Probing Macromolecular Motions and Couplings Using Elastic Network Models

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Macromolecular dynamics provide essential links between biomolecular structures and functions. The all-atom molecular dynamics and its variations have been developed to simulate and analyze macromolecular dynamics. However, given the state-of-art computing capacity, its use is limited in both time scale and system size. Many biologically interesting macromolecular motions span a time scale of microseconds to seconds which is beyond the reach of all-atom molecular dynamics.

In this talk, we will present a set of novel methods that probe macromolecular dynamics based on a coarse-grained physical model (elastic network model or ENM). Recent findings suggest that a handful of lowest normal modes solved from the ENM give surprisingly good descriptions of many protein conformational changes observed between different functional states. By combining this coarse-grained modeling technique with the basic theories of perturbations and correlations from statistical physics, we have developed a set of highly efficient methods that probe several key aspects of macromolecular dynamics: first, dynamical effects of point mutations; second, long-range dynamical couplings that mediate molecular signaling; third, the quantitative relationship between the global dynamics of the whole protein and the local dynamics of its functional site. This method is applicable to dynamics/motions of large macromolecular complexes with long time scales.