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Protein jamming on DNA ZEBBA WUNDERLICH, Harvard, MICHAEL SLUTSKY, MEHRAN KARDAR, LEONID MIRNY, MIT — The mechanisms by which DNA-binding proteins find their sites on DNA have been the subject of intensive research in biophysics. Most theoretical models consider proteins searching naked DNA for their binding sites. In the cell, however, myriads of proteins and protein complexes (*e.g.* nucleosomes) are constantly binding DNA. What is the effect of DNA-bound proteins and nucleosomes on the rate of protein-DNA association and dissociation? Here we study how a protein finds its site on DNA, and how long it stays on its site, considering DNA that is bound by other proteins. The process of association and dissociation is modeled by rounds of 3D diffusion and 1D sliding. We assume that proteins bound to DNA act as reflecting boundaries and obstruct sliding of other proteins. We demonstrate that if the density of proteins on the DNA is above a critical level, a protein's mobility on DNA is significantly reduced, leading to jamming. We find that proteins bound to DNA in the proximity of the specific site can (i) significantly increase the time it takes for the protein to find its site, and (ii) simultaneously increase the time a protein spends on its site. The increase in the residence time of a protein on its site can have important biological implications. Our results are consistent with recent experiments on p53 and the organization of nucleosomes in yeast promoters. The structures of eukaryotic enhancers also suggest that jamming may play a role in the assembly of protein complexes on DNA.

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