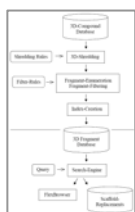


Welcome to the 13th edition of the BioSolveIT newsletter!

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

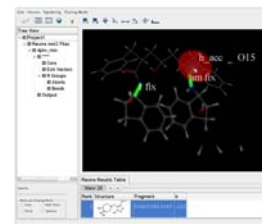
[Recore – new, 3D-compatible scaffolds in seconds](#)

[Recore](#) is a 3D ligand scaffold replacement tool that allows the user to generate new ligand cores in the blink of an eye. The tool was co-developed between our academic partner the [Center for Bioinformatics \(ZBH\)](#) at the University of Hamburg and [F. Hoffmann-La Roche AG](#). The method is an ideal solution for evading patent issues whilst working with competitor's molecules and was published in the Journal of Chemical Information and Modeling (reviewed in this month's [literature corner](#)). It recently received special attention in Nature Reviews Drug Discovery (May 2007 Research Highlight).



Given a user-defined central unit of a molecule, the core, the best possible replacement – whilst keeping all connected atoms, i.e., the side chains in place – is identified from a 3D fragment database of possible moieties. Solutions can be influenced interactively by defining priority constraints, such as H-bond acceptor/donor interactions in a particular vicinity etc., these constraints act like pharmacophores. A typical workflow is a two stage process shown in the diagram to the left (click to enlarge), of which Stage A needs to be performed only once.

Infinite replacement scaffold moieties are obtained by shredding drug-like molecules in 3D molecular libraries to obtain maximum success and synthesizability. A graphical user interface for *Recore* (pictured) will be released in the New Year whilst a command line version is available now. You can view a [tutorial movie](#) and also have the possibility of using this interesting unique tool with a [free evaluation](#).



[align, analyze and visualize scaffold hops with FTreesXL](#)

FTreesXL is a graphical user interface for the highly popular and successful scaffold hopping *FTrees* ligand similarity search engine. The GUI facilitates seamless handling of extensive datasets for virtual screening workflows. Screening datasets from multiple sources can be compiled using ultra-large file sizes (>2GB) so segmenting your data will be a thing of the past. *FTrees* results can then be efficiently analyzed and visually inspected.

Standard *FTrees* provides much more than just a typical similarity score. Due to *FTrees*' powerful scaffold hopping capabilities solutions sometimes may appear to be unrelated, however unlike many other ligand based tools *FTrees* provides an alignment of ligands within Feature Trees descriptor space by retaining molecular topology. These alignments are one click away with *FTreesXL* and are effortlessly visualized. Such alignments provide a sound physiochemical basis why an *FTrees* hit is classified as highly similar to a query molecule and a sound rational approach for reasoning with medicinal chemists.



The GUI also contains data analysis capabilities as tabulated solution scores can be sorted and filtered in various ways to narrow down hit lists and may be exported for further processing. Whilst utilizing a variety of different clustering algorithms permits classification and identification of different chemical classes of molecules within screening sets. *FTreesXL* is currently in beta-testing and is available for users to evaluate on the Linux platform, please [contact us](#).

[rapidly interfacing into the world of workflows](#)

FlexX and *FTrees* have now been interfaced to the extremely popular Pipeline Pilot by [SciTegic](#). Now your favorite drug discovery workflows within Pipeline Pilot can easily incorporate *BioSolveIT* software as well. Components for *FTrees* and *FlexX* can be effortlessly plugged into your existing workflows diversifying and empowering your pipelines with cutting-edge virtual screening solutions.

The [FlexX-GUI](#) can be utilized to undertake highly detailed protein preparation and parameter adjustment. Subsequently the entire setup may be exported from the GUI and imported into **Pipeline Pilot** with a simplistic drag and drop. A ready-to-use **Pipeline Pilot** interface for *FTrees* can be downloaded from our [web-page](#).



This first release of **Pipeline Pilot** interfaces consist of modules for remote and server computing as well as viewer components adapted specifically for visualizing results from *BioSolveIT* software. The modules facilitate virtual screening of compound libraries and the remote-computation module utilizes PVM to permit parallel computing on clusters. For further details on how to plug in and empower please do [contact us](#).

234th ACS and drug design workshop

The *BioSolveIT* booth at the 234th ACS in Boston was a hive of activity and conversation. Where the new [FlexX GUI](#) was demonstrated to numerous people and some of the most prominent people involved with *BioSolveIT* were present, such as Matthias Rarey, Chris Lipinski (pictured) and Hugo Kubinyi. The winner of the iPod raffle that took place at the meeting was Liying Zhang from the University of North Carolina at Chapel Hill. In addition, Marcus Gastreich from *BioSolveIT* was present again at the mentor luncheon which provides an industry networking opportunity for students. This was organised by Wendy Cornell, the President Elect of the COMP Division for the ACS, who is pictured next to Marcus in the center.

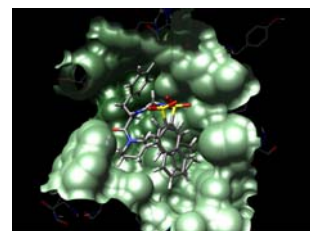


BioSolveIT also recently presented a practical workshop on the *FlexX GUI* at the Drug Design Summer School held in Vienna, Austria. Over 60 participants were tutored during two different sessions on how to use the new *FlexX GUI* to perform successful protein-ligand docking.

tips and tricks – docking with molecular core superposition

This section focuses on troubleshooting and aspects of [FlexX](#) that are either not very well known or are sometimes misunderstood, so we see them as important points to bring to your attention. In this issue we will focus on the docking with molecular core superposition with *FlexX*. [Read more!](#)

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



BioSolveIT news in brief

- Our academic partner [The Center for Bioinformatics \(ZBH\)](#) at the University of Hamburg is now a double consecutive "FIZ Chemie" award winner. The FIZ chemistry prize from the Society of German Chemists for best diploma thesis in cheminformatics was awarded to Ole Kayser for his work on "*Efficient Methods for the Generation of Bioactive Conformers of Small Molecules*".
- Marcin Kolaczowski, Mateusz Nowak, Maciej Pawlowski and Andrzej Bojarski work on the homology modeling of the 5-HT7R receptor and docking with [FlexX](#) has been awarded a prize by the Institute of Pharmacology, Polish Academy of Sciences (IF PAN) for one of the best scientific papers in 2006 (J. Med. Chem., 49 (1), 205 -214, 2006). The work was chosen by IF PAN as one of the 5 best papers from over 100 article submissions.
- A new download package for [CoLibri](#) is available. *CoLibri* 1.1 has now been released and can be accessed from our [download page](#).

literature corner

Discovery and optimization of novel, non-steroidal glucocorticoid receptor modulators

Nicholas C. Ray, Robin D. Clark, David E. Clark, Karen Williams, H.G. Hickin, Peter H. Crackett, Hazel J. Dyke, Peter M. Lockey, Melanie Wong, René Devos, Anne White, and Joseph K. Belanoff.

Bioorg. Med. Chem. Lett., 17, (17), 4901-4905, (2007)

[details here](#)

GPCR Structure-Based Virtual Screening Approach for CB2 Antagonist Search

Jian-Zhong Chen, Junmei Wang, and Xiang-Qun Xie

J. Chem. Inf. Model., 47 (4), 1626 -1637, (2007)

[details here](#)

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](#)

Supervised Scoring Models with Docked Ligand Conformations for Structure-Based Virtual Screening

Reiji Teramoto and Hiroaki Fukunishi

J. Chem. Inf. Model., 47 (5), 1858 -1867, (2007)

[details here](#)

upcoming articles

- *FlexX* and *FTrees* in MOE
- Preferred Partnership Program
- *FlexX* and CORINA

contact

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