Alex Evilevitch

Carnegie Mellon University, Department of Physics, Pittsburgh, PA

Title: "Physical Chemistry of Viral Evolution".

Abstract:

The viral genome is enclosed in a rigid single-molecule-thick protein shell ("capsid"). In many situations the highly negatively charged genome is hundreds of times longer than a capsid's dimension. This physical genome confinement leads to high pressure on the capsid. We address basic conceptual facts that lead to high pressure in the viral capsid, and hence to the virus being infectious. Pressurized double-stranded DNA viruses provide a unique physical system to study the physical chemistry of strongly confined DNA. Since all viral capsids are permeable to water and ions, viral genome interactions are modulated by the chemical potential of water molecules hydrating the DNA. At DNA-DNA separations between 10 and 30Å, the electrostatic forces are dominated by the *hydration force*. With micro-calorimetry (Isothermal Titration Calorimetry) and atomic force microscopy (AFM) a systematic investigation of the role of DNA hydration force on viral genome ejection and packaging was conducted. We found that besides from being responsible for a pressure driven DNA release from a virus, water hydrating the genome inside the capsid is also exerting a supporting osmotic pressure on the interior of the capsid walls. Thus, the hydration force provides mechanical capsid stabilization against external deformation. In order to investigate the effects of the external cellular environment on DNA hydration inside and outside the capsid, packaged DNA length, temperature, salt and osmotic pressure have been varied.

Safekeeping of viral genetic material, successful delivery of the genome into the host cell, and survival between infections when viruses are susceptible to a variety of mechanical damage, defines the concept of *viral metastability*. We argue that the DNA hydration force is responsible for a balance between all of these factors, which are critical to the virion. Since the hydration force is directly dependent on the DNA packaging density, there is an intimate coupling between the *physical-chemical evolution* of the virus' dimensions and the genetic evolution of viruses. Insight into the physical-chemical aspect of viral evolution is provided.