

# 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) [sterratt2011principles](#) Cell type classification is of high importance because the function of different neurons is still largely a mystery.



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# 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.

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### 2.1 The Neuron

Neurons are excitable 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. Sub-cortical. See Hemäläinen 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 consensus is that the basic function of a neuron is to receive and send action potentials and that action potentials are responsible for all cognitive functions. What information is transmitted in the action potentials and how the information is processed is still under much research.

## 2.2 Action Potentials

Describe how action potentials are created.

### Background

Write about Hodgkin and Huxley. [Hodgkin & Huxley 1952 \[1\]](#)

## 2.3 Neuronal Models

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 [Sterratt et al. 2011 \[2\]](#).

### Background

[Hodgkin & Huxley 1952 \[1\]](#) [Connor & Stevens 1971 \[3\]](#) [Sterratt et al. 2011 \[2\]](#)

## 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.

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. This information can be hard to obtain in vitro, but if these values are obtained either using neuron models or physical recordings the extracellular potential is in theory easy to calculate in a computer.

To make calculation easier, some assumptions are made:

1. The permeability  $\mu$  of the extracellular medium is the same as that of vacuum  $\mu_0$ .
2. Assume a quasistatic approximation which lets the  $\partial E / \partial t$  be ignored and as source terms.  
Link to appendix for proof.

Forward problem = calculate the potential from the current source, inverse problem is used in magnetoencephalography (important). The amplitude of a spike in the extracellular potential is usually in the magnitude of  $< 200\mu\text{V}$ . The noise of electrodes vary, but can be as much as  $20\mu\text{V}$ . 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. ([Hämäläinen et al. 1993 \[4\]](#))



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. (Pettersen & Einevoll 2008 [5] ).

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  $\sigma$  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) (Hämäläinen et al. 1993 [4] )

## Background

Electric potential from neurons can either be obtained by measuring the membrane potential or measured from the the extracellular medium. 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. As such it is useful to know the physical origin of the extracellular potential.

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.

## 2.6 Neuron & LFPy

LFPy is a Python module that uses Neuron and the mentioned methods to calculate the electric field outside the neuron. Lindén et al. 2013 [6]

## Background

## 2.7 Cell Type Classification

## Background

It was early observed that the shape of action potentials are different for individual neurons and it has been suggested that action potentials can be used to identify classes of neurons. This the main focus of this article. (Use this source? Mountcastle et al. 1969 [7].

## 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. [Allen Cell Types Database Technical White Paper: Overview 2015 \[8\]](#)

## **Background**

## 3 | Methods

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### 3.1 Pettersen & Einevoll (2008) Reproduction

Pettersen & Einevoll (2008) 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. (Pettersen & Einevoll 2008 [5] )

Write more about the connor stevens model.

#### 3.1.1 Simulation

*Cell:* Used the Mainen & Sejnowski (1996) cell with a passive model, the same model used in the Pettersen & Einevoll (2008). The cell was rotated using PCA (principal component analysis) on the compartment positions so that the first component was parallel to y-axis while the second component was parallel 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 potential was generated using the Connor-Stevens model (Connor & Stevens 1971 [3], Connor et al. 1977 [10] ) using the same parameters as Dayan & Abbott (2001). 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 (2001), but not with Pettersen & Einevoll (2008) which had an amplitude of  $83mV$  from baseline. To compensate for the difference the action potential was normalized to  $83mV$  manually (Figure 3.1).

*Parameters:* Parameters are the same as Pettersen & Einevoll (2008) and Dayan & Abbott (2001) . 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. The action potential was imposed in all soma sections using the "play" vector function

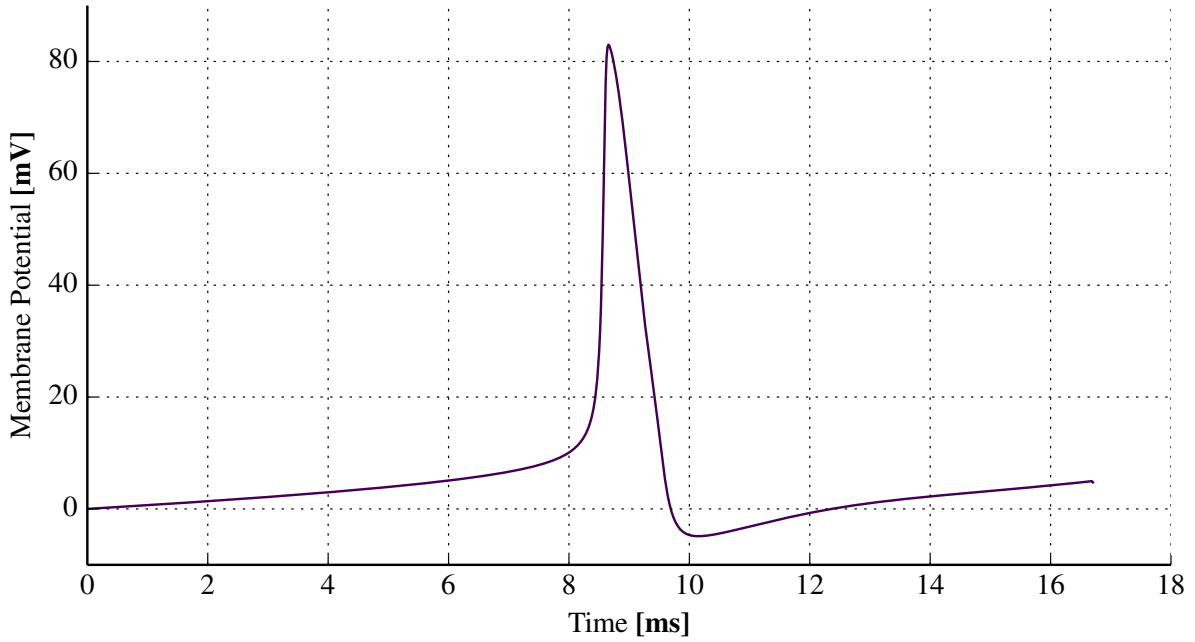


Figure 3.1: Soma membrane voltage.

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 \(2008\)](#). When increasing the resolution to  $dt = 2 \cdot 10^{-6}ms$  the spike width rose to  $0.625ms$ .

### 3.1.2 Results

The action potential that was used in [Pettersen & Einevoll \(2008\)](#) is similar to the one used here. The fourier specter is displayed in Figure 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 Figure 3.3. These results are lower than the widths reported in [Pettersen & Einevoll \(2008\)](#). (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 \(2008\)](#).

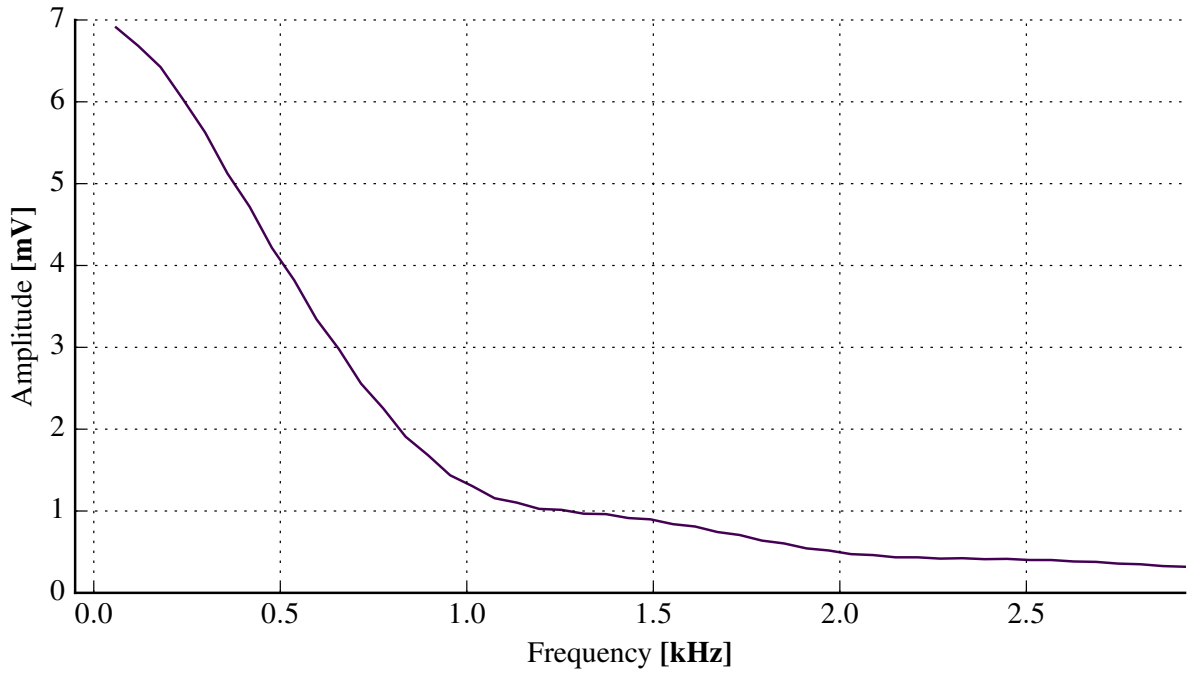


Figure 3.2: Frequency spectrum of simulated somatic membrane potential.

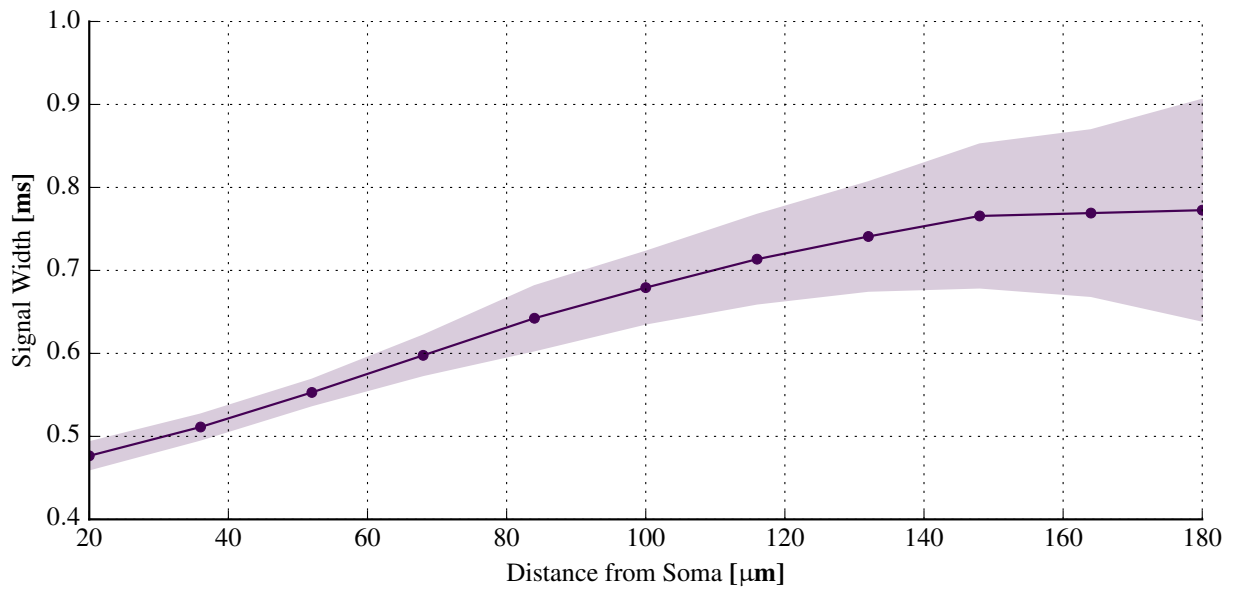


Figure 3.3: Spike width over distance. Mean  $\pm$  1 std.

Pettersen & Einevoll (2008) reports a spike amplitude above  $150\mu V$  at  $20\mu m$ , this does not match current findings. Figure 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 (2008), 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: Clarify this, put reference back to theory chapter.)

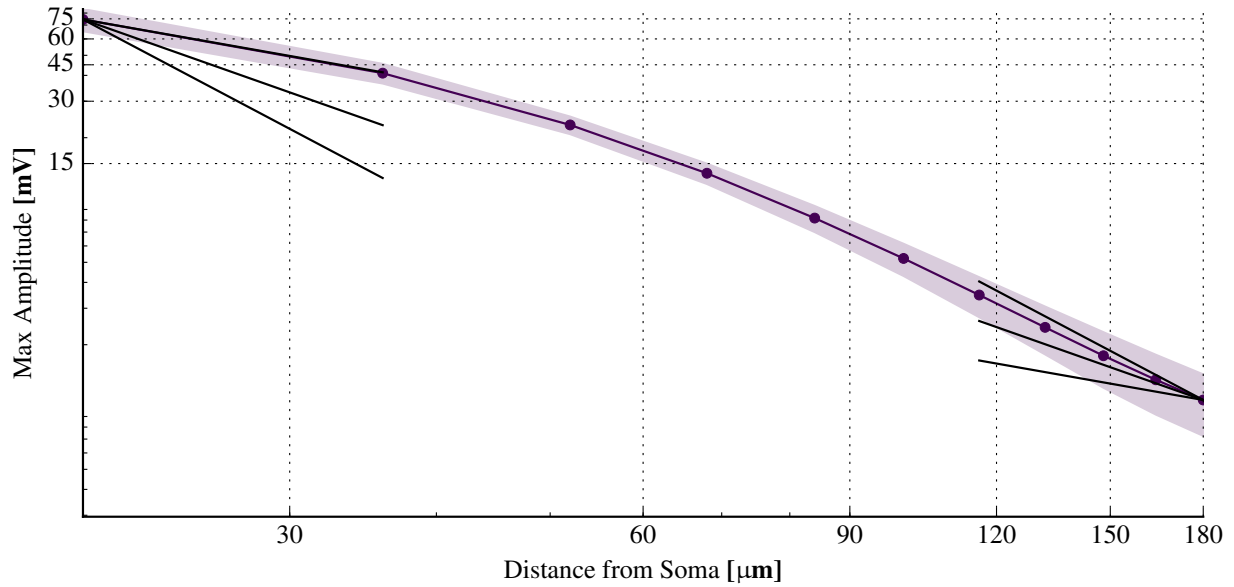


Figure 3.4: Spike amplitude over distance. Mean  $\pm$  1 std. The power law decays  $1/r$ ,  $1/r^2$  and  $1/r^3$  are shown at the leftmost and rightmost data points.

### 3.1.3 Discussion?

## 3.2 Blue Brain

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

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

## 3.3 Allen Brain Institute

My specific 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 available 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.

Reproduction of results from [pettersen2008amplitude](#)

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



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