DNA packing pressure, in the test tube and in the virus

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Apart from its fundamental importance in biology, simply as a charged semiflexible polymer, DNA has many properties only weakly related to its base sequence.

Segments of DNA molecule interact via electrostatic (at larger separations) and hydration (at smaller separation) forces. Both have been quantified in many ionic environments and over a range of temperatures. Both types of forces show a fundamental coupling between interactions and thermally driven conformational fluctuations typical of flexible polymer systems.

In solution DNA makes a wide variety of ordered liquid crystalline mesophases that can be characterized by the type and range of molecular order. In the regime of DNA densities relevant for viral packing, DNA is in a so-called line hexatic phase characterized by long-range bond-orientational order and short-range positional order.

It is widely recognized that in several viruses DNA is packed in an ordered array whose density is comparable to the densities that are easily reached with DNA *in vitro* under the osmotic stress of large polymers excluded from the DNA lattice. This means that we might gauge directly the osmotic pressure within the viral capsid just by translating viral DNA packing density into osmotic pressure.

Our investigations of the equation of state of DNA, i.e., the dependence of its osmotic pressure on its density, must be connected with the physics of viruses. In the absence of condensing ions, a typical viral DNA density would create an outward osmotic pressure inside the capsid on the order of 100 atm. Can this DNA coiled osmotic spring inside the virus be counteracted by an osmotic pressure outside?

Preliminary experiments tell us Yes…but there are discrepancies between measured packing densities *in vitro* and DNA spacings in the virus. The finite volume of a hard viral shell makes a difference to spacing and order under confinement.

Under strongly repulsive conditions, mean DNA densities and measured DNA spacings are strongly correlated inside the viral shell. This indicates that DNA essentially occupies the whole inner-viral volume. However, there might be a tiny decrease in DNA-occupied volume for viruses with shorter genomes. We do not yet have sufficient accuracy to be certain.

The major discrepancy between current understanding and our measurements is how the packaged DNA behaves, its *in viro* equation of state when under spatial confinement. We need better models and experiments to determine the general principles of viral DNA packaging compared with assemblies *in vitro*.