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Long Term Evaluation of the Barrier Properties of Polymer/Metal Oxide Hybrid Layers for Use in Medical Implants

Abstract:

Encapsulation is essential for mechanically flexible and electrically active implants as it protects them from the harsh environment inside the body. Since the performance and longevity of implants depends on the quality of encapsulation, research continues into new and better encapsulation strategies. Chemical vapour deposition can be used to deposit Parylene-C, a biocompatible polymer, at room temperature. Plasma enhanced atomic layer deposition can be used to deposit ultra-thin, conformal, and hermetic metal oxide layers. These strategies are both used for the encapsulation of implants. In this work, these two methods are combined to create a polymer/metal oxide hybrid system in which a layer system of metal oxides is sandwiched between two Parylene-C layers. DC leakage-current measurement and elevated temperature are used to qualify the barrier property of the layer-system. After more than one year, the barrier properties still show no significant decrease.

Keywords: Hybrid Layers; ALD; Parylene; Encapsulation

1 Introduction

Thin, mechanically flexible implants such as the retina implant or neural implants adapt to the anatomical structures of the body and require direct contact between their electrodes and the biological tissue. Elevated temperature, physiological salt concentrations and high moisture promote corrosion of unprotected materials inside the human body. The substrate material of the implants does not have sufficient barrier properties to protect the embedded electrical components. Therefore, a suitable encapsulation material is necessary. The longevity, performance and biocompatibility of the active implant depend on the quality of the encapsulation.

Parylene-C is a suiting material for encapsulating implants [1]. The polymer is deposited by chemical vapour deposition (CVD) at room temperature. The layers are pinhole-free, flexible, and have a USP class IV biocompatibility. They provide a good barrier to ion permeation [2] and thus suppress corrosion. A major drawback of Parylene-C is the adhesion, which is greatly reduced due to moisture penetration, leading to failure of the encapsulation.

Atomic layer deposition (ALD) is used to apply wafer-thin, conformal, and defect-free layers of metal oxides that have excellent barrier properties. ALD is a highly modified, cyclic CVD process in which layer-forming chemicals are introduced into the reaction chamber in clearly separated steps. They react with the surface in a self-limiting manner, leading to a layer-by-layer growth. The energy required for the reaction is provided either by elevated temperature or, for the coating of temperature-sensitive materials, by a plasma.

Aluminium oxide applied by the plasma enhanced ALD process has excellent barrier properties but dissolves slowly in contact with water. Chemically stable titanium oxide can be used to protect the aluminium oxide. Thus, a sandwich-layer can be produced in which aluminium oxide is protected by the titanium oxide.

In this work, a polymer/metal oxide hybrid layer system is deposited on a nonflexible microelectrode array (MEA) to test its barrier properties. A metal oxide sandwich-layer is deposited by ALD and sandwiched with Parylene-C. The objective is to produce a high-performance barrier layer, combining the advantages of both layer types. The coated MEAs were exposed to phosphate buffered saline (PBS) at elevated temperatures for accelerated aging. Measurements of DC leakage-current were performed to test the long-time barrier properties. This work is a continuation of the work that tested the barrier properties of ALD layer coatings on the same type of MEAs [3].

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2 Materials and Methods

2.1 Measurement Setup

The experimental setup to test the barrier properties of the layer is schematically shown in **Figure 1 a.)**. A high resistance Source Measurement Unit (SMU) 6517B (Keithley Instruments, Inc., Cleveland, Ohio, USA) with integrated DC power supply was used to measure the leakage current down to pA. The multiplexer containing DR-SDS relays E48393 from NAIS (Matsushita Electric Works, Holzkirchen, Germany) was used to switch the electrical path and thus measure up to nine different channels in one run. BNC cables with 7080-TRX-GND adapters (Keithley Instruments, Inc., Cleveland, Ohio, USA) were used to connect all units with each other. Since currents down to the pA are measured, the measurements were carried out in a Faraday cage, ensuring electrical shielding, and the ground potential was looped through the entire setup to obtain a defined potential. A voltage of U = 1 V was applied between the AgCl counter electrode in PBS and the electrodes on the sample. Measurements were carried out automatically via a custom programmed LabView VI (National Instruments, Austin, Texas) [4]. Leakage currents from the samples were recorded in the first month every third day and after that weekly. Between the measurements, the samples were stored on a hotplate (Stuart SD 500, Cole-Parmer, Staffordshire, UK) at 60 °C for accelerated aging [5].

Figure 1 b.) shows a sample which consists of a lid with a AgCl electrode, a glass tube filled with PBS, and a coated substrate with gold leads.

2.2 Sample Preparation

The MEAs were produced using the bottom-up method utilizing standard microsystems fabrications techniques. Wet oxidised 4-inch silicon wafers (100) with an oxide thickness of 3.2-3.4 μm were used as substrate. Photolithography was performed using a Karl Süss Ma6 Mask Aligner and the photoresist AZ5214E (MicroChemicals, Ulm, Germany). After the development of the structures, a metal layer stack of 10 nm titanium, followed by 50 nm gold, and 10 nm titanium was applied by physical vapor deposition using an Edwards Auto306 (BOC Edwards, West Sussex, UK) without vacuum breakage. The lift-off process was carried out using acetone in an ultrasonic bath. The processed wafers were sliced in 24x24 mm² pieces and cleaned in an ultrasonic bath with acetone, followed by isopropyl and then rinsed with DI-Water. The produced electrode structures are shown in **Figure 1 c.)**.
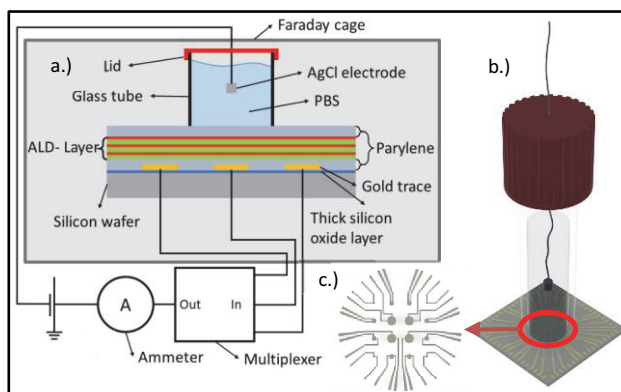

Figure 1: Experimental setup for the evaluation of the long-term stability of the barrier properties
  a.) Schematic of the experimental setup. A Faraday cage is used for electric shielding
  b.) An illustration of the sample
  c.) Electrode layout

The four big electrodes in the centre have a diameter of 500 μm, the medium ones at the edges have a diameter of 250 μm, and the four small corner electrodes have a diameter of 125 μm. Each electrode has two leads with contact pads at the edge of the sample for short-circuit measurement, which was carried out before every measurement to assure electric contact of the sample.

Since the surfaces of the electrodes, as well as parts of the leads, are in contact with the PBS, the combined surface was considered for the calculation of the current density. The sizes of the areas are shown in **Table 1**. The designation of the electrodes starts in the north-west of **Figure 1 c.)** and follows the clockwise direction. The names big, medium, and small electrodes correspond to the electrodes with a diameter of 500 μm, 250 μm and 125 μm, respectively.

Table 1: Area used for the calculation of the current density

Electrode	Area exposed to PBS [mm²]
Big Electrode 1 and 2	0.7738
Big Electrode 3	1.0130
Medium Electrode 1 and 2	0.6427
Medium Electrode 3	0.6412
Small Electrode 1 and 2	0.3136
Small Electrode 3	0.4018

2.3 Coating of the samples

Before coating of the MEAs, the contact pads were masked with Kapton tape. Parylene-C was deposited using the Labcoater 300 (Plasma Parylene Systems, Rosenheim,

Germany). An oxygen plasma pre-treatment was performed for 300 s with 300 W at 40 Pa. Afterwards, silane A-174 was introduced as adhesion promoter. Thickness measurements were performed by reflectometry (NanoCalc-XR, OceanOptics, Largo, USA) on enclosed silicon wafer pieces. One sample was coated with 715 nm and another with 3 µm Parylene-C. The latter is used for the polymer/metal oxide hybrid system.

The application of the Al_2O_3 and TiO_2 layers were carried out with the MyPlas-PEALD system (Plasma Electronic GmbH., Neuenburg, Germany). Precursors Trimethyl-aluminium (TMA) and Titanium (IV)-isopropoxide (TTIP) were used for Al_2O_3 and TiO_2 growth, respectively [3, 6]. Oxygen plasma was used as co-reactant for both precursors. The deposition temperature was 100 °C. The sample with 3 µm layer of Parylene-C was pre-treated with an oxygen plasma for 300 s with 150 W at 2.25 Pa inside the ALD recipient. A layer-system of 15 nm Al_2O_3 and 5 nm TiO_2 was applied 3 times in a row, resulting in an overall thickness of 60 nm, which was confirmed with reflectometry on an enclosed silicon wafer. After ALD coating, the sample was coated with a 5 µm thick Parylene-C layer. The same pre-treatment methods for Parylene-C as previously described were used. Silpuran®4200 (Wacker, Munich, Germany), a biocompatible adhesive, was used to glue the glass tube onto the coated substrates. It was filled with PBS so that the coated electrodes were in direct contact with the solution. The lid with the AgCl electrode reduced the evaporation of the PBS.

3 Results and Discussion

Current densities over a period of one year at 60 °C (polymer/metal hybrid layer sample), and for 400 h at room temperature (Parylene-C sample) were measured, respectively. For the sample with the hybrid system, 5 measurements were taken per electrode in each run. Error bars represent the standard deviation. The sample with 715 nm Parylene-C was measured in one run.

Figure 2 shows the calculated current densities of the sample with a coating of 715 nm Parylene-C. The barrier effect begins to weaken after 15 hours. A steep increase in current density is observed at Big Electrode 2 and successively the other electrodes begin to show an increase in current density. The PBS probably penetrated through the layer near Big Electrode 3 and caused the increase in the current density. The PBS spread at the interface between the Parylene-C and the silicon oxide. To examine the surface morphology of the Parylene-C after the measurement, the adhesive between the glass tube and the Parylene-C layer was carefully loosened.
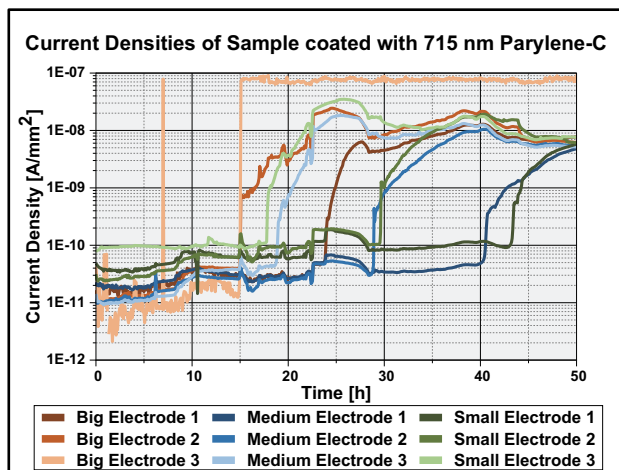
Figure 2: Representation of the calculated current density of the sample with 715 nm Parylene-C.

The Parylene-C detached from the substrate but remained attached to the glass tube in the form of a thin skin. Thus, the Parylene-C was penetrated at one point and the water spread underneath it, resulting in weak adhesion. In this setup, a current density of more than 1E-9 A/mm^2 indicates a failure of the barrier properties.

In the upper left corner of **Figure 3** an overview of the corroded electrodes is shown. The white border within the image is the adhesive residue of the glue after the glass tube was removed. The main picture shows a corroded electrode.

Figure 4 shows the calculated current densities of the layer system with 3 µm Parylene-C + 3x (15 nm Al_2O_3 +5 nm TiO_2) ALD + 5 µm Parylene-C. In the first month of measurement, the values follow a slightly decreasing trend and start to fluctuate strongly after 3 months. The negative currents measured may be noise signals, but it cannot be excluded that electrochemical processes are taking place at the interfaces of the layers [7]. Although Parylene-C has a good ion barrier property, thin layers can still be penetrated by ions over long
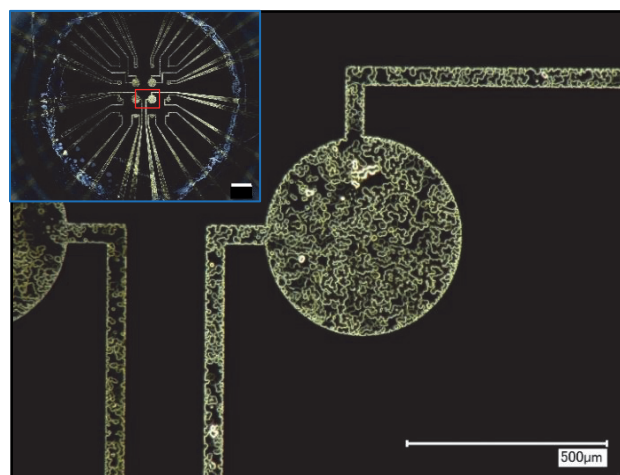
Figure 3: Corroded electrode of the sample coated with 715 nm Parylene-C after 400 h of measurement. Scale bar in inset:1 mm
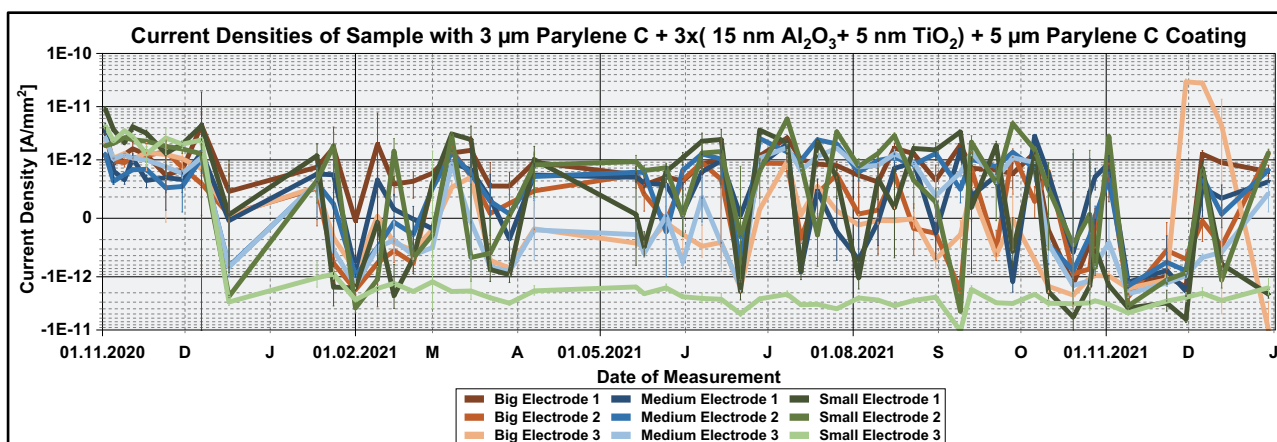
Figure 4: Calculated current densities of the 9 different electrode areas over a period of more than one year. The measurements show fluctuations in few pA range. The value of 1E-9 A/mm2 was not exceeded.

time periods and contribute to corrosion and electrochemical reactions [8].

As shown in the first measurement, a current density of 1E-9 A/mm^2 indicates a failure of the barrier layer. However, this value was not exceeded nor reached during the entire time of measurement. The barrier effect of the layer system is therefore still sufficient and corresponds to 5 years at 37 ℃.

It should be noted, even biocompatibility can be assumed for Parylene-C, a possible degradation of the same during long-term exposure was not investigated within the scope of this work. Therefore, the barrier properties given apply to a physiological environment, but without foreign body reaction. This may lead to premature degradation of the encapsulation, which should be investigated in further studies.

4 Conclusion

The barrier properties of a 715 nm Parylene-C layer and a polymer/metal oxide hybrid layer with 3 µm Parylene-C + 3x (15 nm Al$_2$O$_3$ +5 nm TiO$_2$) ALD + 5 µm Parylene-C were tested using DC leakage-current measurement. The coating with 715 nm Parylene-C, which was tested at room temperature, failed already after 15 h, as the current density increased abruptly. The exceeded value of 1E-9 A/mm^2 was used as a benchmark for the failure of the barrier properties. The hybrid system was stored at 60 ℃ and measured at room temperature. Even after more than one year, the value of 1E-9 A/mm^2 was not exceeded. The barrier property of this coating is therefore still sufficient and corresponds to 5 years at 37 ℃.

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