## Methodological approaches to recording neuronal activity

(emphasis on high fidelity methods capable of resolving signals from individual neurons)

Electrical Methods for single neurons

Two electrode methods

Hodgkin Huxley

Microelectrode-based approaches

**Glass electrodes** 

Sharp microelectrodes

Patch pipettes

Whole cell recording

Cell free patch clamp

Extracellular recordings

Metal electrodes

Pt/Ir alloys, Tungsten, Gold plating, coatings

Tetrodes

A bit about spike sorting

Multielectrode arrays

Utah array, Si-fabricated probes, Neuropixel probes

Optical methods for single neurons and populations of neurons

Small molecule Ca<sup>++</sup> indicator dyes

GECIs (Genetically-Encoded Calcium Indicators)

GCaMPs, RCaMPs

Small molecule Voltage dyes

Genetically-encoded voltage indicators

Discussion of pros and cons of different methods

## **References:**

Bezanilla, F. Nerve simulation Program: <u>http://nerve.bsd.uchicago.edu/</u>, Univ. Chicago Website with simulation programs of squid giant axon biophysics based on the Hodgkin Huxley models. The site has models of voltage clamp, whole axon current clamp, and propagation of membrane potential in space and time. It also models electrodiffusion across membranes with user defined permeabilities.

Buzsáki, G. Large scale recording of neuronal ensembles. *Nature* **7**: 446-51 (2004) *Review about tetrodes and microelectrode arrays and their utility in recording activity from populations of neurons.* 

Chen T-W, et al. Ultrasensitive fluorescent proteins for imaging neuronal activity. *Nature* **499**:295–300 (2013)

The GCamp6 paper.

Hodgkin AL, Huxley AF, Katz B. Measurement of the current voltage relations in the membrane of the giant axon of *Loligo*. *J. Physiology* **116**: 424-48 (1952)

The classic study using two electrode voltage clamp to dissect the ionic currents underlying the AP.

Jun et al. Fully integrated silicon probes for high density recording of neural activity. *Nature* **551**: 232-5 (2017)

Neuropixels probe paper.

Molecular Devices. The Axon Guide. 3<sup>rd</sup> Ed. (2012)

https://mdc.custhelp.com/euf/assets/content/Axon%20Guide%203rd%20edition.pdf

Comprehensive review of basic membrane biophysics, intracellular recording approaches, and experimental instrumentation used to measure transmembrane electrical signals from single neurons.

Recce ML & O'Keefe J. The tetrode: a new technique for multi-unit extracellular recording. *Soc. Neurosci. Abstr.* **15**: 1250 (1989) *First description of tetrodes!* 

Scanziani M and Häusser M. Electrophysiology in the age of light, *Nature* **461**: 930-9. (2012) *Review of optical approaches for recording and stimulating the activity of single neurons.* 

Schwiening CJ. A brief historical perspective: Hodgkin and Huxley, J. Physiol. 590.11: 2572-75 (2012) A very nice historical account of the Hodgkin Huxley discoveries.

Sutter Instrument Co. Pipette Cookbook 2018. <u>https://www.sutter.com/PDFs/pipette\_cookbook.pdf</u> *Everything you would <u>ever</u> want to know about micropipettes.* 

Xu et al. Voltage imaging with genetically encoded indicators. *Curr. Opin. Chem. Biol.* **39**: 1-10 (2017) *The state of play in genetically encoded voltage indicators.*