Design and microfabrication strategies for thin-film, flexible optical neural implant*

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***Abstract*— Advanced polymer science and design technologies are constantly evolving to meet ever-growing expectations for flexible optical MEMS. In this work, we present design and microfabrication considerations for designed flexible Polymeric Opto-Electro-Mechanical Systems (POEMS). The presented methods integrate waveguide fabrication and laser diode (LD) chip assembly with Lawrence Livermore National Laboratory's (LLNL's) flexible thin-film technology to enable LLNL's first neural optoelectrode that can deliver guided light for neural activation. We support our findings with electrical and optical bench verification tests, present thermal simulation models to analyze heat dissipation of laser light sources on polymer substrates and discuss potential modifications for next generation prototypes. This fully integrated approach will allow spatial precision, scalability and more particularly, longer lifetime, needed to enable chronic studies of brain activities.**

I. Introduction

The development of polymer micromachining technologies has enabled application of microelectromechanical systems (MEMS) in wider variety of applications, especially in the biomedical device industry. Softness and flexibility of polymers like polyimide, parylene and silicones allow for better mechanical match at device-tissue interface prolonging device lifetime in biological environments. In recent years, polymer chemistry and microfabrication advances have driven new application avenues and better device performance. Lawrence Livermore National Laboratory (LLNL) has developed a series of thin film polymer implants for research and clinical applications [1-5], including the first FDA-cleared retinal implant in the world [6]. The polyimide-based retinal implant has been implanted in human patients for over 10 years, demonstrating exceptionally long device lifetime for a microfabricated implant.

The potential to integrate optics with electronics is of a great advantage in biomedical instrumentation. In this work, we report on the integration of thin film polymer technology with microscale-optical elements enabling a Polymer based Opto-Electro-Mechanical Systems (POEMS) based neural implant. POEMS can enable higher performance, more compact and cheaper systems allowing selective sensing and actuation capabilities across many biomedical applications such as imaging and optogenetics. Optogenetics involves genetically engineering neurons to express proteins, called opsins, which are sensitive to incident light of specific light wavelength and can be used to activate or silence neurons. For freely moving animals, simultaneous optogenetic stimulation and recording of brain activity requires optoelectrodes that can generate a spatial and temporal pattern of light and detect electrical activity generated by manipulated neural networks. Previous optoelectrode designs, that assembled separate components for light emission and electrical sensing together, were physically large and bulky [7], [8] or not selective [9], [10] activating many unmonitored neurons. Light sources coupled to glass fibers were attached to commercial silicon recording probes [11] for stimulating more than one cell-type but required labor-intensive manual assembly resulting in large device size. More recent studies reported direct integration of LEDs on the probe shank [12], [13], making optoelectrodes fiber-free. But strong electromagnetic interference (EMI) coupling between stimulating and recording channels gives rise to stimulation-locked artifacts in neurophysiology that obscure neural activity near the stimulation site for tens or hundreds of milliseconds. EMI coupling between stimulating and recording channels was significantly reduced in follow up work [14] but local tissue heating remains a concern for implanted light sources. Gradient index lens (GRIN) coupled waveguides offered a multicolor, thermally safe and very low EMI design for multiple cell-type stimulation [15], [16]. All the above discussed optoelectrodes use silicon and its compounds for device fabrication. Silicon, a commonly used material for neural probes, is brittle with high Young's modulus (130-200 GPa) and can potentially cause more tissue damage compromising recording quality over time. Recent research studies have also reported polymer optoelectrodes [12], [17-21]. However, these either offer partially flexible device

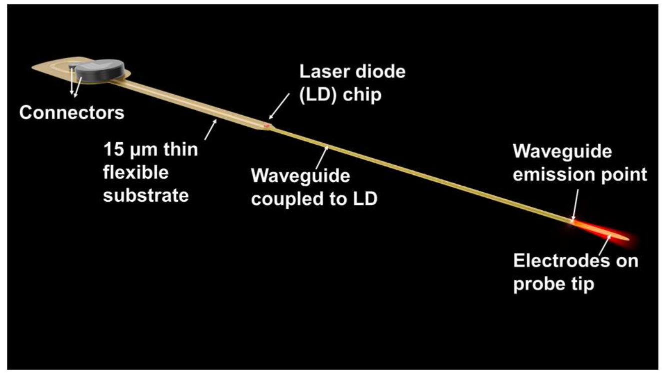

Figure 1. Schematic of a single shank all-polymer optoelectrode with flexible waveguide on probe shank butt-coupled to laser diode (LD) on probe backend.

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solutions [17-19], use low optical transmission materials like SU-8 [18], [20] or are susceptible to local heating [12], [21] and EMI [11], [17], [19].

In this work, we present a novel thin-film, all-polymer optoelectrode made of materials with Young's Modulus between 1-4 GPa (Fig. 1). We present thermal and electrical design advantages of our flexible optical neural implant with supporting data and discuss potential design improvements for future prototypes.

II. THIN-FILM NEURAL IMPLANT DESIGN

A. Device Fabrication

The fabrication process is based upon LLNL's thin film polymer device fabrication process flow [2] followed by precise and customizable flexible waveguide fabrication and laser diode (LD) chip assembly, all integrated onto a 15 µm thick neural probe (Fig. 2). The fabricated waveguide has a 10 µm-thick and 10 µm-wide polymer core made from two different materials with different refractive index (RI), EpoCore-5 (micro resist technology, Germany; RI = 1.55) or OrmoClearFX (micro resist technology, Germany; RI = 1.58) with a 2.5 µm-thick Cytop cladding (AGC Chemicals, Japan; RI=1.34), achieving an exceptionally high waveguide numerical aperture (NA) of between 0.77 to 0.83. The inherent stress of flexible polymers is not as high as semiconductor dielectric films and can be compensated by optimizing film thicknesses for core and cladding layers. An indium-gold eutectic pad was patterned as the anode pad for the laser chip [22] that is butt-coupled to the fabricated waveguide in the assembly step.

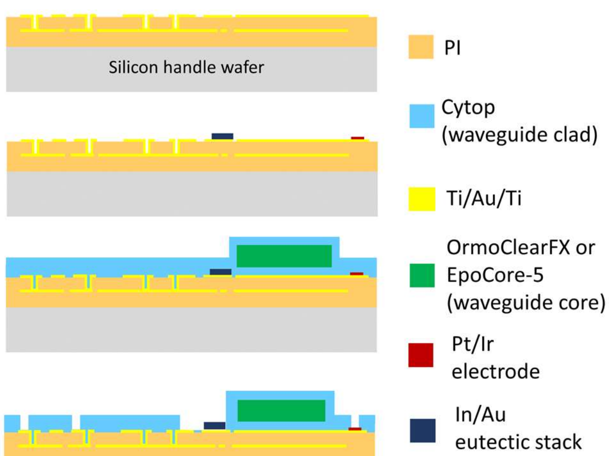


Figure 2. Process flow for optoelectrode fabrication.

Recent advances in nanoscience and polymer chemistry have led to the invention of polymers with superior properties and degradation resistance. EpoCore is an improved version of SU-8, a PMMA (Polymethyl methacrylate) based material, with easy microfabrication processability and better optical properties. OrmoClearFX is a hybrid (organic-inorganic) polymer made from Ormocers® [23] and exhibits high optical transmission and optical clarity in visible range (400-800 nm), which is not common for other microfabrication-friendly polymers. Cytop is an amorphous perfluoropolymer with high electrical resistivity, very low refractive index and high resistance to moisture absorption, making it a suitable material for electrical and optical insulation of optical bioMEMS.

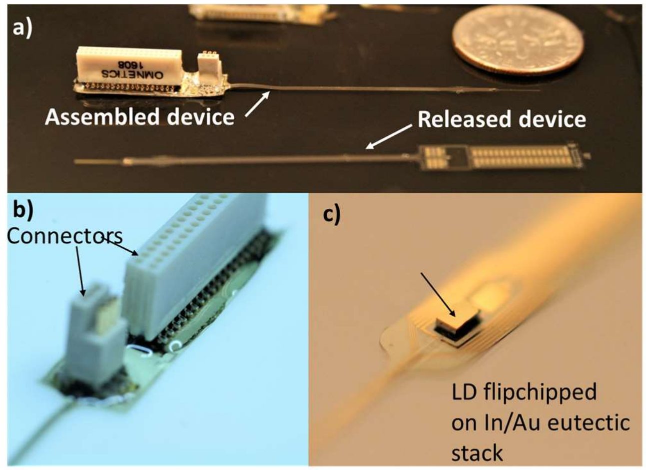


Figure 3. a) Assembled optoelectrode with flip-chipped b) connectors and c) laser diode (LD) bare die. All flip-chipped components are assembled directly on thin film substrates avoiding use of bulky PCBs.

B. Device assembly

Electrical connectors and LDs are assembled directly onto the thin-film polymer substrate without the need for conventional bulky Printed Circuit Boards (PCBs). Devices released as thin films serve as substrates for electrical connectors' and laser chip assembly. First, Omnetics connectors for driving laser diodes and for recording from electrodes (A79026-001 and A79607-001 respectively, Omnetics Connector Corporation, Minneapolis, MN, USA) are flip-chipped on Au bond pads patterned on thin film probes using conductive epoxy (Epo-Tek H2OE-FC, Epoxy Technology, Billerica, MA or Silver Paste Plus 05063-AB, SPI Supplies, West Chester, PA). All electrical connections are sealed in an insulating epoxy (Epo-Tek 301-2, Epoxy Technology, Billerica, MA). Next, 5 mW laser diode chips (U-CP-63051B3, Union Optronics Corp., Taiwan), 200 µm by 300 µm in size, are flip-chipped onto microfabricated In-Au anode pad (Fig. 3) and the diode's cathode is electrically connected to a nearby Au bond pad using conductive silver epoxy. The laser chip is assembled at the backend of the waveguide such that the emitted light is directed and focused into the distal end of the waveguide on the probe shank. All-optical coupling junctions can be secured with a drop of index-matching epoxy to reduce Fresnel losses at the interfaces. Laser diode-waveguide alignment is a critical step and must be optimized by precise definition of waveguide film etches during microfabrication and use of a sub-micron bonder tool (Lambda Flipchip bonder, Finetech, Germany).

The fully packaged device can be mounted on a silicon shuttle for insertion during tissue implantation [3], [5].

III. RESULTS AND DISCUSSION

B. Optical characterization

We measured the 635 nm diode's wall-plug efficiency as 6.8% (at threshold current ~ 20mA, 2.2V) and 5.3 % (at maximum operating current ~ 35mA, 2.3V) for packaged laser diodes (n=3). The waveguide transmission loss was calculated using direct cut-back method and measured as 7.6

dB/cm in EpoCore-5 and 4.8 dB/cm in OrmoClearFX for 10 x 10 µm waveguide cross-section. The power measured at waveguide output was 80-120 µW (at maximum LD efficiency) which translates to 800-1200 mW/mm^2 in intensity. Optogenetics experiments typically require 10 mW/mm^2 to activate opsins that respond in the higher end of visible wavelength spectrum. Future microfabrication and assembly modifications will focus on reducing coupling loss between the LD and waveguides in future prototypes.

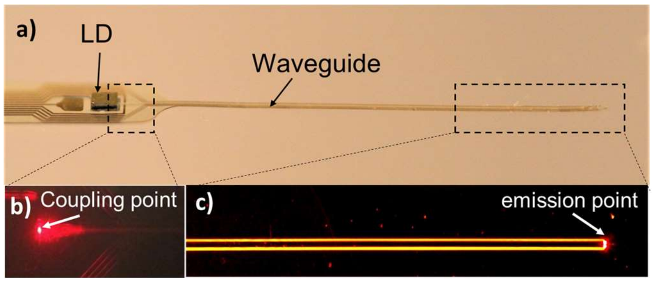
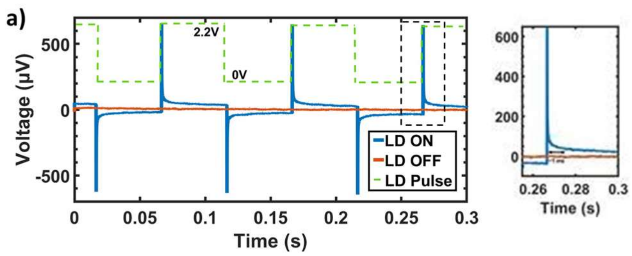


Figure 4. 635 nm bare die laser diode assembled on released thin film probe. a) Optical coupling junction between LD and waveguide. c) Light emission from 10 µm x 10 µm waveguide tip.

B. Electrical characterization

Impedance and electrical noise of recording channels were analyzed in 1x phosphate buffered saline (P0205, Teknova Inc, Hollister, CA) with an RHD2164 amplifier connected to an RHD2000 Evaluation System (Intan Technologies, Los Angeles, CA). The average impedance of 100 nm-thick Pt-Ir electrodes with 314 μm^2 recording area was recorded as 413 ± 54.6 kΩ (mean ± std. error) at 1 kHz (N=15 electrodes from 2 devices with one non responsive channel), which is adequate to record neural signals with good signal-to-noise ratio. The average baseline noise picked up by the recording channels in absence of light stimulation was 14.5 ± 2.4 µV (mean ± std. error) peak-to-peak.



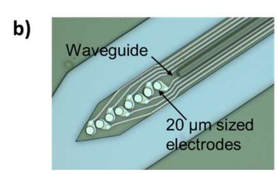


Figure 5. a) Baseline signal (red) and stimulation locked artifacts (blue) recorded on 100 nm Pt-Ir electrodes when laser diode current is off and on (dashed green, 20mA, 2.2V). Inset shows zoomed-in view of a transient peak with decay time. b) Electrodes at probe tip.

When trains of 635 nm light pulses (50 ms pulse width, 50% duty cycle, 20 mA, 2.2 V) were applied on the LD channels, voltage transients were picked up on the recording channels (Fig. 5). While these transients are smaller in magnitude than previously reported for un-shielded polymer optoelectrodes [21] or unshielded silicon optoelectrodes [13], [22]; shielding and grounding strategies will be implemented in future prototypes to further bring down the transient amplitude below 100 µV. Since polymer substrates are non-conductive unlike silicon substrates, they are the preferred substrate choice for low-noise systems in micro-/nano-scale optoelectronics but may require additional shielding.

C. Thermal considerations

Polymers are also good thermal insulators as compared to their silicon counterparts and this can be used to advantage for managing heat flow in optoelectrodes. If light sources are designed to be far away from the implantation site, as is possible in an implanted waveguide style probe, heat from light sources can be sufficiently managed to not flow from the source to the implant site.

We developed a heat transfer model (COMSOL Multiphysics, Burlington, MA) (Fig. 6) to simulate temperature rise of electro-optical components and the surrounding tissue around the optoelectrode. There are two requirements for optoelectrode thermal design. First, the temperature rise at the tissue should not fluctuate during device operation [24]. We defined the design threshold as a 1°C temperature rise from the baseline tissue temperature of 37 °C [22] [25]. Second, the temperature of the LD should be less than its thermal maximum (80 ºC) to prevent permanent

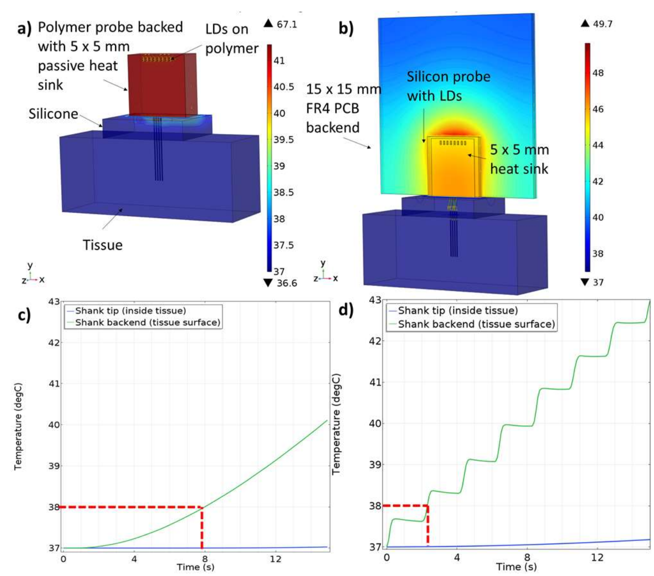


Figure 6. COMSOL heat transfer model for multi-shank optoelectrode. a) Polymer optoelectrode compared to b) silicon optoelectrode, shows surface temperature rise at device components and tissue surface when eight LDs are operated at 10% duty cycle power. c), d) Tissue temperature rise over time for models shown in (a, b) when total input electrical power delivered to the device is 80 mW/LD. Results show that 8 LDs can be operated for 8s and 2.5s before tissue temperature rises above 1°C for polymer and silicon optoelectrodes, respectively.

diode damage. System thermal efficiency is critical when scaling an optoelectrode system up to 8 or more independent sources for multi-shank probes. Assuming diode operation at maximum power rating of ~80 mW (~35 mA, 2.3 V), the simulation results indicate that 8 LDs flipchipped on a multi-shank design can operate continuously for 8 s (200 ms pulse width, 10% duty cycle), which is more than adequate for various optogenetic applications [11]. This will require use of a passive 5 x 5 mm conductive heat sink (aluminum) at the backend of the polymer probe. The results also show that our polymer optoelectrode with 5 x 5 mm heat sink increases continuous device operation time by at least 3 times as compared to a similar silicon optoelectrode connectorized on a 15 x 15 mm printed circuit board (PCB). Silicon based optoelecrodes show a fast, oscillatory temperature rise in tissue [22] whereas, polymer optoelectrodes exhibit slow and gradual temperature rise because of thermal insulation properties of polymers.

IV. CONCLUSION

We fabricated, assembled, and characterized LLNL's first thin film neural optoelectrode with EpoCore and OrmoClearFX waveguides butt-coupled to 635 nm bare die laser diodes. The optoelectrode offers a compact, thermally safe and flexible solution that can facilitate long term chronic brain studies. The designed waveguides with Cytop cladding offer minimal transmission loss between 4.8-7.6 dB/cm for 10 x 10 µm waveguide cross-section, the lowest reported value for polymer waveguides to our knowledge. Future studies will focus on optimizing LD hermetic sealing and implementing grounding and shielding techniques to reduce stimulation locked artifacts.

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