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HIGH-DENSITY NEURAL ACTIVITY RECORDING WITH NEUROPIXEL PROBES REVEAL MULTIDIMENSIONAL SENSORY-MOTOR REPRESENTATIONS

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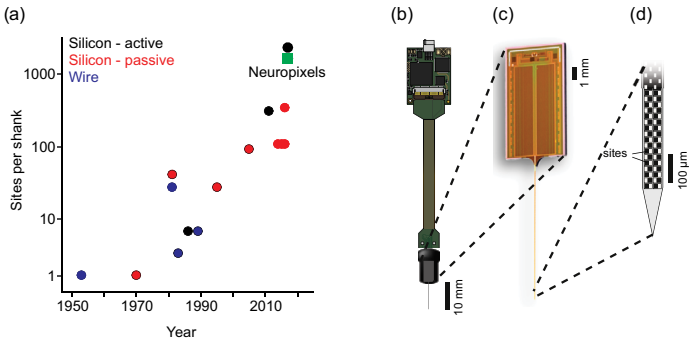
ABSTRACT

Behaviorally relevant sensory-motor processing is conducted by large neuronal populations accross the brain. An ideal experiment to study this would involve recording brain-wide neural activity of each neuron with sub-millisecond temporal resolution. Although still unchievable, development of extracellular recording techniques has enabled scaling the experimental yield from few (single channel metal microelectrodes) to few tens (wire tetrodes) to few hundreds (silicon probes) of simultaneously recorded neurons[1]. Here we describe the latest technology improvement, called Neuropixel probe, that enables yet another order of magnitude scaling to few thousands of simulatenously recorded neurons. Exciting experimental results are also shown to demonstrate the power of the new technology.



(A) Extracellular probe development over time. (B) Schematic of the Neuropixel probe with headstage. (C) CMOS element including the shank and the signal processing base. (D) Recording site arrangement.[1]

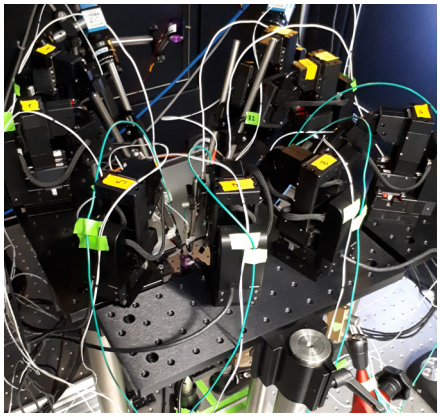
NEUROPIXEL PROBES

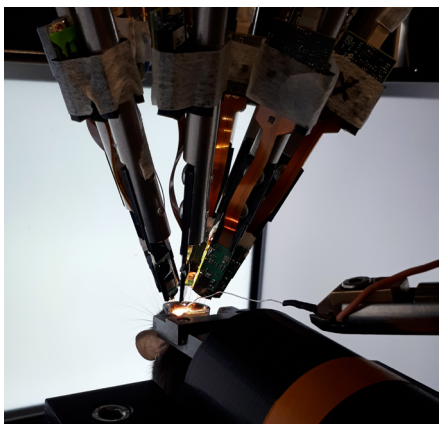
The Neuropixel probes are CMOS technology based devices tailored for rodent experiments that offer 960 per 70 × 20-µm cross-section shank, out of which any combination of 384 sites can be simultaneously recorded[2]. The probes include on-board amplification, multiplexing and digitization integrated to 6 x 9-mm size base to minimize number of signal lines despite of large recording site counts. The 12 × 12-µm recording sites are made from TiN6 substrate that provide low impedace required to achieve low noise levels 5.1 ± 0.6 µV (mean ± s.d. ; bandwidth 0.3-10 kHz).

8 PROBE RECORDINGS

Mice were head-fixed to a setup with three computer screens positioned around them at right angles. The probes had a silver wire soldered onto the reference pad and shorted to ground; these reference wires were connected to a Ag/AgCl wire positioned on the skull. The craniotomies as well as the wire were covered with saline-based agar. The agar was covered with silicone oil to prevent drying. Each of the 8 probes were mounted on a rod held by motorized micromanipulator (uMp-4, Sensapex Oy) and were then advanced through the agar and through the dura. Once electrodes punctured dura, they were advanced slowly (ca. 10 um/sec) to their final depth (4 or 5 mm deep). Electrodes were allowed to settle for approximately 15 minutes before starting recording. Recordings were made in external reference mode with LFP gain=250 and AP gain=500, using SpikeGLX software. The mice were in a light-isolated enclosure and, during the part of the recording considered here, the computer screens were black.

*All experimental procedures were conducted at the UCL according to the UK Animals Scientific Procedures Act (1986) and under personal and project licenses released by the Home Office following appropriate ethics review.

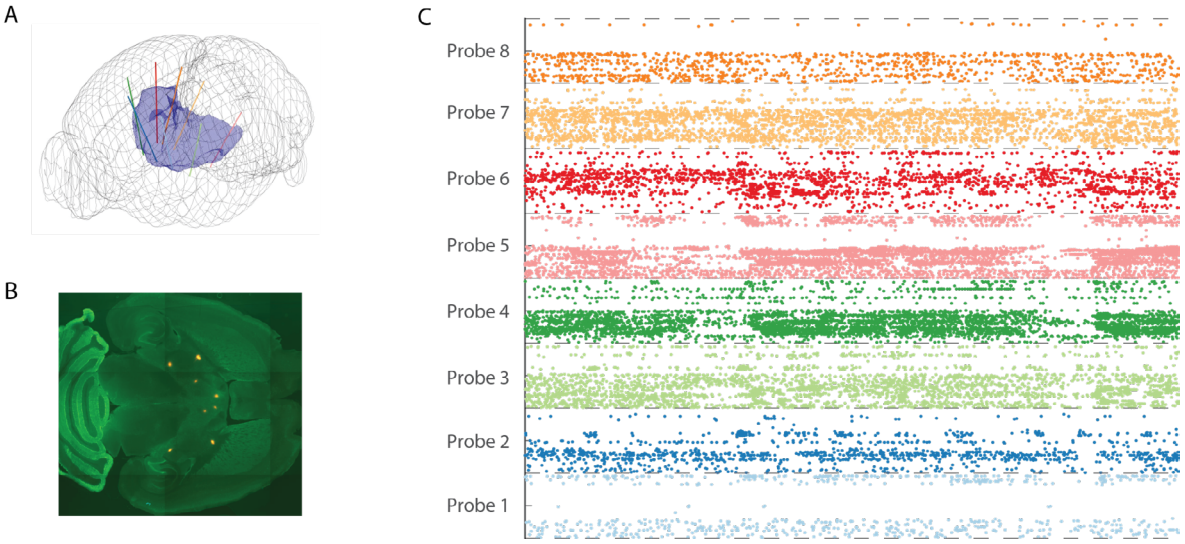




"Neuropixels probes have revolutionized electrophysiology by providing a step change in the quantity and quality of data we can acquire. Using Sensapex manipulators for these experiments allowed us to quickly and easily scale up the technique to its full potential, by enabling us to use eight probes at a time in confined spaces with high precision. "

Dr. Nick Steinmetz

RESULTS



Recording from >3000 sites simultaneously in awake mice. (A) Location of recording sites in mouse brain with thalamus highlighted. (B) Horizontal slice of histology showing probe locations. (C) Spike rasters where each tick represents a spike, plotted at the depth on the probe that the spike occurred. Each probe spanned 4mm.

To understand behavior and cognition, we require the ability to monitor the activity of large neuronal populations at the relevant spatial and temporal scales. It is now possible to record the activity of hundreds to thousands of individual neurons at millisecond temporal resolution across multiple brain regions with Neuropixels probes. We have recently demonstrated the use of eight probe experiments to record simultaneously from nearly 3,000 neurons from parts of neocortex, hippocampus, thalamus, basal ganglia, and the midbrain in awake mice[3]. In this work, led by our collaborators Carsen Stringer and Marius Pachitariu, we used these data to ask: how do distributed populations of neurons across many brain regions represent spontaneous behaviors that the mice engage in?

Surprisingly, we found that neurons across the forebrain encode detailed information about the ongoing behaviors of the mouse. Rather than representing just one global 'arousal' variable, even areas that are nominally sensory instead represent information about at least 30 dimensions, or unique features, of spontaneous behaviors that could be captured on video. By recording from large populations of neurons, we were further able to reveal that population activity is even higher dimensional than the subspace representing behaviors, as at least 125 dimensions of neuronal activity were shared across neurons.

HIGHLIGHTS

- Eight Neuropixels probes can be used to record from up to 3000 neurons simultaneously in awake mice
- These recordings revealed complex population activity and widespread behavioral representations
- Future experiments will be able to utilize this approach to understand previously inaccessible aspects of neural coding in many brain areas in awake mice.

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