Structure and self-assembly of viruses

In a landmark paper Sir Aaron Klug and Don Caspar have established a theory that predicts the surface structures of viruses in terms of a family of polyhedra [1]. It is fundamental in virology and has a broad spectrum of applications, ranging from image analysis of experimental data to the construction of models for the self-assembly of viral capsids (i.e. of the protein shells encapsulating, and hence providing protection for, the viral genome). Despite its huge success, experimental results have provided evidence for the fact that this theory is incomplete, and in particular cannot account for the structure of viruses in the family of Papovaviridae, which are of particular interest for the public health sector because they contain cancer-causing viruses. Based on group theory and tiling theory we have developed a theory that closes this gap [2,3]. It leads to a new series of polyhedra, the triacontahedral series [4], that corresponds to the particles observed during the self-assembly of the major capsid proteins of viruses in the family of Papovaviridae. Among others, it allows to classify the malformations that may occur during self-assembly (e.g. [5]). The new theory has opened up various areas of application.

In this talk, we will focus in particular on our models for the self-assembly of viral capsids and the classification of crosslinking structures, which have been featured recently by Science News (Sept. 2005, Vol. 168, No. 10). Moreover, we will report on our recent results concerning the RNA-organisation within viral capsids.

(1) Assembly models: Our theory for the structural description of viruses encodes the locations both of the capsid proteins and of the bonds (dimer- and trimer-interactions) between them, and hence predicts the local bonding structure in terms of the locations of the C-terminal arm extensions of the proteins. We use this information to derive graphs that encode the structure of the intermediate species occurring during self-assembly of the capsid proteins. These graphs are combinatorial objects that are used to derive quantities of interest such as the concentrations of the assembly intermediates, and they hence characterize the assembly process [6]. Moreover, they allow us to determine the dominant pathways of assembly and hence to develop strategies of interference with the assembly process [7].

(2) Crosslinking structures: Crosslinking structures are additional covalent bonds that provide particular stability to the viral capsids. We have shown that our approach can be used to classify crosslinking structures, and that it provides a theoretical tool to probe whether crosslinking is possible for general types of viruses [8].

(3) RNA organisation within viral capsids: Many single-stranded (ss)RNA viruses organise a significant part of their genome in a dodecahedral cage as a RNA duplex structure that mirrors the symmetry of the capsid. We have further developed a model by Bruinsma and Rudnick for the structural organisation of the RNA in pariacoto virus based on results from graph theory and DNA network engineering [9]. We show that it is a representative of a whole family of cage structures that abide to the same construction principle, and derive the energetically optimal configurations.

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