Virus-like particles, packaging signals and assembly pathways

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1. Abstract

Many viruses have evolved signals in their genome consisting of sequence motifs which have strong affinity for their cognate capsid proteins, combined with secondary structures which reliably present them in their structure. The motifs, termed packaging signals, ensure that the assembly of the virus is efficient, specific and reliable in the crowded intracellular environment. These packaging signals play crucial roles in the viral life cycle, triggering protein expression and directing the assembly of new virus particles. Using efficient virion assembly as a measure of viral fitness, we construct a genotype-phenotype map using packaging signals of a simplified virus model. Simulating viral assembly using a Gillespie algorithm, the genotype-phenotype map reveals that evolution selects assembly pathways that avoid error, as well as maximising specificity. We use this understanding of efficient assembly to interpret the packaging in directed evolution of virus-like particles, finding a jump in assembly efficiency and specificity when packing signals organised similarly to those seen in the model evolve. The same increase is seen in designed virus-like particles when packaging signals are synonymous recoded into the VLP genome. The efficiency of VLPs engineered using packaging signals shows great potential for applications.

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