Fabrication of Nanoporous Membranes for Tuning Microbial Interactions and Biochemical Reactions

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New strategies for combining conventional photo- and soft- lithographic techniques with high-resolution patterning and etching strategies are needed in order to produce multi-scale fluidic platforms that address the full range of functional scales seen in complex biological and chemical systems. Microfluidic fabrication techniques have expanded significantly with each method having unique material and scale restrictions. Micromachining and micro-powder blasting that yield higher throughput, lack the resolution needed to fully address biological and chemical systems at the cellular and molecular scales. Achieving such nanoscale resolution relies on techniques such as electron beam lithography or nanoimprinting, which are traditionally considered costly and slow. Other techniques such as photolithography or soft lithography help fill the gap between these extremes. In this study we look at combining photolithography and electron beam lithography to produce nanoporous membranes to control species transport in a fluidic device while maintaining satisfactory throughput and cost.

Fluidic devices can be designed to provide tunable levels of control over the fluidic environment based on connectivity and flow control. With adequate control of physical structure, molecular or cellular species of interest can be contained while the local fluid environment is altered around it. In this work we describe the fabrication of systems used in cell culture and cell-free protein synthesis reactions. For cell culture, media flow is used to replenish nutrients consumed by multiple bacterial species and requires membranes having pores on the scale of 100-200 nm. These membranes facilitate chemical communication between species and nutrient exchange with the environment while containing the bacteria for microscopic observation. *Figure **1***a shows the culture chamber. Flow of a cell culture causes microbes to become trapped behind the membrane. *Figure **1***b shows a close up of the nanomembrane. Moving to a smaller scale, *Figure **2*** shows a device with smaller pores designed to regulate molecular transport of raw materials and energy needed to support a cell-free protein synthesis reaction. *Figure **2***a shows the nanomembrane separating two microchannels. *Figure **2***b is a view of the nanomembrane under higher magnification. The inset shows a pore that has been reduced in size by oxide deposition to regulate transport.

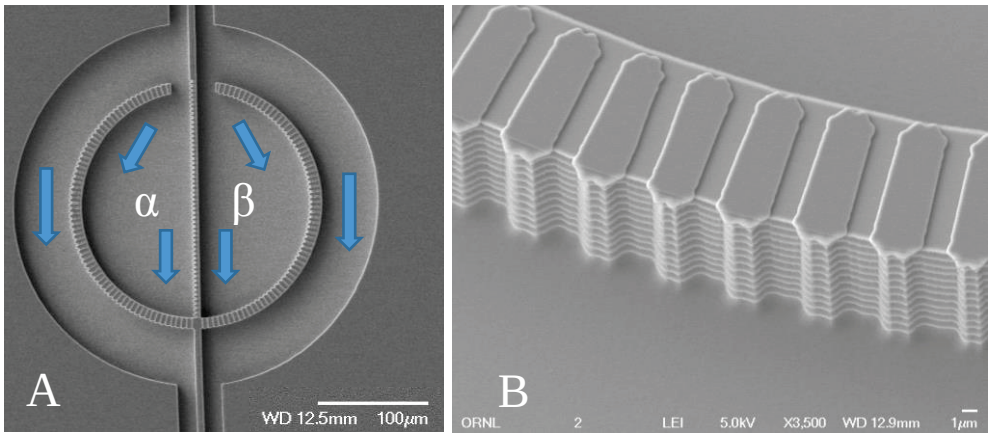

Figure 1 A) SEM image of cell culture device. Flow of culture media along the arrows loads the inner ring of the device with microbes. The culture media is replaced with media to remove microbes outside the culture chamber and provide nutrients. Two species can be loaded into chamber α and chamber β to analyze their interactions. B) The membrane traps microbes with a 200 nm gap. Support material maintains the structure.

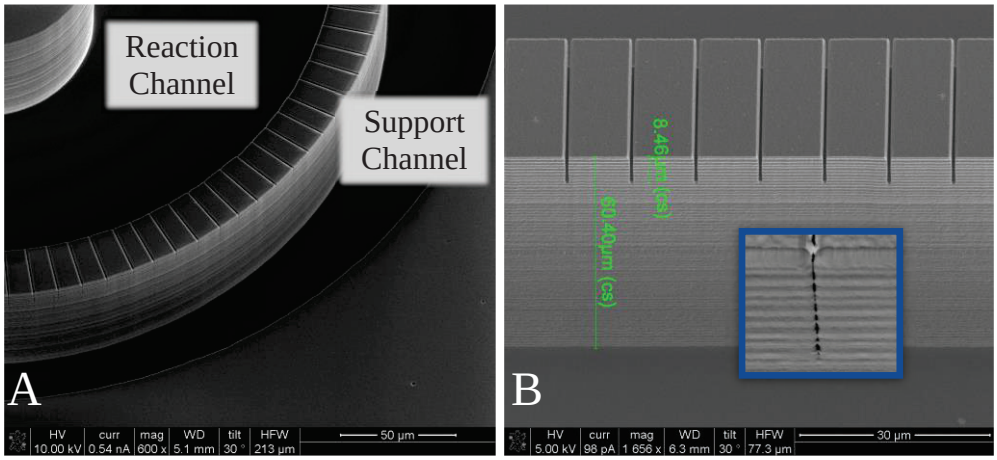

Figure 2 A) SEM image of an electron beam lithography patterned nanoporous membrane with photo patterned fluid channels. B) An expanded view of the membrane with a magnified inset of the pore shows the pore after oxide deposition. The size of the pore was altered with SiO_2 deposition to control the molecular weight cutoff of the membrane.