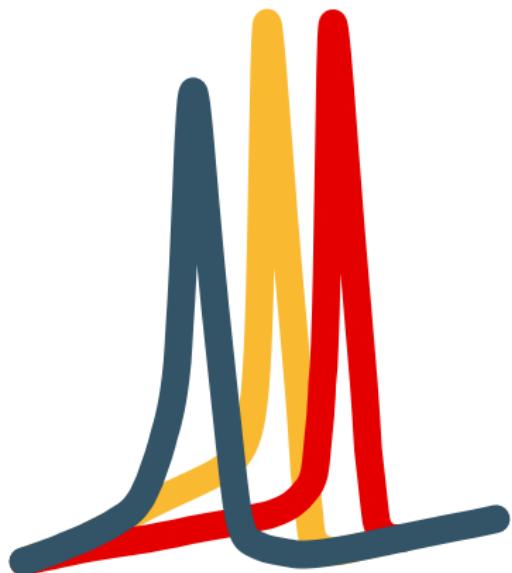


How to model effects of uncertain model parameters with Uncertainpy

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University of Oslo, CINPLA



Overview of this talk



Why do we need uncertainty
quantification and what is it

Overview of this talk



Why do we need uncertainty quantification and what is it



How to perform an uncertainty quantification

Overview of this talk



Why do we need uncertainty quantification and what is it



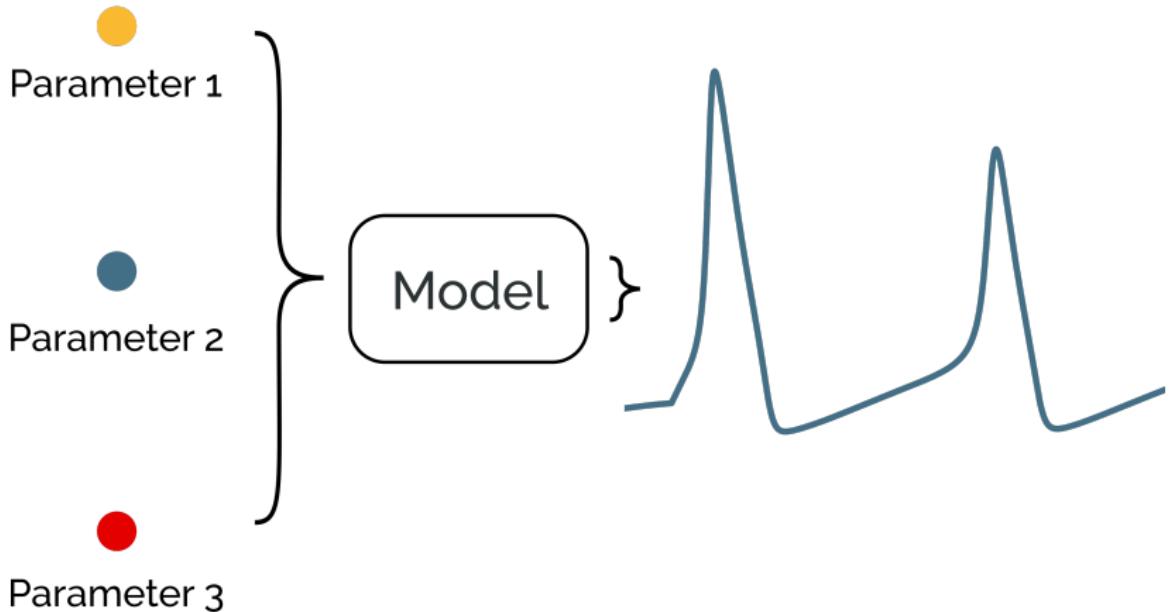
How to perform an uncertainty quantification



Comparison problems

?

Computational models contain parameters



The example we use is the Hodgkin-Huxley model

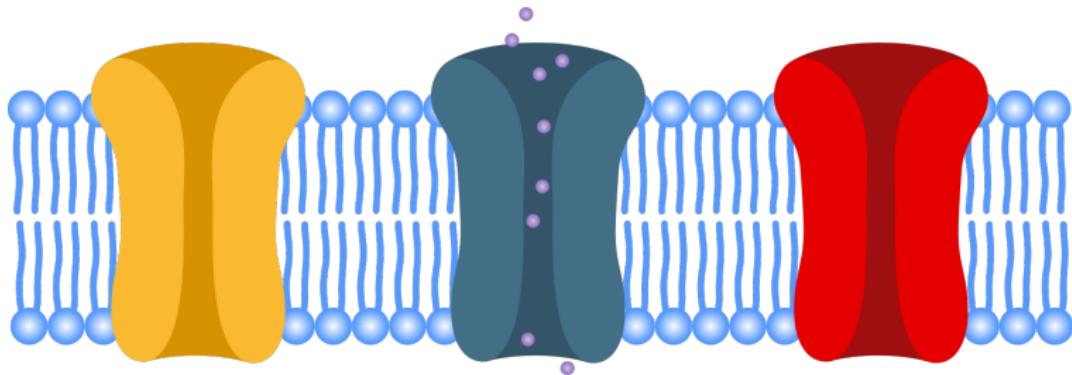
$$I = C_m \frac{dV_m}{dt} + \bar{g}_K(\dots) + \bar{g}_{Na}(\dots) + \bar{g}_L(\dots)$$

The example we use is the Hodgkin-Huxley model

Current through the ion channels

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

The Hodgkin-Huxley model has three types of ion channels



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

Potassium
conductance



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

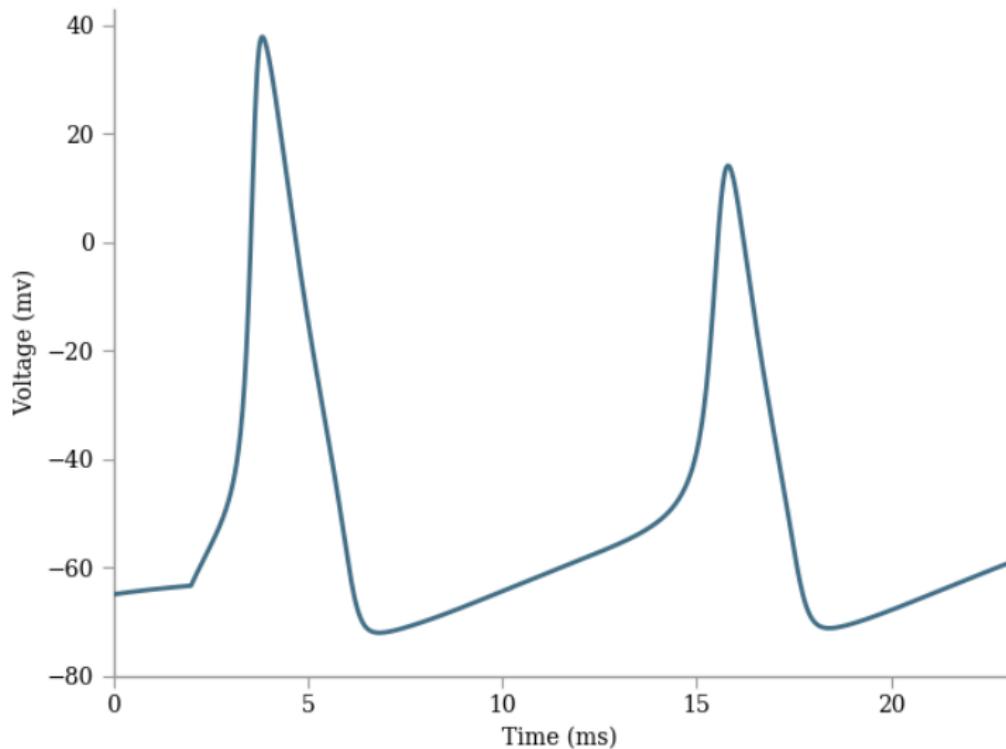
Sodium
conductance



$$\bar{g}_l$$

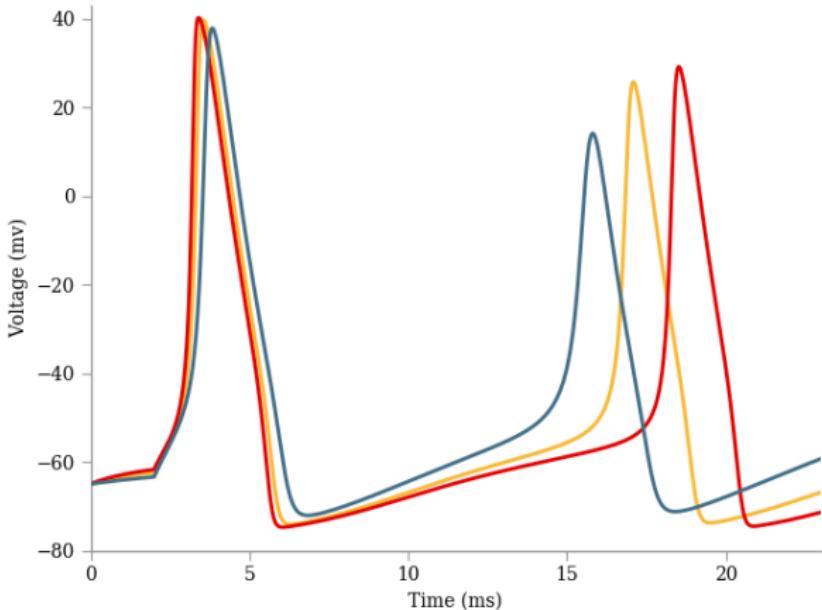
Leak
conductance

Membrane potential of the Hodgkin-Huxley model

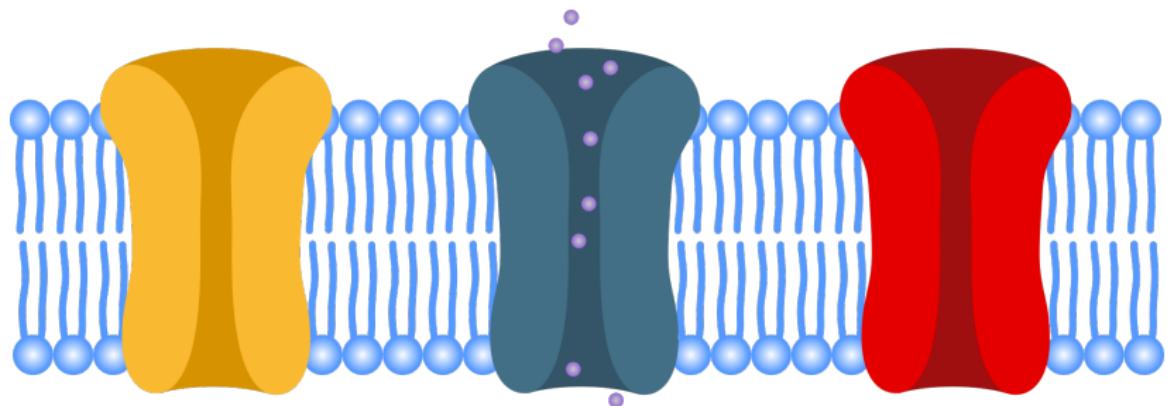


Changing the parameters give different results

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



The parameters do not have exact fixed values



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

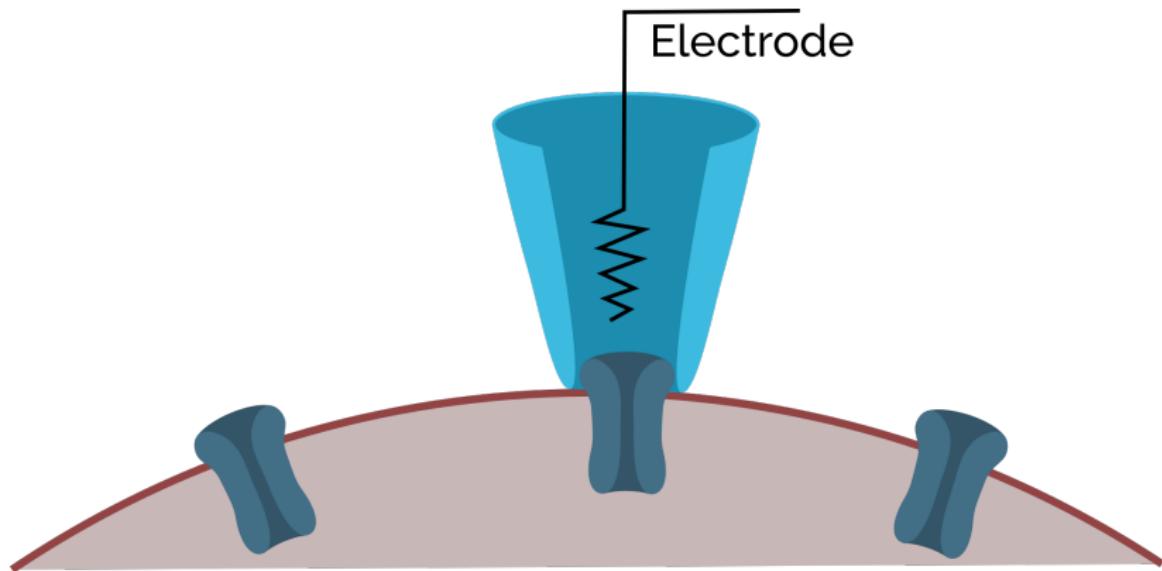


$$\bar{g}_{\text{K}}$$



$$\bar{g}_l$$

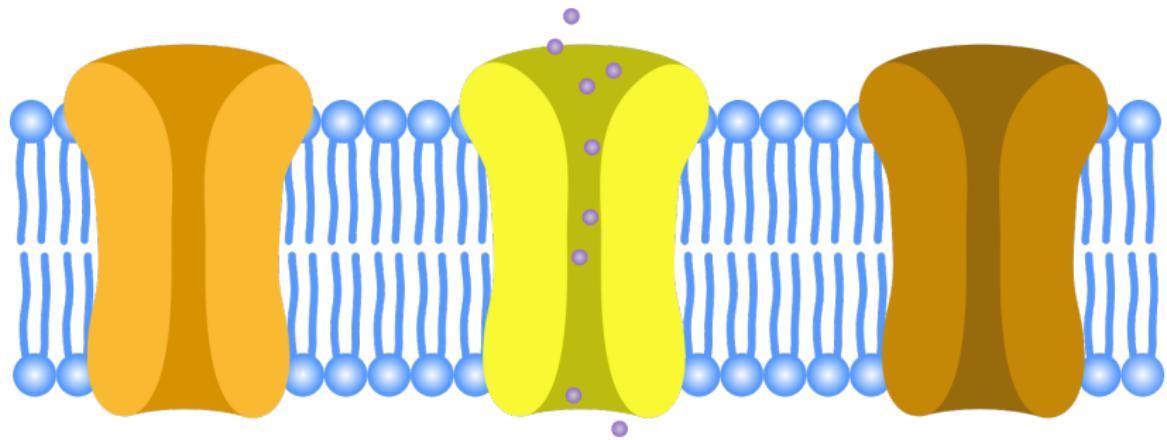
Measurement uncertainty



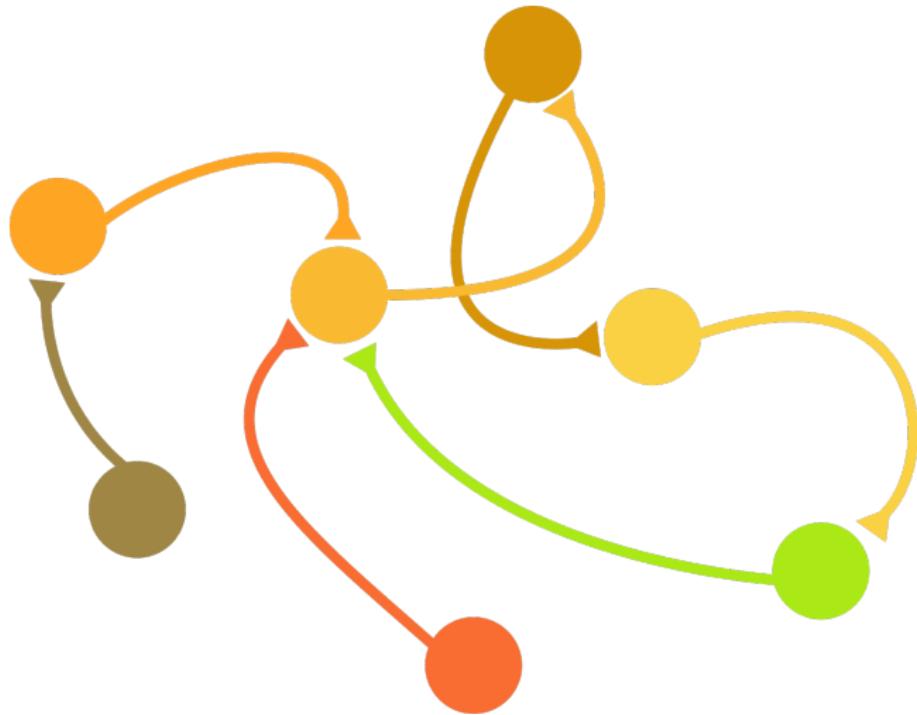
Biological variability: parameters change over time



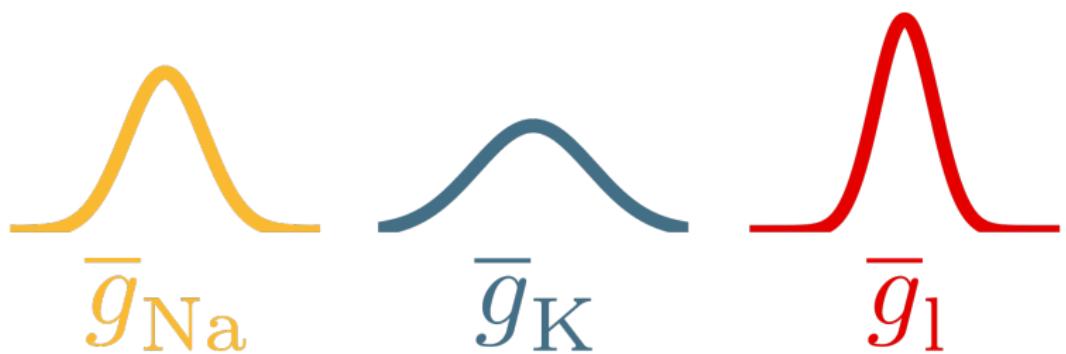
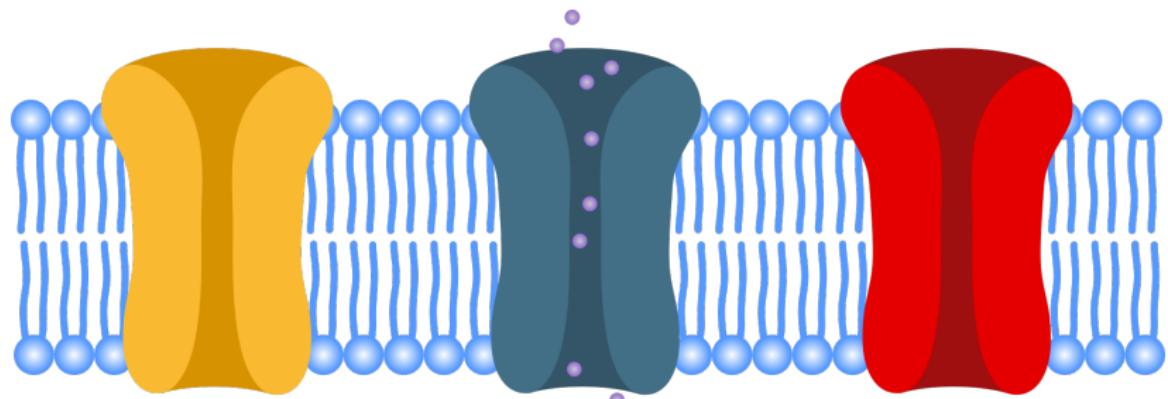
Biological variability: parameters vary within a neuron



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

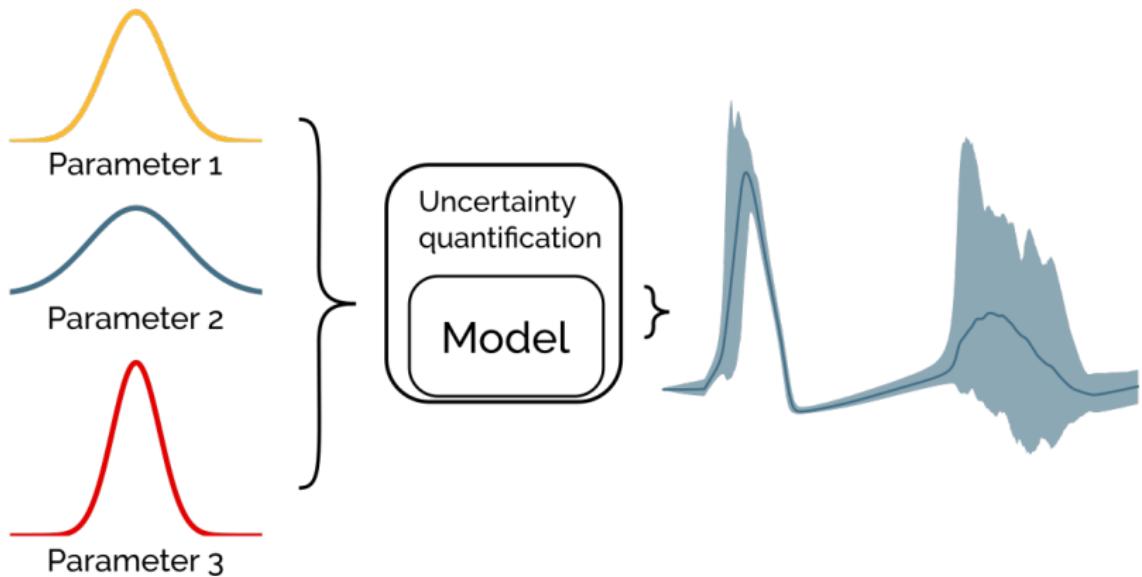


Parameters are best described by distributions

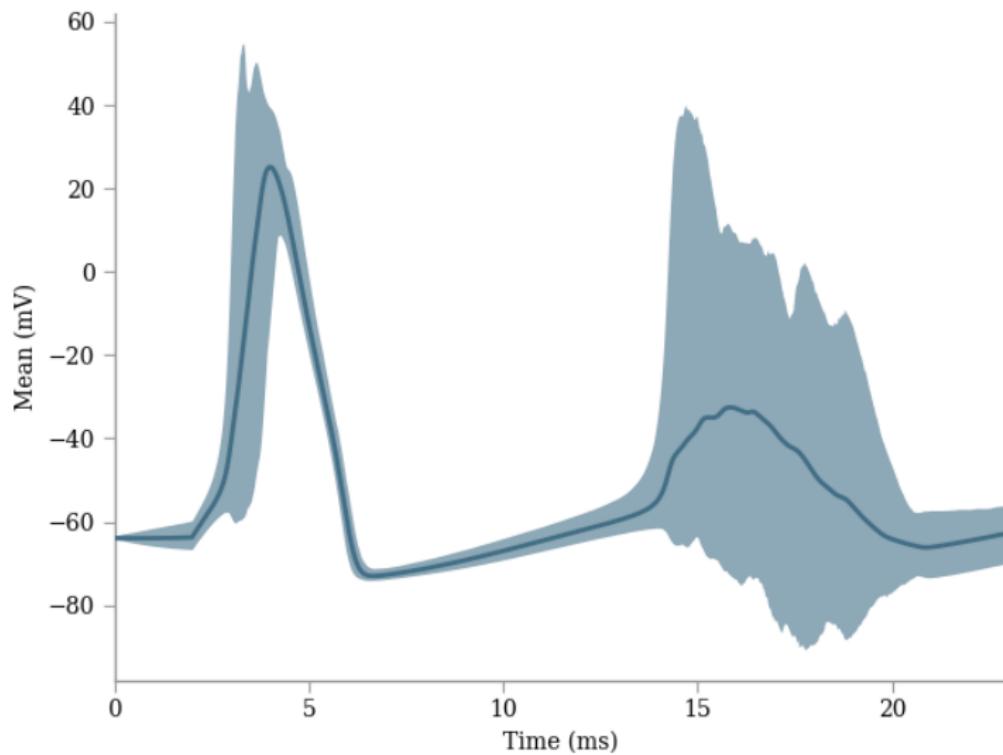


Uncertainty quantification enables us to take the effects of uncertain parameters into account

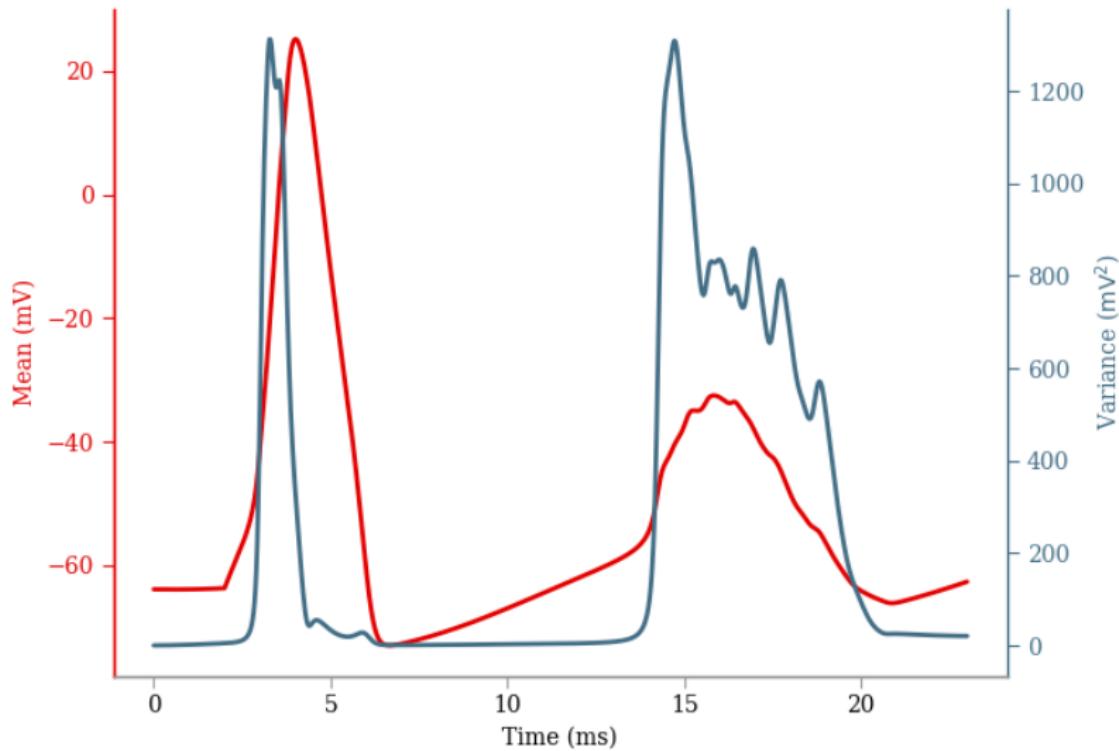
Uncertainty quantification is the process of quantifying the effects of uncertain parameters



90% prediction interval of the Hodgkin-Huxley model

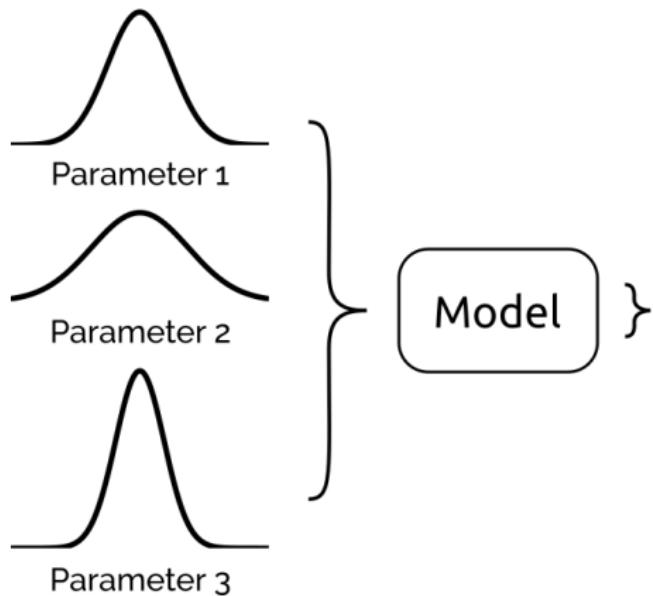


Mean and variance of the Hodgkin-Huxley model

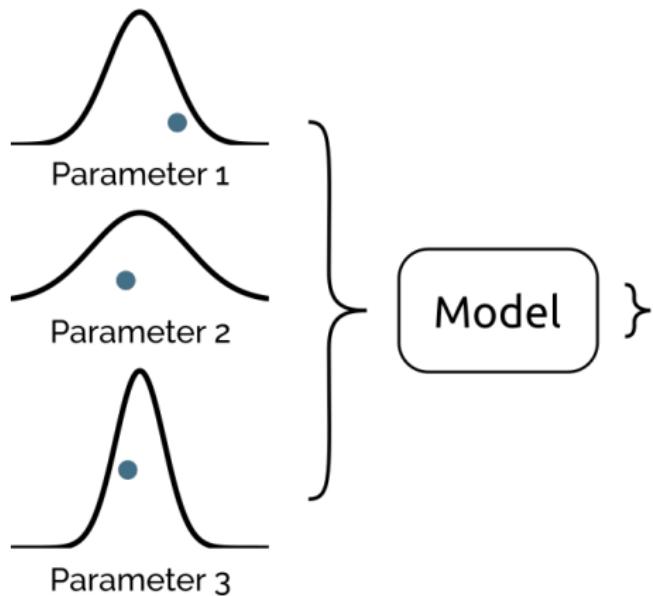




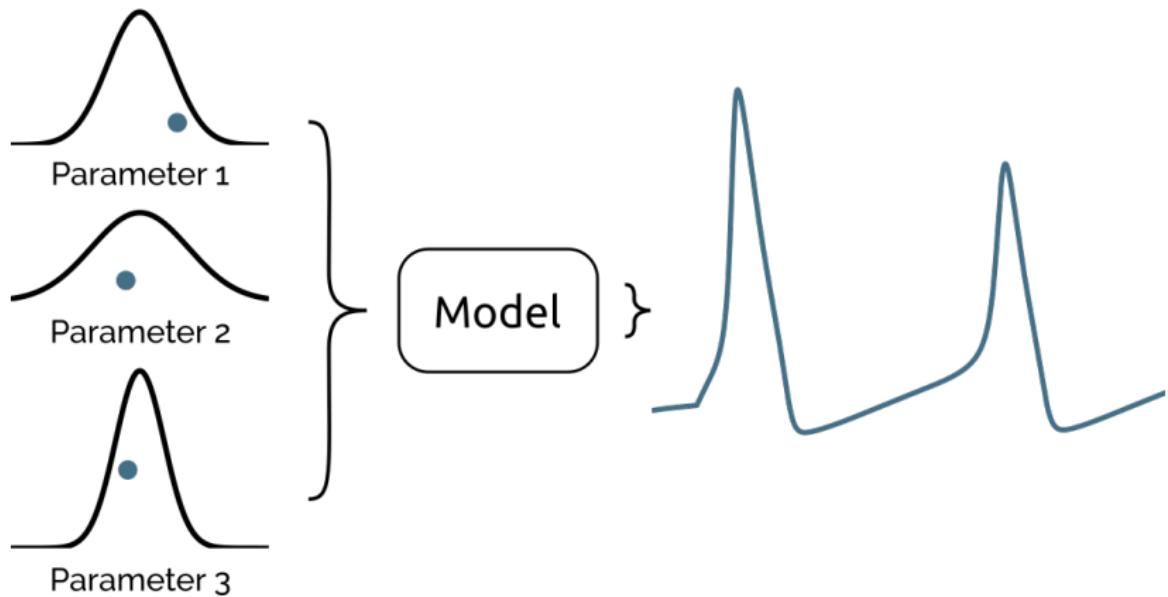
The Monte-Carlo method uses random numbers to perform the uncertainty quantification



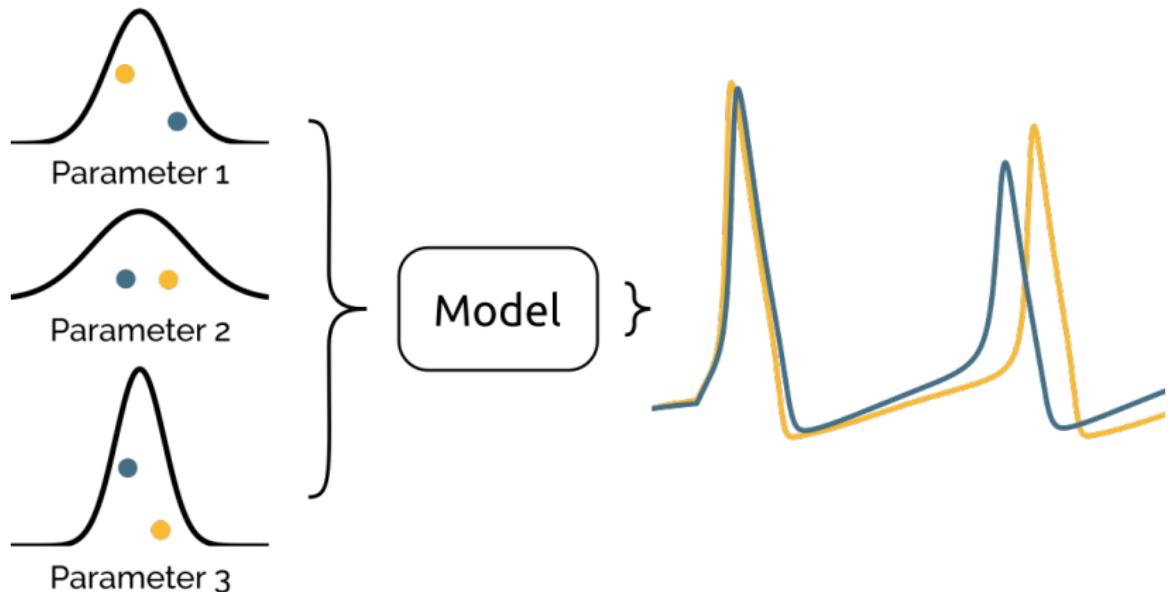
The Monte-Carlo method uses random numbers to perform the uncertainty quantification



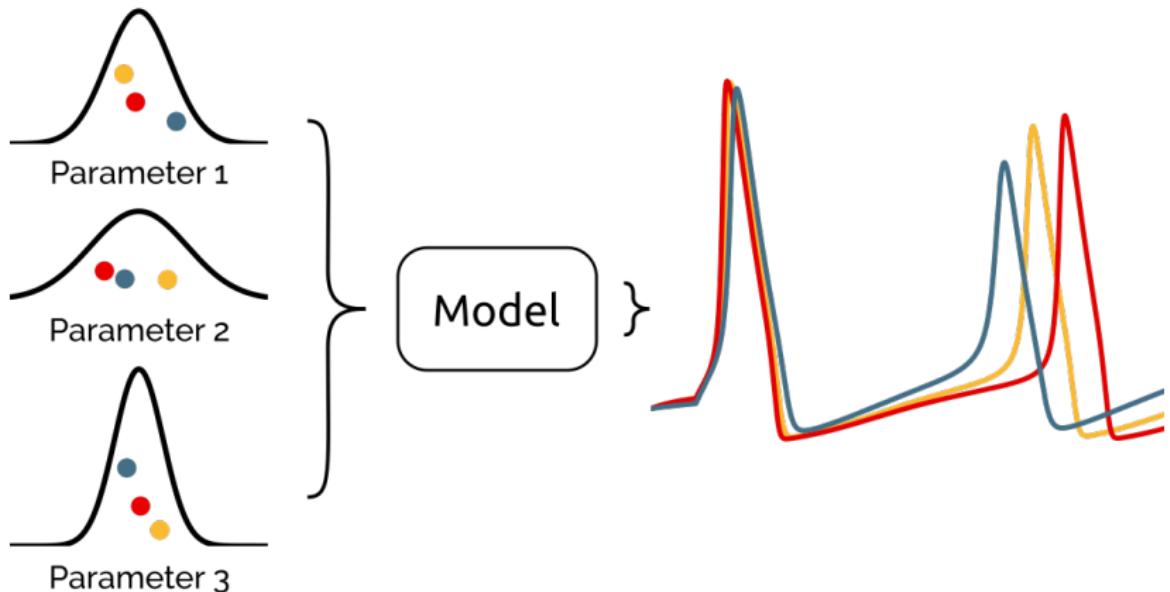
The Monte-Carlo method uses random numbers to perform the uncertainty quantification



The Monte-Carlo method uses random numbers to perform the uncertainty quantification



The Monte-Carlo method uses random numbers to perform the uncertainty quantification





A Python toolbox for uncertainty quantification

Found at:

<https://github.com/simetenn/uncertainpy>

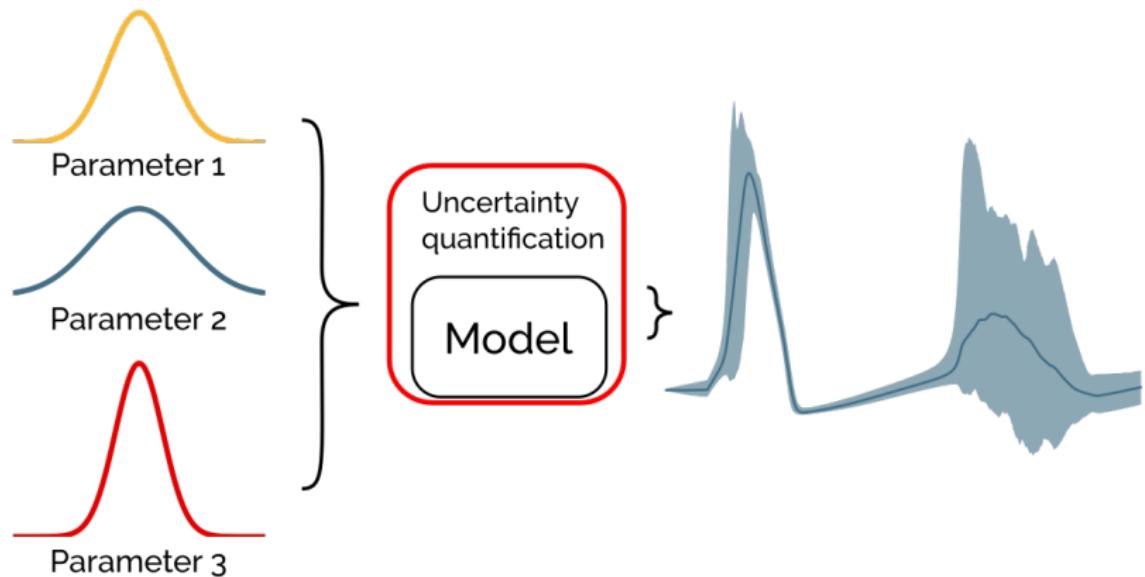
Installation:

```
pip install uncertainpy
```

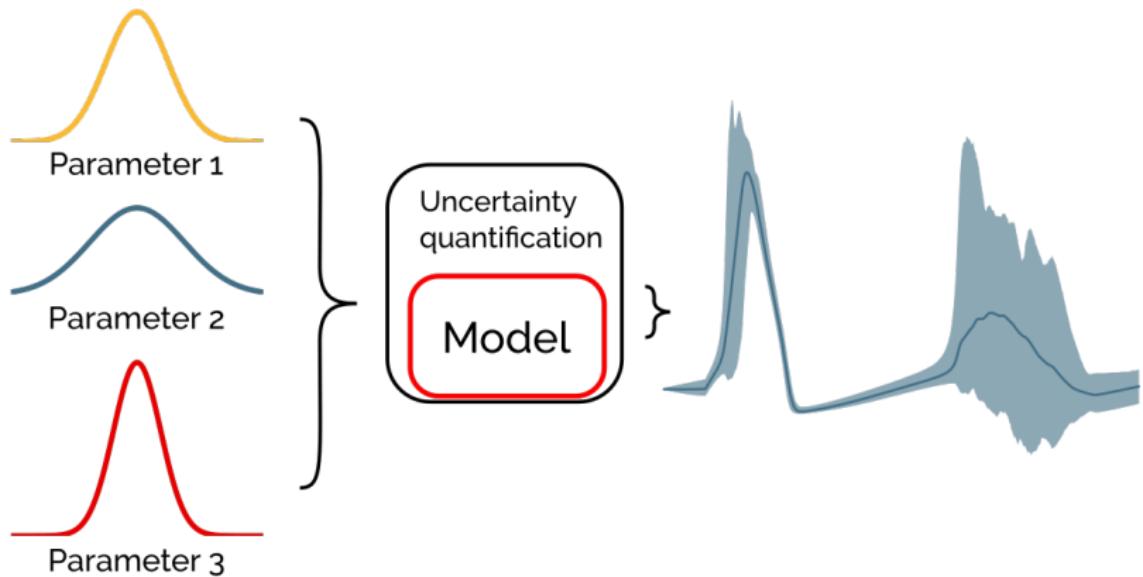
Preprint found at:

www.biorxiv.org

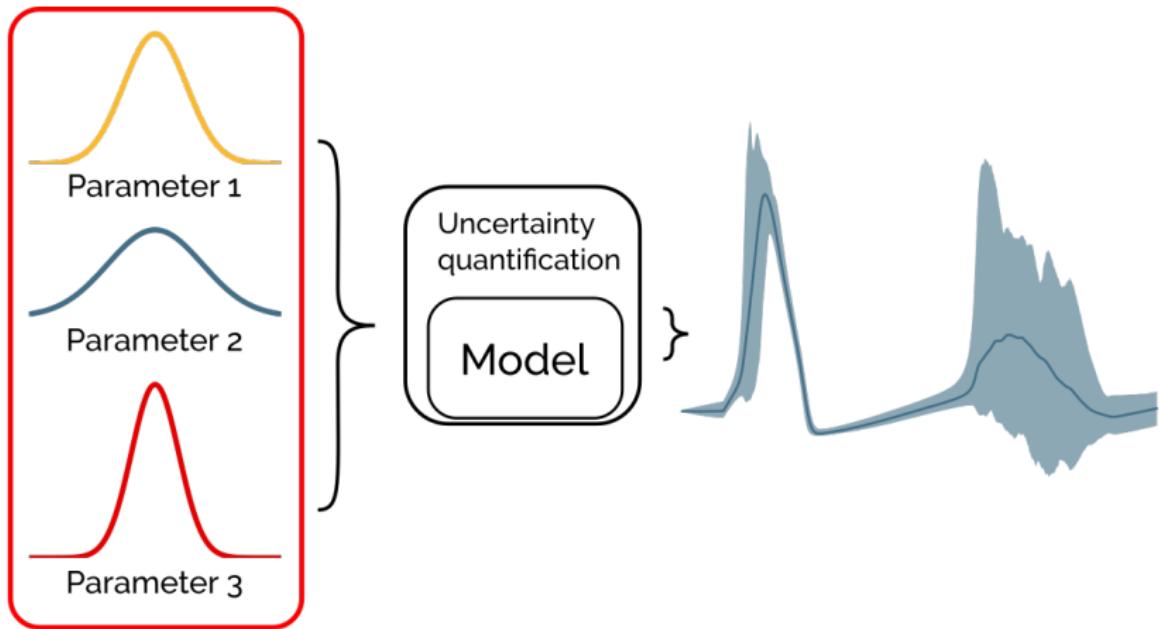
Uncertainpy performs all uncertainty calculations and requires the model and parameters



Uncertaintypy performs all uncertainty calculations
and requires the model and parameters



Uncertaintypy performs all uncertainty calculations and requires the model and parameters



The problem is set up using the
UncertaintyQuantification class

```
import uncertainpy as un

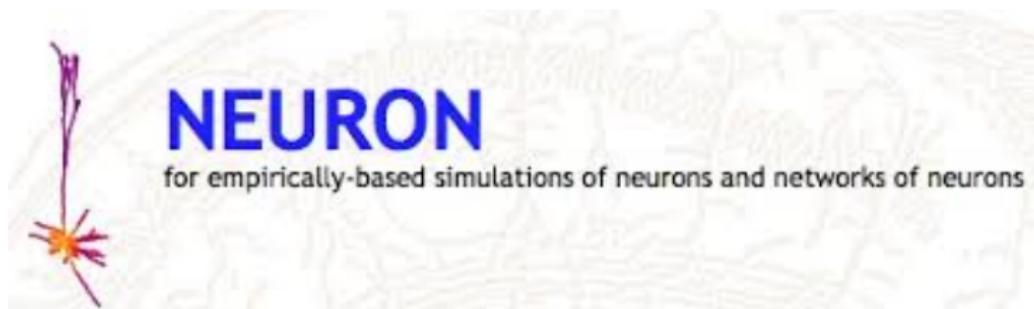
UQ = un.UncertaintyQuantification(
    model=...,
    parameters=...
)
```

Models are created as Python functions

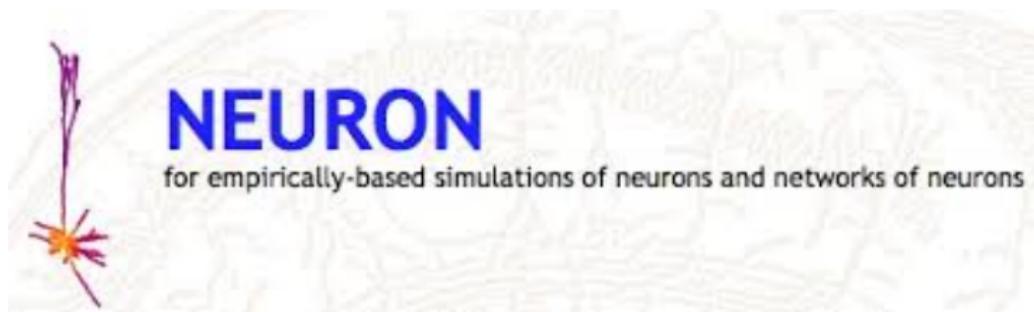
```
def hodgin_huxley(gbar_Na, gbar_K, gbar_l):
    # Calculate the membrane potential using
    # gbar_Na, gbar_K and gbar_l
    ...
    return time, membrane_potential
```

```
UQ = un.UncertaintyQuantification(  
    model=hodgin_huxley,  
    parameters=...  
)
```

Uncertainty has support for multi-compartmental models



Uncertainty has support for multi-compartmental models and network models



Parameters are given as a Python dictionary

```
parameters = {"name": distribution}
```

Parameters are given as a Python dictionary

```
import chaospy as cp

uniform_distribution = cp.Uniform(2, 5)
normal_distribution = cp.Normal(12, 2)
```

Parameters are given as a Python dictionary

```
parameters = {                                # Original
    "gbar_Na": cp.Uniform(60, 180),          # 120
    "gbar_K": cp.Uniform(18, 54),            # 36
    "gbar_I": cp.Uniform(0.15, 0.45)        # 0.3
}
```

```
UQ = un.UncertaintyQuantification(  
    model=hodgkin_huxley ,  
    parameters=parameters ,  
)
```

We perform the uncertainty calculations
with quantify()

```
UQ = un.UncertaintyQuantification(  
    model=hodgkin_huxley,  
    parameters=parameters  
)  
  
results = UQ.quantify()
```

Overview of the Hodgkin-Huxley example

```
def hodgkin_huxley(gbar_Na, gbar_K, gbar_l):
    # Calculate the membrane potential using
    # gbar_Na, gbar_K and gbar_l

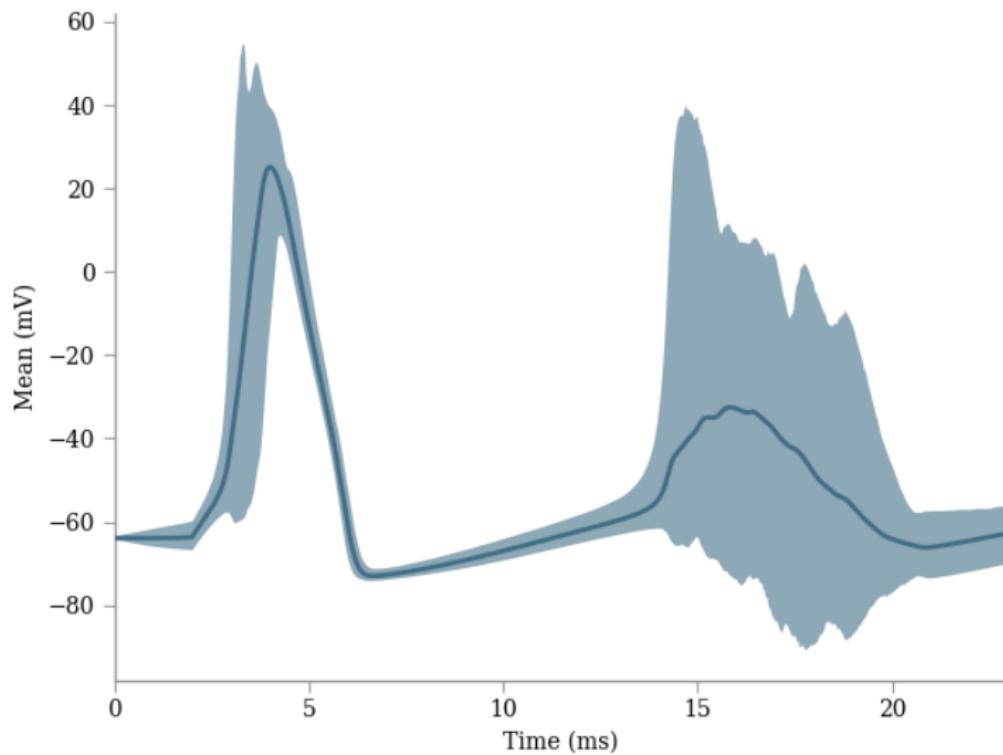
    return time, membrane_potential

parameters = {                                     # Original
    "gbar_Na": cp.Uniform(60, 180),           # 120
    "gbar_K": cp.Uniform(18, 54),              # 36
    "gbar_l": cp.Uniform(0.15, 0.45)}         # 0.3

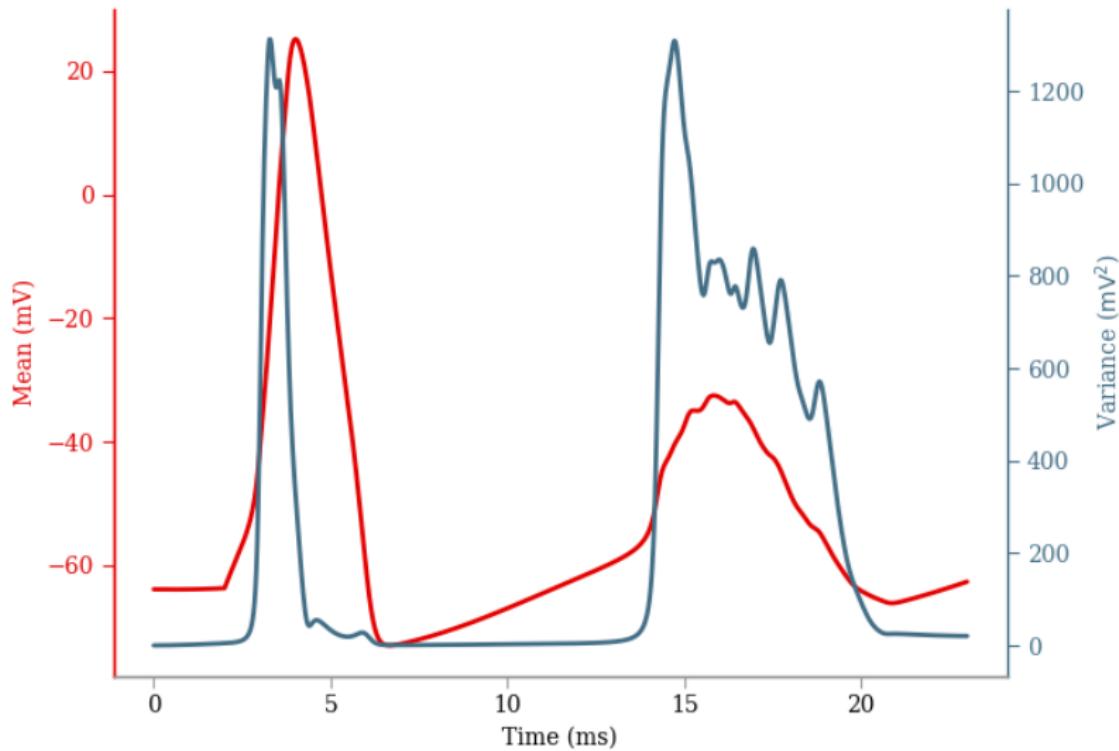
UQ = un.UncertaintyQuantification(
    model=hodgkin_huxley,
    parameters=parameters)

results = UQ.quantify()
```

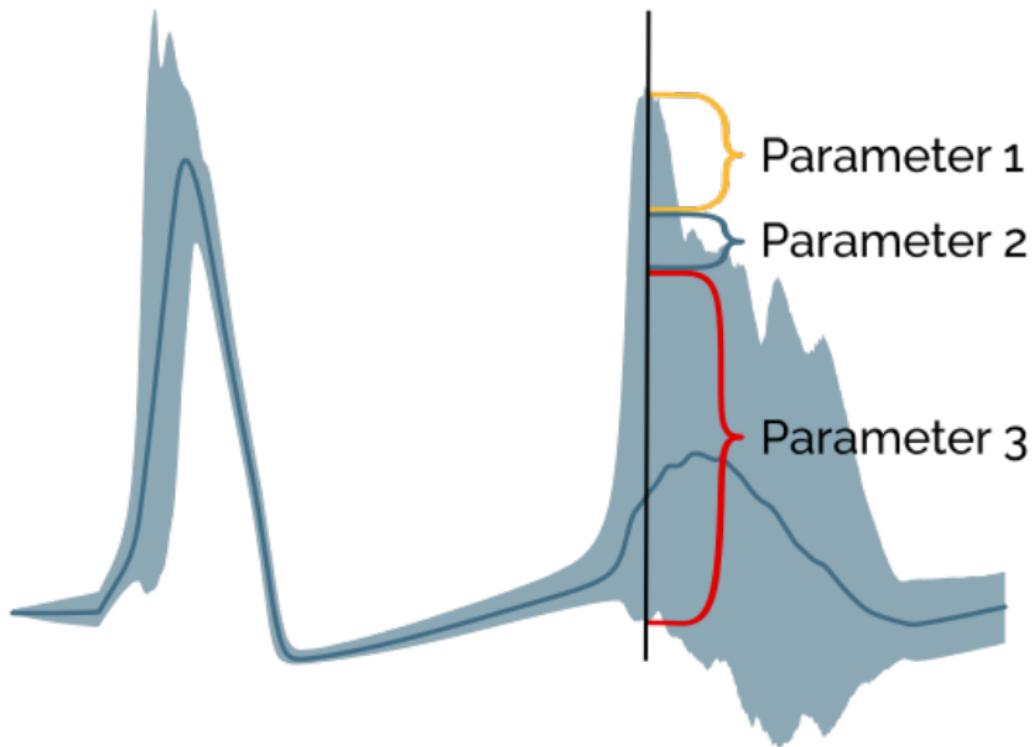
90% prediction interval of the Hodgkin-Huxley model



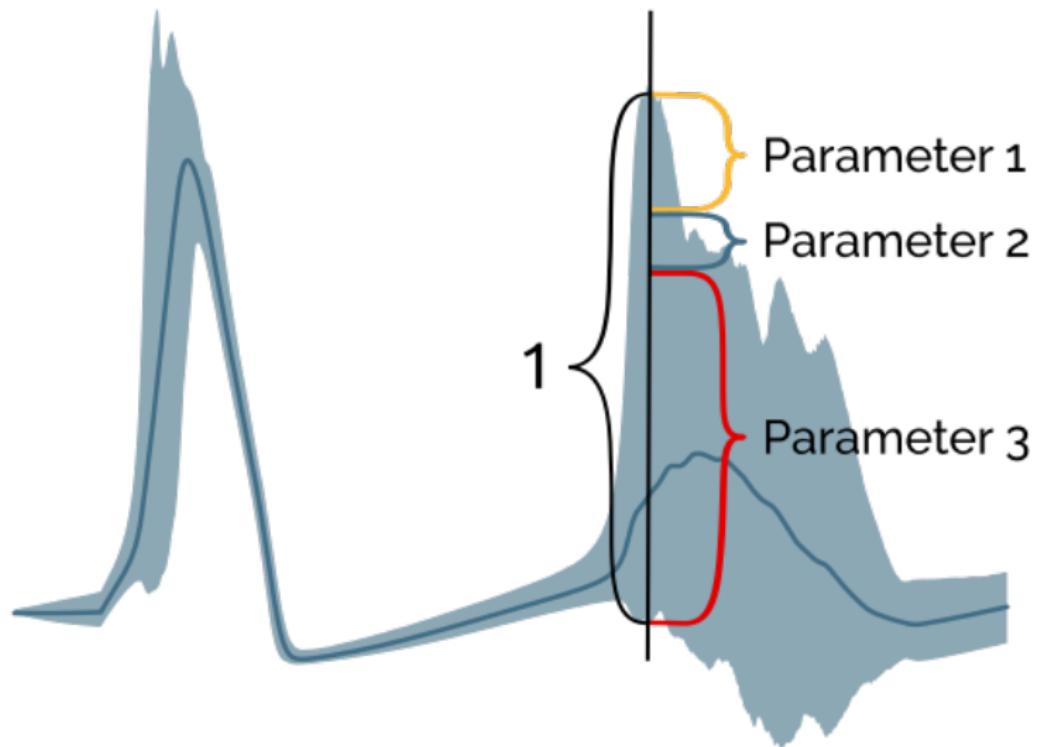
Mean and variance of the Hodgkin-Huxley model



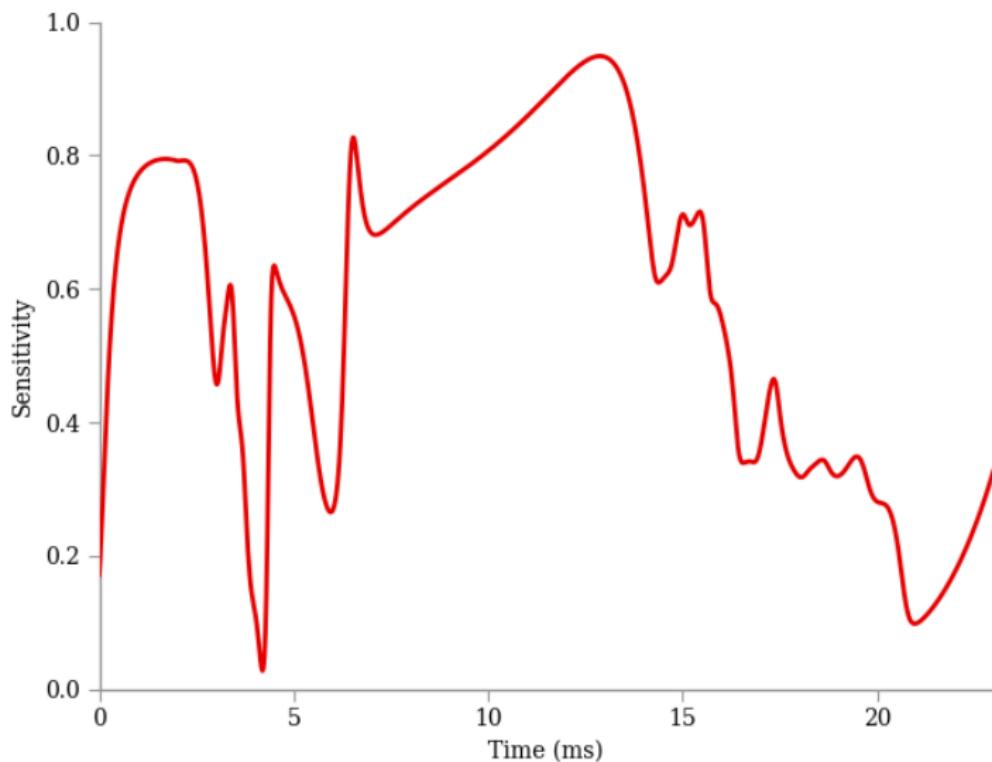
Sensitivity analysis quantifies how much of the uncertainty each parameter is responsible for



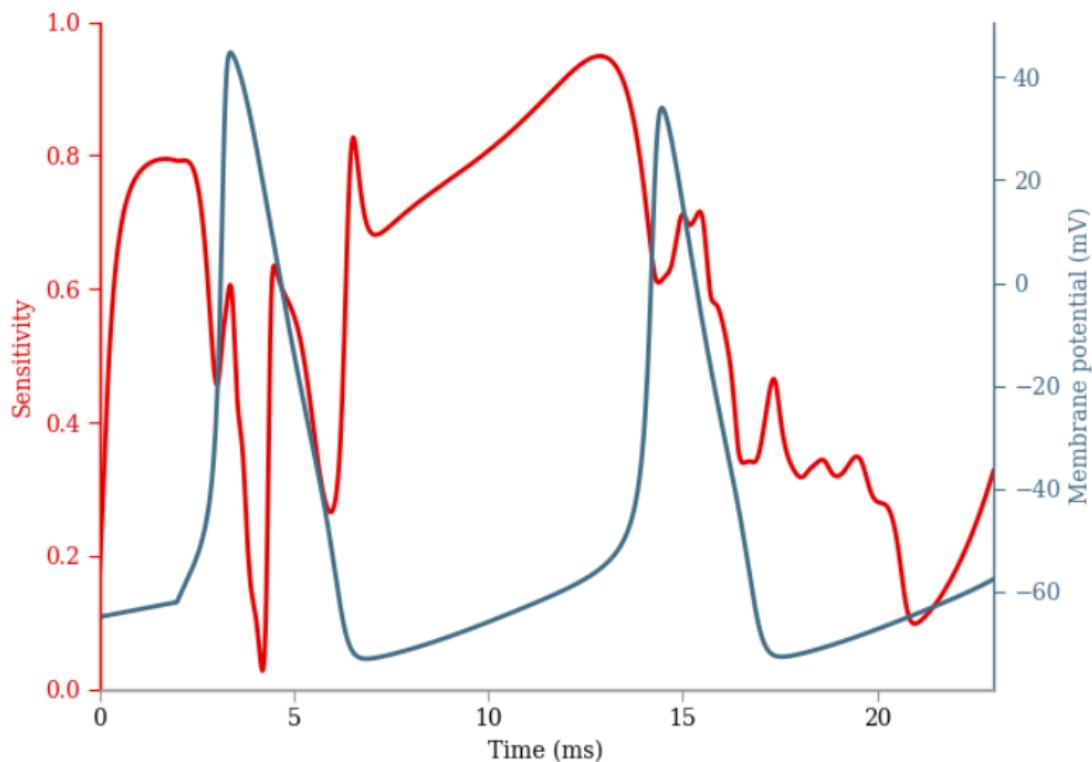
Sensitivity analysis quantifies how much of the uncertainty each parameter is responsible for

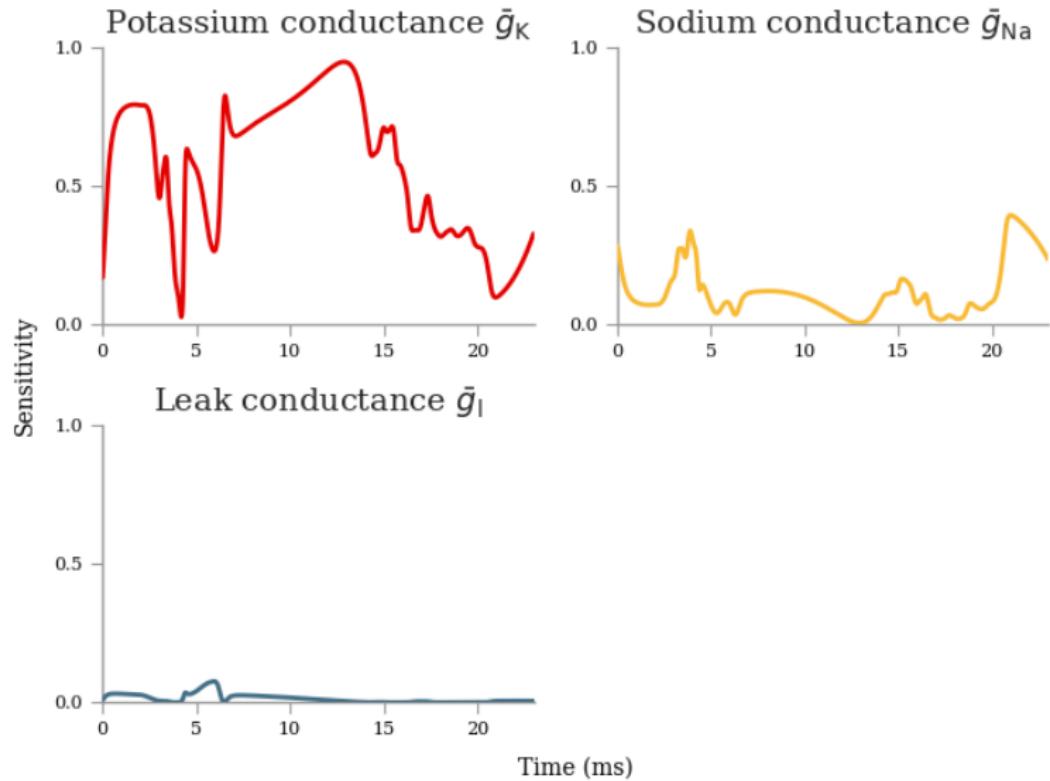


Sensitivity of the potassium conductance \bar{g}_K in the Hodgkin-Huxley model



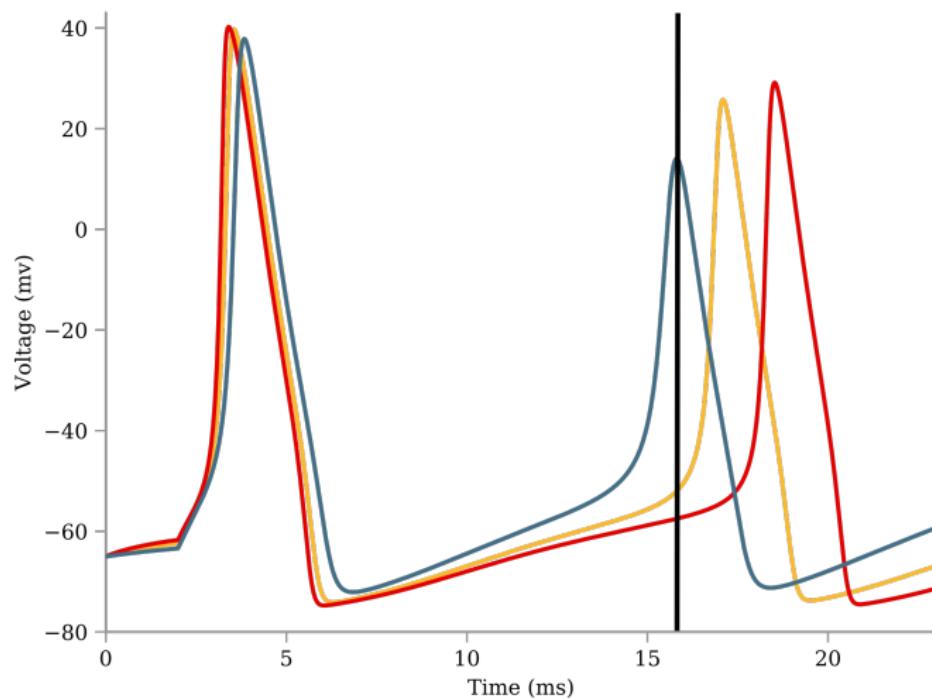
Sensitivity of the potassium conductance \bar{g}_K in the Hodgkin-Huxley model



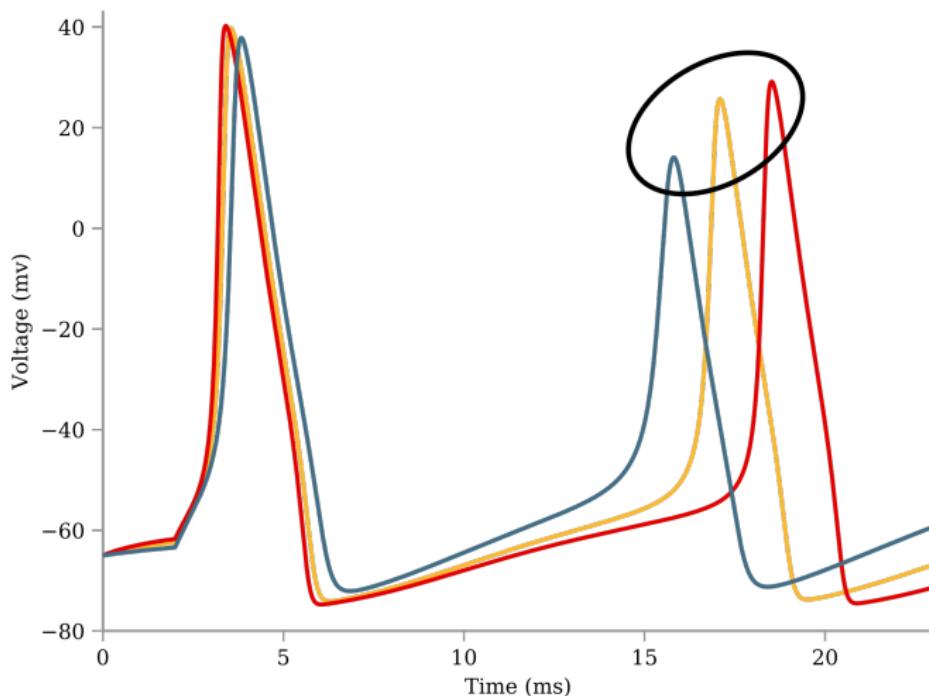




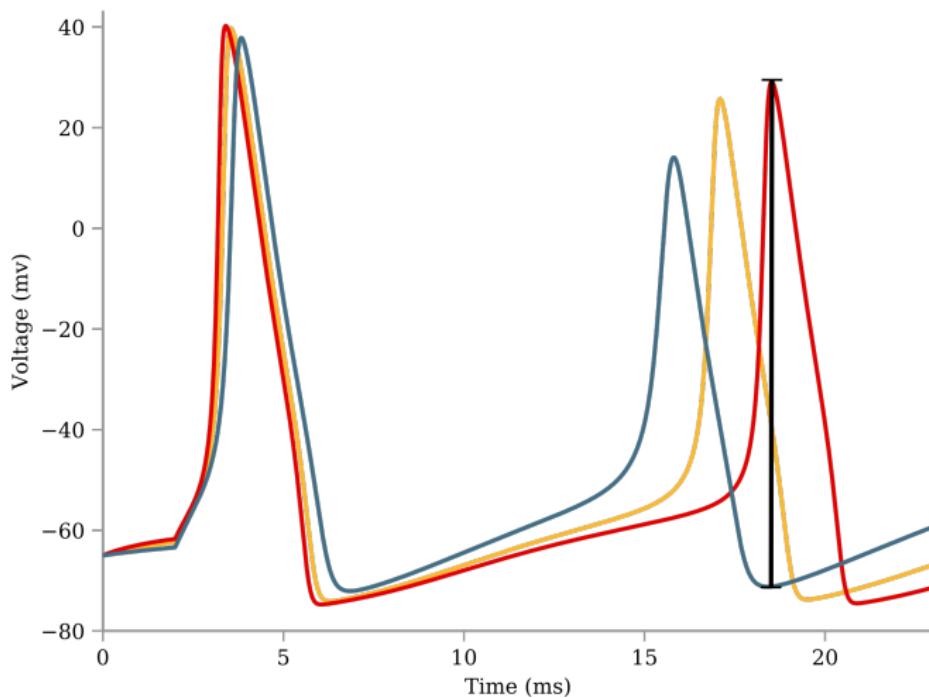
Pointwise comparison of model results give large differences due to small time shifts in spikes



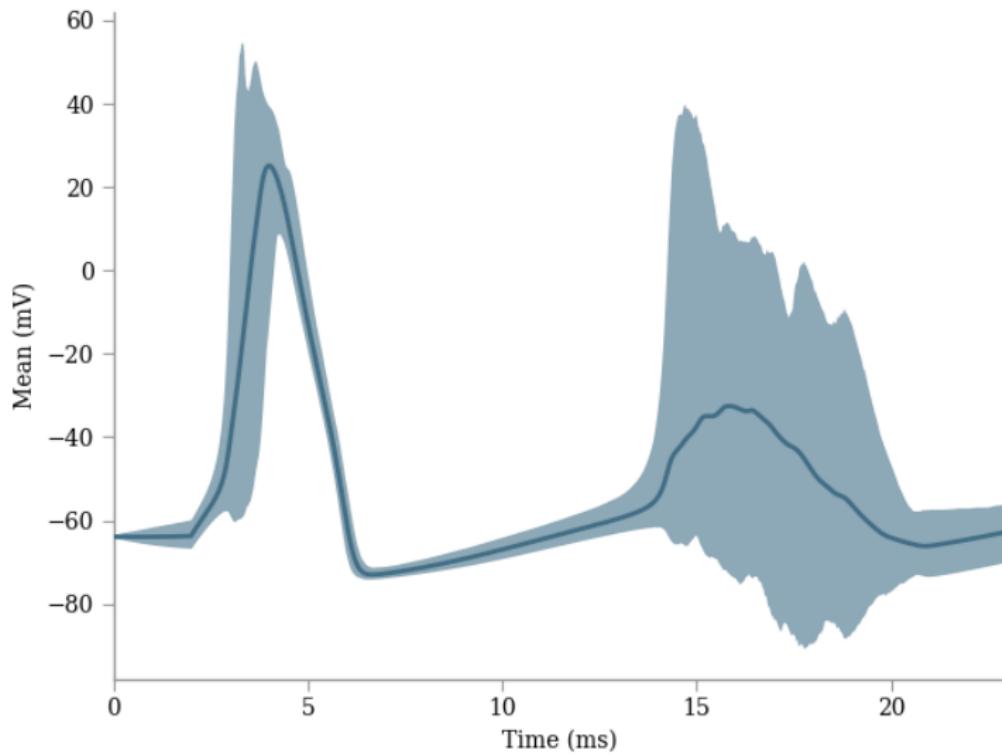
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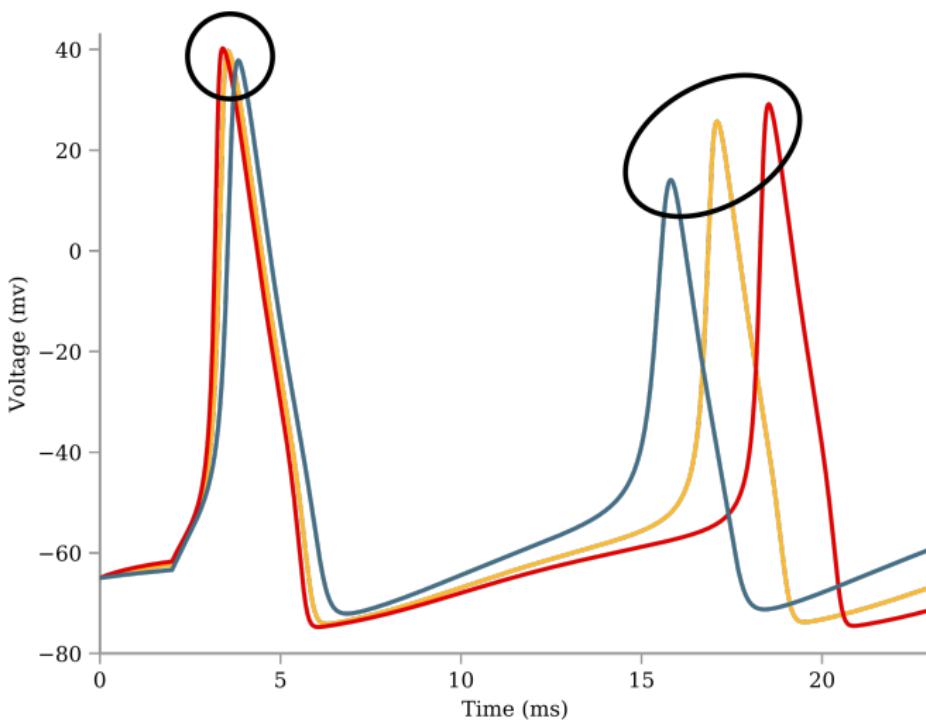
Pointwise comparison of model results give large differences due to small time shifts in spikes



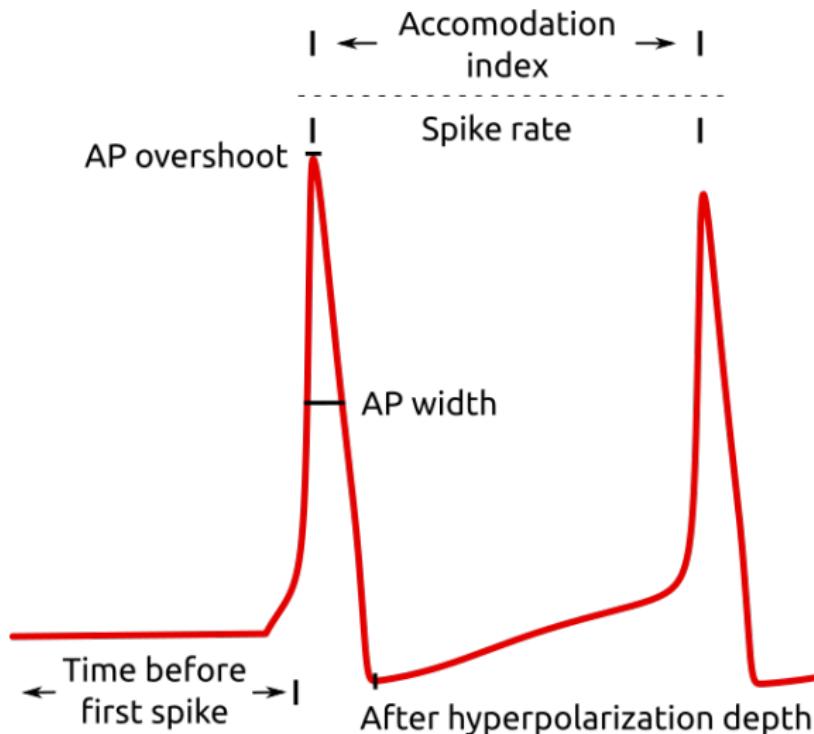
The time shifted spikes cause large variance



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



Uncertainpy comes with pre-defined features that can be directly used with the `features` argument

```
UQ = un.UncertaintyQuantification(  
    model=hodgkin_huxley,  
    parameters=parameters,  
    features=un.SpikingFeatures()  
)
```

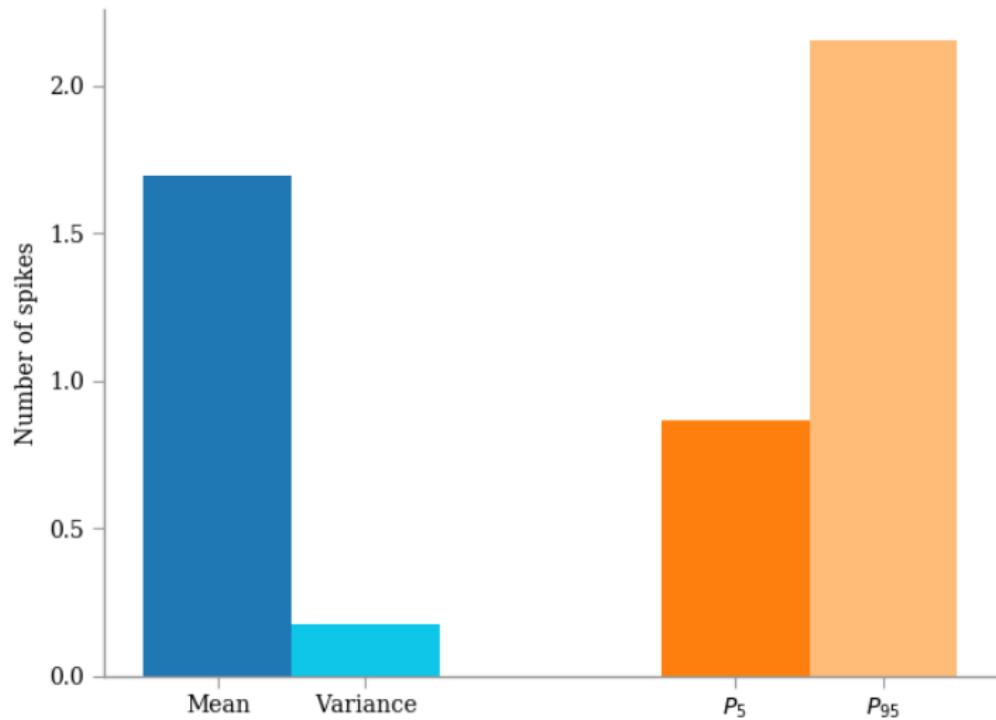
Features are defined as Python functions

```
def nr_spikes(time, membrane_potential):
    # Calculate the feature using
    # time and membrane_potential
    ...
    return time, nr_spikes
```

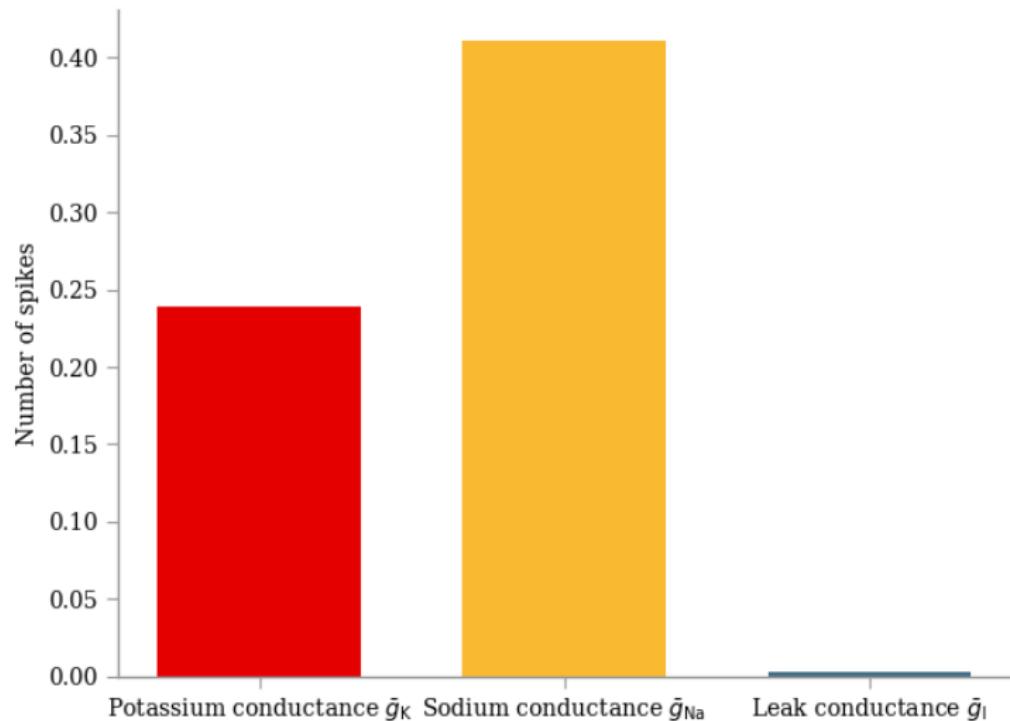
A list of feature functions is given with the features argument

```
UQ = un.UncertaintyQuantification(  
    model=hodgkin_huxley,  
    parameters=parameters,  
    features=[nr_spikes, spike_rate]  
)
```

The number of spikes of the Hodgkin-Huxley model



Sensitivity of the number of spikes of the Hodgkin-Huxley model



Summary:

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

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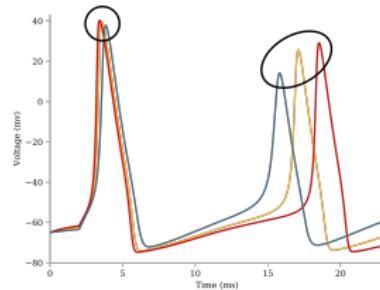
performs all calculations without the need for detailed knowledge

Summary:

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



performs all calculations without the need for detailed knowledge



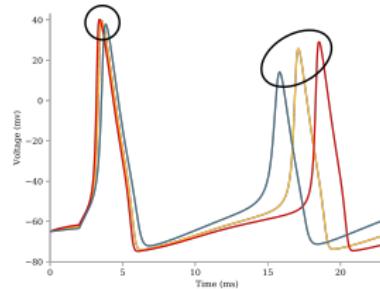
Features are useful when comparing spiking results

Summary:

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



performs all calculations without the need for detailed knowledge



Features are useful when comparing spiking results

Questions?