



THE CHINESE UNIVERSITY OF HONG KONG

Department of Physics

SEMINAR

# Computational Tools for Enhancing Conformational Sampling of Biological Macromolecules

by

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ALL INTERESTED ARE WELCOME

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## Abstract

Conformational changes are crucial for a wide range of biological processes including biomolecular folding and the operation of key cellular machinery. Probing the mechanisms of conformational changes at atomic resolution is difficult experimentally and computer simulations may complement experiments by providing dynamic information at an atomic level. One of the main challenges for computer simulations is the insufficient sampling, interesting conformational changes occur at timescale of at least microsecond while atomic simulations tend to be about nanoseconds. Popular enhanced sampling algorithms such as Replica Exchange Method (REM) and Simulated Tempering (ST) use high temperatures to help systems cross energetic barrier, while their efficiency is limited by the entropic barriers. I will introduce the Adaptive Seeding Method (ASM) for studying the thermodynamics of conformational changes of biological macromolecules. By applying the ASM to RNA hairpin folding I will demonstrate that it is significantly more efficient than REM and ST. Only local equilibrium is necessary for AMS so very short seeding simulations may be used. Markov State Models (MSMs) are then used to extract the global equilibrium populations from these short simulations. In the future, I will continue developing new methods and use them to understand conformational changes in complex biological macromolecules, like bio-molecular folding, and mechanisms of cellular machines such as RNA transcription complex.