

Piet's dream travelled the world

From 1 ISFET per chip to more than a million per chip

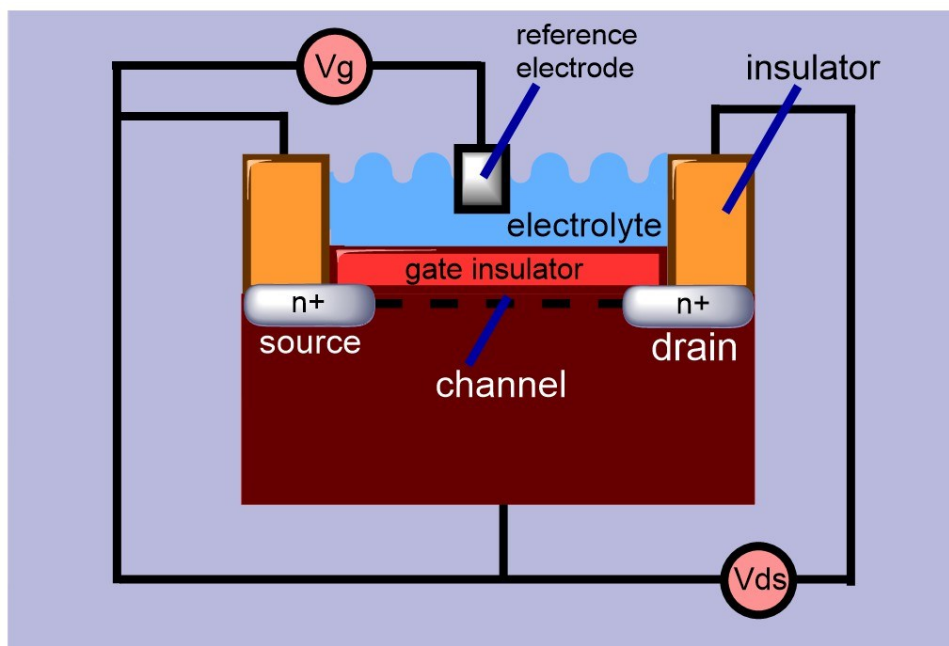
It all started with an invention of which, in fact, horrified the transistor builders of the time. But Piet Bergveld persevered and developed his ISFET. Today, there are DNA-chips consisting of 660 million ISFET's on one chip!

In the second half of the sixties, the young researcher Piet Bergveld (25), was involved in research on Parkinson's disease. His dream, by then, was a sensor that he could put directly on a nerve or muscle, or even in the brain. Piet, by the time, working in the Medical Electronics group: already in the early years of the University of Twente ('Technische Hogeschool Twente' by then), there was medical research, as a very early predecessor of the current Technical Medical Centre (TechMed) of the university.

For his sensor, he would like to use a transistor, the electronic building block that later shaped our current information society. It was in the early days of chips, containing 64 chips. Your current iPhone has more than 10 billion of them, on a chip!

One single transistor was a small tin box with three wires, the inside was hermetically protected against light, dirt and moisture. And what did Piet Bergveld do? He sawed the lid off, his plan was to let fluid in. Not at all a good plan, according to the transistor manufacturers. But his idea was that by doing so, you could create a sensor for detecting charged particles, ions. The common FET (*Field Effect Transistor*) then became an ISFET (*Ion Sensitive Field Effect Transistor*).

If we take a look at an ordinary FET, it has three connections: the gate, the source and the drain. With a tiny voltage on the gate, you can influence the current that flows through source and drain. This can work because the gate has a thin insulating layer with a metal layer on top. Instead of this metal layer, Piet wanted to introduce a liquid – by letting drops inside or by putting the ISFET upside down and dipping it in the fluid. Or, the basis of his first ideas, bringing it into contact with a muscle or a nerve.



The ISFET, cross section: the usual metal layer on top of the 'gate insulator' (in bright red) is replaced by a (bio)chemical substance. The amount of charged particles, ions, in this fluid determines the current between source and drain.

In 1970 en 1972 he published about this remarkable ideas, and the ISFET also became the basis of his PhD thesis in 1973.

Until then, it was still pioneering and convincing people. But the next step was that the Cordis company, producing pacemakers, catheters and other medical equipment in Roden, The Netherlands, showed interest. Together with Piet's group, Cordis developed a catheter with a pH sensor for measurements in blood, in the body. Piet kept on developing ISFET's for other purposes, like the EnzymeFET and the ImmunoFET.

In those years, they also presented a system we would call 'lab-on-a-chip' today: a full analysis system with an ISFET-chip, components for fluid flow and electronics. Together, the components formed the first '*dipstick titrator*' in the world. Still, today, the commercially available titrators have an ISFET inside.

Piet developed more sensors with medical and other applications, like pressure sensors, a tiny microphone for a hearing aid, an accelerometer, a gyroscope (multidirectional movement detector) and a microdialysis chip. The Biosensor Technology (BIOS) group was born, and Piet was appointed Professor in 1984.

The R&D department of Cordis, in the meantime, moved into a new company called Sentron. This company continued exploring ISFET applications, for food and agro, bio industry and environmental applications. One of the latest products is the 'pH Plus Bolus', monitoring cow's health, together with Austrian company Smaxtec.

Piet kept on dreaming, even in one of his latest keynote lectures. Why not build a 'chemical camera', consisting of many ISFET's, each with a specific protein attached? Reading out the camera, you can directly see the local protein binding. Like the dream of the first ISFET, this is a dream that now comes true as well. The Ion Torrent company has built a chip with many tiny wells for measuring DNA sequencing. Their latest version has 660 million ISFET's on one single chip!