Microfluidic platform for studies of self-organizing processes in a bacterial cell

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Cells maintain their structure and reproduce through numerous self-organizing processes. The common approach to understand how cellular organization is maintained is to perturb this organization and then observe a response from the cell. Essentially all approaches used by cell biologists in these studies enable the assessment of only ensemble-averaged responses, overlooking significant cell-to-cell variations that exist in a population. The current methods are also not suitable to study processes in cells with fast response times. Here, we describe the development of two microfluidic platforms that allow mechanical and chemical perturbation of cellular organization while following the cellular response at single cell level in real time using a high resolution fluorescence microscope.

The platform designed for studies involving chemical perturbation consists of PDMS channels with lateral dimensions comparable to the diameter of a bacterial cell (Figure 1). Each channel connects to a larger flow channel allowing for controlled and rapid introduction of different chemical agents to the growth medium. While the fluidic portion of the platform functions as expected, our studies show that cells have growth limitations in the channels. We will discuss the origin of this limitation.

The platform designed for studies involving mechanical perturbation consists of pressure actuated microvalves (Figure 2). Bacteria are placed under a valve that when closed leads to bacterial deformation and shape changes. As we have shown before a long term deformation of bacterial cell leads to drastic changes in its morphology. The platform enables to systematically study the effect of cell shape on cellular function.

The two platforms present promising complementary approaches to probe, in a quantitative and systematic way, processes that maintain cellular functions. In addition to bacterial cells, these two platforms can also be useful in studies of yeast and other single-celled organisms.

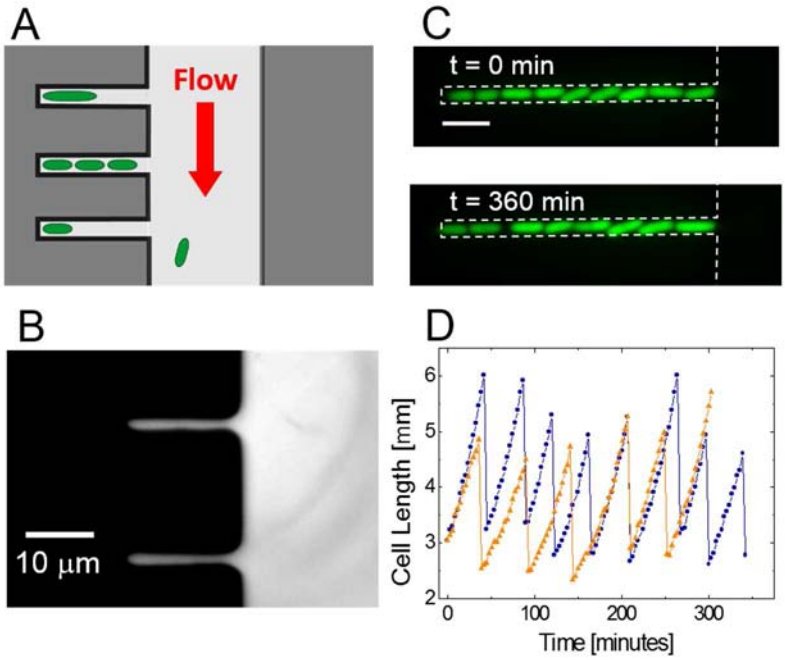

Figure 1: Platform for studies involving chemical perturbations: A) Schematics of the microfluidic system. Cells grow in large numbers of dead-end channels. The flow in the large vertical channel allows for a quick exchange of chemical composition of cell medium and to flush away extra cells. B) Image of a completed chip from an optical microscope. C) *Escherichia coli* cells growing in one of the completed devices. Cells carry a fluorescent GFP label and are imaged in a fluorescence microscope. Scale bar is 5 μm. D) Growth curves of two cells in the channel.

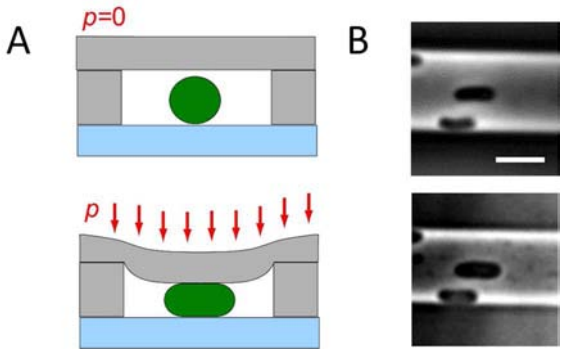

Figure 2: Platform for studies involving mechanical perturbations:
A) Schematics of the microfluidic system. Shown is a cross-sectional view of a pressure-actuated valve and a bacterial cell. Valve closing by externally applied pressure (p) deforms bacterial cell. B) Phase contrast images of *E. coli* cells before (top) and during application of mechanical pressure (bottom). Noticeable broadening of cell contours can be seen. Scale bar is 5 μm.