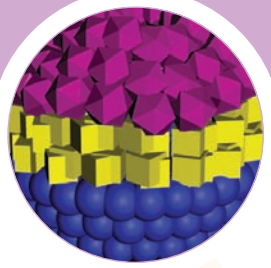


New wrinkle in digital microfluidics

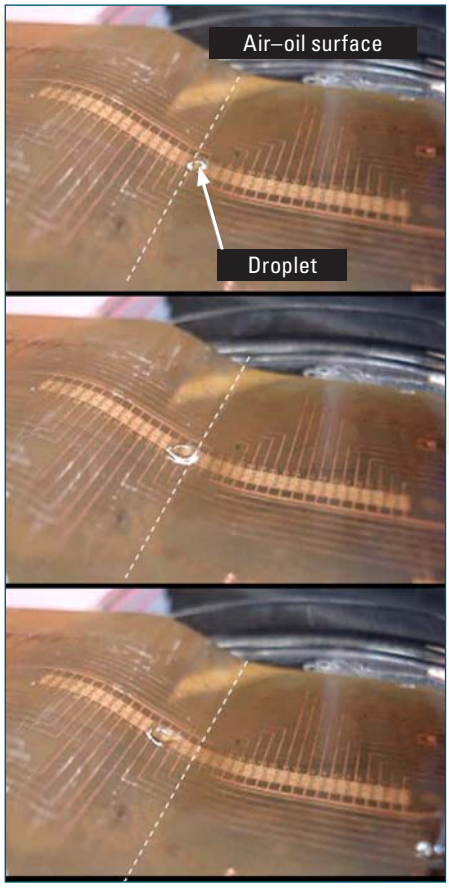
Moving individual droplets over a 3D terrain offers a simple method for performing multiphase extractions on a microfluidic platform.

Despite its relative youth, digital microfluidics—the ability to move, combine, separate, and analyze individual droplets over a well-defined path—is on its way to commercialization. At least one company, Advanced Liquid Logic, has encapsulated the decade-old concept in a compact benchtop immunoassay analyzer that is now undergoing validation in several clinical laboratories. But digital microfluidics lacks the extensive set of tools and component structures available for more traditional continuous fluid-flow microfluidics. To remedy that shortcoming, Aaron Wheeler and his colleagues at the University of Toronto have created a terrain over which individual droplets can be moved in three dimensions. More importantly, they have used this special terrain to teach a new dog an old trick (*Lab Chip* **2008**, *8*, 672–677).

In the early days of nucleic acid analysis, the standard method for purifying DNA from biological specimens depended on a phenol extraction to remove proteins and other biomolecules from an aqueous sample. Although that technique is still considered to be the optimal method for extracting DNA, it has been replaced by solid-phase chromatography in microfluidic devices, largely because it is easier to pack a solid-phase support into a microfluidic channel than to create the microfluidic circuitry needed for a two-phase extraction.

Wheeler and his team stumbled upon an easy way to perform two-phase extractions by digital microfluidics. The key was their unexpected discovery that they could drive individual fluid droplets up and down sharp slopes on a flexible, copper-clad polyimide substrate coated with PDMS and Teflon-AF. "To our surprise, we found that we could move droplets over virtually any geometry," says Wheeler.

He and his collaborators create their "all-terrain" microfluidic devices with a commercially available, flexible substrate consisting of a 9-μm-thick layer of copper on a 50-μm-thick polyimide film. They embed 1 × 1 mm electrode arrays in this substrate, spaced 60 μm apart, by standard photolithography and wet etching before depositing a 9-μm-thick dielectric layer and a 50-nm-thick hydrophobic layer of PDMS and Teflon-AF1600. Droplets are driven across the arrays by sequential activation of neighboring pairs of electrodes, thanks to a process known as electrowetting-on-dielectric. To reduce nonspecific adsorption of biomolecules in the droplets to the device, the researchers either coat the substrate with a thin layer of silicone oil or supplement the carrier buffers in the droplets with small amounts of Pluronic F127.



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Sequence of frames from a movie (top to bottom) depicting a droplet of water moving through an interface between silicone oil and air.

The ability to move droplets over this flexible microfluidic track allowed the researchers to direct protein- and DNA-loaded aqueous droplets down a slope into a petri dish filled with a phenolic extraction medium and then back out of the extraction medium. MS analysis of the droplets before extraction failed to detect any DNA, whereas a sharp peak corresponding to the DNA analyte was easily identified after extraction.

"The ability to do fast and efficient liquid–liquid extractions on a microfluidic platform is novel and potentially quite powerful," says James Landers of the University of Virginia. Implementing such a scheme on integrated PCR microfluidic devices, such as the ones that Landers and others are developing, could simplify device construction and lower the costs per assay. Orlin Velev of North Carolina State University adds, "This is an interesting technique, which adds new tools and capabilities to the ongoing research effort in fabrication of clinically robust microdevices. I think this demonstration is important because it shows that we've barely scratched the surface when it comes to using digital microfluidics in innovative ways."

As a proof of concept, Wheeler and his team have shown that they can use their all-terrain droplet actuation to cycle droplets between regions of distinct temperature or oxygen concentration. The former could be advantageous for PCR applications, whereas the latter could lead to the creation of biofuel cells that require rapid cycling between aerobic and anaerobic conditions. ◥

—Joe Alper