Chronic Single Neuron Electrophysiology in an Alzheimer's Disease (AD) Mouse Model

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Abstract

Because Alzheimer's disease affects the brain over time, understanding the neurobiological basis of the disease requires high resolution chronic recordings. Here, ultra-flexible, brain-like mesh electronics are used to record Alzheimer's disease (AD) mice brains over 6 months. Signal analysis and spike sorting of the recordings show that neuronal firing decays between Month 4 and 6. Ultimately, this research presents a model to study the long-term effects of AD with high resolution.

Introduction

Single Neuron Recording on Chronic Time Scale

- Single neuron recording is important because it allows for understanding of what is happening to individual neurons and how they are affected by aging or neurodegenerative processes (1).
- Neurodegenerative diseases such as Alzheimer's Disease affect neurons over long time periods. Chronic recording is important to understanding how neurons evolve over time and the disease progress (1).

Mesh Electronics

- Devices that provide single neuron resolution such as tetrodes or Utah arrays often cause immune responses due to the mechanical mismatch between the material (stiff) and the surrounding neural tissue (soft). This reduces the ability for the device to record long-term (2).
- This presents a need for the use of ultra-flexible, brain-like mesh electronics with recording sites that are of similar size to the soma of a neuron. (2).
- Thus, mesh electronics provides a unique platform for neural activity for single neuron resolution and chronic stability. The mesh-like, interpenetrable structure used in this study encourages re-growth of surrounding tissue and allows for chronic recording.

Alzheimer's Disease (AD)

- Alzheimer's disease represents one of leading causes of death in developed countries (3).
- It is estimated to affect 6 million people in the US and 44 million people worldwide (3).
- Because Alzheimer's disease affects the brain over time, understanding the neurobiological basis of the disease requires high resolution over an extended time scale.

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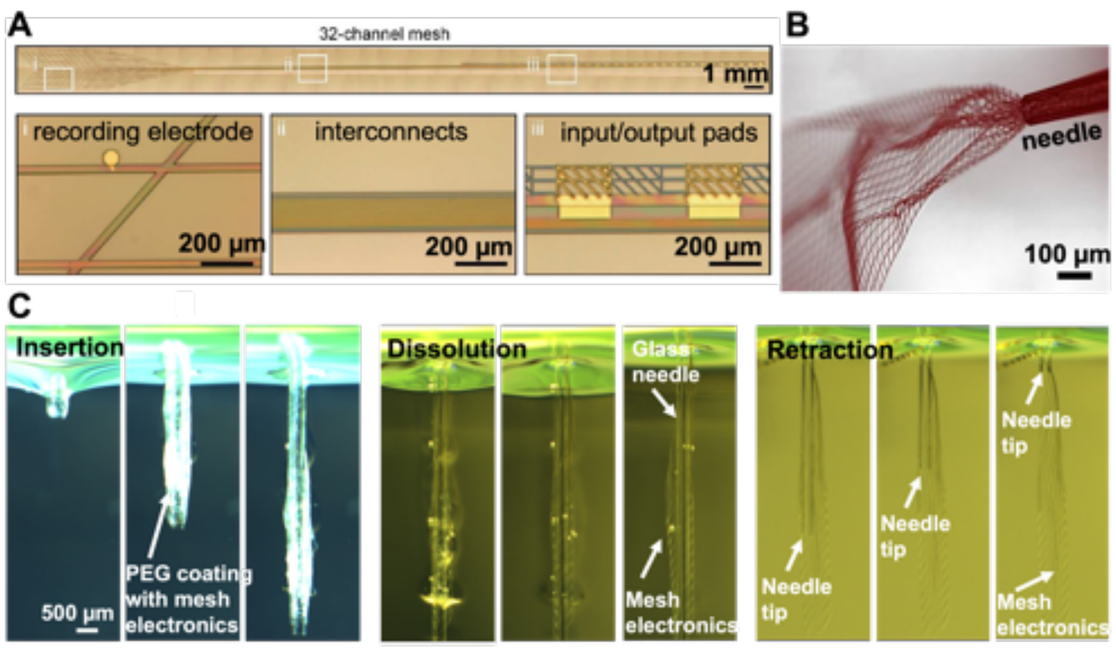
3. 2020 Alzheimer's disease facts and figures. (2020). Alzheimer's & Dementia, 16(3), 391–460. https://doi.org/10.1002/alz.12068

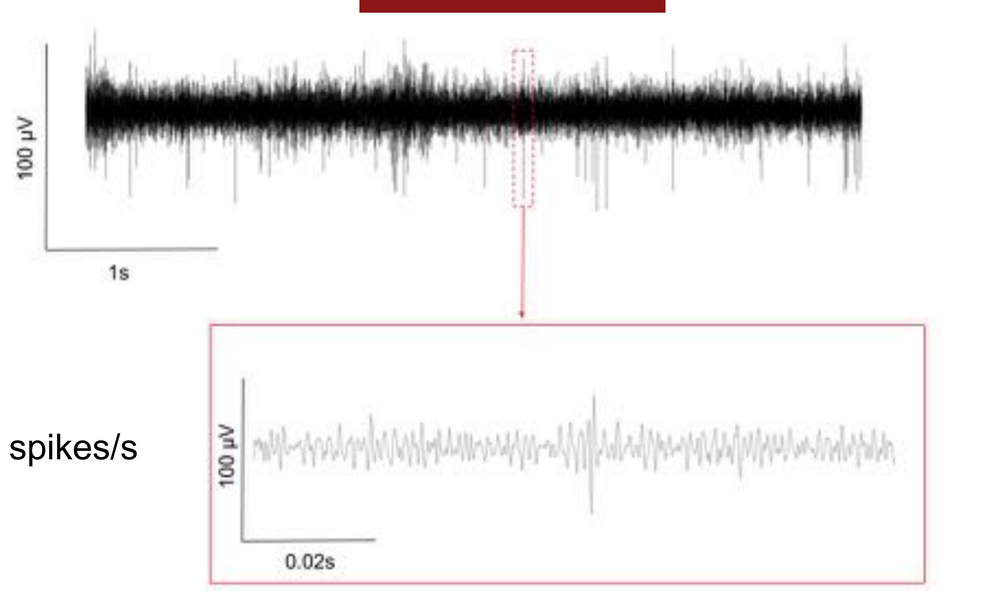
Device Fabrication



(**A**) Optical microscope images of flexible electronics with a mesh structure. The bottom images show a zoom-in view of the recording electrodes (i), the interconnects (ii), and the input/output (I/O) connection pads (iii). (**B**) Photograph showing the injection of mesh electronics into water with a glass needle. (**C**) Mesh electronics can be delivered into a soft medium, such as the brain, with precise targeting ability via a PEG-assisted temporary engaging approach. Mesh electronics can be attached to a glass needle with polyethylene glycol (PEG) for insertion (left), followed by dissolution of PEG (middle) and retraction of the needle (right).

Chronic Single Unit Electrophysiology in the Aging AD Mouse Brain

Month 4 Data



25 spikes/s

The spikes contain the same waveform, suggesting they all originate from a single neuron.

Month 6 Data

7 spikes/s

Conclusion & Outlook

Conclusions:

- Long term single-neuron recording of Alzheimer's disease will allow for greater understanding of the progression of the disease.
- There is a decay of firing rate during aging of mice brain with Alzheimer's disease.

Outlook:

- Increase number of replicates to improve accuracy of data.
- Record over a year to understand the progression of the disease over longer time periods.

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