Many enveloped viruses exit cells by means of budding from the plasma membrane. The driving force for budding is the interaction of an inner protein core with transmembrane glycoproteins. The molecular details of this process are ill defined. Alphaviruses, such as Sindbis virus (SINV) and Semliki Forest virus (SFV), represent some of the simplest enveloped viruses and have been well characterized by structural, genetic and biochemical techniques. Although a high resolution structure of an alphavirus has not yet been attained, cryo-electron microscopy (cryo-EM) has been used to show the multilayer organization at 25 Å resolution (Cheng et al., 1995). In addition, atomic resolution studies are available of the C-terminal domain of the nucleocapsid protein (Choi et al., 1991) which has been modeled into the cryo-EM density (Cheng et al., 1995).

Three different crystal structures, containing five independent copies of Sindbis virus capsid protein (SCP), show that amino acids 108 to 111 bind into a specific hydrophobic pocket in neighboring molecules. It is proposed that the binding of these capsid residues into the hydrophobic pocket of SCP mimics the binding of the E2 glycoprotein carboxy terminal residues into the pocket. Mutational studies of capsid residues 108 and 110 confirm their role in capsid assembly. Structural and mutational analyses of residues within the hydrophobic pocket, residues 108 to 111 of the capsid protein and residues in the carboxy terminal region of E2 in Sindbis virus and Semliki Forest virus, suggest that budding results in a switch between two conformations of the capsid hydrophobic pocket. This is the first description of a viral budding mechanism in molecular detail.


The structure of the Carnation Mottle Virus (CMV) capsid protein has been determined at 3.2 Å resolution by the method of molecular replacement. The virion consists of the protein shell, a molecule of genome RNA and two short non-genome RNA fragments. The capsid is composed of 180 copies of the same protein with molecular weight of 37,780 Da arranged in accordance with T=3 icosahedral symmetry. X-ray data (140,483 unique reflections; Rmerge=8.2%; completeness=91%; sp. gr. 123; a=382.6 Å; z=2) were collected only from 4 crystals using the synchrotron radiation with an image plate as detector. The coordinates of TBSV were used as a searching model at 6 Å resolution. Refinement has been performed using XPLOR with 5-fold non-crystallographic symmetry constraints. An R-factor of 18.3% (r.m.s. deviation from ideality for bond distances are 0.02 Å and for angles are 4.15°) in the resolution range 6.0-3.2 Å (using 140,248 unique reflections) for the final model of CMV, containing 7,479 independent non-hydrogen atoms, three calcium ions and three sulphate ions. No water molecules are included in the model. The structural and biochemical results lead us to consider an alternative assembly pathway.

The structure of the Porcine Vesicular Exanthema virus (PVEV) capsid protein has been determined at 3.1 Å resolution by the method of molecular replacement. The virion consists of the protein shell, a molecule of genome RNA and two short non-genome RNA fragments. The capsid is composed of 180 copies of the same protein with molecular weight of 37,780 Da arranged in accordance with T=3 icosahedral symmetry. X-ray data (140,483 unique reflections; Rmerge=8.2%; completeness=91%; sp. gr. 123; a=382.6 Å; z=2) were collected only from 4 crystals using the synchrotron radiation with an image plate as detector. The coordinates of TBSV were used as a searching model at 6 Å resolution. Refinement has been performed using XPLOR with 5-fold non-crystallographic symmetry constraints. An R-factor of 18.3% (r.m.s. deviation from ideality for bond distances are 0.02 Å and for angles are 4.15°) in the resolution range 6.0-3.2 Å (using 140,248 unique reflections) for the final model of CMV, containing 7,479 independent non-hydrogen atoms, three calcium ions and three sulphate ions. No water molecules are included in the model. The structural and biochemical results lead us to consider an alternative assembly pathway.