Suitability of SU-8, EpoClad and EpoCore for flexible waveguides on implantable neural probes

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***Abstract*—In neuroscience optogenetics was established as common research method. However, the devices used for optogenetical stimulation, so called optrodes, are often made of stiff materials which lead to cell damage. We investigated the suitability of the epoxy based polymers SU-8, EpoClad and EpoCore for the fabrication of bendable thin-film waveguides. With the integration of such waveguides into neural electrodes flexible optrodes could be realized which would allow simultaneous stimulation at different sites. Three different waveguide types were fabricated with SU-8 and EpoClad as cladding and EpoCore as core materials. The optical losses were measured from 12.9 dB (SU-8 and air cladding) over 14.4 dB (SU-8 cladding) to 22.4 dB (EpoClad cladding). Aging in air at 23 °C for a time period of 80 days led to a continuous increase of the losses, which seemed to adapt to an upper limit of over 20 dB. Samples aged in saline solution at 37 °C showed a faster increase in the first 20 days, but a similar upper limit.**

I. Introduction

In the last decade optogenetics became a popular research method for neuroscientists. The possibility to excite and inhibit specific cell types with light in very precise time scales makes optogenetical stimulation advantageous over the popular electrical stimulation and pharmacological manipulation [1]. However the devices, which are commonly used for optogenetical stimulation and simultaneous recording of the action potentials, so called optrodes, usually do not meet all requirements. For acute experiments neuroscientists often use self-made optrodes, where glass fibers are simply attached, mostly glued, to a tungsten wire [2, 3]. More effort has been made for chronic applications. Here, glass fibers were prepared with ferrules and then glued to electrode arrays [4–6]. Thereby, the implanted arrays can be plugged to the external stimulating devices only during experiment performance, allowing the animals to move freely during the rest of the time. Until now most of the optrodes are mechanically stiff, as they have to withstand the forces during insertion through the pia mater in the brain. However once implanted, stiff electrodes often lead to tissue damage. This is especially critical when not only one but a complete array of shaft electrodes is to be inserted in the cortex. To minimize chronic damage flexible devices are preferable. These would also allow an adaption to the curvature of the biological texture for surface electrodes like ECoG-arrays.

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Approaches of combining microscale light-emitting diodes (µLED) with flexible electrodes were realized [7, 8]. Besides flexibility such devices have the further advantage to simultaneously stimulate at different sites. However in vivo long-term stability of these optrodes is not yet proven, although, depending on the application, this can be an indispensable requirement.

With the integration of waveguides in flexible nerve electrodes the advantage of simultaneous stimulation at different sites would be given as well. Furthermore packaging problems of electrical components, like µLEDs, could be avoided with waveguides leading directly to the stimulation sites. The list of requirements on materials used for the realization of such waveguides, however, is long: Adjusted refractive indexes of the core and cladding materials, biocompatibility, long-term in vivo functionality and the ability of integration in flexible nerve electrodes (concerning adhesion as well as process integration) are only some of them. We investigated the suitability of the epoxy based polymers SU-8, EpoClad and EpoCore for the realization of such waveguides as we suspected that they might have the potential to fulfill at least some of these requirements.

II. Materials and Methods

EpoClad, EpoCore (micro resist technology GmbH, Berlin, Germany) and SU-8 (MicroChem Corp., Newton, US-MA) are epoxy based negative tone photoresists for micro systems technology. Like the names may suggest, EpoClad and EpoCore are specifically designed for optical applications, having adjusted refractive indexes to serve as cladding and core materials for optical waveguides. We used EpoClad_20 and EpoCore_20 to get thicknesses in the range of 20 µm. Datasheets promise high transparency to visible light and with the indicated Cauchy coefficients their refractive indexes at a wavelength of 477 nm could be determined to 1.609 (EpoClad) and 1.619 (EpoCore), respectively.

SU-8 3025 was also used as cladding material. Its refractive index at a wavelength of 477 nm is 1.588 (according to the Cauchy coefficients of the datasheet). SU-8 used as substrate material is normally stiff and brittle. Nevertheless with careful adaption of the process parameters it is also possible to fabricate freestanding bendable structures, like cantilevers [9]. Slow temperature changes during the diverse bake steps are required.

SU-8 has already been under investigation concerning its biocompatibility [10] whereas no data could be found for EpoClad and EpoCore. This is why it was tested if for the cladding, which would be in direct contact with the tissue, the EpoClad could be replaced by SU-8.

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A. Fabrication of waveguides

Simple multimode slab waveguides were fabricated, showing core dimensions of 100 µm width and approximately 20 µm height and lengths between 10 and 15 mm.

Three different waveguide variations were processed, type 1, type 2 and type 3. For type 1 samples SU-8 3025 was used as lower cladding material but no upper cladding was deposited on the core. The waveguides of type 2 were processed with upper and lower claddings of SU-8 3025 and those of type 3 with upper and lower claddings of EpoClad_20. For all types the core consisted of EpoCore_20. The cores of type 2 and type 3 overlapped the upper cladding by 10 µm to make light coupling easier.

The different samples were fabricated as follows: First a sacrificial layer of 300 nm SiO_2 was deposited (PECVD, PC310 reactor by SPS Process Technology Systems Inc, San Jose, CA USA) on a 4" Si wafer. 4 ml of SU-8 3025 (type 1 and 2) and EpoClad_20 respectively (type 3) were spin coated (30 s @ 3000 rpm). After a repose of 10 min a soft bake (SB) was performed (type 1 and 2: 3 min @ 65 °C and 20 min @ 95 °C; type 3: 5 min @ 50 °C, 5 min @ 90 °C and 10 min @ 120 °C). The wafers were exposed via a chrome-on-glass mask with a mask aligner (MA/BA6, SÜSS MicroTec, Garching, Germany) with i-line filter (365 nm, type 1 and type 2:160 mJ/cm²; type 3: 490 mJ/cm²). After a post exposure bake (PEB, type 1 and type 2: 2 min @ 65 °C and 3 min @ 95 °C; type 3: 5 min @ 50 °C and 10 min @ 110 °C) EpoCore_20 was spin coated on the wafers (4 ml, 30 s @ 3000 rpm). A SB (5 min @ 50 °C and 15 min @ 65 °C) was performed before exposure (350 mJ/cm²) via a chrome-on-glass mask. After the PEB (2 min @ 50 °C and 60 min @ 60 °C) the lower cladding (SU-8 and EpoClad respectively) was developed together with the core (6 min in mr-Dev 600) whereas the perimeters of the waveguides and the core structures were formed. The upper cladding was spin coated for type 2 and type 3 (30 s @ 3000 rpm) and a SB (type 2: 3 min @ 65 °C and 20 min @ 95 °C; type 3: 5 min @ 50 °C, 5 min @ 90 °C and 15 min @ 120 °C) was performed before exposure via the same mask as used for the lower cladding (365 nm, type 2:160 mJ/cm²; type 3: 490 mJ/cm²). After the PEB (type 2: 2 min @65 °C and 3 min @ 95 °C; type 3: 5 min @ 50 °C and 10 min @ 110 °C) and development (6 min in mr-Dev 600) a hard bake (HB) was performed for the wafers of type 3 (30 min @ 120 °C and 30 min @ 140 °C).

An etch bead removal (EBR) was necessary after the SB steps to avoid sticking of the wafers to the photo mask. Slow heating of less than 2 °C/min was applied during all bake steps (SB, PEB and HB). As final clean room step the SiO_2 sacrificial layer of the wafers was etched in hydrofluoric acid (1 % HF) and the relieved waveguides were rinsed in deionized water.

B. Loss measurement of waveguides

The waveguides were characterized with a laser (Argon-Ion Laser, BeamLok 2065-5S, Spectra-Physics, Mountain View, US-CA) and a photodiode (OSD60-5T Id, Centronic, Surrey, UK). Using a chuck with micrometer screws the samples were precisely aligned to the laser beam (wavelength of 476.5 nm) until this was coupled into the core. To determine the loss of the waveguides the power of the laser beam was measured once with (P_{out}) and once without (P_{in}) the waveguide in the beam. The measurement was performed over time with a frequency of 5 Hz and the mean value was determined. The read out of the photodiode was performed via computer with a LabView program (National Instruments, Austin, US-TX) and data was analyzed with the software Mathematica (Wolfram Research, Champaign, US-IL). The total loss in dB consisting of coupling loss due to reflections and scattering at the inlet and outlet of the waveguides as well as of losses inside the waveguides, like scattering, absorption and evanescent waves, was calculated with equation (1).

$$L = -10 * \log_{10} \frac{P_{out}}{P_{in}} \quad (1)$$

C. Comparison of different fabrication types

The losses of 16 different waveguide samples of each fabrication type were measured. The mean values of the three types were compared and tested for significance with Student's t-test.

D. Aging

Intended use of the waveguides are in vivo applications where the waveguides would be exposed to aqueous solutions. To simulate the influence of water and ions to the behavior of the waveguides one sample of type 1 and type 2 respectively was put in phosphor buffered saline solution (PBS) and stored at 37 °C. The losses were measured before PBS-storage and after approximately 8, 40 and 70 days in PBS. For comparison two further samples (one of type 1 and one of type 2) were stored under normal conditions in air at 23 °C. The samples were investigated over a time period of 79 days while their losses were measured approximately every ten days.

III. RESULTS

With all three fabrication types bendable waveguides could be fabricated which successfully guided the coupled laser light. However waveguides of type 3 did not perform as good as the others.

A. Fabrication

The thicknesses of the SU-8 layers were in the range of 30 µm and those of EpoClad and EpoCore in the range of 20 µm. A problem was posed during fabrication of type 3 waveguides: The 10 µm long core-inlets of the waveguides often were covered with a very thin layer of the upper cladding. Variations in exposure time, bake parameters and development time did not affect this phenomenon.

B. *Loss measurement*

Coupling of the laser light into the waveguides resulted to be very difficult and its success depended strongly on the quality of the inlet of the waveguides. Lots of waveguides of type 3 could not be characterized at all, as the inlets were covered by the upper cladding. Independent of the fabrication type the measurement of one and the same sample varied with the inlet of the waveguide (left or right) used for coupling the laser beam. The influence of the coupling loss on the total measured loss was that big that no influence of the waveguide lengths between 10 mm and 15 mm could be observed. Therefore only the total optical loss (in dB) was considered and not the typically used loss over length (in dB/cm). Fig. 1 shows a waveguide sample where the light coupling worked well.

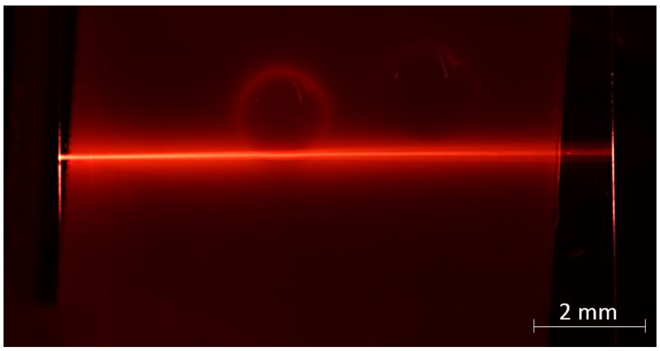

Fig. 1: Photo of a slab waveguide where light could be coupled successfully (The photo was taken with a filter, which why the blue laser beam appears red.).

C. *Comparison of waveguide types*

The three different fabrication types showed significant difference in their light coupling and guiding performance. In Fig. 2 the mean values of the measured losses of 16 samples of each fabrication type ranged from 12.9 dB (type 1) over 14.4 dB (type 2) to 22.4 dB (type 3).

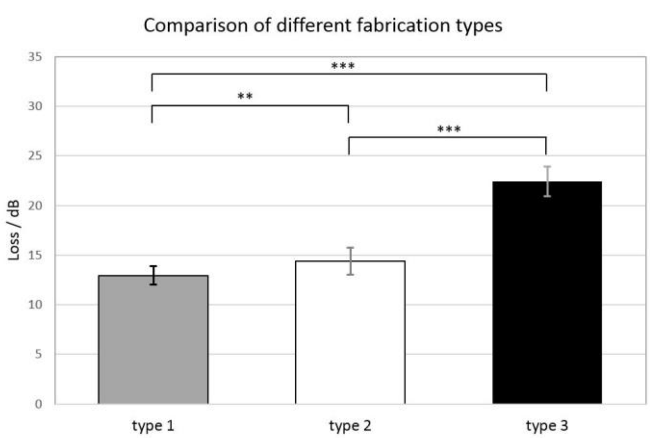

Fig. 2: Mean values of the measured light losses with standard deviations for the three fabrication types (with n = 16 for each): 12.9 ± 0.9 dB for type 1, 14.4 ± 1.3 dB for type 2 and 22.4 ± 1.5 dB for type 3. Mean values of type 1 and 2 differ significantly ($p = 0.05$, indicated by two stars) whereas the difference of type 1 and type 3 and type 2 and type 3, respectively, is highly significant ($p = 0.001$, indicated by three stars).

Differences were significant between type 1 and type 2 ($p = 0.05$) and highly significant between type 1 and type 3 and type 2 and type 3 ($p = 0.001$), respectively.

C. *Aging*

Aging in air as well as in saline solution led to an increase in light loss for all the investigated samples (Fig. 3). The samples (s1 and s2, type 2) were measured from both sides (except in the first two measurements of s1) what is indicated by the two bars of each sample in one time interval. From day 20 on the sample aged in air (s1) showed a continuous rise of loss from less than 15 dB up to over 20 dB, which seemed to adapt to an upper limit. The loss of the sample aged in PBS (s2) rose more quickly from less than 15 dB to over 18 dB in the first 20 days.

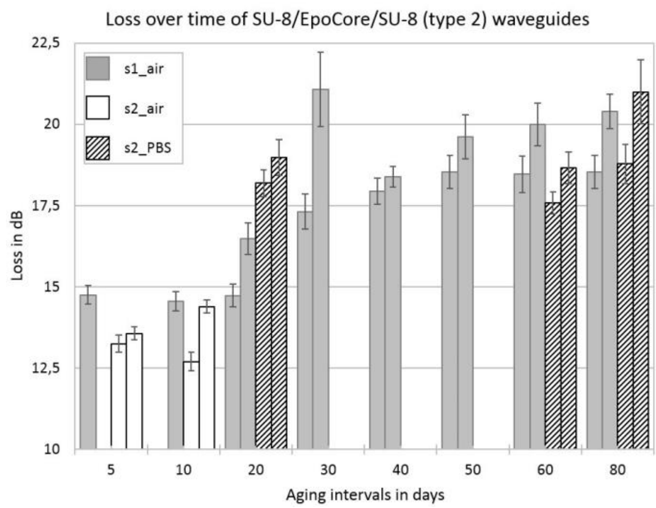

Fig. 3: Influence of aging in air and in PBS on two samples (s1 and s2) of fabrication type 2. The optical losses increase continuously over time. From day 20 on s1 increased from less than 15 dB to over 20 dB. In PBS the losses of s2 rose more quickly from less than 15 dB to over 18 dB in the first 20 days.

The samples of type 1 showed a similar behavior of increasing loss over time (tab. 1). However it is noticeable that during aging in PBS, the increase of the sample of type 1 (without upper cladding), was greater than that of the type 2-sample. It increased from 13.4 dB to 22.8 dB.

Tab. 1: All loss values measured for four aged samples (two of type 1 and two of type 2).

Aging / days	Losses / dB				Days in PBS	Losses / dB		
	Type 1		Type 2			Type 1 in PBS	Type 2 in PBS	
0-5			14.6 ± 0.3	14.8 ± 0.3	0	13.4 ± 0.2	13.3 ± 0.3	13.6 ± 0.2
5-10	12.5 ± 0.2	12.7 ± 0.2					12.7 ± 0.3	14.4 ± 0.2
20	11.8 ± 0.3	14.7 ± 0.3	14.7 ± 0.3	16.5 ± 0.5	8	18.8 ± 0.7	18.2 ± 0.4	19.0 ± 0.6
22	13.7 ± 0.2	15.1 ± 0.3						
27	13.9 ± 0.3	18.4 ± 0.6	17.3 ± 0.5	21.1 ± 1.2				
41	15.1 ± 0.3	19.0 ± 0.8	17.9 ± 0.4	18.4 ± 0.3				
43	14.7 ± 0.3	19.1 ± 0.5	18.5 ± 0.5	19.6 ± 0.7				
55			18.5 ± 0.6	20.0 ± 0.6	43	22.0 ± 1.0	17.6 ± 0.3	18.7 ± 0.5
79	16.8 ± 0.3	22.2 ± 1.2	18.5 ± 0.5	20.4 ± 0.5	67	22.8 ± 1.1	18.8 ± 0.6	21.0 ± 1.0

IV. Discussion and Conclusion

Even though EpoClad and EpoCore are sold for waveguide applications samples of type 3 showed the highest light losses and it is doubtful if they are also useful for implantable systems. The phenomenon of the slightly covered core inlets by the upper EpoClad layer is probably caused during its photolithographic exposure. Light reflections of the well guiding core structures may lead to illumination of the surrounding cladding where it normally should be protected by the photo mask. Further investigations with variations of process parameters have to be performed to check this hypotheses. However, with an increase of the core overlap (e.g. 100 µm instead of 10 µm) this problem could be avoided easily. Another reason for the different performance of the three waveguide types is their different numerical aperture (NA) at a wavelength of 477 nm. The gradient of the refractive indices between EpoCore and air is 0.619 (part of type 1), between EpoCore and SU-8 it's 0.316 (type 2 and part of type 1) and between EpoCore and EpoClad it's only 0.180 (type 3). Best combination for an implantable multimode waveguide would be a core of EpoCore with a complete cladding of SU-8 (type 2) to have a good coupling angle (better than type 3) and to protect the core from the harsh environment inside the body (better than type 1).

With the integration of such waveguides into neural probes, flexible optrodes could be realized. Very good coupling of light into the waveguides would have to be performed with e.g. glass fibers, laser diodes or vertical external cavity surface emitting lasers (VECSEL) which are fixed to a substrate and perfectly aligned to the waveguides to minimize further light losses of the system (Thicker core structures could improve the coupling quality, however the waveguides would lose their mechanical flexibility then.). It is believed that like this optrodes suitable for optogenetical applications could be realized, as the measured losses of the waveguides are in the same range like those of already successfully established optrodes [11], furthermore the core cross sections are more than 11 times smaller, leading to much higher power densities.

For chronic implantation the most critical aspect is certainly the aging behavior of the waveguides. As could be demonstrated, once exposed to saline solution, their light guiding quality is badly influenced (most probably due to water absorption). In addition during aging of the samples in PBS the suspicion arose that they lost their flexibility and became brittle. Therefore further long-term studies have to be performed and more detailed investigation is necessary where the influence of a hard bake should be considered as well.

SU-8, EpoClad and EpoCore for flexible waveguides on implantable neural probes bring along restrictions like missing knowledge of biocompatibility, at least for EpoClad and EpoCore, small core cross sections (thin layers are necessary to maintain flexibility), which increase the light coupling loss and uncertainty of long term stability for chronic applications. It is therefore doubtful if it is worth to spend further time in investigating these materials or if it would be better to concentrate on more promising materials, like for example medical grade silicone rubber.

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V. References

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