

Manipulation and Analysis of Single Cells using Microfabricated Fluidic Devices

J. Michael Ramsey, Oak Ridge National Laboratory

There has been an interest in using microscale chemical separations techniques to analyze the contents of single cells for more than a decade. A typical cell has a sub-picoliter volume, and thus techniques for analyzing single cell contents must employ similar volumes so as not to dilute the analytes. Capillary electrophoresis and capillary chromatography have been used to assay single cells for various components such as electrolytes, peptides and neurotransmitters. The steps of lysing a cell and injecting its contents into a capillary have been clumsy to implement using conventional technology. Current state-of-the-art analysis rates using the conventional approach is approximately 10 cells per day. We have developed a microfabricated fluidic device to automate the manipulation, lysis, injection, and electrophoretic separation steps of a single cell assay that uses non-adherent cells. This device hydraulically transports cells from a reservoir through a delivery channel that intersects with an electrophoresis channel. The electric field present in the electrophoresis channel is sufficient to lyse a cell when it enters into transport and electrophoresis channel intersection. The lysis event conveniently dumps the spatially confined contents of the cell into the electrophoresis channel, forming a well-defined injection volume. Electrophoretically separated components can then be detected at the distal end of the separation channel. This device has been demonstrated using cytosolic dyes loaded into Jurkat cells. Complete lysis was accomplished in < 33 ms. The total separation time was ~ 2.2 s with absolute migration time reproducibilities $< 1\%$ and efficiencies ranging from 2300 to 4000 theoretical plates. Cell analysis rates of 7-12 cells/min were demonstrated and are >100 times faster than those reported using conventional approaches.

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