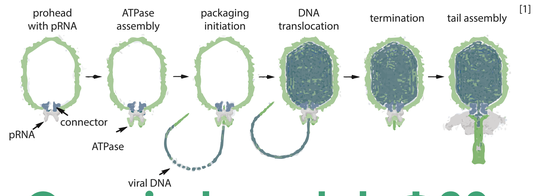
Molecular Simulation of DNA Packaging into the Φ29 bacteriophage

Nour-Saïda Harzallah & Francis W. Starr

Physics Department, Wesleyan University, Middletown, CT 06459

Introduction

Viral assembly remains one of the most fascinating biological processes that nature has ever engineered. A virus first exists as a shell called a capsid. For tailed bacteriophages and herpesviruses, viral assembly starts with DNA packaging. This process, during which the DNA is compacted to a nearly crystalline density into the capsid, is governed by a strikingly powerful molecular motor.[1] This motor is capable of overcoming the DNA repulsive electrostatic interactions and entropy barriers and results in a tightly packed DNA conformation ready to be ejected into a host cell. In our previous project, we took a close look at the dynamics of DNA ejection. Here, we study the dynamics of DNA packaging.

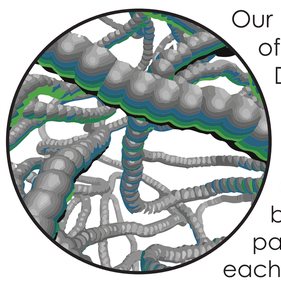


[1]

Our viral model: Φ29

We study the ejection of double-stranded DNA from the Φ29 phage using a simplified DNA and capsid model, which we simulate via molecular dynamics using LAMMPS.[2]

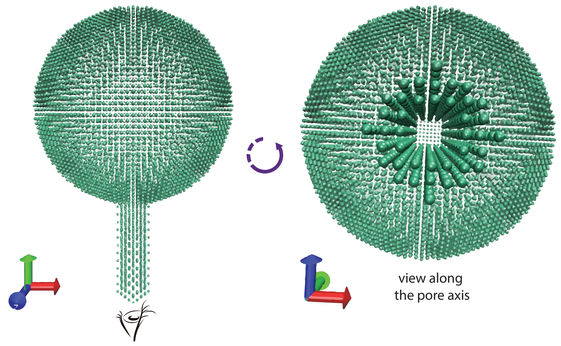
1/ Viral DNA:



Our coarse-grained model of the double-stranded DNA is represented by a chain of 5,000 beads modeling the Φ29's genome(19.3Kb). One coarse-grained DNA bead represents 8 base pairs. The diameter of each bead is 25Å (the double-helix diameter). The bond length is 12.5Å giving the DNA a cylindrical geometry consistent with known DNA structure.

2/ Viral Shell

The viral shell is composed of a capsid modeled by a hollow sphere of particles connected to a tail modeled by a hollow cylinder with both ends open. We chose the particle spacing to prevent any DNA leakage from anywhere but the capsid pore. The viral shell is kept fixed throughout the entirety of the simulation.



Simulation Setup

We define the DNA-DNA beads and DNA-capsid beads interactions using a 12/6 Lennard-Jones potential, given by:

$$U_{LJ} = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

We also define the net attractive electrostatic interactions between DNA-DNA beads using the standard Coulombic interaction potential with an additional damping factor to mimic the screening potential of a polar solvent:

$$E = \frac{Cq_iq_j}{\epsilon r}\exp\left(\frac{r}{\lambda}\right)$$

where lambda is the debye/screening length.

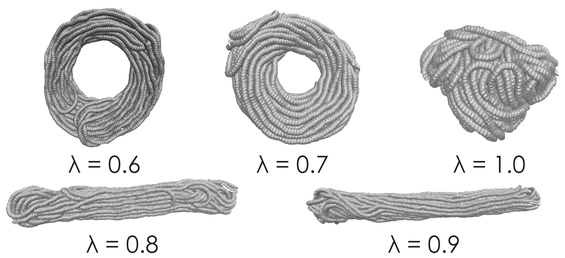
The connectivity between the DNA beads is maintained by a Hookean spring:

$$U_{bond} = K_{bond}(r' - r_0)^2$$

The angle potential between DNA beads is represented by the cosine potential to get the correct persistence length:

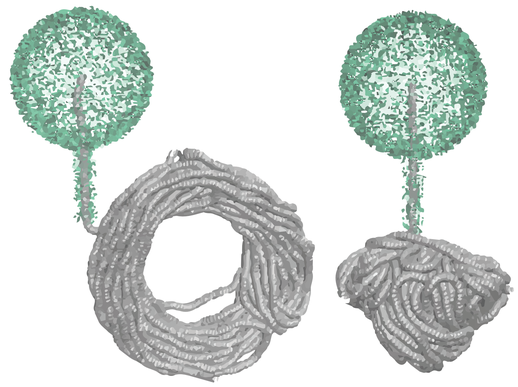
$$U_{angle} = K_{angle}(\cos\theta - \cos\theta_0)^2$$

1/ Preparing for Packaging

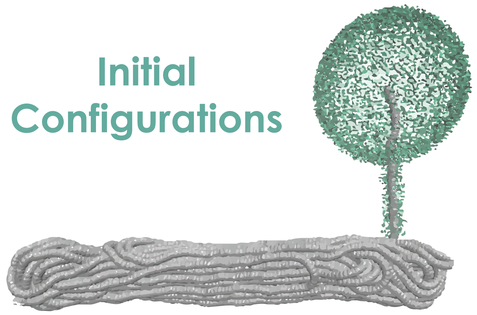


We carry 5 simulations with different lambda values to observe its conformational effect on the viral DNA.

At λ = 0.6 and 0.7, we observe toroids. At λ = 0.8 and 0.9, we observe rods. Both toroids and rods are conformations observed experimentally. At λ = 1.0 we observe an unorganizoned cluster of beads.



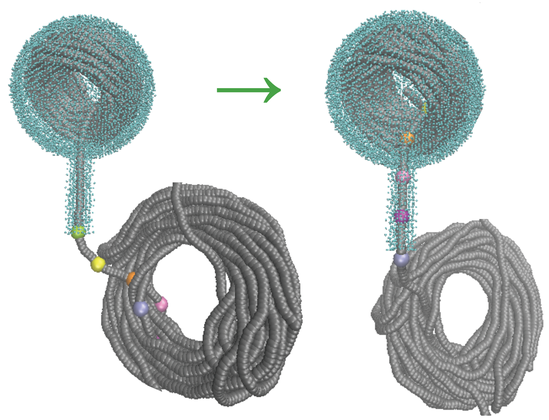
Initial Configurations



2/ Packaging

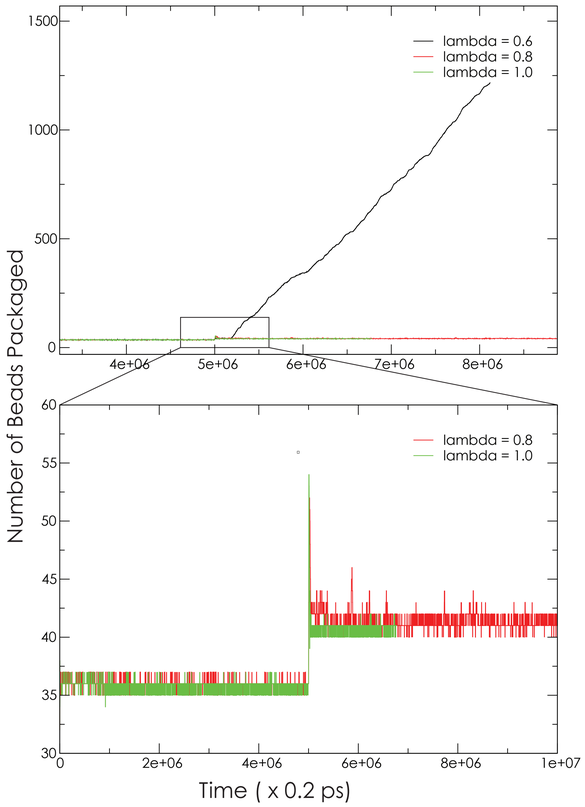
Next, we introduce the viral shell. We carry three simulations with different lambda values that give us three distinct initial conformations.

An upward force, analogous to the force induced by the ATP-driven motor in our phage model, is applied on the beads at the bottom of the feeding tube.



Results

We follow the time evolution of DNA packaging for each of the 3 simulations. We count the number of DNA beads that are confined in the viral shell.



Packaging is successful only for lambda = 0.6. The packaging force is strong enough to counteract the DNA-DNA attraction. The toroidal conformation unravels as the force pulls the DNA inside the capsid. We observe complete stalling for lambda = 0.8 and 1.0. The DNA-DNA electrostatic interactions lock the DNA in its initial conformation (rod or unorganized cluster) outside of the capsid rendering the packaging force ineffective. These conformations lead to DNA jamming. This stalling pattern is observed experimentally in a positively charged environment. Our results indicate that this stalling is due to jamming outside of the capsid rather than inside.

Moving forward, we will test the sensitivity of packaging dynamics to a wider range of lambda values to confirm the location of DNA jamming.

Acknowledgments

Special thanks to Prof. Starr for being an inspiration and an unparalleled support system.

Thank you to WesMaSS for funding my summer research!