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Confinement of DNA in small channels Applications and fundamental issues

Depending on the degree of confinement, excluded volume, inherent elastic properties of the double helix and entropic exclusion contribute to the extension of DNA in channels with cross sections on the order of the persistence length of the polymer. The exact buffer conditions set the scale of the electrostatic interactions determining the persistence length and the effective width of the polymer as well as the interactions of the polymer with the confining walls of the device. Open questions remain with regards to the exact individual contributions of each mechanism.

One great benefit of confinement from an application point of view is that the entire DNA can be easily visualized along with any labels. Typically, labels are chosen to create a pattern that is a function of the underlying sequence. Using hybridization probes or restriction enzymes, the exact sequence can be locally determined. Using more general probes in for example chromosome banding, a rough estimate of the base pair composition is the result at a resolution exceeding several tens of Mbp. We have developed a simple labeling scheme that provides a map at a resolution of 1-10kbp of the local AT-concentration along the DNA using standard intercalating dye molecules combined with gradual denaturation of the double helix. The result is a gray scale barcode that can be used to identify specific locations along the double helix and thereby give information about large-scale genetic variations along the genome. The technique is based on standard fluorescence imaging of *single* molecules, something that in turn opens up for high-throughput single-cell genomics studies. An important question is to what *extent* the resulting barcode can be used as an identifier for different parts of the genome. What factors limit the resolution of the technique? How long a stretch of DNA needs to be considered for *uniqueness*?

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