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END-COLUMN DETECTOR FOR CAPILLARY ARRAY ELECTROPHORESIS: DESIGN AND APPLICATION TO ARRAYS OF 25, 100, AND 10,000 CAPILLARIES

Craig R. Forest; Willaim G. Thilly; Ian W. Hunter;
Massachusetts Institute of Technology, Cambridge, MA

Abstract

Ultra-high throughput capillary electrophoresis comprising 10,000 channels holds the promise of sorting through the requisite 10^{12} gene fragments to discover statistically significant correlations between mutation and disease. The discovery of the genetic causes for common diseases could lead to simple genetic tests for risk and to targeted preventative or therapeutic strategies.

The foremost challenge in the design of such an instrument is the detector. Current scanning detectors are limited by duty cycle, while in most imaging detectors, laser intensity is attenuated by reflection and refraction at capillary walls. Previous work in 2-D capillary array detection which avoids these problems using sheath flow can not scale to such large arrays due to limitations in laser power, detector area, and lens diameter.

We have created an end-column detector which is capable of exciting and collecting fluorescence from the tips of capillaries arranged in tightly packed rectangular arrays. The system relies on a cooled light-emitting-diode (LED) array for excitation, lenslet array for high numerical aperture fluorescence excitation and collection, and astronomy-grade CCD for imaging. Fluorescence from the entire array is imaged continuously with no moving parts. We can detect as few as 10^{7} (~1 nM) fluorescently-tagged DNA molecules undergoing electrophoresis. There appears to be no residual fluorescence after the DNA has exited the capillary into the buffer reservoir; the DNA moves rapidly out of the lenslet focal volume upon entering the buffer electrolyte solution from the polyacrylamide gel.

To test the end-column detector, we constructed arrays of 25, 100, and 10,000 capillaries 300 mm long, spaced 1 mm apart, and aligned at both ends. We report progress in the detection of DNA electrophoresed through the capillaries under both denaturing and non-denaturing conditions. Mobility differences based on length are measurable under non-denaturing conditions. Under denaturing conditions, we are able to resolve single-base differences in sequences several hundred bases long. We report progress on demonstrating field of view and sensitivity of detection for up to 10,000 capillaries.

Options**A travel stipend is requested.**

Requested presentation:**Oral**
Requested session:**Instrumentation and Fundamentals: Detection methods**
Correspondent:

Craig Forest
MIT
77 Massachusetts Ave. Room 3-147
Cambridge, MA 02139
USA
617-324-2398
617-252-1849
cforest@mit.edu