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MOE: New Features that Enhance the Drug Design Process

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MOE (Molecular Operating Environment) is the leading software system for drug design and protein modeling in the pharmaceutical industry.

Fragment Based Design has recently assumed great prominence as a strategy for lead optimization. Methods like Scaffold Replacement, Breed, MedChemTransformations and Combinatorial Builder produce huge libraries of potential leads. Unfortunately many of them will fail later in the process because of incompatibilities with the binding pocket. Chemical Computing Group has brought these methods in context with the binding pocket. Using the 3D information of the active site helps the researcher to focus on structures with high potential. A common interface gives the user flexible control over all tools.

For the analysis of non-bonded interactions Extended Hückel Model calculations have been implemented in MOE. Researchers can investigate interactions like hydrogen, halogen, proton-π or CH-X bonds in 2D and 3D diagrams. Desolvation binding free energy maps can be calculated in minutes using the 3D-Reference Interaction Site Model (RISM). Water, salt and hydrophobe solvation densities can be visualized for the complex or the apo structure.

For protein modeling, Kinase and GPCR family databases and analysis tools have been developed. The Kinase Explorer allows browsing aligned kinases based on core, pocket or canonical structural views. The GPCR tools identify and annotate transmembrane regions automatically. Alignment constraints can be added by a few mouse clicks to improve the sequence alignment of GPCR's. Kinase and GPCR databases can be augmented with in-house data by an automated protocol.

All these tools can now be used together with well-known MOE applications for QSAR-, homology-, Pharmacophore modeling.