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DNA intercalation by ethidium bromide: A quantitative binding study using DNA stretching and force-induced melting MARK C. WILLIAMS, IOANA VLADESCU, MICAH MCCAULEY, Department of Physics, Northeastern University, IOULIA ROUZINA, Department of Biochemistry, Molecular Biology, and Biophysics, University of Minnesota — The interactions between single DNA molecules and the non- covalent binding agent ethidium bromide are investigated using an optical tweezers instrument and the effects of this intercalator on the structure and mechanical stability of DNA molecules are quantitatively analyzed using our model of force- induced melting. The DNA force-extension cycles in the presence and absence of drug are recorded. It is found that the drug binds preferentially to double-stranded DNA and stabilizes the double helix. There is clear evidence of the force induced melting transition at low concentrations of drug, while at higher concentrations the drug is able to prevent the melting transition. The DNA contour length is obtained as a function of ligand concentration directly from the stretching curves. From this data we obtain the complete ethidium bromide dsDNA binding isotherm, which is used to find the binding constant and the binding site size of the intercalator. Out data also allows us to quantify directly the effect of ethidium bromide on the free energy of the helix-coil transition in dsDNA. This single molecule study brings new insights into the molecular mechanisms which drive drug-DNA complex formation.

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