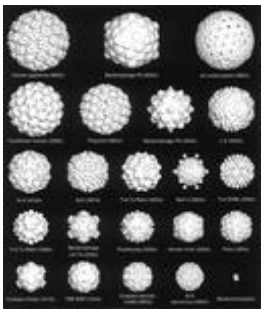
The Origin of Icosahedral Symmetry in Viruses

Research Capsid Icosahedral Monte-Carlo Simulations Theory Thermodynamics



Certainly one of the most intriguing facts about viruses is that the large majority of them display full icosahedral symmetry, arguably the highest and also the most esthetically-pleasing symmetry shown in Nature. The elements of icosahedral symmetry involve 6 five-fold rotation axes, 10 three-fold, and 15 two-fold. The figure to the right shows a number of examples, including the 60nm-diameter human papilloma virus at one end and 28nm CCMV near the other; similar image reconstructions for still larger viruses, up to the 100nm-diameter herpes simplex virus, are available from cryo-EM and X-ray work (Figure from **Review by Baker et al.**). Before the brilliant conjectures of Crick and Watson in 1956, and the pioneering structural virology principles laid out by Casper and Klug in 1962, the large majority of viruses (indeed, all apart from the minority that were cylindrical) were believed to be spherical. But spherical symmetry gave way to icosahedral as soon as sufficiently high resolution X-ray and EM studies became available.

Why? What is the basis for icosahedral symmetry being so strongly preferred by viruses? Following up on the implicit conclusions drawn by Crick and Watson and by Casper and Klug almost 50 years ago, we have recently argued (**2003 PRL** and **2004 PNAS**) that there is indeed a simple physical basis for this special symmetry shown by viruses of so many different kinds, involving so many different capsid proteins. In particular we demonstrate that icosahedral symmetry allows for the lowest-energy configuration of particles interacting isotropically on the surface of a sphere. More explicitly, we find that the energy-per-particle is a minimum for configurations that involve 12 five-fold defects at the vertices of an icosahedron, and that these configurations are especially favored for "magic" numbers of particles corresponding to the "triangulation" ("T") numbers of Casper and Klug.

It turns out, however, that - even though the capsid shapes of a large majority of viruses do indeed conform to these structures - there are important exceptions. Notable among them are the cone-like shapes shown by retroviruses like Human Immunodeficiency Virus (HIV); see figure on left from **Ganser et al**. Note that once again there are 12 five-fold defects in the otherwise hexagonal lattice formed by the capsid proteins; but now they are distributed at the two ends of the truncated cone, 7 at the top and 5 at the bottom. (According to Euler's theorem, 12 is the minimum number of disclinations needed to form a closed shell from a 2D hexagonal network.) It turns out that the relative stabilities of structures of this kind, relative to closed-end cylinders and "spheres" (truncated icosahedra), can be understood in terms of the continuum mechanics of closed hexagonal lattices. More explicitly, one can formulate a Hamiltonian consisting of just a few essential ingredients: the in-plane stretching energy of the lattice, and an out-of-plane bending term involving a spontaneous curvature, i.e., a preferred local radius for the bending of the closed shell. In this way one can demonstrate how cones like that

shown on the right become competitive with spheres and cylinders as a function of the spontaneous curvature and ratio of stretching to bending moduli (**link to LANL preprint**).