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Free Energy Calculations for DNA Near Surfaces Using an Ellipsoidal Geometry

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Abstract. The change in some thermodynamic quantities such as Gibbs' free energy, entropy and enthalpy of the binding of two DNA strands (forming a double helix), while one is tethered to a surface and are analytically calculated. These particles are submerged in an electrolytic solution; the ionic strength of the media allows the linearized version of the Poisson-Boltzmann equation (from the theory of the double layer interaction) to properly describe the interactions [13]. There is experimental and computational evidence that an ion penetrable ellipsoid is an adequate model for the single strand and the double helix [22–25]. The analytic solution provides simple calculations useful for DNA chip design. The predicted electrostatic effects suggest the feasibility of electronic control and detection of DNA hybridization in the fast growing area of DNA recognition.

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Key words: Microarrays, genetic analysis, analytic Poisson-Boltzmann.

1 Introduction

The thermodynamics of the binding of free DNA species differs with the binding of DNA species immobilized on surfaces because of the interaction with the surface. Polarization fields change the electrostatic contribution to the binding free energy [8–10]. While simulation shows many packing complications near surfaces [11, 12], electrostatics is clearly a dominant driving force in hybridization that is altered by surfaces.

On a DNA chip, or DNA micro array, we have thousands of single strand DNA fragments (probes) immobilized within a square micron on a surface as well as a similar

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amount of free single strand DNA fragments (target) in solution that will bind to (hybridize) the probes forming a double helix DNA (complex). By this process one may perform a massive parallel DNA sequence analysis. This is of great interest because of applications like genetic screening, drug discovery and design, DNA computing and other related applications [13]. The DNA micro array is a fundamental tool which is transforming genetic science into genetic technology as has been proved by its widespread implementation [13].

In the last few years great effort has been made to analyze this problem by experimental [22,23] and computational [24,25] approaches, but there is not much progress on faster analytical models. Previous work in this laboratory used a spherical representation for the short DNA oligomers such a system (Vainrub and Pettitt) [8–10]. While much information was obtained from such an approach a more realistic model would be desirable. We propose an analytic solution to the electric potential for ellipsoids over a plane using the linearized version of the Poisson-Boltzmann equation, this will allow us to calculate some thermodynamic properties of the system. We model the DNA species (double helix and single strand) as an ellipsoid. The surface effects may be considered for either the case of a dielectric surface where we have a constant charge distribution or a conductor such as a metal where the potential is constant. Note that in the classical method using image charges one will have a sign reversal for the interaction with the images in these two cases. We consider both types of surfaces below.

2 Thermodynamics of binding

The most important thermodynamic features to analyze to have a better picture of the phenomena and improve DNA microarray design are the Gibbs free energy change ΔG, the entropy change ΔS and the enthalpy change ΔH upon hybridization. These quantities determine the melting temperature of the system and ultimately the efficiency of the microarray. Assuming that the process is reversible, the free energy is a state variable, and hence, we make use of the fact that we need not construct a hybridization coordinate but simply require knowledge of the work to bring a single strand versus a double strand to within a certain distance and angle of a surface.

We take a closer look to the process we are analyzing. We have a DNA segment tethered to a plane in a single strand configuration. At the same time we have a finite concentration of DNA segments floating freely in a dielectric liquid, usually salt water and/or formamide. A diffusive search begins for the strands complementary to the one tethered which will hybridize to it. We expect there will be a change in the free energy, the enthalpy and the entropy for the system due to the presence of a surface. Our interest is to understand the influence of the plane or surface to this reaction. In other words, we want to calculate the difference in the binding's free energy when it happens in the bulk liquid electrolyte and when it happens near the surface.

We call G the Gibbs' free energy of formation in the bulk and G^i the Gibbs' free energy