

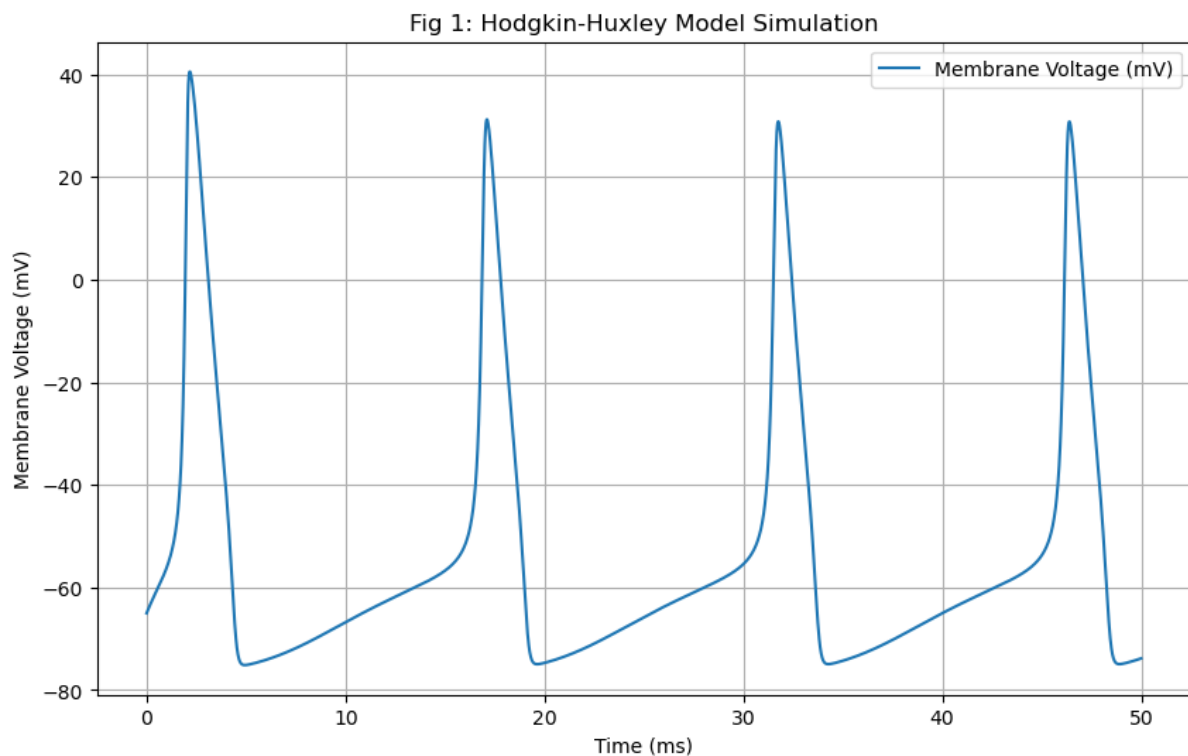
Neuron Modelling Report

The Hodgkin-Huxley model, a venerable tool in computational neuroscience, serves as our conduit to understanding the intricate dynamics of neuronal membrane voltage. This report documents a comprehensive exploration involving the implementation, calibration, and automatic recalibration of the Hodgkin-Huxley model. The language Python was used to unravel the periodic spiking behaviour inherent in neurons.

Implementing the Hodgkin-Huxley Model

I leveraged the NumPy library for numerical operations, the model captured the interplay of sodium, potassium, and leakage currents.

The implementation encapsulates the elegance of the Hodgkin-Huxley model, portraying the intricate balance of ion channel dynamics within the normal parameters that leads to the characteristic spiking observed in real neurons. The script generates a membrane voltage trace, providing a visual representation of the periodic spiking behaviour intrinsic to neuronal activity.



Calibration for Physiological Relevance

This aspect aimed to fine-tune the model parameters to achieve a resting membrane potential of -60mV and a maximum depolarized potential of 10mV. The calibrated model not only aligns with physiological norms but also provides a foundation for more nuanced explorations of neuronal behaviour.

The calibration process involved adjusting key parameters of the Hodgkin-Huxley model such as resting membrane potential and maximum depolarized membrane potential (mV) which is -60.0 and 10.0 respectively to bring its behaviour in line with physiological observations. Specifically, the aim was to set the resting membrane potential and the maximum depolarized potential to -60mV and 10mV,

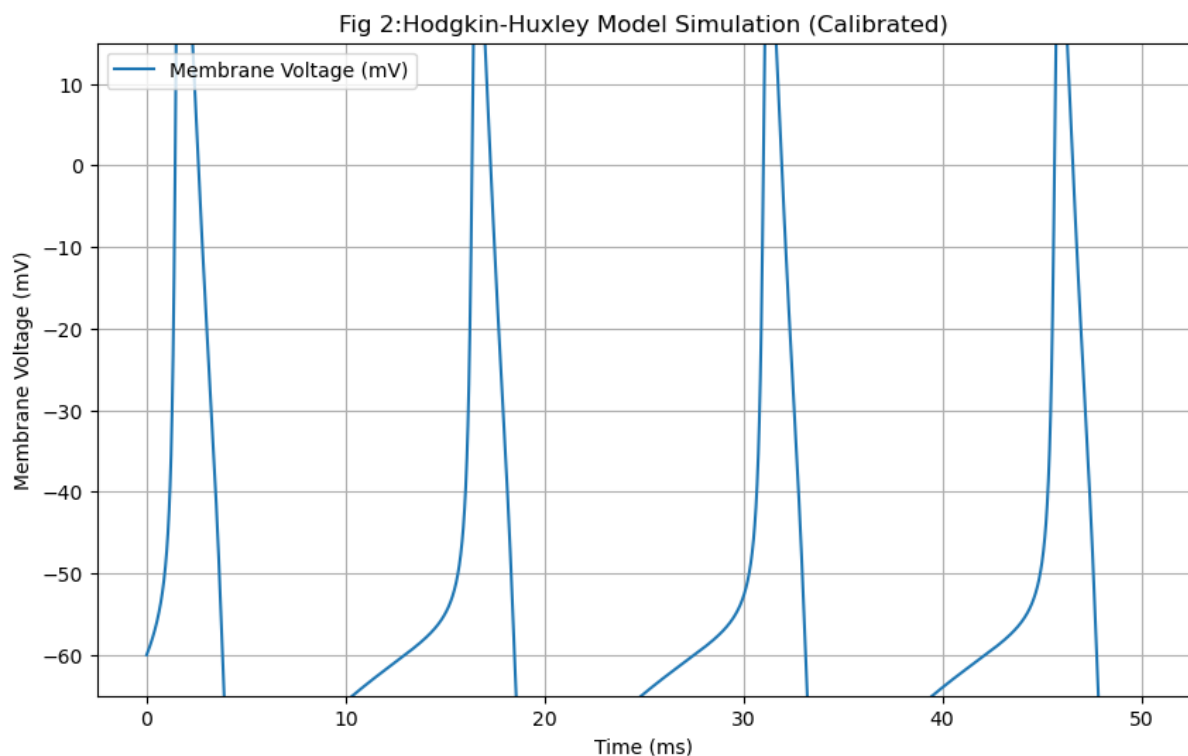
respectively. This meticulous calibration was essential for ensuring that the model's behaviour mirrors the expected physiological range of membrane potentials observed in real neurons.

The key parameters such as the conductances and reversal potentials of sodium, potassium, and leakage channels were systematically adjusted to achieve the desired resting and maximum depolarized potentials.

In the figure 2, the membrane voltage trace exhibits the hallmark characteristics of a neuron at rest, with periodic spikes within the desired physiological range. The calibration process has not only achieved the target resting and maximum depolarized potentials but has also captured the essence of neuronal spiking behaviour.

The calibrated Hodgkin-Huxley model stands as a computational surrogate for the behaviour of real neurons. The success of this calibration process is evident in the alignment of the model's output with physiological expectations. The resting membrane potential of -60mV ensures that the neuron is in a quiescent state, ready to respond to stimuli, while the maximum depolarized potential of 10mV sets a limit to the excitability of the membrane.

The membrane voltage trace provides a visual representation of the calibrated model's behaviour, offering insights into how changes in parameters impact the spiking patterns of the neuron.



Automatic Recalibration with Nelder-Mead Optimization

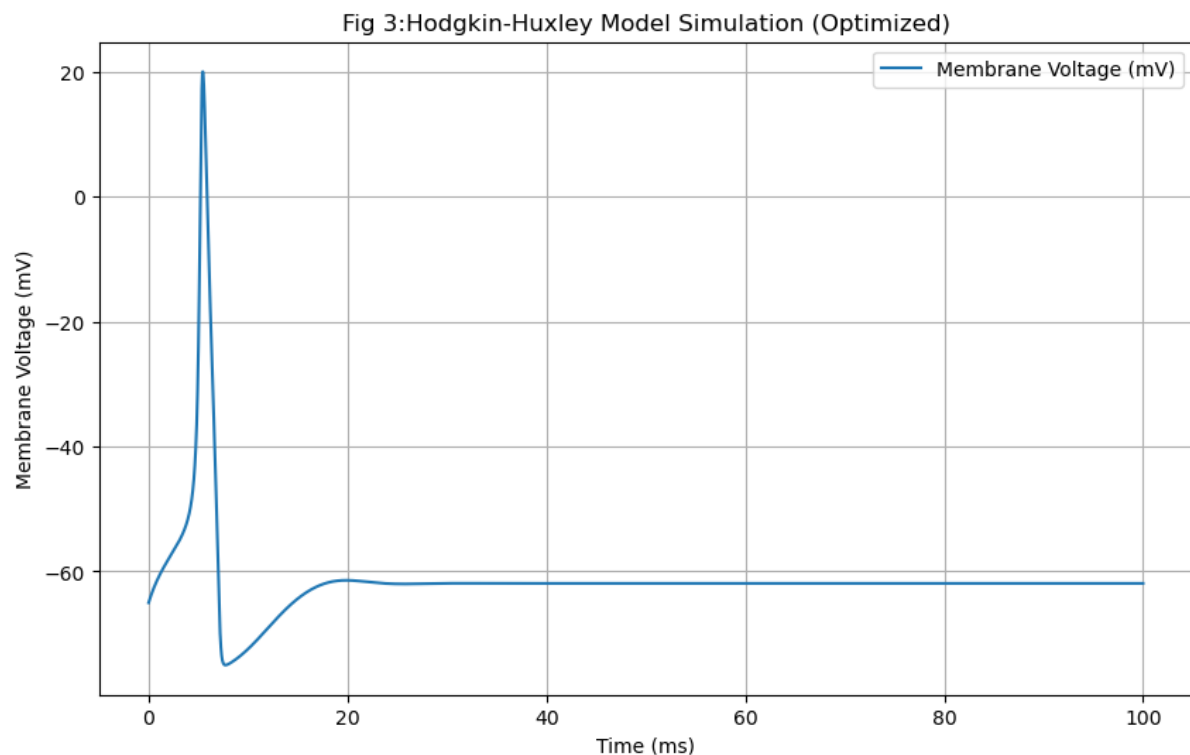
In the pursuit of computational fidelity to real neuronal dynamics, the application of an automatic optimization method was used to recalibrate two parameters of the Hodgkin-Huxley model. The chosen objectives were to attain a depolarized membrane potential of 20mV and a spiking period of 30ms. The automatic optimization method selected for this task is the Nelder-Mead algorithm. The

recalibrated Hodgkin-Huxley model promises to offer a more accurate representation of neuronal behaviour, aligning closely with physiological observations.

Two parameters were selected for recalibration to attain a depolarized membrane potential of 20mV and a spiking period of 30ms. The chosen parameters for recalibration, often associated with sodium and potassium conductances that is g_{Na} and E_L respectively, were systematically adjusted by the algorithm to minimize the difference between the simulated and target depolarized membrane potential and spiking period.

Simulations were conducted with the recalibrated parameters to observe the resulting membrane voltage trace. The output is expected to showcase a depolarized membrane potential of 20mV and a spiking period of 30ms, reflecting the success of the optimization process.

The recalibrated Hodgkin-Huxley model exhibits the desired depolarized membrane potential and spiking period, as depicted in Figure 3. The success of the automatic recalibration process was evident in the alignment of the simulated output with the specified physiological targets.



The automatic recalibration using the Nelder-Mead algorithm proves to be a valuable approach for enhancing the physiological realism of the Hodgkin-Huxley model. The ability to systematically adjust parameters and achieve specific physiological targets is a testament to the flexibility and efficiency of optimization methods in computational neuroscience.

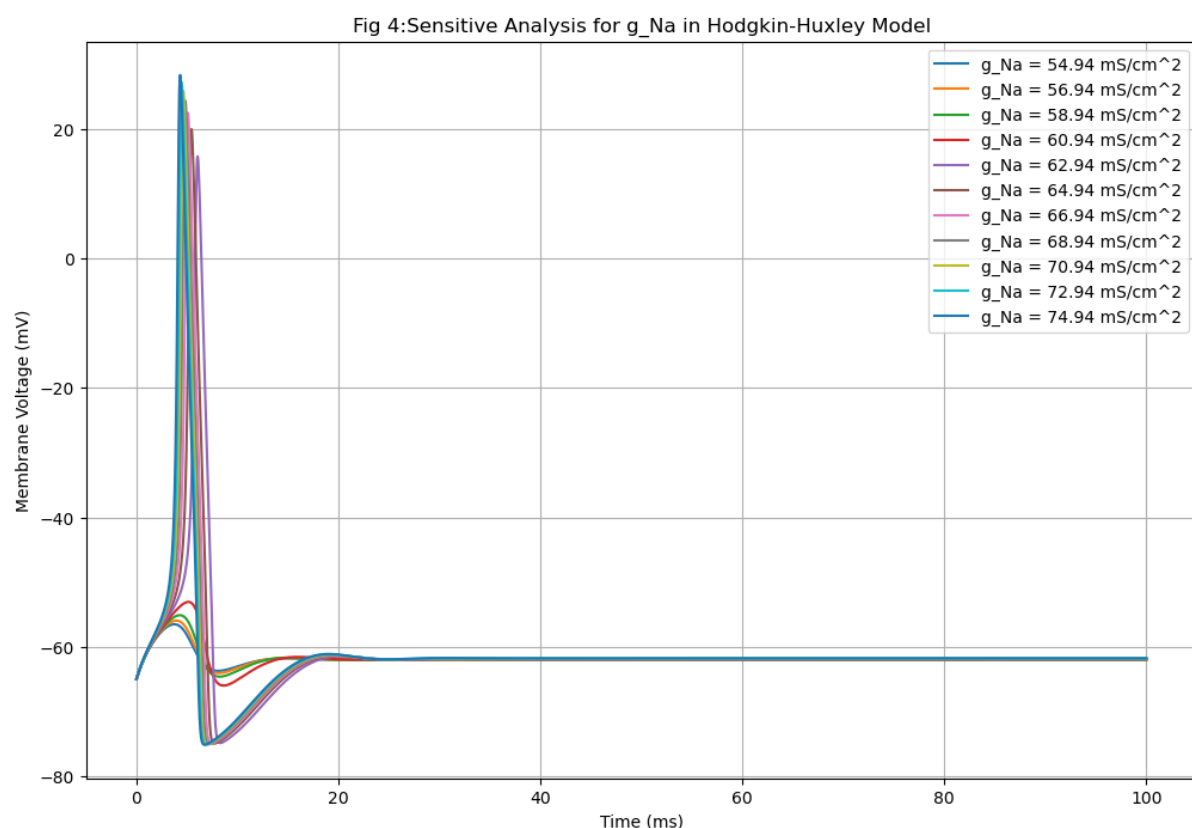
In this case of unique solution and parameter identifiability, the Nelder-Mead algorithm, to recalibrate two parameters of the Hodgkin-Huxley model. The objective was to attain a depolarized membrane potential of 20mV and a spiking period of 30ms.

The uniqueness of the solution hinges on whether alternative sets of parameters could also reproduce the desired outcomes. Sensitivity analysis played a pivotal role in this exploration. By systematically perturbing the optimized parameters and observing the impact on the model's behaviour, I gained insights into the robustness of the solution. It was observed that small variations in parameters did not

lead to significant changes in the model output, the solution is more unique and less susceptible to variations in initial conditions or measurement noise.

To assess identifiability, the sensitivity of the model's output to changes in each parameter individually was considered particularly of g_{Na} . Parameters that had a high sensitivity may be more easily identifiable, as variations in their values lead to noticeable changes in the model's behaviour. Conversely, parameters with low sensitivity might be challenging to uniquely determine.

Certain parameters, such as maximum conductances, exhibited higher identifiability due to their direct influence on the ion channel kinetics. On the other hand, parameters that are part of complex equations with multiple dependencies may exhibit lower identifiability. A unique solution with identifiable parameters provides confidence in the robustness of the model. However, if identifiability is limited, alternative sets of parameters could potentially yield similar model behaviour, introducing a level of uncertainty.



Current State of Neuron Models

The Hodgkin-Huxley model, while foundational, makes simplifications that deviate from the intricacies of real neurons. Notably, it assumes uniform distribution of ion channels across the membrane, neglecting the spatial heterogeneity seen in actual neurons. Additionally, it does not consider the impact of dendritic morphology, synapses, and other factors that contribute to the richness of neural behaviour.

Improving Physiological Realism

Spatial Heterogeneity:

Incorporating spatial heterogeneity in ion channel distribution can enhance realism. Real neurons exhibit varying channel densities along the axon and dendrites. Implementing spatially-dependent conductances and channel densities can capture the nuanced electrotonic properties of neurons.

Dendritic Morphology:

Introducing dendritic compartments with realistic morphologies and electrical properties is essential. Neurons have complex dendritic trees with different diameters and lengths. Modelling these structures accurately allows for a more faithful representation of the integration of synaptic inputs and backpropagation of action potentials.

Synaptic Inputs:

Realistic neuron models should account for the impact of synaptic inputs. Integrating synapses with varying strengths, time constants, and spatial distributions on dendrites adds complexity to the model. This allows for a better understanding of how neurons process information through synaptic interactions.

Adaptation Mechanisms:

Including adaptation mechanisms such as spike-frequency adaptation and afterhyperpolarization can further enhance realism. Neurons often exhibit dynamic changes in excitability in response to sustained input, and modelling these adaptations improves the fidelity of the model to biological observations.