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Abstract

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PI Name:	BARRON, ANNELISE E.
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PI Title:	ASSISTANT PROFESSOR
Project Title:	THERMO REVERSIBLE GELS FOR MICROCHANNEL SEQUENCING DNA

Abstract: Cutting-edge DNA sequencing technologies rely upon the use of miniaturized electrophoresis channels microfabricated on chips or provided by large arrays of fused-silica capillaries. Microchannel electrophoresis systems are easily automated, allow the use of large voltage gradients for rapid DNA separations, and consume very little sample. With these advantages, miniaturized systems have the clear potential to deliver both the order-of-magnitude increase in sequencing throughput and substantial decrease in the cost per base that are called for by Human Genome Project. However, the full speed-increase and cost-saving potentials of miniaturized sequencing systems will only be realized with the development of a new class of replaceable DNA sequencing gels that will provide both long read lengths and rapid, low-pressure, microchannel loading, characteristics that are mutually exclusive in media formulated from conventional water-soluble polymers. Here, we present results clearly demonstrating the potential of thermo-responsive polymers to decouple the loading and sieving properties of microchannel sequencing gels, by simultaneously providing the high-resolution, long-read-length DNA separations typically expected from high-viscosity solutions of high- molecular-weight polymers, and the rapid, low-pressure loading usually considered possible only with low-viscosity, low-molecular-weight-polymer solutions. This superposition of desirable gel properties is achieved with polymers designed and synthesized in our laboratories to have a thermally-controlled viscosity switch. Using acrylamide-based formulations, we will develop 'thermo- melting' gels enabling rapid, low-pressure loading at 65 C and high-resolution sequencing at 45 C. We will also develop 'thermo-gelling' formulations for application in high-temperature sequencing -- gel that will be easily loaded at 25 C, and can be run at 75-85 C. High-temperature runs eliminate sequence-dependent compression zones occurring in repetitive regions of genomic DNA. Finally, we aim to develop advanced gel formulations with thermally-tunable meshes, to push back the limits in sequencing read lengths. The sequencing and loading performance of these novel gels, designed specifically for microchannel electrophoresis, will be tested both in capillaries and on microchips.

Thesaurus Terms:

capillary electrophoresis, gel, nucleic acid quantitation /detection, nucleic acid sequence, polymer, reagent /indicator, technology /technique development
miniature biomedical equipment, thermodynamics

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