to other drawing tools is that it is atom based, i.e. each interaction is resolved down to the interacting atoms.
PoseView has lately been used to generate a 2D image of the vast majority of protein-ligand complexes in the [RCSB PDB](#).
- Dates for your diary:** BioSolveIT will be present at the following events:

May 26	UK-QSAR and Cheminformatics Group Spring Meeting , Manchester, UK
June 5 - 9	9. International Conference on Chemical Structures , Noordwijkerhout, NL There will also be a workshop hosted by BioSolveIT covering the new Medicinal Chemistry Toolkit. This workshop will take place Sunday, June 5 2011, prior to the ICCS conference. There are only a few seats left, so save your spot in the high quality and free of charge workshop .
August 28 - September 01	242nd ACS National Meeting & Exposition , Denver, CO, USA Please check our web site for abstracts of talks.

If you would like to meet one of our representatives to discuss any questions or have any kind of feedback please email us at Contact@BioSolveIT.de.

literature corner

- Reducing Docking Score Variations Arising from Input Differences**
Miklos Feher and Christopher I. Williams
J. Chem. Inf. Model., 2010, 50 (9), pp 1549-1560
[details here](#)

- Three-Dimensional Pharmacophore Modeling of Liver-X Receptor Agonists**
Wenxia Zhao, Qiong Gu, Ling Wang, Hu Ge, Jiabo, Li, and Jun Xu
J. Chem. Inf. Model., Article ASAP
[details here](#)

upcoming articles

- HYDE protein-ligand complex scoring
- KNIME**[®] nodes

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