Abstract

Abstracts do not include sources, but are here for the purpose of notes.)

The physical processes that creates electrical signals in neurons are well understood, but how the signals are processed into actions and thoughts has yet to receive a scientifically robust answer (add more sources) [10]. Cell type classification is of high importance because the function of different neurons is still largely a mystery.

Contents

1 | Introduction

Introduce the topic, the problem and how the problem is being solved.

Since the conception of neuroscience the neurons function have been studied on many levels and with many perspectives, from a single neuron level to networks of neurons with chemistry, physics, medicine and psychology to name some.

2 | Theory

Each section introduces topics that are referenced frequently in the article. At the end of each section there is a background subsection. These subsections contain information about the current state of research on the topic and previous work.

2.1 The Neuron

Neurons are excitiable brain cells capable of transmitting voltage changes across its structure which again can excite other neurons. These sharp voltage changes are called action potentials and when a neuron creates an action potential it is said to "fire".

(TODO: Add picture of neuron and explain all the parts.)

(TODO: Add more, citations.)

Topic to mention: Neuron cell types, pyramidal neurons, basket neurons interneurons, what are they. The term "morphology". Intracellular also referred to as membrane potential. Subcortical. Se hemalainen p.421. for a good summary. What is transmembrane current. Impulse. Apical dendrites. Grey matter. Spines. Synapses. Quiescent neuron.

Background

The physical processes in and around neurons are well understood in comparison to the function they serve. The basic function of a neuron is to receive and send action potentials to process information. What information is transmitted and how it is processed is still being researched.

2.2 Action Potentials

Describe how actionpotentials are created.

Background

Write about hodking and huxley. [5]

2.3 Neuronal Models

The electrical activity of neurons are caused by different concentrations of ions in the extracelluar and intracellular medium. The cell membrane consists of a $5\,\mathrm{nm}$ lipid bilayer and is impenetrable to ions. The gradient is created by differnt ionpumps in the cell membrane which can selectivly push ions through. The most significant ions in this process are sodium (Na^+)

There are multiple models for neurons, some of the main groups are point models and compartmental models. List many models? Multi-compartmental models can be useful to understand the processing of neurons with complex morphological structures

Background

Hodgkin & Huxley [5], Connor & Stevens [1], and Sterratt et al. [10]

The temperature is important.

2.4 Electrodes

2.5 Calculating Extracellular Potential

The extracellular potential is the electric potential generated from the transmembrane currents in the neurons. When a neuron fires this can be seen from the extracellular potential which will have a spike which is similar to the intracellular spike.

By modelling the neuron as compartments and approximating each compartment as a spherical volume current source at position $\mathbf{r_0}$, the potential at at position $\mathbf{r}$ at time t will be,

$$\mathbf{E}(\mathbf{r},\mathbf{t}) = \frac{1}{4\pi\sigma}\frac{I_0(t)}{|\mathbf{r}-\mathbf{r_0}|} \tag{2.1}$$

$$\mathbf{E}(\mathbf{r},\mathbf{t}) = \sum_{n=1}^{N}\frac{1}{4\pi\sigma}\frac{I_n(t)}{|\mathbf{r}-\mathbf{r_0}|} \tag{2.2}$$

Potential from compartments modelled as line sources.

$$\mathbf{E}(\mathbf{r},\mathbf{t}) = \frac{1}{4\pi\sigma}\sum_{n=1}^{N} I_n(t)\frac{dr_n}{|\mathbf{r}-\mathbf{r_0}|} \tag{2.3}$$

$$= \frac{1}{4\pi\sigma}\sum_{n=1}^{N} I_n(t)\frac{1}{\Delta s_n}\log\left|\frac{\sqrt{h_n^2+\rho_n^2}-h_n}{\sqrt{l_n^2+\rho_n^2}-l_n}\right| \tag{2.4}$$

Taken from Lindén et al. [6]

This equation rests on two assumptions,

1. The permeability μ of the extracellular medium is the same as that of vacuum μ_0.
2. The quasistatic approximation which lets the time derivatives, $\partial E/\partial t$, be ignored as source terms. See appendix A.1

The extracellular potential can be calculated using Maxwell's equations and the continuity equation if the spatial distribution (morphology) of transmembrane currents and the extracellular conductivity is known.

In the quasistatic approximation, since $\nabla \times \mathbf{E} = \mathbf{0}$, the electric field can be expressed with a scalar potential.

Forward problem = calculate the potential from the current source, inverse problem is used in magnetoenchephalography (important). The amplitude of a spike in the extracellular potential is usually in the magnintude of $< 200\mu$V. The noise of electrodes vary, but can be as much as 20μV. This limits the range electrodes can record from.

The currents sum to zero, while the spike is very visible, there are many small currents in the dendrites with opposite current. ([4])

The extracellular spike width tend to increase with distance from soma because of the neuronal morphology. This article used a passive neuron model with different morphologies to show that the spike width increases with distance to soma. The spike amplitude also decreases with distance to soma and seems to follow a power law. ([9]).

The shape of extracellular spikes are mainly depedent on the membrane currents and the morphology of the cell. Some of the effects from the morphology of the cell are increased spike width and decreased amplitude from distance to soma.

Many things here from around page 245. When the conductivity σ and the current generators are know, Maxwell's equations and the continuity equation equation can be used to calculate the electric field E and magnetic field B. (TODO: Copied text) ([4])

Background

Recording is usually done using electrodes, this makes recording the membrane potential more challenging than recording from the extracellular medium as the electrode has to be very close or inside the cell. At the time of writing, recording the membrane potential of a concious subject is nearly impossible, this makes understanding extracellular potentials vital for current research.

Early calculations was done by Rall 1962 investigating the interaction between action potentials and synapes using cylinders as the current source. (TODO: Read article, make more understandble.) Holt and Koch 1999 added comparmental models to reconstruct pyramidal neurons.

The information about the transmembrane current is usually difficult to obtain, as well as the morphology.

2.6 Neuron & LFPy

LFPy is a Python module that uses Neuron and the mentioned methods to calculate the electric field outside the neuron. [6]

Background

2.7 Cell Type Classification

Background

It was early observed that the shape of action potentials are different for individual neurons. Mountcastle et al. [8] discovered what they called regular spiking , fast spiking [8].

2.8 Allen Cell Types Database

The Allen Brain Institute have gather individual neuron data from lateral geniculate nucleus (LGN) and primary visual cortex (V1) of young laboratory mice. The data's main categories are electrophysiology, morphology and modeling. With the morphological data the extracellular potential can be calculated given a model for the transmembrane currents.

3 | Methods

3.1 Pettersen & Einevoll (2008) Reproduction

Pettersen & Einevoll [9] shows some features of extracellular spike modulation and results presented here are comparable to results in the paper. See chapter something for extracellular spike modulation. ([9])

Write more about the connor stevens model.

3.1.1 Simulation

Cell: Used the Mainen & Sejnowski [7] cell with a passive model, the same model used in the Pettersen & Einevoll [9]. The cell was rotated using PCA (principal component analysis) on the compartment positions so that the first component was paralell to y-axis while the second component was paralell to the x-axis. This rotates the cell so most of the dendrites are along the y and x-axis. (TODO: show the morphology of the neuron)

Spike Generation: An action potental was generated using the Connor-Stevens model [1, 2] using the same parameters as Dayan & Abbott [3]. This had an amplitude of $107.6mV$ from baseline with the peak at $48.21mV$. These values are similar (TODO: how similar?) to Dayan & Abbott [3], but not with Pettersen & Einevoll [9] which had an amplitude of $83mV$ from baseline. To compensate for the difference the action potental was normalized to $83mV$ manually (fig. 3.1).

Parameters: Parameters are the same as Pettersen & Einevoll [9] and Dayan & Abbott [3] . Membrane resistance $R_m = 3 \cdot 10^4 \Omega/cm^2$, membrane capacitance $C_m = 1\mu F/cm^2$, axial resistance $R_a = 150\Omega/cm^2$, time resolution $dt = 2^{-6}ms$. The reversal potential was set to zero.

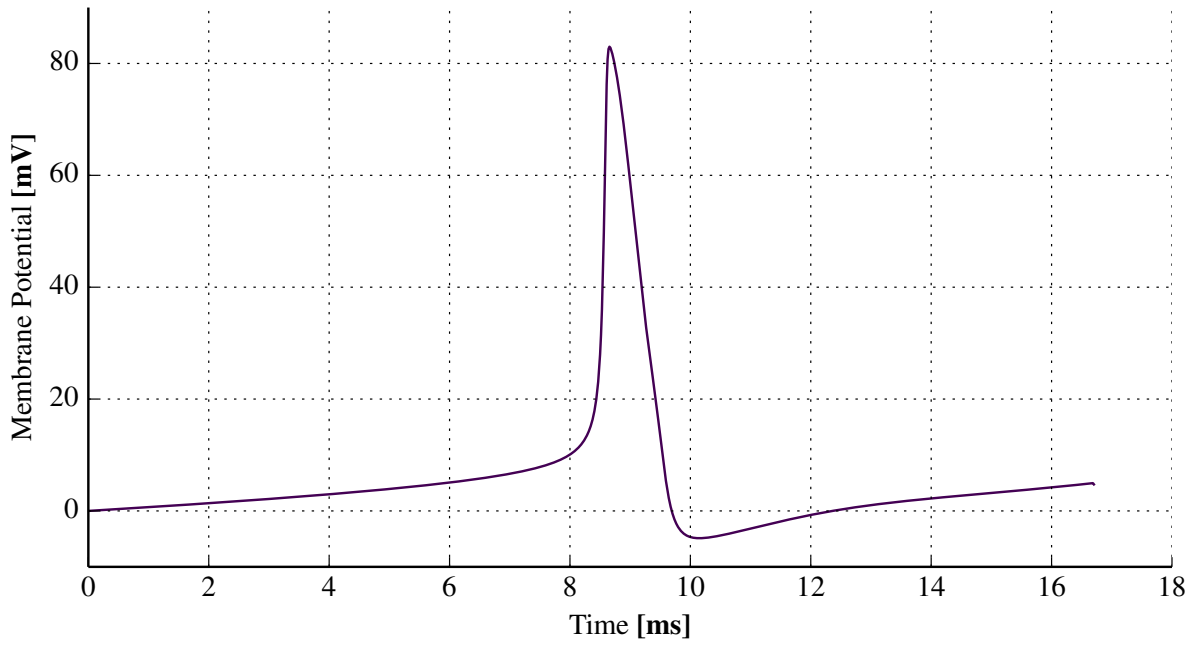

Figure 3.1: Soma membrane voltage.

The action potental was imposed in all soma sections using the "play" vector function in Neuron.

Electrode Positions: Recording sites were placed in the xz plane at 11 linearly spaced positions along 36 lines with equal angular spacing. (TODO: Show the electrode positions.)

Spike Width & Amplitude: A baseline was set as the value at the start of the signal. Amplitude was calculated as the difference between maximum absolute value and the baseline. The spike width was calculated at half width at maximum amplitude.

Spike width was recorded at $0.5625ms$ for $dt = 2 \cdot 10^{-5}$, similar to $0.55ms$ from Pettersen & Einevoll [9]. When increasing the resolution to $dt = 2 \cdot 10^{-6}ms$ the spike width rose to $0.625ms$.

3.1.2 Results

The action potental that was used in Pettersen & Einevoll [9] is similar to the one used here. The fourier specter is displayed in fig. 3.2 . The graph displayed in the paper and the one shown here are nearly identical. (TODO: Rewrite, be more spsific here?)

The spike width increases with the distance from soma as seen in fig. 3.3 . These results are lower than the widths reported in Pettersen & Einevoll [9]. (Use more time on editing the Connor-Stevens model to come closer to an max.amplitude on 20mV?).

Sudden changes in spike width was experienced with increased distance from soma. Above $200\mu V$ the spikes shapes are not well defined. This was also reported in Pettersen & Einevoll [9].

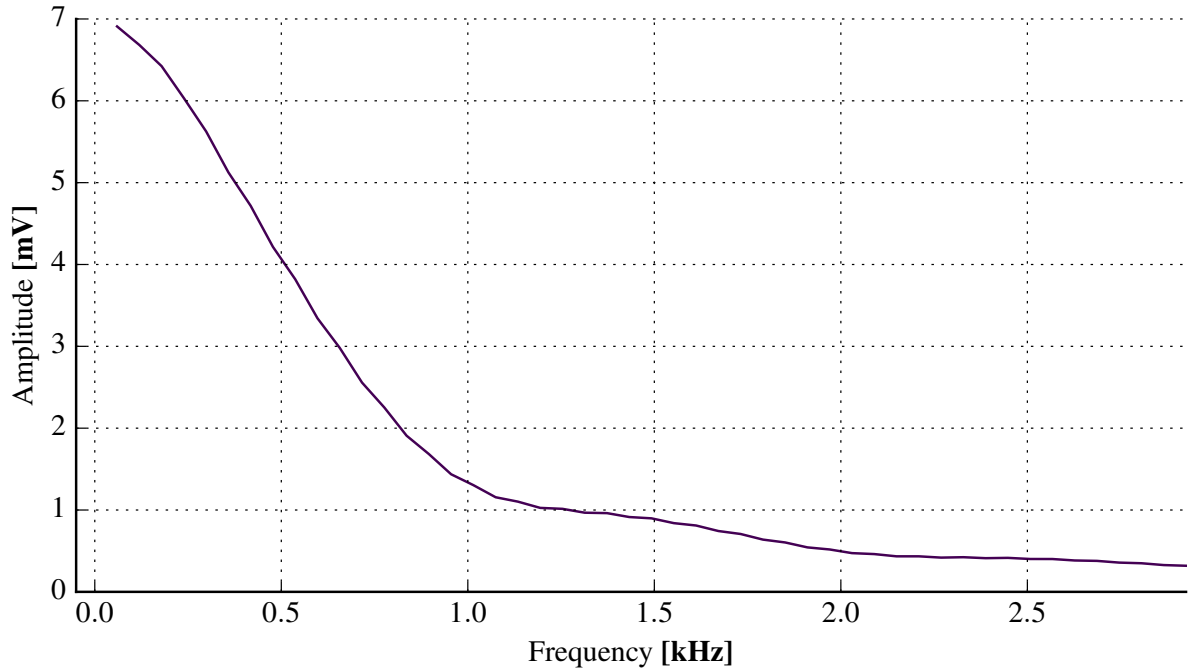

Figure 3.2: Frequency specter of simulated somatic membrane potential.

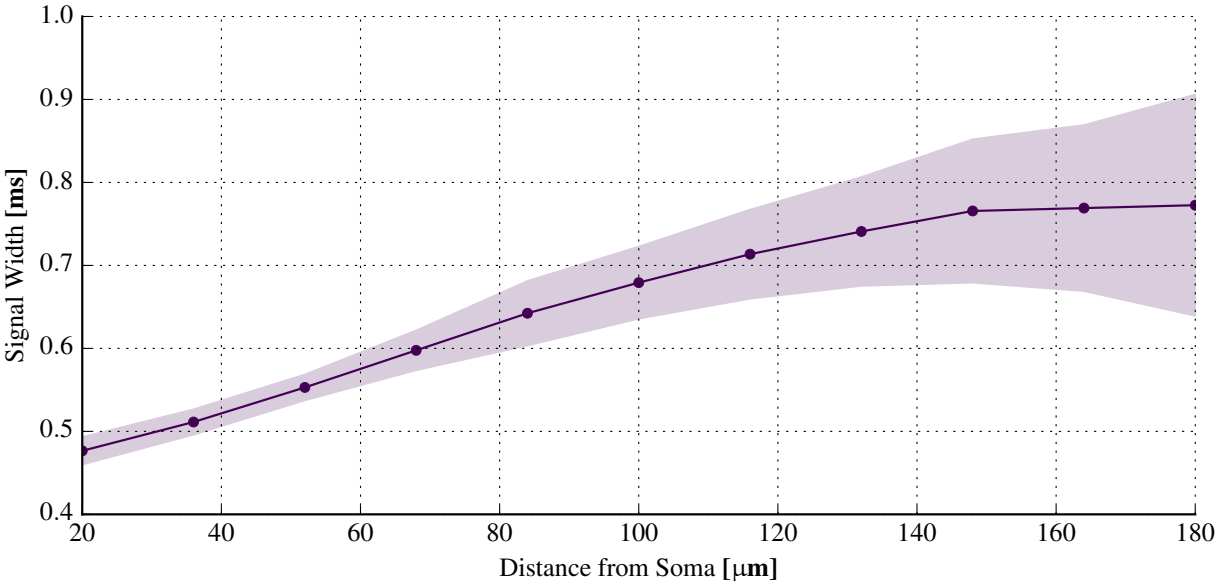

Figure 3.3: Spike width over distance. Mean +/- 1 std.

Pettersen & Einevoll [9] reports a spike amplitude above $150\mu V$ at $20\mu m$, this does not match current findings. fig. 3.4 shows spike amplitude with logarithmic axes. (TODO: Is numbers on the power law decays necessaryy?) Although the data does not match Pettersen & Einevoll [9], it is comparable with what is expected in the near and far limit field of a ball and stick neuron. In the near field the the expectation is a $1/r$ decay and in the far field it is $1/r^2$ or $1/r^3$ depending on distance. (TODO: Clearify this, put reference back to theory chapter.)

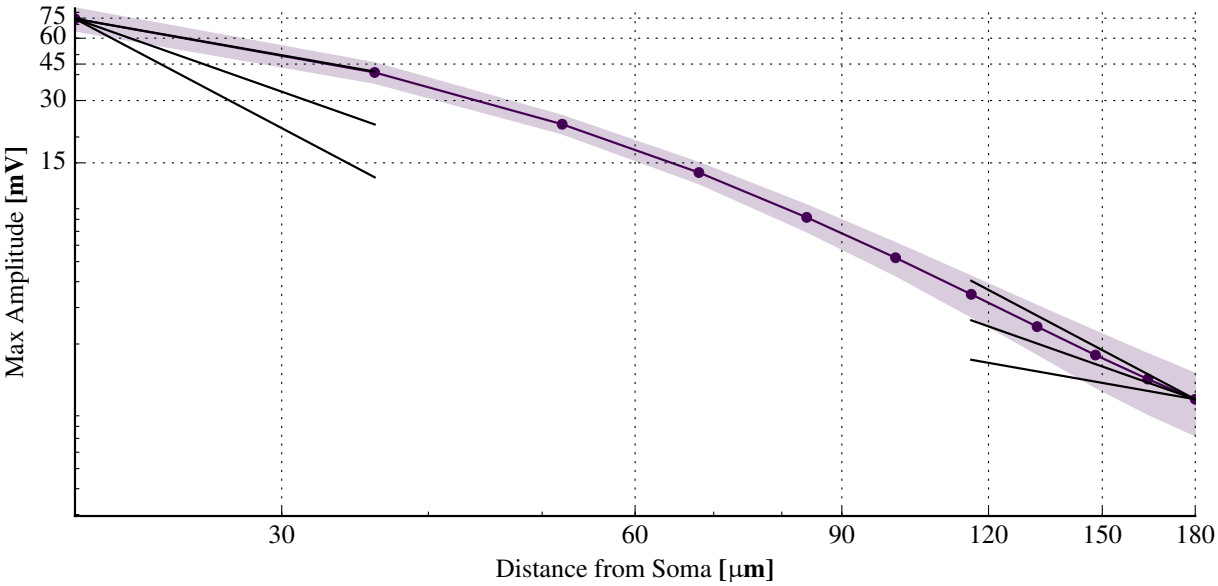

Figure 3.4: Spike amplitude over distance. Mean +/- 1 std. The power law decays $1/r$, $1/r^2$ and $1/r^3$ are shown at the leftmost and rightmost data points.

3.1.3 Discussion?

3.2 Blue Brain

Use the models. Write code to capture one action potential. Bursting neurons often hav adapting action potential, what to do there.

Have a volume of electrodes, calculate the amplitude and where they stop being noticable. Plot where the signal can be recoqnized.

3.3 Allen Brain Institute

My spesific implementation of LFPy and Neuron.

The recording site for the electrophysiological data is soma for all neuron in the data from Allen Brain Institute. The currents in the dendrites are not avaiable and is modelled using a passive neuron model. Write how the simulation is set up.

Create convincing results that shows that the simulations are correct and can be trusted.

- Action potential width and amplitude is correct.
- Fourier specter is correct.

- Extracellular width and amplitude matches the article.
- Create same plots.
- Calculate the same parameters, power law?

How different are action potentials generated from the same cell. How does the "mean" spike look from the experimental data.

Data from Blue Brain and Allen Brain Institute.

Allen Brain Institute Questions:

- How much does the experimental spikes differ.

4 | Results

Use membrane potentials from Allen Brain Institute and Blue Brain and look at width from different cells.

5 | Discussion

Nothing here yet.

A | Appendix

A.1 Quasistatic Approximation in Neural Tissue

A quasistatic approximation implies that the equations have a form that does not include time derivatives (static). Some quantaties can be allowed to vary over time, but slowly. Here we show that the quasistatic approximation is a valid assumption in neural tissue. First start with Maxwell's equations.

$$\begin{aligned} \nabla \cdot \mathbf{E} &= p/e \\ \nabla \times \mathbf{E} &= -\partial \mathbf{B}/\partial \mathbf{t} \end{aligned} \tag{A.1}$$

$$\begin{aligned} \nabla \cdot \mathbf{B} &= 0 \\ \nabla \times \mathbf{B} &= \mu_0(\mathbf{J} + \epsilon_0 \partial \mathbf{E}/\partial t) \end{aligned} \tag{A.2}$$

In a passive nonmagnetic medium, **J** is the sum of ohmic volume current and the polarization current

$$\mathbf{J} = \sigma \mathbf{E} + \partial \mathbf{P}/\partial t \tag{A.3}$$

where $\mathbf{P} = (\epsilon - \epsilon_0)\mathbf{E}$ is the polarization and ϵ is the permitivity of the material.In neuromagnetism, we generally deal with frequencies that are below 100 Hz. Cellular electrical phenomena contain mostly frequencies below 1kHz. Let σ and ϵ be uniform and let us consider elctromagnetic wave at frequencty f.

$$\mathbf{E} = \mathbf{E}_0(\mathbf{r}) \exp(i 2\pi f t) \tag{A.4}$$

With eqs. (A.2) and (A.3) we get,

$$\nabla \times \mathbf{B} = \mu_0(\sigma \mathbf{E} + (\epsilon - \epsilon_0)\partial \mathbf{E}/\partial t + \epsilon_0 \partial \mathbf{E}/\partial t) \tag{A.5}$$

For the quasistatic approximation to be valid, it is necessary that the time-derivative terms be small compared to the ohmic current.

$$\left|\epsilon \mathbf{E}/\partial t\right| \ll |\sigma \mathbf{E}| \rightarrow 2\pi f \epsilon/\sigma \ll 1 \tag{A.6}$$

With $\sigma = 0.3\,\Omega^{-1}\,\mathrm{m}^{-1}$, the value of brain tissue, $\epsilon = 10^5 \cdot \epsilon_0$, and $f = 100\,\mathrm{Hz}$, we find

$$2\pi f \epsilon/\sigma = 2 \cdot 10^{-3} \ll 1 \tag{A.7}$$

In addition, $\partial \mathbf{B}/\partial t$ must be small. from eqs. (A.1) and (A.2) ,

$$\begin{aligned} \nabla \times \nabla \times \mathbf{E} &= -\frac{\partial}{\partial t}(\nabla \times \mathbf{B}) \\ &= -\mu_0 \frac{\partial}{\partial t}(\sigma \mathbf{E} + \epsilon \partial \mathbf{E}/\partial t) \\ &= -i2\pi f \mu_0 (\sigma + i2\pi f \epsilon)\mathbf{E} \end{aligned} \tag{A.8}$$

Solutions of this equation have spatial changes on the characteristic length scale

$$\lambda_c = \left|2\pi f \mu_0 \sigma (1 + i2\pi f \epsilon/\sigma)\right|^{-1/2} \approx 65\,\mathrm{m} \tag{A.9}$$

This length is much longer than the diameter of the head. This implies that the contribution of $\partial \mathbf{B}/\partial t$ to $\mathbf{E}$ is small. Theautorefor, the quaasistatic approximation appears justified. This does not mean that we should forget time-dependent phenomena altogether. For example, the capacitative current through the cell membrane is significant in determining the properties of the action potential. Nevertheless, this so-called displacement current, $\epsilon_0 \partial \mathbf{E}/\partial t$, need not be taken into account in the calculation of $\mathbf{B}$.

Copied from Hämäläinen et al. [4]

Bibliography

[1] J. A. Connor & C. F. Stevens. “Prediction of repetitive firing behaviour from voltage clamp data on an isolated neurone soma.” In: *The Journal of Physiology* 213.1 (1971). 00704, pp. 31–53.

[2] J. A. Connor, D. Walter, & R. McKown. “Neural repetitive firing: modifications of the Hodgkin-Huxley axon suggested by experimental results from crustacean axons.” In: *Biophysical Journal* 18.1 (1977). 00236, pp. 81–102.

[3] Peter Dayan & Laurence F. Abbott. *Theoretical neuroscience*. Vol. 806. 03314. Cambridge, MA: MIT Press, 2001.

[4] Matti Hämäläinen et al. “Magnetoencephalography- theory, instrumentation, and applications to noninvasive studies of the working human brain.” In: *Reviews of modern Physics* 65.2 (1993). 03322, p. 413.

[5] Alan L. Hodgkin & Andrew F. Huxley. “A quantitative description of membrane current and its application to conduction and excitation in nerve.” In: *The Journal of physiology* 117.4 (1952). 16698, pp. 500–544.

[6] Henrik Lindén et al. “LFPy: a tool for biophysical simulation of extracellular potentials generated by detailed model neurons.” In: *Frontiers in neuroinformatics* 7 (2013). 00015.

[7] Zachary F. Mainen & Terrence J. Sejnowski. “Influence of dendritic structure on firing pattern in model neocortical neurons.” In: *Nature* 382.6589 (1996). 00880, pp. 363–366.

[8] Vernon B. Mountcastle et al. “Cortical neuronal mechanisms in flutter-vibration studied in unanesthetized monkeys: Neuronal periodicity and frequency discrimination.” In: *Journal of neurophysiology* (1969). 00592.

[9] Klas H. Pettersen & Gaute T. Einevoll. “Amplitude variability and extracellular low-pass filtering of neuronal spikes.” In: *Biophysical journal* 94.3 (2008). 00120, pp. 784–802.

[10] David Sterratt et al. *Principles of computational modelling in neuroscience*. 00081. 2011.