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Engineering Sciences and Applied Mathematics

ESAM Seminar Series

Simulations of virus assembly around RNA and a general method to apply Markov state models to self-assembly

Presented by:

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For many viruses, the spontaneous assembly of a capsid shell around the nucleic acid (NA) genome is an essential step in the viral life cycle. Understanding how this process depends on the charge and structure of the nucleic acid could promote biomedical efforts to block viral propagation and guide the reengineering of capsids for gene therapy applications.

In this talk I will first discuss the dynamics and thermodynamics of virus assembly, evaluated from simulations that employ coarse-grained models for capsid proteins and NAs. We find that capsids spontaneously 'overcharge'; that is, the NA length which is kinetically and thermodynamically optimal possesses a negative charge greater than the positive charge of the capsid. When applied to specific virus capsids, the calculated optimal NA lengths closely correspond to the natural viral genome lengths. These results suggest that the features included in this model (i.e. electrostatics, excluded volume, and NA tertiary structure) play key roles in determining assembly thermodynamics and consequently exert selective pressure on viral evolution. Secondly, I will discuss an approach to use Markov state models (MSMs) to enhance sampling in simulations of virus assembly and other self-assembly problems. In this approach, the time evolution of system properties on long timescales is determined from many short trajectories run in parallel. This approach was recently developed in the context of protein folding, where it has been demonstrated as a powerful method to capture protein folding dynamics on experimentally relevant timescales. I will describe an adaptation to the MSM technique that enables its application to a wide variety of self-assembly problems.

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For further information see http://www.esam.northwestern.edu

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