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Expandohedra: Modeling Structural Transitions of a Viral Capsid

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Abstract

Inspired by natural phenomena and mathematical theory this paper presents the development of a model, based on the dodecahedron, that visualizes the structural transition and expansion of a capsid (viral protein shell).

Introduction

Most viruses are made up of a protein shell, called the capsid, which encapsulates the viral genomic material. Viral capsids are a fascinating example of symmetry in nature: in fact, a significant number of capsids displays icosahedral symmetry, being almost spherical objects whose shape resembles a soccer ball. Mathematics, in particular geometry, plays a crucial role in the description of these biological structures. Specifically, inspired by the works of Buckminster Fuller on the geodesic dome, in 1962 Caspar and Klug derived a series of polyhedra with icosahedral symmetry (named icosideltahedra), to predict the locations and orientations of capsid proteins [1], and this theory still remains a fundamental framework in virology.

During the infection cycle many viruses undergo conformational changes resulting in a symmetry breaking of the capsid in order to release the genomic material inside. Little is known about the way this process works. Experiments show that for some classes of viruses the capsid expands so that the initial configuration and the final state after the expansion retain icosahedral symmetry [2]. Figure 1 illustrates the example of the Equine Rhinitis A Virus (ERAV) capsid before and after maturation. Geometrically, its shape can be approximated as a dodecahedron in its initial state and as an icosidodecahedron after expansion.

In the past few years several mathematical models have been derived to analyse structural transitions of viral capsids [3, 4]. Moreover, based on Fuller's Jitterbugs [5], a series of mechanical models collectively known as expandable polyhedra or expandohedra have been studied and designed to model viral capsid expansion [6, 7]. Motivated by these results we have visualized a virtual model in addition to constructing a physical artistic representation of an expandohedron, which represents the mathematically predicted transition of ERAV. In this paper we review these results and the interdisciplinary project that brought together mathematics, biology and design.

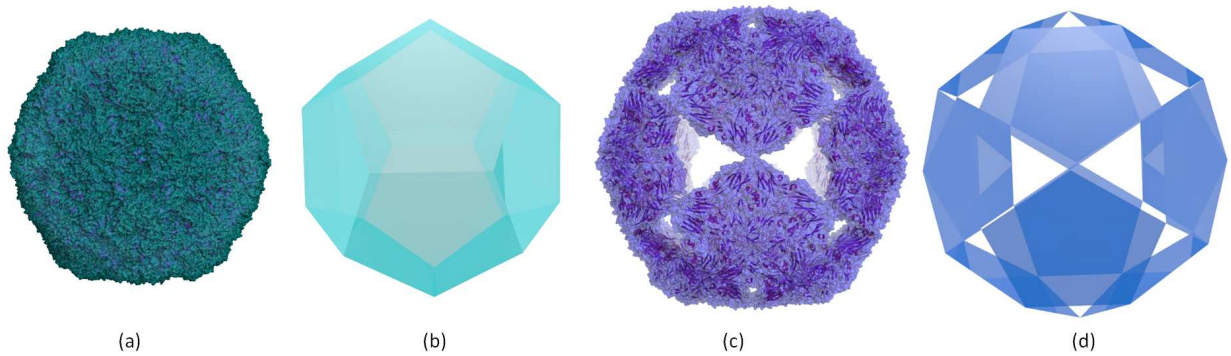

Figure 1 : *Conformational changes observed in the capsid of ERAV: closed state (a) and final state after expansion (c). Geometrically, the two states can be shaped as a dodecahedron (b) and an icosidodecaheron (d), respectively.*

Mathematical model

The capsid is assumed to have the shape of a dodecahedron: each pentagonal face, called a pentamer, represents a protein building block of the virus and acts as a rigid unit during the transition. Specifically, we assume each pentagon to be free to move and rotate along an axis perpendicular to it and passing through the center of the face (see Figure 2). Moreover, we assume that an elastic, but almost inextensible, protein thread links two adjacent pentagons keeping the integrity of the capsid shell.

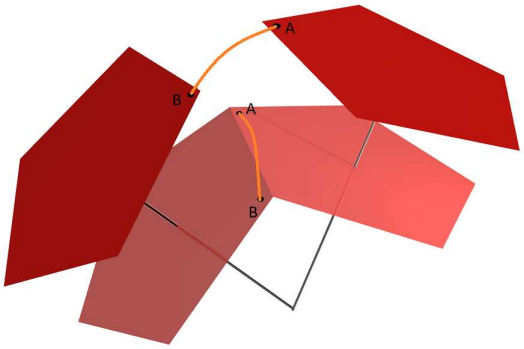

Figure 2 : *Expansion of the capsid: each face moves and rotates, and adjacent faces are linked by elastic, but almost inextensible, protein threads.*

The dynamics of the capsid is governed by the translation and rotation of each face, thus creating a system with 24 degrees of freedom. The mathematical and physical principles underpinning the expansion pathway are described in [3]. From a biological point of view, there are no information on how the expansion works. Mathematical models and stochastic simulations predict that, even if the initial and final configurations are highly symmetrical (they retain icosahedral symmetry), the symmetry of the capsid is broken during the expansion, i.e. the expansion pathway is asymmetrical. In particular, this event occurs in a cascade-like manner: one pentagons detaches, then followed by its adjacent faces and so on until the final state is attained. Here we give a visual representation of this mechanism (see Figure 3), based on numerical simulations. This contrasts a dodecahedral jitterbug model in which a symmetrical expansion occurs when all 12 pentamers move simultaneously in the same direction.

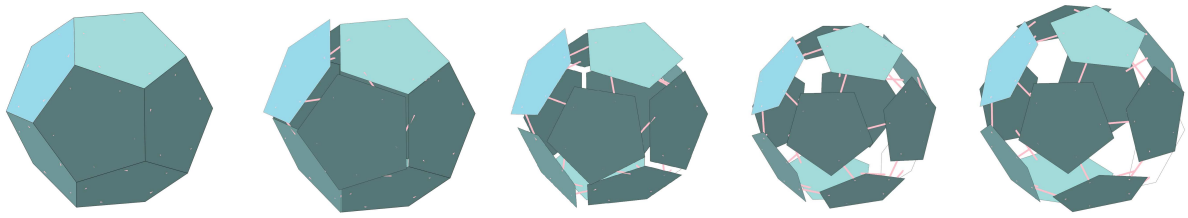

Figure 3 : *Snapshots of the asymmetric expansion pathway of the capsid: one pentagon detaches, then its adjacent faces start moving until the capsid reaches the final expanded state, which possesses full icosahedral symmetry.*

Expandohedra

In order to visualize this transformation for public engagement initiatives both virtual and physical representations were generated. This work first focused on purely geometric visualization of the dodecahedral expansion (as in Figure 3), with the aid of Python programming language and the software PyMOL [8] to simulate representations of the ERAV structure and animate the process of expansion, based on the computations in [3, 4]. Figure 4 shows a snapshot taken from the animated expansion pathway of the capsid illustrating the relative positions of the protein threads that maintain the integrity of the structure.

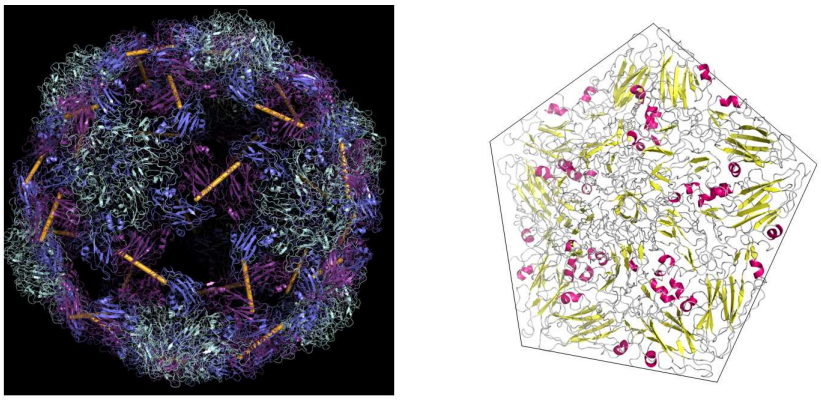

Figure 4 : *(a) Snapshots of the simulated expansion of the ERAV capsid. (b) Close-up view on a single pentagonal unit of the capsid.*

An artistic model was created from Plexiglas in order to create a physical interpretation of the expansion process. In order to combine both geometric and biological structures the ERAV protein surface pentamer was 3D-printed and resin casts were created to visualize the virus surface. Two dodecahedra were modeled, one nested within the other, constructed at different stages of expansion with colored wire filament connecting adjacent faces across axes of two-fold rotation in an equivalent manner as the protein thread (Figure 5). Identically sized faces and lengths of wire were used in the construction of both shells but the differing stages of expansion enabled the nested construction. Differing shades of color were used to visually distinguish the inner and outer capsid shells, while some of the acrylic pentamers were etched with pattern corresponding to the tiling structure underlying the symmetrical arrangement of proteins.

This paper presents on-going work exploring models, both virtual and physical, by which virus expansion may be explained. Little is known about this process although mathematical simulations has

Figure 5 : *ERAV Expansion # 1, acrylic and fiberglass, 2014.*

indicated asymmetric pathways between the symmetrical states. We hope to continue this interdisciplinary investigation combining mathematical modeling, biological experimentation and mechanical modeling in order to further investigate the expansion process. The work presented in this paper has been successfully used for public engagement activities to demonstrate the role mathematics has to play in aiding our understanding of biological structures.

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