High-Density, Integrated, Multi-Functional Neural Probe for Small Animals

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Principal Investigator(s): Azahara Oliva Gonzalez, Antonio Fernandez-Ruiz
User(s): Lindsay Karaba, Jaehyo Park, Zifang Zhao

Affiliation(s): Neurobiology and Behavior, Cornell University

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Contact: aog35@cornell.edu, afr77@cornell.edu, lak256@cornell.edu, jp2597@cornell.edu, zz833@cornell.edu

Research Group Website: braincomputation.org

Primary CNF Tools Used: Parylene Coater, SUSS MA6|BA6 Aligner, Nanoscribe GT2 Two-Photon Lithography System, Heidelberg DWL2000, CHA Mark 50 E-beam Evaporator

Abstract:

Micro-fabricated neural probes serve as important tool for probing neural activities. There is an increasing need for developing high-density, multi-functional device for monitor electrical and electrochemical signal with minimal invasive and long-operation time in physiological environment. We have designed and fabricated high-density neural interface in conformable parylene-C substrate. Our probe has a cross-section of 3 x 126 μm^2, ensure low damage to brain tissues. To achieve wireless neural activity recording in rodents during unrestrained behavior, we designed a light-weight wireless high-channel count headstage and performed parylene coating to ensure all-weather operations. We used a low temperature solder bonding process to achieve high-density soft-hard circuit bonding, this enables connector-free, direct integration of probe to circuit board that allows a total system weight < 4 grams. With this system, we successfully recorded high-quality data from freely moving animal in naturalistic environment.

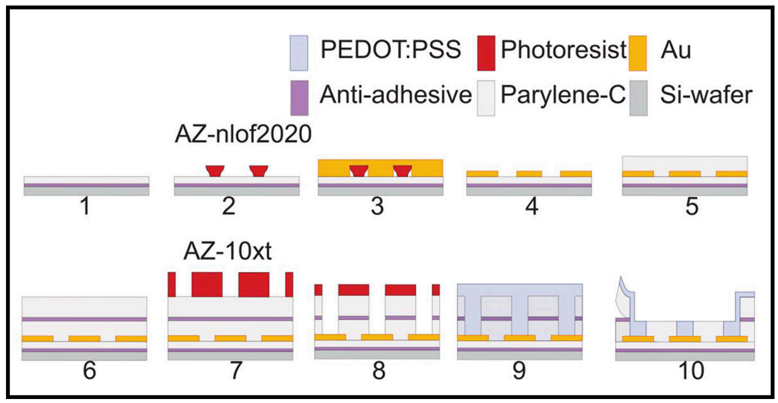

Figure 1: Microelectrode fabrication processes.

Summary of Research:

Recent advances in neural interface enabled recording high-resolution neural activities up to a few thousand channels [1]. However, most high-density neural interfaces are built with rigid, silicon-based substrate [2].

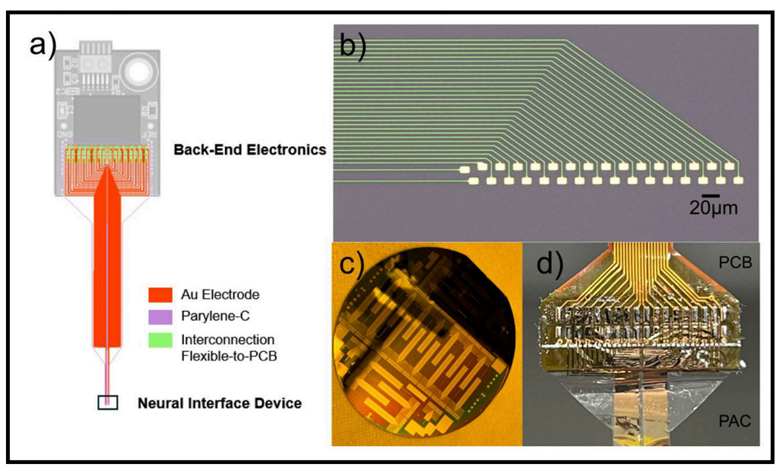

Figure 2: Light-weight, high-density neural probe. a) Illustration of wireless, light-weight neural monitor system. b) High-density, microelectrode on parylene substrate. c) 27 electrodes fabricated in a 4-inch wafer. d) soft-rigid electronic bonding with low-temperature solder.

This leads to physical damage to brain tissue during implantation and micro-electrode movement, and eventually degraded the signal quality. In order to solve this, we are building implantable microelectrodes with conformable, organic materials. We fabricated high-density conformable neural probe with parylene-C with similar process as previously reported [3] (Figure 1). In short, we used metal lift-off process to pattern a 150 nm Au layer on parylene-C substrate, then used dry etching process to pattern the opening in parylene-C passivation layer. We designed high-density neural probe with stackable design with 32ch in each probe unit to be directly bonded with back-end electronics (Figure 2a). Using CNF, we have optimized the lift-off process to reduced interconnect line width to 3 μm (Figure 2b). To achieve effective electrical bonding between parylene-C based neuro probe to a printed circuit board, we used a low-temperature solder bonding processing with a low melting point solder paste (137°C). We achieved reliable bonding without damaging parylene substrate (Figure 2c). Direct bonding of microelectrode and back-end circuit removed the need for complicated bonding process or bulky connectors and lead to a reduced form factor and system weight. We achieved 1.86 grams total system weight, with additional 2 grams for the lithium battery. This system could wirelessly record neural activity with a configurable channel number ranging from 64 channels to 256 channels. We used parylene-C for coating the back-end device for weather-proof coating. This allows us to record in freely moving rodents in outdoor, naturalistic environment in Liddel field campus. With this system, we have recorded high-quality electrophysiology signal in both rat and mouse hippocampus, to study the learning and memory function of related neural networks.

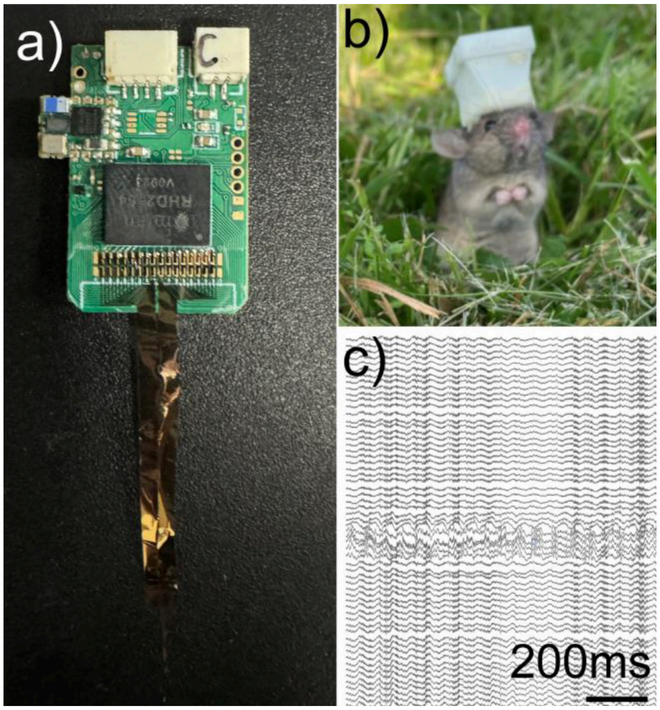

Figure 3: Wireless electrophysiology system for study unbounded animal behavior. a) Assembled wireless device with microelectrodes. b) A mouse with 3D printed carrier for wireless headstage. c) Recorded high quality electrophysiology during animal locomotion.

Conclusion and Future Steps:

We have fabricated conformable, high-density micro-electrodes with CNF tools and they have advanced our capability of study animal neural activity in traditionally challenging, unconventional environments. In the future, there are many possible directions we could work on to extend this work.

1) Multi-modal sensing: Currently, we are only using passive electrode to record electrical activity produced by neurons. Neural networks also rely on chemical signaling system, such as neurotransmitters. We are looking into how to effectively use different materials to electrically interact with neurotransmitters to actively sense the concentration of neurotransmitters, with multi-channel electrodes.

2) Neuro-modulations: Neuroscience also require tools to perturb neural circuits to investigate its functions. Importantly, optogenetics can modulate a subgroup neuron's function through opto-stimulation. We are currently exploring the possibility to build thin-membrane microelectrode on top of a thin wave-guide with the NanoScribe.

References:

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[3] Zhao, Z., Cea, C., Gelinas, J. N., and Khodagholy, D. Responsive manipulation of neural circuit pathology by fully implantable, front-end multiplexed embedded neuroelectronics. Proc. Natl. Acad. Sci. U. S. A. 118, e2022659118 (2021).