

What's New in Discovery Studio 2.5

Discovery Studio® takes modeling and simulations to the next level. It brings together the power of validated science on a customizable platform for drug discovery research. From project conception to lead optimization, Discovery Studio includes a diverse collection of sophisticated software applications all conveniently packaged into a single, easy-to-use Linux- or Windows-based environment. Because Discovery Studio is built upon Pipeline Pilot™, Accelrys' scientific operating platform, any software that you need can be integrated into the research environment, whether it's software from Accelrys, in-house developers, or other vendors. Notable enhancements and features since Discovery Studio 2.1 are listed below:

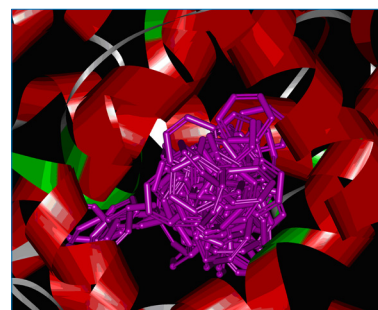
New features and Usability Enhancements

- A new welcome page opens when you start the application that provides quick access to sample files, guide you through basic tasks, new tutorials, and include links to important information sources
- New Discovery Guides allow you to combine scientific algorithms and/or existing Discovery Studio functionality to create personalized workflows
- View and manipulate your data in the new Molecule Window designed for improved performance and visualization
- Filter, sort, tag and edit large datasets in the Molecule Window without loading structures into memory until requested, which improves performance
- View the 2D chemistry of small molecules interactively with the Molecule Window, allowing you to make selections on a three-dimensional structure from a two-dimensional representation
- Automatically extract sequences and secondary structures properties from PDB and Mol2 files, enabling you to align structural data sets by sequence and secondary structure without loading the 3D structures into memory
- Lock the visibility of individual molecules
- Undock tabbed windows and manage them separately outside of the main application window frame for multiple monitor use
- Conveniently color atoms with a new toolbar containing various options
- You can now show the pi-pi, cation-pi, and

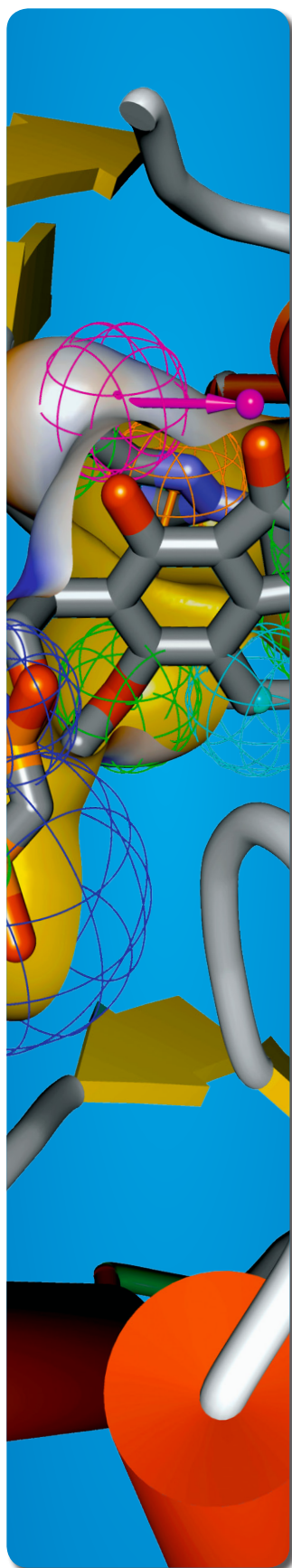
sigma-pi interactions with a new monitor type, Pi Interactions

- Automatically assign color to different molecules using the updated Atom Display Style dialog
- Access several general purpose protocols from a new folder to address routine tasks in Discovery Studio. These protocols include ligand preparation, protein preparation, filter by SMARTS, ligand efficiency calculation, molecular property calculation, etc.
- Many short running protocols that require minimal setup can now be run as quick launch protocols from the Tools Explorer

New scientific functionality – Fragment Based Design

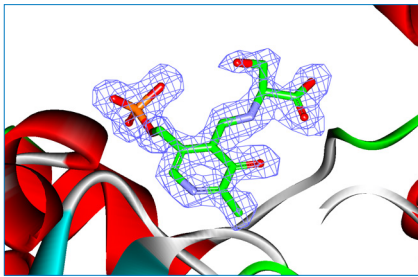


- Access a new protocol, Dock Fragments (MCSS), to place fragments in a receptor active site. This protocol uses the well validated and published Multiple Copy Simultaneous Search (MCSS) algorithm that generates a collection of positioned and oriented chemical functional groups that interact in some way with the binding-site region of a molecule
- Optionally generate fragment conformations prior to docking



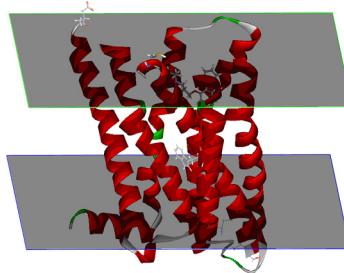
- Perform fragment minimization using CHARMM
- Use post-processing steps for clustering and removing fragments
- Analyze SAR data with a new protocol, Calculate Ligand Efficiency protocol
- Calculate Ligand Efficiency with several normalization options: Heavy Atom Count, All Atom Count, Molecular Weight, Fit Quality, and Ligand-Lipophilicity Efficiency

New scientific functionality – X-ray



- Access new collection of protocols for building and refining molecular structure models from X-ray crystallographic data
- Access the CNX, popular X-ray refinement program, as standalone application or as component collection
- Generate electron density maps for crystal structures in CNX/CNS format
- Detect water molecules in an electron density map of a fully or partially refined protein structure, and add them to the initial structure
- Generate an electron density map and use this map to automatically place one or more ligands into non-occupied X-ray electron density with real-space refinement of the ligand into electron density
- Perform full refinement of a crystal structure with a single workflow, enabling rigid-body minimization, simulated annealing, coordinate minimization, occupancy minimization, or B-factor minimization
- Validate your crystal structure using various test criteria

New scientific functionality – Transmembrane Protein Analysis



- Access a new tool panel to analyze and edit transmembrane proteins. The panel includes a simple tool for performing transmembrane helix identification from protein sequences using a Hidden Markov Model (HMM) approach
- Use the Transmembrane Protein tool panel to add implicit membranes to a protein structure with capabilities to manually edit the orientation and position of protein in membrane
- Automatically select the helix segments that are embedded inside the membrane and separate them into individual chains
- Access to several enhancements in protocols to work with protein in membrane environment. The Add Membrane and Orient Molecule protocol uses CHARMM solvation models to optimize the location of a molecule with respect to membrane

New scientific functionality – ADMET

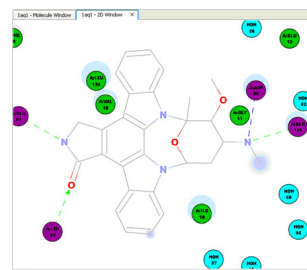
- Access new TOPKAT models, which provide improvement upon previous versions by using greater amounts of data. They are also built with more advanced algorithms, and are also extensible
- Add your own data to extend the toxicity models and improve their applicability to specific data sets

New features – Pharmacophore Analysis

- Run Pharmacophore Database Building and Searching protocols in parallel to take advantage of multi-core and multi-processor computers, resulting in greatly improved performance

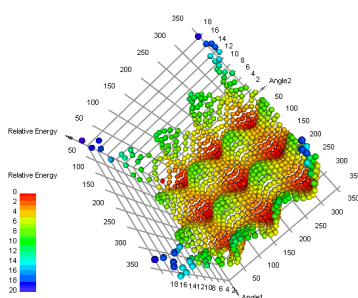
- View details of the database in a report format, such as the number of molecules built and the average conformers
- Easily map a single atom to more than one pharmacophore feature or to designate a feature as a NOT feature
- Define a sketched molecule as input for the Enumerate Library protocol

New features: Receptor-Ligand Interactions and Simulations



New features – QSAR, Library Design and Small Molecules Analysis

- Generate a classification decision tree with a new protocol, Create Recursive Partitioning, and view the results in the new dendrogram window
- Access enhanced QSAR model generation methods. Many of the learners have optimum prediction space and feature tracking capabilities
- Access a new folder, Conformations, for performing conformational searching and analysis with all methods consolidated in one place
- Use a new protocol, Generate Conformations, to specify a subset of rotatable bonds for torsion searches
- Easily Perform calculations to minimize conformations, either in gas phase or in solution using various solvation models and force fields

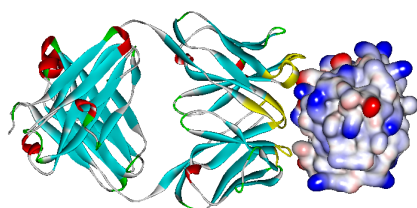


- Draw 2D ligand interaction diagrams with a new tool to compute a representation of a three-dimensional ligand-receptor binding site.
- Objects selected in the diagram are automatically selected in other views, which makes it easy to select items of interest in more complex views.
- Compute the conformational entropy of the ligand in the enhanced version of the Calculate Binding Energies protocol. This adds a term to account for the loss in conformational entropy in going from the starting set of conformations to a single docked conformation
- Access the popular GOLD docking program, licensed by CCDC, in the Dock Ligands (GOLD) protocol
- Access improved performance in all of the high-throughput docking protocols using CHARMM
- Use the upgraded protocols in the Simulation folder for projects dealing with protein membrane systems more effectively.
- Add customized residues, new atom types, and new parameters directly into the forcefield editor
- Prepare your ligand data files with ionization based on customizable business rules, tautomer ranking, and filtering. Run the
- Assess conformational diversity and coverage of small molecule conformations using a new protocol, Analyze Conformations. Measure specific constraints (such as distances, angles, and torsions) across all conformations
- Quickly examine the conformations of common cores of molecules using the new Align by Substructure protocol

Prepare Ligand protocol in parallel for improved performance

New features – Protein Modeling and Analysis

- Build homology models with updated protocols: select a template and fix part of the model structure according to that template, specify nucleic acid residues to be copied from template to model structure, etc.



- Model antibody loops by fixing the framework of the antibody structure as its input coordinates and only optimize the loop region. Alter the loop definition and create groups for each loop on the input structure and the newly created models
- Superimpose proteins structures based on a set of selected residues, e.g. ligand binding site residues using the enhanced Align and Superimpose Proteins protocol

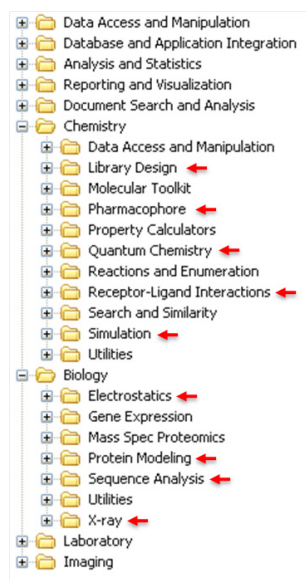
Documentation Enhancements

- A new comprehensive user guide is available that provides an overview of the product and how it compliments other Accelrys products, information about visualizing and editing data, guidelines for performing computational analyses, methods for extending the product using scripting and Pipeline Pilot, and useful deployment information.
- A set of tutorials are available to walk you through basic features, areas of technical expertise, and advanced lessons for modifying protocols.

- The help system is enhanced to provide easier navigation, improved organization, and better search capabilities.

Pipeline Pilot Integration Enhancements

- Customize any DS protocols or components using Pipeline Pilot Professional Client, also referred to as the [DS Developer Client](#)
- Access several grid enabled protocols for high performance computing. Out-of-the box support for SGE, PBS, LSF
- DS components collections are now installed into the functional categories introduced in Pipeline Pilot 7.5



Product Updates

- Accelrys provides regular updates for the DS Component Collection and the client. You can easily check for updates from the client by choosing “Help | Check for Updates” from the menu bar