ABSTRACT

Wang, Fen, M.S.E., Purdue University, May 2007, Microfluidic delivery of small molecules into mammalian cells based on hydrodynamic focusing. Major Professor: Chang Lu

Cell-based assays on a microfluidic platform have received widely scientific interest in chemistry and biomedical fields. Microfluidics-based cell assays offer high levels of automation and integration, and allow multiple assays to be run in parallel, based on reduced sample volumes. These characteristics make them attractive for studies associated with drug discovery. Controlled delivery of drug molecules or other exogenous materials into cells is a critical issue that needs to be addressed before microfluidics can serve as a viable platform for drug screening and studies.

In this study, we report the application of hydrodynamic focusing for controlled delivery of small molecules into cells immobilized on the substrate of a microfluidic device. Fluorescein dye and yellow-green fluorescent beads were used to visualize the laminar flow pattern in this cross chamber. Several flow ratios were applied to the chamber. A simple mathematical model for prediction of diffusion width as a function of flow rate and diffusion coefficient was proposed. It was shown that the model describes the experimental data reasonably well for different flow rate. Further we applied the method to the application on cell-based microlfudic analysis. We delivered calcein AM which was permeant to the cell membrane into cells, and monitored its enzymatic conversion into fluorescent calcein during and after the delivery. Different ratios of the sample flow to the side flow were tested to determine how the conditions of

hydrodynamic focusing affected the delivery. A 3D numerical model was developed to help understand the fluid flow, molecular diffusion and delivery based on hydrodynamic focusing. The results from the simulation indicated that the amount of calcein AM delivered was strongly correlated with its concentration distribution on the cell surface, which was in turn determined by the hydrodynamic focusing. We have demonstrated the feasibility of using microfluidic hydrodynamic focusing for potentially quantitative delivery of exogenous molecules into cells at the single cell or subcellular level. We expect that our technique will pave the way to high-throughput drug screening and delivery on a microfluidic platform.