Multiscale Modeling of Virus Capsid Formation and Evolution

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Introduction to viruses

Viruses are contagious agents and can cause epidemics and pandemics. They grow and/or reproduce inside a host cell. Figure 1 shows four typical virus morphologies. Virus infection starts with the attachment of a virus on the host cell surface, with possible fusion of viral capsid surface and the host cellular membrane, followed by virus penetration into the host cell. These processes involve mostly non-bonding interactions between the virus capsid surface and the aquatic environment, as well as the host surface membrane or receptor. An average virus comprises of millions of atoms. The real time dynamic simulation of viral attachment, fusion and penetration of a host cell in the aquatic environment requires microsecond or millisecond simulation time and is technically intractable with full-atom models at present. We therefore introduce a multiscale virus model based on differential geometry of the surfaces.

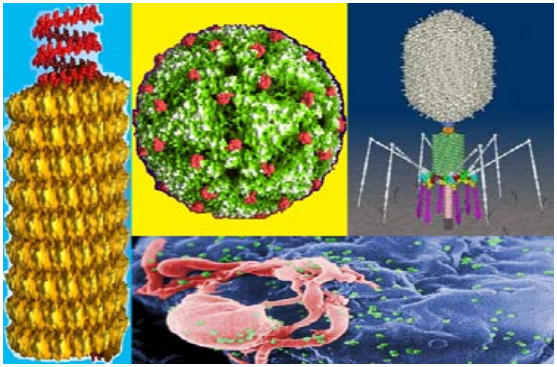

Figure 1: Four typical types of viral morphologies. Left: helical type; Top middle: spherical type (the given example is the Foot-and-Mouth disease virus); Top right: complex virus; Bottom right: viral envelope type (the given example is an HIV virus).

Multiscale model

First, we use continuum mechanics and hydrodynamics to describe the aquatic environment, and discrete atoms and/or coarse grained particles to describe the virus. As such, the interaction between virus capsid and water environment is modeled by the surface tension. The non-bonding interactions between the virus capsid subunits and between virus surface and host cell membrane or receptor are modeled by the van der Waals and the Coulomb interactions. We use the differential geometry theory of surfaces to model the boundary between the continuum domain and the discrete domain. By minimizing the free energy functional and using the steepest decent method, we arrive at a multiscale partial differential equation describing the time evolution of the boundary, i.e., the surface of the virus molecule

$$\frac{\partial S}{\partial t} = \|\nabla S\| \left[\nabla \bullet \left(\frac{\gamma \nabla S}{\|\nabla S\|} \right) - V(r) \right] \qquad (1)$$

where, S is a hypersurface function that characterizes the multiscale boundary and γ is the surface tension. Here the interaction potential is of the form

$$V(r) = \sum_i \varepsilon_i \left[\left(\frac{\sigma_i}{r - r_i} \right)^{12} - \left(\frac{\sigma_i}{r - r_i} \right)^{6} \right] + \frac{q q_i}{r - r_i} \qquad (2)$$

where ε_i, σ_i and q_i are potential well depth, van der Waals radius and charge for particle I, respectively. Equation (1) is intrinsically multiscale comprising continuum and discrete parts.

Coarse grained description

Some large viruses contain as many as tens of millions of atoms. It is impossible to handle such excessively large data set in visualization and simulation. In this case, we introduce a coarse grained model to further reduce the data size and enable the dynamic visualization. As such, we add an extra scale in our multiscale model

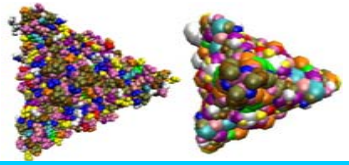

Figure 2: Coarse graining model of a viral protein subunit. Left: the full atomic model of a protein subunit of the Nodamura virus (PDB ID: 1nov); Right: the coarse graining model with each particle representing an amino acid residual.

Utilizing symmetry

Viruses typically encode a few genes. To form protective capsids, viruses usually make use of symmetries. Commonly occurring symmetries are the spherical type, helical type, circular type, and dihedral type. We utilize virus symmetries to simplify our computations. We therefore generate a virus subunit by Equation (1) and construct the whole virus capsid by symmetry.

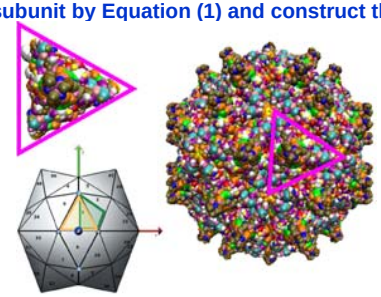

Figure 3: Illustration of virus surface construction from a facet patch by using symmetry. Top left: the generating subunit (facet patch) of the Nodamura virus (PDB ID: 1nov); Bottom left: icosahedral transformation frame used for constructing the full surface from a facet patch; Right: the full surface of the Nodamura virus constructed by symmetric assembly.

Results

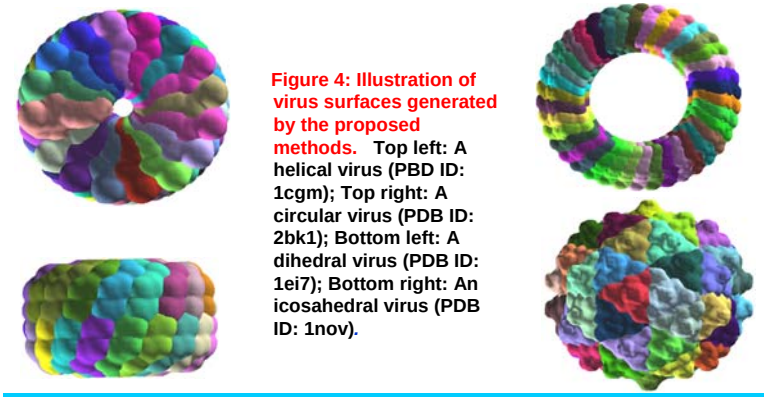

Figure 4: Illustration of virus surfaces generated by the proposed methods. Top left: A helical virus (PBD ID: 1cgm); Top right: A circular virus (PDB ID: 2bk1); Bottom left: A dihedral virus (PDB ID: 1ei7); Bottom right: An icosahedral virus (PDB ID: 1nov).

Conclusion

A mutiscale model based on differential geometry is introduced for virus capsid formation and evolution as shown in Figure 4.

Acknowledgement

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