Breakthrough towards lab-on-chip system for fast detection of single nucleotide variations in DNA

I-Micronews

A SNP is a single nucleotide replacement in a DNA sequence which can result in different reaction by people to pathogens and medicines. Detection of these SNP's is therefore becoming increasingly important with the move towards more personalized healthcare.

Existing methods to detect SNP's require many sample processing steps in dedicated medical tools at medical laboratories. Such tests are labor intensive, time-consuming and expensive. Moreover, rather large blood samples are needed. A lab-on-chip device can bring huge advantages both to the patient and the healthcare system. Such devices enable fast, easy-to-use, cost-effective test methods which can be performed at regular times in a doctor's office or even near the patient's bed. This is very interesting for point-of-care applications such as personalized medicine.

By combining advanced micro-electronic fabrication processes with heterogeneous integration, imec and Panasonic aim to realize a state-of-the-art microfluidic device for SNP detection. In order to do this, advanced microfluidic components have been fabricated and optimized, such as a miniaturized pump for on-chip generation of high pressure, a micropillar filter optimized for DNA separation achieving world-record resolution, and a SNP detector allowing on-chip detection using very small sample volumes.

The entrance unit of the SNP detection system samples very small volumes of blood. This entrance unit features a miniaturized high-pressure pump based on an advanced conductive polymer actuator. After optimization, the actuator generates high pressures (up to 3MPa) at low voltage (~1.5V). The high pressure is essential to generate a fluid flow through the next unit of the SNP detection system. The on-chip low voltage operation is important because it opens the path to autonomy and portability of the lab-on-chip device.

Next, the DNA separation unit featuring an advanced micro-pillar array filter was developed. This deep-UV patterned silicon pillar array was realized using advanced MEMS technology. It consists of many micron-scale pillars, being typically 20µm high and with 1-2µm inter-pillar distance. The pillar array is used for DNA separation based on ion-pair reversed-phase (IR-RP) liquid chromatography. Imec and the VUB (Vrije Universiteit Brussel), a scientific partner of imec, optimized the pillar-based IR-RP liquid chromatography technique for DNA separation. This resulted in the first miniaturized on-chip system that enables fast and highly selective separation of short, double stranded DNA strands which only differ 50 base pairs in length. The resolution of the system is the highest in the world and proves the potential to handle 5 SNPs at the same time in the final SNP detection system.

The other functional units of the SNP detector are a unit for DNA extraction and polymerase chain reaction (PCR) using heaters and temperature sensors, and a SNP detection unit based on electrochemical sensors. The miniaturization of these sensors was of crucial importance, since the minimum required sensor volume determines the blood sampling volume needed for the SNP detection, and hence the dimensions of all components of the device. Scientists of Panasonic and imec demonstrated SNP detection capabilities using on-chip sensors handling a volume as small as 0.5µL.

Imec's Human++ program provides a multidisciplinary R&D platform for industrial partners to collaborate on finding industry-relevant solutions for future healthcare and wellness needs by combining nanoelectronics and biotechnology into heterogeneous systems for diagnosis and therapy. Human++ partners build on imec's 25 years of expertise in micro- and nanoelectronics and expertise in several healthcare-relevant domains.

About imec
Imec performs world-leading research in nanoelectronics. Imec leverages its scientific knowledge with the innovative power of its global partnerships in ICT, healthcare and energy. Imec delivers industry-relevant technology solutions. In a unique high-tech environment, its international top talent is committed to providing the building blocks for a better life in a sustainable society.

Imec is headquartered in Leuven, Belgium, and has offices in Belgium, the Netherlands, Taiwan, US, China and Japan. Its staff of more than 1,750 people includes over 550 industrial residents and guest researchers. In 2009, imec's revenue (P&L) was 275 million euro.
Further information on imec can be found at www.imec.be.

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About Panasonic
Panasonic Corporation (based in Osaka, Japan) is a worldwide leader in the development and manufacture of electronic products for a wide range of consumer, business, and industrial needs.

About VUB
The VUB offers a quality education to more than 9000 students and hosts more than 150 research teams working on its campuses, and is one of the biggest centres of knowledge in the capital of Europe. Thanks to this expertise and its strategic location, the Vrije Universiteit Brussel is the ideal partner for prestigious research and education with an outlook on Europe and the world.The Department of Chemical Engineering of the VUB (Free University of Brussels, Belgium) aims at

developing creative solutions to challenging problems in the field of separation technology and catalysis by exploiting the new possibilities in materials engineering and nanotechnology. Key to this development process is a thorough understanding of the fundamental events, from the molecular scale to the real life application level. In our group, advanced experimental techniques (lab on a chip, high-throughput experimentation, …) are combined with state-of-the-art computer modeling methods, including molecular modeling and computational fluid dynamics, to obtain insight in the fundamental adsorption, diffusion, reaction and mass transfer effects. Since 2004, the major research activity has been focusing on the design and development of perfectly ordered microfabricated support structures in separation columns. The group is the academic founder of the Flanders' Microfluidics and Microreactor Centre.

SOURCE [1]

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http://www.mdtmag.com/news/2010/12/breakthrough-towards-lab-chip-system-fast-detection-single-nucleotide-variations-dna

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[1] http://www.i-micronews.com/lectureArticle.asp?id=5973