Laser adds extra dimension to lab-on-chip

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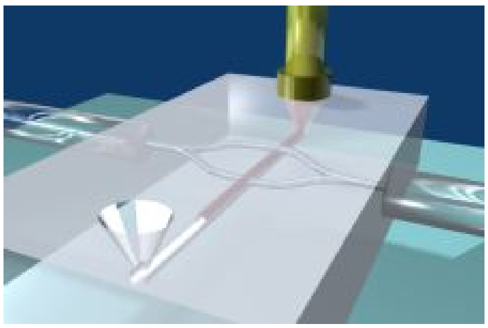

(PhysOrg.com) -- A European research project has shown how to build optical sensors directly into the structure of labs-on-chips. The breakthrough paves the way for on-the-spot medical diagnostics.

People have been working on the 'lab-on-a-chip' concept for more than a decade. The idea relies on microfluidics, where tiny volumes of sample liquids move along microscopic channels cut into a variety of substances including silicon, glass and plastic. True, this technology has progressed phenomenally: it is now possible to separate samples at the molecular level on a chip which is no larger than a postage stamp.

But the lab-on-chip hype usually fails to address a 'big' problem: you usually still need large-scale equipment to detect and identify the molecules flowing inside the microfluidic chips. The fluidics is certainly at the microscale, but the optical molecular detection is still firmly rooted in the macro world of life-size laboratories.

Laser lights the way

Except now an EU-funded project has been able to 'inscribe' features into microfluidic chips, making integrated optical detection a possibility for the first time.

The HIBISCUS consortium, involving academic and industrial partners, used a technique called femtosecond laser micromachining. The femtosecond laser emits extremely short light 'flashes' - each lasting no more than a few millionths of a billionth of a second. This pulsation makes the laser beam extremely intense, and can alter materials in unusual ways. By focusing the beam you can use the laser like a microscopic tool or pen and 'draw' physical features in three dimensions into a thin wafer of glass.

This micromachining technique has already been used to cut intricate components, like gears and motors into silicon. The HIBISCUS team was able to inscribe tracks, called waveguides, into labs-on-chips. The waveguides channel light through the chip, across the microfluidic channels and back out of the chip where it is detected. They could also use the laser to produce the microfluidic channels themselves.

It is now possible to shine a light source (usually a laser) into the sample fluid and detect its absorption or other optical activity directly in the chip, rather than having to take a sample from the chip and analyse it with laboratory equipment.

"This is the first time that waveguides have been put into a lab-on-chip using the relatively straightforward femtosecond laser micromachining process," explains Giulio Cerullo who coordinated the project. "It now means that at last a lab-on-chip can finally be shrunk fully, with optical detection and analysis taking place within the chip."

One exciting demonstration by the project shows that it is possible even to detect small changes in the refractive index of a sample flowing in a microchannel using a three dimensional detector called an optical interferometer. In this case the waveguides are laid out so that one passes through a microfluidic channel while the other one passes just above it. The liquid flowing in the channel induces a tiny change in the path length of the light between the two waveguides, which is picked up by the interferometer. This makes it possible to detect very small changes in the sample composition.

Immediate results

The project has made prototype labs-on-chips with integrated waveguides for several biological applications, including a DNA-fragment separation and detection assay (which could be used to detect specific disease markers in patient samples) and a chemical microreactor for protein synthesis.

Cerullo's dream is that the lab-on-chip could help doctors perform virtually immediate medical diagnoses in their own practices. They could take a sample from a patient and immediately run it through a small device, which would be able to detect marker molecules - protein markers for a disease or the telltale DNA sequence of a genetic disorder.

"Once you make detection part of the lab-on-chip, you have miniaturisation of an entire analytical laboratory," remarks Cerullo. "It brings diagnosis to the point of care. A patient goes home without that awful sense of uncertainty hanging over them until they get their test results back. Or they can receive urgent medical treatment - a day or two's advance on treatment can mean life or death for some cancer patients."

The HIBISCUS consortium includes three commercial SME partners that are all exploiting the results of the project. High Q Laser in Austria is already selling the femtosecond laser that it developed for the project. Lionix, based in the Netherlands, manufactures microfluidic chips and is now looking to make labs-on-chips that incorporate the waveguides. The Dutch firm Zebra Bioscience is developing kits for point-of-care diagnostics.

Disposable diagnostics?

Cerullo reckons that an integrated lab-on-chip would not be prohibitively expensive for medical professionals. He estimates that the initial investment for a lab-on-chip manufacturer to set up the micromachining technology for the waveguides would be around €200,000. Total investment to manufacture fully integrated labs-on-chips may reach several million euros. But this outlay is relatively low once it is spread across the millions of disposable chips that could be sold to medical practices and hospitals around the globe.

The integrated optical detection also makes feasible the idea of using microfluidics as an efficient and more eco-friendly production method for pharmaceutical products.

"Our project is the last piece in the lab-on-chip puzzle," concludes Cerullo. "It will open the door to many exciting applications, especially much faster, on-the-spot medical diagnosis."

More information: HIBISCUS project - www.polimi.it/hibiscus/

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