

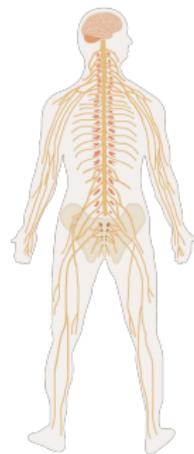
UNCERTAINTY QUANTIFICATION IN NEUROSCIENCE

Simen Tennøe



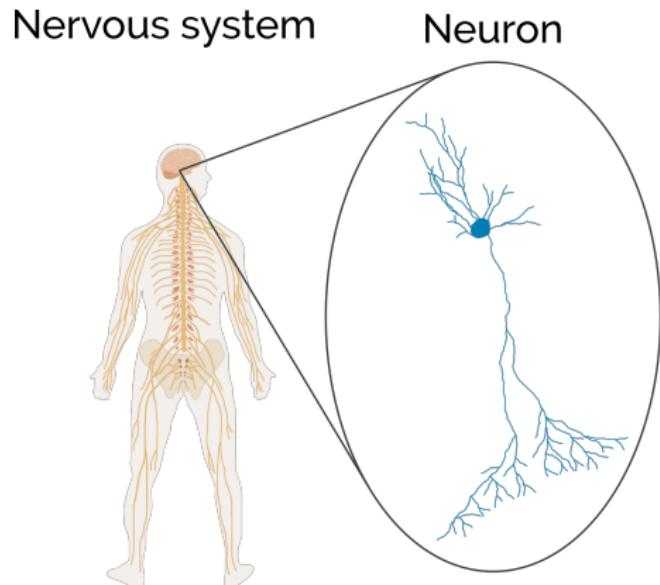
Neuroscience is a diverse field

Nervous system



Source: Wikimedia commons
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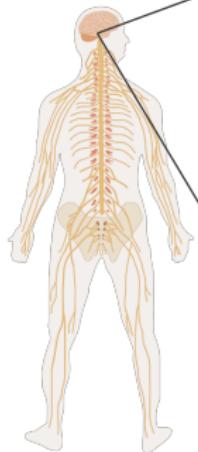
Neuroscience is a diverse field



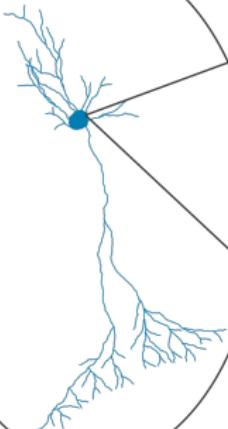
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Neuroscience is a diverse field

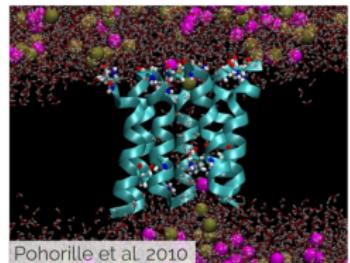
Nervous system



Neuron



Ion channel



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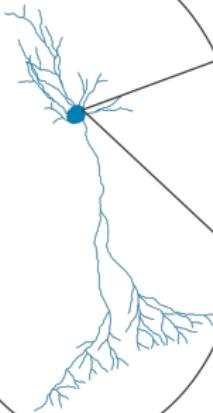
Neuroscience spans a wide range of temporal scales

Nervous system

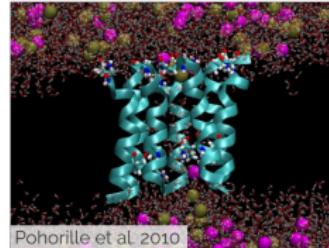


Source: Wikimedia commons
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Neuron



Ion channel



Aging

~ 100
years

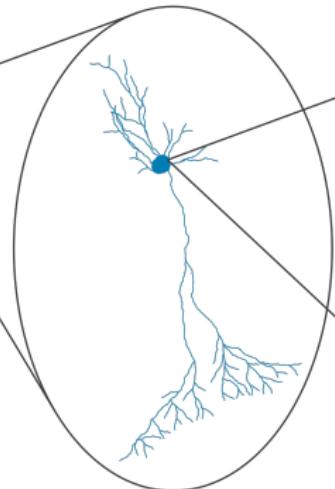
Neuroscience spans a wide range of temporal scales

Nervous system

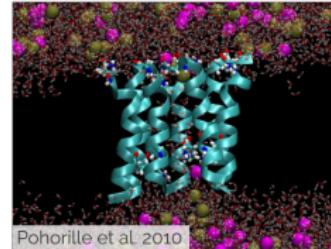


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Neuron



Ion channel



Aging

~ 100
years



Molecular dynamics

0.000000000001 s
 10^{-12} s

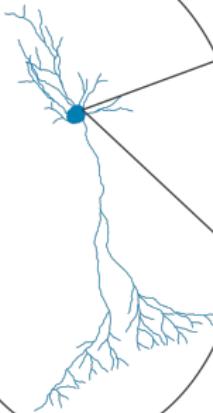
...and spatial scales

Nervous system

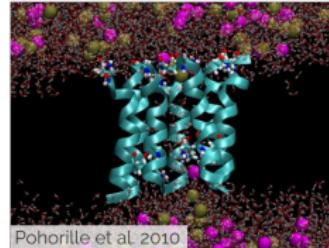


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Neuron



Ion channel



Longest
nerves

~ 1 m

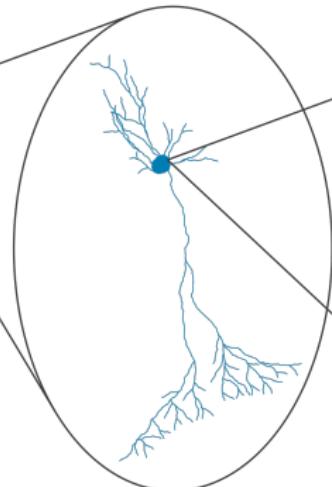
...and spatial scales

Nervous system

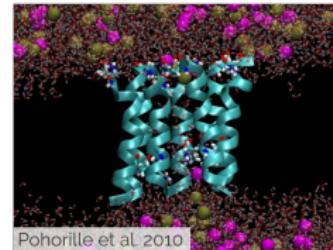


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Neuron



Ion channel



Longest
nerves
 ~ 1 m



Molecular dynamics
0.000000001 m
 10^{-9} m

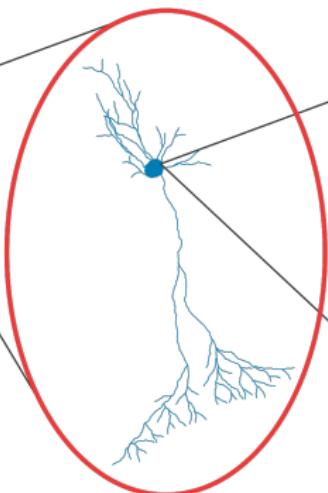
My work has been on the scale of neurons

Nervous system

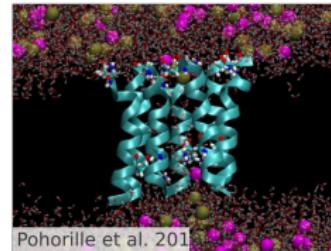


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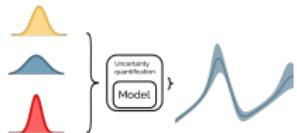
Neuron



Ion channel

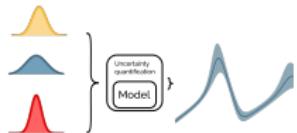


Overview of the thesis and this presentation



Uncertainty quantification
and sensitivity analysis

Overview of the thesis and this presentation

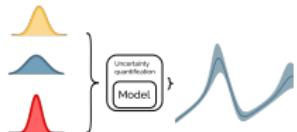


Uncertainty quantification
and sensitivity analysis



Data storage

Overview of the thesis and this presentation



Uncertainty quantification
and sensitivity analysis

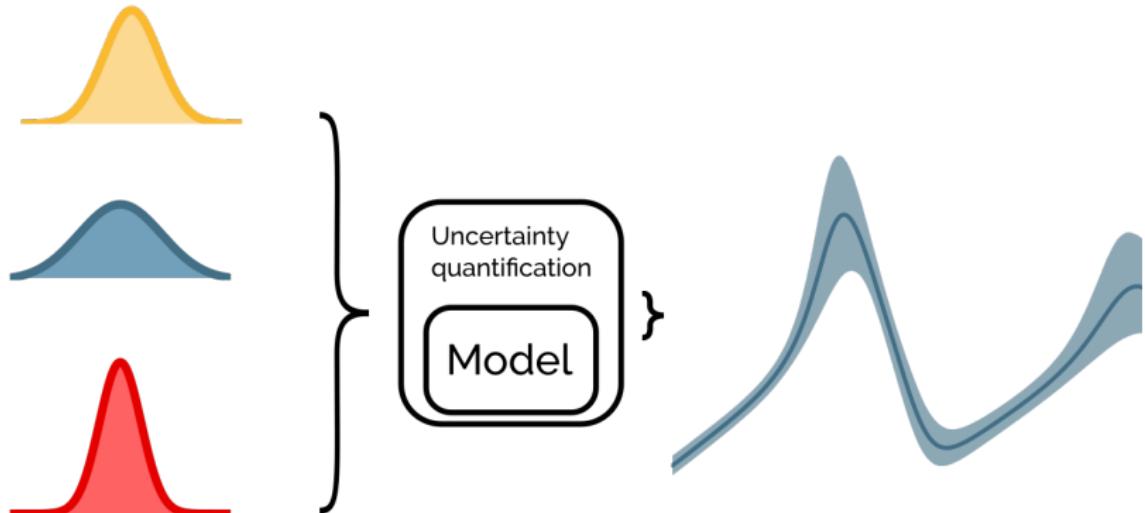


Data storage

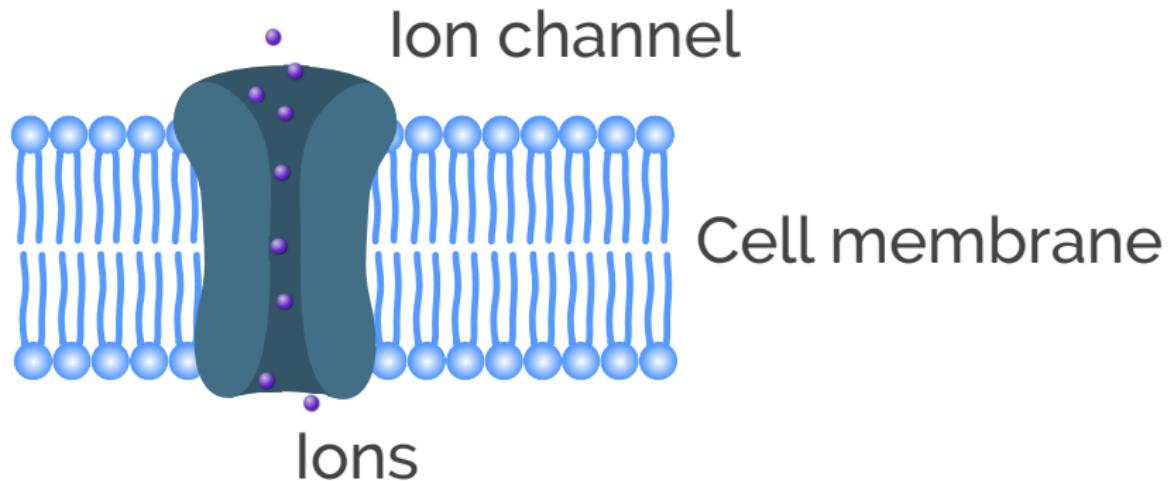


Education

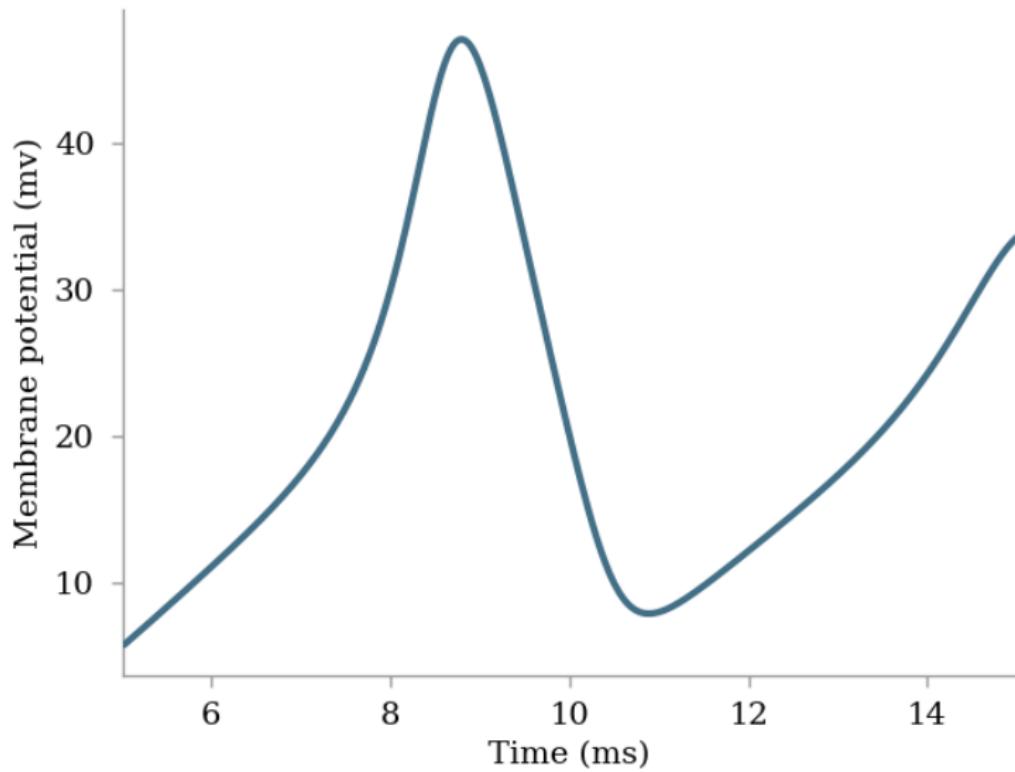
Uncertainty quantification and sensitivity analysis



Neurons generate action potentials by sending ions through ion channels



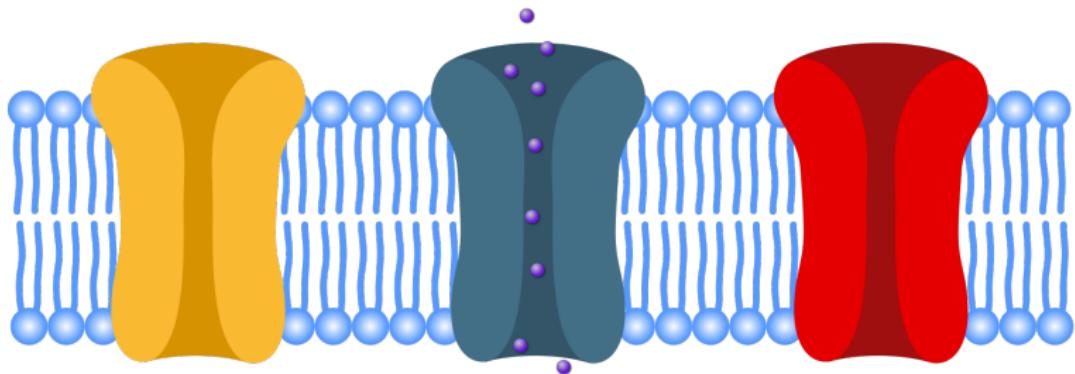
Membrane potential of the Hodgkin-Huxley model with a step current



The equation describing the Hodgkin-Huxley model

$$I = C_m \frac{dV_m}{dt} + \bar{g}_K(\dots) + \bar{g}_{Na}(\dots) + \bar{g}_I(\dots)$$

The Hodgkin-Huxley model has three types of ion channels



$$\bar{g}_{\text{Na}}$$

Potassium conductance



$$\bar{g}_{\text{K}}$$

Sodium conductance

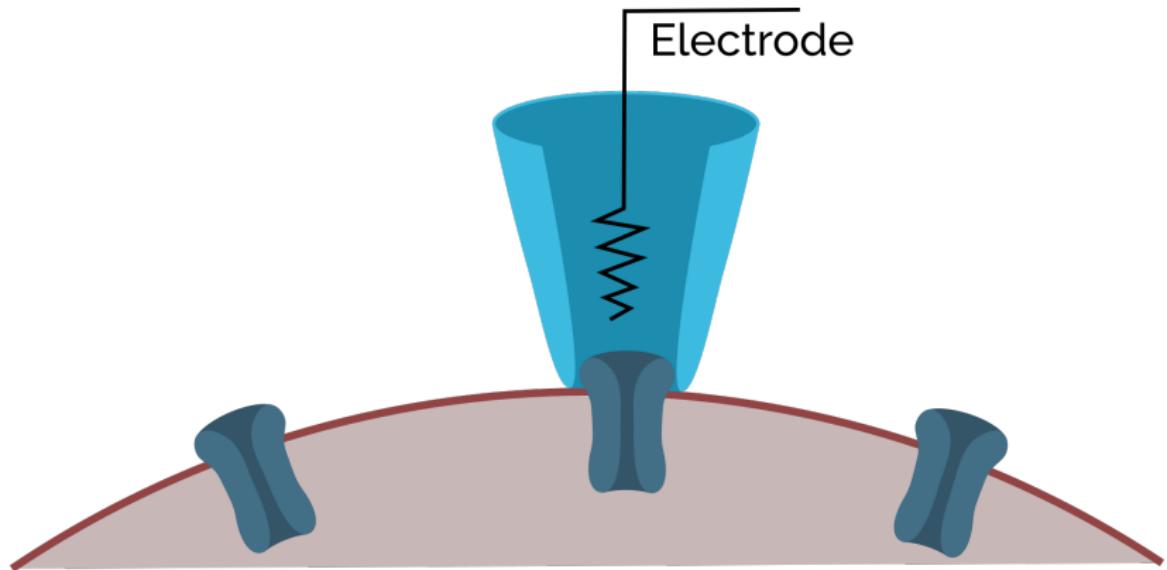


$$\bar{g}_l$$

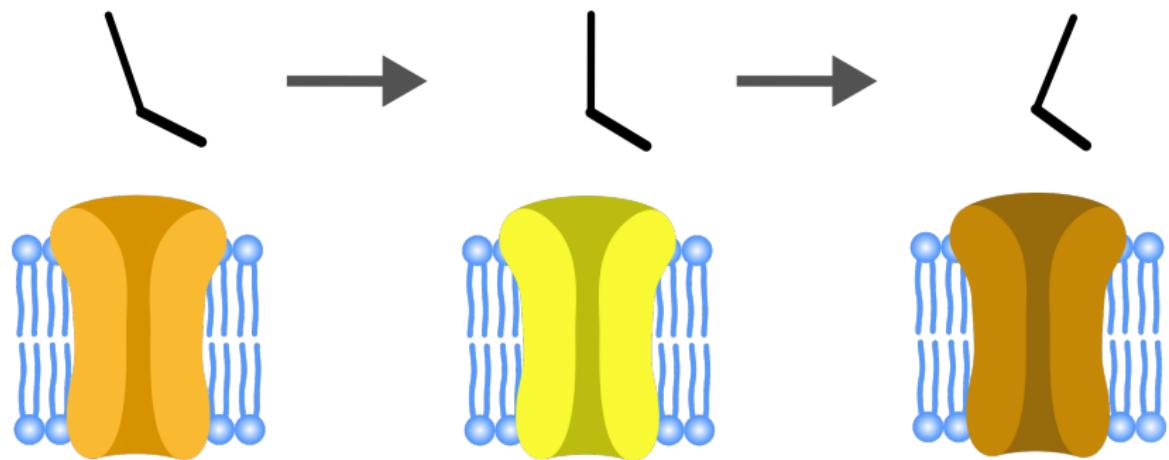
Leak conductance

Problem: the parameters do not have exact
fixed values

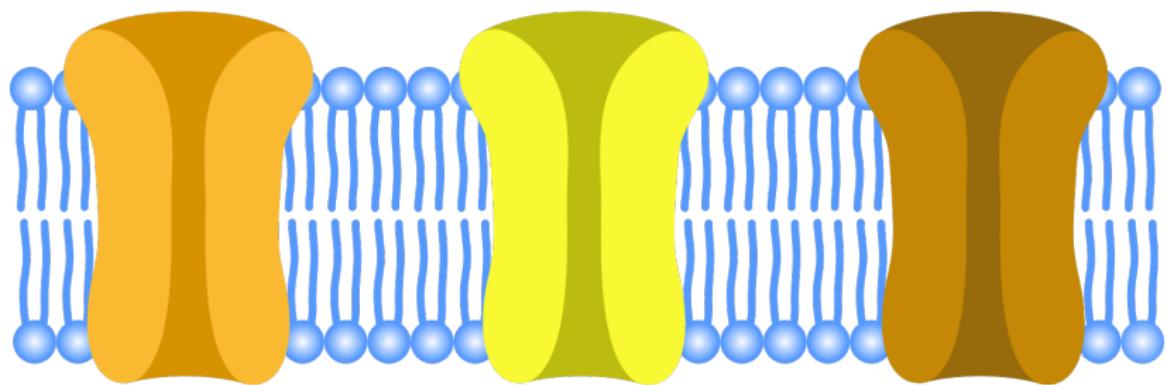
Measurement uncertainty



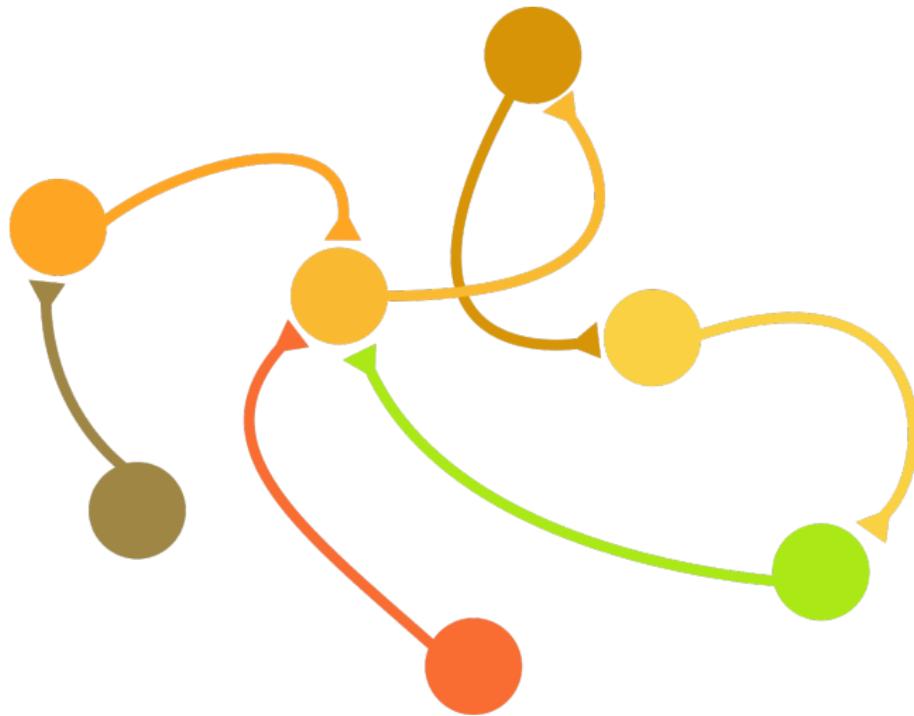
Biological variability: parameters change over time



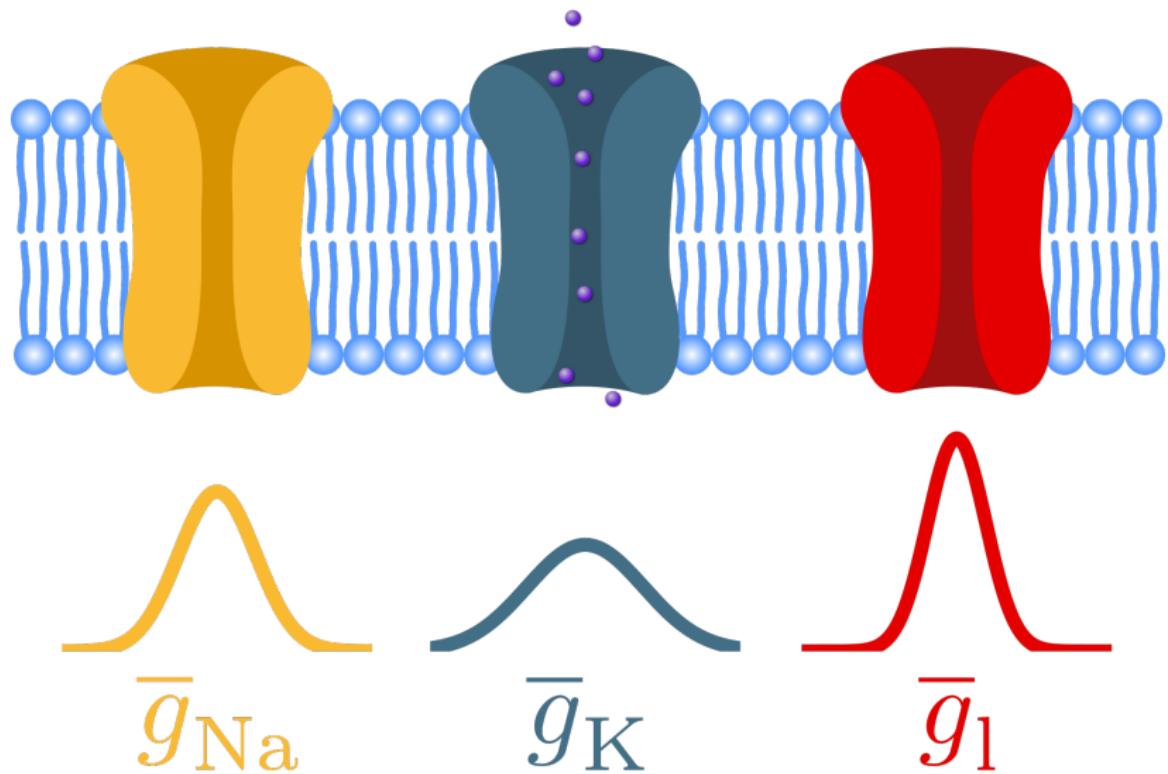
Biological variability: parameters vary within a neuron



Biological variability: parameters vary between several neurons of the same type

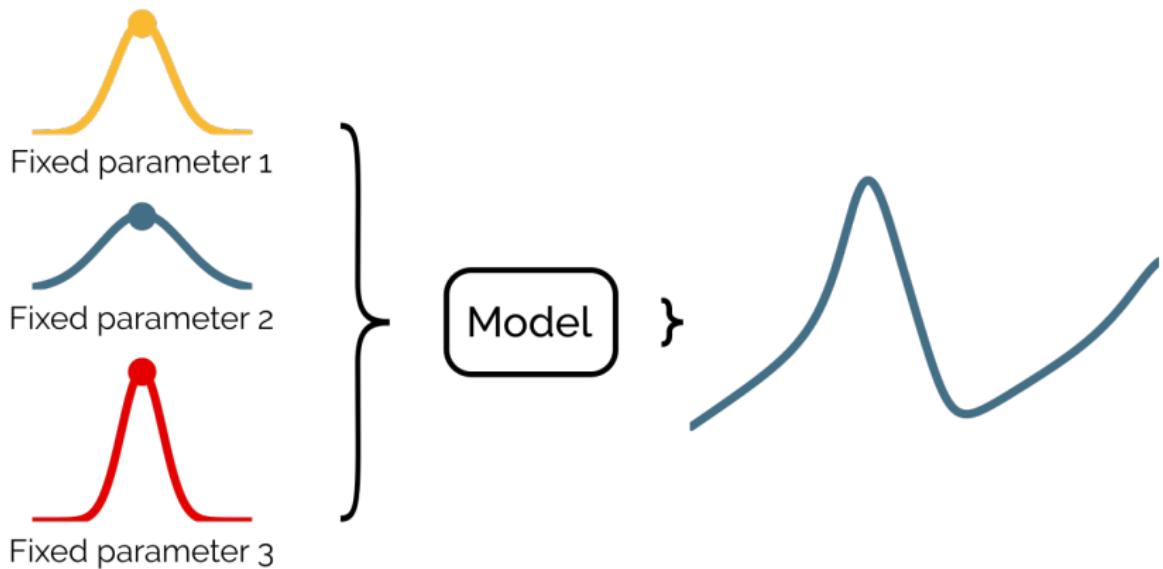


Parameters are best described by distributions

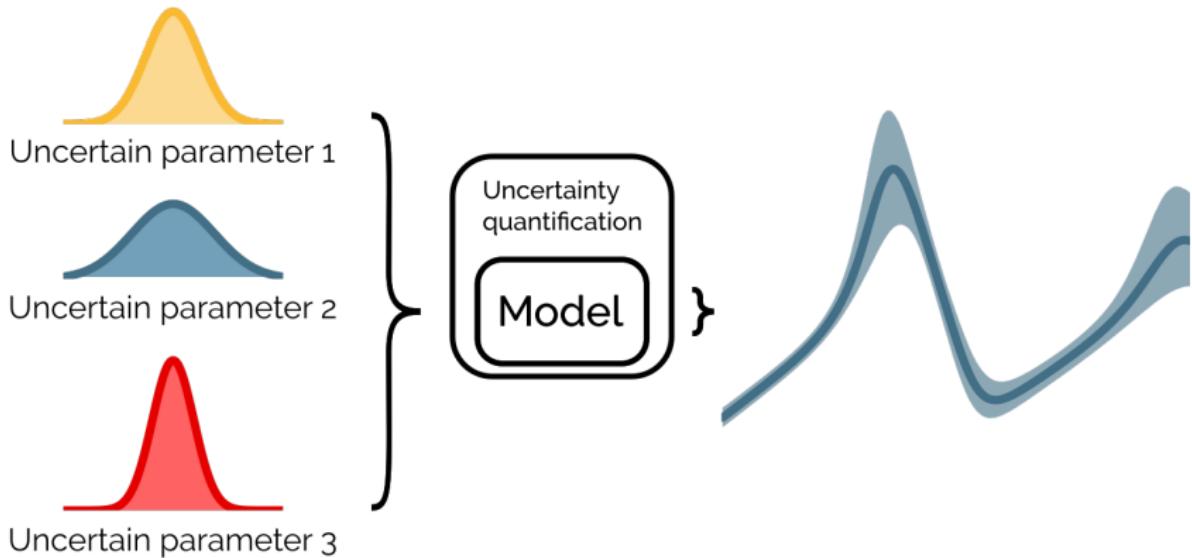


Uncertainty quantification enables us to take the effects of uncertain parameters into account

Uncertainty quantification enables us to take the effects of uncertain parameters into account



Uncertainty quantification enables us to take the effects of uncertain parameters into account





A Python toolbox for uncertainty quantification

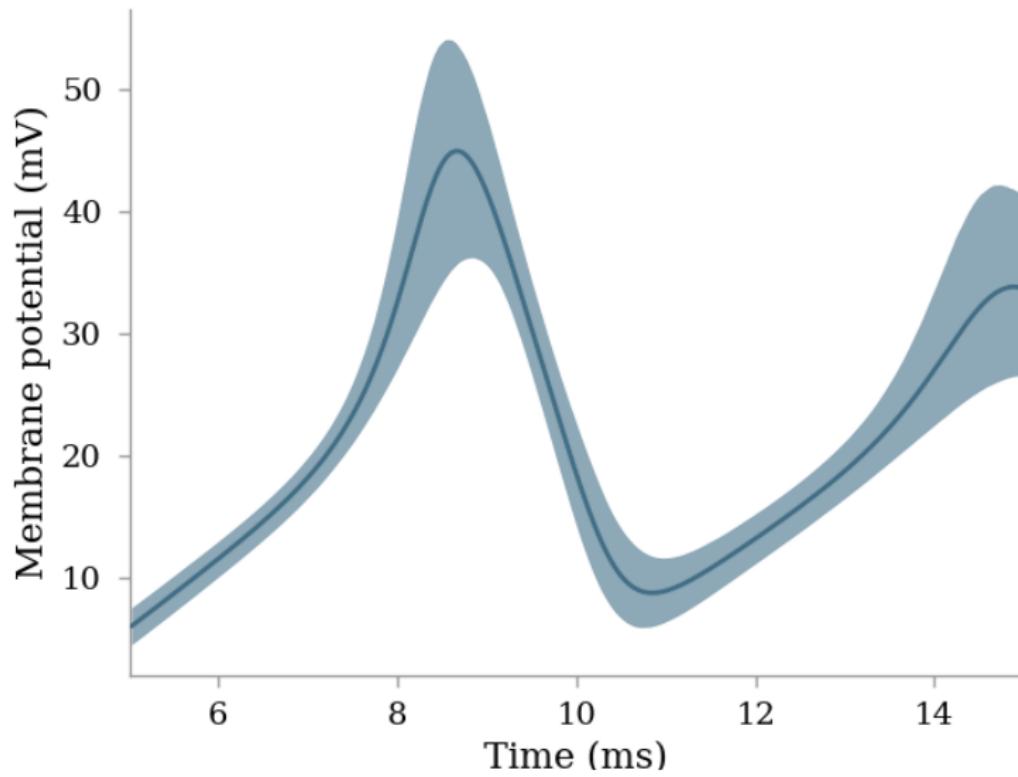


A Python toolbox for uncertainty quantification

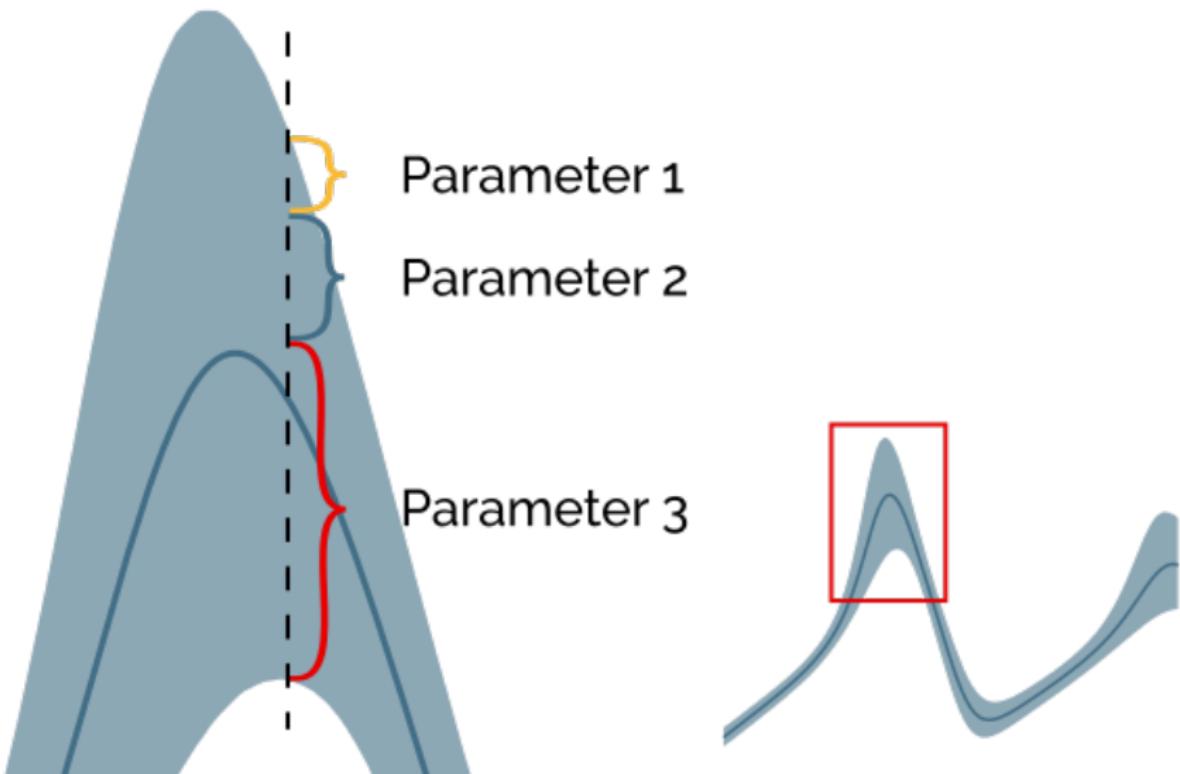
Uses both:

- ▶ Highly efficient **polynomial chaos expansions**
- ▶ Traditional **quasi-Monte Carlo methods**

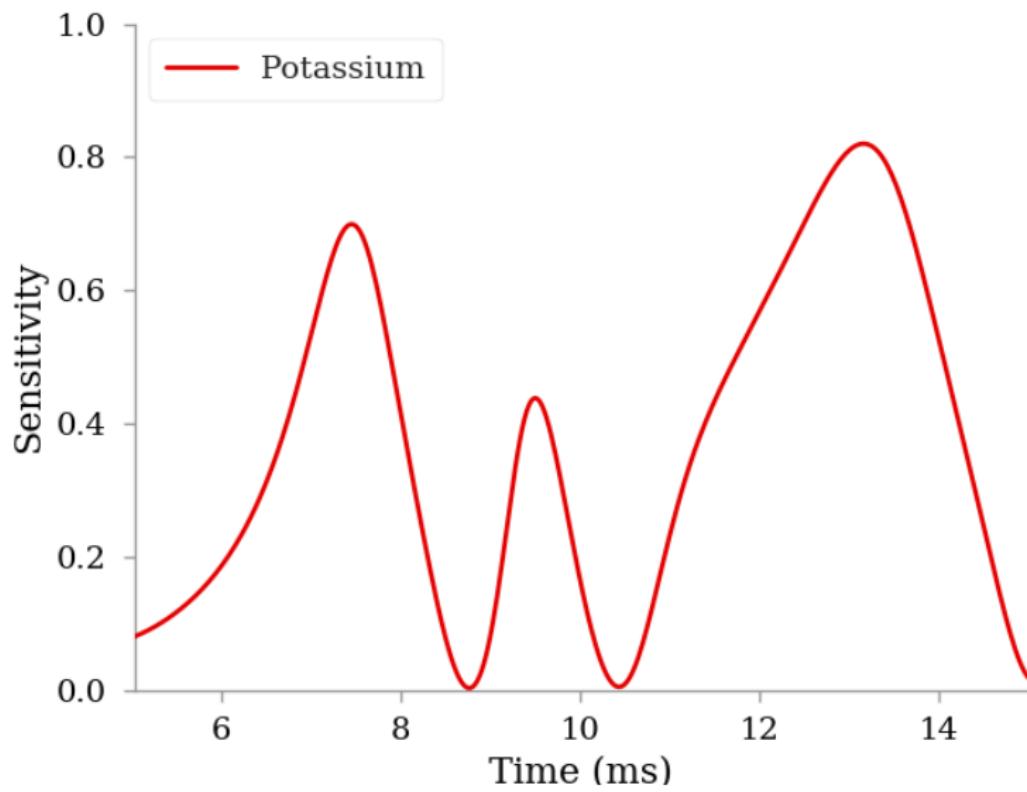
90% prediction interval of the Hodgkin-Huxley model



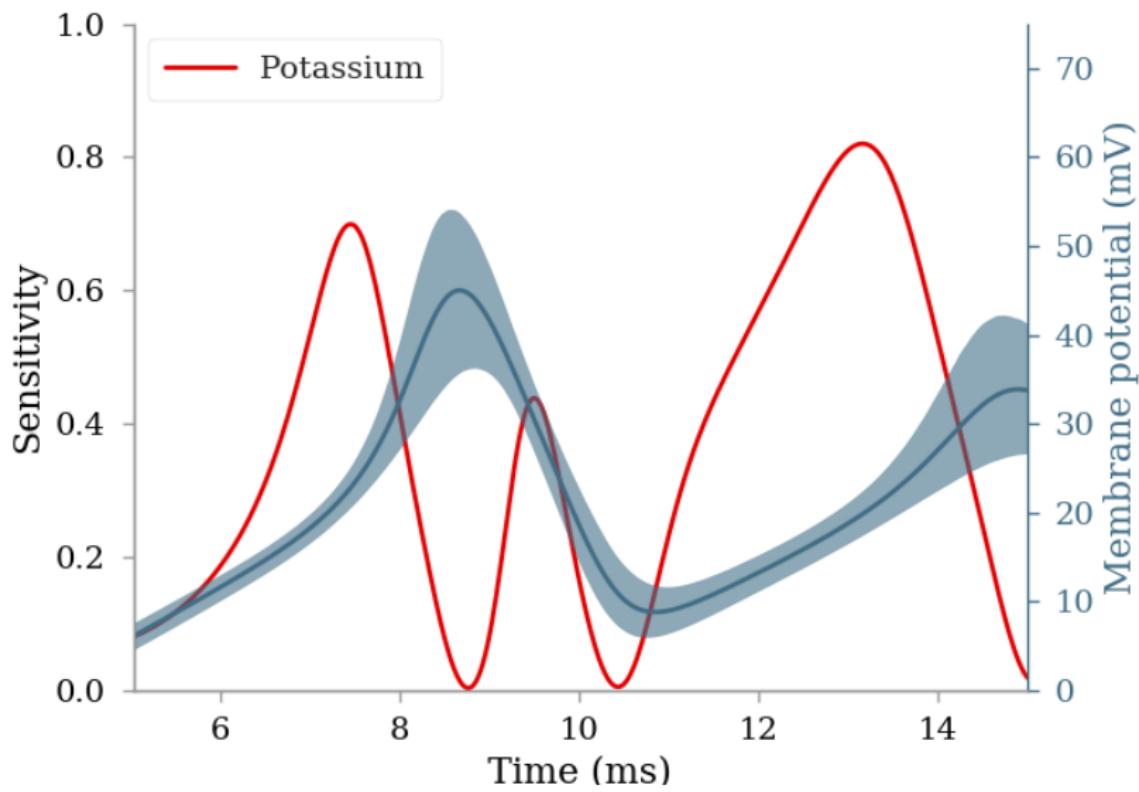
Sensitivity analysis quantifies how much of the uncertainty each parameter is responsible for



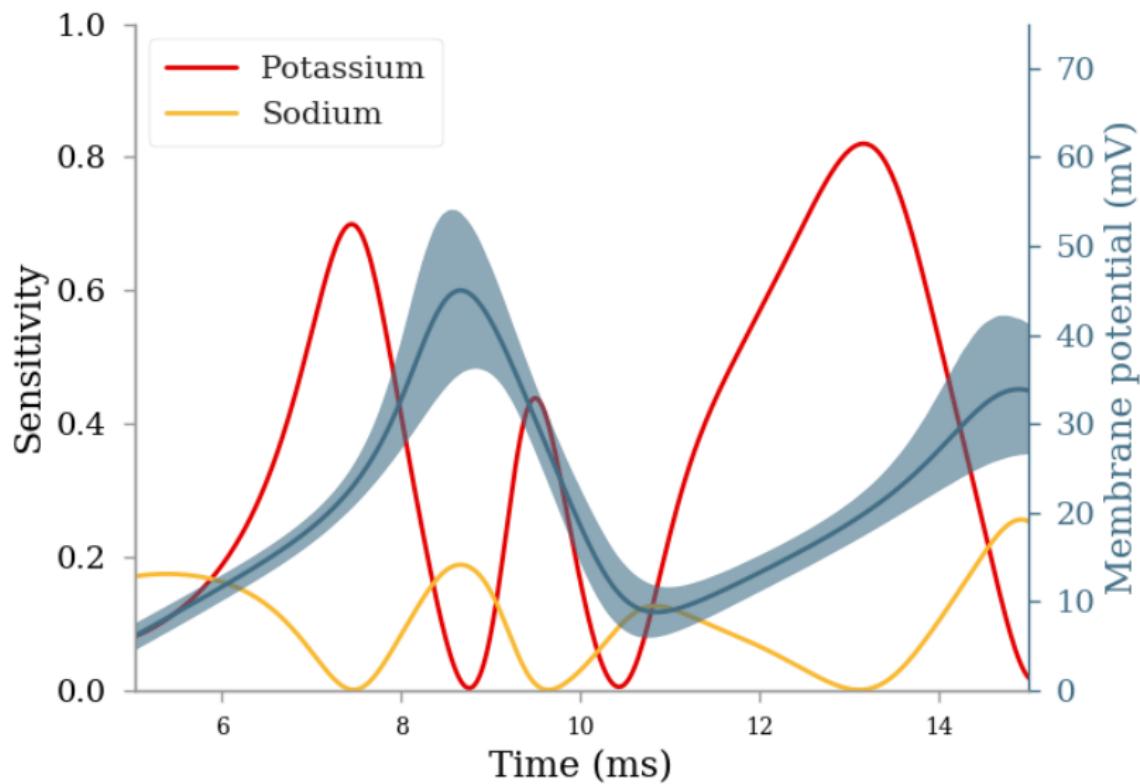
Sensitivity of the conductances in the Hodgkin-Huxley model



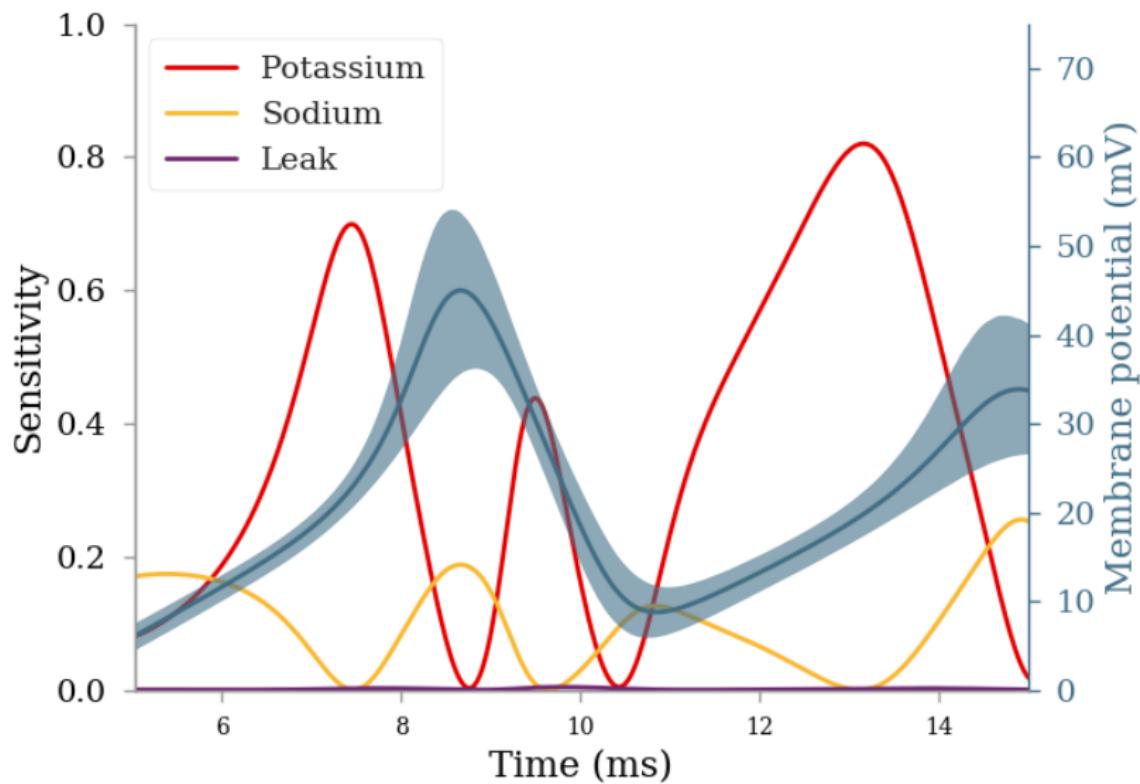
Sensitivity of the conductances in the Hodgkin-Huxley model



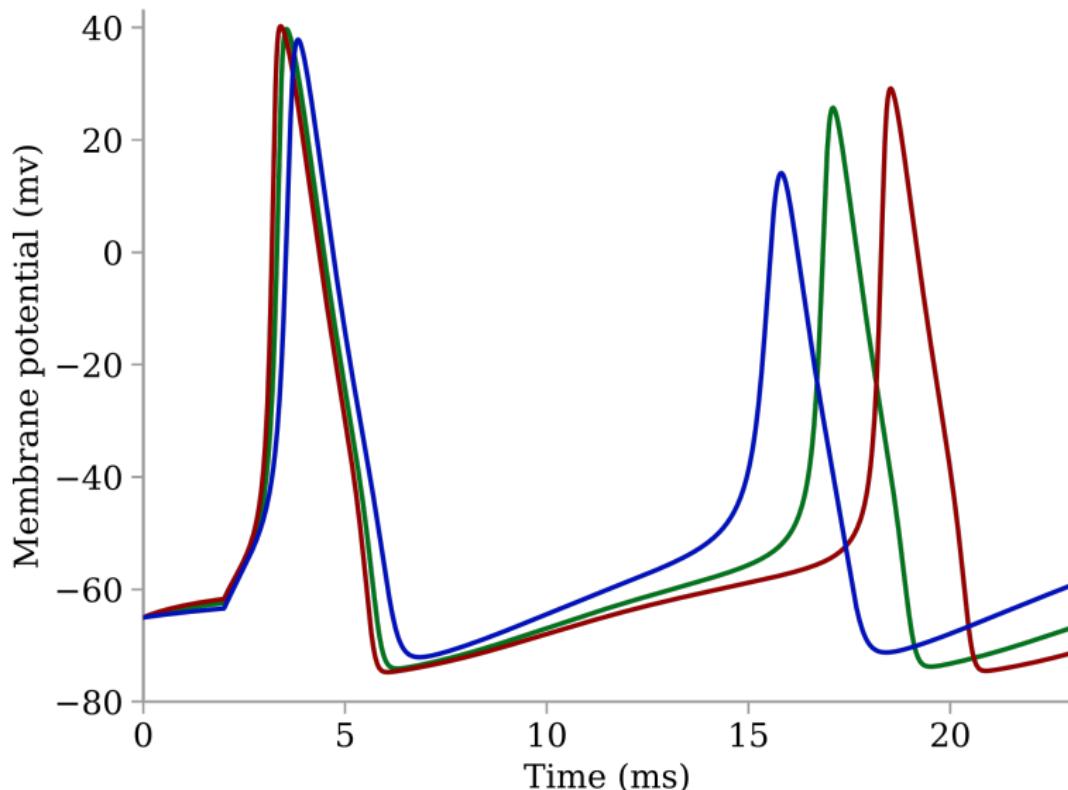
Sensitivity of the conductances in the Hodgkin-Huxley model



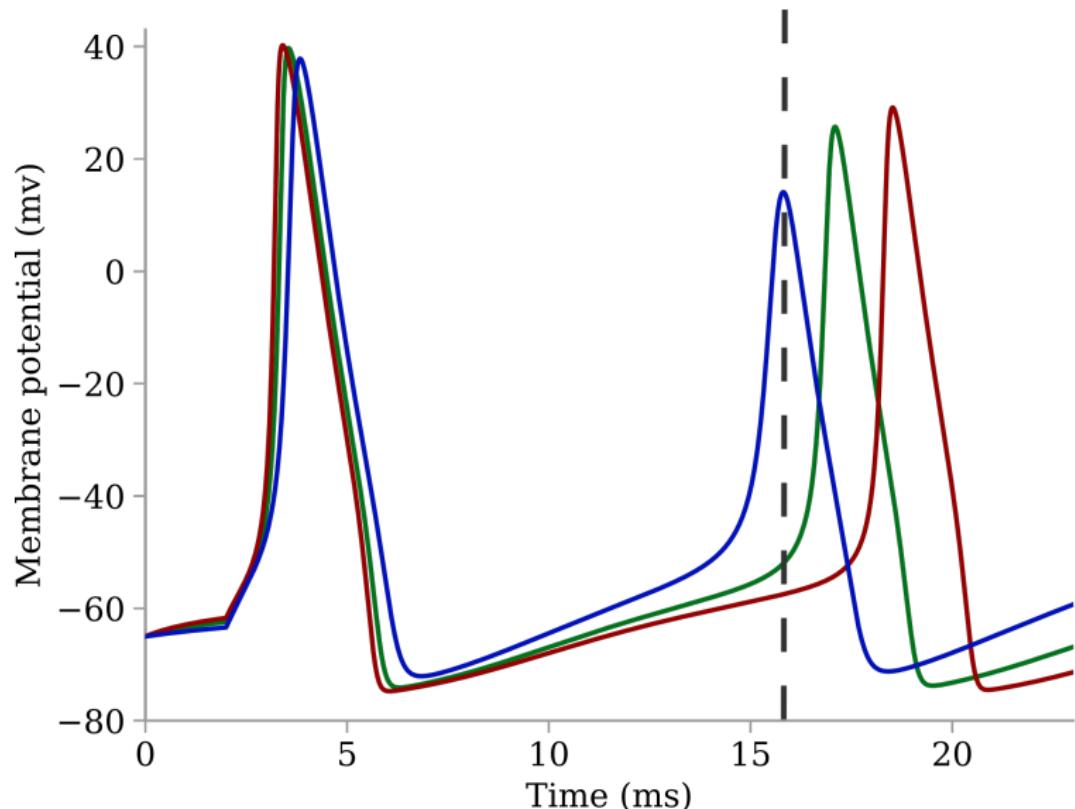
Sensitivity of the conductances in the Hodgkin-Huxley model



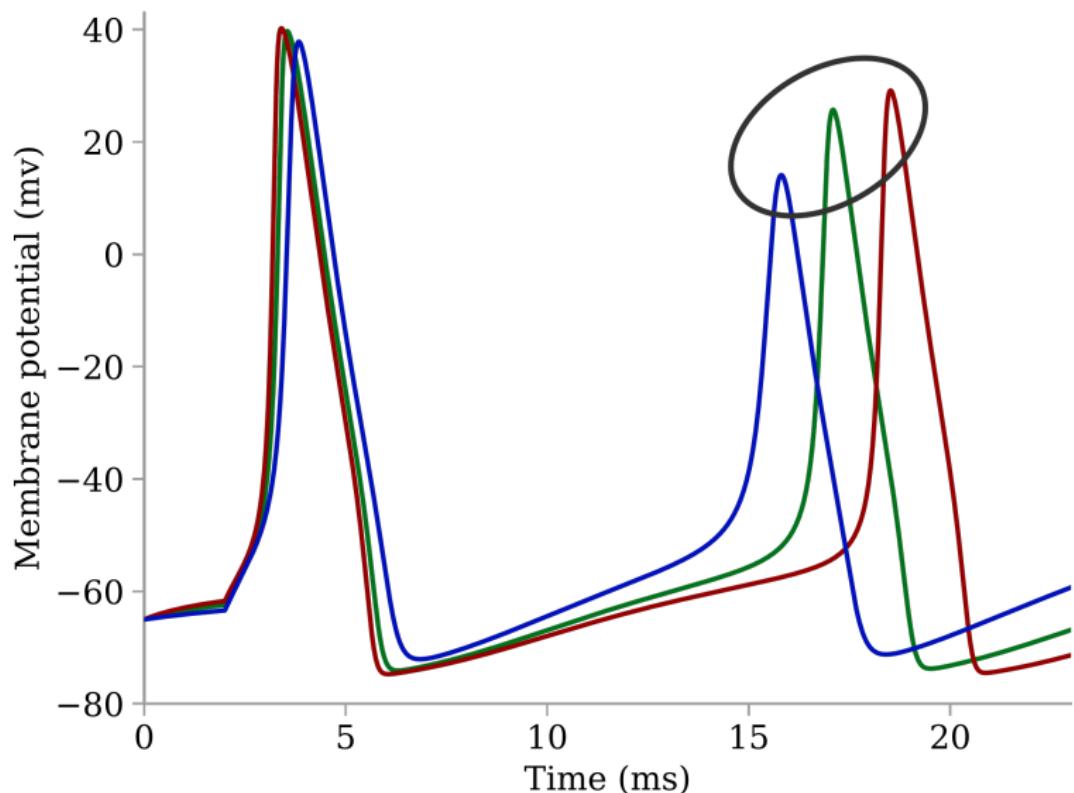
Pointwise comparison of model results give large differences due to small time shifts in spikes



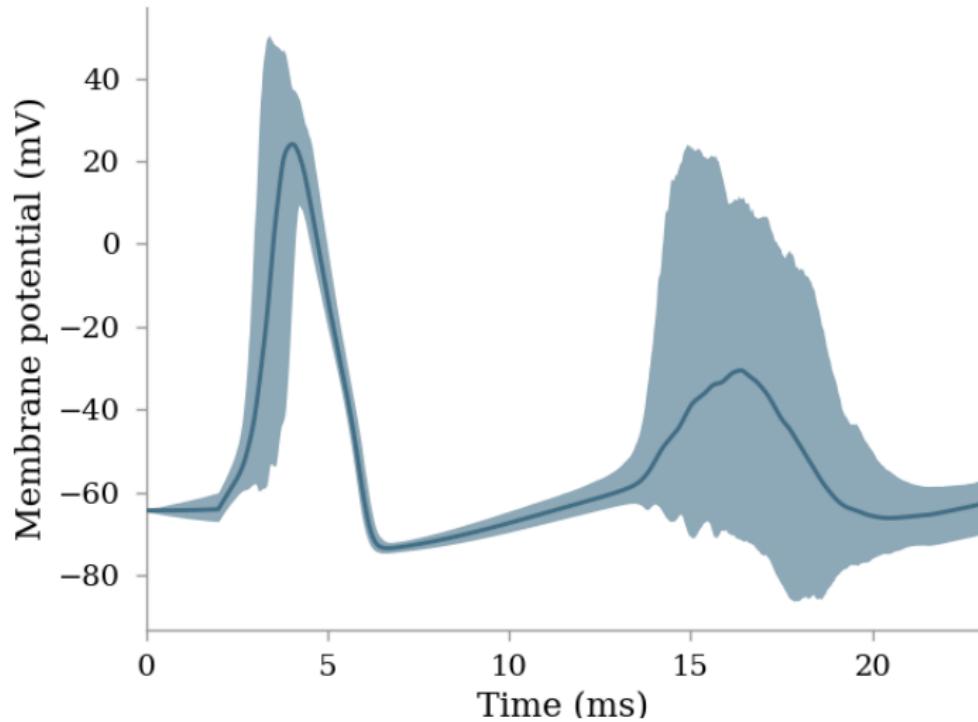
Pointwise comparison of model results give large differences due to small time shifts in spikes



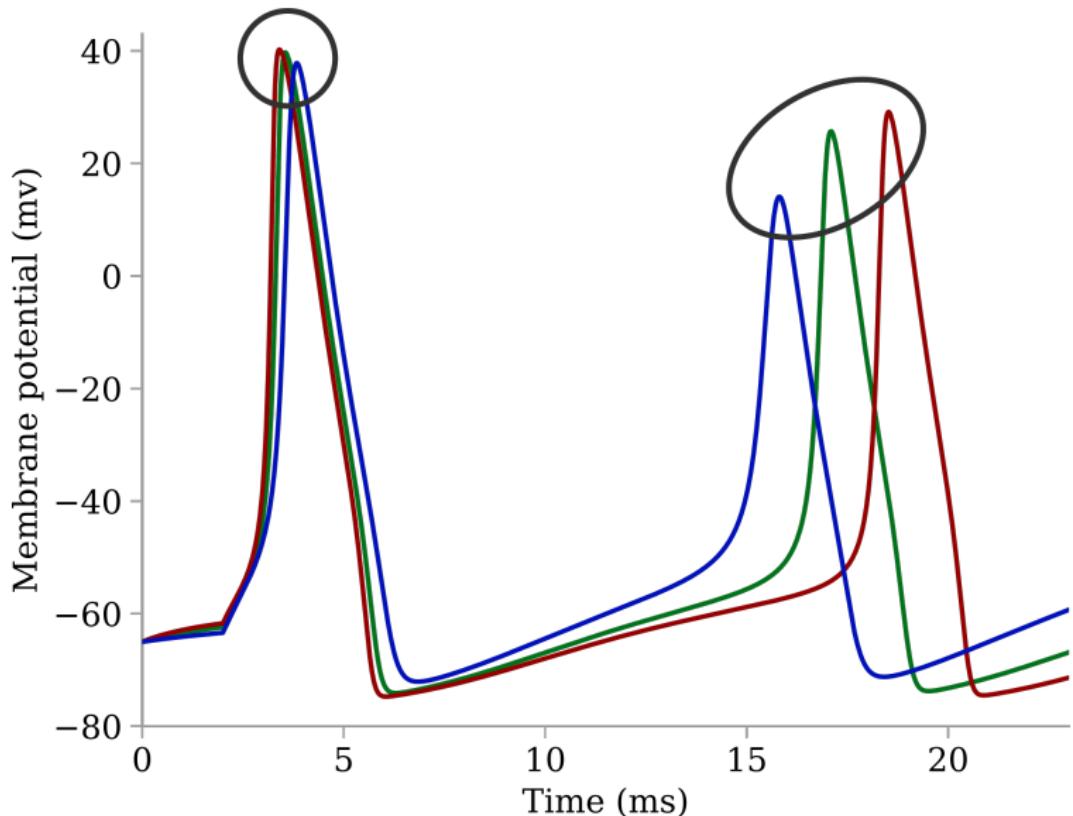
Pointwise comparison of model results give large differences due to small time shifts in spikes



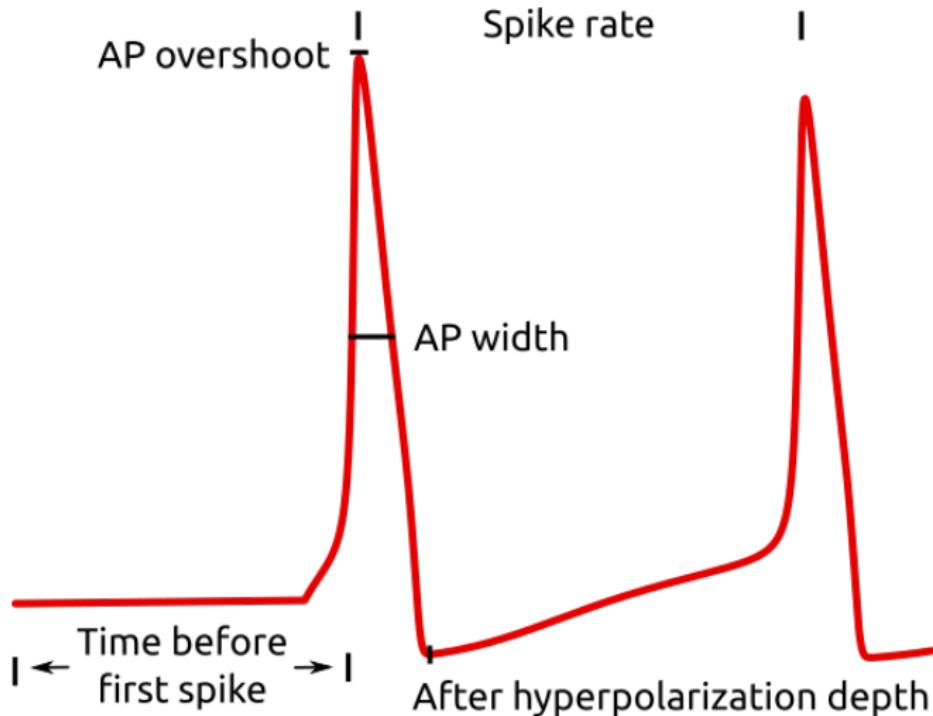
The time shifted spikes cause large variance



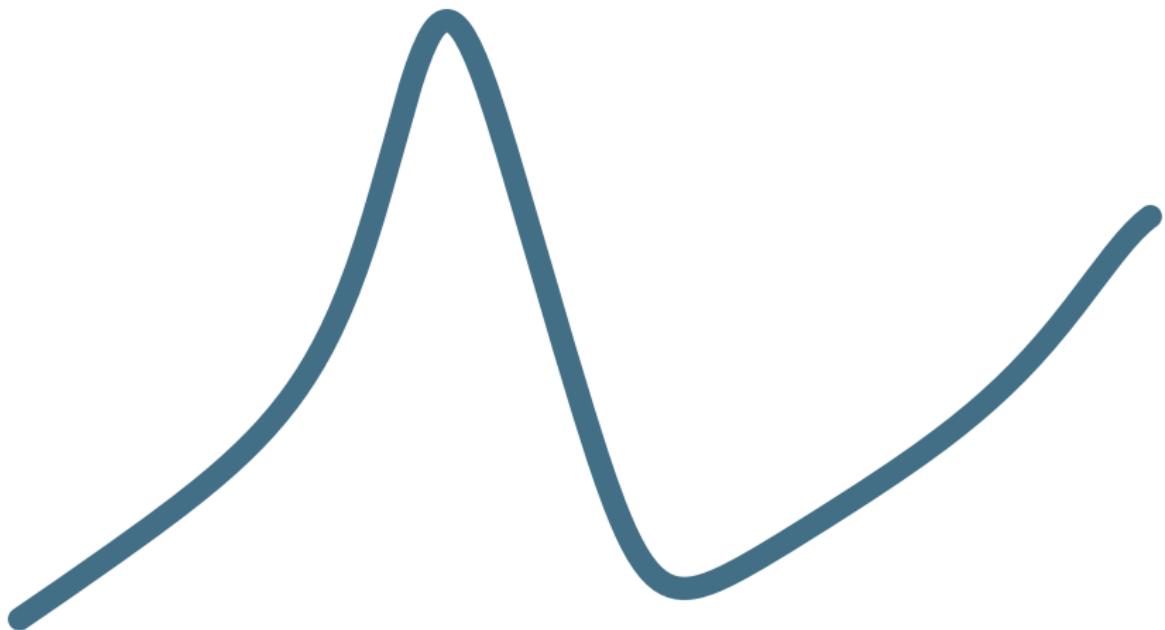
The solution is to compare features of the model, such as the number of spikes



Uncertainty calculates the uncertainty for a user selected set of features of the model



Endocrine pituitary cells behave similar to neurons

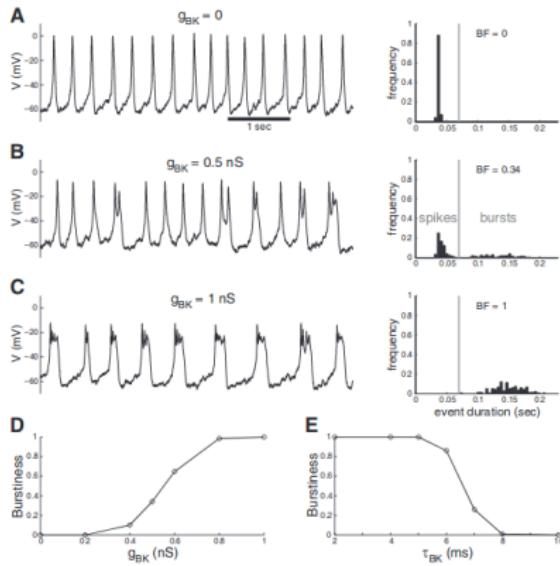


Replicated the results of a previous model of endocrine pituitary cells in rats

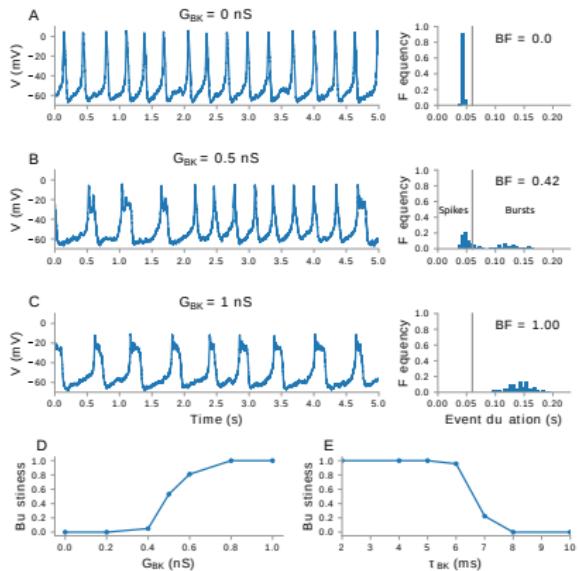


Source: Wikimedia commons - Joanna Servaes

Replicated the results of a previous model of endocrine pituitary cells in rats

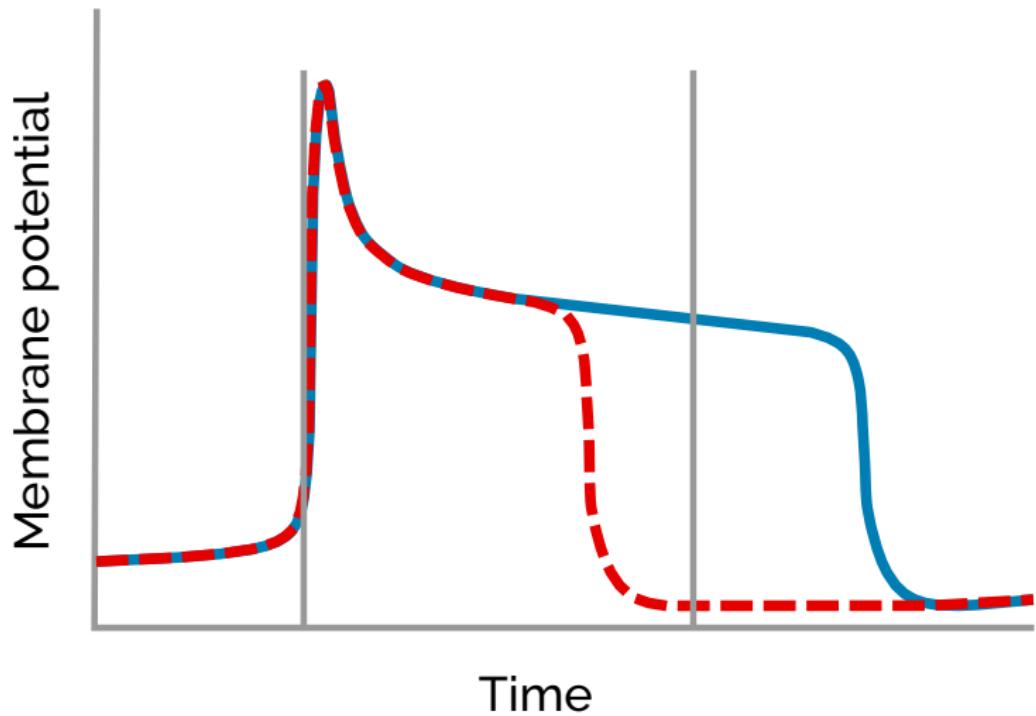


Original result

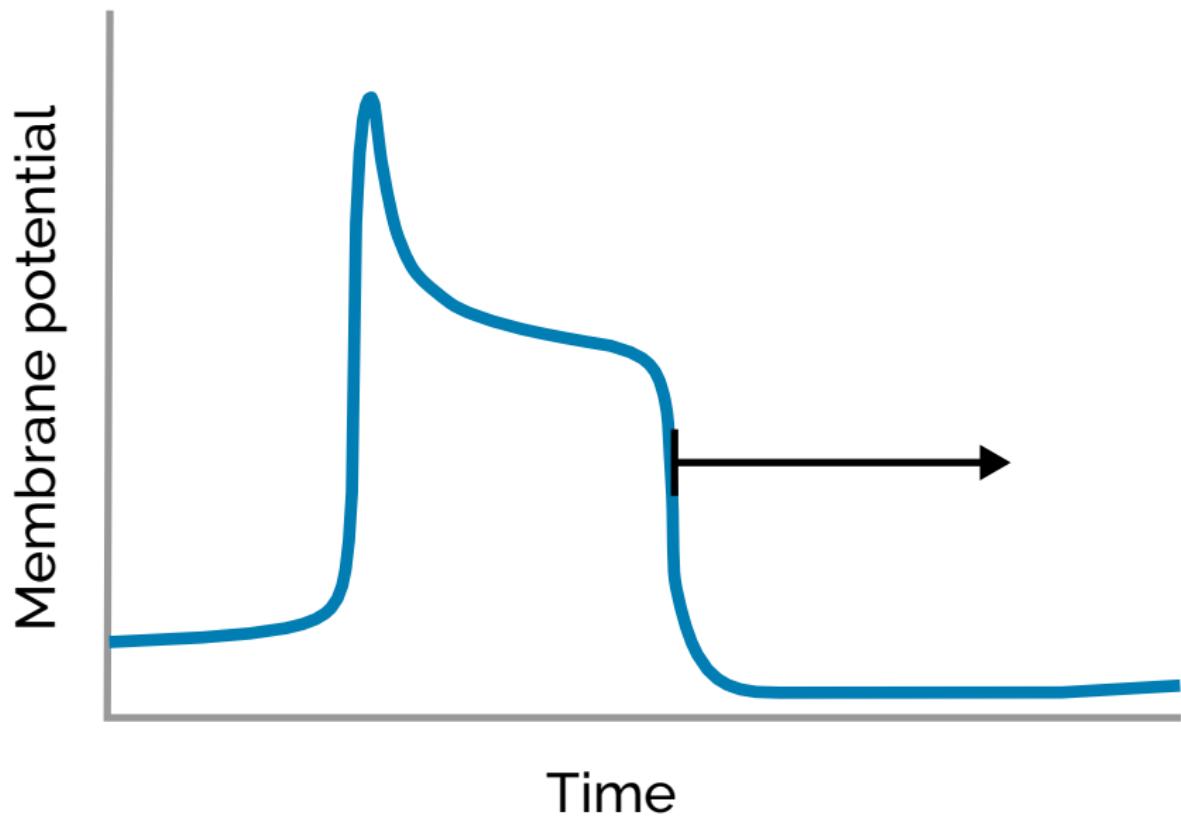


Replication

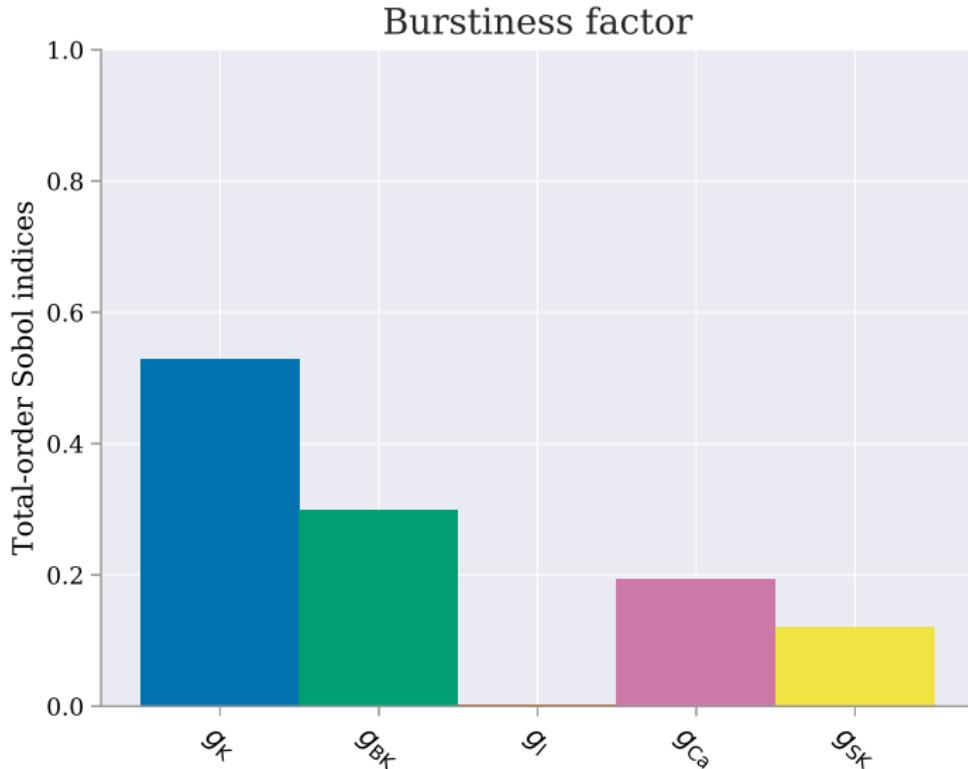
Burstiness measures the amount of action potentials with a duration longer than 60 ms



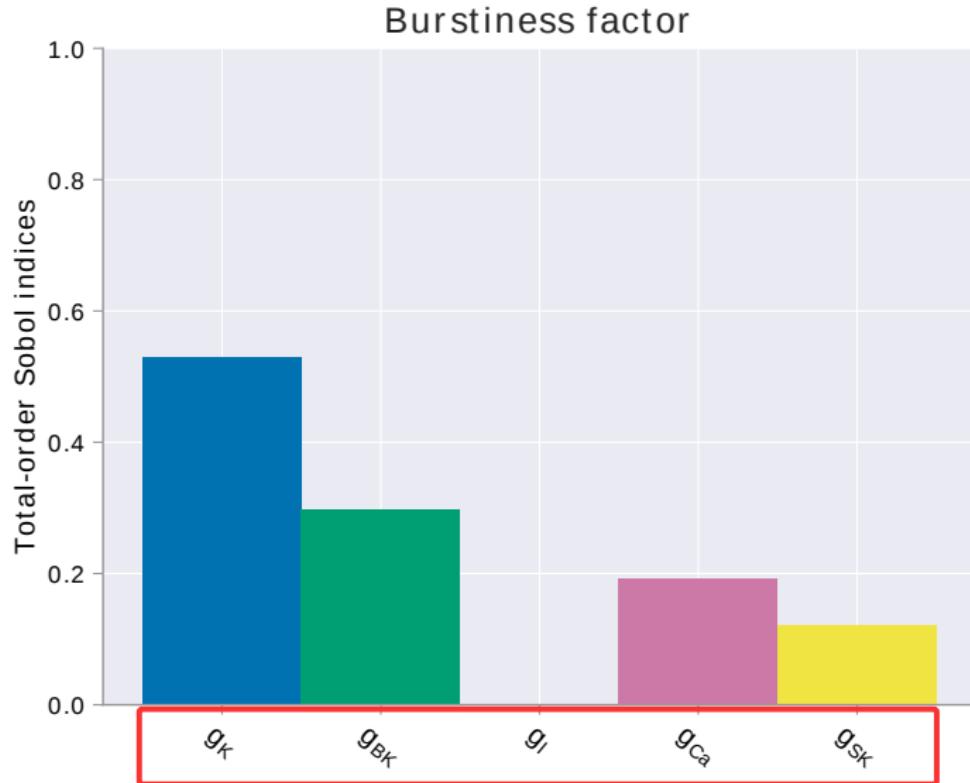
Previous results was that the big conductance potassium (K^+) current is important for bursting



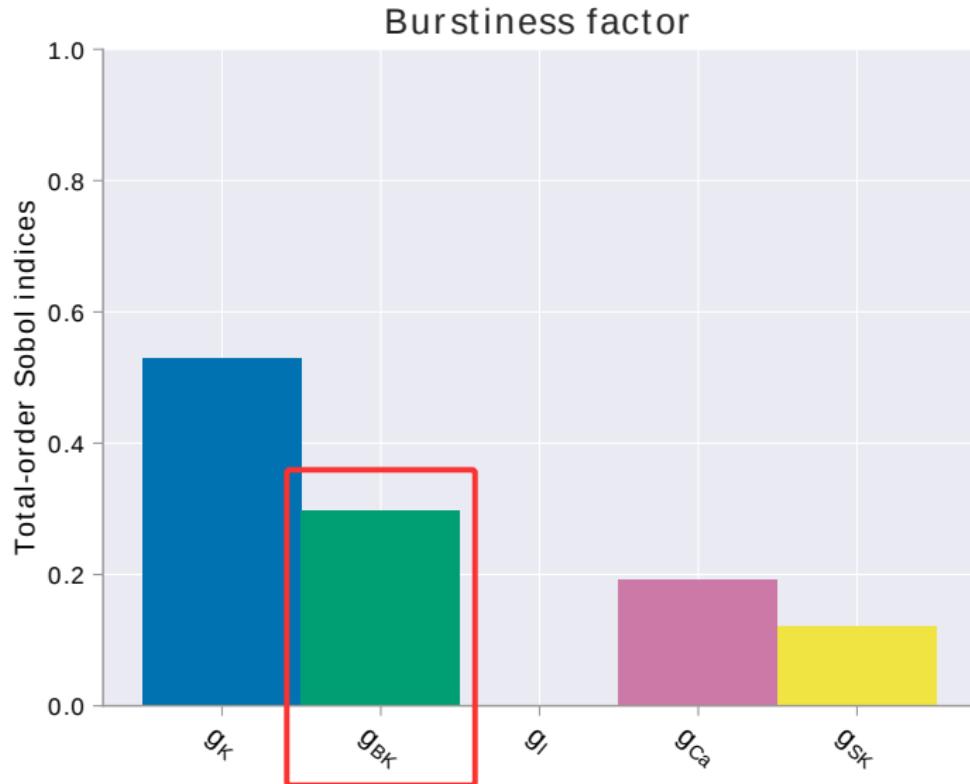
Performed an uncertainty analysis



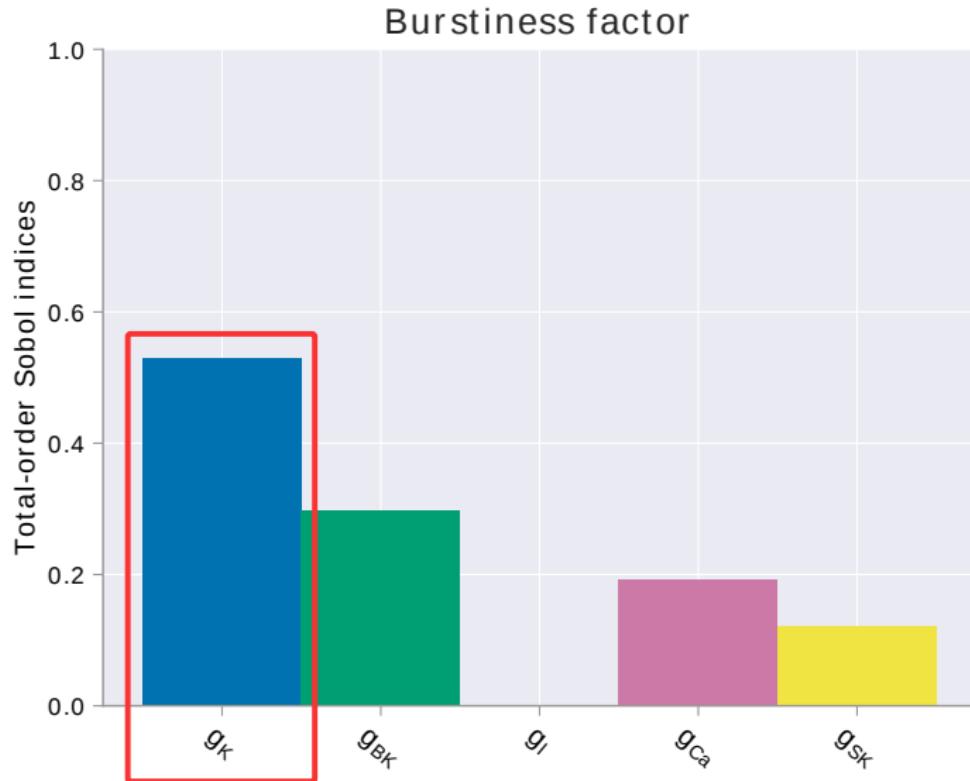
Sensitivity of the burstiness factor for each ion channel conductance



Previous results was that the big conductance potassium (K^+) current promotes bursting



We found that rectifying potassium (K^+) current had a greater effect

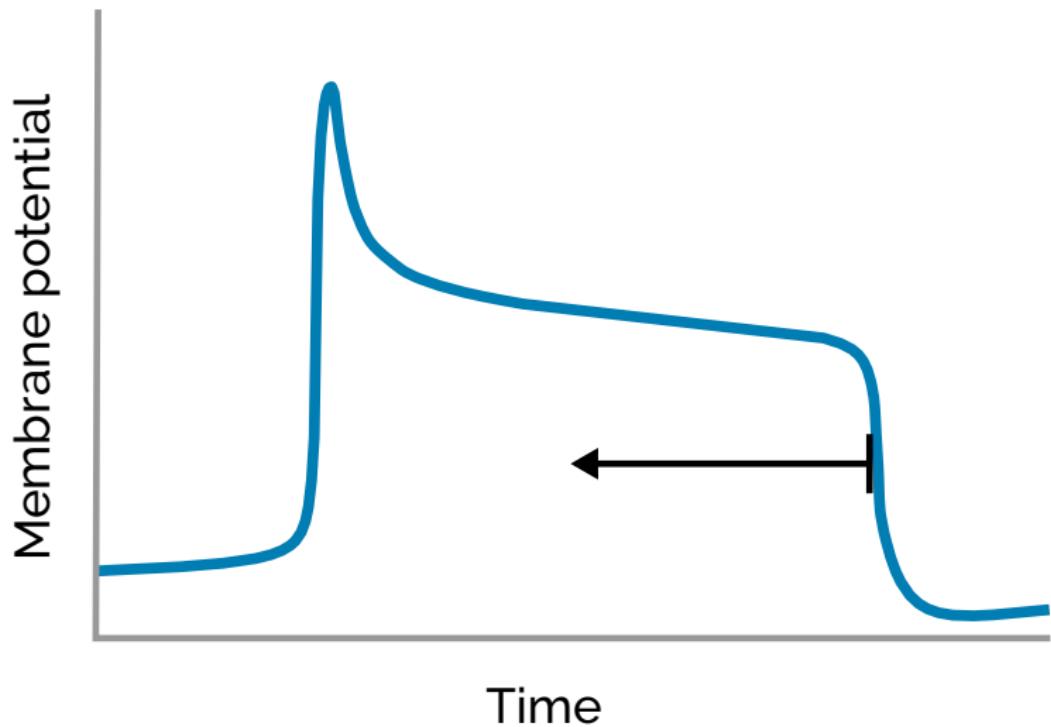


Created a model from experimental data for endocrine pituary cells in Japanese rice fish



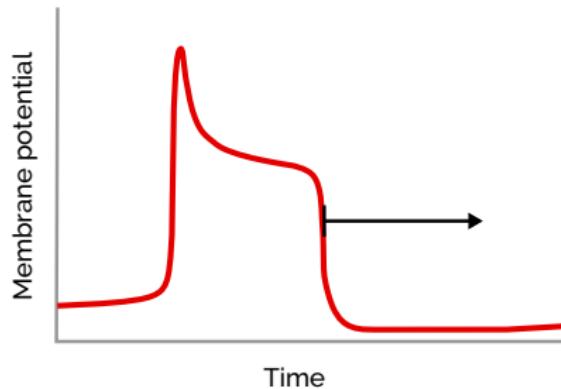
Source: Wikimedia commons - Seotaro

Big conductance potassium (K^+) makes action potentials narrower in Japanese rice fish

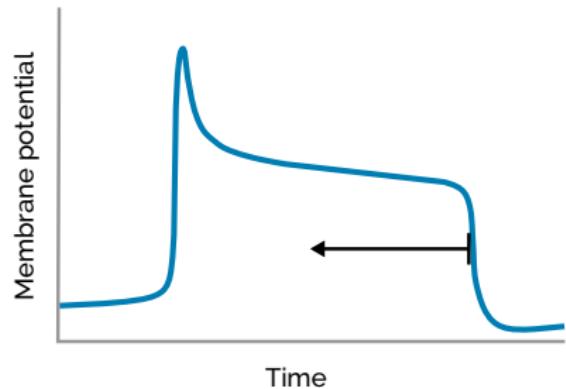


Big conductance potassium (K^+) makes action potentials narrower in Japanese rice fish

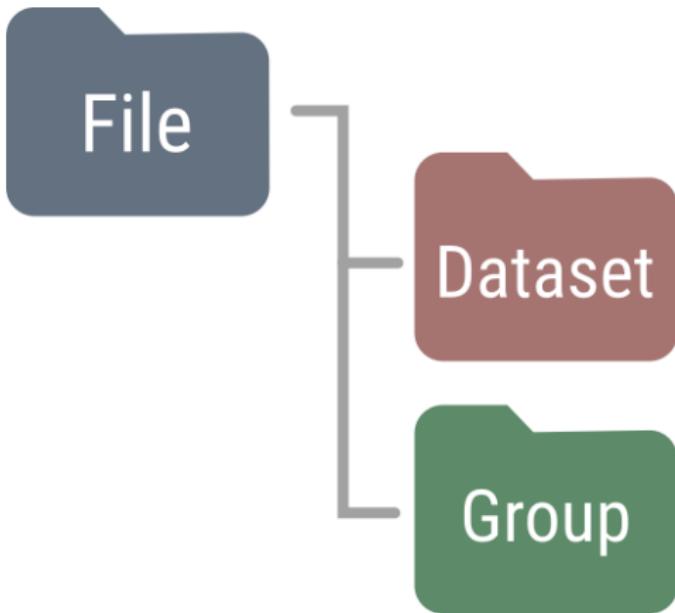
Rat



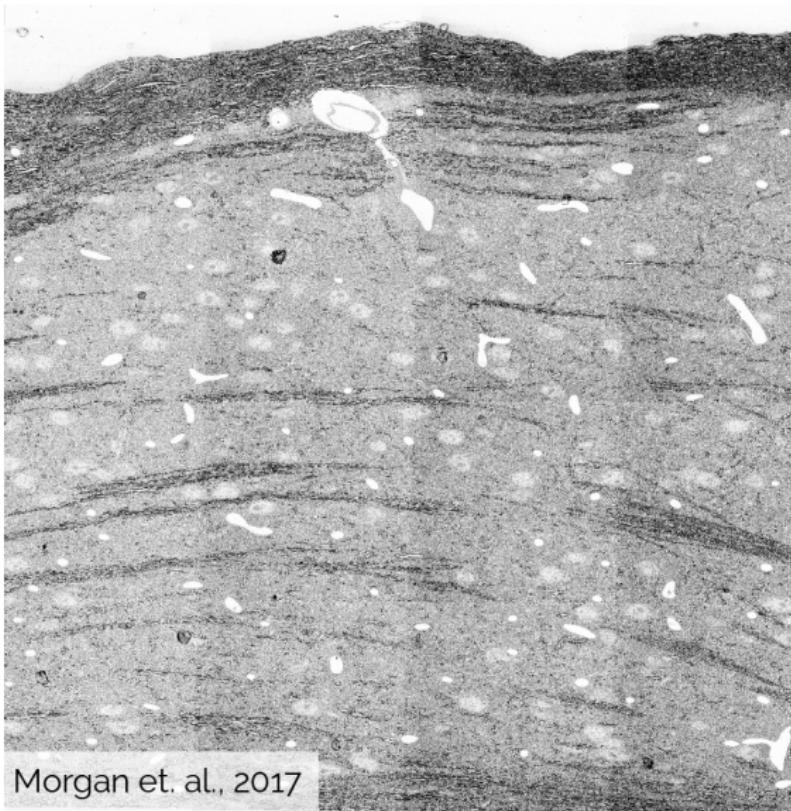
Japanese rice fish



Data storage

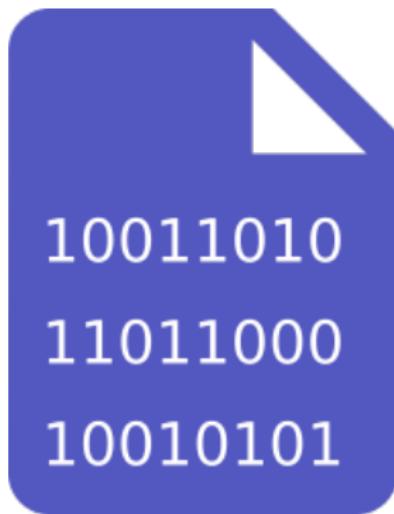


Neuroscience generates huge amounts of data

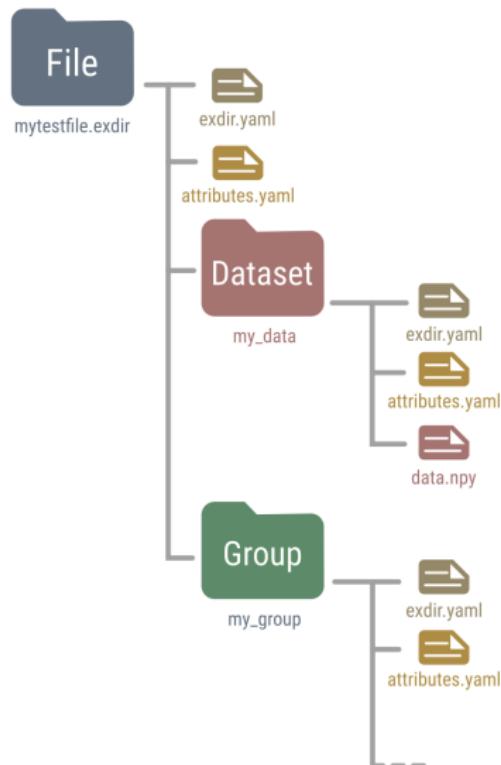


Morgan et. al., 2017

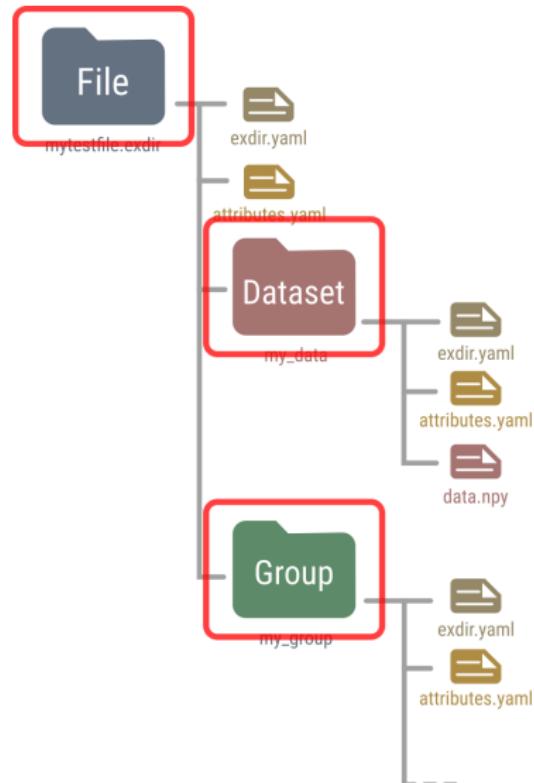
HDF5 is a popular data format for storing data in a hierarchy within a single binary file



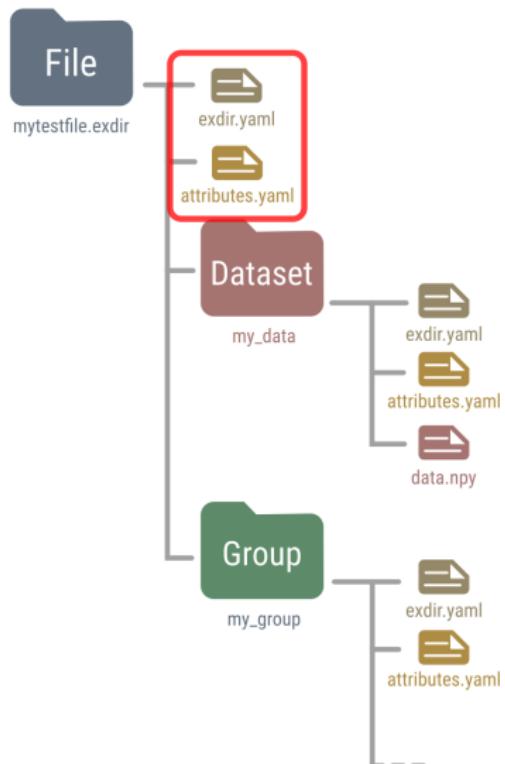
Exdir is a specification organizing data in a hierarchy using file-system directories



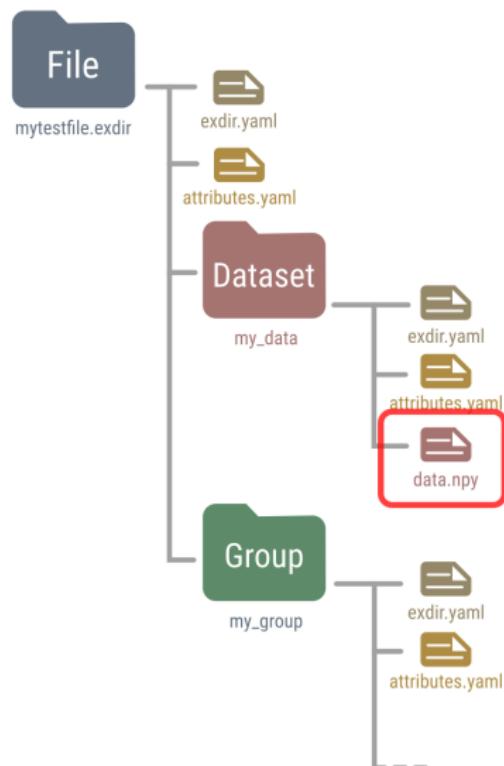
Exdir is a specification organizing data in a hierarchy using file-system directories



Exdir is a specification organizing data in a hierarchy using file-system directories



Exdir is a specification organizing data in a hierarchy using file-system directories



Education



Problem: the computational aspects of
neuroscience education is lacking

Neuronify is an educational neural network simulator

Continue

New

Examples

Save

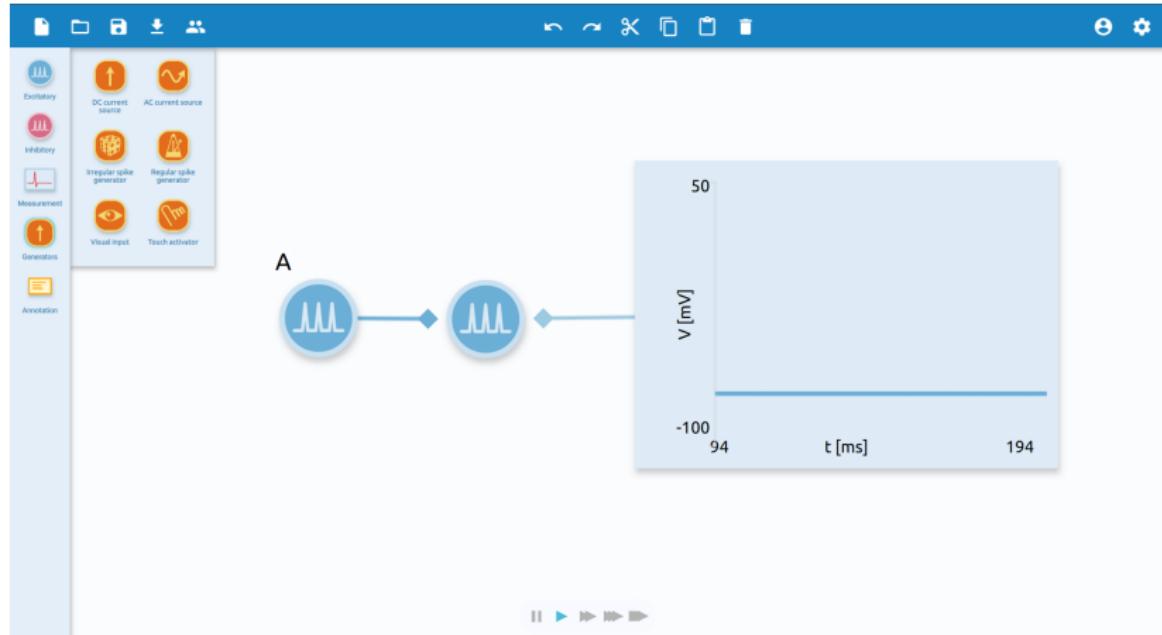
Load

About

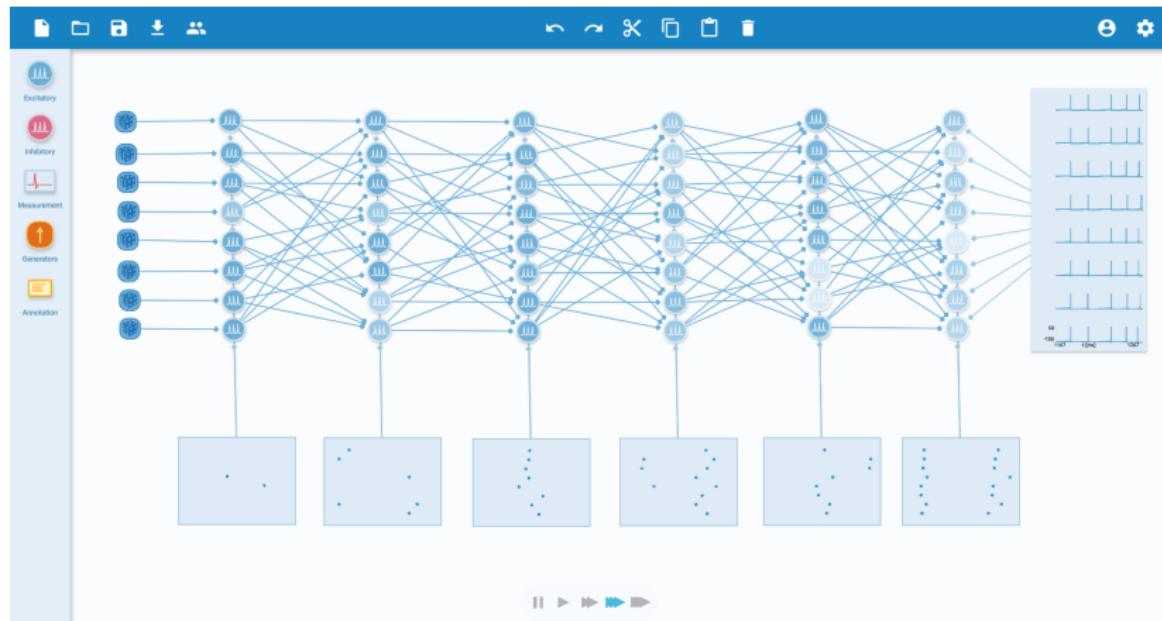
Neuronify



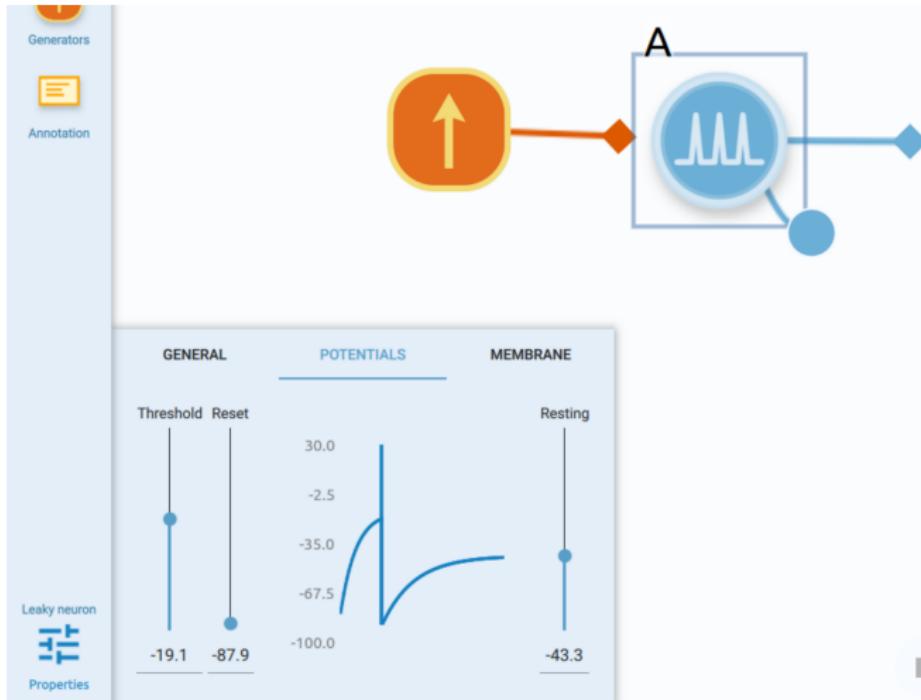
Neuronify is an educational neural network simulator



Neuronify is an educational neural network simulator



Neuronify is an educational neural network simulator



Neuronify has been downloaded $\sim 63,000$ times and used in research and several neuroscience courses



ARTICLE

DOI: 10.1038/s41467-018-07113-0

OPEN

Perineuronal nets decrease membrane capacitance of peritumoral fast spiking interneurons in a model of epilepsy

Bhanu P. Tewari  ¹, Lata Chaunsali¹, Susan L. Campbell^{1,2}, Dipan C. Patel¹, Adam E. Goode³ & Harald Sontheimer  ^{1,4}

Introduction to analysis and modeling in biology with Python

Chapter 1

Using Python as a Scientific Calculator



Figure 1.1 A DNA double helix. A 3D rendering of a molecular model of a DNA double helix. Labels indicate the nitrogenous bases, phosphate groups, and sugar groups that make up the structure.

Chapter 2

Analyzing bacterial population growth



Figure 2.1 Bacteria. Bacteria are unicellular, prokaryotic microorganisms. Shown here is a scanning electron micrograph of a bacterial colony.

Chapter 3

Modeling unlimited bacterial population growth

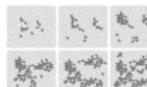


Figure 3.1 Bacterial growth. On the left, a model of bacterial growth is shown. On the right, a grid of four panels shows bacterial growth over four time steps.

Chapter 4

Models for limited bacterial population growth

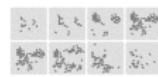


Figure 4.1 Bacterial growth model. In the model in section 4, limited population growth is simulated. The population grows until it reaches a plateau. The plateau is then maintained until the next time step. The growth rate is then reduced. This is a model of bacterial growth in a limited environment.

Chapter 5

Modeling plant population growth



Figure 5.1 A green plant. This is a green plant. It has leaves and a flower bud. The flower bud will open into a flower. The flower will then produce seeds. The seeds will then grow into new plants. This is a model of plant population growth.

Chapter 6

Inheritance



Figure 6.1 Pea plant. This is a pea plant. It has green pods. The pods will open to reveal green peas. The peas will then grow into new plants. This is a model of plant population growth.

Chapter 7

DNA sequence analysis

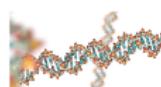


Figure 7.1 DNA sequence analysis. This is a DNA sequence analysis. It shows a DNA double helix. The sequence of nucleotides is shown along the length of the DNA.

Chapter 8

Mutations and DNA



Figure 8.1 A mutation. This is a mutation. It shows a DNA double helix. A mutation is a change in the DNA sequence. It can be a single nucleotide change, or it can be a larger change, such as a deletion or insertion of a entire segment of DNA.

Chapter 9

Modeling epidemics



Figure 9.1 A simulation of an infection that is spreading through time and space. This is a simulation of an infection that is spreading through time and space. The infection starts in one place and spreads to a new place after a short period of time. It is then spread to another place, and so on. This is a model of an infection that is spreading through time and space.

Summary:

Performed uncertainty analysis and created software for:



Uncertainpy

Uncertainty quantification
and sensitivity analysis

Summary:

Performed uncertainty analysis and created software for:



Uncertainty quantification
and sensitivity analysis



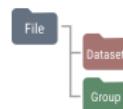
Exdir: Specification for data storage using file system folders

Summary:

Performed uncertainty analysis and created software for:



Uncertainty quantification
and sensitivity analysis



Exdir: Specification for data storage
using file system folders



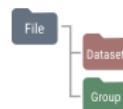
Neuronify: Educational neural
network simulator

Summary:

Performed uncertainty analysis and created software for:



Uncertainty quantification
and sensitivity analysis



Exdir: Specification for data storage
using file system folders



Neuronify: Educational neural
network simulator

Thank you for your time