Model of DNA Bending by Cooperative Binding of Proteins

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We present a model of non-specific cooperative binding of proteins to DNA in which the binding of isolated proteins generates local bends but binding of proteins at neighboring sites on DNA straightens the polymer. We solve the statistical mechanical problem and calculate average properties such as site occupancy, cooperativity and effective persistence length. We predict that cooperativity leads to non-monotonic variation of the persistence length with protein concentration, and to unusual shape of the binding isotherm. The results are in qualitative agreement with recent single molecule experiments on HU-DNA complexes. Further experimental tests of our model are proposed.

Keywords **— Key words or phrases in order of importance, separated by commas. Key words are optional. Use no more than three lines.**

I. Introduction

Numerous proteins modify the elastic properties of DNA by introducing local bends and by changing its bending and twist rigidity. In prokaryotes the packaging of DNA is facilitated by nucleoid-associated proteins such as HU, IHF, H-NS and others. In eukaryotic chromosomes, in addition to nucleosome-forming histones, there are non-histone DNA bending proteins such as HMGB. In some cases (IHF and HMGB) measurements of force-extension curves of single DNA molecules [1] and of force-free thermal fluctuations of surface-grafted DNA [2] show that the bending rigidity of the DNA-protein complex decreases and eventually saturates with increasing protein concentration. In other cases (H-NS) binding of proteins leads to progressive stiffening of the complex [3]. Both types of effects have been modeled by describing the DNA-protein complex as a worm-like chain whose elastic properties (persistence length and bending angle) depend in a linear fashion on the concentration of bound proteins [4]. Even more intriguing behavior takes place in HU-DNA complexes (EcoHU proteins from E. coli [1]and in BstHU from thermophilic bacteria [5]), where the effective persistence length initially decreases with protein concentration as above, but at higher concentrations begins to increase and can even exceed that of bare DNA, presumably due to formation of a stiff HU-DNA filament [6,7]. Reentrant behavior was also observed in FRET experiments where the energy transfer efficiency was found to increase, reach a peak and then decrease with HU concentration [8]. The above results can be interpreted as a signature of cooperativity due to interactions between proteins bound to DNA. As far as theoretical modeling is concerned, cooperative effects on binding of proteins to DNA were considered by previous researchers who used a linear (in the concentration of bound proteins) energy functional that contained both bending and Gaussian elasticity [9]. In ref. [9] cooperativity was introduced in an indirect manner via the mean spherical approximation that leads to effective non-linear coupling between elasticity and protein concentration. Cooperativity was also introduced in the form of a tension-mediated non-contact interaction between two proteins bound to DNA [10]. In this work we introduce an exactly solvable model of protein binding to DNA which captures both the effect of cooperative binding on the spontaneous curvature of the polymer and the effect of elasticity on the binding isotherm.

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