

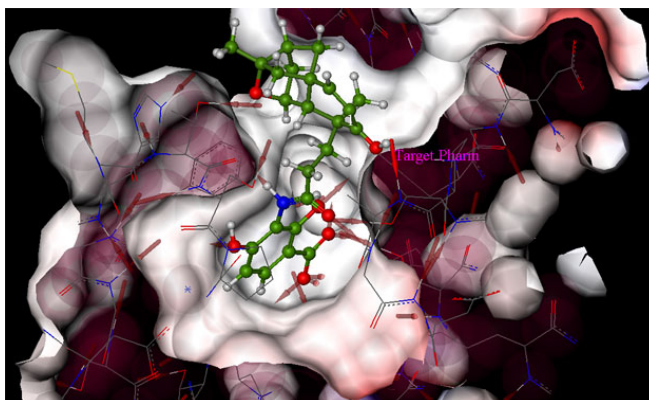
Welcome to the 18<sup>th</sup> edition of the BioSolveIT newsletter!

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

### [LeadIT simply clicks with FBDD and SBDD](#)

BioSolveIT GmbH is pleased to announce the release of *LeadIT*, a powerful, new, aggressively easy to use platform for FBDD and SBDD. The team building software is a computational fusion of bioisosteric replacement, fragment evolution, merging and growing fragments, and traditional protein-ligand docking. *LeadIT* redefines the current state of the art in modeling software interface design and re-invents user interaction. Creating a slide show of novel, synthetically accessible chemical ideas in seconds couldn't be easier. Stimulate medicinal chemists' minds with an investment of literally only 5-10 mouse clicks! Pick and choose molecules, refine results with a chemist and/or virtually validate them via docking with just a few more clicks. Designing and docking novel ideas was never simpler!

With *LeadIT*'s fragment evolution capabilities users can grow known fragment hits to user selected receptor targeted interactions to efficiently transform leads into drug candidates. Alternatively propose molecules employing a different strategy of merging existing known ligand binders for a target. Or try linking together fragment binders found in different sub-pockets. Furthermore, performing scaffold replacements to bust any IP issues you may have is just as simple. The versatility and diversity of proposals to medicinal chemists is multi dimensional and not even limited to the billions of fragment combinations we ship with the tool.



BioSolveIT ships *LeadIT* with a sandbox fragment set, based on the DUD subset of ZINC. This allows you to play with all the functionality within *LeadIT*. Additionally, you may download a much more comprehensive fragment database created from 3.27 million molecules of the ZINC 'Lead Like' set. All compounds with unique Murcko scaffolds were taken into account. But there are no limitations with *LeadIT*, create your own fragment database with its built in shredding functionality. Many companies have already created, manipulated and conformationally enumerated fragments to successfully search their in-house data. If you fancy picking up this super playful tool just [grab a copy](#).

### [leveraging LeadIT to team up MedChems and CompChems](#)

Leveraging *LeadIT* in organizations bridges the gap between medicinal and computational chemistry. It improves productivity by facilitating the groups to work closer together in a team to interactively explore ideas and loop through the drug design cycle more effectively. The intuitive design and pedigree of algorithms within *LeadIT* allows quick interactive exploration of design ideas and hypothesis. This provides a novel way for medicinal chemists to collaborate with modelers. Traditionally the approach to CADD is to run calculations, identify molecules and present these to chemists for potential synthesis. This approach delays the feelings of accomplishment and promotes frustration on both sides due to bottlenecks, days can be spent feeling 'unfulfilled'. *LeadIT* turns this philosophy on its head: The tool is quick and playful and allows an interactive and dynamic approach to novel ideas generation. MedChems and CompChems can generate the results on-the-fly. In front of the screen together! We have experienced this avoids frustration, creates motivation and fun, and drastically speeds up your lead finding and optimization. Read on:



ideas that have been generated straight away.

With *LeadIT* it takes only a matter of seconds to explore a multitude of ideas on a project. MedChems and CompChems may just brainstorm over a cup of coffee in a one-on-one session or even on-the-fly within the design team meetings. Either way a slide show of possibilities is created on demand depending on the views and prerogatives of the project and chemists in question. Solutions generated in such collaborative approaches can be taken onto further stages of modeling and validation by potential synthesis, or – if desired – medicinal chemists may even be inclined to start working on these novel

Working closely together in such a manner allows project dependent information or properties of molecules (be they desirable or not) to be easily fed back into the design cycle creating an opportunity for a more trusting, talkative and productive relationship! The options for design are numerous and the choice is entirely up to the group in charge. *LeadIT* truly does empower MedChems and CompChems to work and think in different ways! For more information on collaborative approaches for design with *LeadIT* (e.g. through sharing projects via email) please [contact us](#).

### synthetic info with *LeadIT* produces joint success

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In principle medicinal chemists can make almost any compound, however they have to question if it is reasonable to do so and if they are inclined to do so! An effective approach is to incorporate the personal mindset of the medicinal chemist in a modelers design procedure. In one respect the medicinal chemist is the customer of the modeler, and, hey, don't we all want happy customers? *LeadIT* provides a system using substructure boundary conditions for incorporating project dependent synthetic information and filters that allow a medicinal chemist to influence modeling to their own personal synthetic taste within a project. *LeadIT* delivers proposals in seconds, so why not share the screen with a coffee as a team of MedChem & CompChem?

If a medicinal chemist is involved in the design process with their desired chemistry and selectively pick molecules from a slide show proposed by *LeadIT* they will begin to have a sense of ownership of the molecules from the start. The trust as well as fragments evolve with *LeadIT* so that chemists can perform reactions and not get the synthetic blues. Hence, the more molecules proposed in the realm of a chemist's synthetic capability, the more molecules are actually made. The chance of success rises with the increased number of diverse modeling-validated molecules being synthesized. You get 'diverse modeling validated' molecules made with *LeadIT*, best to experience the *LeadIT* success 'effect' for yourself. If you have any further wishes or remarks please get in touch with us [here](#).

### join Profs Kubinyi and Rarey at *LeadIT* Workshop at the 239<sup>th</sup> ACS

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BioSolveIT will host a free FBDD and Scaffold Hopping workshop at the 239<sup>th</sup> ACS in San Francisco, CA, USA. The workshop will be the world premiere of our new state of the art software platform



Prof. Hugo Kubinyi

*LeadIT*, integrating *ReCore* and *FlexX* functionality into a super easy to use intuitive GUI. In hands on sessions we will highlight how to solve selected scaffold hopping and fragment-based design problems with *LeadIT*. We are proud to announce two world renowned speakers at this seminar. First of all Prof. Hugo Kubinyi, a medicinal chemist with 40+ years of experience in drug discovery will give an introductory presentation on scaffold hopping. In his talk titled 'Scaffold Hops – Fact or Fiction?', he will provide a critical view on the needs, the opportunities and the pitfalls of successful scaffold hopping. Second Prof. Matthias Rarey, the main author



Prof. Matthias Rarey

of ground breaking software tools like *FlexX*, *FTrees* and now *ReCore*, will provide an insight on his latest research projects. Medicinal chemists and modelers alike are encouraged to attend to learn how to grow and link frag-

ments, merge ligands, and perform scaffold hopping with simple mouse clicking. Come and actively learn about team-building software that will allow you to bridge the gap between medicinal and computational chemists. Attendees who register BEFORE Valentine's Day (Feb 14<sup>th</sup>, 2010) will participate in a laptop raffle. Also all participants will receive a FREE 3 months license to practice what was learned in the workshop and apply this on their own personal projects. For more information and to sign up please visit [our web page](#). Space is limited, so make sure to register shortly! We look forward to seeing you in SF!

## tips & tricks: *LeadIT* – the basics

The section today focuses on the basic aspects of *ReCore* within *LeadIT*, so we see these as important points to bring to your attention. In this issue we present a series of tutorial movies for our tips'n'tricks which will help you learn how to work effectively with *LeadIT*, perform core replacement and fragment growing! [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](mailto:support@BioSolveIT.de).

## BioSolveIT news in brief

- In conjunction with the CCDC the world class CSD data is now available for download and utilization with *LeadIT* [here](#).
- Recently released BioSolveIT Software: Updated *Pipeline Pilot*<sup>®</sup> and *KNIME*<sup>®</sup> components, *FTrees* 2.1.2 and *CoLibri* 1.2.0.
- In December 2009 recent tours presenting BioSolveIT software were undertaken in China and India with Cloud Scientific Technology Co Ltd and Apsara Innovations Pvt Ltd respectively. For information on BioSolveIT software in China please contact [Tao Huang](#) at Cloud Scientific and for India [Ashok Betraj](#) at Apsara Innovations.
- Katrin Stierand and Andrea Volkamer, members of Prof. Matthias Rarey's group, a founder of BioSolveIT, obtained poster prizes at the 5<sup>th</sup> German Conference on Chemoinformatics in Goslar for their work on *PoseView* (2D ligand depiction) and active site analysis for drugability respectively.
- Dates for your diary: BioSolveIT will be present at the following events:



Andrea Volkamer (left) and Katrin Stierand (right), winners of poster prizes in Goslar.

Mar 20 <sup>th</sup>	<a href="#">Cutting Edge Approaches to Drug Design 2010</a> , London, UK
Mar 21 <sup>st</sup> - 25 <sup>th</sup>	<a href="#">239<sup>th</sup> ACS National Meeting &amp; Exposition</a> , San Francisco, CA, USA – <a href="#">Conformational sampling for large-scale virtual screening: Accuracy vs. ensemble size</a> (T. Lippert and M. Rarey) – <a href="#">Exploring the chemical universe</a> (C. Lemmen, C. Detering, M. Gastreich, and H. Claußen) – <a href="#">Computational methods for 2D-visualization of molecular interaction patterns</a> (K. Stierand, M. Rarey, and C. Lemmen) – <a href="#">Leading fragments to lead structures: Fragment evolution, merging and core replacement, and ... docking</a> (C. Detering)
Apr 08 <sup>th</sup> - 09 <sup>th</sup>	<a href="#">6<sup>th</sup> Annual MedChem Europe</a> , Munich, Germany – <a href="#">Interactive Fragment Growing, Linking, and Merging</a> (P. Oledzki)

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](mailto:Contact@BioSolveIT.de).

## literature corner

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- ReCore: A Fast and Versatile Method for Scaffold Hopping Based on Small Molecule Crystal Structure Conformations*  
Patrick Maass, Tanja Schulz-Gasch, Martin Stahl, and Matthias Rarey  
J. Chem. Inf. Model., 47 (2), 390 -399, (2007)  
[details here](#)
  
- ReCore*  
John H. Van Drie  
J. Am. Chem. Soc., 131 (4), 1617, (2009)  
[details here](#)
  
- Structure-Based Rational Screening of Novel Hit Compounds with Structural Diversity for Cytochrome P450 Sterol 14 $\alpha$ -Demethylase from *Penicillium digitatum**  
Qingye Zhang, Ding Li, Pei Wei, Jie Zhang, Jian Wan, Yangliang Ren, Zhigang Chen, Deli Liu, Ziniu Yu, and Lingling Feng  
J. Chem. Inf. Model., Publication Date (Web): January 20, 2010  
[details here](#)

## upcoming articles

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- CSD data with *LeadIT*
- PoseView* - 2D depiction of 3D interactions

## contact

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For further information please contact:

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