

Welcome to the 11th edition of the BioSolveIT newsletter!

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

FlexNovo

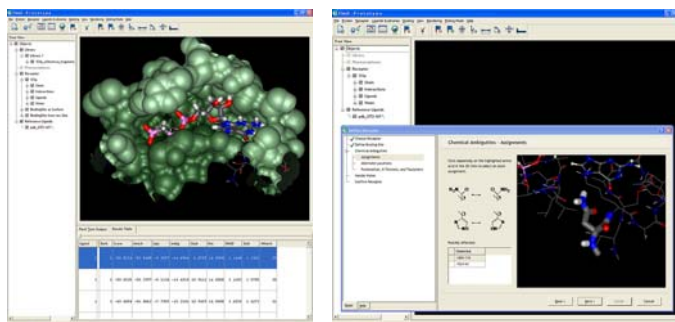
[FlexNovo](#) is a new software tool developed by Joerg Degen and Matthias Rarey at the Centre for Bioinformatics, University of Hamburg. It permits structure-based searching within large chemical fragment spaces, concatenating together the fragments according to certain rules that specify how these fragments can be connected. Like its sibling [FlexX](#), it consists of an incremental construction algorithm. During the build-up process, several filters (Lipinski, pose-geometry, diversity) can be activated. The software has been tested on four different targets DHFR, CDK2, COX-2, and ER and has shown very promising results. [FlexNovo](#) generated diverse sets of molecules that are highly complementary to the binding site of the protein and that exhibit structural motifs of the binding modes of known actives. For the original publication, please take a look [here](#) and for additional information on [FlexNovo](#) from Hamburg University please take a look [here](#). [FlexNovo](#) is available for beta testing. Please contact us either through our [support page](#) or via e-mail at FlexNovo@BioSolveIT.de.

better, faster, more: the new FlexX Release 2.1

[FlexX Release 2.1](#) is the latest edition of the well established and popular [FlexX](#) protein-ligand docking tool. The software is supported on Linux, Microsoft® Windows®, SGI® IRIX®; we also have a significantly faster 64 bit Linux version available; additional operating systems are available on request. [FlexX 2.1](#) now supports very large input/output files to allow millions of ligands in libraries to be handled with ease. The software can be accessed from the familiar molecular modeling environments of SYBYL® and MOE®. The new MOE-FlexX interface combines the strengths of MOE's data preparation and results analysis capabilities with [FlexX's](#) fast precise docking calculations. [FlexX-Screen](#) is a new module for rapidly screening vast corporate compound libraries at less than 1 second per compound with no loss in accuracy compared to standard [FlexX](#). In addition, the module also contains many different customizable filters for toxicity, reactivity and drug-likeness (Lipinski). If you are interested in evaluating the new [FlexX](#), please write to FlexX@BioSolveIT.de or visit our [web page](#).

FlexX is going graphical: a new GUI for structure-based drug design

BioSolveIT will soon be proud to present [FlexX](#) in its newest clothes. Preparing receptor description files, editing **config.dat** files will soon belong in the past. The avid modeler will only need to start the program and will be guided by [FlexX's](#) intuitive graphical user interface workflow. From receptor and ligand preparation – alternate locations of amino acid side-chains, protonation in the active site, ligand initialization and removal of ambiguities – can now be handled automatically, but of course still allowing the user the possibility to tweak specifically desired parameters within the GUI. Here are a couple of sample screen shots.



CoLibri

[CoLibri](#) is a library design tool conceptualized and implemented in conjunction with Pfizer and Boehringer Ingelheim. The tool has been designed for intricate compound handling during virtual screening experiments. Vast compound collections can be assembled from multiple sources containing various different input formats whilst removing duplicates. Assessing distributions of physico-chemical properties of compounds, chemically selecting/filtering based on property thresholds, molecular name-patterns or absence/presence of a particular substructure motif can be achieved effortlessly. In addition, [CoLibri](#) can be used to create fragment libraries in two ways. Firstly ligands are decomposed into fragment libraries, which can then follow customizable retrosynthetic ligand reconstruction to form a library of novel molecules. Secondly, multiple combinatorial libraries can be assembled into non-redundant fragment combi-chem spaces. Fragment spaces have the advantage of covering a large area of chemical

space with only a small number of fragments and can be used with [FTrees-FS](#) and [FlexNovo](#). [CoLibiri](#) version 1.0 will be shortly available for download. If you would like to evaluate [CoLibiri](#), lease the software from us or have any questions relating to [CoLibiri](#) please don't hesitate in contacting us either through our [support page](#) or via e-mail at CoLibiri@BioSolveIT.de.

tips and tricks from the world of FlexX

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 protein-ligand clash treatment in [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@BioSolveIT.de.

BioSolveIT news in brief

Dates for your diary: BioSolveIT will be present at the following conferences:

- March 12-15 [Drug Discovery Technology](#), Europe : Better tools for early decision-making, London, UK
- March 25-29 [233. ACS Spring Meeting](#), Chicago. BioSolveIT will talk about ['Fragment-based de novo design'](#) (COMP 71) and ['Analyzing docking results by substructure search in Euclidean space'](#) (CINF 72)
- March 26-29 [New Approaches in Drug Discovery and Design](#), Rauschholzhausen, Germany
- April 24 [UKQSAR Spring Meeting](#), AstraZeneca, Alderley Park, UK

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

Interpretation of Scoring Functions Using 3D Molecular Fields. Mapping the Diacyl-Hydrazine-Binding Pocket of an Insect Ecdysone Receptor.

B. Bordas, I. Belai, A. Lopata, and Z. Szanto
J. Chem. Inf. Model., 47 (1), 176-185 (2007)

[details here](#)

A Structure-Based 3D-QSAR(CoMSIA) Study on a Series of Aryl Diketoacids (ADK) as Inhibitors of HCV RNA-dependent RNA Polymerase.

J. Kim, J. H. Han, and Y. Chong
Bull. Korean Chem. Soc. 27, 11, 1919-1922 (2006)

[details here](#)

Docking studies of agonists and antagonists suggest an activation pathway of the A₃ adenosine receptor.

S. Kim, Z. Gao, L. S. Jeong, and K.A. Jacobson
J. Mol. Graph. Model. 25 (4), 562-577 (2006)

[details here](#)

upcoming articles

- The New [FlexX](#) GUI: Hassle Free Docking
- FTrees-XL: The Latest Graphical Interface for [FTrees](#)
- [FlexX](#) and [FTrees](#) in Pipeline Pilot

contact

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