

# What's New in Discovery Studio 2.1

Discovery Studio® provides the most advanced modeling and simulation software solutions for life science researchers available today. From project conception to lead optimization, Discovery Studio includes a diverse collection of sophisticated software applications in a single, easy-to-use Linux- or Windows-based environment. Because Discovery Studio is built upon Scitegic Enterprise Server™ platform, Accelrys' scientific operating platform, any software that you need can be integrated into the research environment, whether it's from Accelrys, in-house developers, or other vendors to provide a truly customized solution.

## Major New Functionality: Protocol Customization

- Leverage unprecedented graphical customization of protocols using DS Developer Client (a scaled down version of Pipeline Pilot Professional Client that is available as a part of the Discovery Studio 2.1 release)
- Customize 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 or proprietary codes

## Major New Functionality: QM/MM

- Increase accuracy of protein-ligand interaction modeling during lead optimization using a combination of Density-Functional Theory (QM) and CHARMM (MM)
- Perform single point energy calculations or geometry optimization using a wide variety of exchange-correlation functionals and basis sets
- Obtain accurate partial charges for ligands for docking or simulation applications
- Model specialized interactions such as cation-Pi, Pi-Pi and metal-ligand-receptor interactions

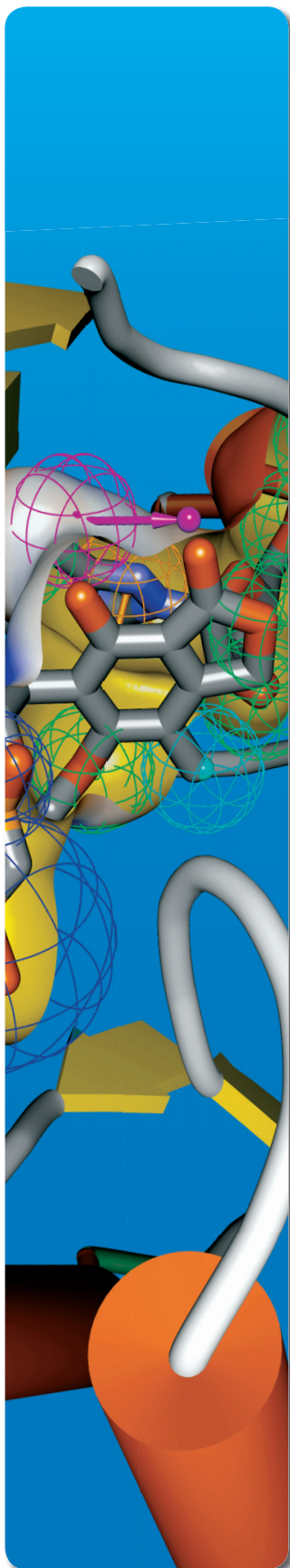
## Major New Functionality: HypoDB

- Access thousands of pharmacophore models from our partner database, Inte:Ligand, for activity profiling

- Help identify potential mechanism of action of compounds
- Screen early for potential adverse targets or finding new targets
- Determine compound selectivity to projected target families
- Create ensemble therapeutic pharmacophore screens
- Screen against ADMET Pharmacophore models

## Visualization

- Quickly create a Group from the current selection in the Hierarchy View using a shortcut key (context menu)
- Edit and save forcefield parameters interactively from the DS Visualizer Client
- Navigate easily through the Tools Explorer using a scroll bar. Access buttons instead of dropdown lists in the tool panel title bars
- Calculate solvent accessibility while taking presence/absence of ligand into account
- Explore multiple binding sites in the docking protocols due to the ability to support structures with more than one site sphere
- Access hydrogen bond angle data in the Data Table View of the 3D Window
- Specify the angle criteria for Hydrogen Bond monitors
- Seamlessly export data from a plot to a comma separated value file
- Add error bars to a 2D plot
- Import all charges from MOLV3000 files
- Merge pharmacophores with a single click



- Add/remove query/bond/atom labels from the display in a single click
- Add excluded volumes by distance from a known binding site
- Highlight minimum and maximum values in the Heat Map to improve visualization
- Track the alternate conformations removed from a protein structure via the Protein Clean report
- Retain customized coloring schemes for sequence alignments in BSML files.

### **DiscoveryScript Perl Application Programming Interface (API)**

- Access a large collection of customized scripts for specific scientific tasks through the Scripts menu in DS 2.1, as well as from the Accelrys Community website (Accelrys.org)
- Create scripts using more than 70 common high-level operations in the user interface using a new category called Commands that replicate UI actions or act on DS data models
- Improve customization by defining the folder used when running protocols via DiscoveryScript
- Directly enter input parameters for scripts from the UI in the Arguments tab of the Script Window
- Run DS protocol through a script using the RunPath path specification
- Color proteins using the proteinColorByMolecule data type, that has been added to Mdm::ProteinColorScheme
- Quickly list all property names for an object using a function
- Run the following commands/tools via scripting: molecular overlay, predict DSC secondary structure, Electrostatics tools, manage constraints/restraints, current window extents

### **ADMET**

- Filter a set of small molecules and select only those molecules that meet the rules specified by the set of selected SMARTS® rules.

### **Electrostatics**

- Access the reference titration curves for each titratable residue in a protein while running the Calculate Protein Ionization and Residue pK protocol

### **Library Design and Analysis**

- Filter out ligands with missing properties in the Find Similar Molecules by Numeric Properties protocol
- Specify a Custom Score protocol and a Custom Score Property when using both the Optimize Subset Library with Pareto Method and Optimize Combinatorial Library with Pareto Method protocols, using an example protocol (accessible via DS Developer Client or Pipeline Pilot Professional Client)

### **Pharmacophore Analysis**

- Quickly convert SMARTS rules to Discovery Studio pharmacophores using a protocol
- Customize conformation generation by defining rigid fragments in the CAESAR protocol
- Customize conformation generation by constraining bonds and atoms in the CAESAR mode of the Diverse Conformation Generation protocol
- Analyze results of the Cluster Pharmacophore protocol by accessing Inter-feature distances and RMS values used to calculate the distance matrix
- Visualize pharmacophores aligned to the ligands after running the Ligand Profiler protocol
- Append to databases created with earlier versions of Catalyst using catDB.
- Access Customized Features that have the following enhancements
  - Improved feature visualization for quick analysis of chemistry associated with the feature
  - Elements in the Hierarchy view renamed for the standard pharmacophore features to aid understanding
  - Create queries of the type (Pharmacophore A OR Pharmacophore B) with one click
  - Automation when creating customized queries to improve usability (e.g. aromatic bonds are automatically perceived and set) added
  - Ability to use Customized Feature in Feature Mapping protocol added

- Improved error handling (check features before adding to the dictionary and disallow additions of bad queries)
- Browse for Database Files, and get a report of the failed compounds, in the Build 3D Database protocol
- Get a report of failed compounds in the Build 3D Database protocol
- Analyze non-fitted ligands in the Screen Library protocol
- Catalyst Server enhancements:
  - Create and modify large (>2 GB) database files
  - Append to and merge databases in the legacy format
  - Access efficient shape indexing which is now done on disk rather than in memory and uses very little memory.

### Protein Modeling

- Employ the accurate ZRANK scoring option for the ZDOCK Protein docking protocol
- Use secondary structure information for improved alignments in the Align and Superimpose protocol
- Import Insight II – ZDOCK data into DS 2.1 using a utility protocol
- Access the updated ZDOCK server (version 2.3) (2.1 also available for backward compatibility)

### QSAR

- Delete user models generated by Discovery Studio using a protocol
- Access molecular properties in the Calculate Molecular Properties protocol in pre-organized form in 1D, 2D, and 3D categories
- Run DMol<sup>3</sup> geometry optimization as an option in the Calculate Molecular Properties protocol

### Receptor-Ligand Interactions

- Run the Flexible Docking protocol efficiently due to significant performance (disk space and memory) and usability improvements, as well as elimination of redundant poses

- Increase accuracy of docking using the Dock Ligands (LibDock) protocol due to improved hotspot matching. Track the hotspots used for docking in the LibDock protocol

### Simulations

- The performance of all CHARMM based protocols has been improved by using the FAST nonbond routine using lookup tables for solvent-solvent, solvent-solute and solute-solute interactions
- All protocols have been enhanced to use the newly optimized Generalized Born parameters by default
- The Calculate Interaction Energies protocol has been enhanced to report residue level interaction energies
- Track the charging algorithm for each molecule in the Data Table View of the 3D Window for several protocols
- Choose from van der Waals or user specified radii for GBMV, GBSW, and PBSA implicit solvent models
- Access the GBMV option in the minimization and molecular dynamics protocols
- Use the molecular surface definition for the dielectric boundary in the GBSW protocol
- Specify the salt concentration for the GBSW implicit solvent model
- Quickly identify the forcefield used in all protocols in the output Report.html file
- Access the enhancements available in CHARMM version updated to CHARMM34b1
  - Column fft for better parallel performance in PME
  - Image facility added to the Constant pH molecular dynamics (CPMD) module to use on periodic boundary systems
  - Parallelization of the SCP-ISM solvent model using standard MPI routines