Smart Optrode for Neural Stimulation and Sensing

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Abstract—Implantable neuro-prosthetics have provided considerable clinical benefit to a range of neurological conditions. Optogenetics is a particular recent interest which utilizes high radiance light for photo-activation of genetically altered nerve cells. This can provide improved biocompatibility and neural targeting over electrical stimuli. To date the primary optical delivery method in tissue for optogenetics has been via optic fibre which makes large scale multiplexing difficult. An alternative approach is to incorporate optical micro-emitters directly on implantable probes but this still requires electrical multiplexing. In this work, we demonstrate a fully active optoelectronic probe utilizing industry standard 0.35µm CMOS technology, capable of both light delivery and electrical recording. The incorporation of electronic circuits onto the device further allows us to incorporate smart sensors to determine diagnostic state to explore long term viability during chronic implantation.

Keywords—optogenetics; optrode; micro-LED; temperature sensor; biomedical implant; biophotonics

I. INTRODUCTION

Neural prostheses are used to treat a wide range of neurological conditions such as blindness (retinal prostheses), deafness (cochlear prosthesis), spinal cord injury (bladder prostheses) and motion disorders such as Parkinson disease (Deep Brain Stimulation) [1,2]. Optogenetics – the optical stimulation of genetically photosensitized cells could potentially provide the next generation of therapeutic systems [3]. The key caveat with optogenetics is the requirement of intense blue light (typically up to 1mW/mm² on the nerve cell surface) [4]. As nervous tissue scatters blue light strongly, this light must be delivered locally.

Traditionally, in-vivo light delivery has been achieved with optic fibre and connected light sources. More advanced opto-electrodes (optrodes) have combined such fibres with recording electrodes which are commercially available. Microstructures with incorporated light emissive elements (micro-LEDs) [5-9] can simplify address and negate the need for complex optical alignment. The challenge in creating devices which can both optically stimulate and electrically record is to address the different electronic components [2,10,11]. Furthermore, as such relatively complex devices move towards clinical practice, it is desirable to monitor their long term viability [6]. In particular, if there is any fracture of the device shaft on probe insertion, it is desirable to check before providing full power. Similarly, it would be useful to monitor long term drift in device performance.

One method is to simply provide sufficient contact points to access optrode sub-components [10,11]. Control electronics can therefore be wire bonded or directly bump bonded. However, we argue in this work that a desirable alternative is to use the electronic substrate itself as the optrode. This allows for incorporation of local control circuits throughout the optrode.

One strong argument against the use of implantable optical emitters for optogenetics is the fear of thermal damage to tissue. Although the overall power through the micro-LEDs is small, it is localized to an area of typically 400µm and could therefore cause localized tissue damage. We have therefore utilized the ability to create circuits throughout the optrode by developing a temperature monitoring system to ensure operation within safe thermal limits.

We summarise this work as an implantable CMOS-based active optrode for brain neural stimulation and recording with self-diagnostic functions. Key functionality is as follows:

1. Electronic recording of local field potentials from independent shaft electrodes and ADC conversion.
2. Digital control of optical intensity and pulse width modulation of independent light emitting units.
3. Diagnostic determination of:
   a. Probe fracture
   b. LED viability
   c. Probe temperature.

Fig.1 depicts an inserted optrode in brain for neural stimulation and recording.

Fig.1. Optrode concept. The optrode is designed to be implanted at the brain surface to emit light stimulus whilst simultaneously recording electrical signals. This allows for closed loop neuroprosthetic applications.

This work is sponsored by the Engineering and Physical Research Council and the Wellcome Trust (www.cando.ac.uk). We would also like to thank the European Commission for the Erasmus Mundus project which funded Dr Ahmed Soltan’s PhD exchange program. Finally, Mr Hubin Zhao would like to thank the Chinese CSC scheme for funding his current PhD.
II. OPTRODE DESIGN METHODOLOGY

Fig. 2(a) shows a cartoon of the active optrode structure. It has a pin formation with a head 1.5mm wide and shaft 280µm wide. The length of the shaft is 2.7mm. The creation of the optrode from a CMOS substrate allows the incorporation of stimulation, recording and diagnostic circuits in the shaft. Fig. 2(b) shows a functional model of the on-board finite state machine (FSM) which acts as digital command and control core of the optrode and interfaces with the Serial Peripheral Interface (SPI) unit. The key operative functions are summarised in TABLE I.

A. Stimulation sub-system

The optrode has two blocks of 3x independent stimulation sites which are placed at key intervals along the shaft. Addressing and control circuitry exists in the head, and front end mixed signal circuitry per optical emitter is placed in the shaft. In addition to the diagnostic circuits described below, each LED control sub-circuit can read-out its current state.

Fig. 3(a) shows the structure of the stimulation sub-system. A digital to analogue converter (DAC), a transconductance amplifier (TCA) and an H-bridge current driving circuit are employed in each site to attain the needed intensity modulation. The designed TCA and H-bridge are shown in Fig. 3(b). TCA provides the current in to its input voltage received from DAC. The H-Bridge is implemented to achieve bio-directional stimulation function.

B. Recording sub-system

Four electrical recording channels continuously observe the local field potential (LFP) at the sites along the optrode shaft. LFP signal has an amplitude of 5~10 mV with a power spectrum predominantly below 100~200 Hz.

The recording channels utilize a shared ADC and the corresponding control logics. Each channel has a low-power and low-noise front-end amplifier [12,13] and a gain stage. The output of the gain stages are fed into an analog multiplexer which is controlled by the selection signal from recording control block. To drive the relatively large capacitive load of the ADC input, a buffer stage is used after the multiplexer output (Fig. 4).

![TABLE I Key operative functions of the optrode](image)

<table>
<thead>
<tr>
<th>Mode</th>
<th>Description</th>
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<tr>
<td>Electrical</td>
<td>Measuring the local field potential (LFP) in the recording sites and sending them to the controller via SPI</td>
</tr>
<tr>
<td>Recording</td>
<td>Generating light signal using micro-LEDs and both pulse and intensity control to stimulate the neurons</td>
</tr>
<tr>
<td>Stimulation</td>
<td>Making different tests in stimulating and recording sites and also the supply paths to find any problem or performance degradation and reporting them through SPI</td>
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![Fig. 3. Multi-channel stimulation system (a) overall schematic. Each LED has a unique H-bridge and control circuit with memory cells defining the state of the pulse width control. Globally absolute intensity is set by a DAC and TCA circuit. (b) A transistor level diagram of the TCA and H-bridge circuits. Most of the TCA is global apart from transistor M1.](image)

![Fig. 2. Cartoon of the general construction of the optrode. (a) The active optrode is constructed from a CMOS substrate allowing for incorporation of circuitry throughout the head and shaft. (b) The optrode is controlled by a Finite State machine which has 10 operational states.](image)
Fig. 4. Multi-channel recording system structure. The LNA and linear amplifier for each site sit in the optrode shaft. A multiplexer, buffer and ADC circuit are placed in the head and controlled via FSM (optrode head).

C. Diagnostic sub-systems

The diagnostic system includes different sensory sub-systems to monitor the operational abnormalities and physical variations. Fig. 5 shows the diagram of the diagnostic sub-system and the dependencies between different modules. The LED performance sensor is based on the micro-LED characteristics and detects an open circuit in the LED switching path. The open circuit happens when a micro-LED is not bonded on LED pad properly or the optrode shaft is broken down. The optical stimulation sub-system includes a stimulation control function to control specific LED for neural stimulation and readout the real-time condition of the LED. Also, a self-diagnostic function is built and included in this sub-system to detect any breakage point of optrode [6].

Fracture sensor detects the shaft fracture after the optrode insertion. This sensor provides a very small power line along the shaft and senses the impedance variation. This sensing is done before any other function of the optrode. Another diagnostic sub-system is a diode based temperature sensor. This allows for monitoring of the LED temperature.

III. RESULTS

Fig. 6 shows a microphotograph cut-out of the CMOS implementation. Physical cutting out of the CMOS optrode has not been performed at the time of writing, but we have previously performed exemplar cutting on silicon with laser cutting, mechanical drilling and reactive ion etching approaches. The optrode has individual anodic and cathodic connections for micro-LED bonding which is a post-processing step in the optrode fabrication.

Fig. 7 shows the simulation results of the LED forward current driven by TCA in terms of the DAC values driving the TCA. The emitted radius is assuming the same radiance-current relationship as from previous work [5]. Fig. 8 shows the output voltage of the temperature sensor for a thermal variation of 27–71°C. The conversion and amplification gain of the sensor provide a sensitivity of about 7(mV/°C).

Fig. 9 shows different scenarios for diagnostic LED based on VLED versus the applied voltage on the control transistor. The normal diode behavior is represented by green curve which includes subthreshold region, LED sub operating region (i.e. no light emission) and finally saturation region for the transistor [6]. In the case of optrode breakage, an open circuit will give 5V for VLED. Resistive state is another abnormal condition in which the resistance of LED will be massive because of abnormalities and a resistive curve will be achieved.

Fig. 5. Diagnostic system. Three different sensor forms; LED viability, fracture and temperature. Each has their own amplifier and is multiplexed to a common 8-bit ADC.
In current practice, almost all neuroprosthetic brain devices consist of a subcutaneous implant which acts as a control unit with wires leading to passive electrodes. In our case, as we are incorporating active circuitry within the brain itself (i.e. the optrode), we believe that diagnostic circuitry is vital to monitoring the long term health and variability of the implant.

V. CONCLUSION

We have implemented an ‘active’ optrode for implantable applications in a standard 0.35μm CMOS technology. Our optrode has active circuitry throughout the device area and has pads for 3D implementation of electrodes and photonics. In addition to optical stimulation and electrical recording, our device has the capacity to perform full self-diagnostics.

REFERENCES


