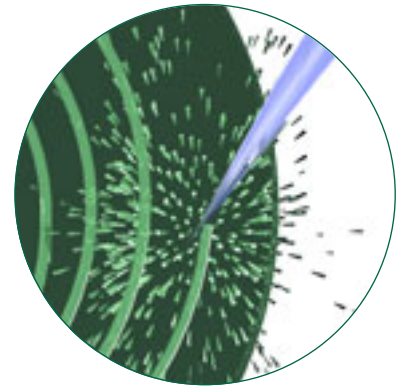
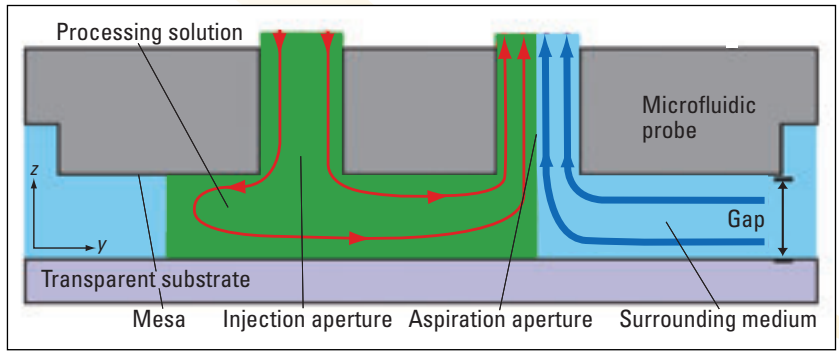
Mobile microfluidic probe unleashed



Like the advances that took phones from wall-bound to wireless, new technology may cut the cord for microfluidic probes. Despite their advantages, microfluidic systems have been hampered by their dependence on stationary, closed channels. David Juncker and his colleagues at IBM Research GmbH (Switzerland) have now overcome this problem with the development of a mobile microfluidic system without channels: a microfluidic probe. The new technology adds to the toolbox both for patterning surfaces and for examining proteins and cells under native conditions (*Nat. Mater.* **2005**, *4*, 622–628).



A cross-sectional schematic illustrates the mobile microfluidic probe surrounded by solution and positioned over a substrate. (Adapted with permission. Copyright 2005 Nature Publishing Group.)

Juncker and colleagues sidestepped the need for channels by building a silicon chip with a large central mesa and two apertures: one for injection and one for aspiration. "The way that we create this laminar environment [is] to have this mesa, this flat surface, and bring it close to the substrate that we want to process. And within the gap that we have there, we have this well-defined microfluidic space. Furthermore, because of the absence of walls, the microfluidic probe is mobile," Juncker explains.

The medium is aspirated through one aperture at a high rate, creating concentric flow fields. When the investigators injected a much smaller volume of a solution at a slower rate, the surrounding medium confined the substrate and created a well-defined liquid boundary, a phenomenon that they call hydrodynamic flow confinement. By varying the distance between the mesa and the surface and the relative injection and aspiration velocities, they could refine the focus of the deposited substrate spots on a surface.

The main difference between micropipettes and the microfluidic probe was that the mesa created a 2-D space that facilitated the full confinement of the dispensed solution. As a consequence, the probe could be rapidly moved with high resolution. By varying the speed at which the probe moved, Juncker and colleagues could create concentration gradients of proteins on the surface, which could be useful in studying biological responses to chemical gradients. The researchers also demonstrated that they could build protein microarrays completely in solution and thereby minimize problems with protein denaturation. Finally, the researchers showed that they could use their system to wash proteins off a surface just as easily, and with the same resolution, as they applied proteins.

Experts are impressed by the cleverness of the idea and its applications. "It really takes to a new level the kind of micropipette perfusion that people have done," says Daniel Chiu at the University of Washington. Sabeth Verpoorte at the University of Groningen (The Netherlands) elaborates, "The beauty of the approach presented in this paper is that one can use laminar flows to locally address surfaces, but it becomes possible to do so in small spots on the surface, instead of having to have the solution come in contact with an entire section of a channel."

Juncker is most excited about the cell biology applications of the system. So far, the researchers can selectively label a surface covered in cells with a confined microjet of fluorescent dye. In the future, the investigators will optimize the technique for further biological experiments. "You could start thinking about using a drug candidate or some other molecule that you would like to study," Juncker explains, citing how chemicals like RNAi could be introduced into individual cells. "Here, you could selectively go to certain cells and keep the other cells as a control."

Chiu notes the delicate equipment and technical skill involved in this work. Although he finds some limitations in the technology, he doesn't see them as a problem. "I don't ever think that this will go submicron, for example, but then for all of the cellular type of studies, you really don't need any small features. You just need things that are tens of microns for single cells, and for those, this technique will work just fine." ■

—Sarah Webb