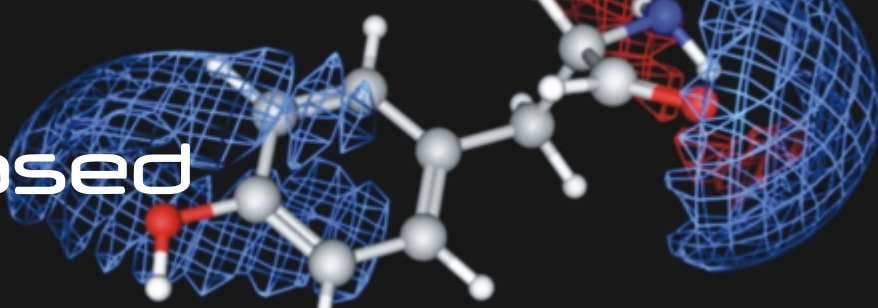


Structure-Based Design



- Active Site Detection
- Electrostatic Maps
- Molecular Surfaces
- Probabilistic Contact Potentials
- Ligand-Receptor Docking
- Fragment-Receptor Search
- Diffraction Simulation

Macromolecular crystallographic data, when available, can be a valuable source of information for discovering active ligands. MOE™ provides a collection of applications for visualizing and understanding details of receptor active sites and receptor-ligand interactions. These applications are used to suggest improvements to ligands or screen ligand databases for candidate binders.

Active Site Detection. Detect candidate protein-ligand and protein-protein binding sites using a fast geometric algorithm, based on Edelsbrunner's alpha shapes. Each site on a macromolecular structure is ranked according to its accessible hydrophobic contact surface. Visualize individual sites or populate them with “dummy atoms” for docking calculations or starting points for *de novo* ligand design efforts.

Electrostatic Maps. Determine favorable locations of neutral, positive and negative features in an active site. The electrostatic maps are calculated by solving the non-linear Poisson-Boltzmann equation for receptor atoms and pseudo-ionic species. The isocontour levels of the generated predicted map are expressed in kcal/mol. The advantage of the present method is that fully screened electrostatic potentials are used and domination of the potential by ionic groups is avoided.

Probabilistic Contact Potentials. Visualize and understand directional details of hydrophobic or hydrophilic contact preferences of a receptor or ligand using probabilistic contact maps. CCG has developed a suite of analytical probability distributions that correspond very well to inter-atomic distance, angle and out-of-plane angle histograms derived from a large collection of crystallographic structures. These distributions are then used to form a composite “preference map” for a given macromolecular structure.

Ligand-Receptor Docking. Dock small molecules in a macromolecular binding site. Supply a database of conformations or generate conformations on the fly based on potential energy models including solvation effects. The poses are scored using a London dG scoring function for estimating binding affinity. Optionally, constrain the generated poses to satisfy a pharmacophore query to bias the search towards known important interactions.

Multi-Fragment Search is an ensemble-based methodology for mapping the preferred locations of specific chemical groups in a receptor structure. An active site of a macromolecular structure is populated with a large number of chemical fragments, which are subjected to an energy minimization protocol. The resulting group locations are clustered, scored (including solvation effects) and output to a database for subsequent visualization and analysis.

Molecular Surface and Maps is an integrated application for active site analysis. Build molecular surfaces, predict contact preferences and calculate electrostatic maps. Color molecular surfaces by choosing from a variety of schemes such as temperature factor, pocket, ActiveLP and electrostatic potential.

Active Site Depiction. Use the protein-ligand interaction diagrams to easily identify polar, hydrophobic, acidic and basic residues. Visualize solvent exposed ligand atoms and residues in close contact with ligand atoms as well as sidechain and backbone acceptor and donor interactions.

MOE

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Protein Modeling and Bioinformatics
Cheminformatics and QSAR
Pharmacophore Modeling

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Molecular Modeling and Simulations
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