

Welcome to the 14th edition of the BioSolveIT newsletter!

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

German efficiency enables Pfizer to find actives from 3 trillion compounds in minutes

With recent trends showing that fragment-based strategies are providing a successful approach to drug design, BioSolveIT leads the way with the fastest of their *de novo* drug design methods, [FTrees-FS](#). Feature Trees Fragment Spaces bridges the gap to experimental techniques by facilitating virtual fragment growing, fragment linking and fragment merging. Recently, a collaboration of Pfizer Inc. with BioSolveIT GmbH came to public fruition with a [J.Med.Chem. publication](#) describing the use of [FTrees-FS](#) on the basis of Pfizer's validated parallel synthesis protocols as a proficient platform for *de novo* drug design. The paper is a shining example of BioSolveIT's approach for retrieving actives from an innumerably large virtual space using German style efficiency.

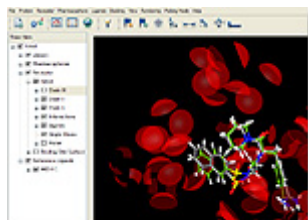
First the [CoLibri](#) combinatorial library toolkit was used to prepare Pfizer's corporate collection of validated synthetic protocols for virtual library design. [CoLibri](#) generates a Fragment Space comprising all virtual compounds that are synthetically accessible. [FTrees-FS](#) was then applied to generate from these 3 trillion virtual molecules similar, yet chemically distinct compounds. Starting from an active hit, it took less than 20 minutes on average to design multiple actives from different chemical series. These designed compounds usually showed low similarity to the active hit by standards of other similarity measures, therefore confirming the uniqueness of the [FTrees-FS](#) results.

The Journal of Medicinal Chemistry publication documents how grouping the virtual hits by their synthetic protocols allows the rapid design and synthesis of multiple follow-up libraries. [CoLibri](#) and [FTrees-FS](#) support hit-to-lead design efforts for tasks like follow-up from high-throughput screening hits or scaffold hopping from one hit to another attractive series. [Contact us](#) today to discuss the use of this powerful approach based on your IP to design libraries and provide virtual hits that won't give your medicinal chemists the synthetic blues.

the accurate and easy docking dream, wake up to FlexX

The need for an intuitive docking tool containing exceptional usability for setting up complex docking protocols in a simplistic way has now become a reality. The [FlexX](#)-GUI provides

- maximum usability with minimum effort
- a wizard for protein preparation
- simple mouse click pharmacophore selection
- drag and drop Pipeline Pilot[®] export
- smooth visualization of results – all in stereo view



The official release of the new visionary [FlexX](#)-GUI provides a docking platform with maximum usability with minimum effort. A step by step wizard can be utilized to overcome the multifaceted difficulties of protein preparation i.e. chemical assignments, co-factors, protonation, tautomers etc. A straightforward ligand library filtering and creation interface is provided, whilst pharmacophore selection is only a simple mouse click of an interaction sphere away (click thumbnail for a larger view).

Clear and uncomplicated parameter manipulation is provided through the interface for users who want to play with default settings, whereas docking novices can simply click the 'dock' button. Rank sort poses by employing user-selected criteria and smoothly visualize results for ease of analysis within a clickable tabulation of all docking solutions. The [FlexX](#)-GUI represents a simplistic way to deal with the highly complex and sensitive procedure of accurate protein-ligand docking. Take a look at the [GUI](#) or obtain your own [evaluation copy](#) today and use this issue's [tips and tricks](#) to get going.

BioSolveIT to host complimentary Interactive *De Novo* Workshop at the 8th ICCS_____

BioSolveIT will be hosting an interactive Workshop on Virtual Screening and *De Novo* Design on the 5th June 2008 following the [8th International Conference on Chemical Structures](#) in Noordwijkerhout, the Netherlands. The workshop will offer an occasion for expert computational chemists and novice modelers alike to learn all about our software in three major areas of drug discovery, structure-based, ligand-based and *de novo* design.

Not only is the workshop free of charge but we'll also provide you complimentary software for you to take home and continue to work with. The only two pre-requisites are:

- to [register](#) early as space will be limited
- to bring your own laptop in order to make this a truly hands-on experience

There is no need for any travel concerns either as BioSolveIT will provide an additional shuttle bus to the airport for all those that need to make their way to the airport at the end of the day. Simply send an email to workshop@biosolveit.de today to join in the fun and save your spot.

nurturing the future and keeping with tradition at the ACS Mentor Luncheon _____

The ACS COMP division celebrated its 3rd Official Mentor Luncheon at the [235th Spring ACS meeting in New Orleans, LA, USA](#). This networking event gave young students the opportunity to quiz people from industry about their everyday life, experiences, or obtain advice on how best to pursue a path into industry. The event has been attended by BioSolveIT from the outset since its conception in 2007.

Co-sponsoring the event, BioSolveIT were once again present with Dr. Carsten Detering attending (click thumbnail for larger view). He was happy to help, for example, on European working conditions, his application procedure experiences, intercultural differences, and many other issues of interest for students. The Mentor Luncheon was free for participating students and was originally coordinated by Dr. Rommie Amaro, an NIH Postdoctoral Fellow in the McCammon Group at UCSD.



tips and tricks – the new FlexX Release 3 - part 1: protein preparation _____

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 begin a two part series of tips and trips which will help you learn how to use the new [FlexX](#)-GUI. [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 _____

- Proteros Biostructures GmbH and BioSolveIT GmbH have recently acquired federal funding of €5.5 Million. The funding will drive a project with two major pharma companies and the University of Marburg for process development of fragment-based crystallography and in silico fragment screening for lead identification.
- Prof. Dr. Matthias Rarey recently presented a talk titled "*To Link or not to Link: That is the Question! Computational Tools for Fragment-Based Lead Discovery and Optimization*" at the largest ever [BAGIM \(Boston Area Group for Informatics and Modeling\) meeting](#) which was hosted by AstraZeneca.
- A new download package for [Recore](#) is [available](#). [Recore](#) is now distributed with a sandbox fragment space and can be accessed from [our download page](#). However, please note this is a very large file.
- Dates for your diary:** BioSolveIT will be present at the following event:

April 24 th	UK-QSAR and Chemoinformatics Group Spring Meeting, Windlesham, Surrey, UK
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If you would like to meet a representative of BioSolveIT to discuss any questions or have any kind of feedback please email us at Contact@BioSolveIT.de.

literature corner

Identification of novel inhibitors of bacterial surface enzyme Staphylococcus aureus Sortase A
Bala C. Chenna, Bidhan A. Shinkre, Jason R. King, Aaron L. Lucius, Sthanam V. L. Narayana and Sa-
danandan E. Velu

Bioorg. Med. Chem. Lett., 18, 380-385, (2008)

[details here](#)

Use of 3D QSAR Models for Database Screening: A Feasibility Study

Alexander Hillebrecht and Gerhard Klebe

J. Chem. Inf. Model., 48 (2), 384-96, (2008)

[details here](#)

*Human Microsomal Prostaglandin E Synthase-1 (mPGES-1) Binding with Inhibitors and the Quanti-
tative Structure-Activity Correlation*

Mohamed D. M. AbdulHameed, Adel Hamza, Junjun Liu, Xiaoqin Huang and Chang-Guo Zhan

J. Chem. Inf. Model., 48 (1), 179-85, (2008)

[details here](#)

SwiFT: an index structure for reduced graph descriptors in virtual screening and clustering

Robert Fischer and Matthias Rarey

J. Chem. Inf. Model., 47 (4), 1341-53, (2007)

[details here](#)

upcoming articles

- [FTrees](#) 2.0
- [FlexX](#) and [FTrees](#) in MOE®

contact

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