Micro-Scale Optoelectronic Transduced Electrodes (MOTEs) for Chronic *in vivo* Neural Recording

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Principal Investigator(s): Prof. Alyosha C. Molnar
User(s): Sunwoo Lee, Shahab Ghajari, Sanaz Sadeghi, Devesh Khilwani

Affiliation(s): Electrical snd Computer Engineering, Cornell University

Primary Source(s) of Research Funding: National Institute of Health

Contact: am699@cornell.edu, sl933@cornell.edu, sg2367@cornell.edu, ss3842@cornell.edu, dk842@cornell.edu

Research Group Website: https://molnargroup.ece.cornell.edu/

Primary CNF Tools Used: ABM Contact Aligner, AJA Sputter, and Westbond 7400A Ultrasonic Wire Bonder, Oxford 100/81/82, UNAXIS Deep Si Etcher, Oxford PECVD/ALD, Anatech, P7 Profilometer, Zeiss SEMs

Abstract:

Elucidating how the brain functions requires chronic in vivo recording of neural activity in live animals. However, existing neural recording technologies have thus far failed to provide a tetherless and fully implantable neural recording unit that can function chronically. Instead, existing techniques typically require electrodes to be tethered to the outside world directly via a wire, or indirectly via an RF Coil [1], which is much larger than the electrodes themselves, causing irrevocable damages associated with the residual motions between electrodes and neurons as the brain moves. On the other hand, optical techniques, which are becoming increasingly popular, are often limited to subsets of neurons in any given organism, impeded by scattering of the excitation light and emitted fluorescence, and limited to low temporal resolution [2]. Here we heterogeneously integrate III-V optical devices on complementary metal-oxide-semiconductor (CMOS) via a layer transfer, creating Micro-scale Optoelectronic Transduced Electrodes (MOTEs), which are powered by and are communicating optically, combining many benefits of optical techniques with high temporal-resolution of electrical recording. Our work not only represents the smallest neural recorder to date but is also the first to be demonstrated to be functional in vivo and chronically (> 5 months) in awake mice.

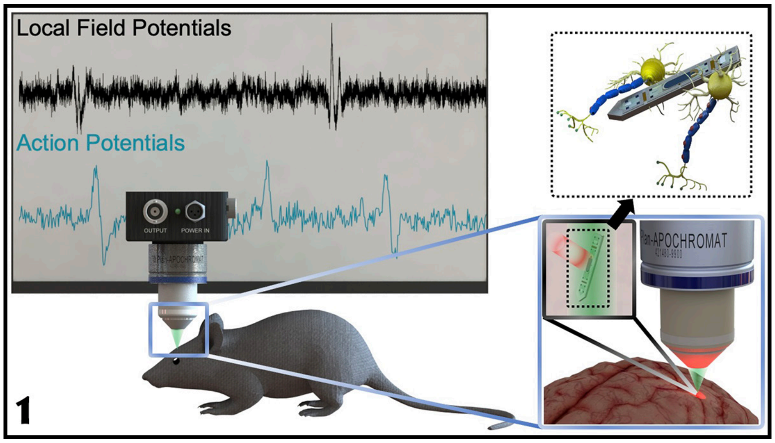
Summary of Research:

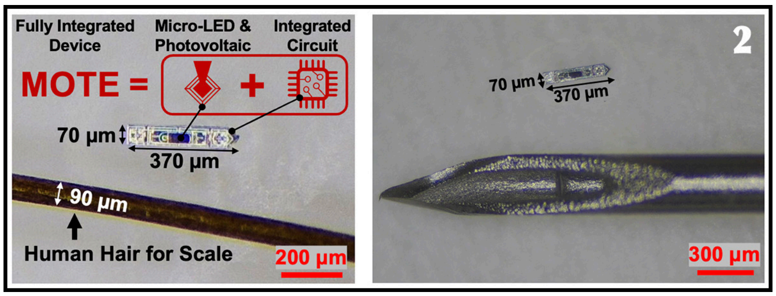
Our fabrication starts with about 5 mm x 5 mm, conventional 180 nm CMOS die, which contains the electronics for signal amplification, encoding, and transmission [3,4]. The CMOS die is then integrated with AlGaAs diode which acts as a photo-voltaic (PV) as well as light emitting diode (LED), hence the diode is abbreviated as PVLED [5]. The PVLED provides an optical link which powers the electronics and transmits encoded signals in optical pulses. The MOTE utilizes Pulse Position Modulation (PPM) for signal encoding for its high information-per-photon efficiency, where the spacing between the output pulses is proportional to the measured electric field of neuronal signals across the measurement electrodes. Figure 1 depicts a conceptual deployment and system description of such MOTE, whereas Figure 2 shows the impressive scaling enabled through the MOTE's heterogeneous integration (< 1 nanoliter in volume and ~1 μg in weight).

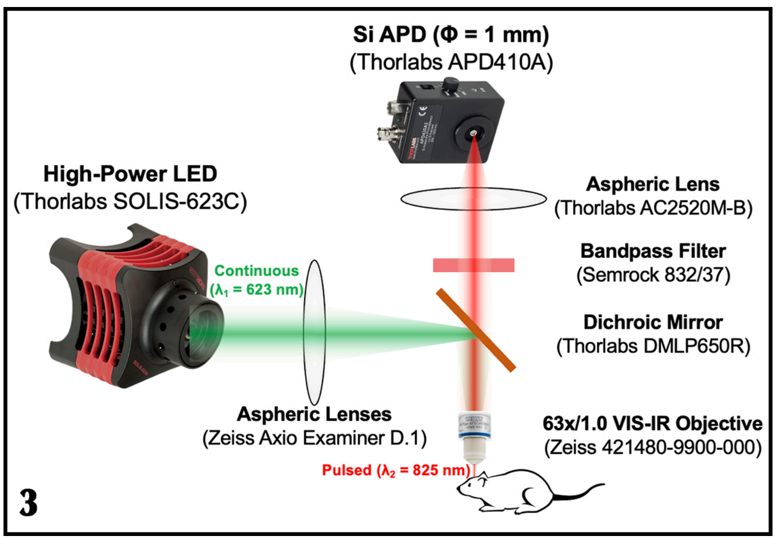
The MOTEs are completely untethered, hence free of any detrimental relative motion often observed in tethered or wired neural recording units. Instead, the MOTEs are powered optically, and through the PPM, emits the measured neural signals optically as well, at a longer wavelength than the "powering" wavelength. Figure 3 illustrates the measurement setup associated with the MOTEs where a 623 nm LED was used to power the MOTE, which in turn emits the PPM pulses that encode the neural activities at the 825 nm wavelength. The MOTEs have been implanted in mouse brains, and we were able to measure the neural activities chronically for more than 5 months (and counting), during which time the foreign body response seemed to be minimal thanks to their miniscule size, and the neural signals were quite stable. Figure 4 provides example measurements of action potential spikes from one such mouse brain where the MOTEs were embedded in its barrel cortex so that the recording can be done in a cause-and-effect fashion (i.e., a touch whisker activating barrel cortex responses).

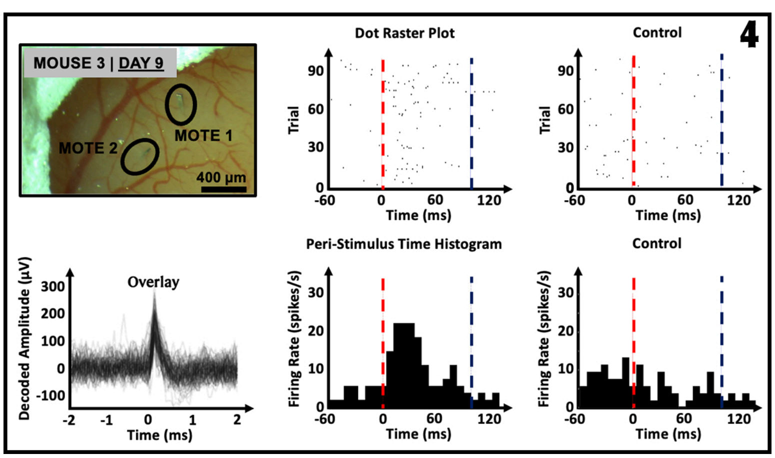
Conclusions and Future Steps:

A MOTE is the smallest electrophysiological sensor of its kind, enabled through an ingenuous heterogeneous integration approach that leverages multiple disciplines:









electronics, optics, nano/microfabrication, and electrophysiology. The next step would entail not only improving the circuits and the devices of the MOTEs but paving the path toward the mass production so to provide interested biolaboratories the MOTEs samples, and to examine the commercial viability. In parallel, applying existing MOTEs to biological studies previously unapproachable such as chronic in-organoid measurements is our near term goal.

References:

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Figure 1: System level description of the micro-scale optoelectronic transduced electrodes (MOTEs) in a mouse brain.

Figure 2: Fully fabricated MOTEs next to S. Lee's hair (left) and a 31-gauage insulin needle (right).

Figure 3: Schematic of the MOTE-based measurement system, which the MOTE is powered and is communicating optically.

Figure 4: In vivo neural recording demonstrating that the MOTEs are indeed able to measure neural activities such as action potentials chronically.