Multiscale fluidic architectures for chemical manipulations of biological domains across length scales

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Chemical signatures in biological systems are dynamic and span intra- and inter-cellular domains with length-scales from nanometers to meters. Resolving spatiotemporal dynamics of biochemical signals is a grand challenge throughout environmental sciences and in other complex systems (*e.g.* biomaterials, chemistry, neuroscience). Solving problems of chemical access and measurement to meet this challenge requires the development of enabling technologies that advance chemical measurement and detection strategies.

Micro and nanotechnologies provide potential advancements in chemical sampling strategies that employ fluidic manipulation and molecular capture structures. Fluidic channels ranging from micrometers to nanometers meet scaling requirements for probing eukaryotic and prokaryotic specimens from the subcellular scale up through the level of functional multicellular communities and tissues (*e.g.* biofilms, tissue culture, neural networks).

We have utilized a combination of electron beam lithography, anisotropic silicon etching and photolithography to define nanofluidic architectures within a microfluidic cell culture environment. Nanochannels were initially left unsealed to allow lower resolution chemical sampling between regions of the microfluidic network. Subsequently, nanochannels were sealed through plasma-enhanced vapor-phase deposition of silicon-dioxide and selectively opened using focused ion beam milling to facilitate higher resolution dosing and sampling. Poly(dimethylsiloxane)-based microfluidics were overlaid onto e-beam defined nanofluidics for flow characterization between microfluidic domains. Figure 1 shows the microfluidic chip architecture (A) with nanofluidic interconnects that enable sampling of a central domain (B). Nanofluidic channel structures are also shown (Figure 1C-E).

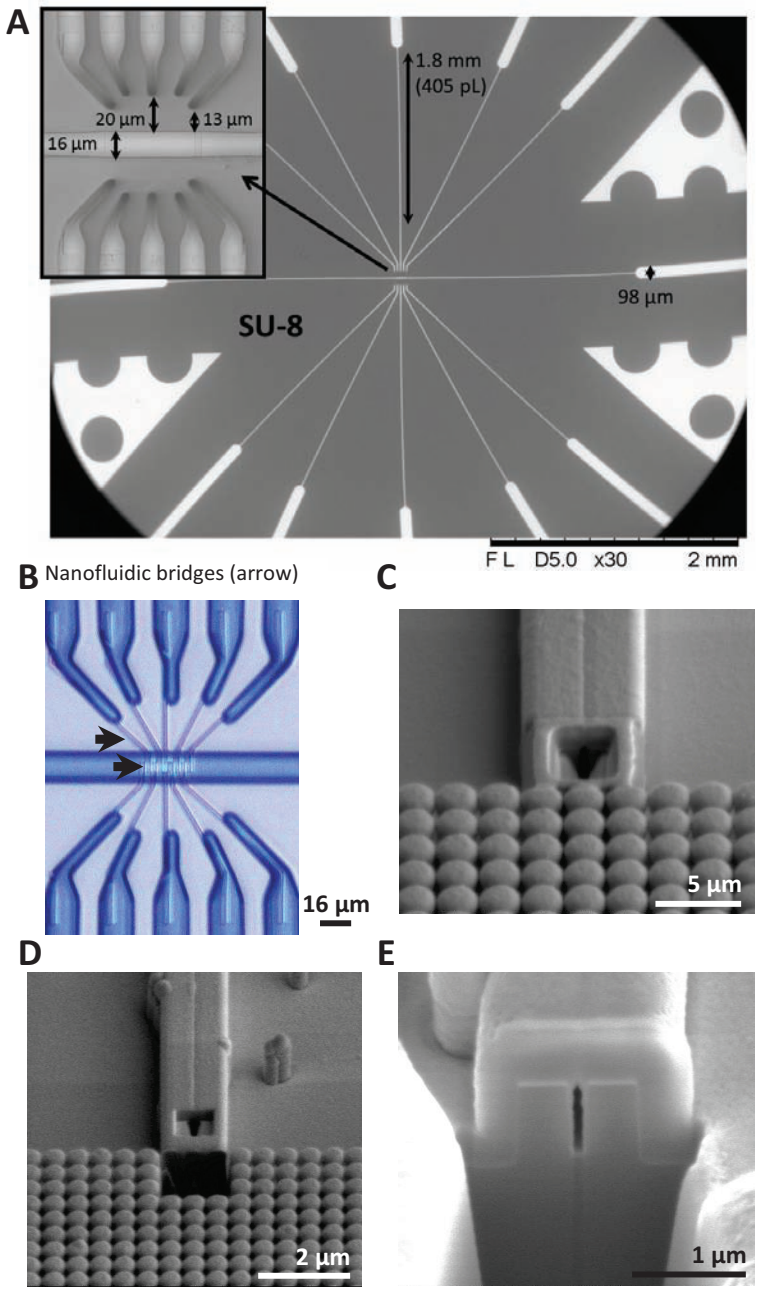

Figure 1: Micro- to nano-fluidic probes: A) SEM image of microfluidic chip with access channels converging on the nanofluidic subcellular sampling channels. B) E-beam fabricated (pre-SiO_2 closure) nanofluidic sampling channels provide fluidic connection between microfluidic leads (two sets of vertical finger-like channels), and the cell culture channel (single horizontal channel). C) SEM image of a single ion-beam milled inlet of a SiO_2-closed nanofluidic channel. D) SiO_2-closed channel and posts for chemical collection. E) Ion-beam-milled, cross-section of SiO_2-closed nanofluidic channel shows SiO_2 on side-walls of the Si-based channel.