

Nanotechnology In Silicon Based Cell And Gas Sensors

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The combination of biotechnology, nanotechnology and Silicon technology promises to bring new developments in the field of Si-based cell and gas sensors. We take a look at the results from three different research initiatives. The first deals with nano-scaled metal-oxide gas sensors, the second with the reduction of surface conductivity in the field of Suspended Gate FET (SGFET) gas sensors and the third with the nanometer-scaled interspace between cells adhering to a substrate or sensor. These projects use widely varying technical approaches ranging from the use of thin metal-oxide layers and flouropolymers for gas-sensors to specially designed CMOS-sensors for the examination of the interspace between cells and substrate. These approaches also indicate the different characteristics that applied nanotechnology can have. In addition, we'll also see promising commercial results of studies on Silicon-based sensors for the analysis of living cells.

Nano-scaled metal-oxide gas sensors

A conventional metal-oxide gas sensor consists of a hybrid assembly, its electronics and the package.

Combining sensor and electronics on a single CMOS chip (for example, a Hall-sensor) fails because of the high working temperatures of about 300°C; at this temperature the CMOS electronics do not work. To overcome this problem a nanotechnology based approach can be used. The basic idea is to control the Fermi-level of the metal-oxide-surface, the location of which influences the sensitivity, by applying local electrical fields. This contrasts with conventional gas-sensor technology, where the temperature is used for this purpose. The essential components are the field electrode and the metal-oxide with an isolator in between. As the Debye length of metal-oxides, taken as a value for the shielding of the material, is typically in the range of 60-80 nm, a sufficient electrical field at the electrode reaches the gas reaction surface only if the thickness of the metal-oxide layer is in the range of or below the Debye-length. Experiments with a 55 nm thick metal-oxide layer (SnO_2) on a 250 nm isolator (Si_3N_4) and simulation results suggest that the performance of the gas sensor at CMOS-compatible temperatures is not only comparable to conventional sensors but even allows to differenti-

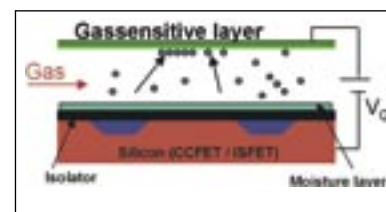


Figure 1 - SG-FET principle

ate between NO_2 and CO by applying different potentials to the underlying electrode (Figure 2). This work was realised in cooperation with Micronas, IPM-FhG both (based in Freiburg) and Professor T. Doll (IMM Mainz).

Suspended Gate FET

The operating principle of a Suspended Gate FET (SGFET) is based on work-function changes of a gas sensitive layer. This work-function shift is measured with a CCFET or ISFET that is placed at a few microns from the sensing layer (Figure 1). One advantage of SGFETs is that the measurement temperature is normally below 100°C, making CMOS integration and a low-power mode possible. However, the low temperature also brings a disadvantage: Ambient mois-

Figure 2 - Measurement with nano-scaled metal-oxide gas sensor

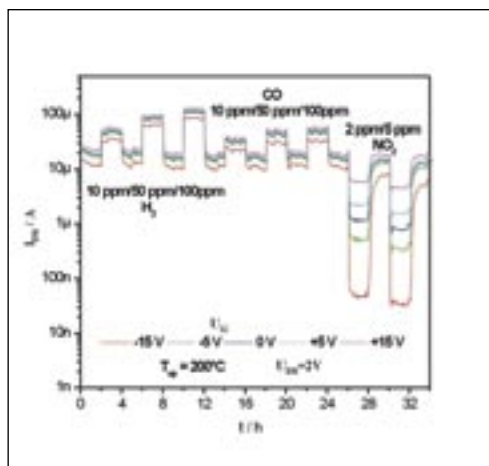
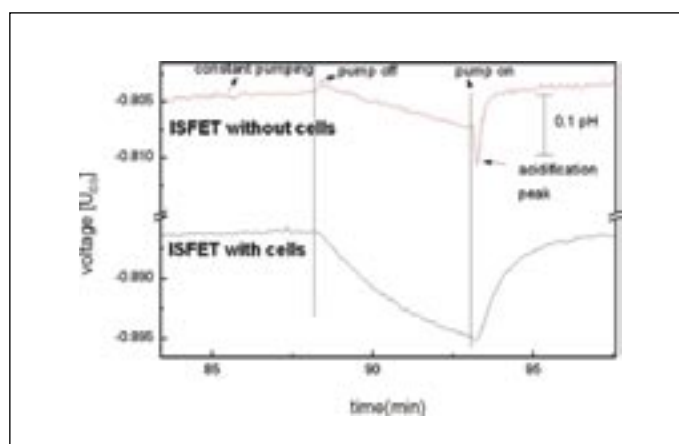


Figure 3 - Typical measurement with cells (LS 174T) covering only one ISFET (cell-ISFET) and with the other ISFET free of cells (ISFET)



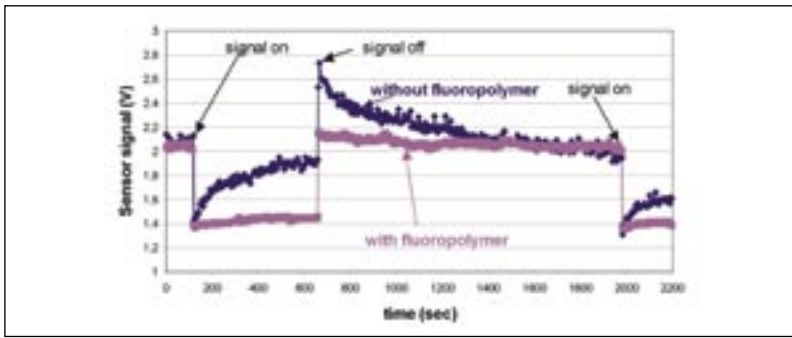


Figure 4 - The influence of nanometer-scaled fluoropolymer films on the sensor performance

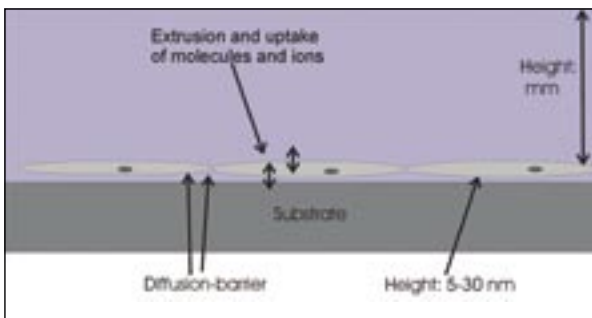


Figure 5 - The general situation of an adherent cell or cell layer on a solid substrate

ture depositing on surfaces, like for example the CMOS passivation layers (silicon nitride or oxide), even if only some nanometers in thickness, affects the gas sensing ability of the sensors. The reason is that a surface current through this moisture layer induced by other environmental potentials counteracts the “real” gas-signal potential. The goal of this research study was therefore to reduce the adsorption of moisture by making the surface ultrahydrophobic. This was realised by a UV-assisted attachment of a 13-15 nm thin film of fluoropolymers onto the silanised SiO₂ sensor surface of the CCFET. The critical surface tension of the modified surfaces is 8 dynes/cm, which indicates a higher hydrophobicity than Teflon (18 dynes/cm). The influence of such nm-scaled fluoropolymer films on the sensor performance can be seen in Figure 4. The measurement without the fluoropolymer shows that after a signal occurs at the sensitive layer (gas signal or applied electrical potential) the sensor signal reacts, but, although the gas signal is still there, the sensor signal starts declining. An electrical model with a resistance and a capacity in parallel (R and C) can describe this performance, (R is the resistance

of the moisture film on the sensor surface and C is the capacity of the CCFET). As a consequence, a high thickness of the moisture film, which means a lower resistance and a higher current, discharges the capacity of the CCFET faster than

the significantly thinner moisture film on the ultrahydrophobic layer. This work was realised in cooperation with Micronas and IMTEK, University of Freiburg (Chemistry and Physics of Interfaces, Professor R  he & MEMS Materials Laboratory, Professor Paul).

Nanometer-scaled interspace between cells and a surface

Adherent cells on solid surfaces is an established in vitro method and the adhesion process of a cell is considered an important trigger for many cell processes (e.g. polarity and tumour genesis), even though not all of the eliciting biochemical or biophysical reactions are yet understood. The general situation of an adherent cell or cell layer on a solid substrate can be described as follows (Figure 5): Two different extra-cellular spaces are defined: the apical side is the one above the cells and is normally in the range of some mm (referred to as ‘mm-space’ below) and the one between the solid surface and the cell membrane (basolateral) in the range of 5-30 nm (referred to as ‘interspace’ in the following). Furthermore, cells have active mechanisms to transport

ions and molecules into and out of both sides of the cell (apical and basolateral). Therefore, in both spaces, ions or molecules are either extruded or assimilated. The diffusion of the molecules and ions from the interspace to the mm-space (and vice versa) is hindered by the cell membranes and when using epithelial cells even by tight cell-cell-connections. The metabolism of a tumour cell, for example, generates as by-products a great number of protons which must be extruded (10⁸ protons/cell/second) outside the cell, otherwise the cell would be too strongly acidified. The important question is: “What happens in the interspace?”

This question is examined with a CMOS-ISFET array of 4 ISFETs each designed for optimal cell growth. The cells directly adhere to the sensitive gate region with a W/L geometry of 100/4 μm². With an assumed cell area of 10*10 μm², approximately 10 cells grow partly on the 400μm² gate region. The ISFET measures the interspace directly.

In Figure 3 a typical measurement is presented with cells (LS 174T) covering only one ISFET (cell-ISFET) and with the other ISFET free of cells (ISFET). It can be assumed that both the apical and the basolateral side of the cells extrude protons. The cell-ISFET measures the acidification in the interspace. This acidification depends on the buffer capacity, the acidified volume and the amount of extruded protons. The basolateral acidification can be calculated with the following equation:

$$\Delta pH = \frac{1}{V_0 \alpha} \sum_{cells} \Delta H^+ cells$$

(V₀ is the volume; α is the buffer capacity and ΔpH the measured pH difference). With an assumed distance between cell membrane and ISFET of 15 nm and with the area of 400μm² the volume is 6 fl (6*10⁻¹⁵l). The cell-ISFET signal shows an acidification of 8.8 mV, which is a pH-decline of 0.16. With the equation above the number of protons per cell and per second calculates to 900. This means that the number of protons extruded to the basolateral side is less than the number extruded apically (cal-

