Towards Entropic Trapping of DNA in Solid-State Nanopores

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Abstract

INTRODUCTION

Better nanofluidic control over DNA will yield exciting leaps in technology, such as biochemical labs-on-a-chip and so-called DNA hard drives. We intend to get a few steps closer by making an isolation chamber to hold single DNA molecule in place. Such an isolation chamber would allow for the outcome of biochemical experiments to be observed on a per-molecule basis. It could also act as a storage medium for data encoded in DNA (recently estimated at a density of 2.2 petabytes per gram). We believe we can create such an isolation chamber based on entropic trapping, and combine it with a molecular detector called a nanopore.

In order to isolate a single DNA molecule in the chamber, we need a way to deliver it and to know when it enters. Nanopores are the ideal device for such purposes. A nanopore is a small hole in a membrane, be it biological or synthetic. Silicon nanopores, also known as solid-state nanopores, consist of a hole approximately 10 nanometers across in some larger piece of silicon. For contrast, double-helical DNA is approximately 2.5 nanometers across. When placed between two reservoirs of ionic solution, solid-state nanopores can detect the passage of a single DNA molecule. This passage event is also known as a translocation. When a voltage bias is placed across the two reservoirs, current forms from ions flowing through the pore. DNA, driven by electrophoretic forces on its slight negative charge, travels toward the pore, eventually getting sucked through. Its passage displaces some flowing ions, causing an observable drop in the ionic current through the pore.

In order to trap DNA in its isolation chamber, we intend to take advantage of the DNAs configurational entropy. At equilibrium, DNA forms a random coil whose spherical shape has a size characterized by the radius of gyration (Rg). If we could get DNA in a cavity roughly the size of the radius of gyration with holes smaller than the radius of gyration on either side, we predict that the molecule will have a near-zero probability of diffusing out (Del Bonis-ODonnel); it would have to squeeze too far out of equilibrium to exit this entropic trap. Figure 1: A schematic of a silicon structure containing a nanopore and adjacent chamber during a DNA translocation event. The structure has 3 main layers. From bottom to top they are the nanopore, the cavity, and a large hole with diameter approximately 500 nm on average.

The device we envisioned to trap individual DNA molecules is shown in Figure 1. (Note

that the molecule pictured is not trapped.) Capturing a DNA molecule in the cavity can be thought of as a competition between two forces: the force pushing the DNA through the structure and the drift of the tip of the molecule due to diffusion and electrophoretic effects. A translocation starts when the leading tip of DNA - or someplace nearby on the polymer - enters the nanopore. A drop in current is observed. The molecule is driven through the cavity by local electric fields. The tip drifts as it crosses the cavity, possibly far enough to no longer enter the large opening when it reaches the far wall. This lateral movement is the crucial step; if the tip enters the large hole the molecule will almost certainly exit the structure, as depicted in Figure 1. The probability of exit is dependent on the cavity length and hole diameter. When the molecule finishes translocating the current will return to its original baseline value. Turning off the driving voltage as soon as possible after the translocation will allow the molecule to equilibrate inside the cavity, trapping it. Waiting too long to turn off the voltage increases the likelihood of exit by continuing to push the skinny, out-of-equilibrium DNA molecule toward the large exit opening. After the molecule has equilibrated, however, its expanded size would keep it in the cavity structure.

Placing such a structure between two reservoirs of ionic solution yields the translocation dynamics described above with a twist: the structures asymmetry means translocations from either side of the pore are not equivalent. Although the effects of the asymmetric structure on translocation dynamics will be touched on, Karri DiPetrillos thesis takes a deeper look at those phenomena. The focus of this thesis will be trapping DNA molecules approaching the exposed nanopore (the bottom layer in Figure 1). Our objectives are thus twofold: to develop the hardware (pores-plus-chambers) and the software (control electronics and data analysis) to make our vision a reality. My contribution was software for analysis and recommendations for programming control electronics. In addition to creating more intricate labs-on-a-chip and possibly storing DNA hard drives, creating such entropic traps would yield deeper understanding of DNA as a polymer more generally.

Trapping DNA in a cavity near a solid-state nanopore would enable for the outcome of biochemical reactions to be probed. DNA is a polymer of particular interest because it propagates life as we know it. Using four bases - A, T, C and G - DNA encodes for the behavior of cells in every living thing, from bacteria to trees to whales. Due to DNAs incredible information density (most recently estimated at 2.2 petabytes per gram), another hot topic in DNA research is information storage and retrieval. An entropic trap could provide a long-term storage system for DNA, enabling humanity to finally do away with tape backups. We believe entropic trapping can be achieved through extremely precise manipulation of forces driving DNA in and around a nanopore, specifically through control electronics.