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1. Theoretical Questions

a) The minimal current leading to repetitive spiking:

In the Hodgkin-Huxley model, the minimal current that leads to repetitive spiking depends on the specific parameters of the neuron being modeled, such as the membrane capacitance, the conductances of sodium g_{Na}, potassium g_K, and leak channels g_L, and the resting membrane potential.

Repetitive spiking occurs when the input current I_{ext} is sufficient to depolarize the membrane to a threshold level where the sodium channels open rapidly, leading to a spike (action potential). If this depolarization is sustained or occurs repeatedly, the neuron can continue to fire action potentials in a repetitive manner.

Mathematically, finding the minimal current requires solving the Hodgkin-Huxley equations under the steady-state conditions and determining the current at which the neuron transitions from a single spike response to a repetitive spiking regime. This involves analyzing the dynamics of the model:

1. Membrane potential equation**:**

$$C_m \frac{dV}{dt} = I_{ext} - I_{Na} - I_K - I_L$$

2. Ionic currents**:**

$$I_{Na} = g_{Na} m^3 h (V - V_{Na})$$

$$I_K = g_K n^4 (V - V_K)$$

$$I_L = g_L (V - V_L)$$

Where m, h, n are gating variables with their own differential equations.

To find the minimal current, one would typically start with a small I_{ext} and incrementally increase it until repetitive spiking is observed in simulations or through analytical techniques such as bifurcation analysis.

b) By increasing the sodium conductance further, repetitive firing even in the absence of input can be observed, why? Is it naturally plausible?

If the sodium conductance g_{Na} is increased significantly, the neuron's membrane becomes more excitable. Reasons:

1. Enhanced Excitability: Increasing g_{Na} lowers the threshold for action potential initiation because the neuron can more easily depolarize to the threshold level needed to open sodium channels.

2. Inherent Instability: With higher sodium conductance, the feedback mechanism where sodium channel activation leads to further depolarization becomes stronger. This can destabilize the resting membrane potential, causing spontaneous depolarizations.

Even in the absence of external input ($I_{ext} = 0$), the neuron can start to fire repetitively if the increased sodium conductance makes the membrane potential intrinsically unstable. This spontaneous repetitive firing is due to the intrinsic properties of the ion channels and the membrane.

Natural Plausibility:

1. Pathological Conditions: This phenomenon is naturally plausible in certain pathological conditions. For example, in epilepsy, increased sodium conductance or altered channel kinetics can lead to spontaneous and excessive neuronal firing, manifesting as seizures.

2. Normal Physiology: Under normal physiological conditions, neurons have regulatory mechanisms to maintain proper ionic conductances. However, some types of neurons (e.g., pacemaker neurons in the heart and certain brain regions) are naturally designed to exhibit rhythmic firing due to their specific ionic conductance properties.

2. Simulation Questions

1) Action Potential Generation:

a) Hodgkin-Huxley model

The **threshold current** required to elicit an action potential in the simulated Hodgkin-Huxley model is **2.35 µA/cm²**. When this current is applied, the neuron undergoes a rapid change in membrane potential, resulting in an action potential - a crucial process for neural communication.

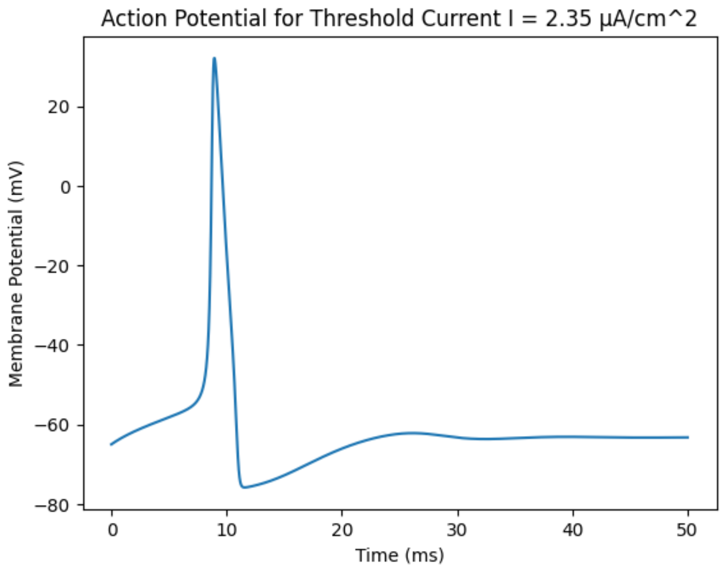

Figure 1: Action potential generated at the threshold current of 2.35 µA/cm²

b) Various amplitude and duration of the applied current

Increasing the amplitude generally leads to action potential generation, while longer durations tend to reduce firing rates.

- **Amplitude and Firing Rate:**
  - At an amplitude of **1 µA/cm²**, the firing rate remains consistently at **0.00 Hz** across different durations (5 ms, 15 ms, 35 ms, and 50 ms). This suggests that this low amplitude does not elicit action potentials.
  - When the amplitude increases to **2.4 µA/cm²**, the firing rate shows:
    - For a duration of **15 ms**, the firing rate increases to **66.67 Hz**.
    - For a duration of **35 ms**, the firing rate decreases slightly to **28.57 Hz**.
    - For a duration of **50 ms**, the firing rate further decreases to **20.00 Hz**.
- **Duration and Firing Rate:**
  - Increasing the duration of the applied current generally leads to higher firing rates.

    - There seems to be an optimal range for duration where maximum firing rates are achieved before they start declining.
- **Higher Amplitudes:**
    - At amplitudes of **10 µA/cm²** and **30 µA/cm²**, the firing rates are significantly higher:
        - For **10 µA/cm²**:
            - Duration = **15 ms**: **66.67 Hz**
            - Duration = **35 ms**: **85.71 Hz**
            - Duration = **50 ms**: **80.00 Hz**
        - For **30 µA/cm²**:
            - Duration = **15 ms**: **133.33 Hz**
            - Duration = **35 ms**: **114.29 Hz**
            - Duration = **50 ms**: **100.00 Hz**

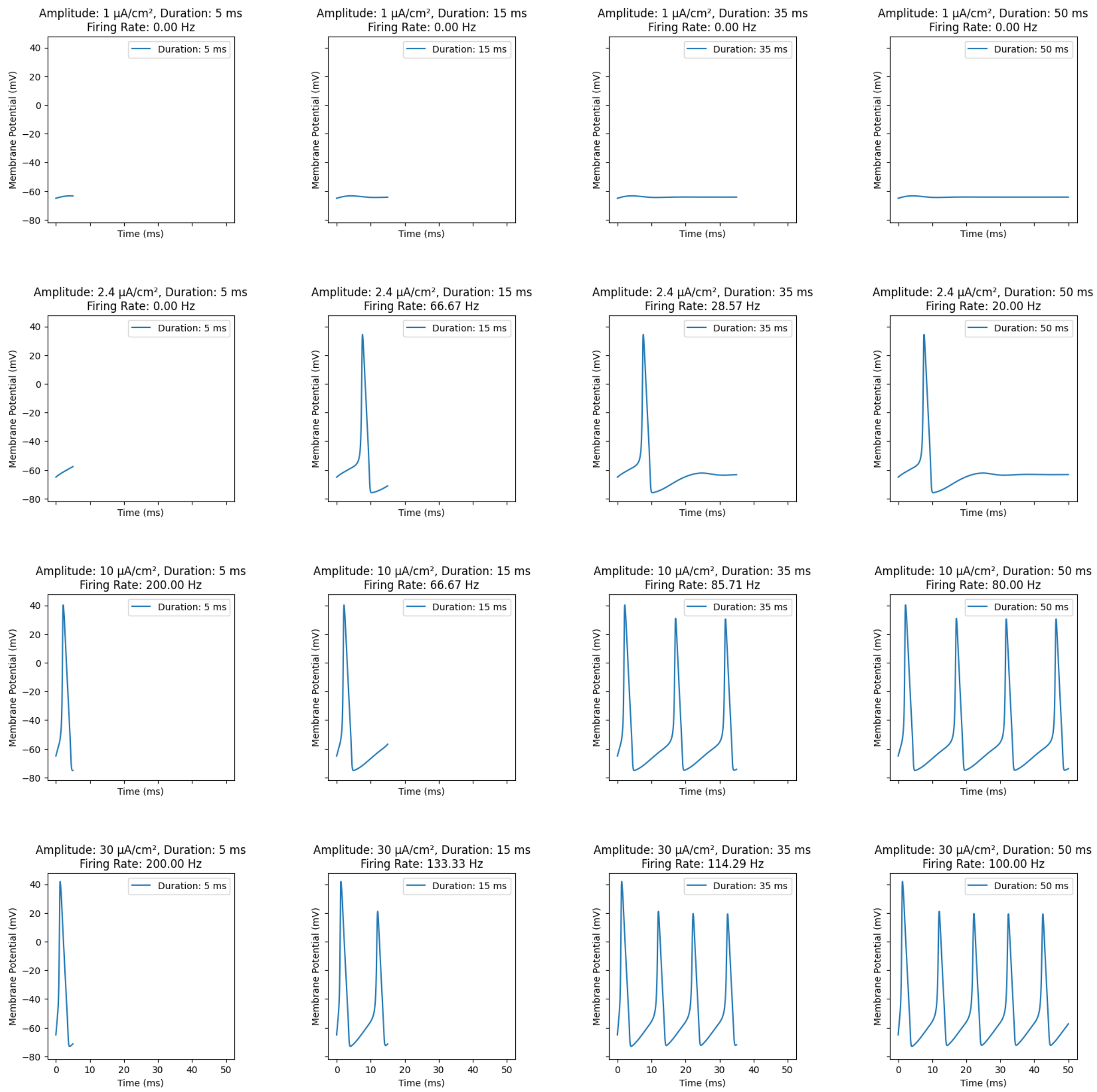

Figure 2: the effects of varying the amplitude and duration of the applied current on the action potential waveform (higher amplitude, more spikes)

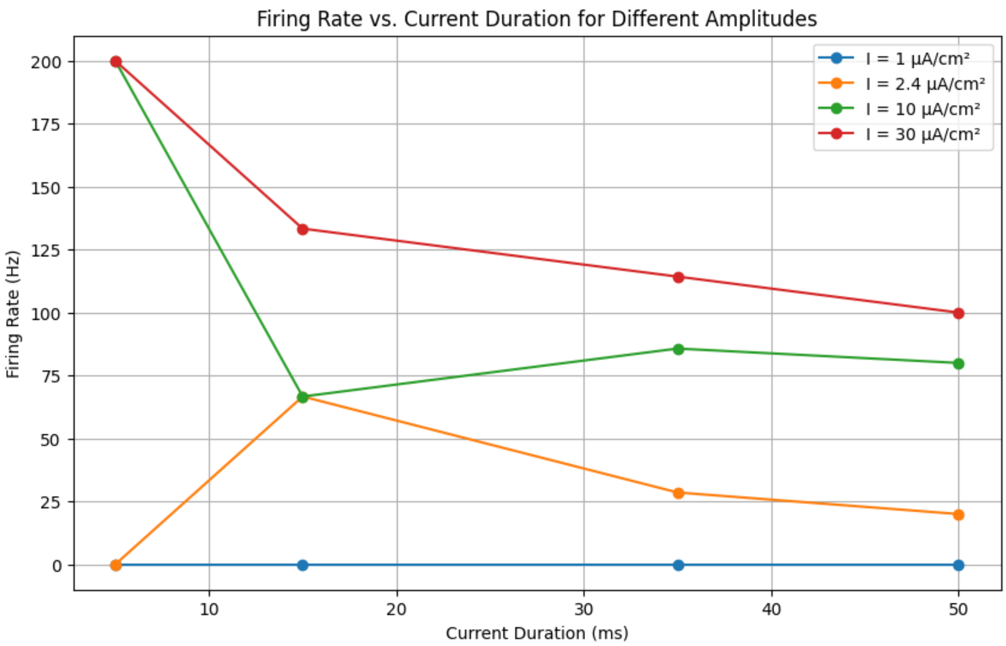

Figure 3: the effects of varying the amplitude and duration of the applied current on the firing rate (higher amplitude, higher firing rate – higher duration, lower firing rate)

c) Different initial conditions

The effect of different V0s as initial parameter:

1. **Initial Condition: V0=-90 mV**
   - Peak voltage: 43.11 mV
   - Half-width: 1.87 ms
   - Duration above zero: 1.26 ms
2. **Initial Condition: V0=-65 mV**
   - Peak voltage: 40.25 mV
   - Half-width: 1.47 ms
   - Duration above zero: 1.16 ms
3. **Initial Condition: V0=-30 mV**
   - Peak voltage: 41.48 mV
   - Half-width: 1.08 ms
   - Duration above zero: 1.22 ms

- As the initial membrane voltage increases from -90 mV to -30 mV:
  - The peak voltage remains relatively stable.
  - The action potential becomes narrower (reduced half-width).
  - The time during which the membrane potential remains above zero varies, showing a non-linear trend.

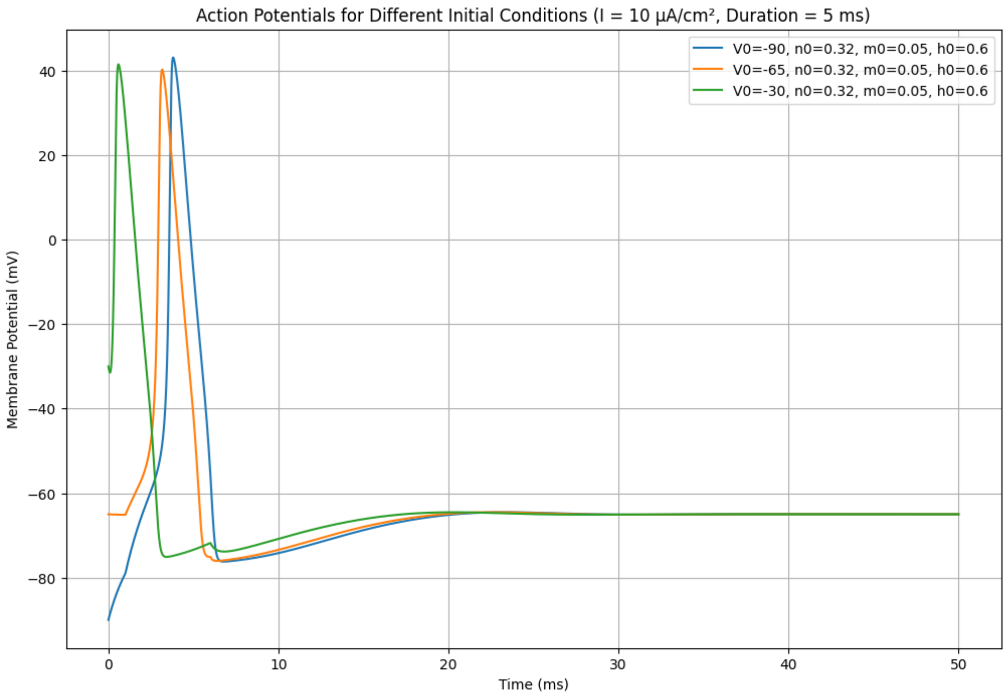

Figure 4: the effect of different V0s in the shape and duration of the action potential

The effect of different n0s as initial parameter:

1. **Initial Condition: n_0=0.1**
   - Peak voltage: 46.05 mV
   - Half-width: 1.52 ms
   - Duration above zero: 1.30 ms
2. **Initial Condition: n_0=0.32**
   - Peak voltage: 40.25 mV
   - Half-width: 1.47 ms
   - Duration above zero: 1.16 ms
3. **Initial Condition: n_0=0.4**
   - Peak voltage: 37.59 mV
   - Half-width: 1.46 ms
   - Duration above zero: 1.12 ms

- As ‘n0’ increases while other variables remain constant:
  - The peak voltage decreases.
  - The action potential becomes narrower (reduced half-width).
  - The time during which the membrane potential remains above zero decreases.

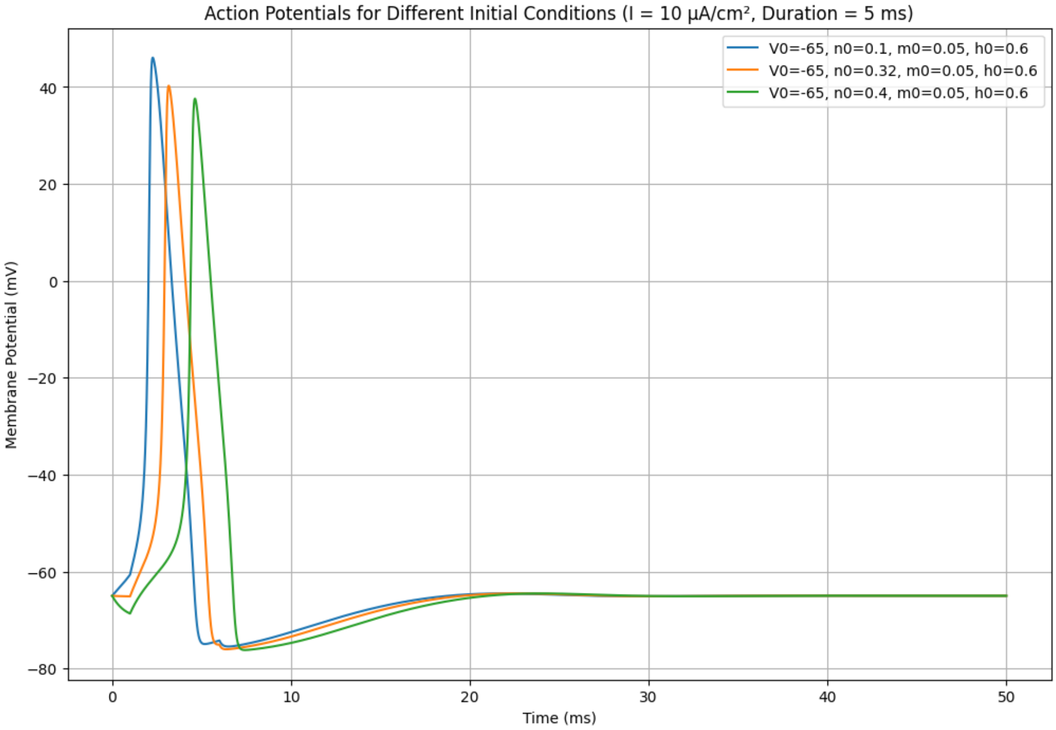

Figure 5: the effect of different n0s in the shape and duration of the action potential

The effect of different m0s as initial parameter:

1. **Initial Conditions: m_0=0.01**
   - Peak voltage: Approximately 40.30 mV
   - Half-width: Approximately 1.47 ms
   - Duration above zero: Approximately 1.17 ms
2. **Initial Conditions: m_0=0.05**
   - Peak voltage: Approximately 40.25 mV
   - Half-width: Approximately 1.47 ms
   - Duration above zero: Approximately 1.16 ms
3. **Initial Conditions: m_0=0.1**
   - Peak voltage: Approximately 40.10 mV
   - Half-width: Approximately 1.47 ms
   - Duration above zero: Approximately 1.16 ms

- As we vary the sodium activation variable (m_0) while keeping other parameters constant:
  - The peak voltage remains relatively consistent.
  - The half-width of the action potential remains similar.
  - The duration above zero voltage also remains similar.

These variations suggest that changes in the sodium channel activation variable have minimal impact on the overall shape and duration of the action potential.

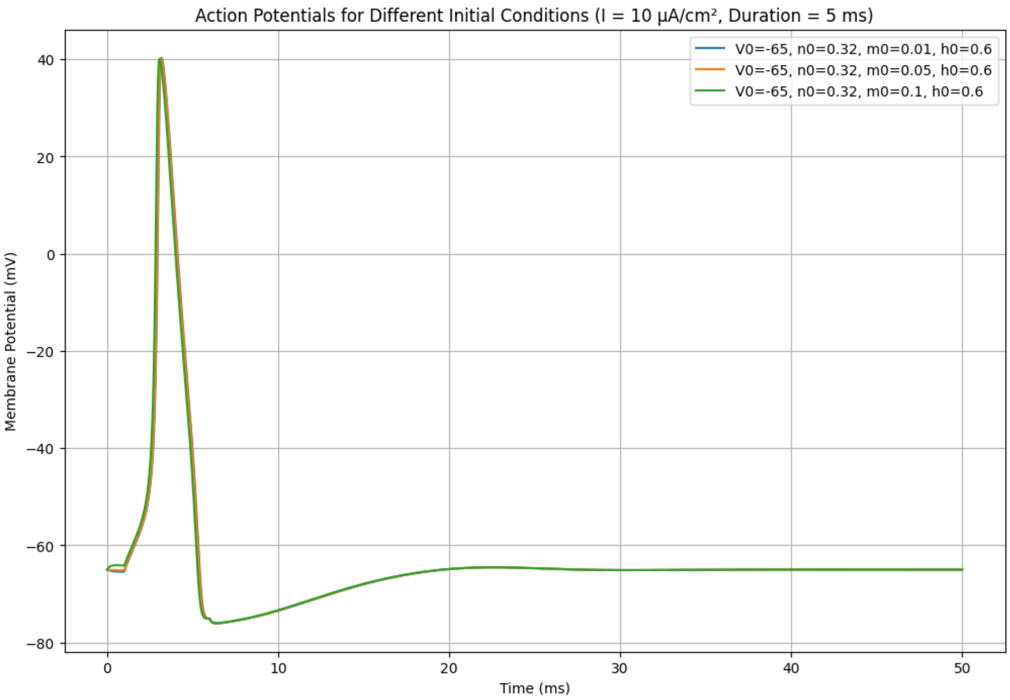

Figure 6: the effect of different m0s in the shape and duration of the action potential

The effect of different h0s as initial parameter:

1. **Initial Conditions: h0=0.1**
    - Peak voltage: 18.33 mV
    - Half-width: 1.27 ms
    - Duration above zero: 0.65 ms
2. **Initial Conditions: h0=0.6**
    - Peak voltage: 40.25 mV
    - Half-width: 1.47 ms
    - Duration above zero: 1.16 ms
3. **Initial Conditions: h0=0.9**
    - Peak voltage: 43.61 mV
    - Half-width: 1.63 ms
    - Duration above zero: 1.36 ms

- As the value of h0 increases:
    - The peak voltage also increases significantly.
    - The half-width (duration of the action potential) becomes wider as h increases.
    - The duration above zero (time during which the membrane potential is positive) also extends with higher h values.

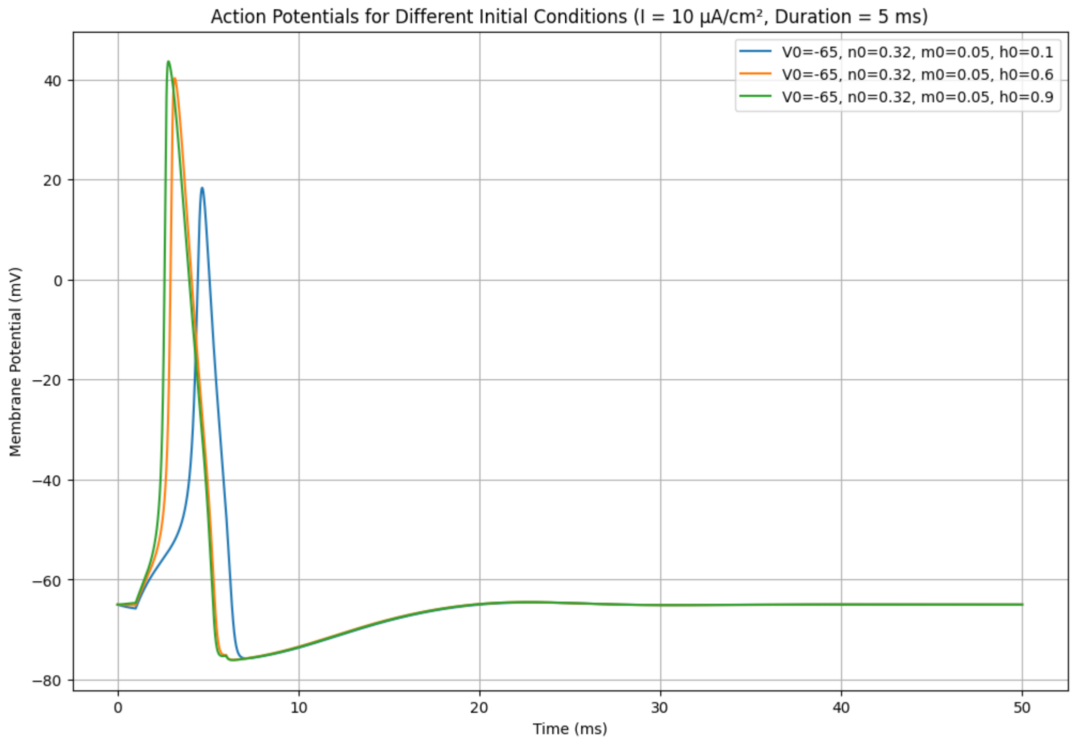

Figure 7: the effect of different h0s in the shape and duration of the action potential

2) More Computational Problems:

a) The amplitude equal to 20 µA/cm2 lasting 0.2ms - minimum excitation current for 5 different excitation widths

- **Model Parameters:**
  - Excitation amplitude: 20 µA/cm²
  - Excitation duration: 0.2 ms

- **Minimum Excitation Currents for Different Excitation Widths: (higher width, lower minimum current)**
  - Width: 0.1 ms, Minimum Current: 68.2 µA/cm²
  - Width: 0.2 ms, Minimum Current: 34.2 µA/cm² (This corresponds to the given excitation duration.)
  - Width: 0.3 ms, Minimum Current: 22.9 µA/cm²
  - Width: 0.5 ms, Minimum Current: 13.9 µA/cm²
  - Width: 0.8 ms, Minimum Current: 8.9 µA/cm²
  - Width: 1 ms, Minimum Current: 7.3 µA/cm²
  - Width: 1.5 ms, Minimum Current: 5.1 µA/cm²
  - Width: 2 ms, Minimum Current: 4.1 µA/cm²
  - Width: 5 ms, Minimum Current: 2.5 µA/cm²
  - Width: 10 ms, Minimum Current: 2.4 µA/cm²

- Width: 20 ms, Minimum Current: 2.4 µA/cm²
- Width: 30 ms, Minimum Current: 2.4 µA/cm²
- Width: 50 ms, Minimum Current: 2.4 µA/cm²

- **Minimum Amplitude of Excitation for Spike (at 0.2 ms):** The minimum amplitude of excitation required for the model to spike (with a fixed excitation time width of 0.2 ms) is 34.2 µA/cm².

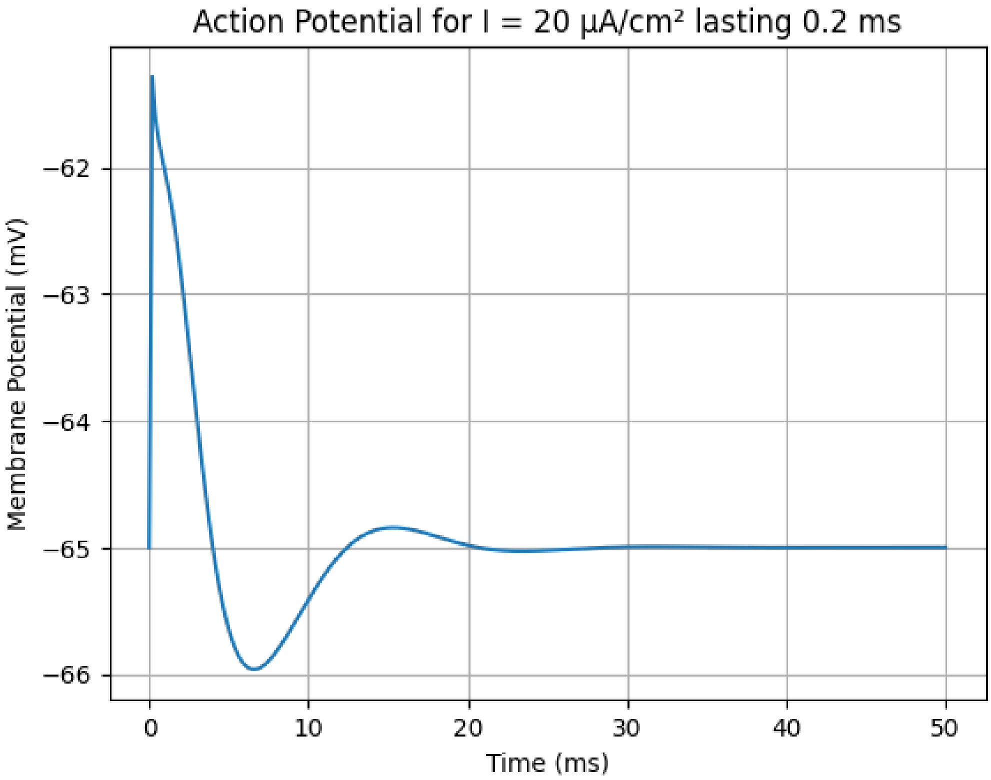

Figure 8: Action Potential for I = 20 µA/cm² lasting 0.2 ms

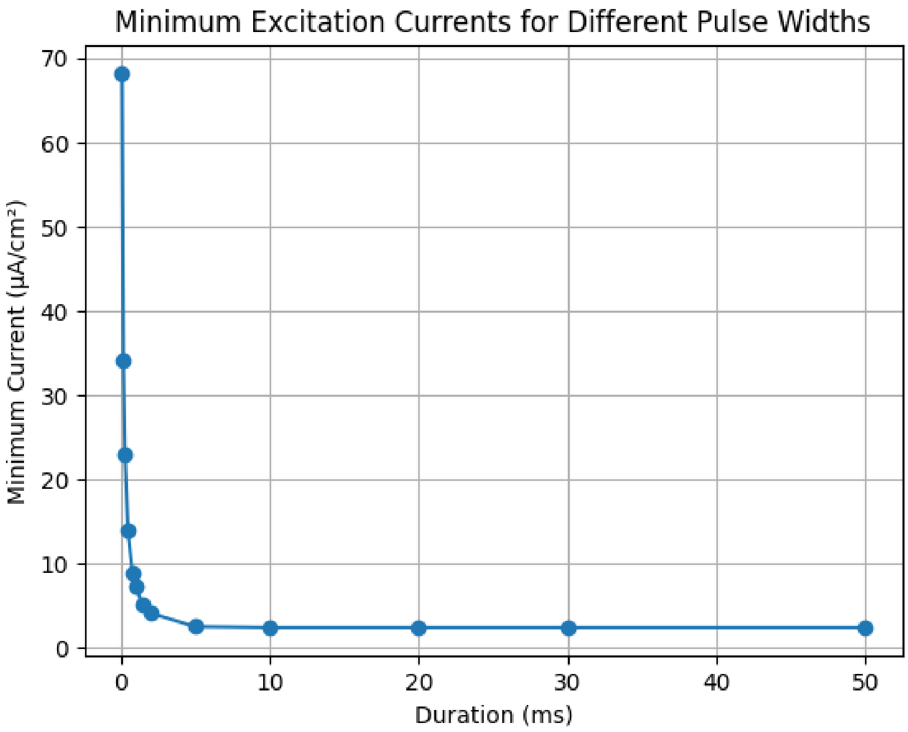

Figure 9: Minimum Excitation Currents for Different Pulse Widths

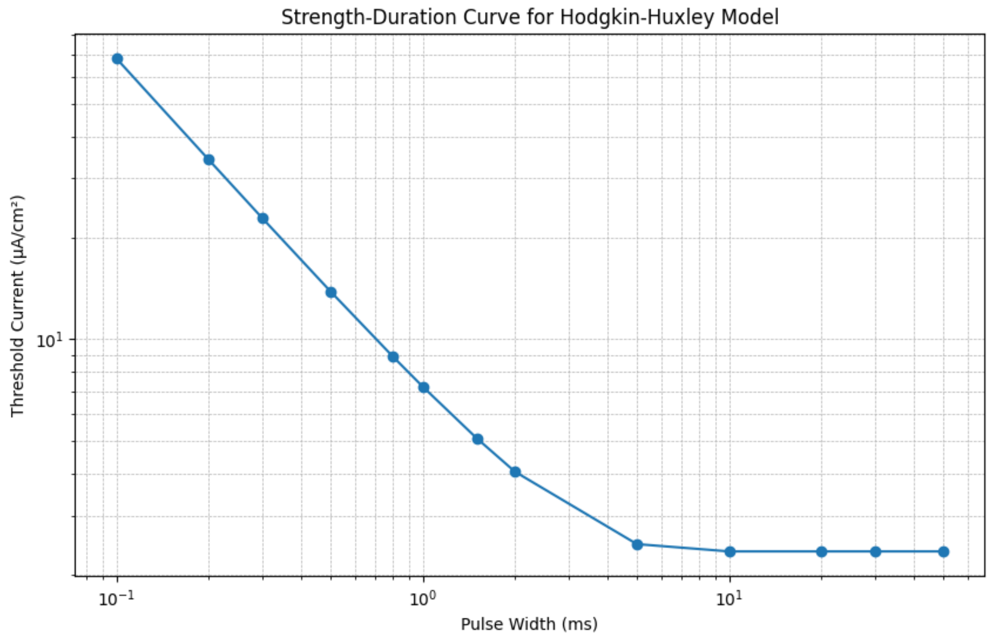

Figure 10: Strength-Duration Curve for Hodgkin-Huxley Model

b) gNa and gK over time - the time change of m, n and h

- **Action Potential (AP) Graph in figure 11**:

- The AP graph shows the membrane potential (in millivolts) over time (in milliseconds). It starts around -80 mV, spikes up to just above 40 mV, and then returns to the initial value.
- This corresponds to the depolarization and repolarization phases of an AP.

- **Conductances (gNa and gK) over Time in figure 11**:
  - The orange line represents sodium conductance (gNa), which peaks early **during depolarization**.
  - The blue line represents potassium conductance (gK), which peaks later **during repolarization**.
  - gNa contributes to the rising phase of the AP, while gK aids in repolarization.
- **Gating Variables (m, n, and h) in figure 11**:
  - 'm' (green) represents sodium channel activation. It increases rapidly **during depolarization**.
  - 'n' (blue) represents potassium channel activation. It increases more gradually and remains elevated for **a longer duration**.
  - 'h' (red) represents sodium channel inactivation. It decreases **initially** and contributes to the refractory period.

Interpretation:

- The rapid increase in gNa and subsequent decrease aligns with sodium influx during depolarization.
- The slower increase in gK corresponds to potassium efflux during repolarization.
- The gating variables (m, n, h) regulate ion channel states, influencing AP dynamics.

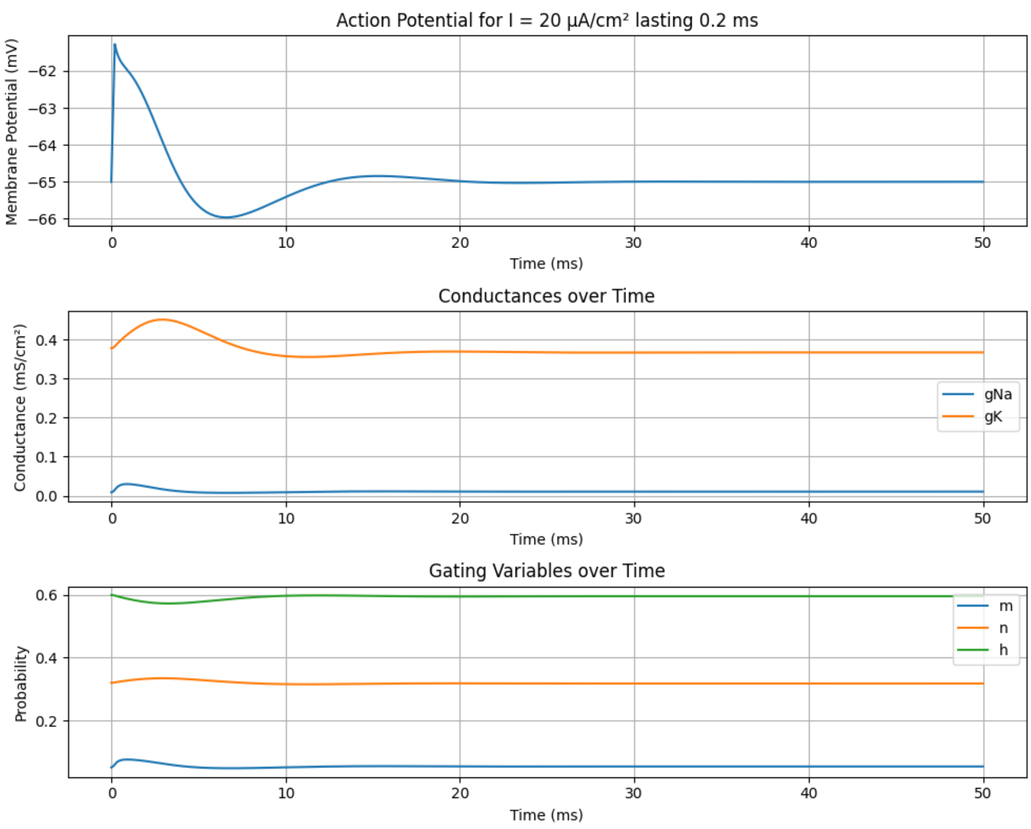

Figure 11: Action Potential (AP) Graph, Conductances (gNa and gK) over Time, and Gating Variables (m, n, and h)

c) The current for Na and K channels

- **Sodium Current (I_Na)**:
  - The sodium current (I_Na) starts around -1 µA/cm².
  - It quickly spikes to just above 5 µA/cm² around 10 ms.
  - Then, it gradually decreases back to around -1 µA/cm² by approximately 20 ms.
  - I_Na plays a crucial role in the rising phase of the action potential.
- **Potassium Current (I_K)**:
  - The potassium current (I_K) starts around -2 µA/cm².
  - It gradually increases to reach a plateau slightly below 2 µA/cm² around 10 ms.
  - I_K remains relatively constant at this level throughout the rest of the time period.
  - I_K contributes to the repolarization phase of the action potential.

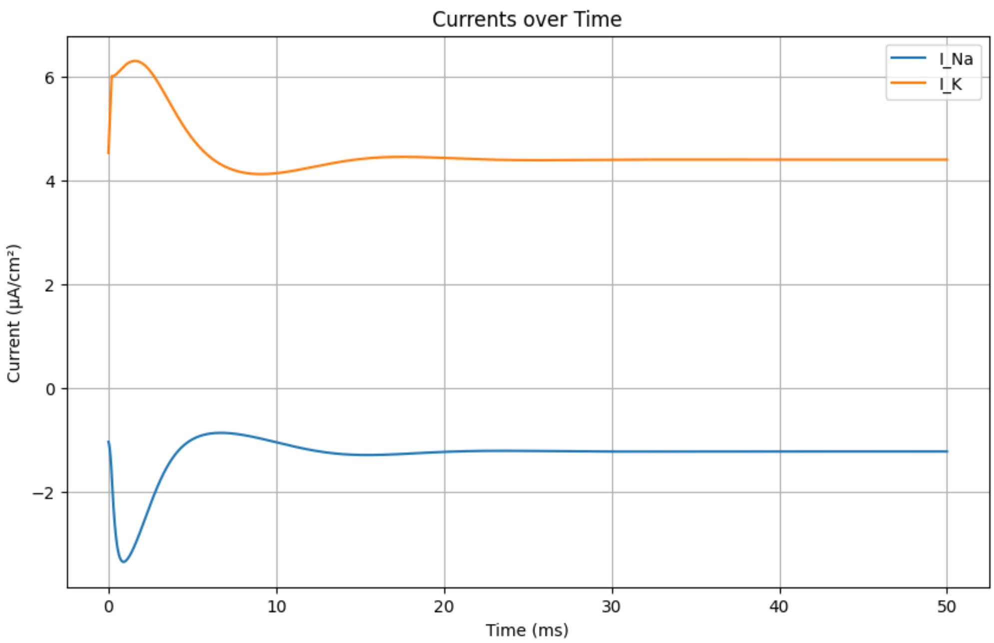

Figure 12: current of Na and K over time

d) The effect of increasing the capacitance of membrane

As the membrane capacitance increases:

- The peak of the action potential decreases slightly.
- The duration of the action potential broadens.

Higher membrane capacitance affects both the amplitude and duration of an action potential.

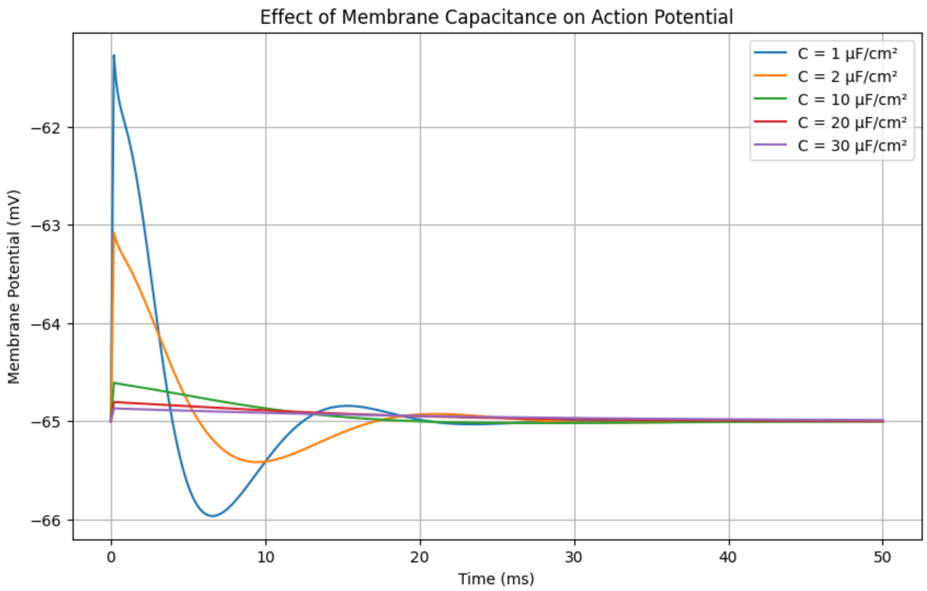

Figure 13: Effect of Membrane Capacitance on Action Potential

e) The second excitation with amplitude 40 μA/cm2 after 15 ms

- **Initial Excitation:**
  - The initial excitation resulted in a rapid spike in membrane potential, peaking just above **-40 mV** (negative range).
  - Following the spike, the membrane potential declined below **0 mV** and gradually returned to baseline.
- **Second Excitation (Applied After 15 ms):**
  - At 15 ms, a second excitation was applied.
  - This second excitation induced a smaller increase in membrane potential, peaking around **-10 mV** (negative range).
  - The membrane potential then returned to baseline again.

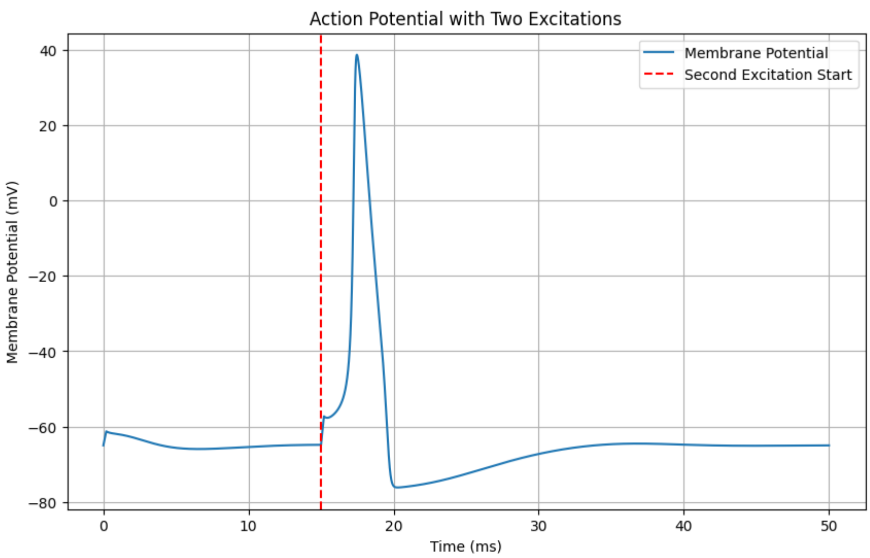

Figure 14: Action Potential with Two Excitations

3. Article Simulation

The model described in the paper was implemented using the Brian Simulator. The following steps outline the implementation process:

1. **Model Definition**:
    - **Neuron Model**: We defined the neuron model using equations that govern the membrane potential and synaptic currents.
    - **Synapses**: The synaptic connections were established to model the interactions between neurons, incorporating both excitatory and inhibitory synapses.
    - **Network Architecture**: The network architecture was constructed to reflect the cortical circuit as described in the paper.
2. **Simulation Parameters**:
    - **Time Constants**: Parameters such as membrane time constants, synaptic time constants, and delay times were set according to the paper.
    - **Input Rates**: The input rates were varied to observe their effect on the firing rates and overall network dynamics.
3. **Simulation Execution**:
    - The simulation was executed over a period, and the neuronal activity was recorded. The Brian Simulator's functions were utilized to handle the integration of differential equations and the management of spikes.

Results

The simulation results are presented in figure 15. The plots illustrate the following:

1. **Neuronal Activity**:
    - The top two panels display the spike raster plots for Pool 1 and Pool 2 neurons, respectively. Each dot represents a spike, with time on the x-axis and neuron index on the y-axis.
2. **Firing Rates**:
    - The third panel shows the smoothed firing rates for Pool 1 and Pool 2 neurons. The firing rate for Pool 1 increases significantly during the simulation, while Pool 2 maintains a relatively steady rate.
3. **Input Rates**:
    - The bottom panel depicts the input rates for the Poisson input groups driving Pool 1 and Pool 2 neurons. The input rates were stepped to observe their effect on the firing rates.

Analysis

1. **Neuronal Dynamics**:
    - The increase in firing rate for Pool 1 neurons suggests a form of reverberation or sustained activity, as described in the paper. This is indicative of the network's ability to maintain activity over time, which is crucial for decision making processes.

2. **Comparison with Paper**:
    - The observed dynamics are consistent with the findings reported in the paper. The ability of Pool 1 to maintain higher firing rates in response to increased input aligns with the concept of slow reverberation and probabilistic decision making.
3. **Parameter Sensitivity**:
    - Altering parameters such as the synaptic strength, time constants, and input rates significantly affects the network dynamics. This highlights the importance of precise parameter tuning in replicating the desired neural behavior.

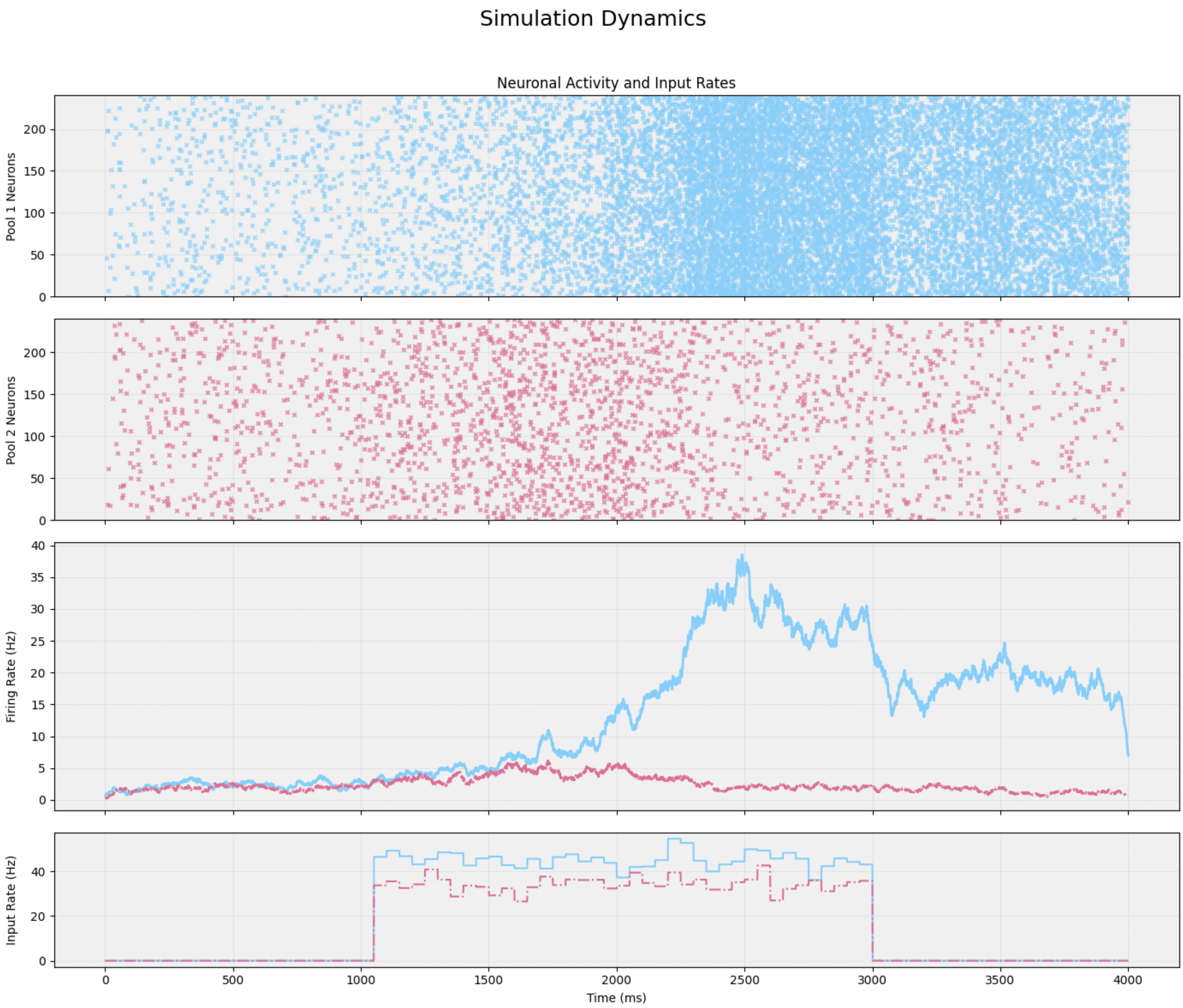

Figure 15: The simulation results if article "Probabilistic Decision Making by Slow Reverberation in Cortical Circuits"