Molecular Modelling of Biological Molecules Using Accelrys Software

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Molecular modelling has shown its potential as a very powerful tool in the life science researches, especially in drug design. The software InsightII from Accelrys provides a full set of tools for molecular modelling which includes molecular graphics and forcefield-based simulations. These tools allow you build, display, manipulate, simulate, and analyse molecular structures, as well as to calculate properties of these structures. The molecules can be as simple as two-atom hydrogen molecules or as large macro-biological molecules which have tens of thousands of atoms.

In InsightII, you can build the molecules easily from scratch or residues. The Bipolymer module makes it easy for you to build and modify peptides, proteins, polysaccharides and nucleic acids.

The fundamental computation at the core of a forcefield-based simulation is the calculation of the potential energy for a given configuration of atoms. The calculation of this energy, along with its first and second derivatives with respect to the atomic coordinates, yields the information necessary for minimisation, harmonic vibrational analysis, and dynamics simulations. This calculation is actually performed by the simulation engine, or forcefield-based program. InsightII provides simulation engines including CHARMm and Discover.

The CHARMm module in InsightII is used to set up and then start a CHARMm calculation in these areas: energy calculation, energy and force calculation, molecular dynamic and free energy simulations. Please refer to the article "The Three Leading Molecular Dynamics Software Pakages" in this newsletter for more details.

Discover module is a very powerful solver in InsightII. It performs energy minimisation, template forcing, torsion forcing, and dynamic trajectories and calculates properties such as interaction energies, derivatives, mean square displacements, and vibrational frequencies. It provides tools for performing simulations under various conditions including constant temperature, constant pressure, constant stress, periodic boundaries, and fixed and restrained atoms. Using appropriate methods and strategies, you can study docking interactions such as enzyme-substrate, polymer-polymer, or receptor-ligand interactions. You can also evaluate the multitude of conformations available to a model, energy refine a model-built structure, and evaluate configurations or chemical perturbations of a system.

Normally, the molecular modelling and structure determination procedures involve three steps: molecular model building, molecular simulations and analysis of the resulting
models and their simulations. While InsightII can be used for the first step, and Discover or CHARMM for the second, the Decipher module tackles the third step.

The analysis step is crucial - to understand the structural basis of a particular biological function, you must analyse the details of each relevant structure, relate and compare conformations of active substructures from different molecules, and relate all of these structural analyses to biological activity to construct a model for the physical origins of a targeted function. A pharmaceutical chemist interested in proposing a new drug or modifying an existing drug to improve its potency will typically analyse hundreds of candidates before a single candidate proves to be successful. For modelling software to be of use, it must provide extensive capabilities to compare these candidates in terms of conformational similarities, property similarities, functional similarities, and whether the 3D structure of the targeted receptor is known, in terms of quality of fit and energy of binding.

At SVU we provide InsightII software with the builder module, the solvers and the analysis modules, which are running on the SGI workstations. Please email ccesvuhelp@nus.edu.sg should you have any queries and problems.