Nanobiotechnologies to Provide a Portable Genetic Biosensor Device

Nanobiotechnology is an exciting and promising field in medicine. It can solve many problems in medicine such as the early detection of cancer, efficient treatment of diseases and reparation of damaged tissues and nerves. It brings about sophisticated diagnostic opportunities and yields more effective therapies by using nano-sized tools. The final objective of nanobiotechnology is to be able to shift the focus of patient care from disease treatments to early detection and prevention of disease, and hence improving the quality of life in patients.

One application of nanobiotechnology is nanobiosensors. These efficient diagnostics tools could provide quick DNA detection for infectious diseases or genetic propensities that would allow physicians to diagnose infected patients in a fast and effective way. The physicians could then tailor treatments for their patients while reducing the chance of any adverse reactions. For several years, my research team has been involved in the production of new biosensors devices at the nanoscale which could be easily integrated in a portable “lab-on-chip” device. This “mini-lab” can perform point-of-care analysis and could even be used inside the human body as “nano-sentinels”.

The European project, Optonanogen, is about this new class of biosensors based on nanomechanics. This biosensors are used for the specific detection of trace amounts of biological molecules in real-time without the need for labeling. The first prototype has been designed for the detection of mutations in the BRCA1 gene, which is responsible for 2.5–5% of breast cancer in women. But the final biosensor microsystem would be able to detect not only the hybridization of nucleic acids partly complementary to human genes, but also chemical contamination in food or water or any kind of biowarfare agents. The final device will be about the size of a human hand, allowing it to be used in doctors’ clinics. It can determine the genetic predisposition of a patient in few minutes. The same analysis in a laboratory, which is generally only used to test high risk groups, can take up to hours or even days.

The heart of the biosensor microsystem consists of an array of 20 microcantilevers (thin slides of silicon, see photograp in Fig. 1) coated with nucleic acids that react with the complementary DNA carrying the genetic anomaly. When the microcantilever detects the DNA to be analyzed, a bending of the cantilever takes place. This bending is in the range of a few nanometers and can be monitored by focusing a laser beam at the end of the lever and measuring the reflection of the laser light in a detector. The sample is then injected into the device via a polymer microfluidic header and the deflection of the cantilevers is measured by an optical detection system based on a photodetector array that collects the light off the cantilevers from a vertical cavity surface emission lasers (VCSELs) array, being capable of measuring with sub-nanometer resolution. Microcantilevers are made of silicon materia which displays dimensions of 200 µm long, 20 µm width and 350 nanometers thick. Fabrication is performed using standard microelectronics technology at clean room facilities.

This biosensor combines nano- and micro-technologies, as there is a need to connect these devices with external usage. The arrays are being fabricated with 20 sensors but the number could be expanded to more than 100 (the technology can be scalable). Moreover, both the cantilever array and the microfluidics header are made from low-cost components that would be disposable. Another advantages of this technology is that it is label free and fast. The result can be obtained in a few minutes with a very small amount of sample from blood or serum (from nanoliters to a few microliters); and the detection limit is very low (close to picomolar) making it suitable for quicker and cheaper biomedical and clinical analysis.
There is a broad variety of applications for this system. Our research team has already applied this technology for the detection of organic pollutant such as pesticides. It can also be applied to clinical diagnostics; genomics and in proteomics; and also for the rapid detection of chemical and biological weapons.

Currently, there are other competing technologies as standard molecular techniques for single nucleotide polymorphism detection. However, these available commercial systems are designed to be used in laboratories but not in field or clinical applications, where portability, sensitivity and rapidity of the detection systems are required. To date, there are three companies selling the microcantilevers biosensing technology. However, we are the first company to develop a fully integrated system on a small scale (expected final size is a hand-held device). We also offer the advantage of individual inlet and outlet for each cantilever rather than one for the whole array.

A consortium was formed with the goal of incorporating this expertise across the European Union (EU). To date, the Information Society Directorate of the EU has funded nearly 2 EUR million (US$2.3 million) and some partners have also received additional funding.

In March 2004, two members of the consortium set up a spin-off company, Sensia, SL, to commercialize this system. Sensia, SL has already commercialized a portable biosensor based on surface plasmon resonance (SPR) developed by CNM-CSIC. Now the company is evaluating whether to commercialize the Optonanogen system on its own or from a larger company.

The initial prototypes are expected to be completed by the end 2005 but there are still many validation steps before commercialization of the final device. We hope to have a commercial device available within one or two years.