Assembly and Maturation of Viral Capsids Probed by Time-resolved SAXS

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Viral capsids form a protective shell composed of hundreds of protein subunits that encapsidate the genetic material of viruses including both non-enveloped (*e.g.* bacteriophages, adenovirus, rhinovirus, *etc.*) and enveloped (*e.g.* Herpes simplex virus, HIV, *etc.*). Formation of the correct final assembly is dependent upon staged polymerization of subunits followed in many cases by a maturation step that converts an assembly-facile but labile immature assembly intermediate into a mature, robust and infectious final capsid. These stages of the viral life cycle can be targets for antiviral inhibition, arresting the formation of infectious particles. Small-angle X-ray scattering is well-suited to characterize both assembly and maturation due to its sensitivity to solute size and conformation. We have carried out static and time-resolved SAXS experiments that reveal that maturation of already formed bacteriophage capsids takes place as highly cooperative two-state switching transitions. Assembly studies of hepatitis B virus capsids reveal a more complex series of polymerization steps proceeding from dimer subunits to intermediate polymers, which then appear to convert to capsids in a cooperative fashion.