Cell Stimulation, Lysis, and Separation in Microdevices

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Sponsorship: NIH

Quantitative data on the dynamics of cell signaling induced by different stimuli requires large sets of self-consistent and dynamic measures of protein activities, concentrations, and states of modification. A typical process flow in these experiments starts with the addition of stimuli to cells (cytokines or growth factors) under controlled conditions of concentration, time, and temperature, followed at various intervals by cell lysis and the preparation of extracts (Figure 1). Microfluidic systems offer the potential to do these experiments in a reproducible and automated fashion.

Figure 1 shows a schematic of a microfluidic device for rapid stimulus and lysis of cells. The fluidic systems with stimulus and lysis zones are defined using soft lithography in a poly(dimethylsiloxane) (PDMS) layer, which is then bonded to a glass slide. Temperature regulation for the two zones is achieved by using a thermo electric (TE) heater at 37°C to mimic physiological conditions during stimulation and a TE cooler at 4°C to inhibit further stimulus during lysis. Mixing in the device is enhanced by the use of segmented gas-liquid flow.

To extract meaningful data from cellular preparations, current biological assays require labor-intensive sample purification to be effective. Micro-electrophoretic separators have several important advantages over their conventional counterparts, including shorter separation times, enhanced heat transfer, and the potential to be integrated into other devices on-chip. A PDMS isoelectric focusing device has been developed to perform rapid separations by using electric fields orthogonal to fluid flow (Figure 2). This device has been shown to separate low molecular weight dyes, proteins, and organelles [1].

Figure 1: A) Typical process flow for cell stimulus. B) Schematic of cell stimulus device. A PDMS fluidic system is bonded to a glass slide and TE elements attached on the back through aluminum heat spreaders, which are used to control the temperature on the device.

Figure 2: Rapid isoelectric focusing of two fluorescently labeled dyes. Flow is right to left. The anode is above the top row of posts, and the cathode at the bottom. Image shows focusing occurs in as little as 10 seconds.

REFERENCES: