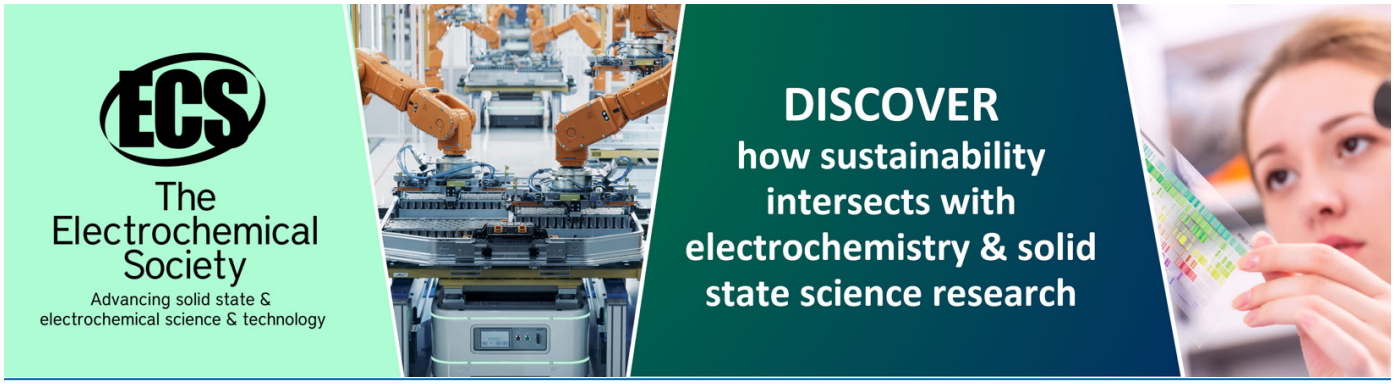
Biostability of an implantable glucose sensor chip



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Biostability of an implantable glucose sensor chip

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Abstract. Surface materials of an implantable microelectronic chip intended for medical applications were evaluated with respect to their long-term stability in bio-environments. The sensor chip shall apply in a glucose monitor by operating as a microviscosimeter according to the principle of affinity viscosimetry. A monolithic integration of a microelectromechanical system (MEMS) into the sensor chip was successfully performed in a combined 0.25 µm CMOS/BiCMOS technology. In order to study material durability and biostability of the surfaces, sensor chips were exposed to various *in vitro* and *in vivo* tests. Corrosional damage of SiON, SiO_2 and TiN surfaces was investigated by optical microscopy, ellipsometry and AFM. The results served for optimizing the Back-end-of-Line (BEoL) stack, from which the MEMS was prepared. Corrosion of metal lines could significantly be reduced by improving the top-most passivation layer. The experiments revealed no visible damage of the actuator or other functionally important MEMS elements. Sensor chips were also exposed to human body fluid for three month by implantation into the abdomen of a volunteer. Only small effects were observed for layer thickness and R_a roughness after explantation. In particular, TiN as used for the actuator beam showed no degradation by biocorrosion. The highest degradation rate of about 50 nm per month was revealed for the SiON passivation layer. These results suggest that the sensor chip may safely operate in subcutaneous tissue for a period of several months.

1. Introduction

The application of microelectronics in the field of biosensorics requires the consideration of certain constraints with respect to the usage of technical materials in corrosive environments [1, 2]. We report here on a sensor chip for the continuous monitoring of glucose operating by the principle of affinity viscosimetry [3, 4]. The development aims at an implantable device for diabetes diagnostics and therapy that shall stay in human subcutaneous tissue for a time span of months. The sensor operates by determining the viscosity of a sensoric liquid that varies in accordance with glucose concentration in the surrounding tissue [5, 6]. The sensor chip is realized as a microelectromechanical system (MEMS) operating with a mechanically bendable beam in an electrostatic actuation scheme and from the bending velocity of which the viscosity can be derived [7].

In contrast to the usual procedure with MEMS being fabricated from the Si bulk, the microviscosimeter presented in this work has been prepared from the Backend-of-line (BEoL) stack [8]. The functional layers staying in contact with the bio-milieu are thus the surface passivation from SiON (Pas), the interlayer dielectric (ILD) from SiO_2 as well as the bendable beam and the ground plate electrode made from TiN. Figure 1 displays a section from the unfilled MEMS cavity that will be

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filled with sensoric liquid during operation. Parts of the beam and ground plate in the vicinity of an anchor point can be recognized that both are fabricated from metallically conductive TiN in order to enable the electrostatic actuation scheme of the BioMEMS. TiN has advantageously been chosen, since the material is well established in semiconductor fabrication technology, where it is used as an anti-diffusion layer below and above lateral interconnects from Cu-alloyed aluminium Al:Cu. The slope observable for the SiO_2 ILD layer has been introduced during etching of the cavity for suspending the TiN beam according to the chronological progression of the etch front, where top layers were subjected to the etchant for a longer time. The top-most layers is formed by the SiON passivation exhibiting a lower etch rate than SiO_2 and forming an overhang after the etch process that stopped on the TiN ground plate.

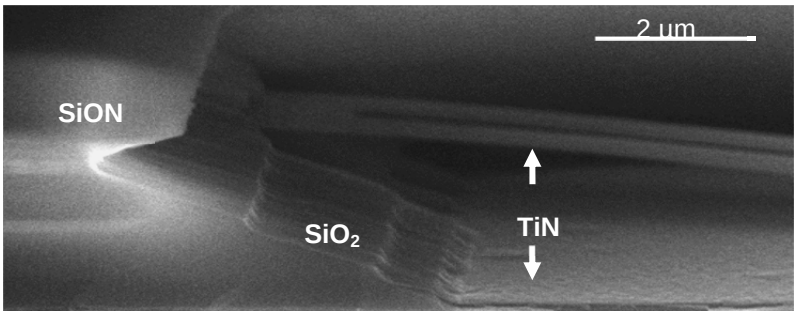

Figure 1. Scanning electron micrograph of a part of the Bio-MEMS displaying the different materials staying in contact with body fluid after implantation of the glucose sensor chip.

Previous investigations revealed TiN to be sufficiently biostable for the applications intended here [9, 10]. The focus of this work was thus on ILD and Pas layers, for which *in vitro* and *in vivo* loss rates should be determined in order to derive a first estimate for a possible life time of implanted biochips in the body tissue.

2. Materials and methods

2.1. Sample preparation

Sensor chips were prepared on 200 mm CZ-Si wafers in a 0.25 µm CMOS/BiCMOS technology [11]. Different variants of the so-called value technology are available with the base variant supplying metal layers M1, M2 and M3 from Al:Cu and sheet resistances of 84, 55 and 55 mΩ/sq embedded in four isolating SiO_2 layers ILD0..ILD3. Furthermore, top-metal layers TM1 and TM2 (16 and 10 mΩ/sq) and additional ILD4 and ILD5 layers may be supplemented, yielding an increased geometrical height of 8 µm of the full BEoL stack. Planarizations of intermediate BEoL stacks are performed in the standard flow after ILD1 to ILD3 by chemical-mechanical polishing (CMP), but not after ILD4 and ILD5.

MEMS actuators were prepared as fourfold clamped X-shaped TiN beams having a width of 6 µm [8], see Figure 2. Due to their small thickness of only 50 nm particular care was taken for the suspension of TiN beams, which was accomplished by critical point drying with supercritical CO_2 after the last etch step in order to avoid beam stiction (‘static friction’) to the ground plate [12]. Electrical testing was performed after stealth dicing the sensor chips from the full wafer [13] and contacting ∅ 80 µm bond pads with a flexible cable via flip-chip bonding.

2.2. in-vitro Tests

Investigations of biostability were performed *in vitro* by exposing the sensor chips to different model solutions and determining the loss rates by comparing selected geometrical parameters in their initial and final state. Figure 2 displays a microscopic view into the MEMS cavity showing the full X-shaped actuator beam that is situated 2.5 µm above the ground plate. Length *L* and width *B* were determined by optical microscopy with a precision of ca. 1 µm before and after the corrosion test.

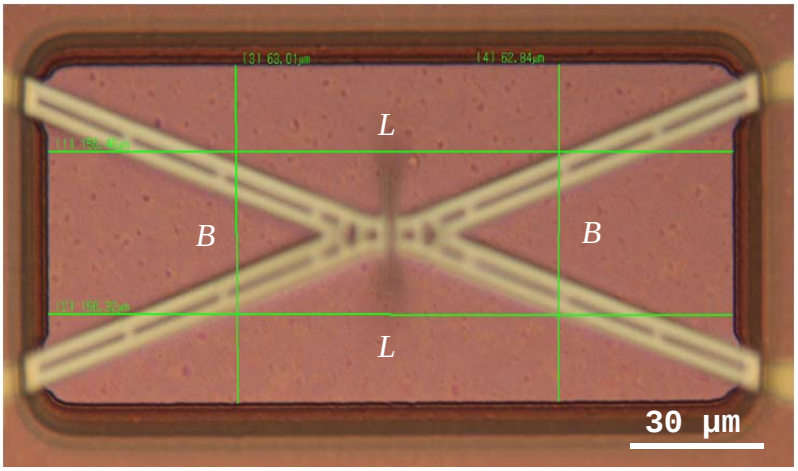

Figure 2. Sensor MEMS cavity showing the X-shaped beam at a height of 2.5 µm above the ground plate that both were prepared from TiN. Green lines indicate the distances *L* and *B* that were determined prior and after corrosion testing.

A possible reduction of top layer thicknesses was examined by spectroscopic ellipsometry. SE measurements were done in the wavelength range of 190-800 nm using an automated, small-spot (14×28 µm^2) spectroscopic ellipsometer with a 71° angle of incidence on the selected area of the chip. The determination of thicknesses (Pas (d_{pas}), SiO_2 (d_{ox}), TiN) of multilayer stack was performed. Surface roughness R_a was determined from topographic AFM scans.

For simulating the body fluid a model solution of isotonous saline PBS-buffered to pH = 7.4 and constantly held at 37°C was applied, into which the sensor chips were completely immersed. Optical and electron microscopy were applied for the inspection of corrosional damage that occurred for some sensor chips during electrical testing in glucose-containing electrolyte.

2.3. in-vivo Test

In order to evaluate the corrosion resistance under realistic operation conditions, sensor chips were also implanted into the abdomen of a volunteer, where they remained for three month before they were explanted and examined. Chips were inserted into polysulfone tubes with a cut-off of 300 kDa and thus allowing for the safe access of corrosion-active components from the body fluid. Corrosion effects were investigated by the methods outlined above by determining variations of thicknesses and other geometry parameters by comparing initial and final state. Disinfection of samples before and after the test was performed by immersing them in ethanol (>70%).

3. Results and discussion

Sensor chips were first subjected to model solutions without bringing them to operation, i.e. no voltage pulses were applied as required for the viscosity measurement. Sensor chips were simply stored in isotonous saline at 37°C and regularly taken out for microscopic inspection. No increase of geometry parameters *L* and *B* of the MEMS cavity could be determined within the measurement precision after

six weeks, $\Delta L \approx 0$ und $\Delta B \approx 0$. Similarly, no significant variations of thickness of the passivation layer d_{pas} or surface roughness R_a of the TiN ground plate could be stated.

Comparable tests were performed with functionally operating sensor chips that were subjected to some 100 ms long DC voltage pulses of 3..4 V at regular time intervals between 10..300 s. Also in this case, no variations of L and B parameters above the significance level could be determined. However, a complete failure of the sensor operation was frequently observed during these tests that could in some cases be traced back to a corrosion of planar interconnects. The phenomenon is illustrated in Figure 3 by optical and electron microscopic views of corroded metal lines. A disruption of the metal line can clearly be recognized that caused parts of the electrical circuit to become disconnected from the voltage source.

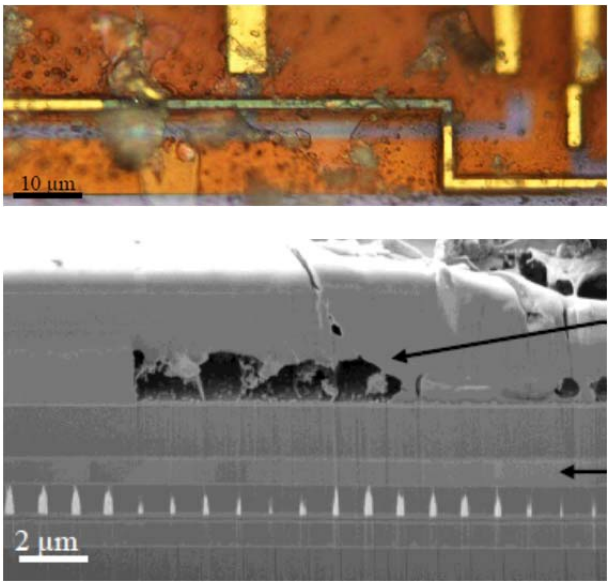

Figure 3. Optical microscope view on chip section showing corroded metal line as yellow line that is greenish coloured in the corroded state (top).

FIB REM micrograph of corroded conduction line of the same area as the top figure showing that the metal layer TM1 below the passivation layer Pas was severely damaged (bottom).

An analysis of the effect revealed that the corrosion originated from a defect in the passivation layer, by which an electrical contact between the electrolyte solution and the metal line TM1 was introduced. It may be suspected that the corrosion process is related to the flow of electrical current in the metal line, since such phenomena were not observed for non-operating sensor chips.

Evidently, such defects have to be completely suppressed for biosensor chips that shall reliably operate in an electrolyte-containing environment. A modification of the top-most layers of the BEoL stack was accordingly tested for solving the problem. Figure 4(a) displays a cross section of the layer architecture from the standard process, where no CMP is applied after depositing ILD4 on TM1. The finally obtained passivation surface then shows protrusions in all those areas, where lateral interconnects made from TM1 can be found below.

It could be assumed that the observed corrosion of metal lines initiated in the vicinity of protrusions being particular prone to mechanical damage upon inadequate handling of sensor chips. Defects would then establish the first contact between electrolyte and TM1 and would act as starting point for the corrosion that would progressively remove increasingly distant parts of interconnect. Figure 4(b) shows the modified BEoL stack, where ILD4 is supplemented by a SiO_2 layer that was subsequently planarized by an additional CMP step. For this architecture, metal interconnects from TM1, firstly, do not cause topographic protrusions on the surface and, secondly, exhibit a larger distance to the surface

that stays in direct contact with the bio-milieu. Both effects preserve the metallic interconnects of TM1 effectively from the corroding environment.

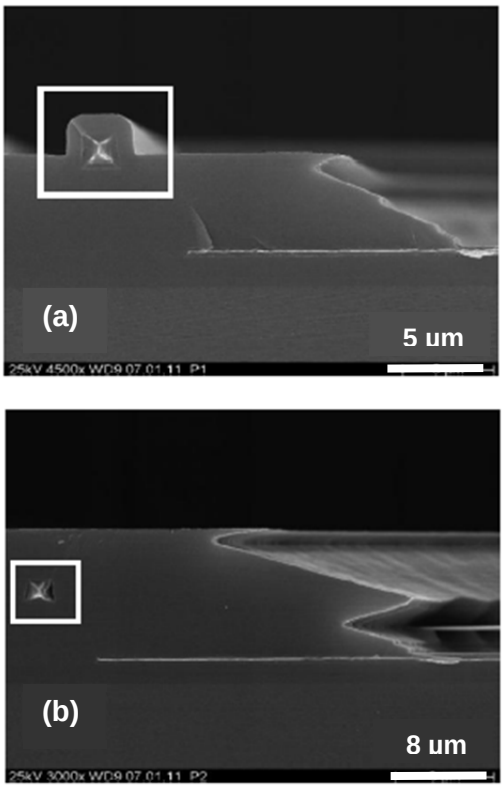

Figure 4. SEM cross sections of two sensor chips close to MEMS cavities showing SiO_2 etch slopes and TM1 interconnects (white boxes). Both chip architectures are finished by a top-most passivation (Pas) layer from SiON. The stack given in (a) has been prepared by the standard process yielding topographic protrusions in the area of TM1 interconnects. In Figure (b), however, the ILD4 layer process was supplemented by depositing another SiO_2 layer and its subsequent planarization by CMP. In this configuration, the Pas layer that stands in direct contact with the bio-milieu is perfectly flat and is less prone to in-creeping electrolyte.

In order to examine the biostability under realistic conditions, *in vivo* tests were performed without supplying a voltage to the sensor chips and without operating them as microviscosimeter. For this purpose, sensor chips were inserted in polysulfone tubes and implanted into the abdomen of a volunteer. Samples were fixed at a depth of 10..20 mm below the skin surface by a medical fathom to prevent migration. Chips stayed for three month in the body and were finally explanted. No significant variations of surface roughness R_a induced by bio-corrosion was observed for the TiN ground plate.

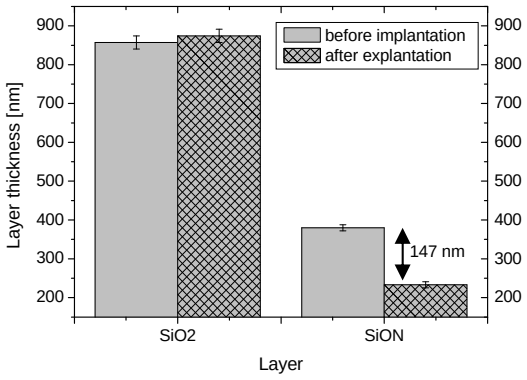

Figure 5. Ellipsometrically determined thickness of top-most SiO_2 and SiON layers within the BEoL stack of *in vivo* tested sensor chips. A loss rate of 147 nm was derived for the SiON Pas layer that stayed in direct contact with body fluid, while the SiO_2 layer below it remained practically unaffected.

Figure 5 gives the thicknesses d_{ox} and d_{pas} of top-most BEoL layers by comparing them before and after implantation. It can be recognized that the SiO_2 layer remained unaffected within the limits of precision of the measurement. This may be understood from the protecting SiON layer situated on top of it. The thickness of the latter, however, has been diminished by 147 ± 8 nm during the experiment. The loss rate of about 50 nm/month compares well to the results of a previous *in-vivo* study that was related to the development of an implantable retina chip [9].

4. Conclusions

The investigations of a biosensor chip intended for long-time implantation presented here revealed no measureable loss rates for exposing the chips *in vitro* for six weeks to model solutions of the body fluid. An improved back-end architecture has been developed to avoid the corrosion of metal interconnects that was frequently observed for electrically driven sensor chips. As a first estimate for a possible life time, it may be deduced from an *in vivo* test that sensor chips may operate for a time span of months in the human body.

5. References

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