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.

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.

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.

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 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

\[
\alpha S \frac{\partial S}{\partial t} = \nabla \cdot \left( \gamma \nabla S \right) - \nabla \cdot V(r)
\]  

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

\[
V(r) = \sum \sigma_i \left( \frac{1}{r_{ij}} \right)^{12} - \left( \frac{\sigma_i}{r_{ij}} \right)^6 + \frac{q_i q_j}{r_{ij}}
\]

where \( \sigma_i \), \( \sigma_j \), 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.

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

Conclusion

Acknowledgement
This work was partially supported by NSF grants DMS-0616704 and IIS-0430987, and NIH grant CA-127189.