

Approaches to understanding the origin and management of DNA stiffness

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Duplex DNA, the genetic material in living cells, is an unusually inflexible biopolymer. The persistence length of duplex DNA corresponds to 150 base pairs under physiological conditions. Surprisingly, the physical origin of this DNA stiffness is unknown. In particular, the contribution of the high negative charge density of DNA to its stiffness remains both uncertain and controversial. The intrinsic inflexibility of DNA is managed in living cells by the formation of nucleoprotein complexes in which DNA is often dramatically bent, kinked and looped.

This presentation will review two related areas of interest to our laboratory. The first concerns approaches to measure or predict the effect of charge density on DNA stiffness. We ask to what extent DNA stiffness is due to DNA charge. The second concerns the mechanism of sequence-nonspecific proteins that stabilize highly-bent DNA structures, thereby reducing the apparent persistence length of DNA. Such proteins include the bacterial HU protein and eukaryotic HMGB proteins. We describe the results of ensemble and single-molecule experiments revealing the effect of HMGB proteins on apparent DNA stiffness. We then describe experiments in living *E. coli* bacterial cells emphasizing the importance of DNA flexibility enhancement by proteins to facilitate gene repression by DNA looping.