EXPLORING FET CONCEPTS FOR LAB-ON-A-CHIP

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Abstract
The initial aim of the ISFET application in the 1970s was to construct a new tool for electrophysiological experiments, but unfortunately, this has never been taken up by the medical field. However, in view of recent experimental results of stimulus-response measurements with protein-covered ISFETs, it may be useful to redo the original measurements. This may result in a lab-on-a-chip for dynamic cell acidification measurements.

From the history of ISFET development, the combination of an ISFET with a pH actuator may be considered as a remarkable achievement. In the first place because it delivered factually the first lab-on-a-chip device and secondly because it can serve as the start of a new type of electrophoretic device for protein separation while simultaneous monitoring of the degree of separation.

Two dimensional ISFET arrays may not fulfill the requirements of measuring many samples in parallel or in series as needed in present lab-on-a-chip devices, due to spatial limitations. A solution may be to apply the read-out concept as used in the presently being developed SeeMOS technology for optical camera s. In stead of photons, the (bio) molecular events at the surface may induce the charges or currents in the sensing MOS structure, or directly, or by means of an ion controlled diode.

The field effect concept can not only be used for the measurement of double layer phenomena at insulator/electrolyte interfaces, but also for manipulation of the double layer and by this for flow modulation, on which effect the so-called FlowFET is based. This control concept may be extended by applying specific electrode configurations and voltage profiles.

Combining flow control and detection in one and the same device may ultimately lead to a lab-on-a-chip design in which all components rely on the FET concept.

Keywords: ISFET, Sensor-actuator, electrophoresis, neuron acidification, FlowFET, chemical camera.

1. Introduction

The history of ISFET development, called ISFETOLOGY by the author and elucidated in detail by him at the 9th International Meeting on Chemical Sensors in Boston (July 7-10 2002) will be published in a coming issue of Sensors and Actuators B. The author realises that historical overviews of scientific research gain in significance in case the historic perspective initiates new research projects. Therefore the current paper

will describe, in addition to a couple of new sensor concepts as launched in the ISFETOLOGY paper, some new ideas in the field of lab-on-a-chip research, all based on the experiences with the FET concept in the past.

2. ISFET sensor/actuator lab-on-a-chip

The PhD-thesis project of Bart van der Schoot in the mid-1980s in the research group of the author was meant to demonstrate that just the very fast response time of an ISFET was the parameter which distinguishes this, at that time rather new device, from conventional pH sensors [1]. Therefore a row of 10 ISFETs was made, per two devices surrounded by a gold electrode. This array was covered with a glass lid in which a channel was etched with an input and an output hole. An electrolyte pumped through this channel could be coulometrically titrated, during continuous flow or by applying a stop/flow protocol. Titration curves of an acid or base could be registered within some seconds, applying current pulses of only 100A s. In fact this system was the first lab-on-a-chip, although not recognized and nominated as such at that time, but it definitely showed for the first time that chemistry can be performed inside a silicon/glass sandwich, using very small volumes (nL s !!) and thus decreasing the time for completion of a chemical reaction drastically.

In the same project the glass cover has also been provided with an additional window, which was covered with an teflon membrane, in order to measure carbon dioxide diffusing into a bicarbonate solution in the channel [2]. This was not performed by a static pH measurement as in the case of the Severinghaus electrode, but by continuous for- and back titration, in intervals of 4 seconds. This showed that dynamic measurements can be performed easily in such small volumes, with the advantage over a conventional static measurement that no liquid filled reference electrode is necessary and that possible sensor drift is not a problem anymore. Again a proof that the lab-on-a-chip approach has many advantages, which can be exploited especially in case sensors are available which can measure very fast and in a small volume, criteria which are fulfilled both by ISFETs.

3. Electrophorese and coulometric actuation

After the successes of the actuator project as described above, the author promptly wrote a new project aimed on separation of proteins in the channel of the chip mentioned above. It was proposed that by means of feedback the pH could be kept at a constant value, different for the distinguishable ISFET/actuator positions in the channel, comparable with the function of the ampholyte molecules used up to then for capillary isoelectric focussing. With the application of a heterogeneous protein mixture, the different proteins were expected to separate according to their isoelectric pH values and thus collect at certain ISFET positions in the channel. However, this research proposal was not granted, most probably because it was not yet done at that moment. There was simply not a lab-on-a-chip mentality at that time.