MOLECULAR MODELING IN DRUG DESIGN AND BIOTECHNOLOGY

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The molecular modeling track provides a forum for contributions describing contemporary computational methods and applications. The current session focuses on drug design and biotechnological problems. In this context, drug design is perhaps best defined as the computer-aided discovery of small molecules which specifically bind macromolecular targets. Biotechnology-related problems include computational approaches to study specific manipulations of proteins (site-directed mutagenesis) and to analyze macromolecular (protein-protein and protein-DNA) interactions.

Six manuscripts are accepted for presentation in the molecular modeling section of PSB'98. Zheng et al. introduce a new concept, based on stochastic algorithms, to generate and analyze virtual combinatorial libraries. Hendrix & Kuntz introduce a new surface descriptor for the DOCK program, which enables targeting to non-concave (eg, flat or irregular) binding sites, a critical feature for the prediction of macromolecular complexes. Moeckel et al. describe the use of the Virtual Reality Modeling Language to identify substrate channels in cytochrome P450 and to analyze the effects of mutations of the P53 tumor supressor. Brown et al. present empirical free energy calculations on repressor-DNA complexes and present thoughtful explanations for the discrepancies between calculated and observed free energy values. Huang et al. introduce the Object Technology Framework program to access and manipulate structural data. Rejto and Verkhivker describe a procedure to determine, in a computationally efficient and straightforward way, linear free energy relationships for ligand-protein binding interactions based on analysis of molecular anchors (key fragments or substituents) attached to a core nucleus.

In addition to these contributions, the molecular modeling track includes invited panel presentations which provide the basis for a separate discussion forum. These presentations represent current technologies in use at major pharmaceutical companies. Bohacek describes a procedure for de novo design of synthetically feasible ligands for target receptor sites. Maggiora presents an additive physicochemical model for rapid and reliable calculation of ligand-protein binding free energies. Kollman discusses the application of molecular dynamics and free energy perturbation calculations to protein structure-function properties and protein-ligands interactions. McMartin describes a method to perform efficient flexible ligand docking for a large combinatorial library of compounds. Blaney discusses some new approaches for flexible ligand docking, including limited receptor site flexibility and new scoring functions.

We would like to thank all of our colleagues for their contributions to the Molecular Modeling track at PSB'98.