Physical principles in the structure of prolate viruses

Antoni Luque* and David Reguera
Departament de Física Fonamental
Universitat de Barcelona
C/ Martí i Franqués, 1, 08028 Barcelona

Viruses are non-living particles which in their simplest form are constituted by an infective genetic material (DNA/RNA) and its protective protein shell (or *capsid*), which is built in a self-assembly process from several copies of the same protein. Viruses can infect a wide variety of organisms -from bacteria to mammals- causing many diseases, which have a huge medical and economical impact. In addition, due to their well-defined size (in the nanometer range), highly symmetrical structure and their ability to self-assemble spontaneously, the interest in viruses has spread also in nanoscience, where several technological and biomedical applications are envisioned.

From the first structural determination of a viral capsid by X-ray analysis back in 1935 to the present days, many different and beautifully symmetrical viral structures have been elucidated, but the physical principles governing their architectures have not yet been fully revealed. About half of the viral species posses a roughly spherical capsid with icosahedral symmetry, characterized by a triangulation number T. However, many other viruses, including various bacteriophages and several plant viruses adopt a *bacilliform* or prolate shape, whose precise geometry is not so well understood. In particular, their non-isometric shape and the lack of well-justified theoretical models constitute handicaps for the current experimental techniques used in the structural characterization of these viruses.

Previously, we have presented a model that successfully explained the origin of icosahedral symmetry for spherical viruses[1]. Here, we extend this model to describe the physical principles underlying the structure of spherocylindrical -or prolate- viruses. The model captures the basic ingredients of the capsomer-capsomer interaction, namely a short-range repulsion to prevent overlapping, and a long-range attraction that drives the self-assembly, and is able to reproduce the equilibrium structures observed both in real prolate viruses as well as in some *in vitro* experiments. T-number icosahedral caps with hexagonally-ordered cylindrical bodies are shown to be local free energy minima (see figure), thus justifying their occurrence as optimal virus structures. Moreover, we find a set of "magic numbers-selection rules– for the number of capsomers that can be present in the cylindrical body, that confirms the geometrical classification put forward by Moody[2]. Finally, we also find other non-icosahedral capped structures that can compete energetically with the T-number capped ones and that resemble the aberrant structures observed in some viruses reconstituted *in vitro*.

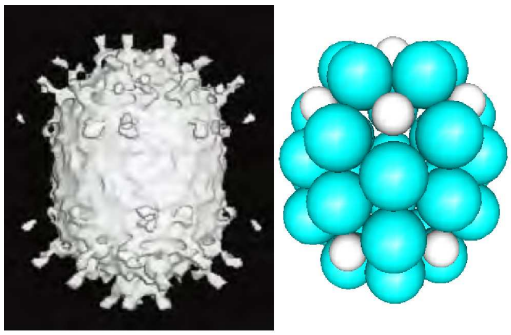

Figura 1. $3D$ reconstruction of a $\phi 29$ virus obtained by cryo-EM[3]. It is a prolate virus with a cylindrical $Q = 5$ body closed by two *spherical* caps having $T = 3$ icosahedral symmetry, according to Moody's classification[2]. On the right there is the side view of the structure corresponding to the free energy minima obtained in our model for $N = 42$ capsomers, which has the same T=3, Q=5 symmetry as the experimental result.

The understanding of the physical principles governing the architecture of these prolate viral capsids might open up new routes to prevent the correct replication of a virus and might pave the way towards the control and tunability of their structure, required for their use in nanotechnological applications.

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* luque@ffn.ub.es

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