

An Ultrahigh Throughput Mutational Spectrometer for Human Genetic Diagnostics

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Discovering the genetic causes of common diseases may require mutation scanning of all genes in a million people. Such discoveries would revolutionize biotechnology, potentially enabling simple genetic tests for risk and targeted preventative or therapeutic strategies. An increase in throughput of genetic analysis instrumentation by several orders of magnitude is essential to undertake such an ambitious task.

In this talk, progress will be presented towards the creation of such a mutational spectrometer containing 10,000 capillary channels for efficient separation, detection, and sequestration of genetic markers. Challenges include DNA manipulation, optical signal detection, macro/micro design integration, precision alignment and assembly, and thermal control. To manipulate DNA, we have utilized a bioMEMS design platform for interfacing to an array of separation channels that enables electrokinetic biomolecule loading, detection, and fraction collection in independent wells. Signal detection is accomplished by a sensitive, scalable, end-of-column fluorescence detection technology that accommodates tightly packed capillary arrays as required for ultra-high throughput electrophoretic separation. Capillary array assembly and constraint technologies have been developed for 2-D arrays containing as many as 10,000 replaceable capillaries. Thermal control requirements of 0.3C over the entire 10,000 channel array are met with a cross-flow water heat exchanger. Achievements thus far will be presented towards the realization of a mutational spectrometer which will enable population-wide pangenomic analyses to uncover the genetic causes of common diseases.

About the speaker: Craig Forest is currently a Ph.D. candidate at the BioInstrumentation Laboratory, led by Prof. Ian Hunter, within the department of Mechanical Engineering at MIT. He received a B.S. in Mechanical Engineering in 2001 from Georgia Tech and an M.S in Mechanical Engineering in 2003 from MIT, in addition to working briefly at Sandia National Laboratories and the NASA Johnson Space Center. His research interests include genetic applications of MEMS, optics, and precision machine design.