

Title of the talk

Genomic and Gene Expression Analysis using Self-Assembled Amphiphilic Materials

Abstract

To better leverage the tremendous advances in our knowledge of the human genome for the treatment of disease, there is an increasing demand to analyze DNA sequence information and quantify gene expression with much greater resolution and speed. To ensure that each patient in the United States has access to their personal genomic information, the NIH is advocating technologies that would allow a full human genome to be sequenced for less than \$1000. This is a lofty goal that will require more than incremental changes to existing sequencing and analysis methods to be achieved.

One of the most time-consuming steps in DNA sequencing is the length-based, electrophoretic separation of enzymatically obtained copies of the sequencing template. Because DNA is a free-draining polymer, its electrophoretic mobility in free solution is not a function of length. Instead, water-soluble polymers or gels are used as a sieving matrix, imposing obstacles on the migrating DNA that retard its mobility in a length-dependent way. Unfortunately, this added friction also makes gel-based DNA separations very slow. An alternative, "end-labeled free solution electrophoresis," has been proposed in which a fast, free-solution separation of DNA is obtained by covalently attaching an uncharged polymer to the end of the DNA. The resulting end-modified DNA has a mobility intermediate between that of the polymer and unmodified DNA, whose value is a function of the DNA length. While promising, this method has not been competitive in DNA sequencing applications, mainly because the end-attached polymers must be extraordinarily monodisperse to enable DNA oligomers differing by only a single base in length to be distinguished.

Here, we present a system in which surfactant micelles are transiently attached to DNA migrating in free-solution electrophoresis. To achieve this, DNA oligomers are alkylated prior to their enzymatic extension, then electrophoretically separated in buffers containing micelles of the nonionic surfactant Triton X-100. Micelle lifetimes are less than one second, and as such, the alkylated DNA will exchange thousands of micelles during its migration. This thermal averaging effect confers a highly uniform drag upon all alkylated DNAs in the sample of interest. Along with its application to rapid DNA sequencing, the micelle tagging method can be also be used to quantify mRNA levels and characterize surfactant microstructures.

Short bio

James W. Schneider is an Associate Professor in the Department of Chemical Engineering at Carnegie Mellon University. He received his B.S. in Chemical Engineering from the University of Wisconsin and his Ph.D in Chemical Engineering under Matt Tirrell at the University of Minnesota. His research interests include the development of novel surfactant-like materials for rapid DNA sequencing and quantification, capillary electrophoresis, and colloidal force measurements. Prof. Schneider was awarded an NSF CAREER award (2001) and a Beckman Young Investigator award (2002).