A Nanofluidic Platform for Single DNA Studies

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The advent of single molecule manipulation techniques has revolutionized biophysical research in the last decade. In recent years, an alternative single molecule manipulation technique has emerged. This technique is based on the confinement of biopolymers in channels with a cross-sectional diameter in the range of tens to hundreds of nanometers in tandem with fluorescence imaging. In this paper, we have investigated the effect of dextran nanoparticles on the conformation and compaction of DNA. Dextran is a generic crowding agent, which is often used to mimic the intracellular crowded environment in vitro. Crowding by neutral background species and confinement in a quasi one-dimensional stationary nanostructure are both known to affect the configurational properties of DNA. The interplay of these two modes of compaction was never studied before, despite the fact that they are intimately related in biology. In this paper, we have presented some counter-intuitive and unexpected results regarding the conformation and the transition to a compact state of crowded and confined DNA. In particular, we observed that crowding in conjunction with anisotropic confinement gives a stretched conformation of DNA and a possibility for condensation at low ionic strength. Our observations and interpretation in terms of concepts from polymer physics indicate that osmotic compaction of the genome by nonbinding protein is a feasible mechanism for gene regulation in bacterial cells.

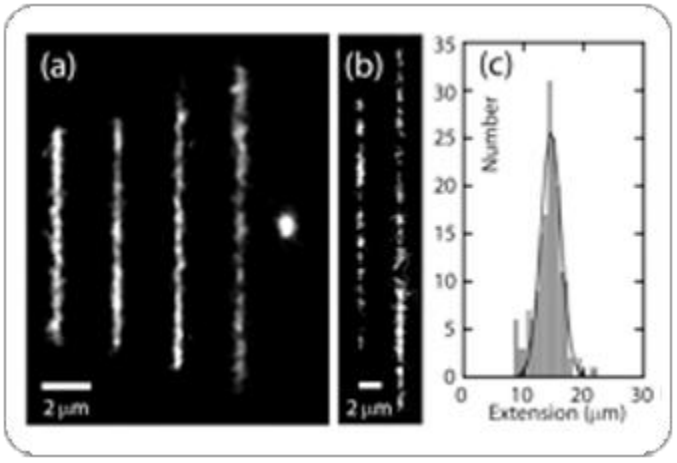

FIGURE 1: (a) Fluorescence images of T4-DNA in 300 x 300 nm2 channels. The molecules are crowded by dextran (radius Rg = 6.9 nm) with volume fraction 0, 4.2 x 10-4, 4.2 x 10-3, 4.2 x 10-2, and 6.3 x 10-2 from left to right. (b) As in panel (a), but in 150 x 300 nm2 channels and volume fraction 4.2 x 10-4 (left) and 4.2 x 10-2 (right). (c) Distribution in extension of a population of 170 molecules in 300 x 300 nm2 channels and volume fraction 4.2 x 10-2.

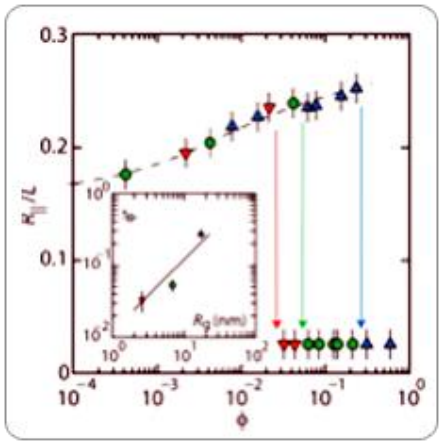

FIGURE 2: Relative extension of T4-DNA in 300 x 300 nm2 channels versus the volume fraction of dextran. Rg = 2.6 (red), 6.9 (green), and 17 (blue) nm. The arrows denote the condensation thresholds. The inset shows the critical volume fraction pertaining to condensation versus Rg.

Publication:

Macromolecular Crowding Induced Elongation and Compaction of Single DNA Molecules Confined in a Nanochannel, C. Zhang, P.G. Shao, J.A. van Kan, and J.R.C. van der Maarel, Proceedings of the National Academy of Sciences of the United States of America, **106**, 16651-16656 (2009), DOI: 10.1073/pnas.0904741106