GSB SEMINAR

From structure to function: the convergence of structure based models and co-evolutionary information

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Date: 12 月 9 日(Wed)
Time: 12:00~13:20 Lunch
13:30~15:20 Academic Seminar
Place: 臺大生科館 3F 演講廳

Understanding protein folding and function is one of the most important problems in biological research. Energy landscape theory and the folding funnel concept have provided a framework to investigate the mechanisms associated to these processes. Since protein energy landscapes are in most cases minimally frustrated, structure based models (SMBs) have successfully determined the geometrical features associated with folding and functional transitions. Structural information, however, is limited with respect to different functional configurations. This is a major limitation for SBMs. Alternatively statistical methods to study amino acid co-evolution provide information on residue–residue interactions useful for the study of structure and function. Here, we show how the combination of these two methods gives rise to a novel way to investigate the mechanisms associated with folding and function.

We will also show how this combined approach can be used to develop a procedure to predict the association of protein structures into homodimers. Coevolutionary contacts extracted from Direct Coupling Analysis (DCA) in combination with SBMs guide the simulations of dimerization. Identification of dimerization contacts using DCA is more challenging than intradomain contacts since direct couplings are mixed with monomeric contacts. Therefore a systematic way to extract dimerization signals has been elusive. We provide evidence that the prediction of homodimeric complexes is possible with high accuracy. The mean RMSD is 1.38 Å for the most accurate conformations of 11 structurally diverse dimeric complexes. This methodology is also able to identify distinct dimerization conformations as for the case of the family of response regulators, which dimerize upon activation.

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