

A Hamiltonian paths approach to RNA virus assembly with implications for viral evolution

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Abstract

Virus capsid assembly has traditionally been considered as a process that can be described primarily as self-assembly of the capsid proteins, neglecting interactions with other viral or cellular components. Recent work on several ssRNA viruses, a major class of viral pathogens containing important human, animal and plant viruses, has shown that this protein-centric view is too simplistic as capsid assembly for these viruses relies strongly on a number of co-operative roles played by the genomic RNA. In this talk I will describe a new generalised framework for modelling assembly that incorporates the regulatory functions provided by cognate protein-nucleic acid interactions between capsid proteins and segments of the genomic RNA, called packaging signals, into the model. Using this approach, I will demonstrate that assembly speed and yield rely crucially on the distribution and nature of the packaging signals, highlighting the importance of the crucial roles of the RNA in this process. I will show that the packaging signals in bacteriophage MS2 and the evolutionarily related GA can be predicted and that their distributions point to an evolutionarily conserved assembly mechanism. I will moreover report on our *in silico* evolution experiments, showing that packaging signals have evolved a specific distribution of affinities that optimises assembly speed and yield.