Govind Menon

Building Polyhedra by Self-Assembly

Gromov begins an interesting—and speculative—recent article [2] with the question, "Is there mathematics in biology?" The answer, I think, is yes, but this is not immediately apparent, since the real underlying question is whether modern biology can inspire new forms of mathematics in a way that compares to the deep ties that bind mathematics and physics. If we believe that an essential aspect of mathematics lies in the discovery of abstract principles from empirical knowledge, there is little doubt that biology today presents us with an abundance of the "raw stuff." What seems much harder is to process this raw stuff into beautiful mathematics, especially if one begins with the genetic code and the theory of evolution.

The topic of my talk is not true biology, but an instance of "synthetic biology." All biological organisms build themselves or "self-assemble." This is, of course, familiar to us from our everyday experience, but my talk will be about much smaller organisms. For the past twenty years, nanotechnologists have been trying to manufacture devices by mimicking biological self-assembly and the exquisite design of molecular machines. The goal of my talk is to advertise one aspect of this rapidly growing field and to explain how an important biological example—the self-assembly of viruses with icosahedral symmetry—can inspire and guide the development of self-assembly in technology.

Viruses are biological organisms that lack the cellular machinery necessary for independent existence. The simplest viruses consist of genomes contained within a protein shield (the capsid). The capsid disassembles when the virus attacks a host cell; the virus genome then hijacks the host cell and uses it to make many more copies of virus genome and proteins, which then rapidly reassemble into new copies of the virus. The natural design of viruses has two elegant features that should appeal to all mathematicians: genetic economy and structural symmetry. The genetic sequences of primitive viruses are very short. For example, the genome of MS2, a well-studied virus, has only 3,569 nucleotides that code for four proteins (lysis, replicase, maturation, and coat protein), each of which has a very specific function. The lysis enzyme degrades the cell wall of the host, and the replicase catalyzes the reproduction of the virus. The other two proteins are used to build the MS2 capsid: it consists of 180 copies of the coat protein, pinned at one end by the maturation protein, in a beautiful arrangement of dimers with icosahedral symmetry (Figure 1). While the genome of MS2 has been known since the mid-1970s, it is only recently that the intricate combinatorial structure of the co-assembly of the capsid with RNA folding was deciphered by Reidun Twarock and her colleagues [1].[1]

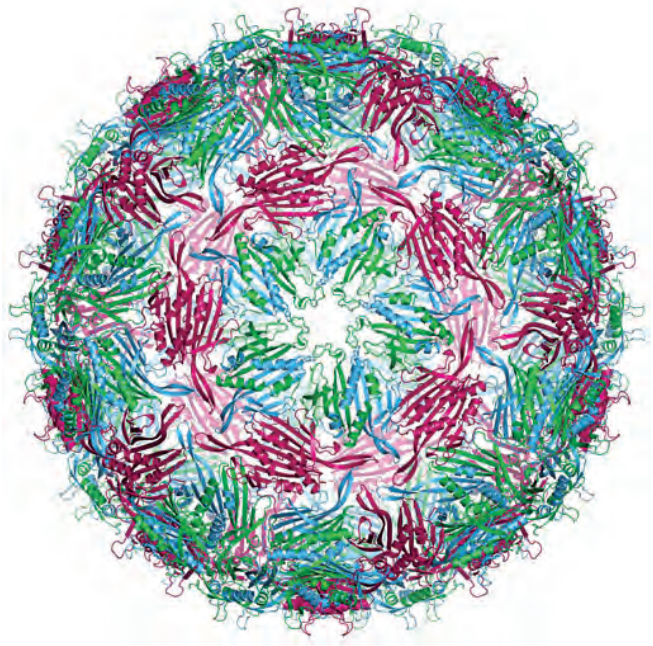

Figure 1. A ribbon-diagram showing the structure of the bacteriophage MS2. The coat protein exists in three distinct conformations (A, B, and C), which merge in pairs into A/B dimers (blue/green) and C/C dimers (maroon). A/B dimers cluster into pentamers around the 5-fold axes of an icosahedron, three alternating A/B and C/C clusters form at the 3-fold axes, and the C/C dimers sit as axes of 2-fold symmetry.

The self-assembly of viruses has inspired many examples of synthetic self-assembly. My work has mainly been in collaboration with David Gracias, an experimentalist at Johns Hopkins University. Over the past fifteen years, David has used photolithography to design many devices and containers that fold themselves into a final shape once they are released from a substrate. The devices built in his lab are small (a hair's width and smaller), but much larger than viruses such as MS2. This allows us to observe the pathways of self-folding, unlike the process of self-assembly of viruses, which must be inferred indirectly (Figure 2).

The unfolding of a polyhedron into a planar net is a classical problem in discrete geometry, and our collaboration began when David asked me what the best net should be for a self-folding dodecahedron. The issue here is a combinatorial explosion. The cube has only 11 nets, each

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[1] *For more on connections between combinatorics and molecular biology, see "Strings, Trees, and RNA Folding" by Christine Heitsch in this issue (page 817).*

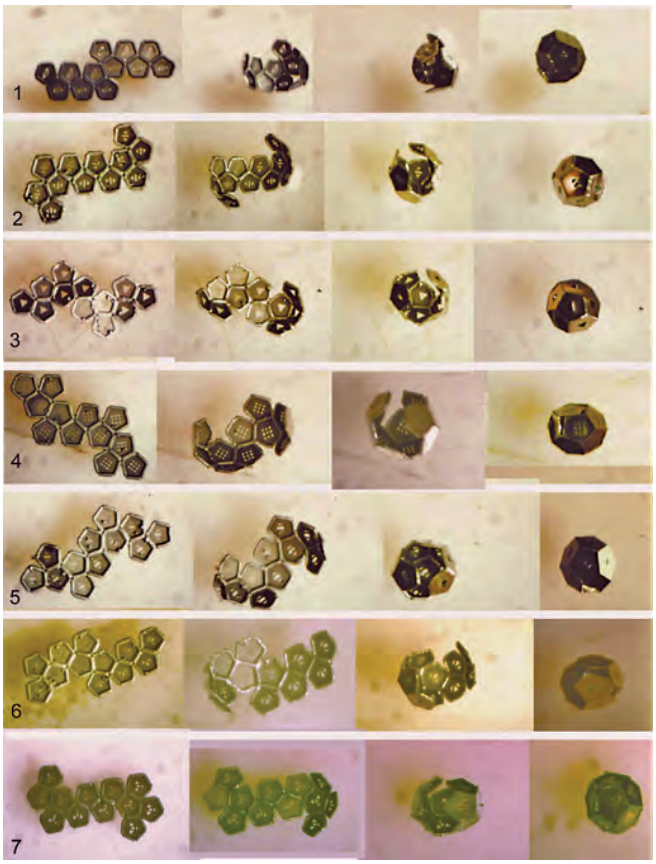

Figure 2. Optical microscope images of surface-tension-driven self-assembly of a dodecahedron from a net. The sides of each face of the dodecahedron are 300 μm.

of which may be tested in the lab. However, the dodecahedron has 43,380 nets, and, to my surprise and delight, simple heuristics along with our computations revealed the best nets in the lab [4]. Since then our work has evolved into a study of the pathways of self-assembly [3]. This has required some surprisingly sophisticated mathematics. My current goal is to understand the conformational diffusion of polyhedral linkages. More formally, this involves a rigorous formulation for Brownian motion on algebraic varieties defined by polyhedral linkages, along with effective algorithms for simulation.

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Figure 2 courtesy of Shivendra Pandey.
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Govind Menon is an applied mathematician at Brown University. He primarily works on the dynamics of disordered systems arising in materials science and physics. This includes models of turbulence, kinetics of phase transitions, and, most recently, random matrix theory and numerical linear algebra.