Network Analysis of Ligand-Perturbed Protein Dynamics

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Dynamics is a crucial part for understanding the function of a biomolecule. Although information about intramoelcular dynamics is difficult to obtain with experiments, 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 and to distinguished different functional types of ligands. Standard analyses for dynamics of biomolecules include atomic fluctuations, dynamic cross-correlation matrix (DCCM), principal component analysis, mutual information analysis, etc. 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, we will demonstrate how more appropriate analyses could be performed with suitable structural alignments, guided by statistical tests. Besides, with the time-lag dynamical cross correlation matrix (tlDCCM) analysis, we will show how long the correlation can persist. We also will illustrate how a membrane protein can be anatomized in terms of dynamics of correlated motions. Specific examples include the human adenosine A_{2A} receptor bound with different ligands, the bacterial efflux pump Sav1866 transporter, and the bacterial leucine transporter LeuT. If time allows, we will also show more recent analyses of molecular dynamics trajectories using Baysian networks.