COMPUTATIONAL APPROACHES TO PROTEIN STRUCTURE DESIGN:

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Computational Approaches to Protein Structure Design: beta-Bellin

Computer analysis of protein models is used to aid design of new protein structures. Using atomic coordinates of beta-bellin, an antiparallel beta-sheeted protein model designed by Jane & David Richardson, characteristics such as solvent-accessible surface, polypeptide backbone twist, beta-barrel geometry, empirical potential energy etc. were computed and compared with values obtained from atomic coordinates of native proteins. This approach involves computer analysis of native proteins as well. In addition to static molecular properties, dynamical behavior of native proteins and protein models is compared using molecular dynamics calculations.

Protein engineering, 3D structure, Molecular dynamics
Annual report on "Computational Approaches to Protein Structure Design: β-Bellin.

The goals of the project are to aid design of new protein structures by computer analysis of protein models. Using atomic coordinates of β-bellin, an antiparallel β-sheeted protein model designed by Drs. Jane & David Richardson, characteristics such as solvent-accessible surface, polypeptide backbone twist, β-barrel geometry (semiaxes of hyperboloidal cross-sections), empirical potential energy etc. were computed and compared with values obtained from atomic coordinates of native proteins. This approach involves computer analysis of native proteins as well. In addition to static molecular properties, dynamical behavior of native proteins and protein models is compared using molecular dynamics calculations.

In the first year of the project, computer analysis of native proteins concentrated on backbone twist of β-sheets and solvent- or large probe-accessible surfaces of selected proteins. Analysis of backbone twists showed large deviations from the average β-strand twist value of +20°. The deviations correlate with anisotropy of non-covalent atomic force distribution throughout the structure. Large probe-accessible surfaces of enzymes were shown to coincide with sites of limited autolysis/proteolysis.

Backbone twist and solvent accessible surface of the β-bellin model were computed and compared to those of native proteins of similar molecular weight and architecture. Quenched molecular dynamics (i.e., a molecular dynamics simulation at 800°K followed by a gradual cooling of the structure) over 10 ps resulted in partial unfolding of the model. More detailed dynamical investigation, at various temperatures (including 300°K) and on improved models, is currently under way.

One paper has been published as a result of this work. Reprints will be sent under separate cover.
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