The ISFET Invention

by Professor emeritus Dr Piet Bergveld

The origin of the chair BIOS, Lab-on-a-chip group, is in fact the invention of the ISFET, the first chip-based chemical sensor, by Piet Bergveld, since 1965 an employee of the chair Medical Electronics, later on called Bio-informatics. Bergveld's interest was the development of a tiny ion sensitive sensor for application in neurophysiology, initiated by his work in the Parkinson project of the chair at the time 1965-1970.

He first published about the necessary electronic systems for measurements with a remote field effect transistor at the place of the actual measurement: inside the brain or on top of a nerve or muscle. In the case that the field effect transistor (FET) could be a MOSFET, at that time developed by the chair Solid State Electronics, Bergveld decided to leave out the metal (M) of the gate of the device, resulting in the ISFET (Ion Sensitive FET), whereas the gate oxide could directly touch a nerve or muscle. The first publications of this new type of chemical sensor appeared in 1970 and 1972, which formed the basis of Bergveld's PhD thesis in 1973.

After the pioneering period, to proof the operation of various ISFET types, the company Cordis in Roden, the Netherlands, started the commercialisation of the ISFET, in close co-operation with the University of Twente, focussed on a catheter with pH sensor for intracorporeal blood measurements. In addition Bergveld developed a whole series of new sensors based on the ISFET principle, such as an EnzymeFET, an ImmunoFET etc.

A complete new approach was the development of an analyser chip for concentration measurements, containing sensor as well as actuator facilities, in fact the first fluidic lab-on-a-chip system. Based on experience with this type of system, a dipstick titrator was developed, also the first in the world.

Beside these new products Bergveld developed a whole series of physical sensors on a chip, such as a silicon microphone, a pressure sensor, an accelerometer, a gyroscope and a micro-dialysis chip. All these activities led to the founding of the chair Biosensor Technology (abbr. BIOS), with Bergveld as the first full professor, in 1984.

In the meantime the R&D division of Cordis was turned into a new company, called Sentron, (1985) which company continued the development of ISFET based products, especially for food, agricultural, bio-industrial, environmental and general applications. One of the recent products is the pH Plus Bolus for monitoring and support of cow rumen health, together with the Austrian company Smaxtec.

In one of the last official keynote lectures before his retirement in 2003, Bergveld predicted the existence of a kind of “chemical camera”, in which the optical pixels of a CCD chip should be replaced by ISFETs with a specific protein attached to the gate. Reading out such a chip should result in an image of local dynamic (bio)molecular binding events.

This idea has been elaborated by the company Ion Torrent, developing a chip with many rows and columns of wells with underlying ISFETs, covered with template-bearing beads. In this way simultaneous detection of independent DNA sequencing reactions is possible by hydrogen ion release upon specific nucleotide incorporation. The most recent DNA chip contains 660 million ISFETs!