

Introducing the DS Developer Client: Customizing and Automating Discovery Studio™ Workflows

“Automated Workflow” or “Customized Workflow” are frequently used buzz words, but what do they really mean to the research scientist? How can they address common hurdles researchers face everyday? With the new release of Discovery Studio V2.1, Accelrys is pleased to announce a new addition to its modeling and simulations environment to address these questions: DS Developer Client.

A major advantage of Discovery Studio (DS) is that it allows users to easily customize an existing protocol or to create a new protocol and publish it within the DS interface for interactive modeling. As shown in Figure 1, DS Developer Client provides a visual and interactive environment to customize such workflows; it consists of a scaled-down Pipeline Pilot client with the necessary component collections to facilitate such customization.

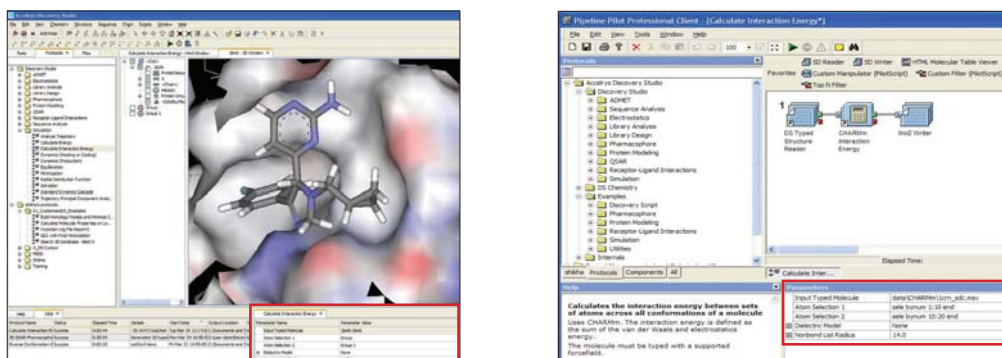


Figure 1. Discovery Studio Visualizer (left) and DS Developer Client (right). The same DS protocol is open in both interfaces (red box)

The DS Developer Client can be used to perform the following levels of customization of DS Protocols:

- Customize (i.e. promote or de-promote) parameters of existing DS protocols/components
- Add or remove available components from existing DS protocols/components
- Create a new component and add to an existing DS protocol
- Increase automation of DS Protocols (e.g. automate DS protocol to run over all files in a specific folder)
- Easily connect to an external relational database
- Integrate third-party algorithms (e.g., CORINA, proprietary codes for descriptor calculations, etc.)

The customized protocols can then be run directly from the DS Developer Client, or saved into a user area and run from the DS interface for interactive modeling. An extensive library of customized components and protocols for Discovery Studio is available for free download.²

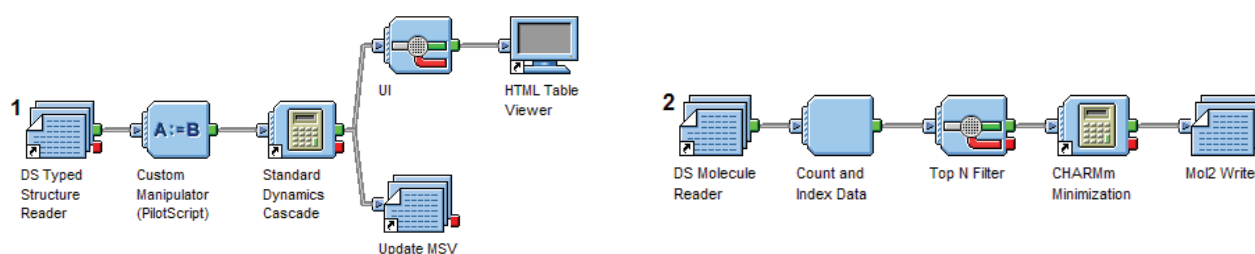
We provide here some useful and simple examples of how users can take advantage of this easy customizability of DS science.

Example 1:

Appending a Final Minimization Stage to the Standard Dynamics Cascade Protocol

This example illustrates how a standard DS protocols can be customized by integrating additional components for a specific task. The existing Standard Dynamics Cascade (SDC) protocol in DS generates trajectory frames from the production phase in the simulation cascade. This custom protocol example adds a second pipeline which selects N conformations with the lowest potential energy from the SDC output, minimizes those conformations and writes out to a mol2 file.

The second pipeline strings together the following standard DS protocol components (DS Molecule Reader, CHARMM Minimization, Mol2 Writer) and the standard Pipeline Pilot generic components ("Count and Index data" to create a numerical index of data records, and "Top N Filter" to sort data records according to specified property and pass the N records at the top or bottom of the list).

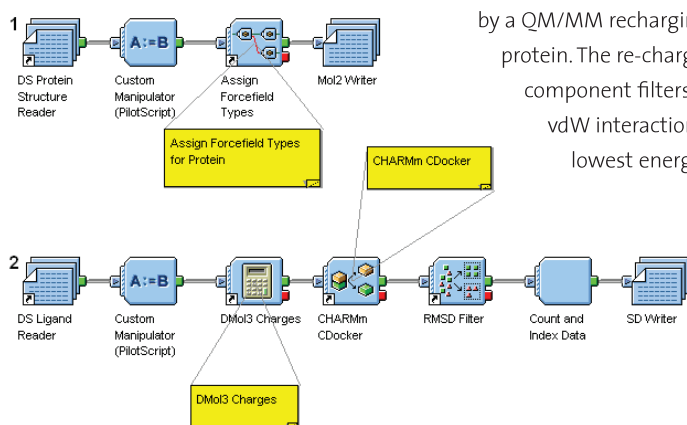


Example 2:

Recharge ligand (QM/MM) component followed by docking

In this example, we show how to add an additional step of recharging ligand atoms by QM/MM method prior to docking. This protocol performs docking using CDOCKER in which the ligands have their default (CHARMM) partial charges replaced by those derived from a QM/MM calculation. In the first pipeline shown below, a protein structure is read in, typed with the CHARMM force field, and written

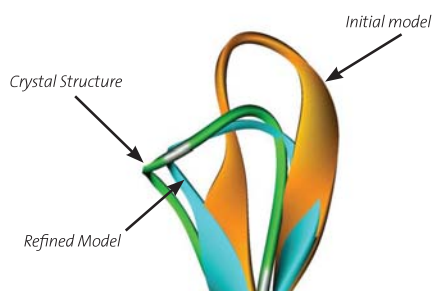
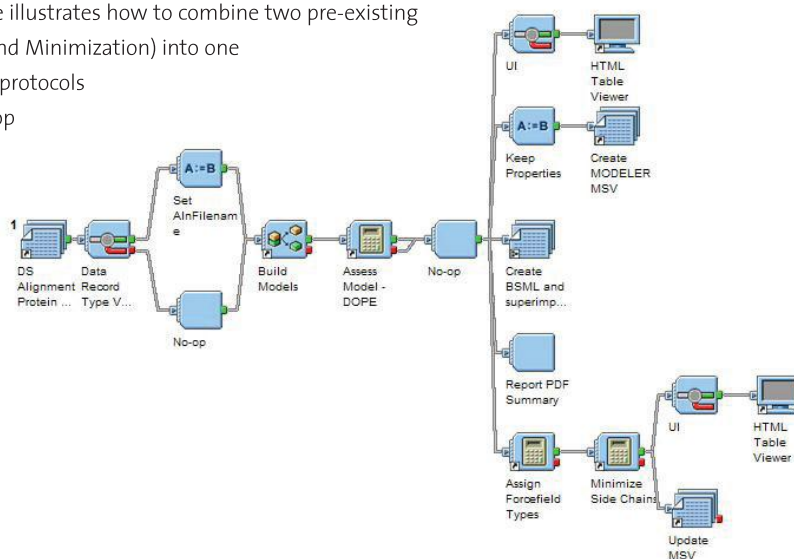
out as a mol2 file. In the second pipeline, the ligands to be docked are read in, followed by a QM/MM recharging of the ligands in the point-charge environment of the protein. The re-charged ligands are then docked using CDOCKER. The "RMSD Filter" component filters the docked poses based on CHARMM energy (electrostatic + vdW interaction energy plus ligand strain energy) and only 'n' poses with the lowest energy are written out to the sd file.



Example 3:

Building homology models and optimizing loops

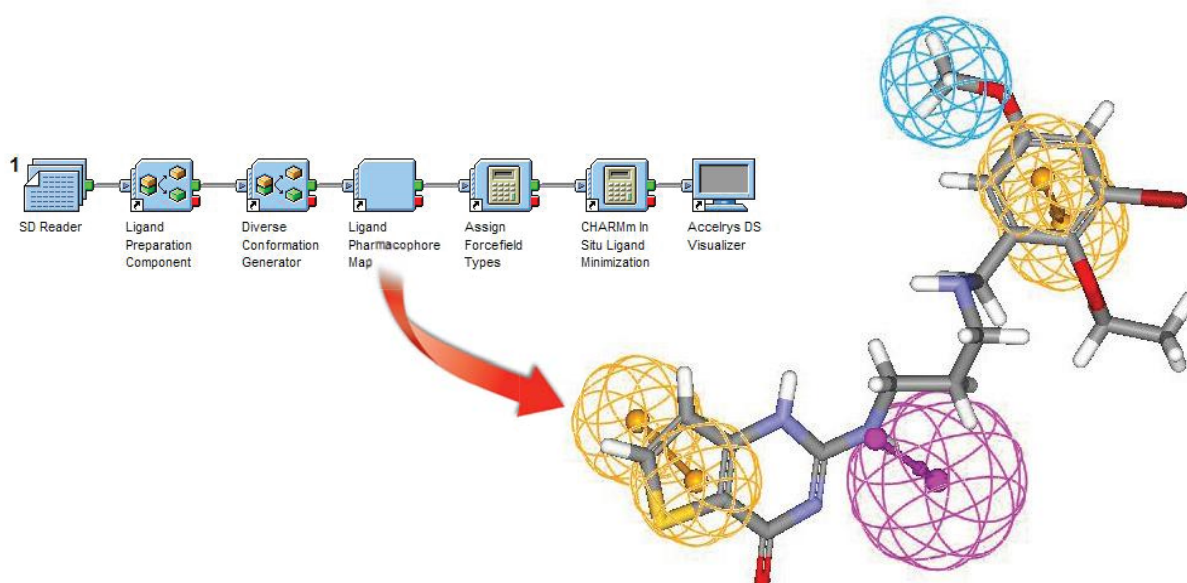
Shown here is a customized workflow that will build homology models using Modeler and then minimizes each model so that the side chain atoms are relaxed. This example illustrates how to combine two pre-existing Discovery Studio protocols (Build Homology Models and Minimization) into one workflow. The user can specify parameters from both protocols including the number of models, the option to use loop refinement, the choice of force field for minimization, etc. The backbone protein atom constraints are hardcoded using the CHARMM syntax.



Example 4:

Processing ligand data with pharmacophore filtering and minimization

It is often necessary to process small molecule data through various filters. The custom protocol below illustrates how several pre-built workflows can be combined together to achieve this. A set of ligands are processed with the Ligand Preparation component (tautomer enumeration, 2D to 3D conversion, etc.) followed by conformer generation using several available options. The resulting conformations can then be filtered by a defined pharmacophore and ranked by a fit value. Finally, these conformations can be minimized *in situ* within a defined protein active site, and the results viewed in DS.



- 1 Varma-O'Brien, S., Brown, F. K., LeBeau, A., Brown, R. D. Changing Paradigms in Drug Discovery: Scientific Business Intelligence™ and Workflow Solutions. *Current Computer-Aided Drug Design*, **2008**, 4, 13-22 13.
- 2 <http://accelrys.org/>