Science at the Edge Seminar Series

Quantitative Biology Graduate Program/ Gene Expression in Development and Disease

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Multiscale Approach for Simulating, Refining and Modeling Supramolecular Complexes

A set of new computational methods has been developed for simulating, refining, and modeling supermolecular complexes at multi-resolution and multi-length scales.

On the resolution scale, quantized elastic deformational model (QEDM) was designed to reliably describe large-scale protein motions in the absence of amino-acid sequence and atomic coordinates. QEDM yields an accurate description of protein dynamics over a wide range of resolutions even as low as 30 Å. On the length scale, substructure synthesis method (SSM) was developed to derive the motions of a given structure as a collection of those of an assemblage of substructures. SSM was applied to F-actin, a typical filamentous system in cells. The results demonstrated that SSM is capable of scaling the simulation of atomic motions of molecular complexes to a macroscopic length scale.

We also report a novel X-ray crystallographic refinement protocol for modeling anisotropic thermal parameters of supramolecular complexes and membrane proteins. Based on that, a very small set of low-frequency normal modes (*e.g.*, 25 ~ 50 modes) was used to reconstruct the thermal motions in X-ray diffraction. The method was applied on a series of supramolecular complexes and membrane proteins, all of which structures were solved at moderate resolutions. The results universally showed that the R_{free} values of the normal-mode-refined models were lower than the original isotropically refined models. Most importantly, the refinement resulted in improvement in electron density maps that allowed for building of a substantial amount of missing atoms including those from functionally important residues. The distribution of anisotropic thermal ellipsoids also revealed structure flexibility that is functionally important. We believe that the new protocol will help to significantly improve the structures of many highly-flexible supramolecular complexes and membrane proteins, for which further refinement is beyond any currently available methods.

Friday, March 28, 2014 at 11:30a.m.
Room 1400 BPS
Refreshments at 11:15