



دانشگاه تهران

پردیس دانشکده‌های فنی

دانشکده‌ی مهندسی برق و کامپیوتر

تمرین امتیازی درس مبانی علوم شناختی

نام و نام خانوادگی:

سینا پیرمرادیان

شماره دانشجویی:

۸۱۰۱۰۱۱۲۵

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1. Hodgkin-Huxley model

1.1 Theoretical Questions

1. How does the Hodgkin-Huxley model explain the generation of an action potential?

The Hodgkin-Huxley model is a mathematical model that describes the behavior of ion channels in the cell membrane during an action potential.

1. **Depolarization:** When the cell membrane is stimulated and reaches a certain threshold potential, voltage-gated sodium channels open. This allows sodium ions to rush into the cell, leading to a rapid increase in the membrane potential. This phase is responsible for the rising phase of the action potential.
2. **Peak of the Action Potential:** At the peak of the action potential, the sodium channels close, and voltage-gated potassium channels open. The closure of sodium channels prevents further sodium influx, while the opening of potassium channels allows potassium ions to move out of the cell, initiating repolarization.
3. **Repolarization:** As potassium ions move out of the cell, the membrane potential starts to decrease, returning to its resting potential. This repolarization phase brings the membrane potential back to its normal negative value.
4. **Hyperpolarization and Restoration:** In some cases, the membrane potential may briefly overshoot its resting potential due to the continued efflux of potassium ions. This phase is called hyperpolarization. Gradually, the ion channels return to their resting state, and the cell membrane potential is restored to its original negative value.

The Hodgkin-Huxley model provides a detailed and accurate description of the underlying mechanisms that govern the generation and propagation of action potentials in excitable cells like neurons and muscle cells. It has been a fundamental model for understanding the electrical behavior of these cells and has greatly contributed to our knowledge of neuroscience.

2. What is the role of potassium conductance in the Hodgkin-Huxley model?

Potassium conductance plays a crucial role in the Hodgkin-Huxley model as it contributes to the repolarization phase of the action potential.

In the Hodgkin-Huxley model, after the rapid depolarization phase of the action potential, when sodium channels have opened and sodium ions have rushed into the cell, the membrane potential reaches its peak. At this point, sodium channels begin to close, and voltage-gated potassium channels open.

The opening of potassium channels allows potassium ions to move out of the cell. This outward flow of positively charged potassium ions repolarizes the cell's membrane, meaning it brings the membrane potential back to its normal negative value. This repolarization phase is crucial in restoring the cell's membrane potential, making it ready for another action potential to occur.

Potassium conductance, represented by the conductance of potassium channels in the Hodgkin-Huxley model, is responsible for the movement of potassium ions across the cell membrane during this repolarization phase. The balance between the inward sodium current during depolarization and the

outward potassium current during repolarization is what enables the cell to generate and propagate action potentials in a controlled and precise manner.

3. How does the Hodgkin-Huxley model account for the refractory period?

The Hodgkin-Huxley model accounts for the refractory period by incorporating the inactivation gating of sodium channels.

During an action potential, when the membrane depolarizes and reaches its peak, voltage-gated sodium channels open, allowing sodium ions to rush into the cell and initiate the rising phase of the action potential. However, shortly after they open, these sodium channels undergo a process called inactivation. Inactivation involves the closure of the sodium channels even though the membrane potential may still be depolarized.

This inactivation mechanism is responsible for the refractory period. While the sodium channels are inactivated, they cannot be opened by further depolarization, preventing the generation of additional action potentials until they have recovered from the inactivated state.

The refractory period is a crucial aspect of the Hodgkin-Huxley model as it ensures that action potentials in excitable cells like neurons and muscle cells are propagated in a one-directional manner and that there is a limit to the frequency at which action potentials can be generated. This property is essential for the proper functioning of the nervous system and muscle contraction.

4. What are the limitations of the Hodgkin-Huxley model?

The limitation includes:

1. **Complexity and Computational Burden:** The Hodgkin-Huxley model is highly detailed and computationally complex. While it provides a comprehensive description of the ionic mechanisms underlying action potentials, this complexity makes it challenging to analyze and simulate large-scale neural networks or complex systems efficiently.
2. **Assumption of Voltage-Gated Ion Channels:** The model primarily relies on voltage-gated ion channels (sodium and potassium) as the main mechanisms for generating action potentials. However, in reality, other types of ion channels, such as calcium-gated channels, play important roles in some cells and under certain conditions. The model's focus on only voltage-gated channels may oversimplify the behavior of some neurons.
3. **Lack of Spatial Variation and Anatomical Detail:** The Hodgkin-Huxley model treats neurons as a single compartment and does not account for spatial variation in ion channel densities or the detailed anatomical structure of neurons. In real neurons, the distribution of ion channels may vary across different regions, and the detailed morphology of neurons can significantly influence their electrical behavior.
4. **Missing Complex Neuronal Phenomena:** The model does not capture certain phenomena observed in real neurons, such as subthreshold oscillations and dendritic integration. Neurons *in vivo* exhibit diverse and intricate responses to various stimuli, and these subtleties are not fully represented in the Hodgkin-Huxley model.

Despite these limitations, the Hodgkin-Huxley model remains a fundamental and groundbreaking model in neuroscience. It has significantly contributed to our understanding of action potentials and the behavior of excitable cells.

5. What is the role of ion channel densities in the Hodgkin-Huxley model?

Ion channel densities in the Hodgkin-Huxley model refer to the distribution and abundance of different types of ion channels along the neuronal membrane. These densities determine the conductance of each ion channel type, which directly influences the dynamics of the action potential.

By adjusting the densities of voltage-gated sodium and potassium channels, the Hodgkin-Huxley model can simulate various types of neurons with different firing patterns and excitability properties. Changes in ion channel densities can have significant effects on several aspects of the action potential and the overall behavior of the neuron:

1. **Action Potential Threshold:** The threshold potential at which an action potential is initiated can be affected by the density of voltage-gated sodium channels. Higher densities of these channels may result in a lower threshold, making the neuron more excitable and more likely to fire an action potential.
2. **Action Potential Shape and Duration:** The density of both sodium and potassium channels influences the shape and duration of the action potential. Higher densities of sodium channels contribute to a steeper rising phase of the action potential, while higher densities of potassium channels can lead to a faster repolarization phase, affecting the overall shape and duration of the action potential.
3. **Overall Excitability:** The density of ion channels determines the overall excitability of the neuron. Neurons with higher densities of sodium channels and lower densities of potassium channels, for example, tend to be more excitable and may fire action potentials more frequently.

Incorporating different ion channel densities in the Hodgkin-Huxley model allows researchers to better understand and replicate the behavior of different types of neurons in the nervous system.

6. What are some modifications or extensions to the original Hodgkin-Huxley model?

Here I explain some modifications and extensions of the Hodgkin-Huxley model:

1. **Incorporation of Additional Ion Channels:** One significant extension involves including additional types of ion channels, such as calcium channels. Different cells in the nervous system express a variety of ion channels, and incorporating these channels allows for more accurate modeling of specific cell types and their electrical behavior.

2. **Complex Channel Gating Mechanisms:** Some modifications introduce more complex gating mechanisms for ion channels. This includes multiple activation and inactivation gates or slow dynamics that better capture the behavior of certain ion channels in response to varying membrane potentials.
3. **Biophysical Factors:** Taking into account the effect of temperature and other biophysical factors on ion channel kinetics can improve the model's accuracy, especially when studying the behavior of neurons in different physiological conditions.
4. **Simplified Models:** To reduce computational complexity while retaining essential features of action potential dynamics, simplified models like the FitzHugh-Nagumo model or the Izhikevich model have been developed. These models provide a more tractable approach for certain types of simulations.

Integration with Other Mathematical Frameworks: The Hodgkin-Huxley model can be combined with other mathematical frameworks, such as network models or stochastic models, to study larger-scale neural activity or incorporate variability and noise observed in real neural systems.

1.2 Simulation Questions

1.2.1 Action Potential Generation

1. Simulate the Hodgkin-Huxley model using the given parameters. What is the threshold current required to elicit an action potential?

Based on the provided information, the threshold current required to elicit an action potential in the simulated Hodgkin-Huxley model is not explicitly mentioned. However, we can infer that the threshold current lies somewhere between the impulse input current ($I(t) = 20\delta(t)$) and the step input current ($I(t) = 20u(t)$).

In the case of the impulse input current, a single action potential is generated, and the membrane potential is depolarized and repolarized, returning to steady-state afterward.

In the case of the step input current, the model generates an action potential but shows a tonic behavior, as the amplitude of the input current is high and prevents the membrane potential from returning to steady state.

To determine the threshold current, one would typically perform a series of simulations with increasing input currents until an action potential is consistently generated. The threshold current is the minimum current required to consistently elicit an action potential in the model.

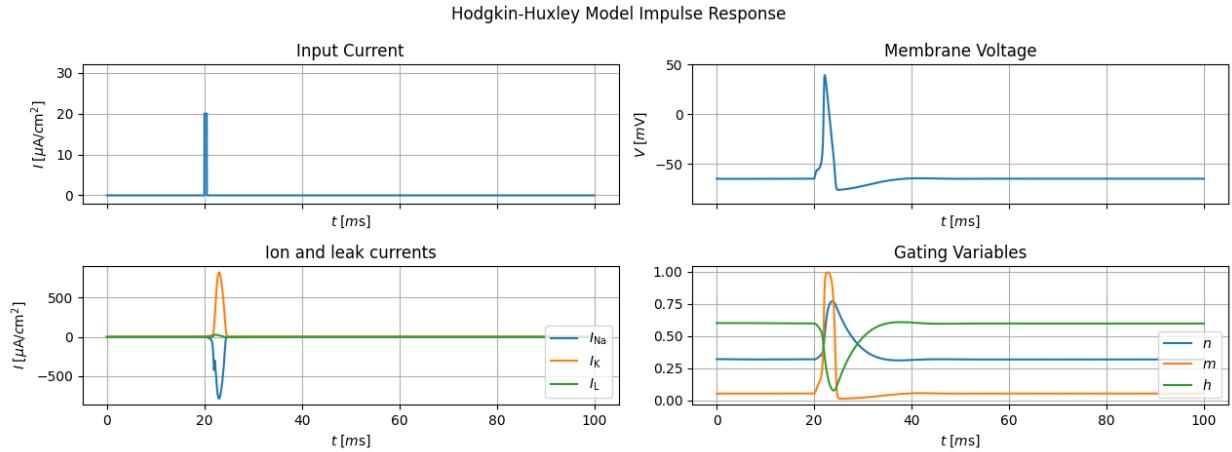


Figure 1

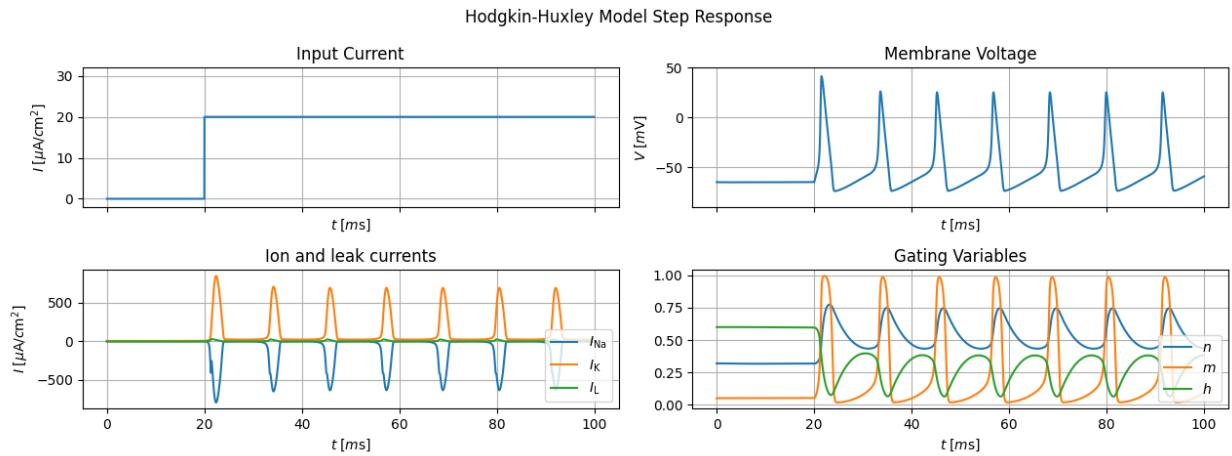


Figure 2

To determine the minimum current required to trigger an action potential (AP), a systematic approach is taken by testing various amplitudes of input currents and monitoring the membrane voltage response. If the membrane voltage (V) exceeds a certain threshold, typically considered as $V > 0$, it indicates the generation of an action potential. By progressively adjusting the input current amplitude and observing the membrane voltage response, the threshold current is identified using this method. This allows us to find the critical current level necessary to consistently elicit an action potential in the simulated Hodgkin-Huxley model.

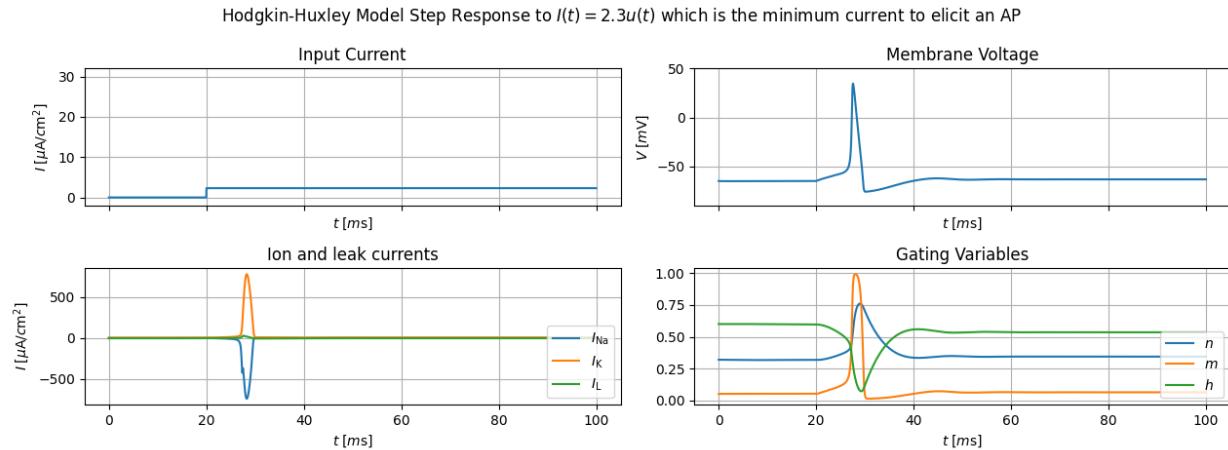


Figure 3

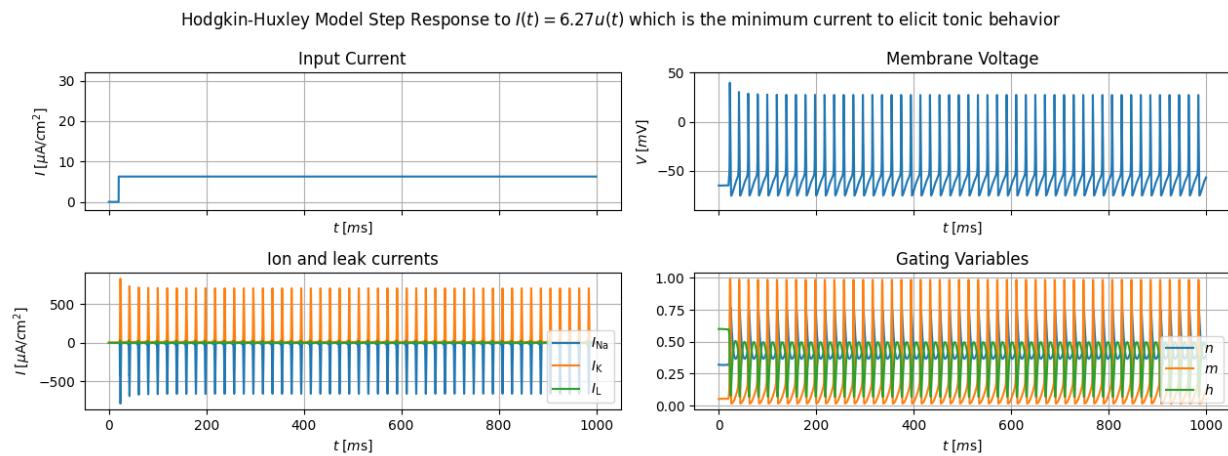


Figure 4

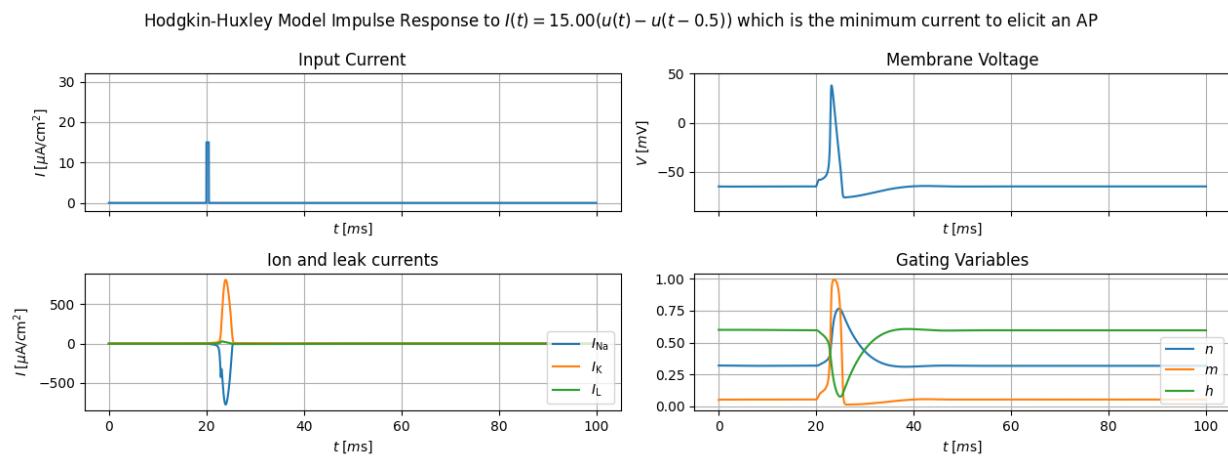


Figure 5

2. Investigate the effects of varying the amplitude and duration of the applied current on the action potential waveform and firing rate.

By manipulating the amplitude and duration of the applied current, we can observe notable effects on the action potential (AP) waveform and firing rate. Altering the current amplitude can influence the generation and shape of the AP. As the amplitude increases, we anticipate a corresponding increase in the frequency of AP production. Moreover, when the amplitude of the step input rises significantly, we may witness a tonic behavior where the membrane potential fails to return to steady state, resulting in continuous firing.

Similarly, adjusting the duration of the input current can also impact the AP characteristics. A lengthier duration of input current may lead to more frequent action potential generation, as it provides an extended depolarization window. This prolonged depolarization phase can result in higher firing rates, contributing to an increase in AP frequency.

By systematically examining various combinations of current amplitude and duration, we can gain valuable insights into the behavior of the Hodgkin-Huxley model and the factors influencing action potential dynamics and firing rates.

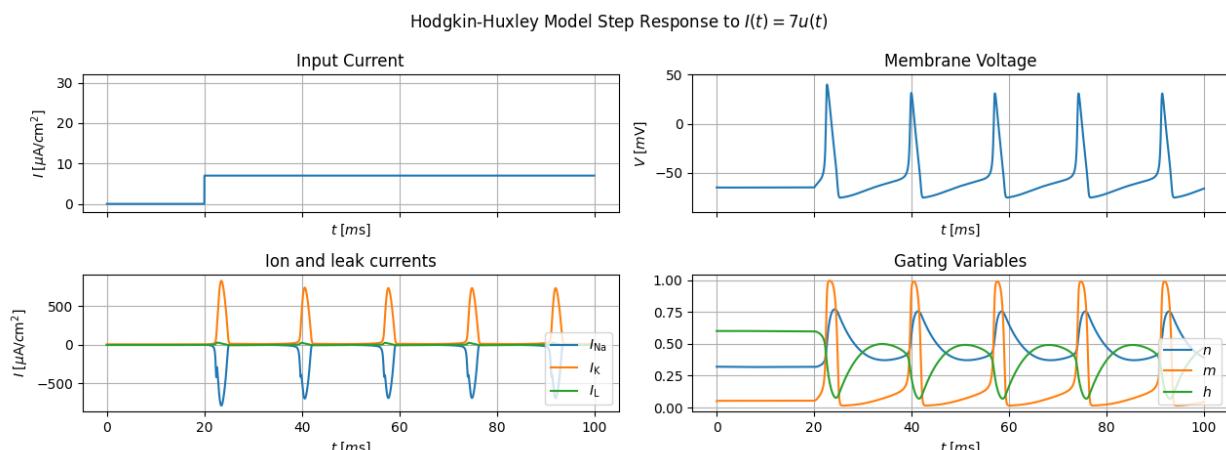


Figure 6

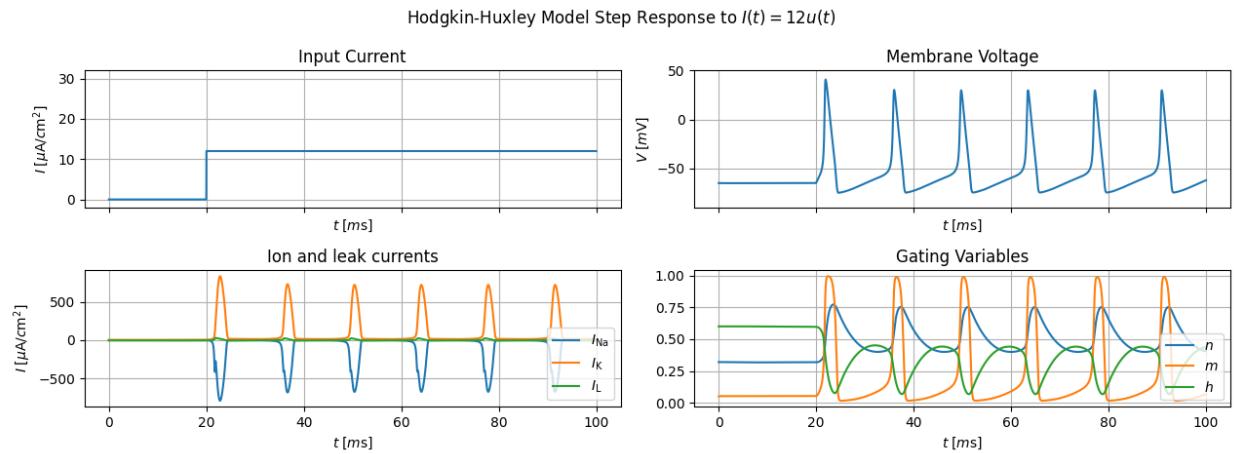


Figure 7

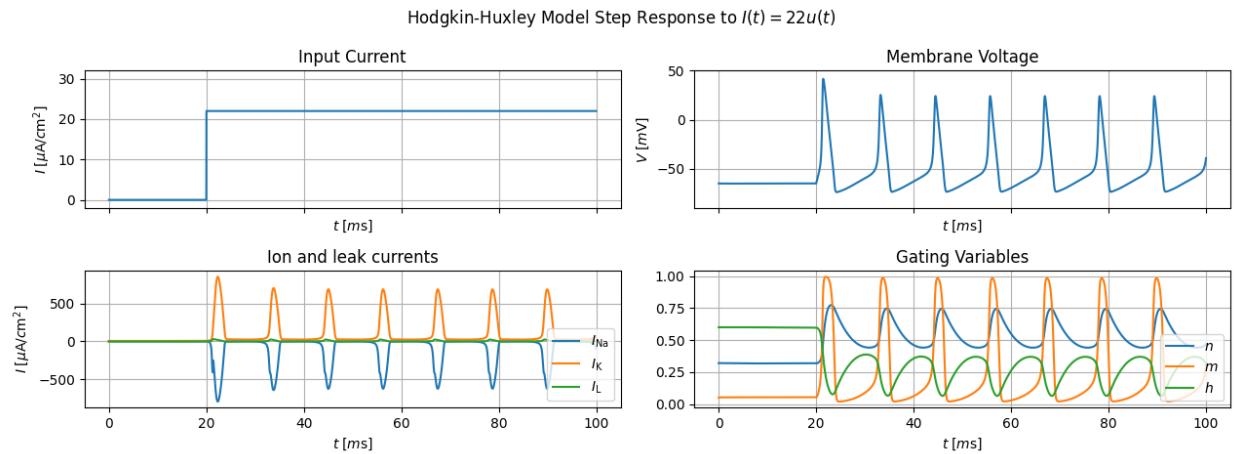


Figure 8

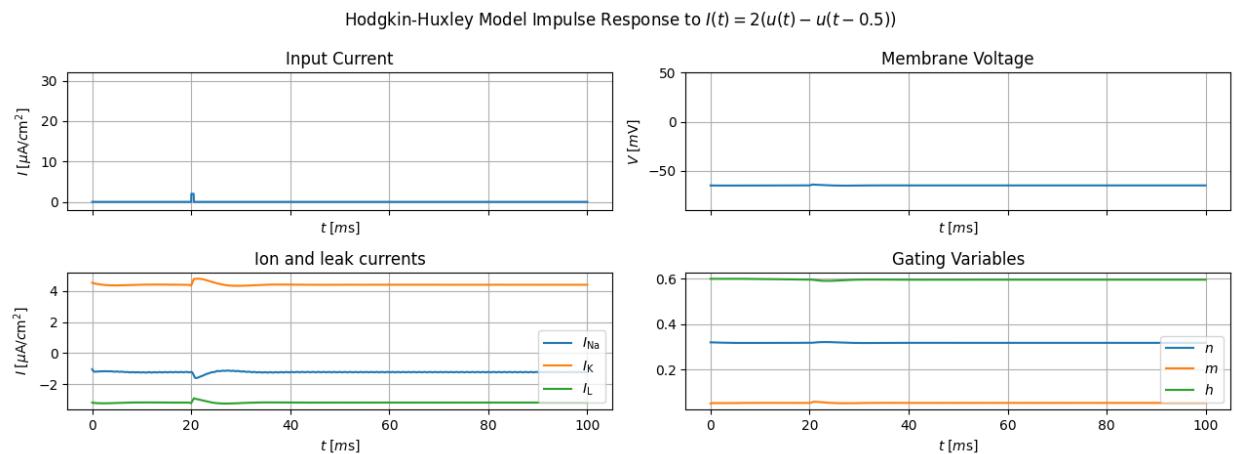


Figure 9

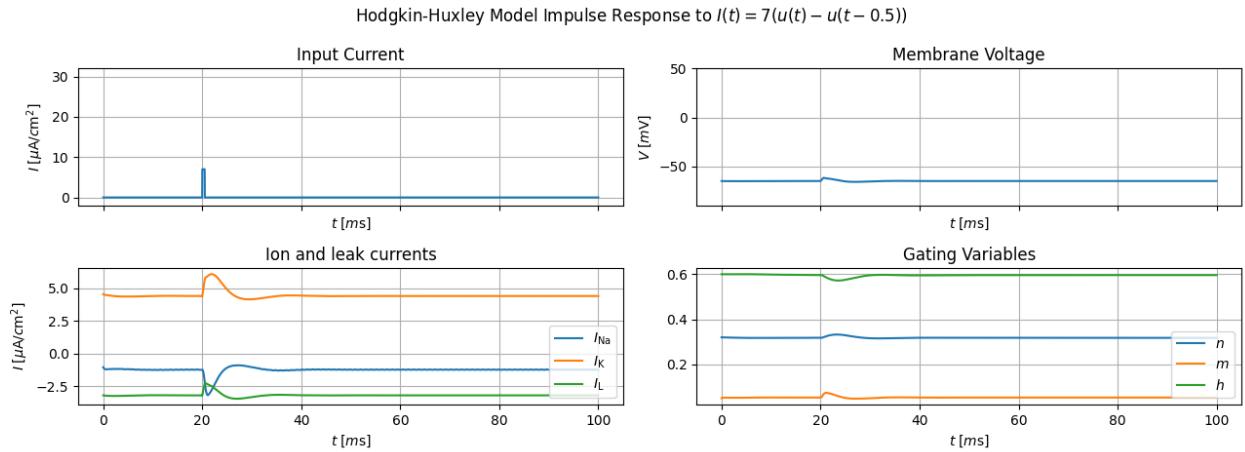


Figure 10

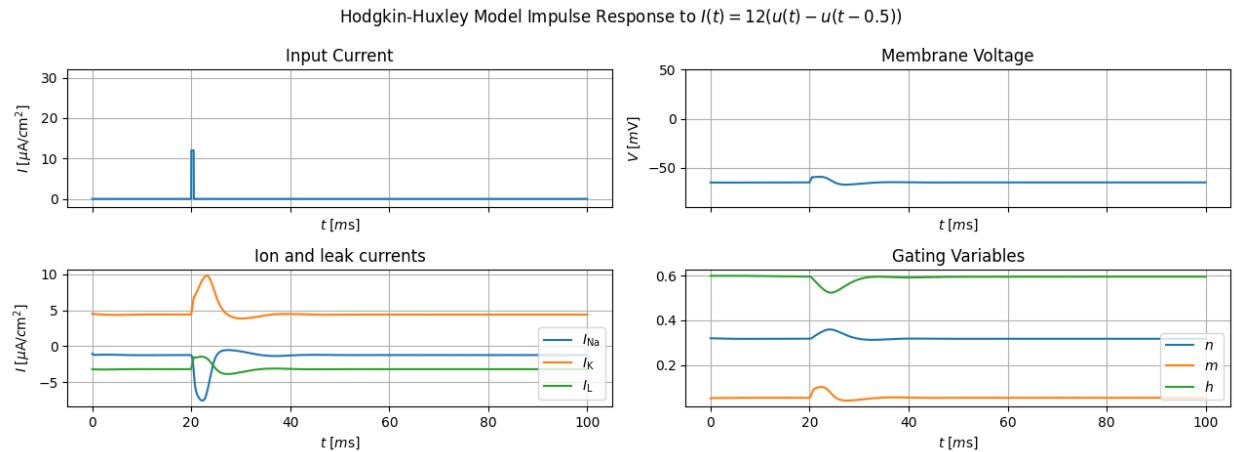


Figure 11

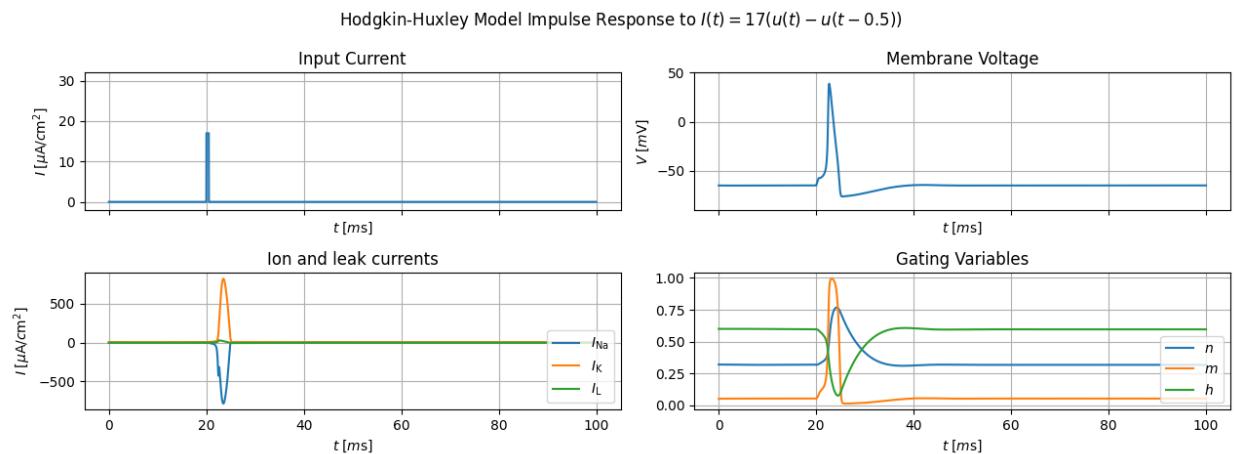


Figure 12

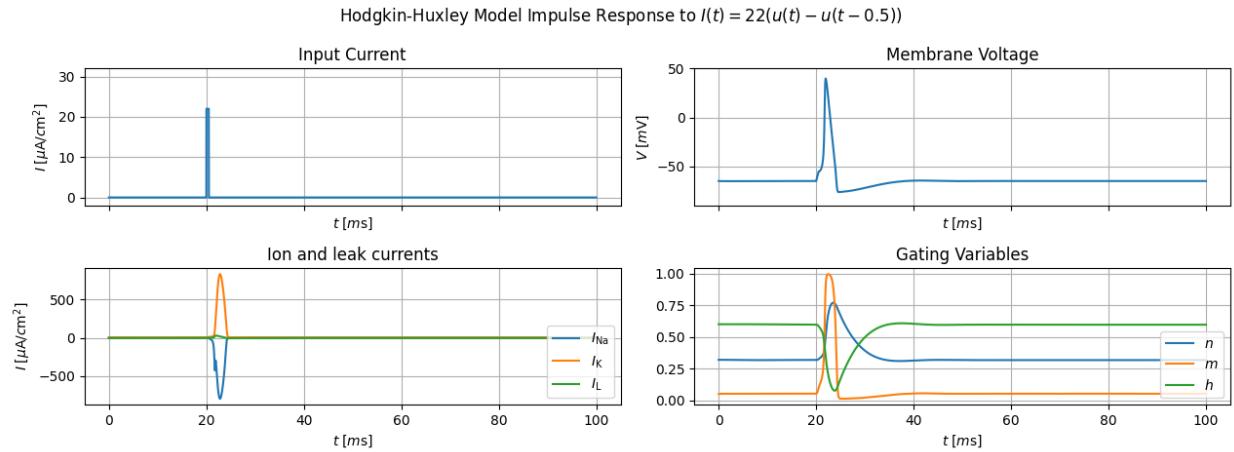


Figure 13

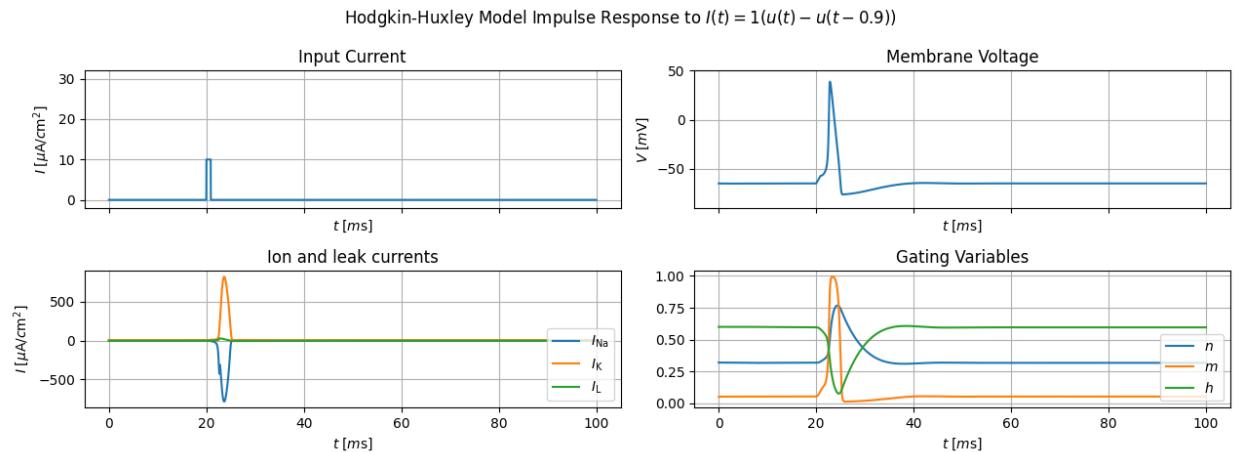


Figure 14

Impulse response Figures illustrates the outcomes of varying the amplitude of the step current on the membrane potential. It is evident that as the amplitude increases, the cell generates action potentials at a faster rate. In above Figure, we observe the impact of altering the impulse amplitude. Notably, as the amplitude increases, the time required to generate action potentials reduces. Figure 8 demonstrates the effects of changing the impulse input's duration. Generally, it can be concluded that augmenting the amplitude or duration of stimulation results in a greater charge accumulation on the capacitor, leading to the generation of action potentials. These observations underscore the importance of current amplitude and duration in influencing the frequency and timing of action potential generation in the Hodgkin-Huxley model.

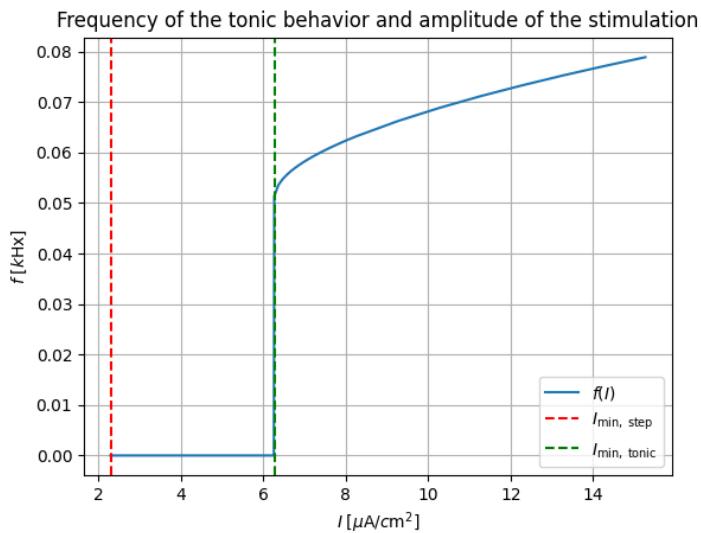


Figure 15

The relationship between the firing rate of the cell and the amplitude of stimulation is evident. By calculating the firing frequency for various amplitudes and plotting a curve using these amplitude-frequency pairs, Figure 15 confirms our expectations. The graph illustrates the expected pattern of increased firing frequency with higher stimulation amplitudes. This observation reinforces the significant impact that stimulation amplitude has on the firing behavior of the cell, as predicted by the Hodgkin-Huxley model.

3. Compare the action potential waveforms generated by the Hodgkin-Huxley model with different initial conditions. How do these variations affect the shape and duration of the action potential?

Modifying the initial conditions in the Hodgkin-Huxley model can result in diverse cell behaviors. When altering the initial conditions of the gating variables, it corresponds to opening or closing the respective ion channels, thereby influencing the amplitude of the input current. Additionally, changing the initial membrane potential can also lead to the generation of action potentials.

To investigate the effects of these variations, we can systematically change the values of the initial conditions one at a time and observe the model's response. By doing so, we can understand how variations in the initial conditions impact the action potential waveforms. Different initial conditions can lead to varying shapes and durations of the action potentials, as they alter the conductance of ion channels and the overall excitability of the cell. Analyzing these changes can provide valuable insights into the sensitivity of the Hodgkin-Huxley model to different starting conditions and its ability to reproduce diverse electrical behaviors observed in real neurons.

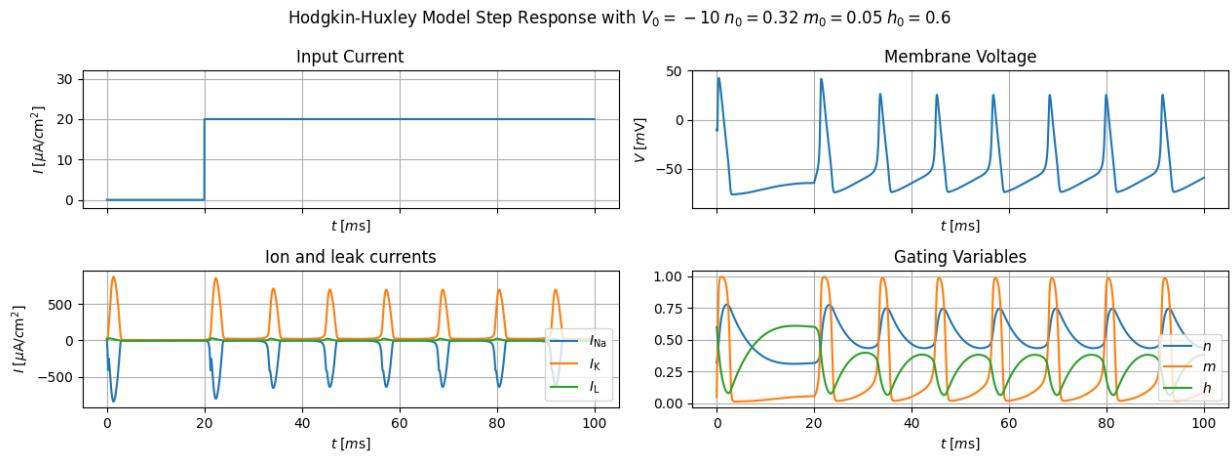


Figure 16

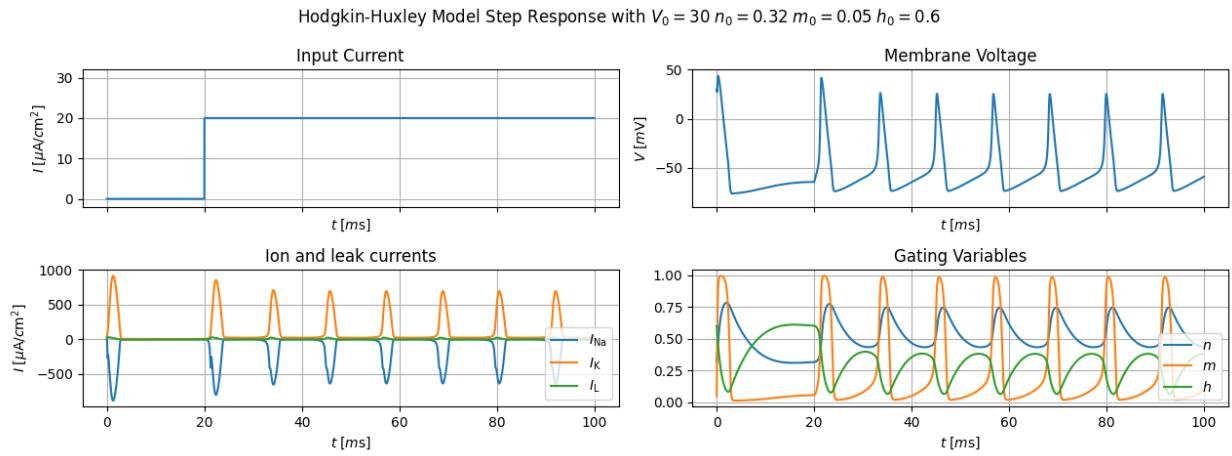


Figure 17

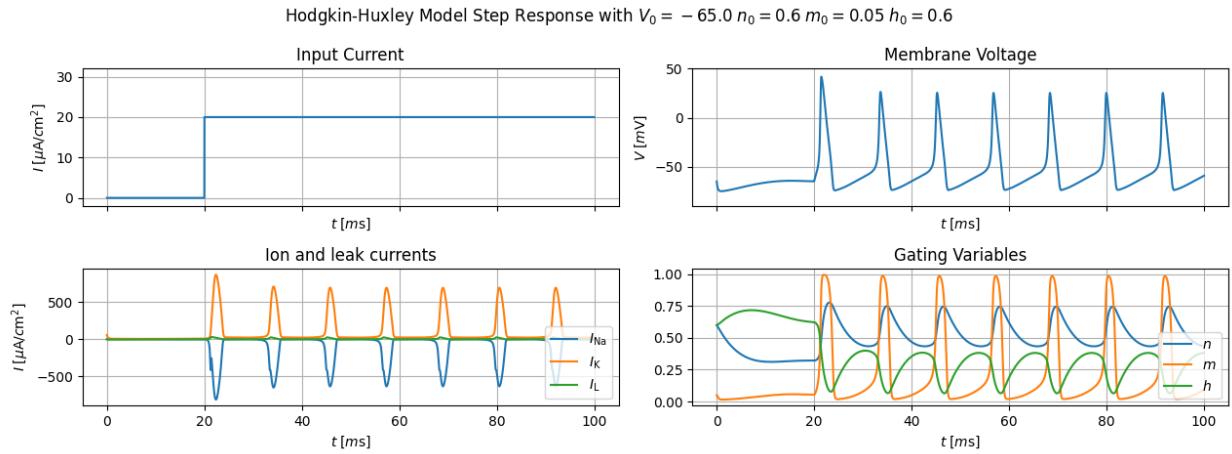


Figure 18

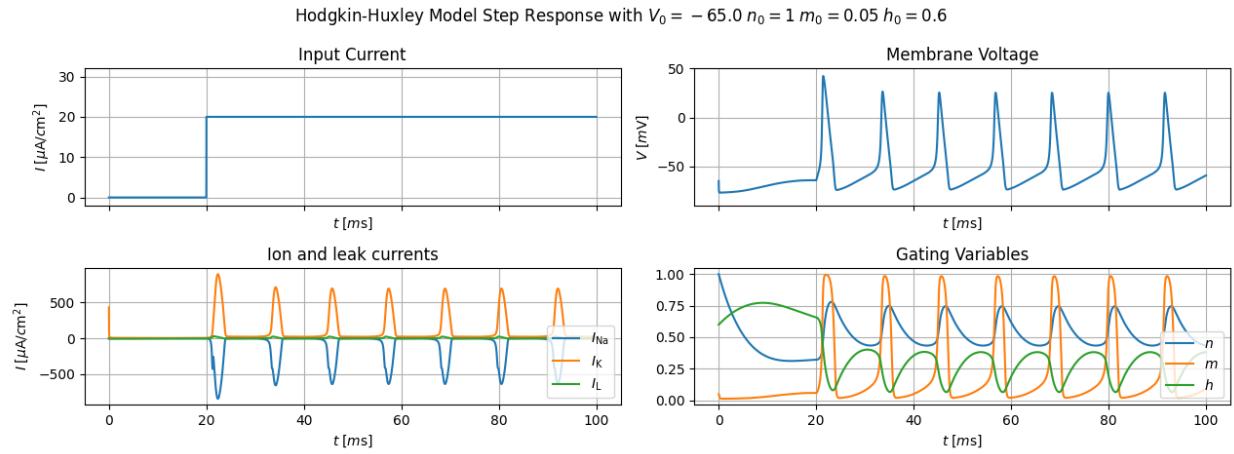


Figure 19

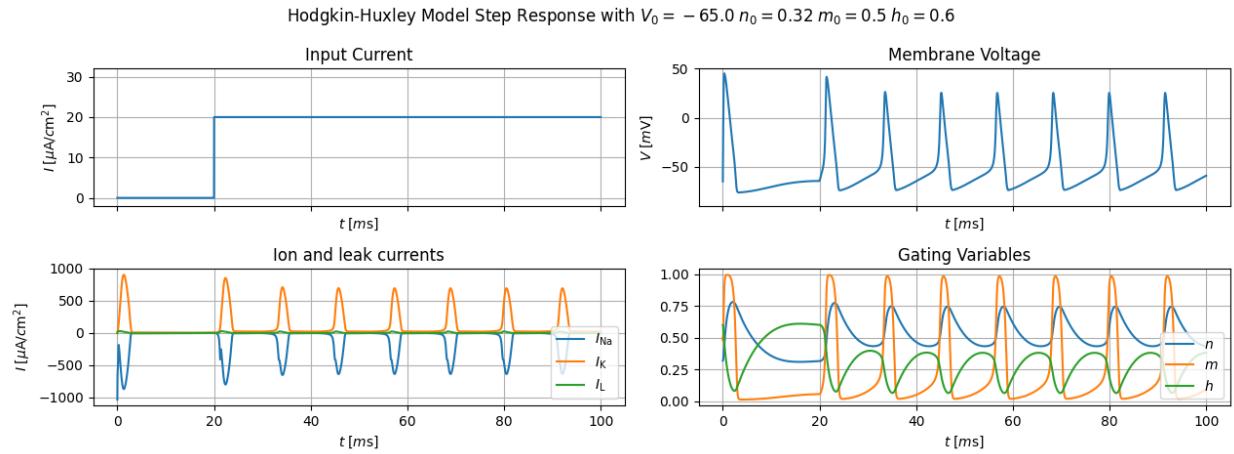


Figure 20

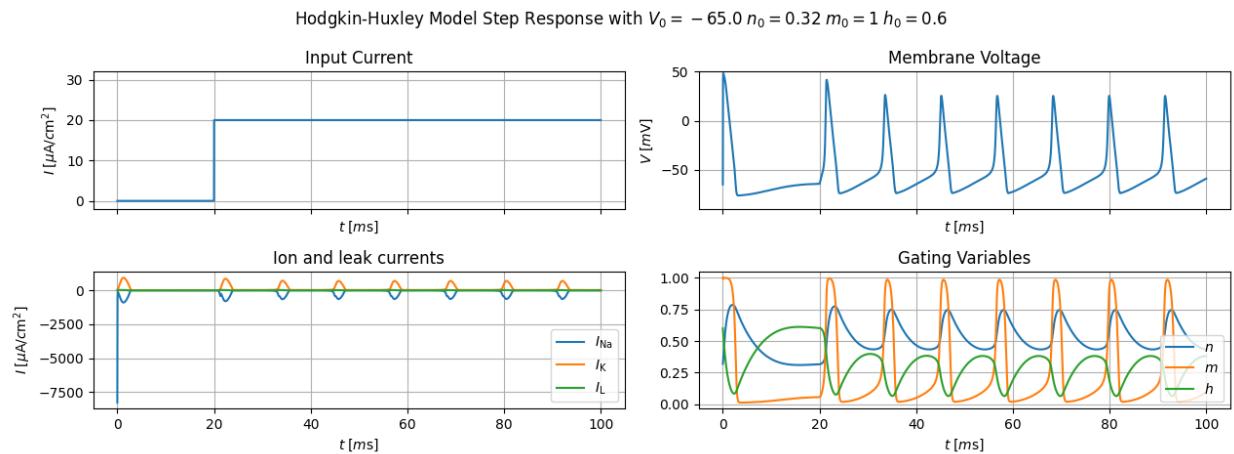


Figure 21

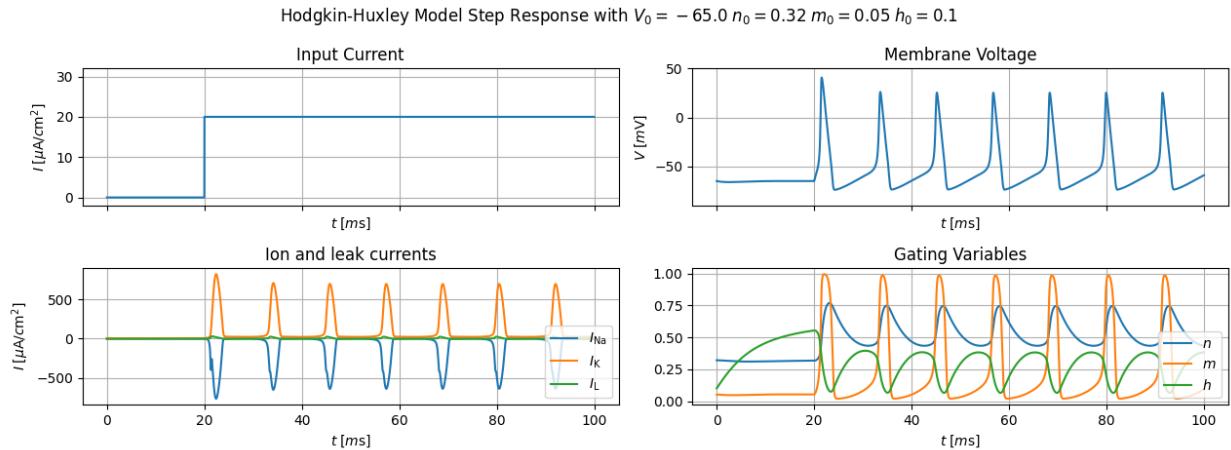


Figure 22

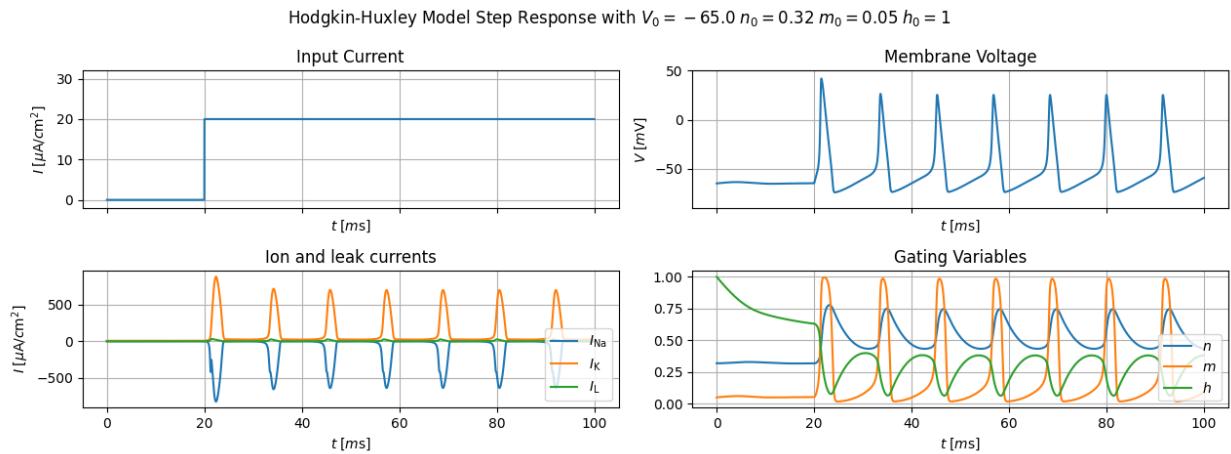


Figure 23

As previously discussed, certain initial conditions can trigger an action potential (AP) in the cell, after which the cell returns to its steady state. Consequently, the initial conditions cannot exert a lasting influence on the cell's behavior, but they can induce action potentials that eventually lead the cell back to its steady state. These transient effects of initial conditions highlight the dynamic nature of the Hodgkin-Huxley model, where changes in ion channel conductance driven by the initial conditions contribute to the generation and termination of action potentials.

1.2.2 Channel Conductance and Dynamics

1. Explore the impact of altering the maximum sodium conductance (g_{Na}) and maximum potassium conductance (g_K) on the shape and properties of the action potential.

By systematically adjusting the parameters of the Hodgkin-Huxley model, such as the maximum sodium conductance (g_{Na}) and maximum potassium conductance (g_K), and carefully observing the cell's zero input response, impulse response, and step response, one can gain insights into the effects of these parameters on the action potential characteristics.

Through these simulations, we can examine how changes in g_{Na} and g_K impact the cell's excitability, the shape of the action potential waveform, and other important properties of the action potential. By analyzing the zero input response, impulse response, and step response, we can discern the specific influences of these conductance parameters on the cell's electrical behavior. This approach allows us to understand how alterations in g_{Na} and g_K can lead to distinct action potential dynamics.

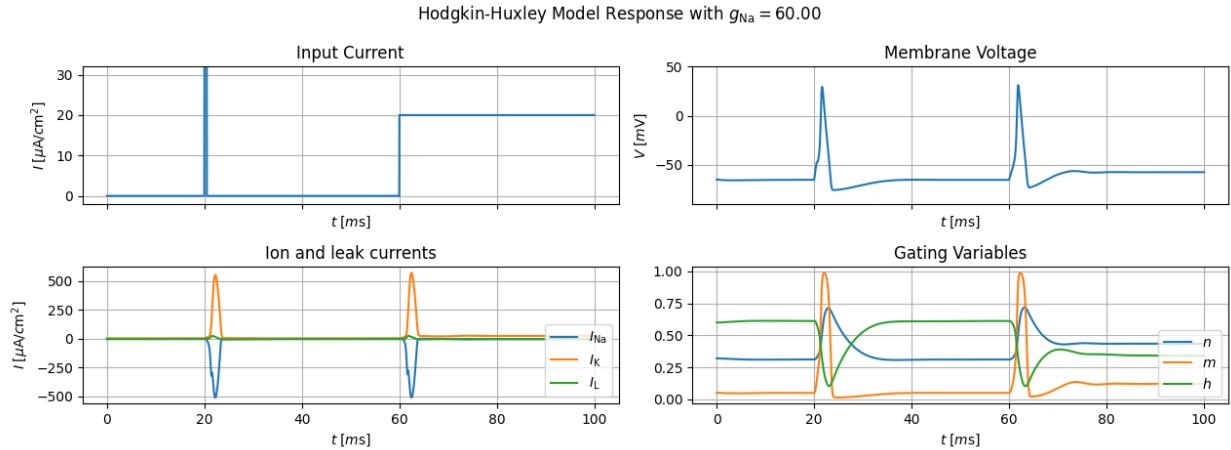


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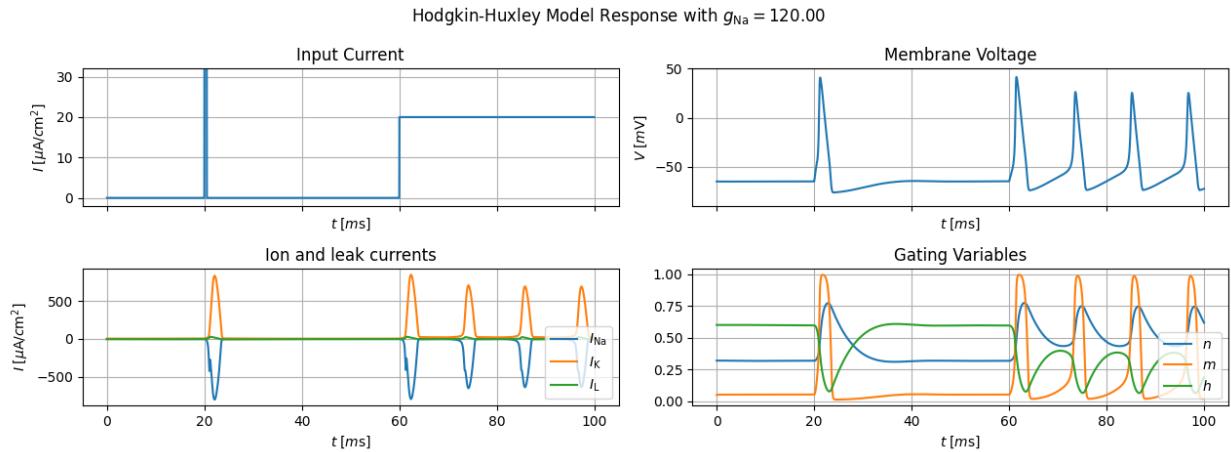


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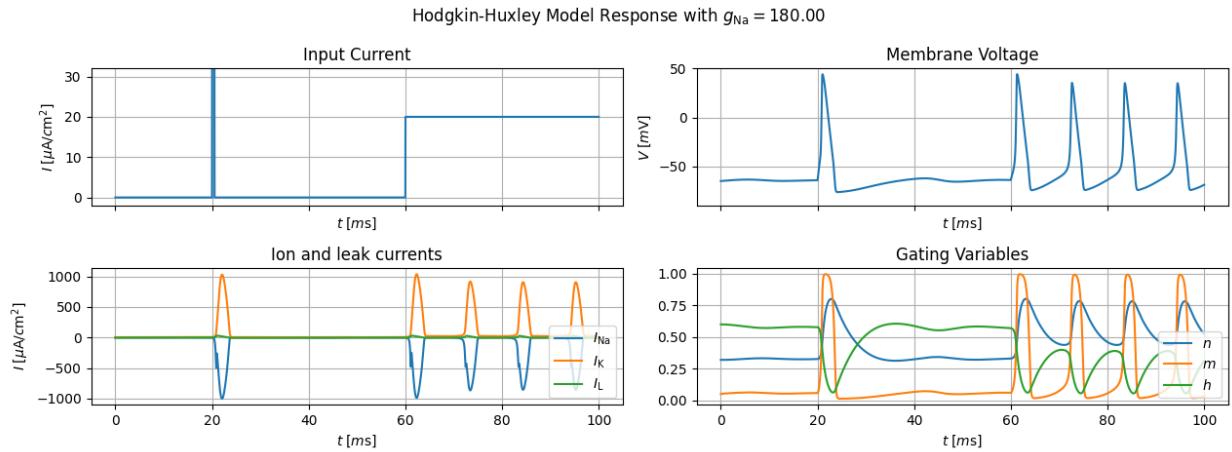


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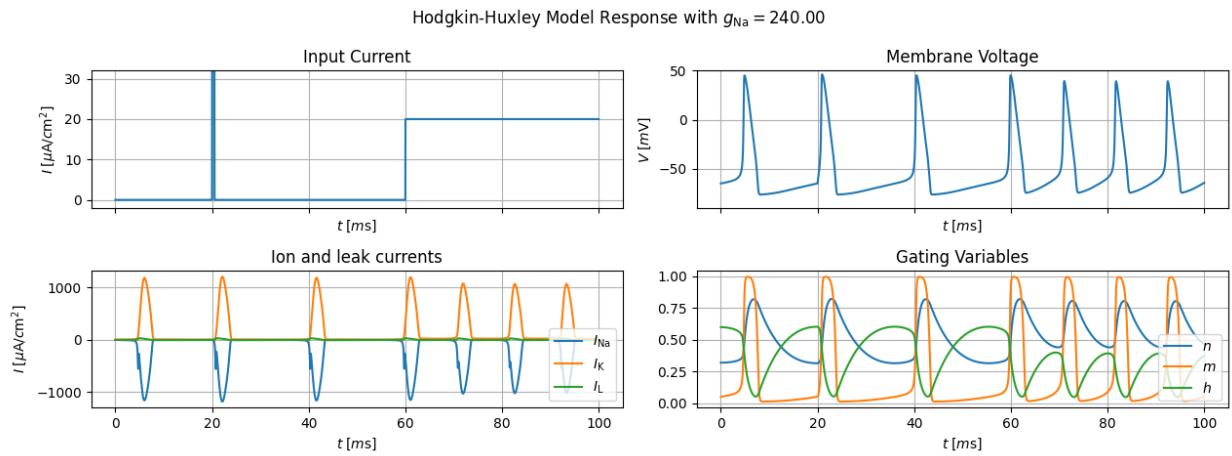


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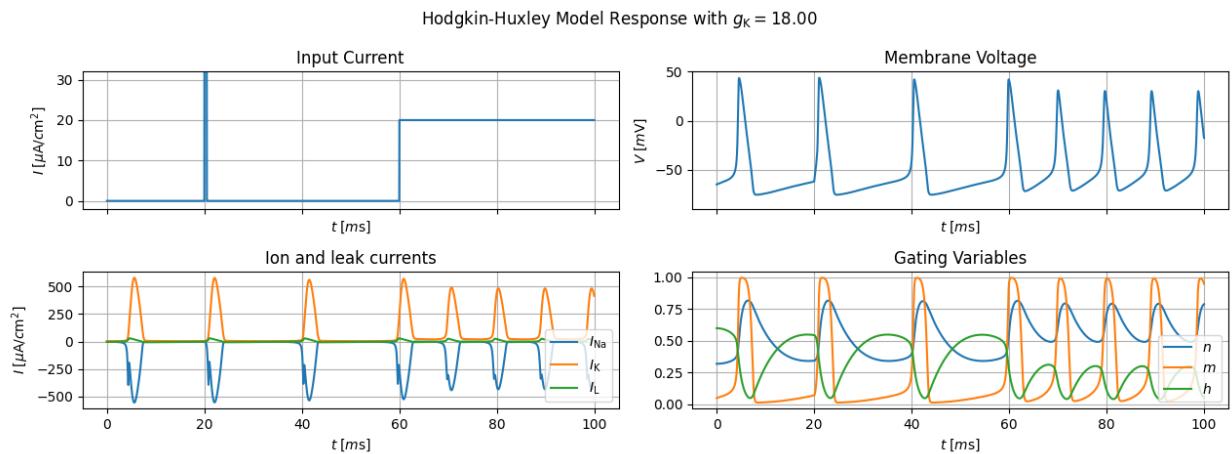


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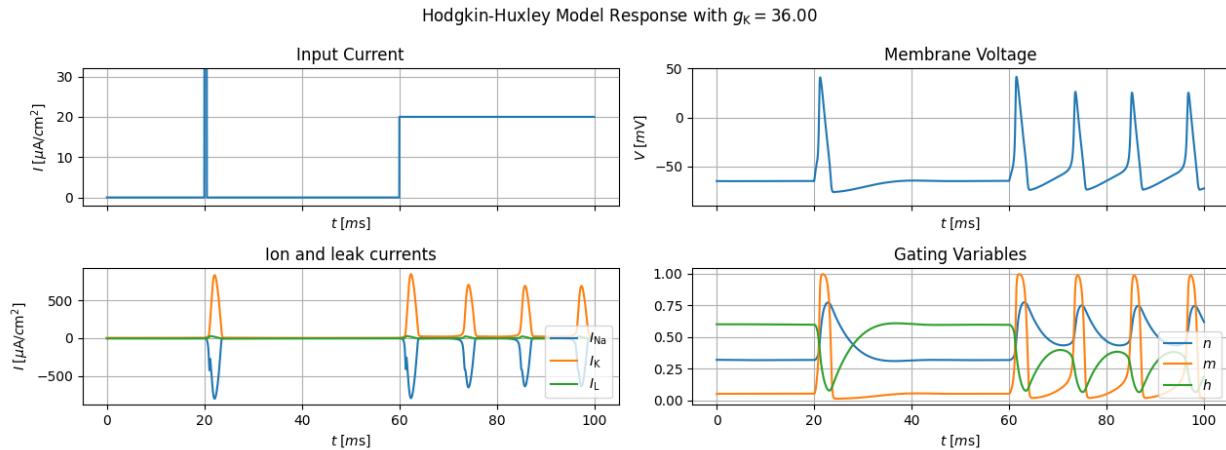


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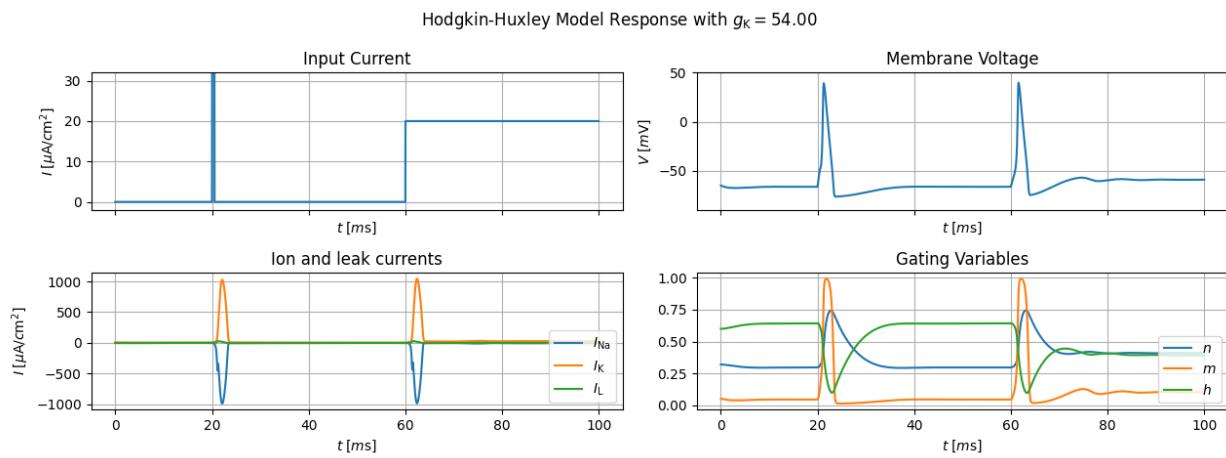


Figure 30

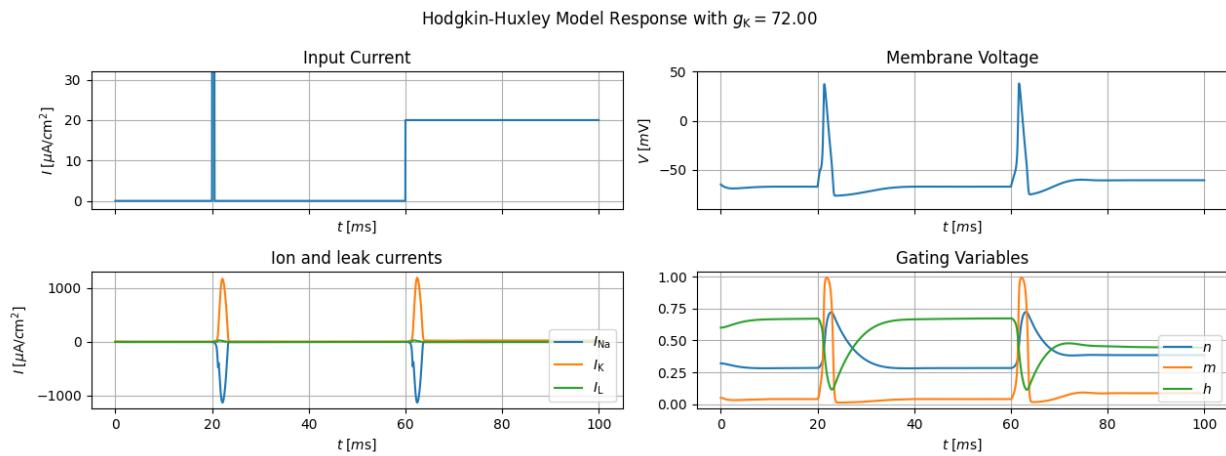


Figure 31

These two parameters have the capacity to modify the cell's excitability. Depending on specific values, the cell may spontaneously generate action potentials (APs). A reduction in g_K can heighten cell excitability,

while an increase in g_{Na} will produce a similar effect. Based on our understanding, an increase in g_{Na} corresponds to a rise in the inward sodium current. This heightened sodium current can excite the cell and accelerate the membrane voltage, leading to AP generation. Conversely, an increase in g_K results in an augmented outward potassium current, which contributes to the cell's repolarization. By bolstering this outward current, it opposes the inward sodium current and dampens cell excitability. However, in some instances, excitability may escalate to the extent that the cell fires spontaneously without any external stimulation. These variations in g_{Na} and g_K provide critical insights into the complex dynamics of action potential generation and regulation in the Hodgkin-Huxley model.

2. Simulate the Hodgkin-Huxley model with different combinations of g_{Na} and g_K . How do these changes affect the excitability and firing behavior of the neuron?

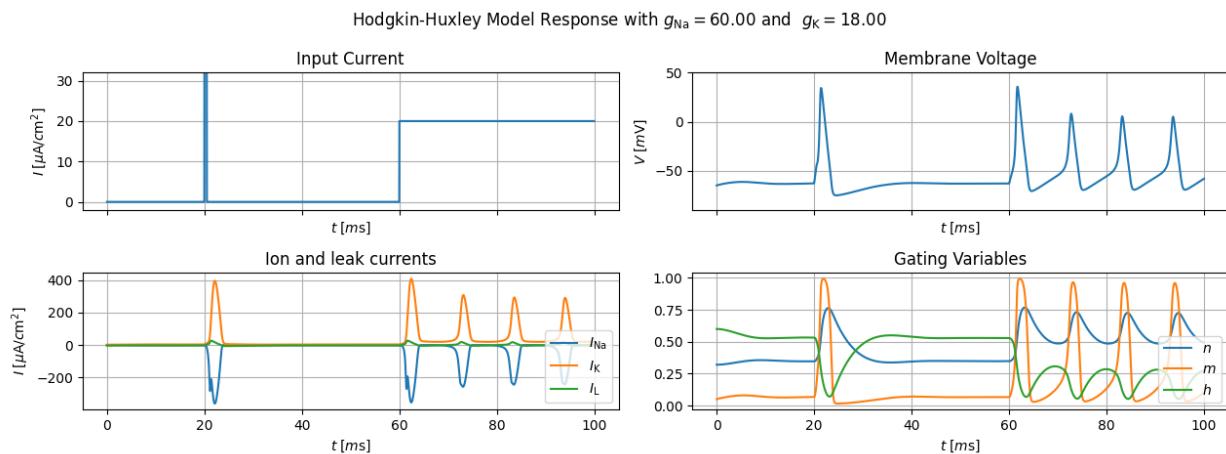


Figure 32

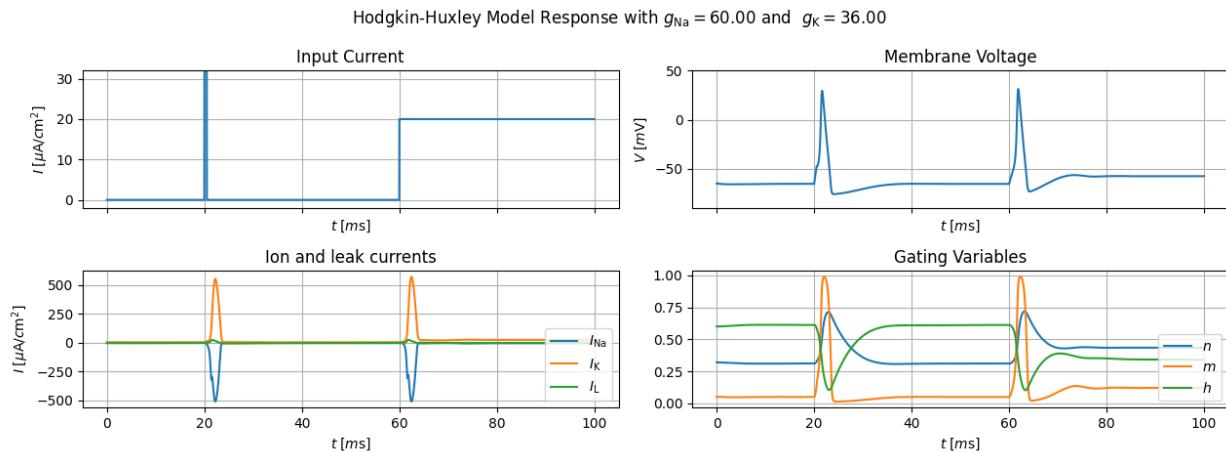


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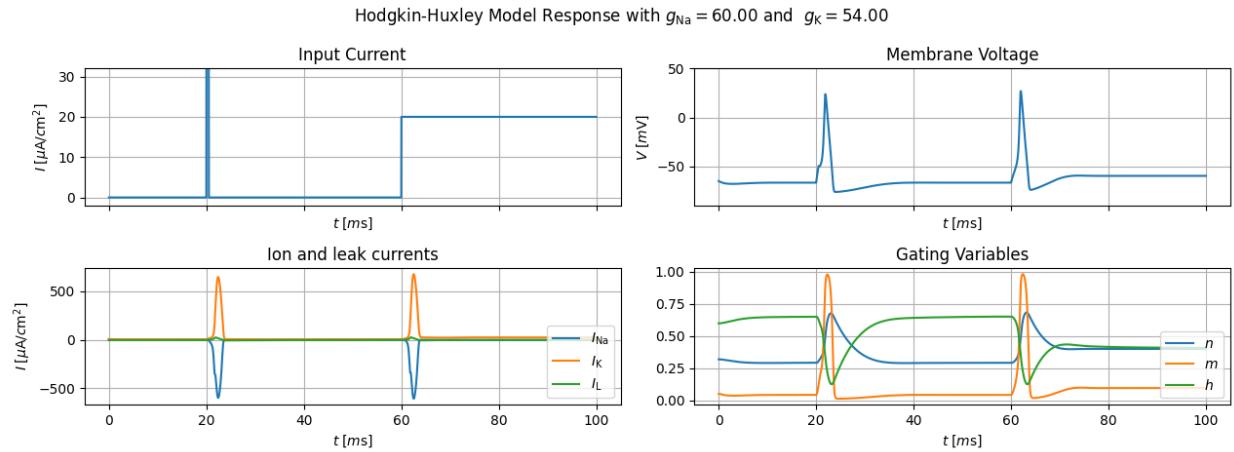


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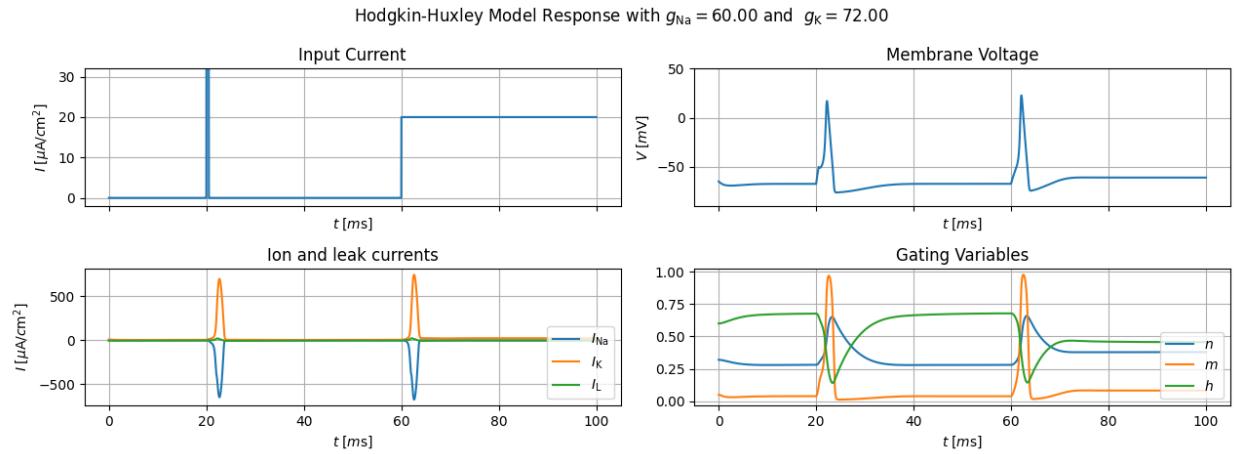


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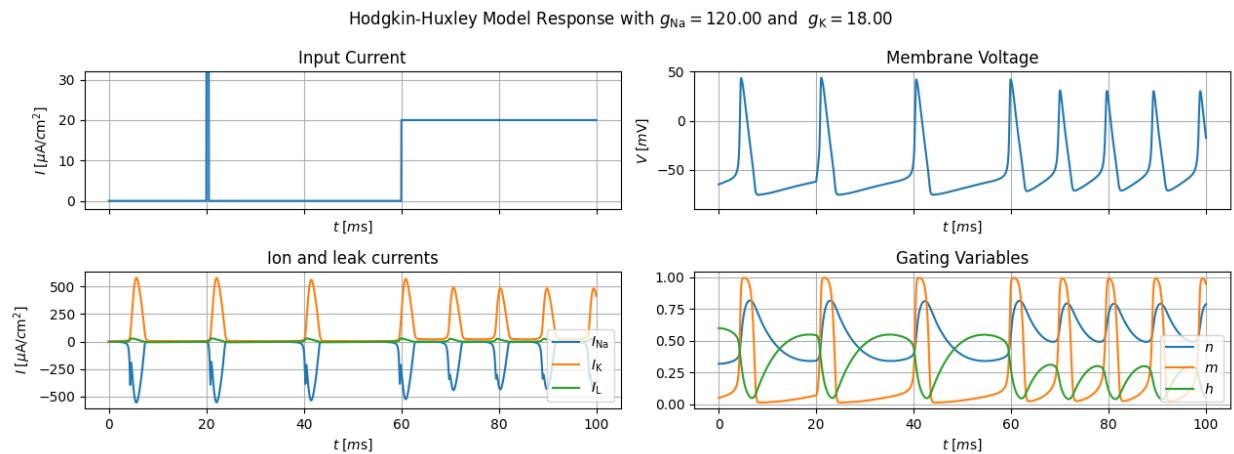


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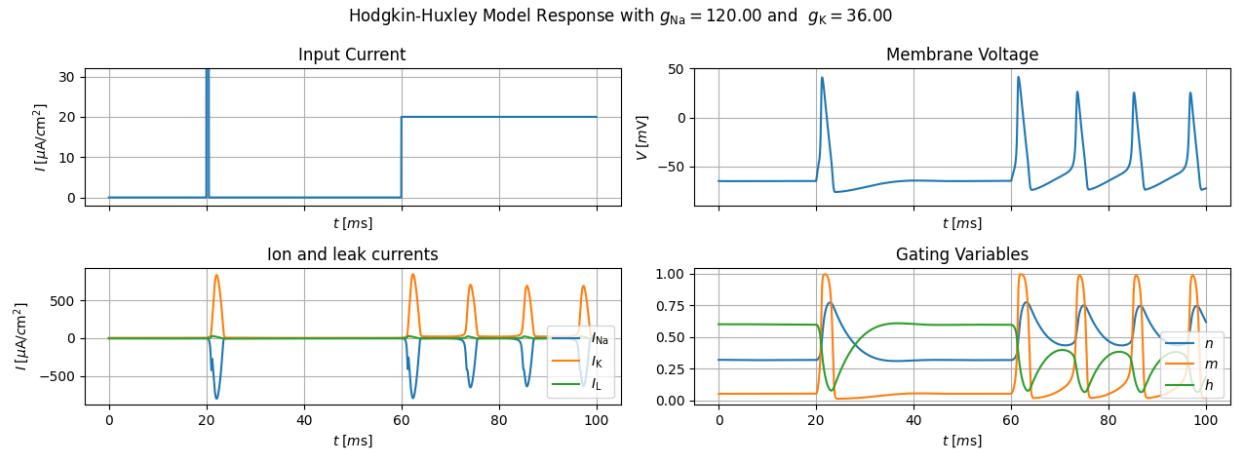


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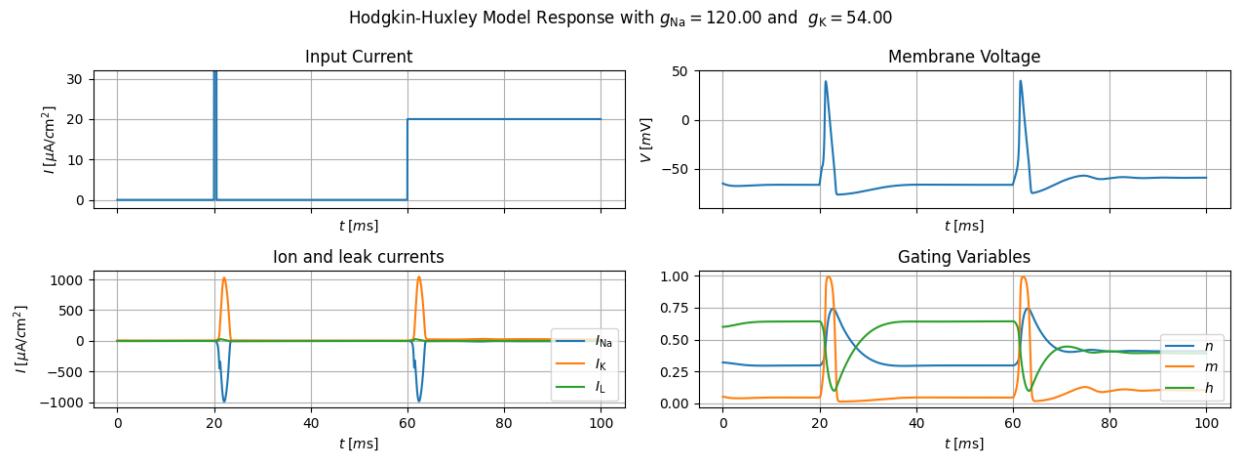


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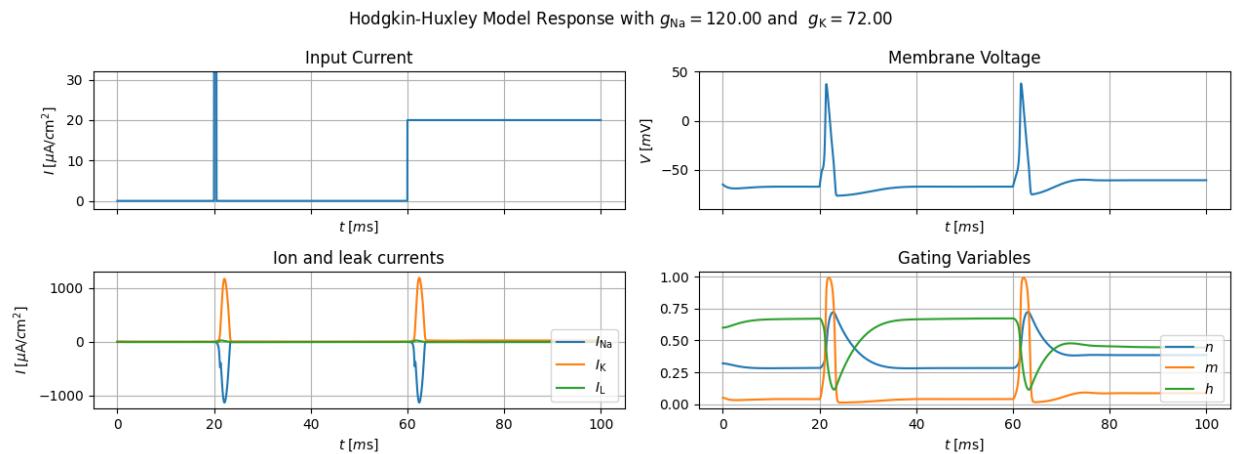


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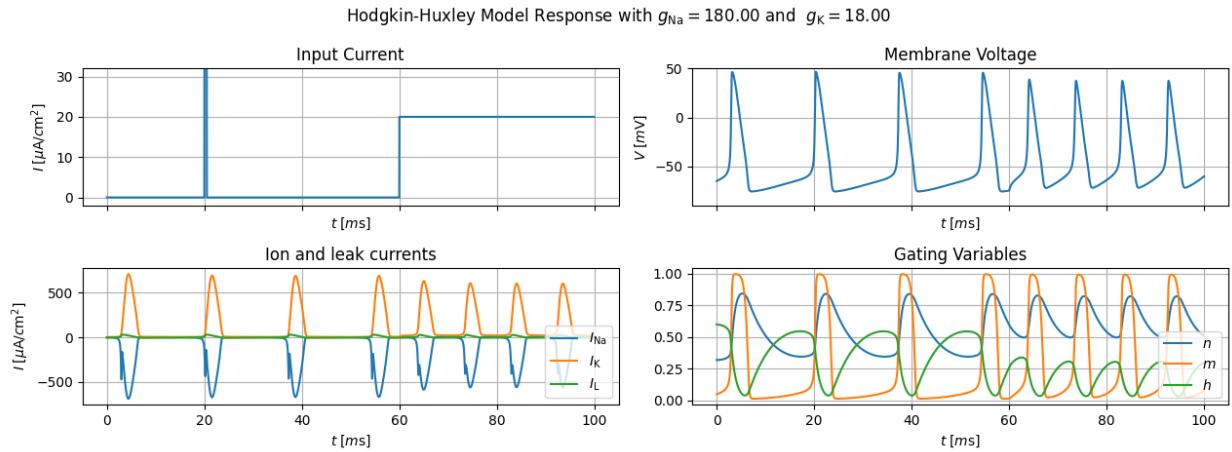


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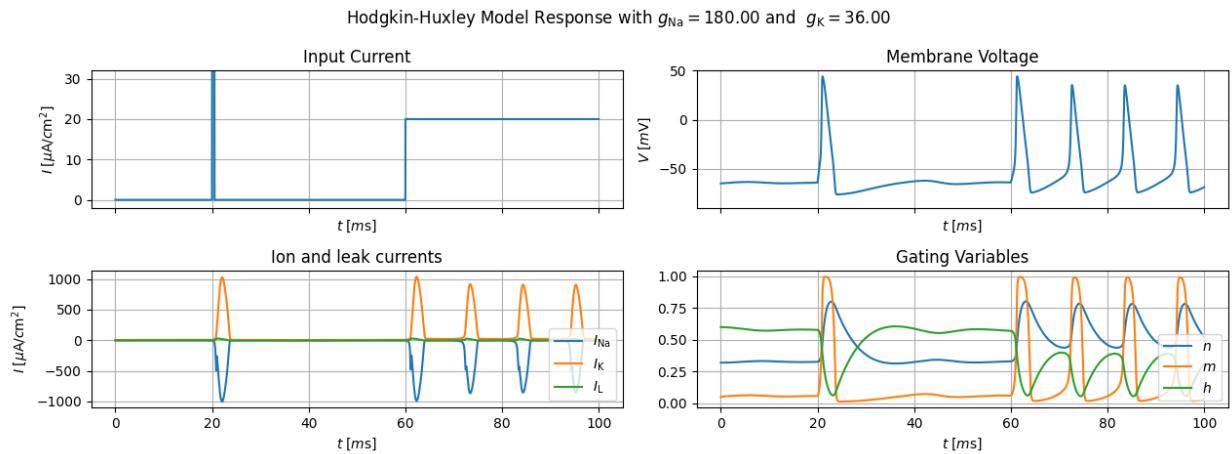


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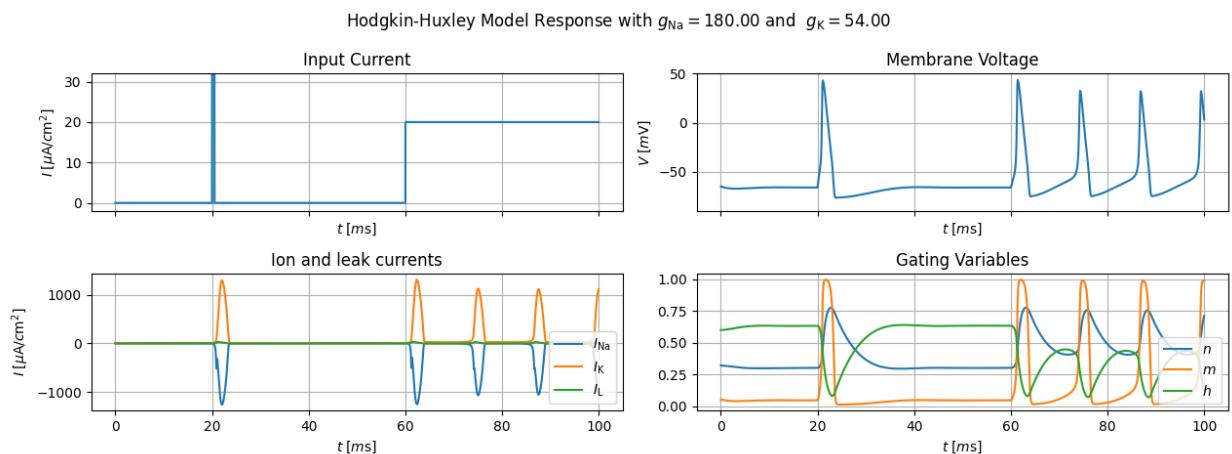


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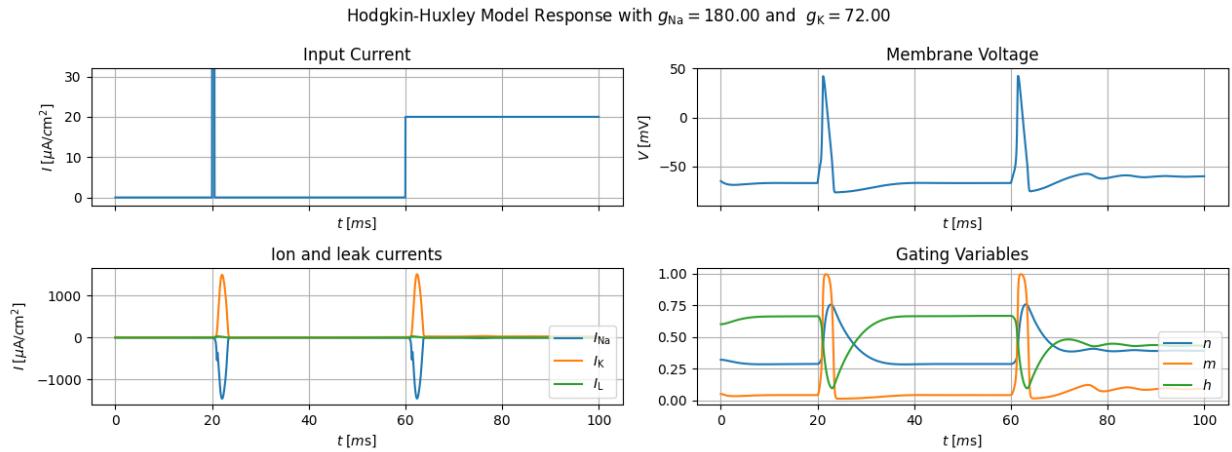


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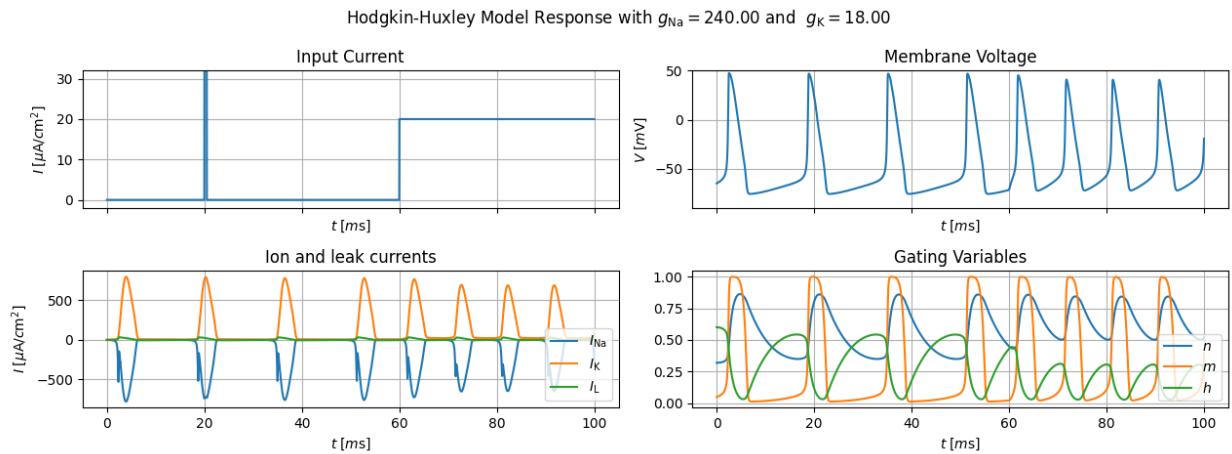


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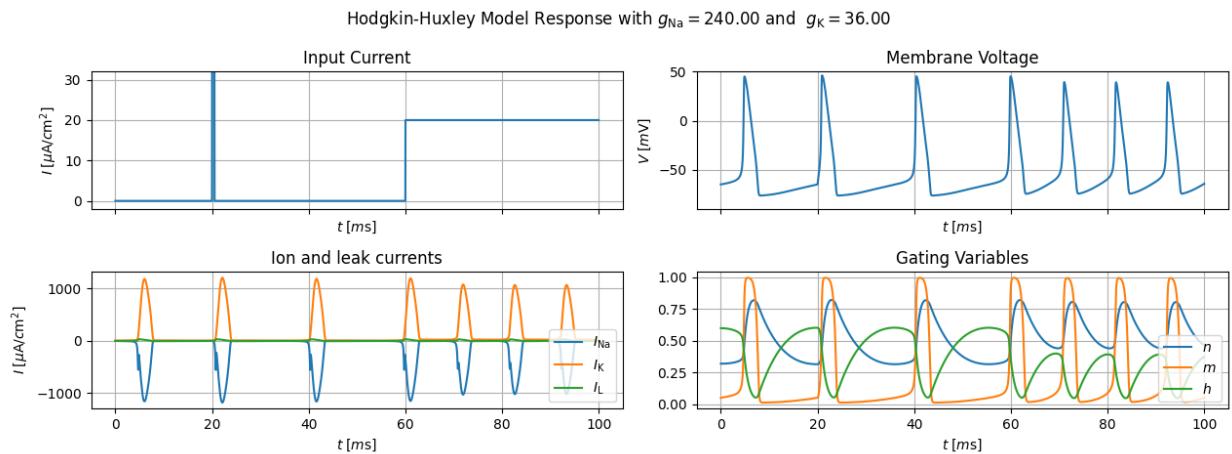


Figure 45

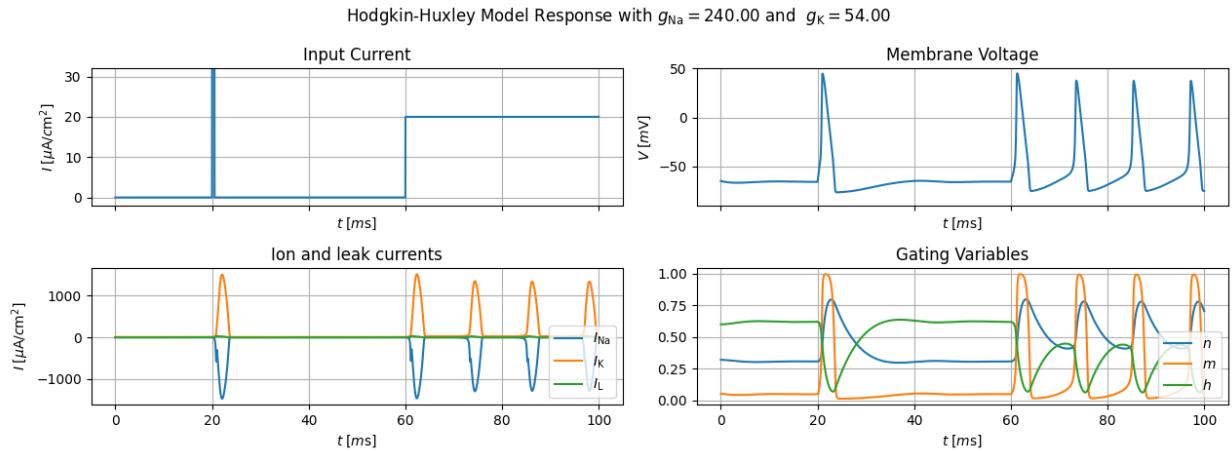


Figure 46

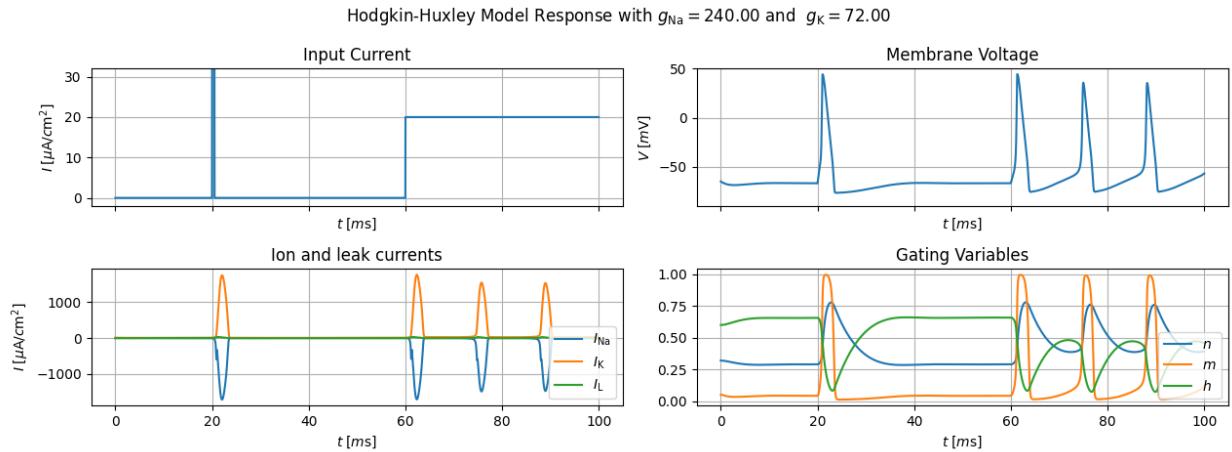


Figure 47

The previous question has already covered the effects of both parameters thoroughly. It is evident that these two parameters exert opposing influences on the cell's behavior. Additionally, it is worth noting that altering only one of these parameters also induces changes in the current of the other ion channel. These interactions demonstrate the interconnected nature of ion channels in the Hodgkin-Huxley model and emphasize the importance of considering both g_{Na} and g_K when studying action potential dynamics. By comprehending these intricate relationships, we can better grasp the complex interplay between sodium and potassium conductance and their impact on the overall excitability and firing behavior of excitable cells.

3. Investigate the role of leak conductance (g_L) on the resting membrane potential and the overall dynamics of the Hodgkin-Huxley model.

By modifying the leak conductance (g_L), we can observe significant changes in the steady-state values of the cell. While keeping the other parameters and initial conditions constant, adjusting g_L can lead to the generation of an action potential, followed by a return to the new steady state. The leak conductance plays

a crucial role in determining the resting membrane potential, as it represents the passive ion flow across the cell membrane when no other ion channels are active.

When g_L is increased, the leak current becomes stronger, affecting the resting membrane potential by bringing it closer to the equilibrium potential of the leak ions (usually close to the potassium equilibrium potential). On the other hand, decreasing g_L will result in a weaker leak current, causing the resting membrane potential to shift away from the potassium equilibrium potential.

Furthermore, changes in g_L can influence the excitability of the cell. A higher g_L might lead to a lower threshold for action potential generation, as it moves the resting potential closer to the firing threshold. Conversely, reducing g_L may require stronger depolarizing inputs to reach the threshold and trigger an action potential.

Overall, the leak conductance (g_L) is a critical parameter that influences the resting membrane potential and the excitability of the cell in the Hodgkin-Huxley model. Understanding the role of g_L allows for a comprehensive analysis of the model's behavior and its response to various physiological conditions or changes in cellular properties

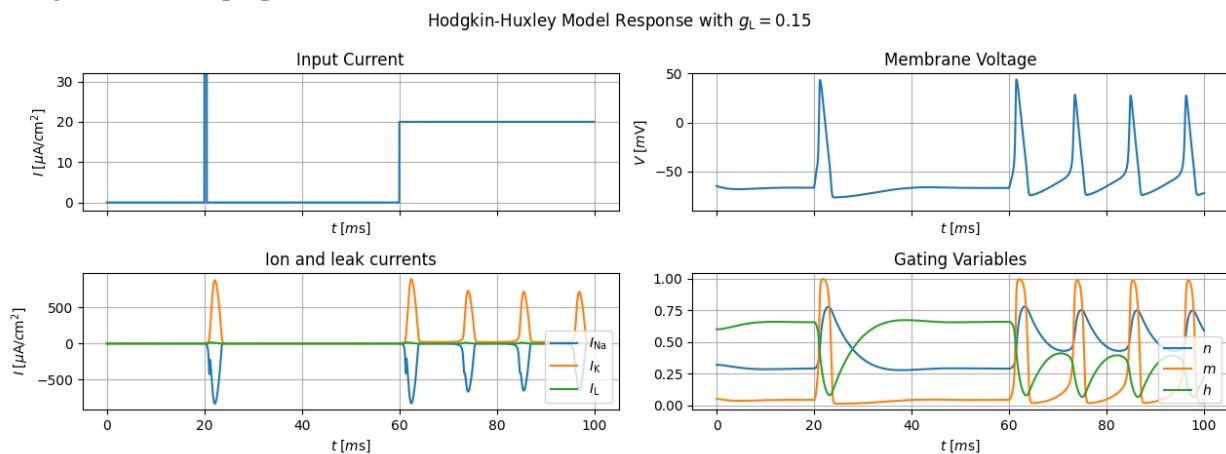


Figure 48

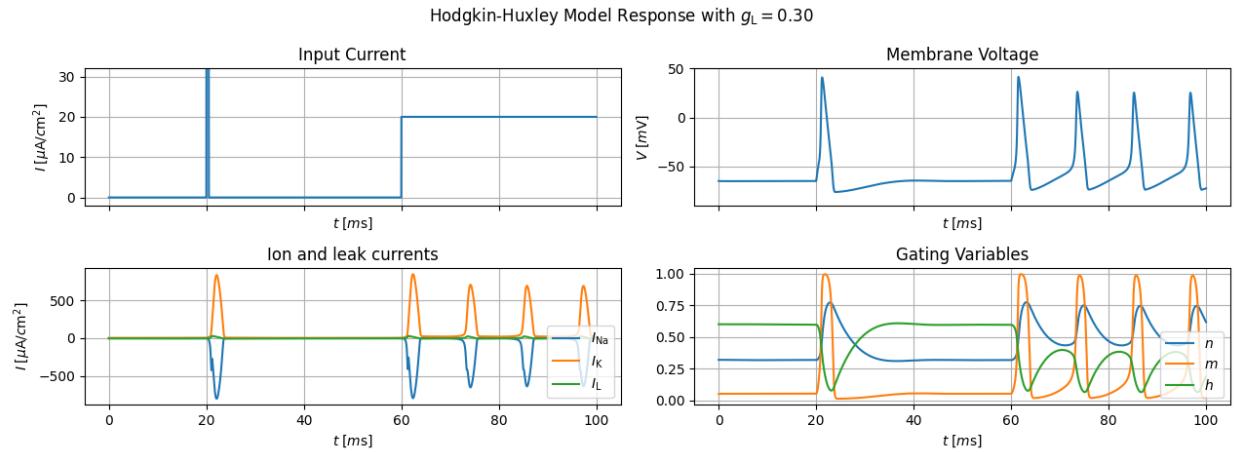


Figure 49

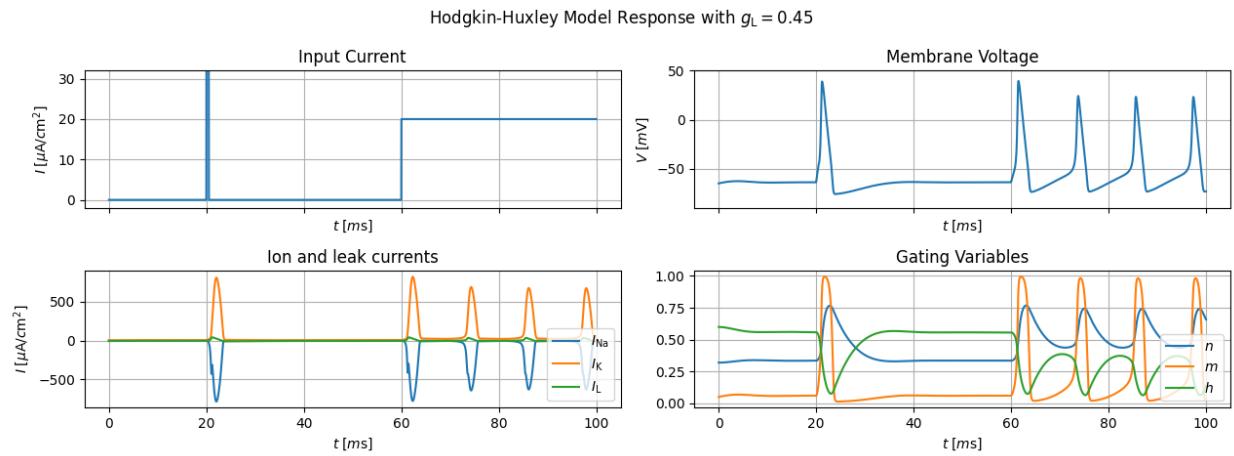


Figure 50

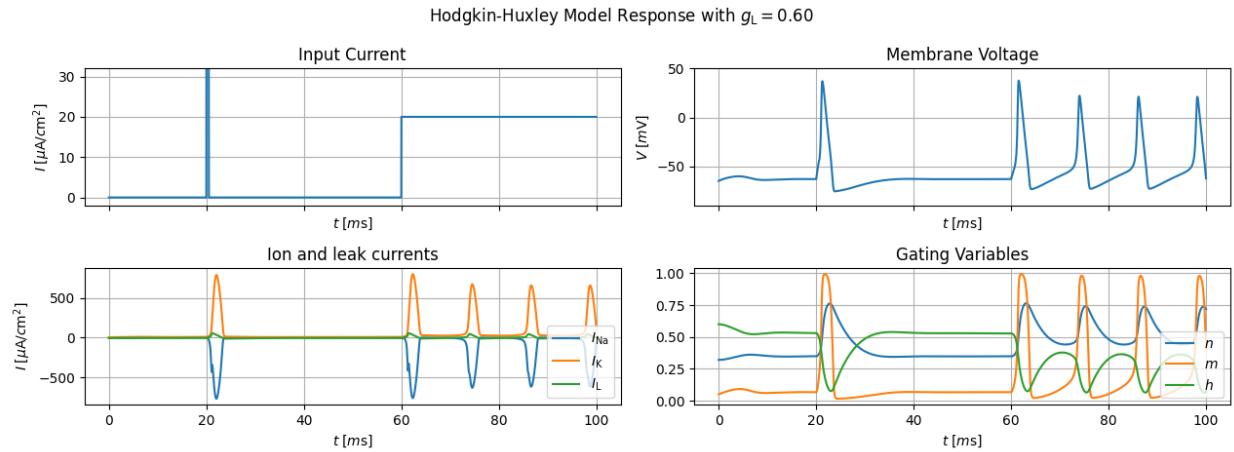


Figure 51

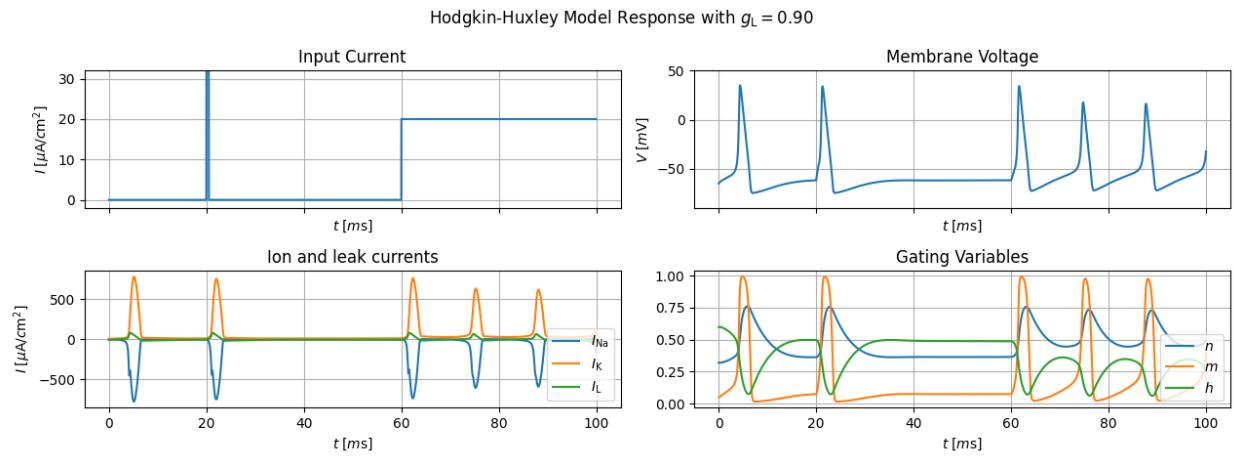


Figure 52

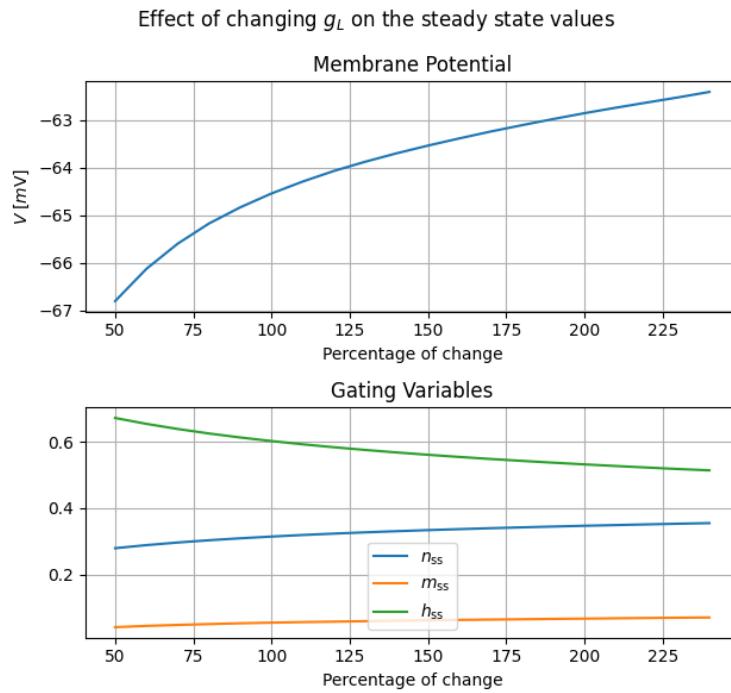


Figure 53

The impact of g_L is predominantly observed in two aspects: the resting membrane potential and the h gating variable. By adjusting g_L , we directly influence the passive ion flow across the cell membrane at rest, which significantly influences the resting membrane potential. Additionally, variations in g_L can have noticeable effects on the h gating variable, one of the key parameters controlling the opening and closing of potassium channels in the Hodgkin-Huxley model.

The leak conductance, g_L , plays a crucial role in shaping the baseline electrical properties of the cell. By affecting the resting membrane potential, g_L sets the starting point for the cell's excitability, determining how close the membrane potential is to the action potential threshold. A higher g_L can lead to a more depolarized resting potential, making the cell more excitable and potentially more responsive to incoming stimuli.

Furthermore, the h gating variable, representing the inactivation of potassium channels, is also influenced by g_L . Changes in g_L can impact the kinetics of h , altering the rates at which potassium channels open and close during the action potential.

In summary, g_L has a substantial influence on the resting membrane potential and the dynamics of the gating variable. These effects, in turn, contribute to the overall behavior and excitability of the cell in the Hodgkin-Huxley model. Understanding the role of g_L is essential for comprehending the intricate interplay of ion channels and their contributions to cellular electrical activity.

1.2.3 Parameter Sensitivity

1. Perform sensitivity analysis by systematically varying each of the model parameters (e.g., g_{Na} , g_K , C) while keeping others fixed. Analyze the effects of these variations on the action potential properties and firing behavior.

In the preceding section, we explored the impacts of altering g_{Na} , g_K , and g_L on the model. In this section, we will solely focus on investigating the effects of changing the membrane conductance, C.

By performing sensitivity analysis, we will systematically vary the value of C while keeping other parameters fixed. Through this approach, we can analyze how variations in C influence action potential properties and firing behavior. The membrane conductance, C, represents the capacitance of the cell membrane, which plays a vital role in determining the membrane's ability to store and release electrical charge during an action potential.

Changing the value of C can have significant consequences for the dynamics of the action potential. An increase in C may enhance the membrane's ability to store charge, leading to longer depolarization and repolarization phases of the action potential. Conversely, a decrease in C may reduce the membrane's capacity to hold charge, resulting in shorter action potentials with faster repolarization.

Additionally, variations in C can impact the overall excitability of the cell. A higher C might lead to a more excitable cell, requiring lower input currents to initiate action potentials. Conversely, a lower C may render the cell less excitable, necessitating stronger input currents to reach the action potential threshold.

By systematically analyzing the effects of changing C, we can gain deeper insights into the role of membrane capacitance in shaping the electrical behavior of the cell in the Hodgkin-Huxley model.

Understanding these relationships is vital for comprehending the underlying mechanisms of action potential generation and the regulation of firing behavior in excitable cells.

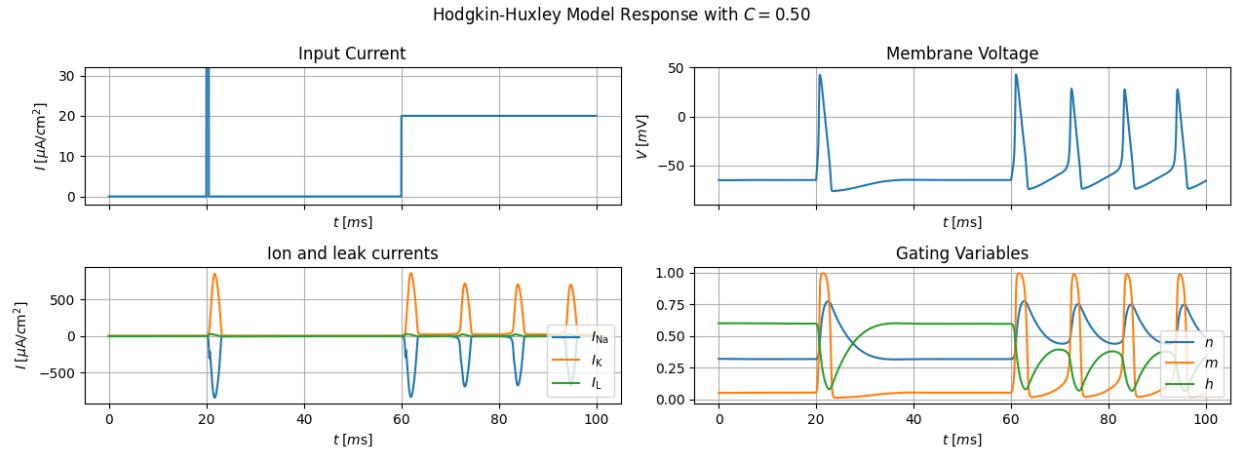


Figure 54

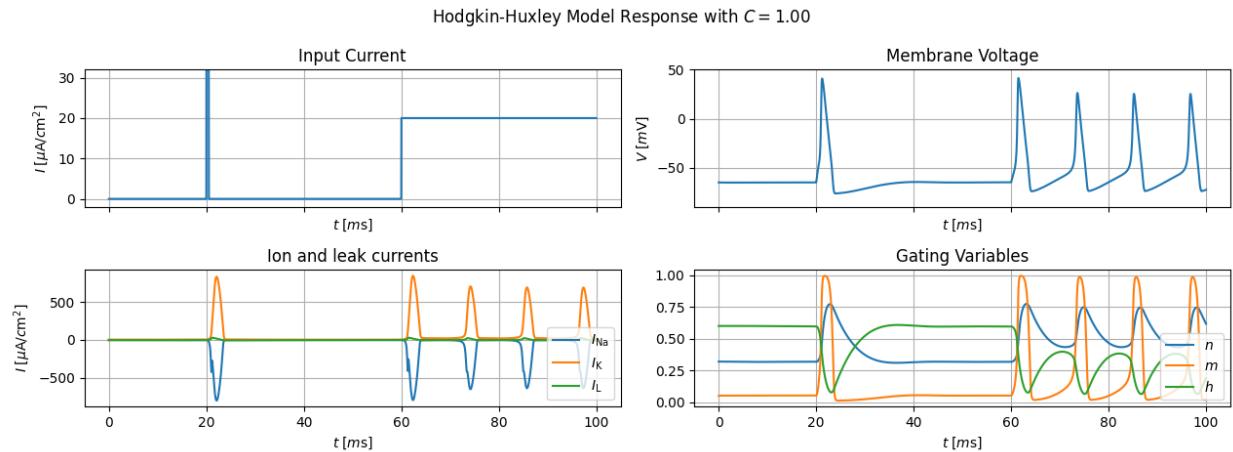


Figure 55

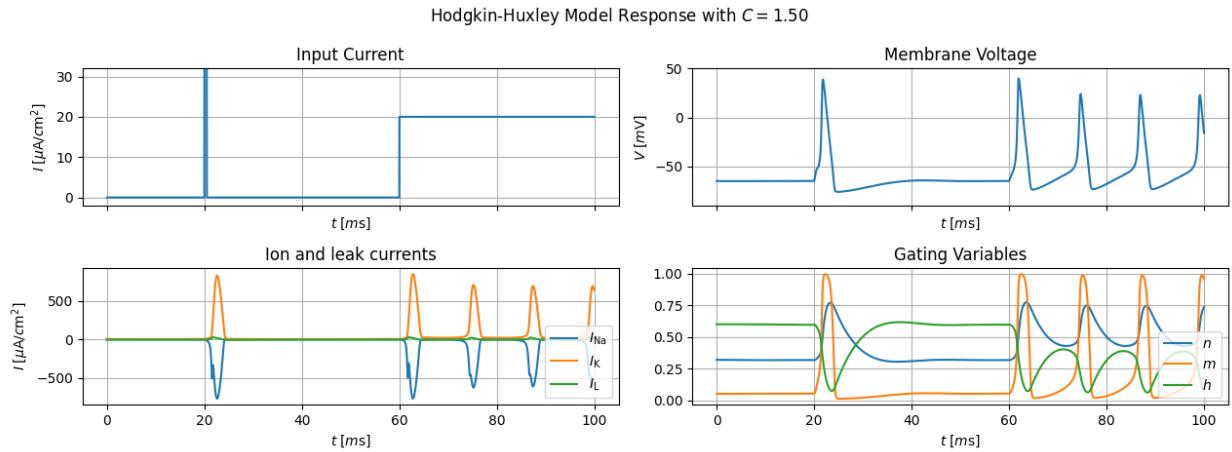


Figure 56

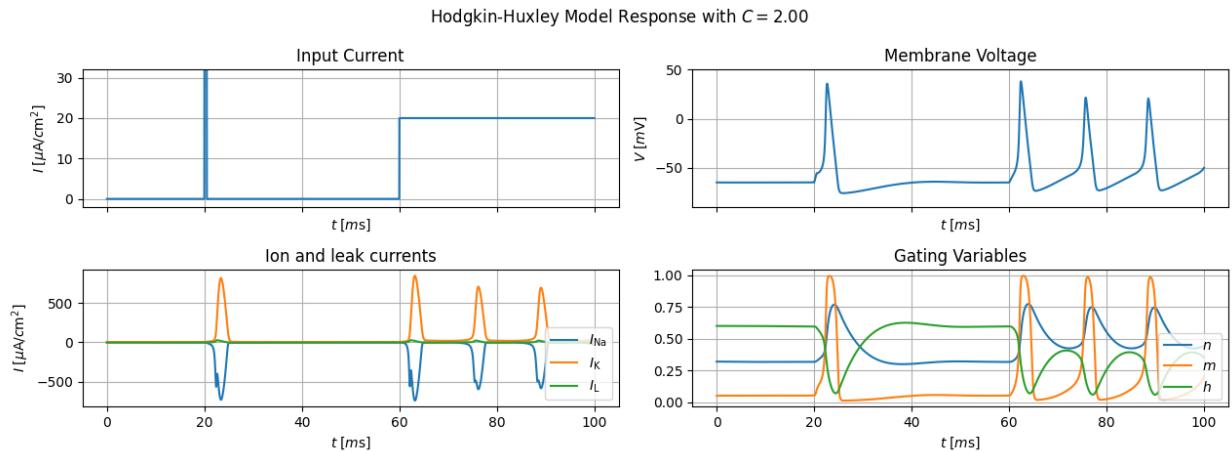


Figure 57

Indeed, these parameters hold the potential to alter both the excitability and dynamics of the system. By systematically varying each parameter while keeping others fixed, we can discern how these changes influence the behavior of the Hodgkin-Huxley model.

The excitability of the cell is profoundly affected by these parameter variations. For instance, alterations in g_{Na} and g_K can directly influence the opening and closing of sodium and potassium channels, leading to changes in the cell's responsiveness to stimuli. An increase in g_{Na} may enhance the inward sodium current, making the cell more excitable and more likely to generate action potentials. Conversely, an increase in g_K could augment the outward potassium current, facilitating repolarization and reducing the likelihood of action potential firing.

Additionally, changes in C can impact the capacitance of the cell membrane, affecting the storage and release of electrical charge during the action potential. A higher C may lead to increased charge storage and

prolonged action potentials, while a lower C might result in quicker depolarization and repolarization phases.

2. Identify the parameters that have the most significant impact on the excitability and firing rate of the neuron. Discuss the implications of these findings in the context of neuronal dynamics.

To explore the impacts of these parameters on the cell's excitability, we can determine and plot the threshold of impulse and step stimulations for various values of these parameters.

By systematically varying the values of g_{Na} , g_K , and other relevant parameters, we can identify the critical thresholds at which the cell transitions from a non-excited state to generating action potentials. These threshold values can be graphically represented for both impulse and step stimulations, allowing us to visualize how changes in the parameters affect the cell's ability to initiate action potentials in response to different types of stimuli.

Through this analysis, we can discern the sensitivity of the cell's excitability to variations in g_{Na} , g_K , and other parameters. Understanding the relationship between these parameters and the threshold of stimulation is vital for comprehending the fundamental mechanisms underlying action potential generation and the overall excitability of excitable cells in the Hodgkin-Huxley model. These insights are crucial for interpreting the behavior of neurons and understanding their response patterns under diverse physiological conditions.

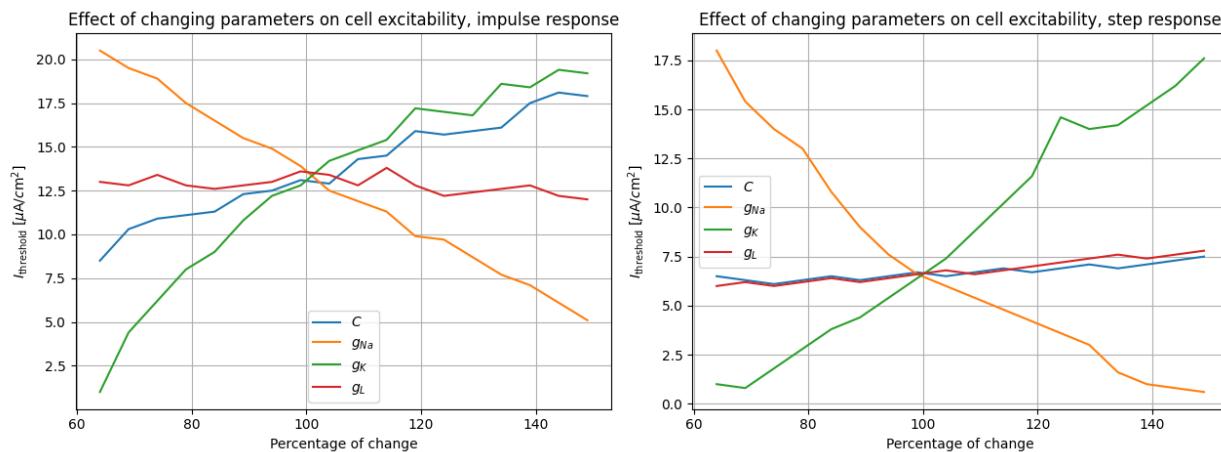


Figure 58

Consistent with earlier findings, Figure 66 confirms that g_{Na} and g_K have a more pronounced impact on the cell's excitability in response to both step and impulse inputs compared to other parameters.

The results indicate that changes in g_{Na} and g_K , representing the maximum conductances of sodium and potassium channels, respectively, play a crucial role in shaping the cell's response to different input

stimuli. Alterations in these parameters can significantly influence the dynamics of the action potential, affecting the generation and propagation of electrical signals within the cell.

While other parameters also contribute to the cell's behavior, the effects of g_{Na} and g_K stand out prominently. Understanding these critical influences is essential for comprehending how ion channels' conductance levels regulate the cell's electrical excitability and firing behavior in the Hodgkin-Huxley model. These observations underscore the significance of g_{Na} and g_K as key determinants in the dynamic behavior of excitable cells and their responses to various inputs.

1.2.4 Subthreshold Behavior

1. Simulate the Hodgkin-Huxley model with subthreshold current inputs. Analyze the membrane voltage response and characterize the subthreshold membrane potential dynamics.

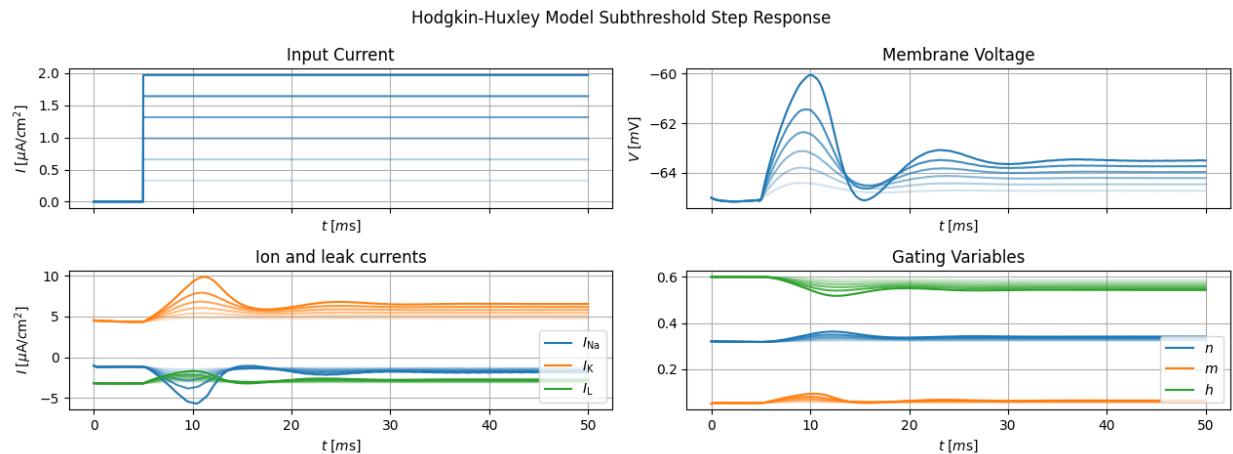


Figure 59

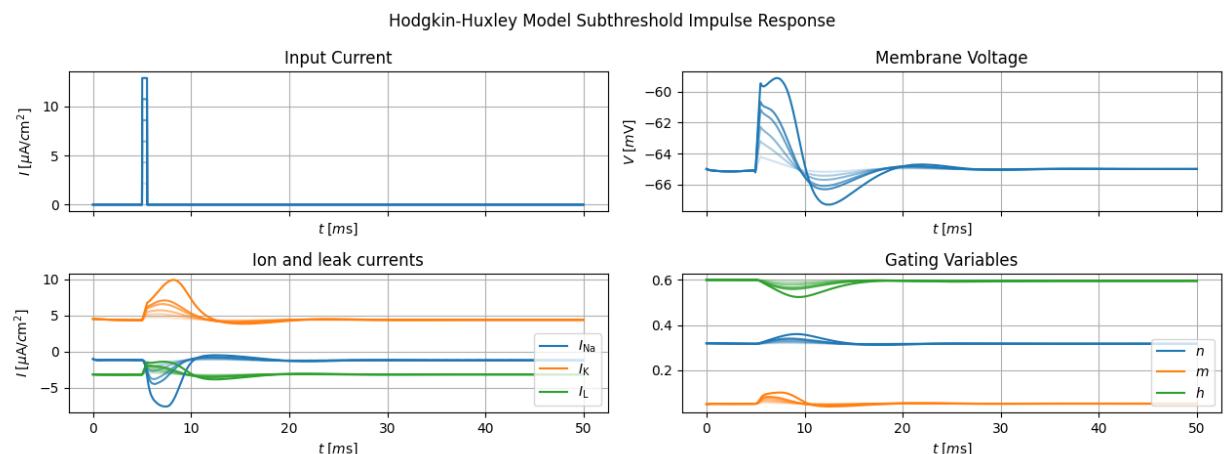


Figure 60

In the subthreshold response, we observe oscillations in the membrane voltage. Notably, these oscillations exhibit larger amplitudes in the step response (Figure 59). The amplitudes of the ionic currents are relatively similar to the leak current, which represents the cellular pumps responsible for restoring the cell to its resting state.

Furthermore, in the subthreshold impulse responses, we notice changes in the steady-state values of the system. These changes are indicative of the system's attempt to counteract the effects of the constant input by adjusting its equilibrium values. This compensatory mechanism allows the cell to maintain a balance and adapt to different levels of stimulation.

The observed oscillatory behavior and adjustments in steady-state values illustrate the dynamic nature of the Hodgkin-Huxley model. These phenomena are essential for understanding how excitable cells respond to various input currents and maintain their stable resting states in the face of different stimuli. The model's ability to capture these subtleties contributes to its effectiveness in simulating the intricate electrical behaviors observed in real neurons.

2. Investigate the relationship between the input current amplitude and the resulting subthreshold membrane potential oscillations or resonance phenomena.

For specific input current amplitudes, the cell may exhibit subthreshold membrane potential oscillations. These oscillations manifest as rhythmic fluctuations in the membrane potential, but they do not reach the threshold required for action potential initiation. The occurrence and characteristics of these oscillations can vary depending on the amplitude of the input current (Figure 60).

Subthreshold membrane potential oscillations represent a distinct electrical behavior of the cell, occurring when the input current is close to the threshold for action potential firing but not strong enough to trigger it. These oscillations are important for understanding the cell's sensitivity to different stimuli and its response patterns to varying input currents. The Hodgkin-Huxley model's ability to capture these subthreshold oscillations contributes to its accuracy in simulating the intricate electrical dynamics observed in real excitable cells.

3. Discuss the role of the activation and inactivation variables (m , h , n) in determining the subthreshold behavior of the Hodgkin-Huxley model.

The activation and inactivation variables (m , h , n) play crucial roles in shaping the subthreshold behavior of the Hodgkin-Huxley model. These variables represent the probabilities of ion channels being in open or closed states, and their values dynamically change over time according to voltage-dependent activation and inactivation equations.

In the subthreshold regime, the behavior of these variables significantly impacts the permeability of sodium and potassium ions across the cell membrane. When the membrane potential is below the threshold for action potential initiation, the m , h , and n variables dictate the conductance of sodium and potassium channels, regulating the flow of ions into and out of the cell. As a result, the subthreshold membrane

potential dynamics are influenced by the changing permeability of these ions, leading to membrane potential fluctuations without reaching the threshold for action potential firing.

Specifically, the m variable represents the activation of sodium channels, while the h variable denotes the inactivation of sodium channels. The n variable, on the other hand, represents the activation of potassium channels. By adjusting the probabilities of these states based on the membrane potential, the model captures the time-dependent behavior of ion channels, which in turn governs the subthreshold response.

2 The Morris-Lecar Model

1. Simulate the full Hodgkin-Huxley model and the Morris-Lecar model using the provided parameter values. Plot the phase portraits for both models, showing the trajectories of the voltage and the activation variable(s) (m and/or w) in the phase plane.

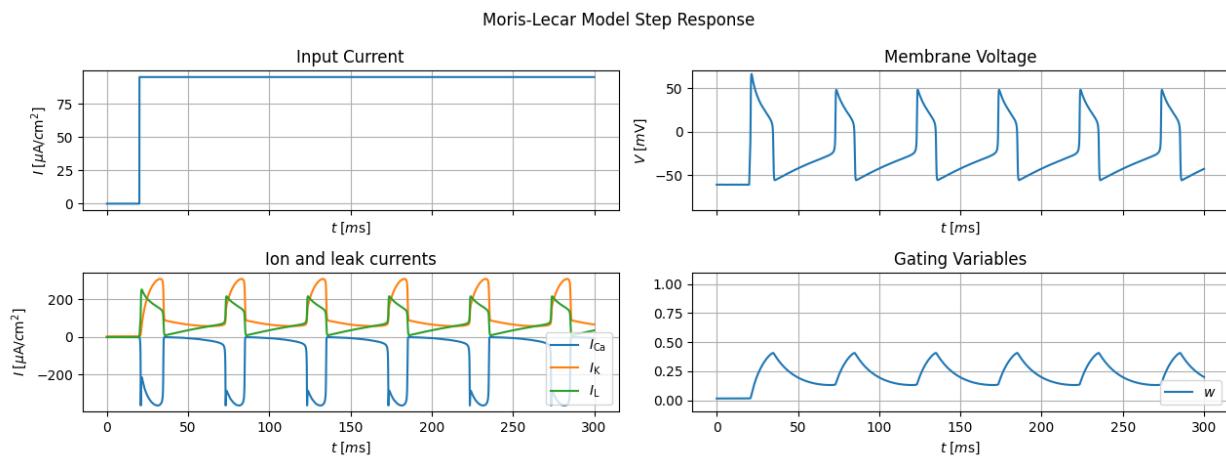


Figure 61

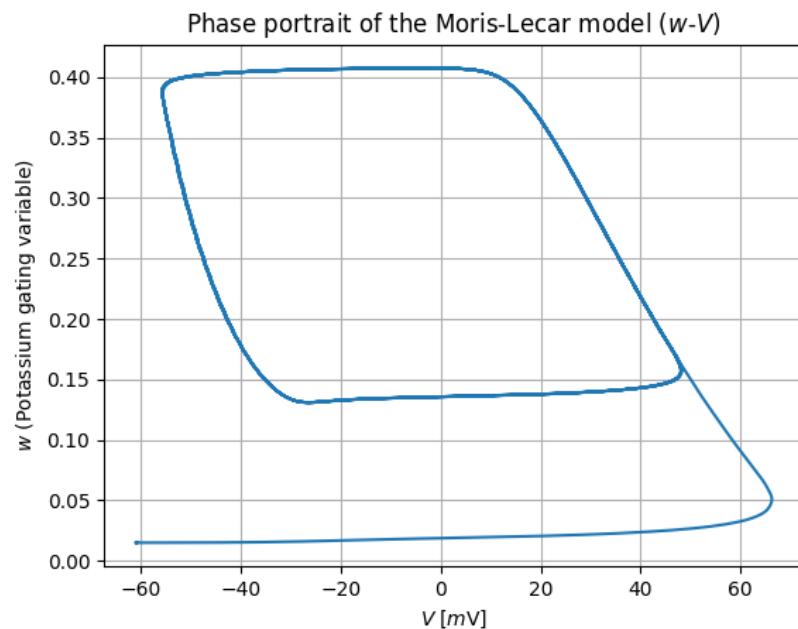


Figure 62

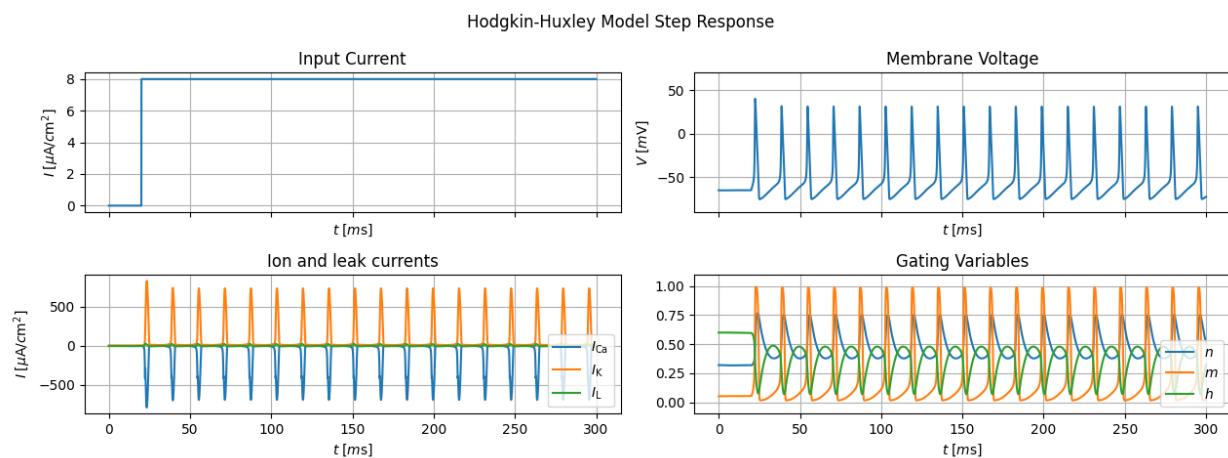


Figure 63

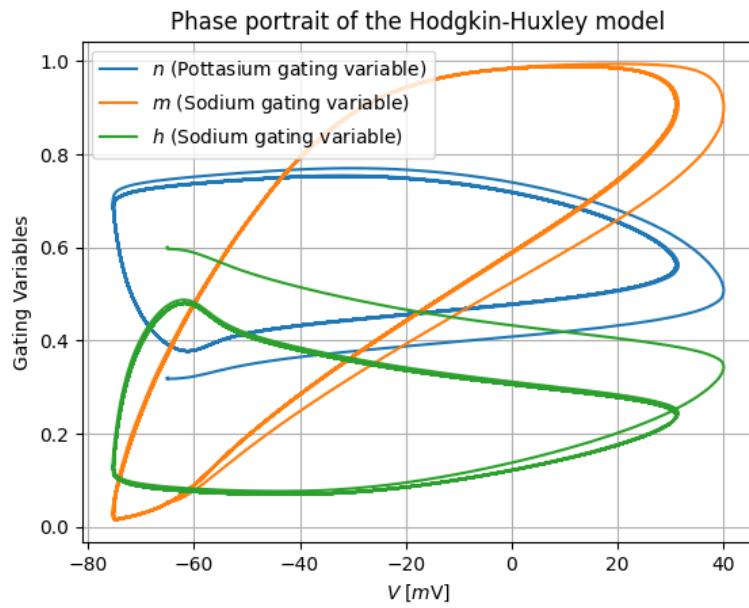


Figure 64

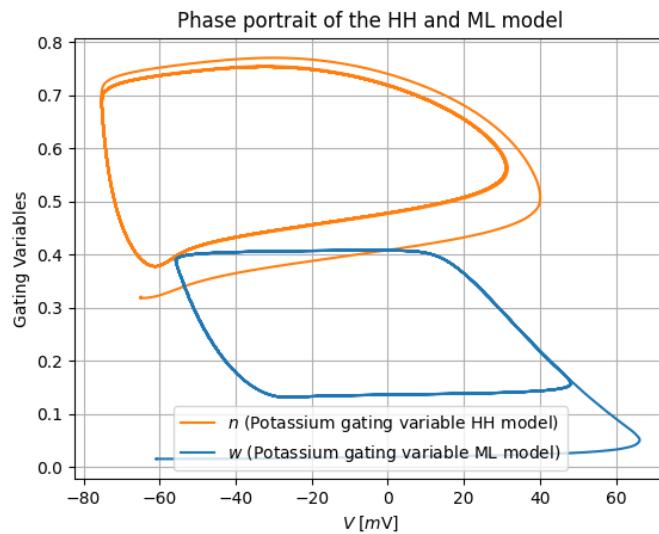


Figure 65

2. Compare the shapes and features of the phase portraits between the two models. Discuss any differences or similarities observed, particularly in terms of the stability and attractor dynamics.

Figure 65 presents the combined phase portraits of the two models. While only two dynamics of the Hodgkin-Huxley (HH) model can be shown alongside the Morris-Lecar model, both phase portraits exhibit limit-cycles, indicating the presence of unstable equilibrium points within the cycles.

A noticeable similarity between the models lies in the presence of limit-cycles, signifying the occurrence of periodic oscillations in the membrane potential. These limit-cycles suggest that both models can exhibit sustained electrical activity without returning to a stable resting state. Additionally, the phase portraits imply that the models share comparable ranges of membrane potential changes during these oscillatory behaviors.

However, some distinctions are observed between the two models. Notably, the limit-cycles in the Morris-Lecar model appear to be slightly shifted when compared to the Hodgkin-Huxley model. This discrepancy may indicate differences in the dynamics of ion channel activation and inactivation processes, leading to slightly altered oscillation patterns.

Regarding stability and attractor dynamics, both models display limit-cycles around unstable equilibrium points. In a dynamical system with limit-cycles, the attractor represents the stable behavior towards which the system tends to converge over time. In this context, both models demonstrate self-sustained oscillatory behavior around these unstable equilibrium points, which function as attractors for their respective oscillation patterns.

Overall, the phase portraits of the two models highlight their shared features, such as the presence of limit-cycles and unstable equilibrium points, while also revealing nuanced differences in their oscillatory patterns. Understanding these distinctions in stability and attractor dynamics provides valuable insights into the underlying mechanisms of electrical behavior and can aid in the interpretation of excitable cell dynamics in different biological contexts.