# Optimized Pathogen Cell Capture using Parallel Bioactivated Microfluidic Channels

M. Javanmard, F. Babrzadeh, R.W. Davis
*Stanford Genome Technology Center, Department of Biochemistry,*
*Stanford University, Palo Alto, CA 94304*
*mehdij@stanford.edu*

Optimization of targeted cell capture with microfluidic devices continues to be a challenge. On the one hand, microfluidics allow working with microliter volumes of liquids, whereas various applications in the real world require detection of target analyte in large volumes, such as capture of rare cell types in several ml of blood. This contrast of volumes (microliter vs. ml) has prevented the emergence of microfluidic cell capture sensors in the clinical setting. Here we present a generalized methodology for maximizing test solution volumes while taking advantage of the benefits microfluidics has to offer, using parallel bioactivated microfluidic channels.

Ideally, in order to be able to assay on the order of a milliliter of blood sample within an hour, it's necessary to operate at rapid flow volumes on the order of around ten microliters per minute. However, the use of rapid flow rates on narrow microfluidic channels results in shear forces flow velocities so high to the extent that cells are unable to be captured. This problem can be overcome by using milliliter wide channels (Figure 1), however at channels this wide, many problems occur such as the emergence of bubbles and non laminar flows.

To overcome this problem, we propose the use of a parallel channel architecture (Figure 2). The device consists of channels in parallel with each other tied to a single channel. Each channel is functionalized with receptor proteins. The parallel architecture allows for high capture rates while using high flow rates. Parallel channels allow low Reynolds number flow and minimize formation of bubbles, something that's difficult to achieve with several millimeter wide devices.

We test our device using cultured pathogenic yeast cells (Candida Albicans) resuspended in PBS buffer pH of 7.4. Monoclonal antibodies against C. Albicans were immobilized on the base of the channel. We flowed yeast cells through the channels at various flow rates up to several microliters per minute for 15 minutes. Beads were counted optically under a microscope (Figure 3). In order to test the selectivity of our platform, we assayed cultured non-pathogenic yeast cells (S. Cerevisiae) resuspended in PBS buffer pH of 7.4. The results of the cell count are plotted in Figure 4.

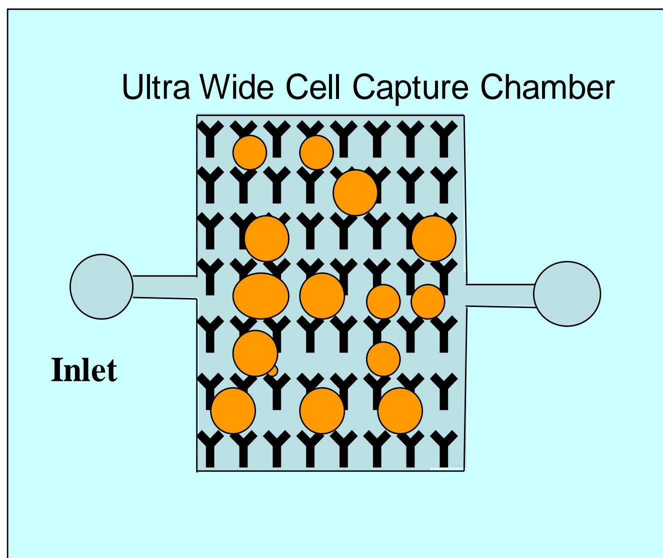


*Figure 1*. Schematic image of ideal ultrawide microfluidic device for capturing cells in large amounts of sample. Antibodies are immobilized on the surface of the channel. Cells are captured as they flow through the device and interact with the surface of the channel. Large width is necessary to process large volumes of fluid.

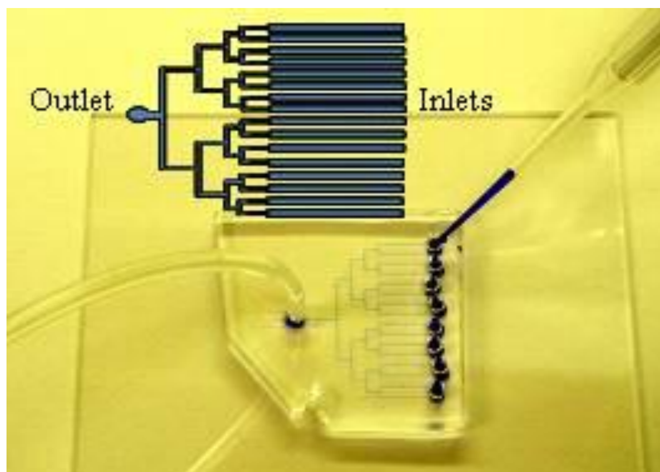


*Figure 2*. Image of 16 channel microfluidic device used for cell capture. Every two channels lead to a well for loading reagents. All channels are tied to a single output where negative pressure is applied. Channels are 25 μm tall and 300 μm wide. Channels fabricated in PDMS and bonded to glass substrate.

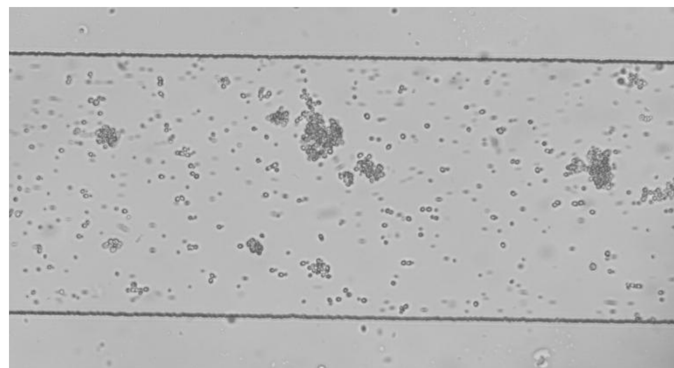

*Figure 3:* Sample is injected into microchannel. If Candida Albicans is present, it will bind onto the surface of the channel. Channel width is 300 um and height is 25 um. Each chip consists of 16 parallel 8 mm long channels. Cells flow through the device for 15 minute. After cells have bound, a flow is applied so that the unbound cells are washed off. Specifically bound cells are counted optically to quantification.

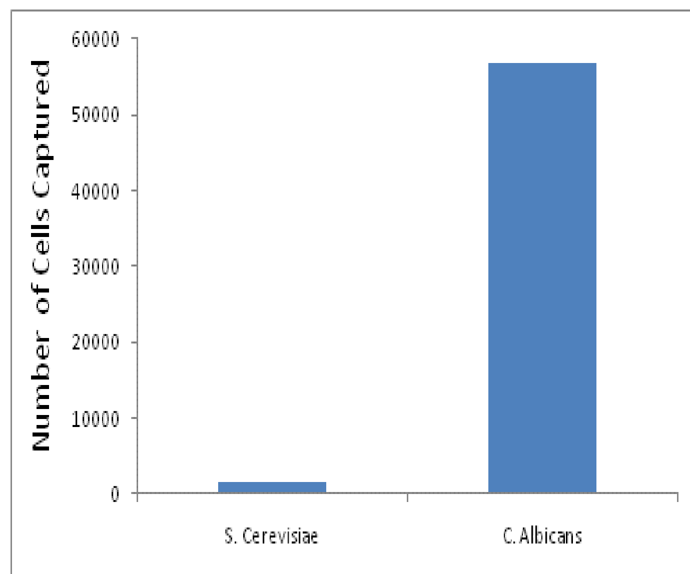


*Figure 4:* After 15 minutes of flowing, beads are counted optically. As a control experiment we separately assayed a sample containing S. Cerevisiae and compared the cell counts for the two samples. The amount of S. Cerevisiae binding to the surface compared to the C. Albicans is negligible.