Self-assembly of viral capsids

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Viruses are biological entities that can infect a wide variety of organisms—from bacteria to mammals—causing diseases that have a huge ecological, medical, and economical impact. In their simplest form, viruses are constituted by an infective genetic material (DNA/RNA) and a protective protein shell, called capsid, which is generally built in a spontaneous assembly process from several copies of the same or similar proteins. In addition, viral shells have a well-defined size in the nanometer range, are usually highly symmetric, and show relevant mechanical properties. All these features have spread the interest for viral capsids in different nanoscience fields, where several technological and biomedical applications have been developed.

Figura 1. Assembly of a viral capsid. We illustrate the process of formation of a viral shell. The spontaneous aggregation of single subunits produces a sequence of intermediates until a closed capsid is formed.

Here we focus on the self-assembly of viral capsids (see Fig. 1). *In vivo* and *in vitro* experiments have shown that empty viral shells can be formed in different conditions, for instance, of pH or salt concentration, leading to different kind of structures. Several studies have pointed out that the free energy minimization principle governs the origin of these viral structures1,2, and that the assembly of viral capsids should be regarded as a thermodynamic process3.

In this contribution, we will show that the assembly and disassembly of viruses have important analogies with the standard vapor-liquid phase transition. We will also demonstrate that classical nucleation theory could be adapted to study the self-assembly of viral capsids4, which provides a solid thermodynamic and kinetic framework to understand viral shell assembly.

In particular, we will investigate in detail the case for spherical capsids, which are the most abundant type of viral shells. We will propose a simple continuum thermodynamic model that captures the main ingredients of viral assembly, and is in agreement with simulation studies5 (see Fig. 2). Then, we will develop the classical nucleation theory of viral capsids for this particular model. We emphasize that this theory will be in agreement with several experiments that show different aspects of virus assembly, e.g., assembly-disassembly hysteresis, capsid production lag time, or capsid formation sigmoidal curves.

Figura 2. Line energy. We show the simulation (points) and theoretical (curves) results for two radii of a spherical capsid made of 32 capsomers (protein tiles). The rim of an intermediate structure (see Fig. 1) is an interface between the free subunit and capsid phases, and has associated a line energy responsible for the energy barrier represented. The points in the last part of the assembly (right) show an interesting phenomena during capsid closure: the implosion effect.

Therefore, this represents an interesting example of how basic physical principles can explain and guide the understanding of biological systems. Due to the generality of the concepts involved, the study could also be adapted to other systems in other scientific fields, such as soft condensed matter.

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Pruebas de la contribución