



Welcome to the 10th edition of the BioSolveIT newsletter!

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

Immediately effective, BioSolveIT guarantees to support ALL users of FlexX/S software ___

Due to [recent developments](#) concerning Tripos® and to avoid any confusion, the users of FlexX/S should be aware of the following announcement: "[Information Related to Recent Developments Associated with Tripos Licenses](#)".

Now you can! — FlexX De Novo Docking Under Pharm Constraints _____

In a *JCAMD* forthcoming special issue on pharmacophores, scientists from Schering and BioSolveIT report on three successful de novo design approaches which rely on the combination of multi-million compound combinatorial docking under receptor-based pharmacophore constraints.

The proof of concept documented in the work sheds light on the enormous potential of this new functionality. Inspired by work from Andrew Leach and co-workers at GSK, the knowledge about some fragments' binding to a protein has been modeled into a receptor-based pharmacophore definition. Linking these fragments is done on-the-fly **during docking**, using huge combinatorial libraries. The advantages: An immense speed-up plus appealing results:

Three sample scenarios as large as 22.4 million compounds have been created to illustrate the method. Docking could be accomplished at rates of a fraction of a second per compound; the results throughout were very encouraging, and enrichment factors of 7000 and higher could be obtained when seeded known actives were retrieved.

Take a look at this product for yourself. We are happy to provide you with free, full-featured evaluation copies of the software and can provide more detailed information about this study if you are interested. Just [let us know!](#)

Academics: Get FlexX-Pharm for free! — New pricing policy for academic users _____

In order to make [FlexX](#) even more attractive for its academic users, BioSolveIT has recently changed its academics pricing policy. This change comprises two advantages:

- All academic licenses now include the best currently available pharmacophore docking module [FlexX-Pharm](#) at no additional cost
- All academic licenses include the ability to temporarily upgrade for free the number of licenses to 1000 — providing you three orders of magnitude more power.

This way all academic users have access to the premier docking engine ([FlexX Release 2](#)) bundled with the most requested extension module for incorporating pharmacophores ([FlexX-Pharm](#)) at the lowest ever rate. Also the temporary upgrades facilitate Xlarge-scale screening campaigns as well as teaching units, providing many students concurrent access.

If you already have a [FlexX](#)-license (e.g. obtained previously through our distributor) we can offer you an even more compelling offer to upgrade to the latest version and become a BioSolveIT-customer with the benefit of our premier service at a minimal cost. If you are interested to evaluate (at no cost), need more information, or are ready to license [FlexX](#), please contact us at license@biosolveit.de.

Managing the tough ones — How to tackle hydrophobic ligands and sites _____

BioSolveIT is proud to introduce a new base placement algorithm, the Single Interaction Scan (SIS). The new approach complements [FlexX](#)'s other two algorithms, the triangle matching algorithm, and the line matching algorithm. New levels of accuracy can now be achieved, especially with hydrophobic ligands where the dominating interactions are non-polar, or where there is only one hydrogen bond possible. The SIS algorithm has shown its complimentary strengths to the other base placement algorithms in in-

house testing (e.g. particular tricky Cytocrome P450 docking cases). Also beta testers have already reported commendatory success e.g. in docking weakly interacting steroidal ligands.

If you have cases, too, where you think that SIS could benefit you, or if you would simply like to evaluate the SIS algorithm, please do [write us!](#)

[BioSolveIT's successful appearance at the 232nd ACS Fall Meeting](#)

BioSolveIT's presence was warmly received at the [ACS Fall Meeting in San Francisco](#). We presented our current line of cutting edge drug discovery tools, as well as many other novelties. Especially noteworthy among the latter is the prototype of the new [FlexX](#) Graphical User Interface, which customers said would set new standards. In addition, the integration of [FlexX](#) into the leading Molecular Operating Environment (MOE[®]) by [Chemical Computing Group](#) created a gasping "Ahhhh" among the crowd. Besides the booth, BioSolveIT was present with two talks. Drs. Christian Lemmen and Holger Claußen reported on the latest crazes in the world of BioSolveIT tools ([talk 1](#), [talk 2](#)).



Several customers presented their productive usage of [FlexX](#), [FlexS](#), [FTrees](#) and more to solve significant problems they faced during their drug discovery endeavors: Pfizer's Dr. Boehm talked about how they searched 3 trillion (!) compounds using [FTrees](#) and our new conformer library generator [CoLibri](#), which was developed in a project between Pfizer and BioSolveIT. Dr. David Clark from Argenta reported time-efficient discovery of a significantly potent and very promising nonsteroidal glucocorticoid receptor modulator using [FlexS](#) as a screening tool.

BioSolveIT will be present again at the next [ACS Spring Meeting in Chicago](#). For other conference participation by BioSolveIT, please visit our [conference pages](#).

["Four Wins": BioSolveIT's FlexX Training Workshop](#)

This year's [FlexX](#) Training Workshop took place in picturesque Santa Clara, just prior to the ACS Fall meeting in sunny San Francisco. Based on another successful collaboration with [SUN Microsystems](#), at the beautiful SUN campus, both new and experienced users of [FlexX](#) learned about how to use [FlexX Release 2](#) at its best, using SUN 64 bit workstations.

In 12 demanding sessions, the attendee's learnt hands on how to prepare ligands and receptors for docking, how to tune parameters for optimal results, to navigate the [FlexX](#) file system, and how to automate jobs with scripting. One participant said: "In this workshop, I have learnt things about [FlexX](#) beyond my expectations".

The next [FlexX](#) Training Workshop will be organized in Europe again in the fall of 2007, so watch our web site for updates or subscribe to our [newsletter!](#) If you would like to be notified about this event please send us an email to workshop@biosolveit.de. However, while waiting for the next workshop, start to learn useful stuff from the world of [FlexX](#) in the [tips & tricks section](#).

[tips and tricks from the world of FlexX](#)

Following established tradition, in this section we focus on 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 planar amides. If you feel that amides in your particular application should be treated as planar, you can force them to be so by adjusting the corresponding section in the static data file `torsion.dat`. Steps to undertake are described on a separate page in the [tips & tricks section](#).

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](#)

BioSolveIT's latest conference presentations:

- At the 232nd ACS Fall Meeting in San Francisco, Dr. Christian Lemmen reported on "[Recent advances in molecular docking](#)"; Dr. Holger Claußen reported on "[Recent developments in the FlexX family](#)".

- At the 16th EuroQSAR in Italy, Prof. Matthias Rarey talked about [Structure-Based Molecular Indexing](#). He was accompanied by Ingo Reulicke, who presented a [new scoring function HYDE](#). Katrin Stierand talked about [PoseVIEW](#), a new tool to draw 2D poses of ligands in their active sites. Further, the Rarey group presented a poster on the [RECORE](#) method for Scaffold Hopping Based on Small Molecule Crystal Structure Conformations, which was done in collaboration with Roche.

literature corner

FlexNovo: structure-based searching in large fragment spaces.

J. Degen and M. Rarey
Chem. Med. Chem., 1(8), 854-68 (2006)
[details here](#)

Prediction of Multiple Binding Modes of the CDK2 Inhibitors, Anilinopyrazoles, Using the Automated Docking Programs GOLD, FlexX, and LigandFit: An Evaluation of Performance.

H. Sato, L. M. Shewchuk, and J. Tang
J. Chem. Inf. Model., ASAP article
[details here](#)

Virtual Screening for beta-Secretase (BACE1) Inhibitors Reveals the Importance of Protonation States at Asp32 and Asp228.

T. Polgár and G. M. Keserü
J. Med. Chem., 48, 3749-3755 (2005)
[details here](#)

upcoming articles

- The [FlexNovo](#) Approach.
- [FlexX](#) goes graphics: The new GUIs for structure-based design.

contact

For further information please contact:

BioSolveIT GmbH
An der Ziegelei 75
53757 Sankt Augustin
Germany
email: newsletter@BioSolveIT.de
www: www.BioSolveIT.de
phone: +49-2241-25 25 0
fax: +49-2241-25 25 525