Microfabricated Fluidic Devices for Cell Lysis and Subcellular Component Separations

Personnel

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Sponsorship

DARPA Bio-Info-Micro

This project is part of the DARPA Bio-Info-Micro program at MIT aimed at understanding cell decision processes, in particular apoptotic (programmed cell death) signal transduction pathways. We focus on the development of advanced micro-scale analytical devices for efficient cellular analysis of small populations of cells. In proteomics and signal transduction studies, the demand to identify the location and amount of proteins poses challenges to subcellular separation and sample preparations. Current technologies involve laborious and time-consuming procedures that require large sample volumes (>10^6 cells). For protein profiling, the organelle separation needs to be fast, parallel, and automated to match the great number of experiments needed. We are developing microfluidic systems that handle small number of cells (~10^2 - 10^3), lyse them, and separate out the organelles of interest. Cell lysis by electroporation is accomplished in a device containing multiple metal posts and a narrow flow channel. Organelles of interest, specifically mitochondria, are separated from the resulting lysate by isoelectric focusing in a microfabricated device (see Figure 8). The performance of the device has been modeled to provide understanding of isoelectric focusing on the micron scale with particles that are amphoteric (such as organelles). Current research extends this method to more separations on the subcellular level and the devices are used to address fundamental biological questions underlying signal transduction pathways.

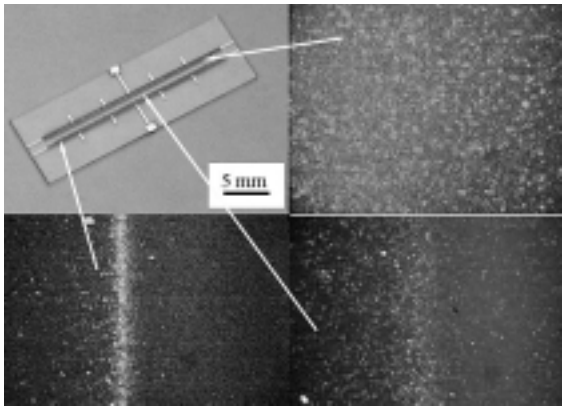

Fig. 8: Example of isoelectric focusing of mitochondria – clockwise from right hand top corner.