生物信息学研究中心
Center of Bioinformatics

学术报告

题 目： Mathematical modelling and computational analysis of protein folding

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地 点： 思源楼 1013 室

摘 要：

Characterizing the equilibrium ensemble of folding pathways, including their relative probability, is one of the major challenges in protein folding theory today. Although this information is in principle accessible via all-atom molecular dynamics simulations, it is difficult to compute in practice because protein folding is a rare event and the affordable simulation length is typically not sufficient to observe an appreciable number of folding events, unless very simplified protein models are used. Here we present an approach that allows for the reconstruction of the full ensemble of folding pathways from simulations that are much shorter than the folding time. This approach is based on partitioning the state space into small conformational states and constructing a Markov model between them. The talk will presented the mathematical theory that allows for the extraction of the full ensemble of transition pathways from the unfolded to the folded configurations, and can be likewise applied to many other complex systems exhibiting metastable effective dynamics. The approach will then be applied to the folding of a small protein, the PinWW domain in explicit solvent, where the folding time is two orders of magnitude larger than the length of individual simulations. The results are in good agreement with kinetic experimental data and give detailed insights about the nature of the folding process which is shown to be surprisingly complex and parallel. The analysis reveals the existence of misfolded trap states outside the network of efficient folding intermediates that significantly reduce the folding speed.

Prof. Christof Schuette is a full professor in mathematics at Freie Universitaet Berlin. His speciality is biocomputing. He is one of the Directors of the Berlin Mathematical School - a joint top graduate school in mathematics of the research universities in Berlin - as well as the Vice Director of the Research Center MATHEON - Mathematics for Key Technologies - funded by the German Science Foundation (DFG) as a center for excellence.