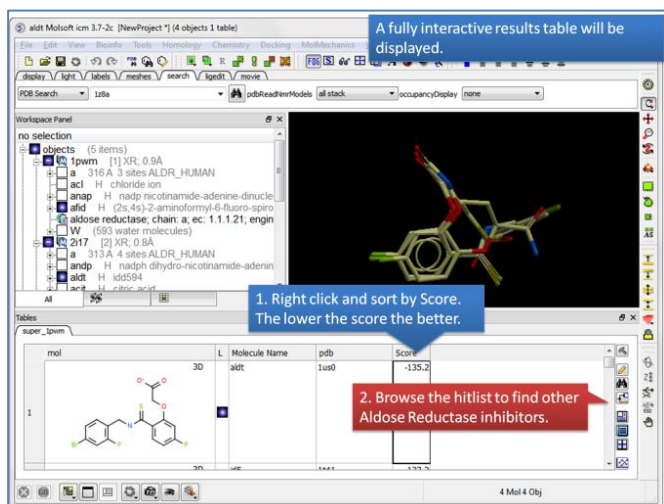# MolSoft

MolSoft ICM Quarterly
February 2012

Thank you for your continued support of MolSoft's ICM software. We hope this newsletter will be useful to keep you up to date with all the latest ICM features and news.

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How to Perform Ligand-Based Screening Using Atomic Property Fields

In the latest version of ICM (3.7-2c) you will find some exciting new tools in the Chemistry menu. Click on the Chemistry menu and then look for the option called "APF Tools". APF stands for Atomic Property Fields and is a 3D pharmacophoric potential implemented on a grid (Totrov 2008 and 2011). APF can be generated from one or multiple ligands and seven properties are assigned from empiric physico-chemical components (hydrogen bond donors, acceptors, Sp2 hybridization, lipophilicity, size, electropositive/negative and charge). An independent study found that APF is the most efficient program for chemical alignment and docking accuracy compared to other commercially available software (Giganti *et al* 2010).
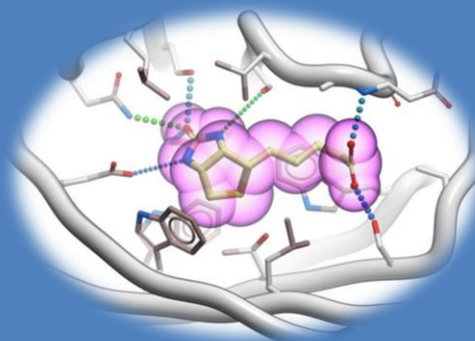
Click here for instructions on how to undertake virtual ligand screening using APF.

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In this issue:

- Ligand-Based Screening
- Multiple Receptor Docking in the 3D Ligand Editor
- Atomic Property Fields Docking
- Additional APF Features
  Virtual Ligand Screening (VLS) Result Analysis Tools
- New VLS Hitlist Visualization Options
- New High Precision Loop Modeling Tutorial
- Join our 2012 ICM User Group Meeting in March

Some Additional APF Features:

- How to calculate a pairwise APF score [More...]
- How to generate a consensus pharmacophore [More...]
- How to perform pairwise APF superposition [More...]
- How to perform flexible APF superposition to a template [More...]
- How to superimpose multiple chemicals in a table by APF [More...]

Dock to Atomic Property Fields in The 3D Ligand Editor

You can now dock directly to APF fields in the 3D ligand editor. Simply select the ligands you wish to generate APF fields for and then proceed using the APF tab in the receptor setup stage. There are more instructions here.

APF References

Totrov M. Chem Biol Drug Des 2008 Jan;71(1):15-27.
Totrov M. BMC Bioinformatics 2011 Feb;15(12):S1:S35
Grigoryan *et al* J. Comput. Aided Mol. Des. 2010 Mar;24(3):173-182.
**Giganti** *et al* J Chem Inf Model 2010 Jun;50(6):992-100

Save the Dates - Upcoming ICM Workshop and User Group Meeting
Please join us at our 2012 ICM User Group Meeting and Scripting Workshop:

- **ICM Scripting Workshop March 28th** This workshop will teach you from first principles all you need to know about ICM scripting so you can automate your work using ICM and write your own macros and scripts.
- I**CM User Group Meeting March 29th-30th 2012** The last ICM User Group Meeting was a great success with many interesting talks and discussions. We recommend this meeting to all our ICM users and anyone who is interested in computational biology or chemistry.

For more information please click here.

How to Undertake Multiple Receptor Docking in the 3D Ligand Editor
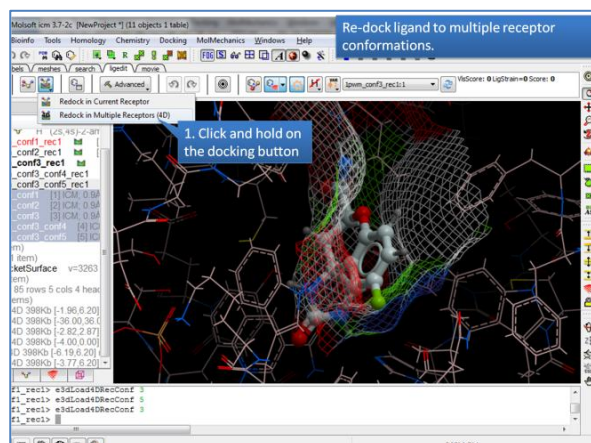
Multiple receptor conformation docking has been shown to be an efficient way of incorporating receptor flexibility into ligand docking (see Bottegoni et al J.Med.Chem 2010). Now you can dock to multiple receptor conformations in the fully interactive 3D ligand editor by selecting the superimposed structures at the receptor setup stage. 4D maps will be generated encompassing all the receptors selected. Instructions on how to do this are here.

How to Highlight ICM Syntax in the Vi/Gvim Text Editor

Many ICM users have asked how to highlight ICM syntax in Vi/Gvim. This is how you can do it:

Linux/Mac:

1. create ~/.vim/syntax in your HOME

mkdir -p ~/.vim/syntax

2. create a link or copy icm.vim file there

ln -s $ICMHOME/icm.vim ~/.vim/syntax/icm.vim

3. paste the line below into ~/.vimrc (create one if it's not there)

au BufRead,BufNewFile *.icm,_*   set filetype=icm

vi/vim/gvim myscript.icm # enjoy syntax highlighting

## Windows:

1. In you home folder ('\Documents and Settings\<username>' on XP or '\Users\<username>' on Vista and Win7)

create folder 'vimfiles' and folder 'syntax' inside it.

2. copy icm.vim (\Program Files\Molsoft LLC\ICM-Pro\icm.vim) there

3. In you home folder create (or edit exiting one) file '_vimrc' and paste line below:

au BufRead,BufNewFile *.icm,_*   set filetype=icm

gvim myscript.icm # enjoy syntax highlighting

VLS Result Analysis Tools

Once you have made a VLS hitlist you can calculate a variety of property expressions associated with the ligands. On the right hand side of the hitlist you will see a panel, press the drop down button next to the Property Expression button. The options include:

- Calculate charge of the ligand.
- Calculate buried surface of the ligand
- Calculate volume change
- Calculate whether the ligand makes a hydrogen bond with a selection. Make a selection of the residue in the receptor first.
- Calculate pharmacophore RMSD. This property expression needs an object called 'pharma' loaded in the workspace, with the pharmacophore in it.
- Calculate cisTransAmide Angle
- Calculate distance to selection. Make a selection of the residue in the receptor first.
- Calculate non-overlap with selection. Make a selection of the residue in the receptor first.

New High Precision Loop Modeling Tutorial Online
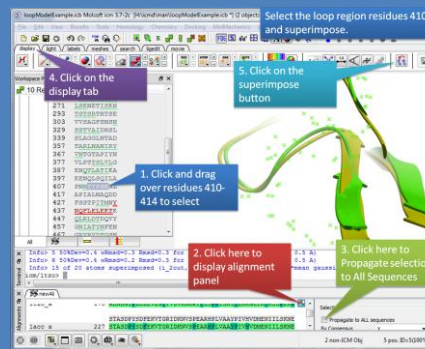
A new tutorial is available which uses the ICM high precision loop modeling method (Arnautova et al Proteins. 2010, 79:477) to model a loop region in the Anthrax Protective Antigen. The loop contains a proline residue where the cis/trans conformation is not clear from the available X-ray crystal structures. The tutorial takes you through the loop modeling steps and determines the most energetically favorable conformation of the proline and the neighboring loop residues. [More here...]

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Each of these properties will be placed in the hitlist table as a new column. You can choose a column name before calculating using the Column name dialog box. Click on the Calculate property button to run the calculation.

New VLS Hitlist Visualization Options

Once you have made a hitlist of the screening results you can use the panel on the right hand side of the hitlist to change visualization options. The available options are:

- pocketSurface = The surface of the ligand binding pocket. White=neutral surface Green=hydrophobic surface Red=hydrogen bonding acceptor potential Blue=hydrogen bond donor potential
- pocketSkin = A skin representation of the neighboring residues.
- Pretty = A default representation for ligand and receptor (see image).
- atomEnergies = An energy value for each atom in the ligand is displayed.Green and low numbers indicate a positive contribution to binding.
- clashVolumes = Highlights any clashes between ligand and receptor.
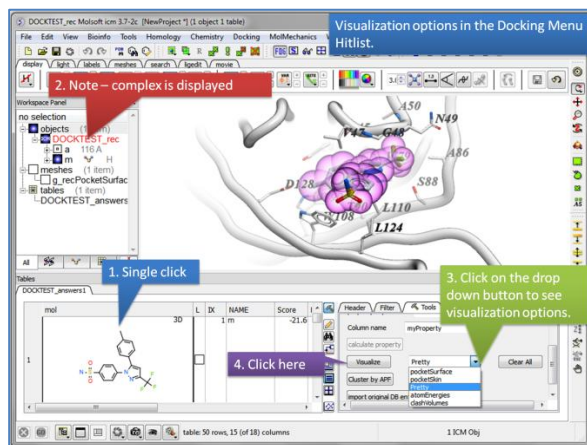
How to Move and Dock Windows in the Graphical User Interface

In the latest version of ICM it has become easier than ever before to tidy and organize the GUI. You can drag and dock the windows virtually anywhere on the screen or in the GUI and the windows are "tabbed" so you can easily toggle from one display to the next. The instructions on how to do this are here.

New Homology Modeling Book
Click image for more details.

Contact Us

Any questions? For more information about MolSoft's products or services please e-mail Andrew Orry (andy@molsoft.com) or call 858-625-2000 x108.

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