COMPANY CREATES CUSTOMIZED BIOCHIPS WITH MIX-AND-MATCH MICROFLUIDIC PARTS

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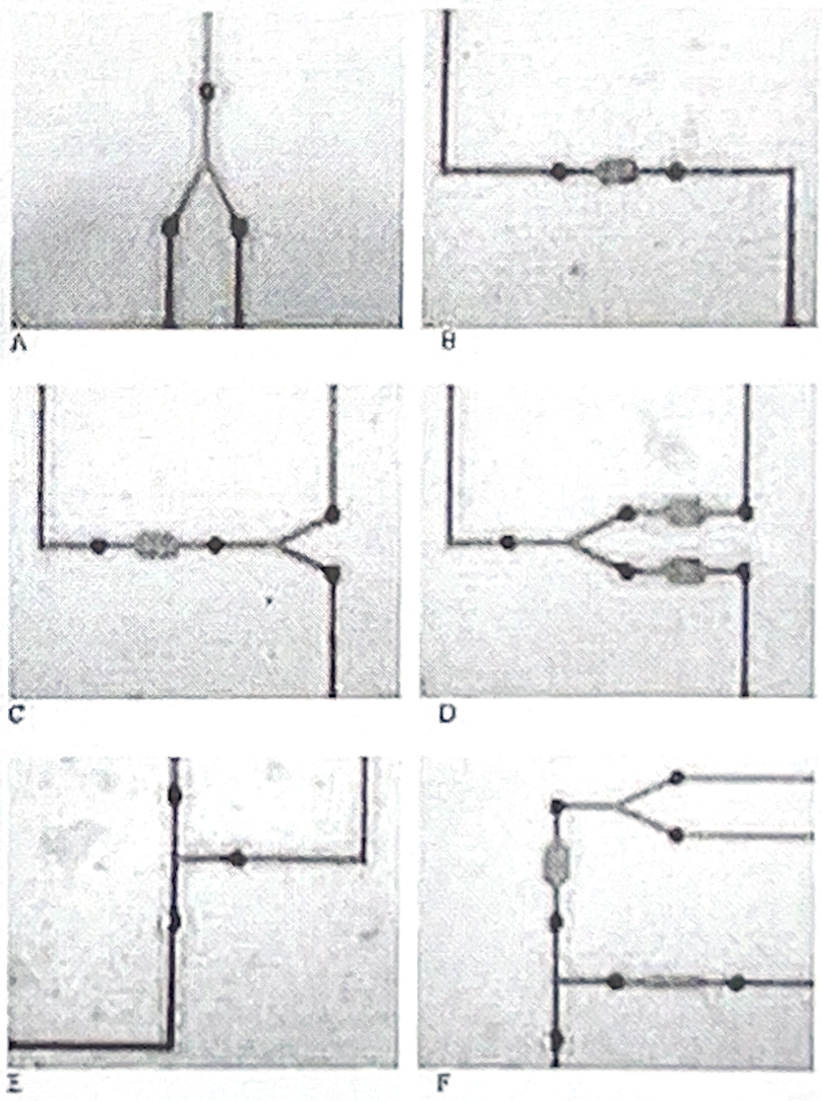
Nov. 20, 2001 – A Pasadena, Calif., company has developed a group of mix-and-match parts for customized microfluidic chips that could allow pharmaceutical companies to screen drugs faster.

"Our microfluidic chips will allow 40,000 samples per day to be done," said Steve O'Connor, president and chief executive of Nanostream Inc. O'Connor wants to knock three years off of drug discovery programs that normally take 12 years. Projects remain in clinical trials for about seven years after possible new drug candidates and targets have been found.

For each new drug, pharmaceutical companies have millions of chemical compounds that require "high throughput screening" – a term used to describe an automated system of testing of compounds that allows large quantities to be analyzed quickly. For drug companies, tests are done on chemicals and proteins to learn how they interact. As genomic researchers find more areas that could be points of intervention for diseases, their targets also need to be screened.

Current macroscopic instruments can screen about 400 samples per day. Nanostream's device will screen tens of thousands of samples per day because it will analyze 100 samples simultaneously, the company said. The product is expected to be complete in about 18 months.



These modules show some of the capabilities of Nanostream's mix-and-match biochip. A. Simple splitter. B. Simple Filter C. Filter then a splitter. D. Splitter followed by two filters. E. Basic check valve. F. Valve, small filter, large filter, splitter.

"The needs of the customers may be very similar, yet each customer wants us to do things a little differently," said O'Connor, 32, a graduate of California Institute of Technology.

Nanostream's chips can be customized and prototyped in a couple of hours and mass fabricated in a day or two. The big time-savers are the modular parts that easily join together.

Felicia Gentile, president of BioInsights, a biotech research firm in Redwood City, Calif.,

said that the customization feature of Nanostream's chips will be one of its biggest benefits to drug companies.

"Each company has its own style or need for its research," Gentile said.

Biological and chemical sample fluids are injected into a postage-stamp-sized chip equipped with microchannels about 50 microns high and up to 300 microns wide. Inside the channel, the flow of fluid can be metered for exact amounts. The samples can be separated and mixed with reagents – substances used to produce reactions -- and then analyzed.

What makes Nanostream's microfluidic chip different from others is its mixer. When fluids are in the scale of microns, they don't efficiently mix together. The fluid molecules can slowly move from one wall of the chamber to the side, but that stalls the screening process. Nanostream's modular mixer gets the fluid to blend immediately.

The modular parts – mixers, splitters, filters and valves – are connected together by various techniques, including the use of ultraviolet light and solvents, said O'Connor. Complex versions of the chips can have channels on different levels that act like elevator shafts connecting fluids.

O'Connor said that while other companies power their microfluidic systems with voltage, Nanostream is using pressure-driven flow, similar to the force that makes water run through a garden hose.

John Baldeschwieler, chemistry professor emeritus at California Institute of Technology, said that Nanostream's technology is inexpensive, versatile and "should be the basis for a wide range of useful and diagnostic tests."

"One of the benefits of Steve's system is that you can make changes very easily."

But, he added, it's full of challenges.

"You don't want fluid to leak out. You look at his demos and you don't see any problems like that. That is one area where I would look carefully," Baldeschwieler said.

In its custom manufacturing process, Nanostream makes the microfluidic channels with a selection of more than 200 polymeric materials. Unlike silicon and glass that are very hard, polymers can be more difficult to harden or cure, so leaking could be a concern.

Also, Baldeschwieler said, most of these systems require some technology to do initial processing. For example, if you're taking samples from people in a clinical setting, some cell preparation usually needs to be done. To get a working system, there may be other parts or functions that need to be developed.

"In the end, there's a systems issue," Baldeschwieler said. "Steve certainly is aware of these things and that he doesn't have a product until all the elements are in place."

Although the biochips might seem like a silver bullet, they won't completely replace current lab-bench equipment such as beakers and test tubes. O'Connor said that of the 40,000 samples that could be screened each day, about 1 percent of them would be transferred to traditional equipment for further research. The "hits" would still need to go through extensive additional testing.

While traditional screening uses about 10 microliters of reagents that can cost up to $1 per test, O'Connor expects that only about 100 nanoliters will be used for the same protocol. Considering price breaks from reagent deals and new reagents under development, the total savings are hard to predict, said a company official.

Aside from the new chip, Nanostream also has another device in the works.

It's developing a high throughput biochemical assay product that analyzes DNA, RNA and proteins for drug research. The sample fluid will be injected into the chip, mixed with a reagent and then "read."

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Overall, analysts say, the market for microfluidics is there, but the industry still needs to mature.

"I think there are opportunities for microfluidics, but it has been a long road for these products to get into the market," analyst Gentile said. These products have to work in high throughput – they can't be monkeying around with this in the lab."

While billions have been spent on pharmaceutical research, microfluidics has not highly penetrated the market, she said.

For instance, Agilent Technologies markets the Agilent 2100 biochip that analyzes DNA, RNA and protein samples. Agilent's overall sales for fiscal 2000 were $10.8 billion; the lab-on-a-chip falls into the company's life science group that brought in about $400 million for the same period.

"It's a very small number," Gentile said.

Environmental engineers are taking a look at Nanostream's chip to reduce costs, sample size and storage problems. Currently, researchers at hazardous waste sites take core soil samples that are 10 feet long and weigh 100 pounds. Soil samples are washed with liquid solvents and then the pollutants are extracted in liquid form.

"Instead of taking it in a van and carting it to the lab, now you could take it in a cooler – there's less volume to store," said Jeremy Semrau, associate professor of civil and environmental engineering at the University of Michigan.

With the new chip, he said, the sample could be cut down to 5 grams. The challenge, however, remains figuring out ways to measure different pollutants at a site and meet the standards of the Environmental Protection Agency.