

New Products and Updates to Existing Products

Schrödinger Suite 2008

New Products

Desmond 2.0

Desmond is a new and highly scalable molecular dynamics software package from D. E. Shaw Research that provides unsurpassed parallel performance, as well as highly accurate computation and competitive single processor performance, for biomolecular simulations. Performance advantages stem from scientific advances in the development of new algorithms for improving the scalability of molecular dynamics calculations. Desmond also relies on novel implementation of numerical algorithms allowing for highly accurate computations even when using single precision. Desmond is fully integrated into Maestro with easy job setup and control.

Key usability features include:

- Automated system setup and equilibration process
- Ability to solvate systems using a variety of existing equilibrated water boxes or custom solvent boxes
- Efficient parallel minimizer application for system setup and equilibration
- Support for a variety of periodic cell configurations (cubic, orthorhombic, triclinic, truncated octahedron, etc.)
- Optional automatic protocol for charge neutralization by the addition of ions
- Ability to manually restrict/select the placement of ions
- Easy-to-use graphical interface for setting up and running free energy calculations
- Ability to calculate absolute and relative solvation free energies
- Ability to calculate absolute and relative binding free energies
- Seamless integration with the OPLS_2005 force field
- Additional force fields such as recent versions of CHARMM and Amber as well as a variety of water models are supported via a template-based command-line tool
- Easy setup for simulations of proteins in explicit membrane environments
- Trajectory viewing tools
- Automated analysis tools for reviewing simulation quality
- Parallel virtual simulation application for analyzing trajectories, extracting interaction energies, etc.
- A plugin that permits writing Maestro structure files and viewing Desmond trajectories in VMD

Key technical features include:

- Scientific advances in the area of developing new algorithms for improving the scalability (i.e., parallel performance) of molecular dynamics calculations
- Novel implementation of numerical algorithms allowing for highly accurate computations (including bitwise reversibility), even when using single precision
- Long range electrostatics rigorously treated via particle mesh based Ewald techniques
- Time-scale splitting and efficient integration using multiple time-step (RESPA) based integrators
- Accurate implementation of constraints to remove highest frequency vibrations and increase the integration time step
- Support for Nosé-Hoover and Berendsen thermostats
- Support for Berendsen and Martyna-Tobias-Klein barostats
- Support for a variety of thermodynamic ensembles including: NVE, NVT, NPT, NPAT (constant surface area), NP(γ)T (constant surface tension)
- Support for isotropic, semi-isotropic and anisotropic pressure coupling
- Ability to restrain the position of selected atoms
- Checkpointing facilities for restarting

WaterMap 1.0

WaterMap is an exciting new product for calculating the chemical potential of water sites in proteins. Key features include:

- Automated identification of key locations for water molecules in ligand-protein binding sites
- Location-specific evaluation of average energy and entropy for water molecules in the binding site
- Intuitive Maestro-based graphical review of results to assist in structure-, energy-, and entropy-based lead optimization
- Ability to calculate binding free energy differences for congeneric ligands resulting from differences in the displacement of binding site waters molecules

ConfGen 2.0

ConfGen, the well-validated conformation generation engine in Glide, is now available as a standalone application. ConfGen reproduces bioactive conformations of ligands with extraordinary speed and accuracy. The fastest mode of ConGen (1 sec/ligand) generates at least one conformer within 2 Å RMSD of the bioactive (crystal structure) conformation for 96% of ligands in an extensive test set of protein/ligand complexes. Remarkably, this is accomplished by generating only 16 conformations per ligand on average. ConfGen supports many options that give the user considerable control over the conformation generation process.

Enhancements to ConfGen Advanced mode (formerly MacroModel Ligand Torsional Search):

- Sampling more conformations for dihedral angles with low rotational barriers
- Exclusion of conformations with clearly unfavorable electrostatics
- Penalty for ring stacking within a ligand

Canvas 1.1 (beta)

Canvas is a powerful and versatile cheminformatics computing suite with state-of-the-art algorithms for fingerprinting, clustering, diversity, and many other applications. Key features include:

- Graphical interface in Maestro for
 - Binary fingerprints
 - Similarity
 - Hierarchical clustering
- Command line tools for the above and for
 - Chemical filtering
 - Diversity Analysis
 - Sphere exclusion diversity
 - Substructure searching
 - Unique SMILES generation
 - Multiple linear regression
 - Partial least-squares regression
 - Principal components analysis
 - Principal components regression
 - Neural networks
 - Naïve Bayes classification
 - Multidimensional scaling
 - Self-organizing maps

Updates to Existing Products and Workflows

CombiGlide Core Hopping 2.0

- Core hopping supported on Windows
- More thorough sampling of proto-core poses during the core-hopping sampling stage
- User-selectable attachment points on candidate replacement cores for core hopping
- Post-docking visualization of core-hopped structures

Epik 1.6

- Better technology for selecting important protonation states
- Improved handling of a number of ionizable groups, including barbiturates, enamines, phosphinic acids, 1,2,4 triazoles, hydantoin, nucleic acids, and xanthenes
- More selective tautomerization of carbonyl groups
- More types of acid/base behaviors and tautomerizations
- More accurate positioning of hydrogen atoms
- Significantly improved throughput for small numbers of ligands
- Support for compressed Maestro files

OPLS2005 Force Field

- Improved handling of metal complexes
- Support for hexacoordinated sulfur atoms (e.g. pentafluoro-sulfanyl)
- Ability to handle dummy atoms to which restraints can be defined
- Support of distance restraints via zero order bonds
- Extended default rules for stretch parameter assignments

Glide 5.0

- Updated XP 5.0 GlideScore with improved performance in virtual screening across a wider range of protein targets
- Enhanced sampling of flexible rings
- Human-readable input file format for simpler wrapping and scripting of Glide experiments
- Per-residue interaction terms (vdW, Coulomb, and hydrogen-bond energies, and minimum distance)
- Atom-based scaling of receptor vdW radii and atomic charges to more finely approximate effects of protein flexibility
- Sharply reduced network traffic when distributing Glide experiments
- Optional rejection of docked poses with twisted or cis amides
- New Glide web interface

Impact 5.0

- Selective thread-based execution (OpenMP) for faster overall turnaround on shared memory computers
- ASL-based definition of restrained and frozen regions

Installation

- Script to check correctness of system configuration at installation time

Induced Fit Docking (IFD)

- Use of selected ligands in the Project Table for input
- Improved robustness

Jaguar 7.5

- Ability to calculate vibrational frequencies, NMR shielding constants, and polarizabilities using the PBF solvation mode
- Geometry scans of one or two coordinates may now be distributed across multiple processors
- New python script (csrch_pka.py) that runs a conformational search using MacroModel to find the best conformation of the protonated and deprotonated forms of the input structure in the aqueous phase and then automatically passes the two structures to the Jaguar pKa module. pKa correction factors have been added for enols
- Ability to calculate molecular surfaces for multiple selected entries in a Maestro project
- Calculations using the hydrogen_bond.py and counterpoise.py scripts can be run on multiple selected entries from a Maestro project
- OLYP and O3LYP density functionals
- The limit on the total number of atoms has been increased from 400 to 1000, and the basis function limit has been increased from 5,000 to 12,000; the limit on the number of basis functions per atom has been increased from 150 to 200
- Pseudospectral parameters for bromine and sulfur have been created for the cc-pVQZ(-g) basis set. This basis set is used in the hydrogen_bond.py protocol, so the calculation of binding energies of molecular pairs containing bromine or sulfur is now possible.
- Task panels for running counterpoise calculations and for calculating binding energies of hydrogen-bonded molecular pairs are now available from the Applications -> Jaguar task list in Maestro.

KNIME Extensions 1.1

- New cheminformatics functionality: advanced fingerprint generation options, additional fingerprint manipulation nodes, and molecular property calculator
- General usability improvements
- Improved performance and robustness

Liaison 5.0

None

LigPrep 2.2

- Better handling of misdrawn nitro groups
- Templates for more than 400 additional ring systems
- Templates for more than 125 additional types of tautomerization
- Better positioning of ring atoms
- Better handling of cage structures
- Better conformations for sulfonamides and sulfones
- Fewer dropped structures
- Support for compressed Maestro files

MacroModel 9.6

- Ability to constrain hydrogen bonds
- Support for compressed Maestro files

MCPRO+ 2.5

- Improved solvent sampling and large speedups in FEP experiments from refinement of default simulation conditions
- FEP experiments can be performed with smaller perturbations near simulation endpoints
- Improved Maestro interfaces, including visualization of solvent volumes, visualization of residues that are neutralized in model system creation, and improved animation of perturbations
- New interface to simplify setup of FEP experiments for examining ring atom structure-activity relationships

Maestro 8.5

- Flexible ligand superposition – uses Phase Shape technology, but does not require a Phase license
- Improved graphics (lighting, materials, colors)
- Improved builder functionality (ChemDraw-like toolbar)
- New panel displays in grid layout 2D structures and user-specified properties of selected Project Table entries (accessible from the Scripts menu)
- New Workspace Assistant panel greatly simplifies generation of high quality figures (accessible from the Scripts menu)
- Calculation of solvent accessible and buried SA
- Protein “Sculpting” – real time minimization following manual perturbation of a protein structure
- Excel-like conditional coloring of the Project Table based on property values
- Creation of movies from selected entries or Desmond trajectories
- Better customization of main menu
- Publication of html summary of Maestro project with annotation and link to the project
- Project backup facility

Phase 3.0

- Shape-based searching and superposition
- Automated pharmacophore perception for n sites, n-1 sites, etc., until common pharmacophores are found
- Clustering of hypotheses by geometric similarity
- QSAR on pre-aligned structures
- Visualization of command-line QSAR models
- Visualization of multiple atom/pharm classes
- QSAR scatter plots
- Freestyle Edit Hypothesis mode
- Advanced matching options for database and file searching
- Visualization of hypothesis matching tolerances

Prime 2.0

- Covalent docking
- Improved accuracy of loop prediction (new variable dielectric model, new hydrophobic backing term, new sampling algorithm)
- Improved robustness
- Significantly faster Build Structure step
- Secondary structure prediction is 100x faster than in previous versions
- Overall speedup of Prime refinement jobs
- Multithreading to take advantage of multicore machines
- DNA/RNA support

PrimeX 1.5

- Control of planarity restraint
- New graphical interface for control of H-bond optimization
- New interface to ligand placement, which includes automatic blob identification
- Improved loop placement
- Maestro sculpting function greatly eases manual adjustments
- ‘Choose best fit’ function in Rotamer Table excludes solutions with clashes
- ‘Optimal’ minimizer selection allows software to choose best method
- Faster R-factor and map calculations
- Grouped B-factors
- Support for import of phased reflections

Protein Preparation

- Interactive H-bond network optimization
- Fully integrated into Maestro
- Water sampling
- Improved speed of Protein Assignment
- Restrained minimization with heavy atoms fixed
- Automatic preparation of structures for use in Prime
- Support for remote job submission

New Python Scripts

New Python scripts are being produced on a regular basis; please visit the Script Center at <http://www.schrodinger.com/scripts.html> for a complete list of scripts or select Update from the Scripts menu in Maestro.

QikProp 3.1

None

QM-Polarized Ligand Docking (QPLD)

- Restartable
- Improved parallelization
- Modular workflow input file for easy customization
- Separate control over the number of Glide and QSite processors

SiteMap 2.2

- Ability to compute binding site volumes
- Improved version of SiteScore that functions as a site druggability score

Strike 1.7

- Use of Maestro files (.mae) for input and output

Virtual Screening Workflow (VSW)

- Support for H-bond constraints
- Ensemble docking capabilities
- Enhanced filtering options
- More scoring options: rigid docking, refine, score-in-place
- XP descriptors
- Optional MacroModel conformational sampling of large rings
- Multiple input conformations from MacroModel

XPVisualizer 5.0

- Calculation and visualization of optimal interactions based on fragment docking
- Display of absolute or relative energies
- Computation of Glide XP interaction-based molecular similarity
- Multiple coloring and sorting options
- Support for XPVisualizer fragment docking