Architecture of the bacteriophage genome: polymorphism and phase transitions

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In double-stranded DNA bacteriophages, the genome is densely packed at very high densities that implies that DNA is compressed in the capsid [1, 2]. In addition, the semi-rigid DNA chain, with a 50 nm persistence length, is confined in a volume of comparable dimension, which imposes high geometrical constraints. The question of the DNA chain organisation inside the capsid is a key element to understand how the genome can be transferred efficiently to the bacteria during the infection process and how it is packaged inside the proteic capsid during phage assembly inside its host cell.

In vitro, it is possible to trigger DNA ejection from a few phage species (λ, T5 and SSP1) by interaction with the purified bacterial receptor. Using cryo-electron microscopy, we analyse the DNA conformation in the full capsid of bacteriophage T5 and follow its conformational changes upon ejection. Among the many models of DNA organisation in the phage capsid, the concentric shell model is the more popular, inspired by the spectacular cryoEM images of T7 [3]. Avoiding averaging methods, we reconsider the question and show that, in T5 (that unlike T7 or ε15, miss an inner core that could help DNA wind concentrically as a spool) the genome is organized into small domains of unidirectionnaly aligned DNA segments (or monodomains), separated by defect walls that form a constrained 3D lattice. During the course of the ejection, the capsid remains homogeneously filled with DNA, independent on the length of the genome. Upon progressive release, it undergoes a series of phase transitions, turning liquid crystalline (2D hexagonal then cholesteric) and finally isotropic [4].

The addition of a DNA condensing agent to a partially filled capsid provokes the condensation of the chain into toroidal globules. The nature (either multivalent cations that diffuse through the capsid wall or polymers such as PEG that does not permeate the capsid) and the concentration of the condensing agent tune both the DNA-DNA interactions between segments of the chain and the interactions between the capsid proteins and the DNA molecule, leading to a variety of shapes and compactness [5, 6].

These results can be discussed with respects to the different forms that may be assumed by a DNA molecule inside the capsid *in vivo*, at the different stages of the infectious cycle (ejection, packaging).

[1] Smith DE, Tans SJ, Smith SB, Grimes S., Anderson DL, Bustamante C. (2001) *Nature* **413**, 748-752.
[2] Kindt J., Tzlil S., Ben-Shaul A., Gelbart W. (2001) *Proc. Natl. Acad. Sci. USA* **98**, 13671-13674.
[3] Cerritelli ME, Cheng NQ, Rosenberg AH, McPherson CE, Booy FP, Steven AC (1997) *Cell* **91**, 271-280.
[4] Leforestier A, Livolant F. (2010) *J. Mol. Biol.*, 396, 384-395.
[5] Leforestier A., Livolant F. (2009) *Proc Natl Acad Sci USA.* 106(23):9157-62.
[6] Leforestier A., Siber A., Livolant F., Podgornik R. (2011) *Biophys. J*. 100, 2209-2216.