

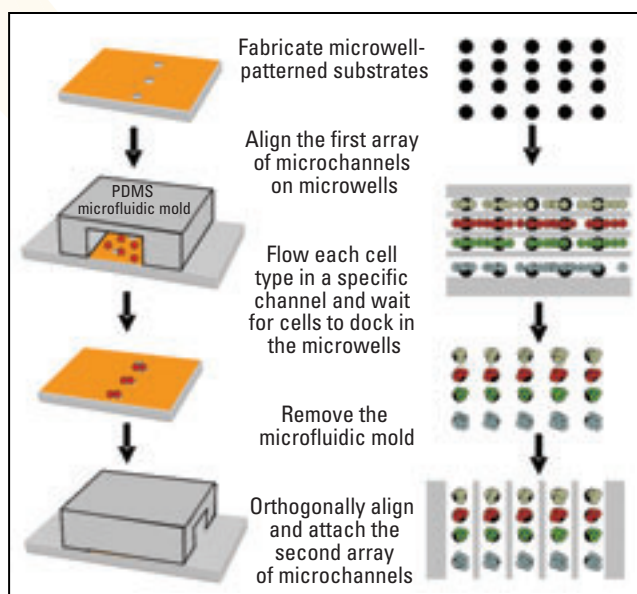
Reversible sealing improves arrays

Researchers have developed an innovative soft lithographic process for the fabrication of patterned microfluidic arrays that could substantially speed up the screening of new drugs. The process, which was reported by Robert Langer, Ali Khademhosseini, and colleagues at the Massachusetts Institute of Technology and Harvard Medical School, uses the reversible sealing of PDMS molds to create an array of microwells with volume capacities as small as 100 μL (*Lab Chip* 2005, 5, 1380–1386).

“If you want to test new drugs, it is desirable to look at the effects of each drug on all the cell types of the body,” says Khademhosseini, the first author on the paper. “Traditionally, people working on drug discovery with cells or tissue cultures have relied on expensive equipment and large robots for rapid screening of drugs. The use of microfluidics may potentially make the process cheaper, more efficient, and [more] sensitive.”

In the new process, the researchers used photolithography to produce patterns of wells on a silicon master, which acted as a template. Two PDMS molds were then fabricated on the silicon template. One mold, engineered with microchannels, was matched with a second mold containing microwells. The chemistry of the mated surfaces was modified to make a tight, but reversible, seal.

After the PDMS microwell and microchannel molds were sealed together, the system was filled under a negative pressure with solutions containing cells. In a typical experiment, each row of mi-



Schematic diagram of reversible sealing of microfluidic arrays onto microwell patterned substrates. (Adapted with permission. Copyright 2005 Royal Society of Chemistry.)

crowells was filled with a different cell type, such as hepatocytes, embryonic stem cells, or fibroblasts. As a solution containing cells flowed through the channels, the cells accumulated in the wells because of decreased shear stress.

The microchannel mold was then peeled off and replaced with a new set of microchannels, which were oriented to allow reagents to be added in a perpendicular direction. “We are working toward a system in which a technician can peel off the channels and put on new ones as well as minimizing the number of inlets and outlets,” says Khademhosseini. “It is a fairly complicated process to optimize the surface chemistries and flow rates.”

“This work is a good demonstration of how microfluidic technology can be used to test large numbers of conditions on cell arrays,” says Albert Folch of the Universi-

ty of Washington. “Cell arrays in microfluidic environments have been demonstrated before, but the challenge that Langer’s group demonstrated successfully is the ability to address many types of array units with different fluids—a paramount goal in high-throughput drug testing. With devices like these, using these arrays in real drug testing is just around the corner.”

Although initially the researchers used 5×5 arrays, Khademhosseini, Langer, and colleagues anticipate creating arrays with as many as 2500 wells/ cm^2 . These arrays will have a far greater density of wells than that of conventional multiwell plates currently in use. In addition to increasing throughput, the microfluidic techniques will significantly re-

duce the necessary volume of samples and reagents.

“This technique fills a vacancy: a well-designed technique for arraying cells and probing them with different reagents that moves the fields of cell biology and tissue engineering one step closer to performing experiments that generate statistically significant data,” says Douglas Weibel of Harvard University. “The arrays are cleverly designed, and the approach is straightforward and should make it possible to probe large numbers of different cells under controlled conditions,” he adds. In the future, the researchers plan to optimize the surface chemistries of the molds, in order to improve the reversible bond between molds and the interaction of microchannel and microwell walls with various types of samples. ▀

—Steve Miller