

PAPER • OPEN ACCESS

Dextran as a fast resorbable and mechanically stiff coating for flexible neural probes

To cite this article: D Kil *et al* 2017 *J. Phys.: Conf. Ser.* **922** 012016

View the [article online](#) for updates and enhancements.

You may also like

- [Production of Dextran from Domestic *Weissella cibaria* Isolated](#)
Saad Shalawy Suheil and Asmaa Sabah Ahmaed
- [Upconverting crystal/dextran-g-DOPE with high fluorescence stability for simultaneous photodynamic therapy and cell imaging](#)
HanJie Wang, Sheng Wang, Zhongyun Liu et al.
- [Synthesis and characterization of Bombesin-superparamagnetic iron oxide nanoparticles as a targeted contrast agent for imaging of breast cancer using MRI](#)
Atefeh Jafari, Mojtaba Salouti, Saber Farjami Shayesteh et al.

ECS
The
Electrochemical
Society
Advancing solid state &
electrochemical science & technology

DISCOVER
how sustainability
intersects with
electrochemistry & solid
state science research

Dextran as a fast resorbable and mechanically stiff coating for flexible neural probes

D Kil, L Brancato and R Puers

KU Leuven dept. ESAT-MICAS, Kasteelpark Arenberg 10, 3001 Leuven, Belgium

Abstract. In this paper we report on the use of dextran as a temporary, fast dissolving stiff coating for flexible neural probes. Although polymer-based neural implants offer several advantages, compared to their rigid silicon counterparts, they pose significant challenges during implantation. Due to their extreme flexibility, they have the tendency to buckle under the axial load applied during insertion. The structural stiffness of the implants can be temporarily increased by applying a bioresorbable dextran coating which eases the penetration of neural tissue. For this application three types of dextran with different molecular weights are analysed. The dissolution rate of the coatings is reported as well as the increased bending stiffness resulting from the dextran coating of Parylene C neural probes. Based on these findings the dissolution rate can be linked to parameters such as molecular weight, coating thickness and the surface area exposed to the dissolution medium. The mechanical characterization yields information on how the structural stiffness of neural probes can be tuned by varying the dextran's molecular weight and coating thickness.

1. Introduction

It is generally known that in the field of neural engineering there is a trend towards the use of flexible polymers as the structural material for neural probes [1]. When neural implants are made out of hard, stiff materials such as silicon [2] these have the tendency to move around under influence of, among others, blood being pumped through the arteries in the brain. These micromotions of the electrode relative to the brain result in a chronic inflammation of the tissue surrounding the implant, which in turn leads to glial scar formation [3]. The dense scar tissue formed around the electrodes effectively isolates them from any surrounding active neurons, interfering with recording or stimulation and rendering the implant useless after a relatively short period of time [4]. This problem can be partially solved by using polymeric materials such as parylene [5] and polyimide [6] which reduce the mechanical mismatch with the surrounding brain tissue and deform as the tissue moves. The downside of this approach is that these thin polymer implants are too flexible to be able to penetrate the neural tissue without buckling.

A frequently used solution is the use of a stiff backbone structure. Examples include stiff backbone layers [7], insertion shuttles [8] and biodegradable coatings [9]. Although these options temporarily increase the structural stiffness of the implant they do come with drawbacks. The stiff backbone layer is intended to remain permanently attached to the implant, it significantly reduces its innate flexibility. Insertion shuttles on the other hand temporarily increase the footprint of the implant, resulting in unnecessary damage to the neural tissue during implantation. The least invasive solution is to temporarily package the implant using a bioresorbable coating such as silk [10] or PEG [11] which stiffens it enough to be implanted. Afterwards the coating dissolves, allowing the implant to regain its



flexibility. A downside to this technique, which should be kept in mind, is that in most cases the coating dissolves so rapidly that there is only one opportunity for implantation.

In this paper, we research the use of dextran for this purpose. Apart from its use in medicine as an antithrombic or volume expander for hypovolaemia [12] it also has excellent functionality as a temporary coating for neural probes. Dextran not only limits non-specific cell adhesion [13] but as it is a complex branched glucan its dissolution rate and mechanical stiffness can be tuned by varying the chain length of the molecule.

Compared to the materials mentioned above, comparable data on the use of dextran as a coating material is not readily available in literature. This work tries to fill that gap and presents an extensive characterization of dextran as a suitable material for this purpose. Ultimately the goal of this paper is to act as a reference guide containing information on how the parameters mentioned above relate to the mechanical stiffness and dissolution rate, allowing the reader to tune his dextran coating to application specific needs, albeit dissolution time or structural stiffness.

2. Experimental details

2.1 Density measurement

Dextran slabs were prepared by dissolving the powder in de-ionized water, creating a highly viscous solution (50 wt%). The mixture was stirred under vacuum to remove any airbubbles. After degassing, the solution was poured into a teflon mould and allowed to dry at low temperature (50°C). When all the water evaporated the dextran slabs were demoulded and weighed.

The volume of the dextran slabs was determined using a water displacement experiment. The samples were immersed in water in a graduated cylinder, and their volume was estimated measuring the increase in the water level. The average density is calculated and summarized in table 1. This experiment was repeated to determine the density of 3 types of dextran with varying molecular weights: 40 kDa, 100 kDa and 500 kDa.

Table 1. Average density of different types of dextran.

Dextran molecular weight (kDa)	40	100	500
Average density (g/mm ³)	2.5E(-3)	2.3E(-3)	1.4E(-3)

2.2 Dextran dissolution rate

Dextran slabs were prepared in a square stainless steel mould as described in section 2.1. After drying, the samples were weighed and submerged in deionized water for a known amount of time. At regular time intervals the samples were removed from the container, allowed to dry, and weighed. This provided an indication on the quantity of dextran dissolved over time. The dextran slabs were submerged while still in the mould in order to keep the surface area exposed to the dissolution medium constant in time, which results in a more accurate representation of the dissolution rate. This experiment was also repeated for the different types of dextran with varying molecular weights.

2.3 Micromechanical testing

In order to quantify the influence of the dextran coating on the mechanical properties of the implants, a set of dummy Parylene C shanks was fabricated and coated using a dipcoating process. The thickness of the dextran coating was measured using a digital micrometer.

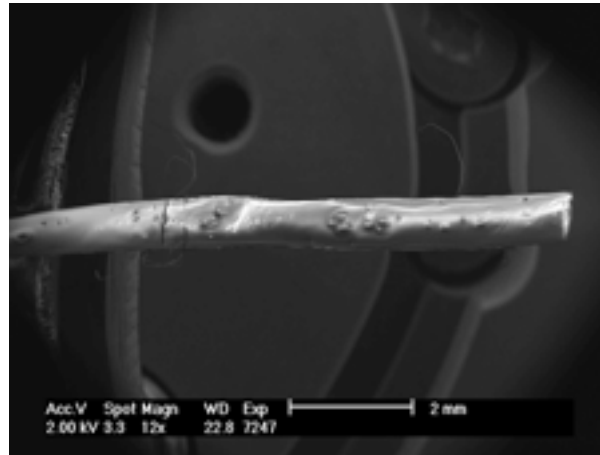


Figure 1. Electron micrograph of a dextran coated Parylene C shank.

The samples were glued to an aluminum oxide substrate, leaving a known part the shank sticking out over the edge. A Femtotools FTA-M02 micromechanical testing system was used to displace the freestanding part of shank. Force measurements were taken during this displacement and used to determine the bending stiffness of the samples. The out-of-plane bending mimics the forces that the shank undergoes during implantation. The Young's modulus E of the samples approximated using the formula for bending of a beam under a point load:

$$E = \frac{k \cdot L^3}{3 \cdot I} \quad (1)$$

With I the area moment of inertia:

$$I = \frac{w \cdot h^3}{12} \quad (2)$$

In these formulas, L represents the distance between the hinging point and the contact point of the indenter tip, w is the measured width of the sample and h is the sample thickness.

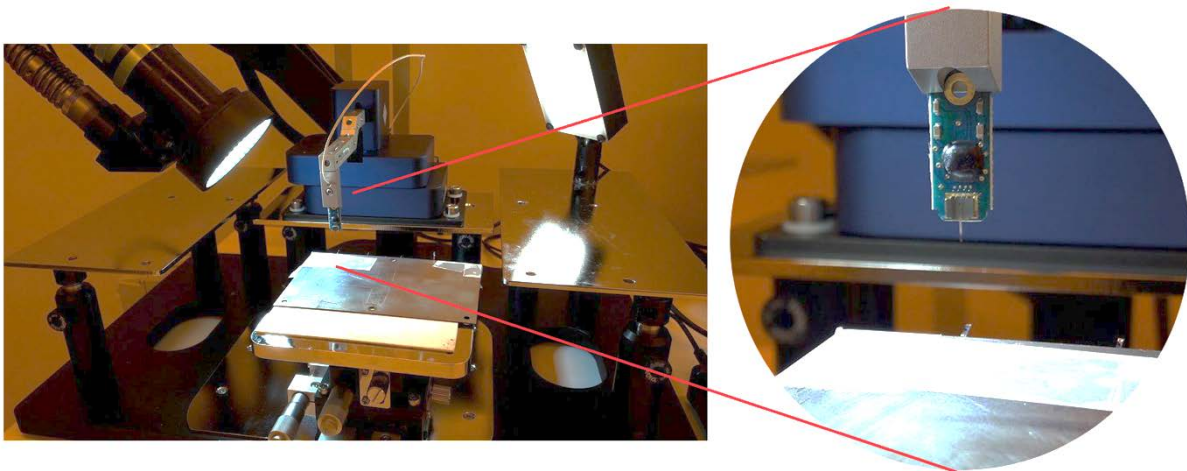


Figure 2. Test setup for measuring bending stiffness using the Femtotools FTA-M02 micromechanical testing system. Close-up shows the vertical indenter probe with integrated force sensor.

3. Results and Discussion

3.1 Dextran dissolution rate

The results of the dissolution experiment are depicted in fig. 3. It is clearly visible that the higher the molecular weight of the dextran, the lower the weight loss over time is. This indicates a strong dependency between dissolution rate and molecular chain length which can be explained by the physical mechanism of sugar dissolution in water.

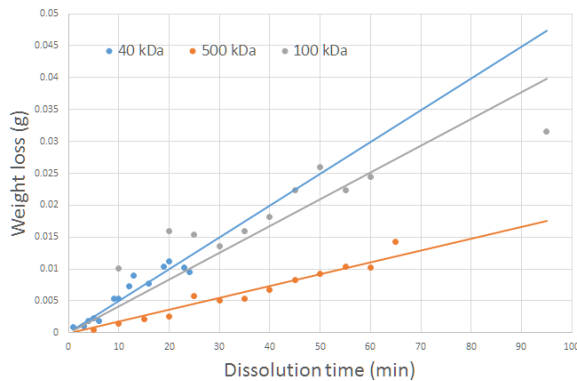


Figure 3. Dextran dissolution rate under influence of molecular weight.

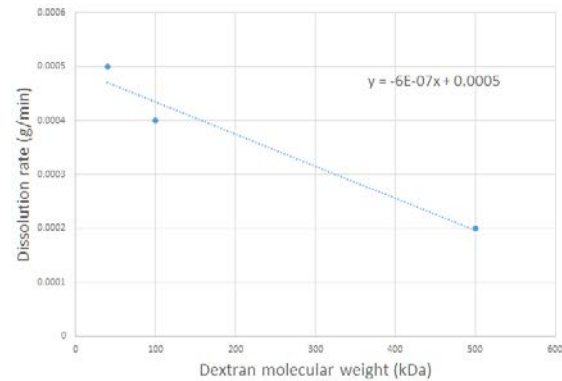


Figure 4. Dextran dissolution rate in function of molecular weight.

Sugar molecules contain a high number of polar oxygen-hydrogen bonds, which have a permanent dipole moment. In the solid crystal structure itself a number of these molecules are held together by weak intermolecular Vanderwaals-forces. When the sugar crystal comes into contact with water, the polar bonds of the water molecules form their own dipole-dipole bonds with the sugar molecules, which are stronger, causing them to separate and bond to the water molecules.

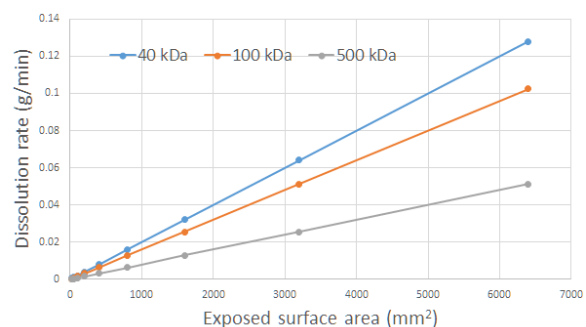
The longer the molecule chain is, the more difficult it is for the water molecules to form dipole-dipole interactions with the functional groups of the sugar. As the folded molecules are much bigger, the surface area of the molecule exposed to the solute is relatively small compared to its size. This effect increases exponentially with the molecular weight and thus the dissolution rate will drop decrease as the molecular weight of the sugar increases. This physical dissolution process offers us the opportunity to tune the dissolution rate of our resorbable coating by varying the molecular weight of the dextran as is shown in figure 4.

It is important to note that these 3 types of dextran can only be compared because the surface area exposed to the dissolution medium was kept constant during the whole experiment. If the surface area is increased, more dextran molecules would come into contact with the medium, increasing the rate at which the coating dissolves. This linear relationship is depicted in figure 5.

Table 2. Average dissolution rate of dextran with varying molecular weights.

Molecular weight (kDa)	40	100	500
Average dissolution rate (mg/min*mm ²)	0.02	0.016	0.008

Figure 5. Dextran dissolution rate in function of the surface area exposed to the dissolution



As the dissolution mechanism is considered as a ‘layer-by-layer’ process the thickness of the coating has no influence on the dissolution rate. As we now have information on all the factors influencing the dissolution time of a dextran coating a formula is presented based on which the dissolution time of an arbitrary dextran coating can be calculated.

$$\text{dissolution time} = \frac{\text{density} \times \text{coating volume}}{\text{dissolution rate} \times \text{surface area}} \quad (3)$$

The density of the coating is dependent on the molecular weight of the used dextran and can be interpolated from the data presented in table 1. The volume of the coating can be measured and the dissolution rate can be deduced from figures 4 and 5, knowing the molecular weight of the used dextran and the surface area exposed to the dissolution medium.

3.2 Micromechanical testing

Measurements were taken of samples coated with the different types of dextran as described in section 2.3 and are summarized in table 3. The thickness measurements are also reported on the graph. The average width of the coating layer was 641 μm . Micromechanical testing revealed an average bending stiffness of 0.029 N.m^{-1} for the uncoated implants. Coating increased this average bending stiffness 361 fold to 10.5 N.m^{-1} . The Young’s modulus of coated sample was measured to be only 0.6 GPa, proving that the enhanced structural stiffness can be mainly attributed to the thickness of the coating and not to the molecular weight of the used dextran.

Table 3. Results of mechanical measurements

	Mean	Standard deviation
Coating thickness (μm)	163	21
Bending stiffness(N.m^{-1}) uncoated	0.029	0.005
Bending stiffness(N.m^{-1}) coated	10.5	5.5
Young’s Modulus Parylene C (Gpa)	2.8	0.4
Young’s Modulus dextran (Gpa)	0.6	0.1

4. Conclusion

By analysing the dissolution rate and mechanical properties of different types of dextran, its use as a biocompatible, stiff and fast resorbable coating for neural implants was proven. A dissolution experiment was performed to determine the dissolution rate of the coatings obtained from dextran’s with three different molecular weights. The results showed a linear dependency of the dissolution rate from the molecular weight. The dissolution rate is influenced from the surface area exposed to the dissolution medium. The enhanced structural stiffness resulting from dextran coating of neural probes was investigated using a Femtotoools micromechanical testing system. Results showed a 361-fold increase in bending stiffness compared to an uncoated Parylene C probe. Finally, a formula is presented which relates all influencing parameters and allows to tune the dissolution time and mechanical properties of dextran coatings.

Acknowledgements

The research leading to these results has received funding from the European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013) / ERC grant agreement n° 340931, and the KU Leuven IDO program, project on electrical brain stimulation IDO/12/024.

References

- [1] Weltman A, Yoo J and Meng E 2016 Flexible, penetrating brain brobes enabled by advances in polymer microfabrication *Micromachines* **7** 180
- [2] Yoon T H, Hwang E J, Shin D Y, Park S I, Oh S J, Jung S C, Shin H C and Kim S J 2000 A micromachined silicon depth probe for multichannel neural recording *IEEE Trans. Biomed. Eng.* **47**, 1082–7
- [3] Biran R, Martin D C and Tresco P A 2007 The brain tissue response to implanted silicon microelectrode arrays is increased when the device is tethered to the skull *J. Biomed. Mater. Res.* **82** 169–78
- [4] Turner J N, Shain W, Szarowski D H, Andersen M, Martins S, Isaacson M and Craighead H 1999 Cerebral astrocyte response to micromachined silicon implants *Exp. Neurol.* **156** 33–49
- [5] Takeuchi S, Suzuki T, Mabuchi K and Fujita H 2004 3D flexible multichannel neural probe array *J. Micromech. Microeng.* **14** 104–7
- [6] Fomani A A and Mansour R R 2011 Fabrication and characterization of the flexible neural microprobes with improved structural design *Sensors Actuators A* **168** 233–41
- [7] Lee K, He J, Singh A, Massia S, Ehteshami G, Kim B and Raupp G 2004 Polyimide-based intracortical neural implant with improved structural stiffness *J. Micromech. Microeng.* **14** 32–37
- [8] Kozai T D Y and Kipke D R 2009 Insertion shuttle with carboxyl terminated self-assembled monolayer coatings for implanting flexible polymer neural probes in the brain *J. Neurosci. Methods* **184** 199–205
- [9] Li W, Rodger D C, Pinto A, Meng E, Weiland J D, Humayun M S and Tai Y C 2011 Parylene based integrated wireless single channel neurostimulator *Sensors Actuators A* **166** 193–200
- [10] Tien L W, Wu F, Tang-Schomer M D, Yoon E, Omenetto F G and Kaplan D L 2013 Silk as a multifunctional biomaterial substrate for reduced glial scarring around brain-penetrating electrodes *Adv. Funct. Mater.* **23** 3185–93
- [11] Chen C-H, Chuang S-C, Su H-C, Hsu W-L, Yew T-R, Chang Y-C, Yeh S-R and Yao D-J 2011 A three-dimensional flexible microprobe array for neural recording assembled through electrostatic actuation *Lab Chip* **11** 1647–55
- [12] Jones C, Payne D, Hayes P, Naylor R, Bell P, Thompson M and Goodall, A 2008 The antithrombotic effect of dextran-40 is due to enhanced fibrinolysis in vivo *Journal of Vascular Surgery* **48** 715–22
- [13] Massia S P, Stark J and Letbetter D S 2000 Surface-immobilized dextran limits cell adhesion and spreading *Biomaterials* **21** 2253–61