Characterization of Biodegradable Polymers with Capacitive Field-effect Sensors

S. Schusser[1,2], *A. Poghossian*[1,2], *M. Leinhos*[1,2], *P. Wagner*[3], *M.J. Schöning*[1,2]

[1] *Institute of Nano- and Biotechnologies (INB), FH Aachen, 52428 Jülich, Germany,*
schusser@fh-aachen.de
[2] *Peter Grünberg Institute (PGI-8), Research Centre Jülich GmbH, 52525 Jülich, Germany*
[3] *Institute for Materials Research, Hasselt University, 3590 Diepenbeek, Belgium*

Abstract

A field-effect capacitive sensor has been applied for the real-time *in-situ* monitoring of degradation of biopolymers for the first time. The sensor is, in principle, capable to detect any changes in bulk, surface and interface properties of polymers induced by degradation processes. The feasibility of this approach has been experimentally proven by using the commercially available biomedical polymer poly(D,L-lactic acid) as a model system. The degradation of the poly(D,L-lactic acid) was accelerated by changing the degradation medium from neutral (pH 7.2) to alkaline (pH 9) condition, resulting in drastic changes in the capacitance of a polymer-modified field-effect sensor.

Key words: Field-effect sensor, real-time monitoring, (bio)degradation, poly(D,L-lactic acid)

Introduction

Although biomaterials have already made an enormous impact in biomedical research and clinical practice (e.g., in drug-delivery systems, as scaffolds for tissue engineering, or orthopedic implants), there is a need for new biodegradable synthetic polymers and implantable devices with controlled/predicted biodegradability [1-5]. For any application, the *in-vitro* study of the degradation kinetics of the biopolymers is essential not only for a fundamental understanding of the nature of the degradation process but also for the design and optimization of implantable biomedical devices. Common techniques used to quantify degradation (e.g., determination of mass loss, shortening of the chain length or shift of the glass transition temperature towards lower values) are not suitable for real-time measurements because of their destructive manner and thus, limit studies on degradation kinetics in respect of throughput and precision [4]. Analyzing techniques capable for a real-time *in-situ* monitoring of the degradation kinetics are therefore highly appreciated. In this report, we present experimental results on polymer degradation investigation by means of capacitive field-effect electrolyte-insulator-semiconductor (EIS) sensors, as a novel and very promising platform for *in-vitro* testing of biodegradability of polymers. The commercially available biodegradable polymer poly(D,L-lactic acid) (PLA) was used as a model system. The benchmark biopolymer PLA (RESOMER®

R 202 H, Evonik Röhm GmbH, Germany) was chosen, because of its exceptional importance, biocompatibility and its use in numerous approved medical devices and pharmaceutical applications [6]. In previous experiments, field-effect sensors have been widely utilized for the detection of various (bio-)chemical quantities, like pH, ion- and analyte concentration, charged macromolecules as well as cellular signals (see e.g., [7-10]).

Sensor principle

Fig. 1 shows a schematic of the layer structure (a) and a simplified equivalent circuit (b) of the polymer-modified EIS sensor (further referred to as PMEIS) consisting of an Al-Si-SiO2-Ta2O5 structure.
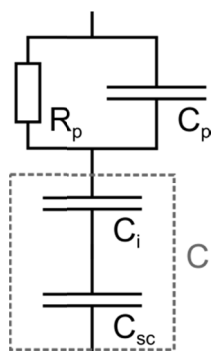
a)
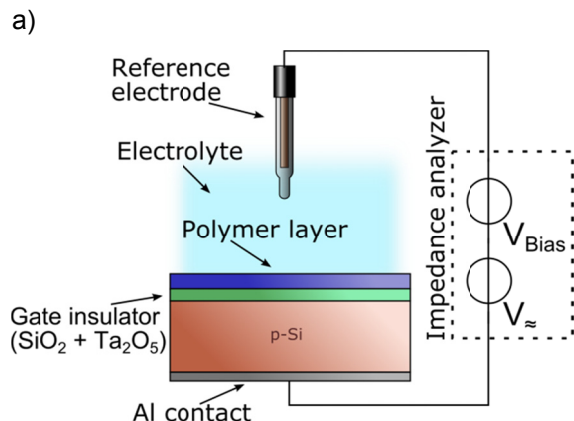
b)

Fig. 1. *Schematic of the layer structure (a) and simplified equivalent circuit (b) of a field-effect PMEIS sensor.*

Fig. 2. *Thickness of the deposited polymer films as a function of polymer concentration.*

For the PMEIS structure, the polymer layer can be described as a parallel network of the polymer geometric resistance, R_p, and the capacitance, C_p, which is in series with the bare insulator-semiconductor structure [10, 11]. The experimentally measured capacitance of the PMEIS structure, C_{meas}, can be expressed as:

$$C_{meas} = C \frac{1 + R_p^2 C_p^2 \omega^2}{1 + R_p^2 \left(C C_p + C_p^2 \right) \omega^2} \qquad (1)$$

where C is the capacitance of the original EIS structure without polymer layer, C_i is the gate-insulator capacitance, C_{sc} is the space-charge capacitance of the Si, $\omega = 2\pi f$ and f is the measuring frequency. Thus, any changes in the polymer resistance/capacitance induced by the polymer degradation will alter the global capacitance/impedance of the PMEIS structure that can be used as an indicator of the polymer degradation.

Fabrication of EIS Sensor and Polymer Deposition

For the degradation experiments, the EIS chips (with chip size of 10 mm x 10 mm) consisting of an Al-Si-SiO$_2$-Ta$_2$O$_5$ structure (p-Si, ρ=5-10 Ωcm, 300 nm Al as rear-side contact layer, 30 nm SiO$_2$; 60 nm Ta$_2$O$_5$) were fabricated. The degradable polymer films with different thicknesses were deposited on the Ta$_2$O$_5$ surface from the polymer solution by means of spin-coating method. The polymer solution was prepared by dissolving the PLA (Mw = 10,000 – 18,000) in acetone. The desired range of layer thickness has been achieved by varying the concentration of the polymer solution (see Fig. 2). The thickness of the polymer layer was defined from profilometry measurements. The deposited polymer films were homogeneous without any visible pores. As an example, Fig. 3 depicts a photo of the PMEIS sensor surface with a 500 nm thick PLA layer.
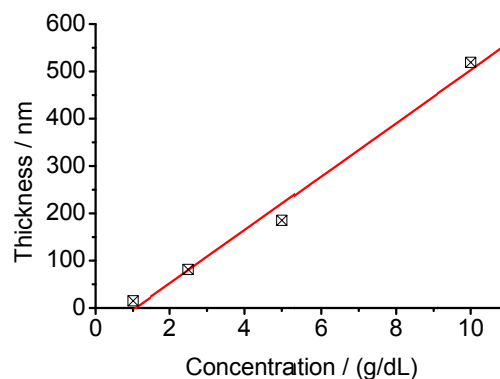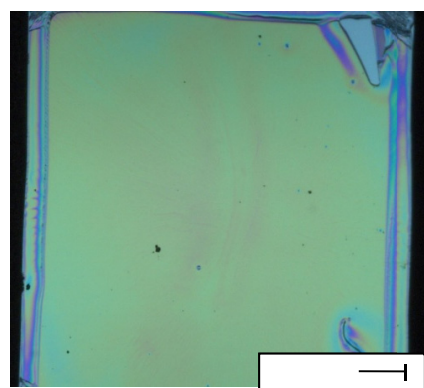

Fig. 3. *Photo of the PMEIS sensor surface with a PLA layer of 500 nm thickness.*

The sensor chip was mounted into a home-made measuring cell and then the PMEIS structure was characterized before and during polymer degradation by means of capacitance-voltage (*C-V*) method. For measurements, a DC polarization voltage is applied between a conventional liquid-junction Ag/AgCl reference electrode (Metrohm) and the rear-side Al contact. A small AC voltage (20 mV) is applied to the system in order to measure the capacitance of the PMEIS sensor. The *C-V* curves were captured every 1 h at a frequency of 100 Hz. The degradation experiments were carried out at a temperature of 37 °C.

Results and Discussion

Fig. 4 represents an example of real-time monitoring of polymer degradation with a field-effect structure. In this experiment, the time-dependent capacitance of the PMEIS sensor with a 500 nm thick PLA layer was recorded in the accumulation region of the C-V curve over the time period of about eight days. It is known, that PLA has a slow degradability in neutral pH solutions and shows a higher degradability in basic solutions [5]. Therefore, during the first 50 h of monitoring, the polymer layer was exposed to neutral pH buffer solution of pH 7.2, which

mimics the physiological conditions of biological fluids. Practically, no changes in capacitance have been observed. Then, in order to accelerate the polymer degradation, the PLA layer was exposed to alkaline buffer solution of pH 9, resulting in drastic changes in the capacitance of the PMEIS structure over time. The degradation rate can be evaluated from the time-dependent C-V curves. These results are supported by optical microscopy of the sensor surface after PLA degradation (Fig. 5).
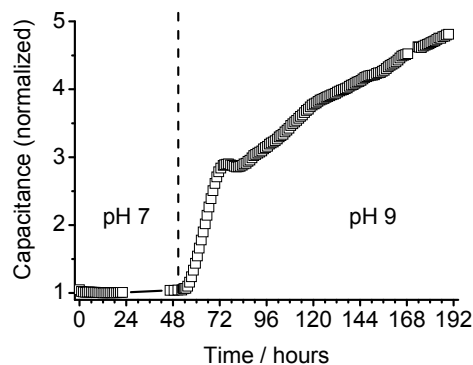

Fig. 4: *Monitoring of PLA degradation with capacitive field-effect sensor: time-dependent capacitance changes induced by polymer degradation.*
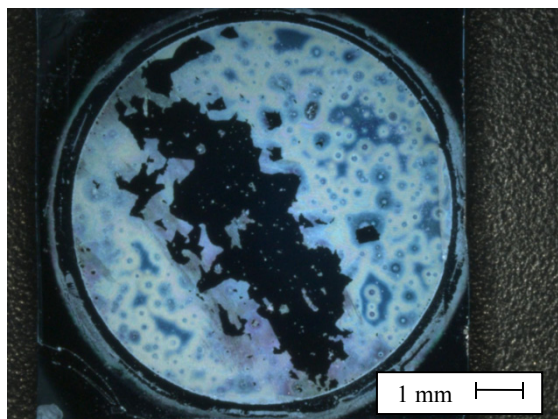

Fig. 5. *Optical microscopy image of the PLA-covered sensor surface after polymer degradation.*

Conclusions

The degradation kinetics of the poly(lactic acid) biopolymer was studied using a field-effect capacitive EIS sensor. These preliminary experiments demonstrate the potential of field-effect devices as a novel and very promising tool for the real-time *in-situ* monitoring of polymer degradation. Further works will be directed to optimize the design of the EIS sensor and measuring conditions.

Acknowledgements

References

[1] L.S. Nair, C.T. Laurencin, Biodegradable polymers as biomaterials, *Progress in Polymer Science* 32, 762-798 (2007); doi: 10.1016/j.progpolymsci.2007.05.017

[2] M. Martina, D.W. Hutmacher, Biodegradable polymers applied in tissue engineering research: a review, *Polymer International* 56, 145-157 (2007); doi: 10.1002/pi.2108

[3] [C.-S. Ha, J.A. Gardella, Jr., Surface chemistry of biodegradable polymers for drug delivery systems, *Chemical Reviews* 105, 4205-4232 (2005); doi: 10.1021/cr040419y

[4] W. Amass, A. Amass, B. Tighe, A review of biodegradable polymers: uses, current developments in the synthesis and characterization of biodegradable polyesters, blends of biodegradable polymers and recent advances in biodegradation studies, *Polymer International* 47, 89-144 (1998); doi: 10.1002/(SICI)1097-0126(1998100)47:2<89::AID-PI86>3.0.CO;2-F

[5] F. von Burkersroda, L. Schedl, A. Göpferich, Why degradable polymers undergo surface erosion or bulk erosion, *Biomaterials* 23, 4221-4231 (2002); doi: 10.1016/S0142-9612(02)00170-9

[6] K.A. Athanasiou, G.G. Niederauer, C. Agrawal, Sterilization, toxicity, biocompatibility and clinical applications of polylactic acid/ polyglycolic acid copolymers, *Biomaterials* 17, 93-102 (1996); doi: 10.1016/0142-9612(96)85754-1

[7] M.J. Schöning, A. Poghossian, BioFEDs (field-effect devices): State-of-the-art and new directions, *Electroanalysis* 18, 1893-1900 (2006); doi: 10.1002/elan.200603609

[8] J.R. Siqueira Jr., M.H. Abouzar, A. Poghossian, V. Zucolotto, O.N. Oliveira Jr., M.J. Schöning, Penicillin sensor based on a capacitive field-effect structure functionalized with a dendrimer/carbon nanotube multilayer, *Biosensors and Bioelectronics* 25, 497-501 (2009); doi: 10.1016/j.bios.2009.07.007

[9] A. Poghossian, S. Ingebrandt, A. Offenhäusser, M.J. Schöning, Field-effect devices for detecting cellular signals, *Seminars in Cell and Developmental Biology* 20, 41-48 (2009); doi: 10.1016/j.semcdb.2009.01.014

[10] Yu. Mourzina, Th. Mai, A. Poghossian, Yu. Ermolenko, T. Yoshinobu, Yu. Vlasov, H. Iwasaki, M.J. Schöning, K+-selective field-effect sensors as transducers for bioelectronic applications, *Electrochimica Acta* 48, 3333-3339 (2003); doi: 10.1016/S0013-4686(03)00402-X

[11] A. Poghossian, D.-T. Mai, Yu. Mourzina, M.J. Schöning, Impedance effect of an ion-sensitive mambrane : characterisation of an EMIS sensor by impedance spectroscopy, capacitance-voltage and constant-capacitance method, *Sensors and Actuators B* 103, 423-428 (2004); doi: 10.1016/j.snb.2004.04.071