

SimBioSys Winter '08 Newsletter

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A Message from Dr. Zsolt Zsoldos, CSO, SimBioSys

The past three months have flown by! So far 2008 has started the way 2007 ended, exciting and very busy. Over the past quarter, we have continued our efforts to develop cutting edge chemistry software while expanding our efforts to reach out into the computational chemistry community. We have started a project to make LASSO descriptors available for all 18+ million structures available in the ChemSpider database and, in addition, have screened the entire database against 40 receptor targets. The results of this very large cross screening experiment are now available through the ChemSpider website. I am also pleased to announce that we have recently entered the blogosphere with our own SimBioSys Blog. Our blog will hopefully serve as another way to interact with the drug discovery community, and a way for you to learn what we are up to. In 2008 we are expanding our travel schedule to try and interact with as many users as possible. I would like to invite you to let us know if you will be attending any of the meetings/conference listed in this newsletter, as we would love to talk with you.

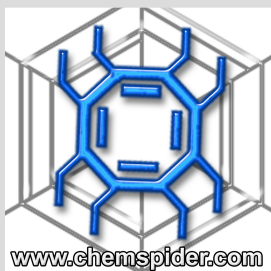


Over 18 Million Molecules Screened against 40 Targets

SimBioSys and ChemZoo have teamed up to provide the virtual screening results for 40 target families on the full ChemSpider Library, currently containing over 18 million molecules. Using the LASSO similarity search tool, SimBioSys has screened the ChemSpider database against all 40 target families from the Database of Useful Decoys (DUD) dataset. In addition to allowing instant ranking results for your particular target of interest (retrieving molecules that are likely to be active for your receptor) this matrix of screening results can be used to find

molecules that have predicted affinity for your target but low predicted affinity for all other targets. Performing such searches promises to improve selectivity and can be a guide to reducing toxicity concerns.

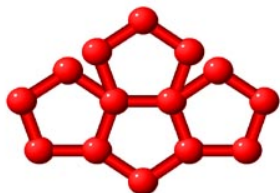
We are now in the process of looking to see what LASSO can and can not do on such a large set of structures, both its limits and its successes. In the spirit of crowdsourcing, we encourage you to check it out and would love to get any and all feedback.



http://www.simbiosys.ca/ehits_lasso/LASSO_on_ChemSpider.pdf

<http://www.simbiosys.ca/blog/2008/02/13/exciting-times-for-lasso-chemspider-and-bio-it-world/>

<http://www.chemspider.com/blog/scaffold-hopping-and-the-search-for-unusual-suspects.html>



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eHiTS and LASSO New Screening Protocol

Getting the most out of your computational tools often comes down to proper usage. At SimBioSys our goal has always been to develop tools that are easy to use, with simple interfaces and a lot of automation. However, even though the scripts are simple, as a user you still need to know the best protocol to get the best performance.

Over the past three weeks, we have been working on the SAMPL project (<http://sampl.eyesopen.com>). SAMPL is a community competition to test protein and ligand modeling. This work has prompted us to formalize the "best practices" protocol for screening with eHiTS and LASSO.

The following graphic illustrates the workflow one should follow when using eHiTS or LASSO for screening databases. The main idea is that we

should first try to generate the best model possible, using all available information prior to performing the screen. As with any modeling approach, testing and validating the model is an essential step prior to applying the model in a predictive way. Thus, in this workflow we have a series of "loops" which involve testing and evaluating the model at that step. Before moving to the next step you must be satisfied with the results.

More information about this new protocol will be available on our blog as well as our website. We encourage users to make comments on this protocol via our blog or through email.

<http://www.simbiosys.ca/blog/>
http://www.simbiosys.ca/ehits/ehits_protocol.html

SAMPL

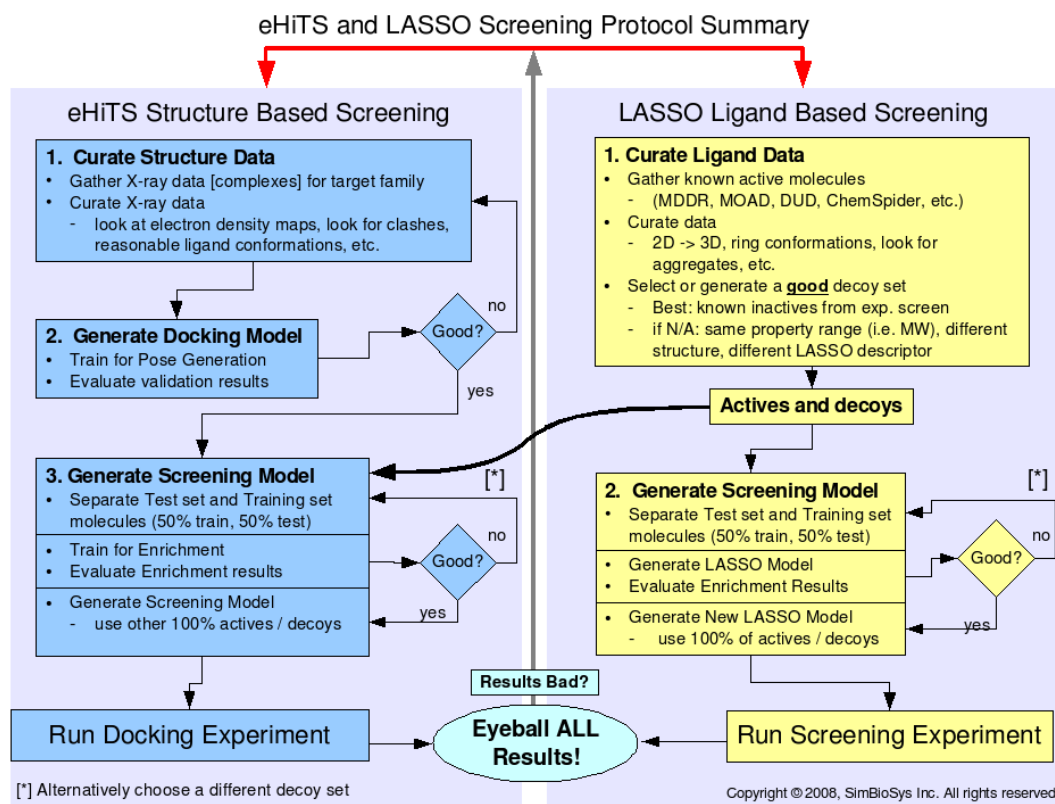
Statistical Assessment of the Modeling of Proteins and Ligands

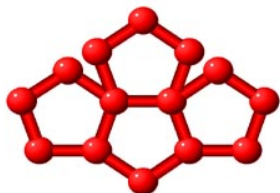
SAMPL is an attempt at prospectively testing protein and ligand modeling. The event focused on virtual screening, prediction of binding poses and prediction of binding affinities. The deadline for submission was Feb 19th, with the results being announced in March 2008.

eHiTS and LASSO Free for open academic research

To request a copy of eHiTS or LASSO, please fill out our Request a Demo form at:

www.simbiosys.ca/





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The Search for Unusual Suspects - BioIT World Article on Scaffold Hopping

A recent article in the February edition of BioIT World, focused on the use of computational tools to expand the range of core molecular shapes for lead generation. We recommend taking a look at the article as it gives a nice overview of the work in scaffold hopping applications. SimBioSys' LASSO ligand based similarity tool was mentioned in this article.

Kenneth Foreman, computational

chemist at OSI Pharmaceuticals summarizes the main purpose of these tools:

"The lack of bias in these computational tools can aid in converting [HTS] hits that have certain undesirable core features into new, IP-able cores," says Foreman.

Rather than go into any more details here, please take a look at the article for yourself at the link below.

<http://www.simbiosys.ca/whatsnew/media.html>

<http://www.bio-itworld.com/issues/2008/feb/cover-story-scaffold-hopping/>

SimBioSys Enters the Blogosphere: www.simbiosys.ca/blog

January 9th, 2008. That's the date SimBioSys entered the Blogosphere. Building upon our efforts to connect more and more with the drug discovery community, we have started our company blog. The blog is designed as another opportunity for our users and friends to find out what SimBioSys is doing and, more importantly, enter into a discussion on various happenings in our field.

Over the coming weeks, we are planning to fill the blog with our ideas and visions for the future of computational chemistry (at least the small portion in which we have our fingers). We hope this will prompt some open and frank discussion. We encourage you to subscribe to our blog, and please, please, comment!

Recent Blog Postings:

Serious Computing on Gaming Hardware

<http://www.simbiosys.ca/blog/2008/02/21/the-next-generation-in-performance-serious-computing-on-gaming-hardware/>

Exciting times for LASSO - ChemSpider and Bio-IT World

<http://www.simbiosys.ca/blog/2008/02/13/exciting-times-for-lasso-chemspider-and-bio-it-world/>

Are you aware of SAMPL?

<http://www.simbiosys.ca/blog/2008/01/26/are-you-aware-of-sampl/>

Roping in your next Scaffold Hop with LASSO

<http://www.simbiosys.ca/blog/2008/01/22/roping-in-you-next-scaffold-hop-with-lasso/>

Interesting Blogs

* ChemSpider

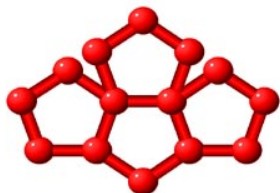
www.chemspider.com/blog/

* Science Blog

www.sciencebase.com/science-blog/

* Useful Chemistry

<http://usefulchem.blogspot.com/>



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Presentations, Publications and User Stories

Presentations from Research Triangle Park Meetings

Last November, SimBioSys joined local experts in the Research Triangle Park area of NC, in a series of meetings discussing virtual screening and docking. Several of the presentations from the two day event are available on our website:

<http://www.simbiosys.ca/science/presentations/index.html#2007>

SimBioSys Publications

http://www.simbiosys.ca/ehits_lasso/publications.html

Darryl Reid, Bashir S. Sadjad, Zsolt Zsoldos and Aniko Simon: LASSO - ligand activity by surface similarity order: a new tool for ligand based virtual screening, in the Journal of Computer-Aided Molecular Design, Published online: 18 January 2008.

<http://dx.doi.org/10.1007/s10822-007-9164-5>

User Publications and Presentations

http://www.simbiosys.ca/science/user_pubs/index.html

Current Pharmaceutical Analysis, Volume 4, Number 1, February 2008, ISSN: 1573-4129. Protein-ligand Docking: A Review of Recent Advances and Future Perspectives. Montserrat Vaque, Anna Ardevol, Cinta Blade, M. Josepa Salvado, Mayte Blay, Juan Fernandez-Larrea, Lluís Arola and Gerard Pujadas

PLoS Computational Biology. 2008 Jan; [Open Access Research Article] In Silico Elucidation of the Molecular Mechanism Defining the Adverse Effect of Selective Estrogen Receptor Modulators. Lei Xie, Jian Wang, Philip E. Bourne. DOI: 10.1371

Structure-based Drug Design: Molecular Docking Studies. Jinxia (Nancy) Deng, PhD, Postdoctoral Research Associate, University of South California, School of Pharmacy. Sept 25, 2007.

"Elucidation of Mechanisms of Action of Molecules with Anti-Cancer Activity Using Molecular Docking." Ines Sousa, Visvaldas Kairys, Jose M. Padron, Miguel X. Fernandes. 2nd Meeting YBIM (Young Biomedical Investigators of the Macaronesia), held on November 10-13, 2007 at Lanzarote, Spain.

Upcoming Events

SimBioSys will be participating in many events and conferences in the coming year, we have listed a few below. We would like to invite you to meet with us at the following events:

- **SBS Conference**
April 6-10, 2008
St Louis, MO
- **235th ACS**
April 6-10, 2008
New Orleans, LA
COMP 57 booth# 432
- **UK QSAR Spring meeting**
Apr 24, 2008
Windlesham, Surrey, UK
- **BIO-IT**
Apr 28 - 30, 2008
Boston, MA
- **8th International Conference on Chemical Structures**
June 1 - 5, 2008
Noordwijkerhout, The Netherlands
- **Structure-Based Drug Design**
June 25 - 27, 2008
Boston, MA
- **Drug Discovery Design & Planning Methods**
July 14 - 18, 2008
Oxford, UK
- **236th ACS**
August 17 - 21, 2008
Philadelphia, PA
booth# 817
- **eChemInfo 2008**
Oct 14-17, 2008
Bryn Mawr, PA

For more information about SimBioSys and our software offerings, please visit our website, email us or contact us by phone:

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