Simultaneous Optical Stimulation and Electrophysiological Recordings in Closed-loop Operation

Thoa Nguyen[1,3], Ling Wang[1,3], Henrique Cabral[1,4], Georges Gielen[2,3], Francesco Battaglia[1,4] and Carmen Bartic[1,3]

[1]*NERF, Leuven, Belgium*

[2]*Imec, Leuven, Belgium*

[3]*Katholieke Universiteit Leuven, Leuven, Belgium*

[4]*Radboud Universiteit Nijmengen, Nijmengen, Netherlands*

1 INTRODUCTION

Closed-loop brain computer interfaces are rapidly progressing due to their application in fundamental neuroscience and prosthetics implemented (Hatsopoulos and Donoghue, 2009; Lebedev and Nicolelis, 2006). The integration of optical stimulation and electrophysiological recordings, on one hand, brings the advantage of cell-type selectivity. On the other hand, it provides an alternative solution to the stimulation-induced artifacts, a challenge in electrical stimulation (Zhang et al., 2009; Zhang and Oertner, 2007; Wininger et al., 2009).

In this contribution, we describe a prototype allowing simultaneous optical stimulation and electrophysiological recordings in a closed-loop manner. The prototype is implemented with online spike detection and classification for selective cell-type stimulation.

2 METHODS

2.1 System Architecture

The implemented system is based on commercial off-the-shelf electronics with three functional parts: (1) data acquisition, (2) LED stimulation, and (3) control software (see Fig. 1).

The acquisition circuitry measures the brain activity collected on 32 channels with respect to the skull reference electrode. The on-board amplifier (Intan chip - RHA2132) amplifies and then multiplexes the signal before delivering it to the analog-to-digital converter (AD7980). The filters integrated in the amplifier are set by external resistors to record the broadband signal, i.e. 0.2 - 5000 Hz. The acquisition headstage is digitally interfaced with the digital I/O board (Data acquisition card (DAQ) - PCI 6259M).

The fiber-coupled LED light source (Thorlab) is controlled by TTL voltage pulses. The pulses are delivered from the analog output of the DAQ card with pre-defined amplitude and duration.

Our custom developed software controls the acquisition, triggers the stimulation, and analyzes the recorded signals. The software is implemented on LabVIEW platform and integrates signal processing code written in Matlab. Data from the headstage are transferred to the computer's memory through a high-speed acquisition loop. In parallel to that, a consumer loop stores and analyzes the data.

A data processing sequence for spike detection and classification is defined for the real-time execution. The implemented spike detection recognizes possible spikes by an adaptive threshold-based algorithm (Quiroga et al., 2004) applied to the band-pass filtered data (300 - 5000 Hz). Next, the detected signals are correlated with previously extracted templates, which were defined offline from a baseline recording period at the beginning of the session. In this first prototype, we employed a simplest form of template matching, i.e. a dot-product, and assigned the spikes to the cluster resulting in the maximum correlated value.

2.2 Microdrive with Optical Fibers

A microdrive is built based on a previous design (Kloosterman et al., 2009) (see Fig. 1). It hosts two separate tetrode bundles with 12 recording tetrodes (Wilson and McNaughton, 1993) and one optic fiber each, allowing recording and optically stimulating neural activity from two different brain regions. Each tetrode consists of a twisted bundle of four or eight polyimide-insulated microwires, fused and cut to create a blunt tip.

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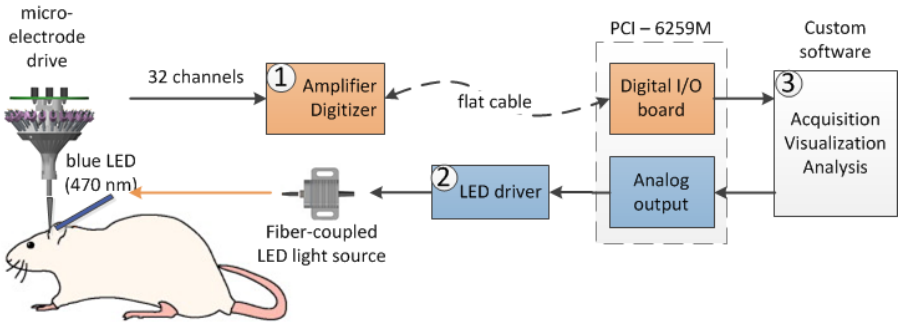

Figure 1: Schematic of experimental setup. The neural signals acquired from 32 channels (1) are detected and classified online (3) for LED stimulation (2).

2.3 Animal Surgery

All *in vivo* measurements were performed in the dorsal hippocampus of awake rats (adult male Sprague-Dawley rats weight >350 g). Experiments were carried out in accordance with protocols approved by the local University animal ethics committee and in accordance with the European Communities Council Directive of November 24, 1986 (86/609/EEC).

During the implantation, rats were anesthetized with 1.5-3% inhaled isoflurane and given a subcutaneous injection of buprenorphine (0.05 mg/kg) to minimize pain. The craniotomy was made over the right dorsal hippocampus, centered at 3.5 mm posterios and 2.8 lateral to bregma, and then sealed with cyanoacrylate glue. The rats returned to their normal housing, and had 5-8 days of recovering before the first recording session. In the mean time, tetrodes were lowered while monitoring activity in order to attain correct position.

3 RESULTS

The prototype was first evaluated in terms of the recording capability in awake rats. Figure 2(bottom) displays a representative recorded trace from a channel in the hippocampus. When comparing the baseline measurements between our custom headstage and the commerical Neuralynx system, we obtained a similar power spectrum (Figure 2(top)), indicating a comparable noise level between two systems.

The system's functionality has been evaluated in three sessions with the awake rat (Figure 3). The brain activities were measured and transferred from the headstage to the computer every 8 ms. The signals are then processed by the embedded Matlab code to detect spikes. After calculating the threshold in the current process, a 32-point waveform segment (8 pre- and 24-post) around the detected peak was extracted. The extracted waveforms for every tetrode (4 channels) were correlated with a set of pre-established waveform templates. Spikes were assigned to the template with the highest correlation score. In Figure 3, when the neuron 16 fires, a TTL pulse of 2 ms is triggered and delivered to the optical fiber to interfere with its activity.

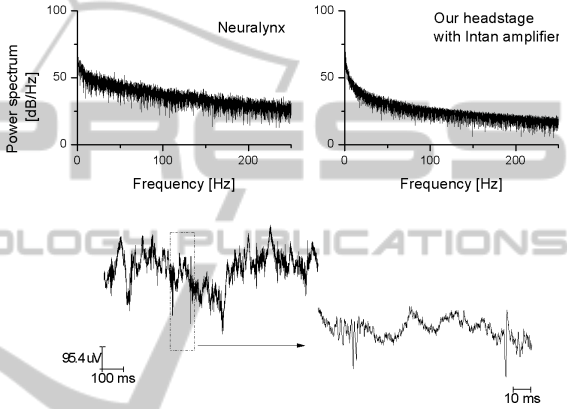

Figure 2: Multi-taper spectrum of the recorded signal by the commerical Neuralynx system (top, left), and by our prototype (top, right). A segment of recordings in a channel with the prototype and its zoom-out are shown in the bottom.

4 DISCUSSION

We have successfully demonstrated the closed-loop operation of our prototype. The optical stimulation is selectively triggered based on the results of the online spike sorting. The processing sequences, from acquisition to spike detection, spike classification, and stimulation, operates in real-time (frame rate of 8 ms) for at least 8 tetrodes (32 channels) on a standard workstation.

Although the implemented processing sequence is the simplest form of template matching, this approach provides a basic single-unit discrimination for non-

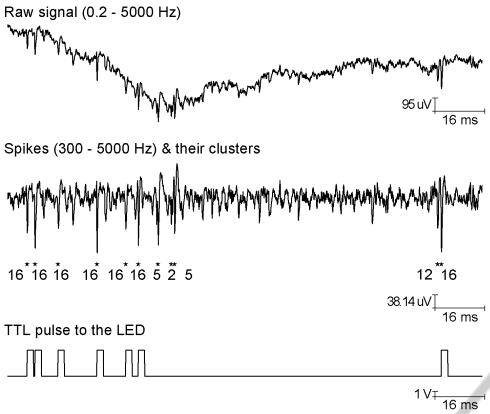

Figure 3: Closed-loop operation of our system. The acquired raw data (0.2 - 5000 Hz) is filtered (300 - 5000 Hz), amplitude-thresholded and classified to clusters with highest score after template matching. The LED is triggered whenever cell 16 fires.

overlapping spike events. More accurate algorithms, that involve matrix to vector multiplications, such as Principal Component Analysis, are tested and should be optimized to cope with the speed requirements.

ACKNOWLEDGEMENTS

This work has been supported in part by the ENLIGHTENMENT project that acknowledges the financial support of the FET program within the FP7 for Research of the EC.

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