

# A Simple Model to Investigate the Stability of Flexible Micromachined Retina Stimulators

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## Introduction

More than one million persons are legally blind in the USA, Australia and Europe. Despite enormous efforts and advances in clinical treatment of eye diseases, there is no established method to prevent or cure degenerative processes in the eye, such as age related macula degeneration or retinitis pigmentosa. Since G.S. Brindley attached 80 electrodes to miniature radio receivers and implanted them in the visual cortex of a blind patient, several attempts have been undertaken to restore vision in blind patients with the means of a technical implant. Nowadays, researchers in Australia, Europe, Japan and the USA work on different concepts for implants to restore vision in the blind. In general, three implantation sites are accessible to interface to the nervous system for electrically evoked light perceptions: the cortex, the optic nerve and the retina.

The cortical implant from W. Dobbelle and his colleagues interfaced with the visual cortex of patients via an array of 64 platinum disk surface electrodes. In another approach, iridium wire microelectrodes could be placed intracortically to stimulate the visual cortex. A four-channel cuff electrode has been implanted in one patient around the optic nerve. After training, the patient could recognize different shapes, line orientations and even letters. The third approach for a vision prosthesis aims to interface with the retina. Subretinal, as well as epiretinal, implantation scenarios have been developed. While a subretinal implant could replace the function of the degenerated photoreceptors, an epiretinal implant could directly interface with the ganglion cells. Therefore, different technical concepts are necessary with respect to electrical stimulation paradigms and electrode and electronics specifications [1].

The general requirements for these electrically driven implants are known, e.g. from cardiac pacemakers and cochlear implants, and include biological as well as technical aspects: the potential damage caused by electrical stimulation, risks of infection and inflammation due to implantation and prosthesis' materials, heat damage during operation, electrode stability, power supply and hermetic sealing of electronic components. The technical requirements for microtechnical realization of epiretinal and subretinal implants differ substantially in detail but must include the general requirements with regard to safety, biostability and all other aspects of biocompatibility. The use of microsystem technology raises even more challenges in comparison to precision mechanics due to concepts without ceramic or titanium housings to integrate a highly complex system in a limited space within the eye.

We are working within the EPI-RET group towards an epiretinal implant [2]. The whole system for a retina implant comprises of three main functional units. The external part includes a high speed CMOS camera to generate the images. It sends the data to a portable box that includes the energy supply (rechargeable batteries) and a signal processing unit, the so-called retina encoder. This retina encoder simulates the spatio-temporal properties of the different layers of the retina and processes the signals from the camera and generates stimulus patterns for the ganglion cells. These data are fed to a telemetric unit for signal and data transmission to the implantable part of the system. In the eye, a telemetry receiver will decode the data and electrodes will be spatio-temporally selected for current stimulation of the ganglion cells. The microtechnical implant is highly complex. It consists of a polyimide-based flexible substrate with a monolithically integrated array of 25 stimulation electrodes and hybrid assemblies of an inductive link for energy supply and selective control of the electrode channels [3,4]. While the first prototypes have been implanted in animal models to evaluate and validate the system concept, we additionally focused on basic investigations on the interfaces at the electrodes and between

the substrate and the encapsulation layers to get a deeper insight on the basic mechanisms that are crucial to ensure long-term stability of microtechnical implants in the eye.

Therefore, we developed a simple optically powered one channel stimulator to investigate the functional stability of the encapsulation of the electronics and the electrode properties. In this paper, we present the design concept and results on *in vitro* investigations of the microtechnical encapsulation approach.

## Materials and Methods

An optically powered one channel retina stimulator has been designed for the proof of principle to use polyimide substrate with integrated platinum electrodes and a parylene encapsulation as insulation layer against ions and moisture (to protect electronic components). The electronic receiver part consists of silicon based PIN photodiodes. Four of them were electrically connected in series to reach a sufficiently high voltage to drive a current to electrically stimulate the ganglion cell layer when the implant lies on the retina. We chose the PIN photodiode SR10 BP-B from ELCOS (Pfaffenhofen, Germany) an SMD component in 1206 series. One PIN photodiode has a typical open circuit voltage of 440 mV and a short circuit current of 7  $\mu$ A when optically powered with 5 mW/cm<sup>2</sup>. The PIN photodiode's spectral bandwidth ranges from 400 nm to 1000 nm, with a peak sensitivity in the near infrared at 900 nm.

The layout of the stimulator substrates with integrated electrodes was designed using a commercial CAD program. The substrate consists of a ring like structure which will be implanted within an artificial intraocular lens. On this ring, four photodiodes will be placed and connected in series. Conductive tracks on a small ribbon cable lead to the stimulation area that will be placed in the macula region of the retina. This stimulator area was originally designed for a manifold of electrodes but in this investigation only one or two electrodes have been integrated. Therefore, three rings of the substrate were arranged concentrically and were connected via s-shaped parts that allow a three dimensional adaptation of the ring to the spherical shape of the eye bulbus. Two versions of the stimulator were designed (Fig. 1, Table 1): One contains a concentric electrode with a dot in the middle and a ring around the dot (bull's eye electrode) and the second version contains two dot electrodes that are placed on the middle ring of the stimulator area (disk electrodes) (Fig. 1).

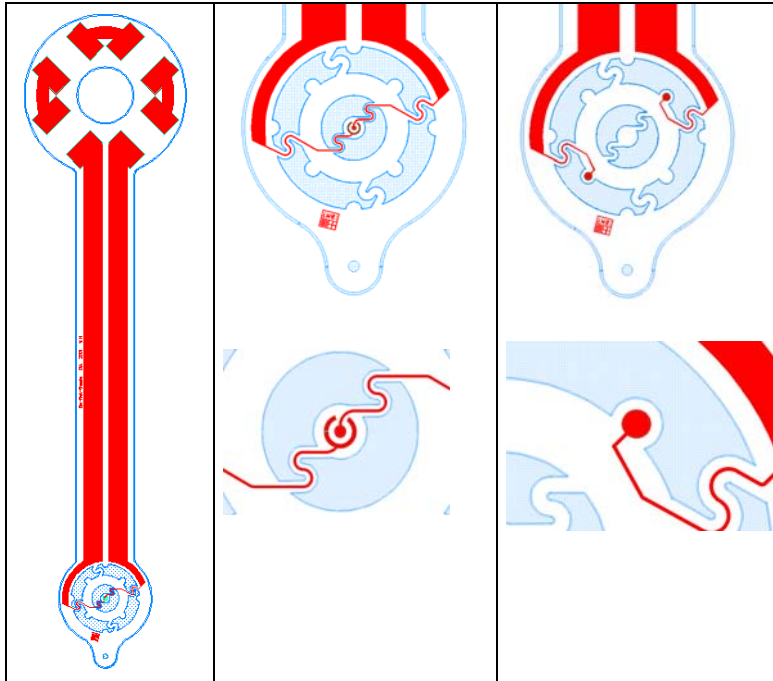


Figure 1. Layout of an optically-powered one channels stimulator (left) with a bipolar concentric electrode (middle) and bipolar disk electrodes (right), respectively. Upper row: stimulator area, lower row: electrode in detail.

The implant substrates were fabricated using micromachining technologies. We developed a process technology for an electrode design, which overcomes the "classical" separation of substrate and insulation layers and allows to integrate interconnects and to generate arbitrary outer shapes [3]. At first, a 5  $\mu\text{m}$  thick layer of polyimide resin (Pyralin PI 2611, HD Microsystems) was spun onto a silicon wafer which serves as a support structure during the whole process. The polyimide was cured in a polyimide oven (PB 6-2, Yes). A metallization layer (30 nm titanium, 300 nm platinum) for connection pads, interconnect lines, and electrode sites was deposited by sputtering (L 420 SP, Leybold) and structured in lift-off technique. A second polyimide layer with a thickness of 5  $\mu\text{m}$  was spun on and was cured to serve as top layer insulation. An aluminum etching mask was deposited and structured with wet etching to define electrode sites, connection pads and the outer geometry of the devices. Reactive ion etching (RIE) with a STS 320 PC generator (Surface Technology Systems) was used to open the electrode sites and connection pads and to separate the devices by etching the outer shapes down to the support wafer. The remaining aluminum etch mask was removed with aluminum etch solution. The wafer was cleaned with isopropanol and deionized water in an ultrasonic bath. Using tweezers, the devices were mechanically stripped from the wafer.

Four SMD photodiodes (SR 10 BP, 1206 Series, ELCOS) were manually aligned on the substrates with the aid of a microscope. They were mechanically fixed and electrically connected with conductive glue (Epo-Tek H20E-PFC; POLYTEC, Waldbronn, Germany) on the pads of the underlying stimulator substrate.

Parylene C was used for encapsulation of the complete device. The deposition of parylene C took place in a "Lab Top 3000" parylene coater (Paratec, Inc.) that uses the standardized Gorham-process. We used plasma activation (49 sccm O<sub>2</sub>, 70 W, 10 s) of the polyimide with the assembled photodiodes before parylene deposition to increase the adhesion between both materials. The electrodes were protected by covering with natural rubber (Fa. Peter Jordan GmbH, PC-Flex-GA) on an aluminium oxide ceramic plate. The implants were

mounted on a stack and a layer of 20  $\mu\text{m}$  parylene C was deposited in the process chamber. After parylene C deposition, the rubber was mechanically removed.

Table 1: Dimensions of the optically powered one channel retina stimulator

stimulator part	dimension / $\mu\text{m}$
diameter of intraocular lens part	7000
diameter of stimulator area	4000
length between middle of IOL and stimulation area	22,000
interconnection cable width	1,200
electrodes: "bull's eye"	
inner dot	70
inner/outer ring diameter	185 / 245
electrodes: "disk"	
Dot	150
distance between dots	2120
thickness of substrate	10

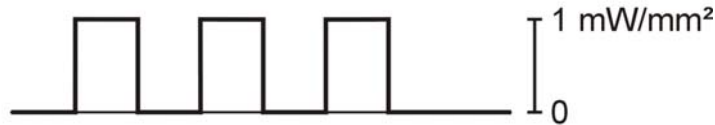
The devices were immersed in physiologic saline solution and stored at room temperature. The integrity and stability of the encapsulation was tested *in vitro* by optically powering the PIN photodiodes with a laser diode (880 nm) at 1  $\text{mW}/\text{mm}^2$ . We applied short laser pulse triplets with a pulse width of 200  $\mu\text{s}$  and an interpulse interval of 200  $\mu\text{s}$ . Pulse testing was done with a repetition frequency of 1 Hz for each triplet. The stimulus pulses were monitored at the electrodes in a differential setup on an oscilloscope (Tektronix TDS3014) of two ball-shaped silver-silver chloride electrodes with a diameter of 0.6 mm at a distance of 0.5 mm from the electrode surface.

## Results

The substrates for the retina stimulators were fabricated by micromachining. The structure for an intraocular lens (IOL) as well as the electrode areas had a very smooth surface with steep etches and smooth electrode surfaces. The IOL part of the stimulator showed a uniform coating of the high aspect ratios on the substrate with the assembled photodiodes after parylene C deposition during optical inspection. The assembly with the photodiodes on the flexible substrates was quite robust during handling, even after pilot implantation in an animal model.

The electrodes showed stable voltage responses in saline solution (Fig. 2). Burst stimulation of triplets for 48 hours with a repetition frequency of 1 Hz remained stable with amplitude variations of less than 10%.

### A IR activation light intensity



### B In vitro voltage response

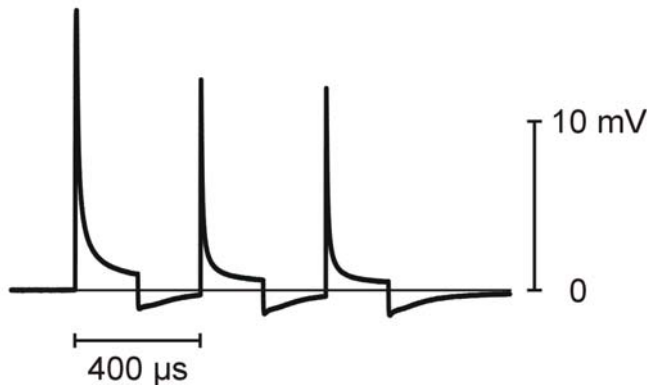


Figure 2. Measurement of in vitro voltage responses over stimulation electrodes after activation of the photodiodes in saline solution.

### Discussion

Polyimide and parylene have already been proved as non-toxic in chronic implantation studies. Their combination as substrate and encapsulation material might be adequate for microtechnical implants with hybrid assemblies of electronic components.

The described model of a simple, optically-powered one channel stimulator showed good stability in saline at the interfaces of the materials with and without electrical bias and allows further investigations on the interface stability of electrodes and insulation materials. So far, polyimide proved its stability in chronic implantations for one year without electrical bias which is promising in comparison to biodegradation that was observed with silicon based stimulation devices [4]. Further work will focus on the long-term stability under repeated electrical stimulation *in vitro* as well as *in vivo*.

### References

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