

Finding actives with diverse chemical scaffolds, but similar surface properties **eHiTS and LASSO**

SimBioSys

Reviewed by Susan Boyd, *CompChem Solutions*

There are plenty of options for molecular docking tools on the market. eHiTS is a bit different from most, in that it combines truly exhaustive, fast docking with a rather neat scoring function, based on projected interaction surface points (ISPs).

These surface points should better represent the interactions which occur in protein–ligand complexes than the more usual atom-based scoring functions and certainly this has been supported by several reported validation tests.^{1,2} This allows it to handle the more subtle interactions, such as those involving π -systems and metals.

Different coloured triangles represent the interaction surface points on a molecule

Another advantage of the scoring function is that it is customisable, to allow it to be trained against particular target families. The speed of eHiTS itself is impressive, with a fully exhaustive docking on a single compound taking under three minutes on a single CPU, but if you need it faster, do explore the add-on, eHiTS-Lightning, which parallelises the jobs. This can run on a PS3 – which retails at considerably less than a mini-supercomputer which is the alternative.

LASSO is the ligand-based equivalent of eHiTS, using the interaction surface points as fuzzy 3D descriptors to identify similar compounds to the input query using a neural network algorithm. Again the speed here is worthy of note.

If 3D coordinates are pre-computed for the datasets being searched (optional), 8 million compounds can be searched in only a couple of minutes.

LASSO can be trained with an input dataset to distinguish active compounds from decoys in an unseen compound collection, and indeed several compound vendors are now using LASSO to create subsets of virtual active molecules against specific target classes.

For more information on eHiTS, eHiTS-Lightning or LASSO, please contact SimBioSys via info@simbiosys.ca

References

1 G B McGaughey *et al*, *J. Chem. Inf. Model.*, 2007, **47**, 1504

2 Personal communication with Fedor Zhuravlev, Technical University of Denmark, Kemitorvet, DTU 201, DK-2800 Kgs. Lyngby, Denmark

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Since chemists first conceived of atoms as the smallest unit of an element, a quest for the means to visualise atoms and their compounds has continued unabated. In the 1850s, state-of-the-art representation consisted of balls and sticks. The problems with these were numerous – primarily in depicting molecular motion, conformations, etc.

The marriage of computers and the ability to render highly accurate images of complex molecules in ChemBio3D makes it possible to produce high-quality images quickly. The ChemDraw program is bundled with ChemBio3D, making it easy to prepare 3D models.

'Model Explorer' is an excellent addition to the software suite, especially thanks to its increased emphasis on proteins, enzymes,

