Valérie Kodeck[1], Karolien Gellynck[2], Ken Kersemans[3], Heidi Declercq[2], Sandra Van Vlierberghe[1], Filip De Vos[3], Maria Cornelissen[2] and Peter Dubruel[1]

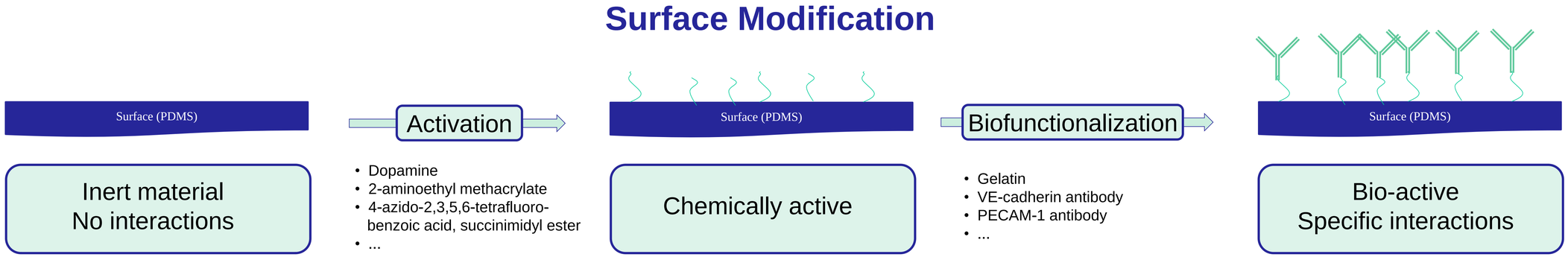
[1]*Polymer Chemistry & Biomaterials Research Group, Department of Organic Chemistry, Ghent University, Krijgslaan 281 S4bis, Ghent, Belgium*
[2]*Department of Basic Medical Sciences, Ghent University, De Pintelaan 185 6B3, Ghent, Belgium*
[3]*Department of Pharmaceutical Analysis, Ghent University, Harelbekestraat 72, Ghent, Belgium*

Functionalization of PDMS to serve as biocompatible packaging material

Introduction

In the present work, polydimethylsiloxane (i.e. PDMS) is applied as a packaging material for the development of an implantable, continuous optical glucose sensor. PDMS is an excellent candidate material since it is transparent in the near-IR region used for glucose monitoring. In addition, PDMS has previously been successfully used as a biomaterial inside the human body [1]. In order to facilitate glucose measurements, the possibility of stimulating angiogenesis close to the implant was investigated by adhering an endothelial promoting antibody (VE-cadherin) to the surface of the implant. To this end, various surface modifications and strategies were characterized and evaluated both *in vitro* as well as *in vivo* to fine-tune the biological response of the implant.

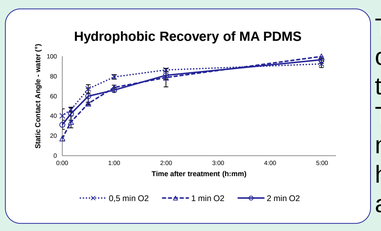
Surface Modification



Surface Characterization

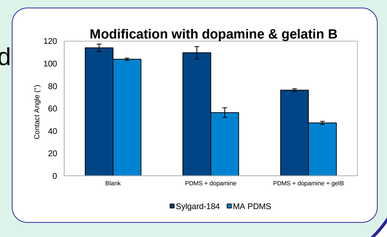
Static Contact Angle Measurements

For all surface modifications, the first characterization is to study the behavior of a droplet of water deposited on the surface. This technique studies the surface wettability.



The hydrophobic recovery of PDMS after plasma treatment was analyzed . The results indicate that the material regains its hydrophobic character after a few hours.

Static contact angles were also determined before and after surface modification. By analyzing the contact angle on different places, the homogeneity of the layer can also be determined.

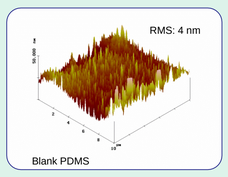


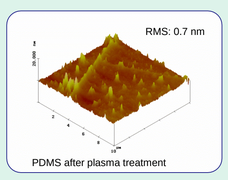
Atomic Force Microscopy

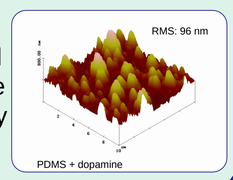
The morphology and roughness of the surface can be analyzed by AFM.

Figures on the right show that after plasma treatment, any unevenness on the blank PDMS surface is etched away. This shows that next to introducing functional groups, the plasma treatment also serves as a cleaning step before further modification takes place.

After the dopamine layer is deposited, the surface roughness increases drastically, compared to both blank and plasma treated samples, confirming the presence of the layer. The homogeneity of the layer can also be determined.







X-ray Photoelectron Spectroscopy

By analyzing the chemical composition of the surface, the presence of a different surface top layer can be confirmed. When this measurement is performed in different locations, the homogeneity of the layer can also be determined.

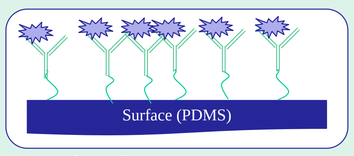
	%Si	%C	%O	%N
Sylgard-184	26 ± 0.5	47 ± 0.8	27 ± 1.1	
Sylgard-184 + dopamine	18 ± 1.7	53 ± 1.3	27 ± 0.8	2 ± 0.4
Sylgard-184 + dopamine + gel B	20 ± 0.6	50 ± 0.4	27 ± 0.2	3 ± 0.1

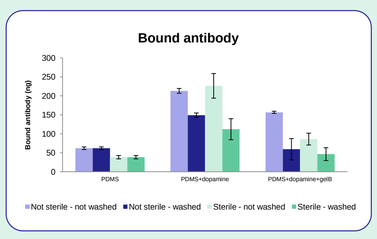
	%Si	%C	%O	%N
MA PDMS	20 ± 1.4	55 ± 0.6	25 ± 1.4	
MA PDMS+ dopamine	18 ± 1.7	56 ± 1.2	24 ± 1.1	1 ± 0.3
MA PDMS + dopamine + gel B	8 ± 0.6	62 ± 0.4	22 ± 0.1	8 ± 0.2

After the surface modification with dopamine, a clear but small N-signal is detected. The subsequent modification with gelatin B results in an increasing N-signal, as anticipated since gelatin B contains a larger number of N-atoms than dopamine.

Radiolabelling

When coupling an antibody (VE-cadherin) to a modified PDMS surface, the amount of bound antibody can be quantified by radiolabelling. Before depositing the antibody, it is labeled with an isotope (^{125}I) via tyrosine and/or histidine sequences present on the antibody.

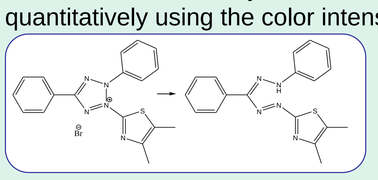




After incubation in the VE-cadherin solution, the γ-radiation emitted from the material surface can be detected and quantified by a Geiger-Müller counter. The deposition of antibody was investigated on several different surface modifications. In addition, the influence of an additional washing step and sterilization was determined.

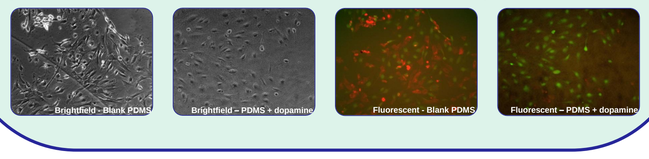
In vitro Assays

The toxicity of PDMS to cells was evaluated using an MTT-assay. The material was incubated in cell medium, creating an extract, which was later added to a human foreskin fibroblast culture. Enzymatic cell activity was then measured quantitatively using the color intensity of the formed formazan.



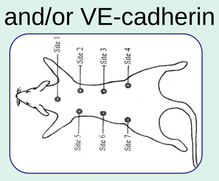
The cell viability for PDMS materials was higher than 80%, indicating PDMS is not cytotoxic.

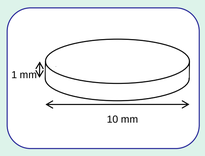
A co-culture of human foreskin fibroblasts (HFF) and human umbilical vein endothelial cells (HUVEC) was stained (red and green respectively) on different surfaces coated with VE-cadherin. The images below clearly show that HUVECs grow preferentially on PDMS coated with dopamine.



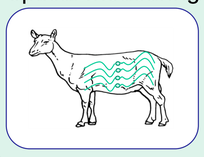
In vivo Assays

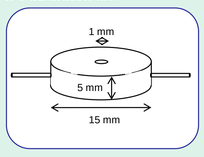
To ascertain the effect of PDMS and its modifications on the body, several *in vivo* studies were performed.
In rats, PDMS coins modified with dopamine, gelatin B and/or VE-cadherin were evaluated.





Some selected modifications were also evaluated in goats. As PDMS will serve as packaging material for an optical sensor, it was used to embed optical fibers. Using this approach both the biocompatibility as well as the *in vivo* optical measuring capabilities could be evaluated.





Conclusion

A PDMS material was developed to function as a packaging material for an implantable continuous optical glucose sensor. Diverse surface modification strategies were investigated and evaluated via *in vitro* and *in vivo* biological assays. The embedding of the sensor was also evaluated via *in vivo* optical measurements. All results indicated that the material is suitable to be applied as packaging material for a glucose sensor.

References

1. Chen, H. et al, *Biocompatible polymer materials: Role of protein-surface interactions,* Progress in Polymer Science, 2008, 33, p1059-1087

Acknowledgement

The authors would like to thank the IWT for the financial support of the SBO proposal GLUCOSENS (2009-2013).