PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Lab on a chip

ArticleInfo		
ArticleID	:	4924
ArticleDOI	:	10.1186/gb-spotlight-20040316-01
ArticleCitationID	:	spotlight-20040316-01
ArticleSequenceNumber	:	276
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2004–3–16 OnlineDate : 2004–3–16
ArticleCopyright	:	BioMed Central Ltd2004
ArticleGrants	:	
ArticleContext	:	130594411

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The development of a microfluidic chip the size of a postage stamp, capable of rapidly processing biological samplesas small as a single cell, means that biologists could soon be carrying their laboratories around in the same way that they now carry around a personal computer, according to a professor of physics at CalTech who developed the chip.

Steve Quake's team describes the general architecture for parallel processing of nanoliter fluids for biotechnology in a letter in the March 15 Nature Biotechnology. "We think it's an important milestone in general biological automation," he told us.

Quake said that, at present, biological automation was like the vacuum tube computer, with large specialized robotic stations that were difficult to string together and to maintain. "We'd like to create fully automated systems that are on chips, easy to use - and general, universal, and inexpensive," he said.

The chip could revolutionize the way biomolecular analysis is carried out in laboratories. "It would greatly reduce the manual labor done by graduate students - make their lives more interesting and so forth - that's the vision," Quake said. The 'lab on a chip' is 1 inch square and supports 100 micron diameter tubing incorporating miniature valves. Biological samples and reagents are individually pumped through the tubes into the chip to be mixed together for cell lysis before the DNA or RNA is bound onto beads ready for eluting and processing (*Nature Biotechnology,* DOI:10.1038/nbt951, March 14, 2004).

The key to this technology lies with the micromechanical valves developed in Quake's laboratory 4 years ago. Cell lysis completes in minutes in a ring of tubing containing three of these valves. "If you have a valve, you can make a pump. If you put three valves in a row, you can pump peristaltically by actuating the valves in sequence," Quake said.

Eric Mazur, professor of physics and of applied physics at Harvard University, who was not involved in the study, told us, "People have had biochips before, but then you had to do pre- and post-treatment of the samples off the chip. Now you can do it all on the one chip. I think that is a major contribution."

"This is what genomics is all about," said Pál Ormos, director of the Institute of Biophysics Biological Research Centre, Szeged, in Hungary. "You have to investigate a large number of small samples, and possibly very fast. During the time for doing one experiment, [here] you are doing three," he said.

Ormos, who was not involved in the study, told us that this illustrates how a hundred experiments at a time could be carried out in parallel in a very small space. At the other end of the scale, because the chips are so miniaturized, very small sample sizes can be analyzed. "In some cases, this is just a practical advantage, but in many cases, it is crucial because you simply don't have a lot of samples," he said.

Quake told us his team has shown that it is possible to use these devices to study gene expression in single cells. "We think it's a really crucial step along the way for making single cell libraries," he said.

"I think the advances described in the paper are both important and exciting," Eric Wieber, director of the Mayo Genomics Research Center and who was not involved in the study, told us in an e-mail. "These developments open the doors to further work that will not only decrease the costs and time required for genomics and systems biology work, but will give us a better understanding of biology at the single cell level," he said.

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