2012 Special Program in Applied Mathematics and Applied Mechanics

Dynamic allosteric communication of biomolecules and drug design

2012 - 11 - 07 (Wed.)
15:00 - 17:00
308, Mathematics Research Center Building (ori. New Math. Bldg.)

Dynamics is a crucial part for understanding the function of a biomolecule. Although information about intramoelcular dynamics is difficult to obtain with experimental approaches, it is rather accessible via molecular dynamics simulations. Recently, microsecond time scale for simulations of membrane proteins, namely, receptors, transporters, pumps, have become widely affordable, and it is therefore timely to ask whether molecular dynamics simulations at this time scale can already provide sufficient dynamical information ready for functional interpretation. Standard analyses for dynamics of biomolecules include atomic fluctuations, dynamical cross-correlation matrix (DCCM), principal component analysis, etc. Recently, use of mutual information to define generalized correlation has also been proposed. However, with the substantial lengthening of time scale, these analyses should be performed with care, especially when molecule conformations are represented in cartesian coordinates. In this talk, I will demonstrate how more appropriate analyses could be performed with suitable structural alignments, guided by statistical tests. Besides, with the dynamical time correlation matrix (DTCM) analysis, we will show how long the correlated motion or dynamical memory within a protein can persist. We also will illustrate how a membrane protein can be anatomized in terms of dynamics of correlated motions. These analyses may help to examine the causality relationships between different dynamics states of the receptor, and provide useful functional information for a drug acting on a given target protein.

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