Capsid assembly and genome packaging in a simple plus-strand RNA virus

Rees Garmann

San Diego State University

1. Abstract

The formation of simple plus-strand RNA viruses is remarkable for at least two reasons: first, their protein capsids are highly ordered structures, consisting of hundreds of copies of the viral coat protein arranged into a non-trivial pattern; second, their RNA genomes are packaged into these capsids with near-perfect selectivity, meaning that very few cellular RNA molecules end up in the capsids, despite the abundance of ribosomal and messenger RNA present in the cytoplasm where assembly takes place. Our lab is working to understand how simple plus-strand RNA viruses manage to pull off these remarkable feats of nanoengineering. Working with bacterial virus MS2, a long-standing model system, we use a combination of sensitive in vitro experiments involving interferometric scattering microscopy to measure the assembly kinetics of individual MS2 capsids around individual strands of RNA. In addition, we perform quantitative in vivo experiments of genome packaging in living cells to better understand the role of the RNA in the packaging process. Our experiments show that MS2 capsids assemble around RNA by a nucleation-and-growth pathway in which the RNA sequence controls the nucleation kinetics. These results provide clues into the mechanisms used by MS2 and related plus-strand RNA viruses to efficiently and selectively package their genomes, and also highlight aspects of the problem that we do not yet understand.