BCS410: HW3 Report

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Problem 1: Simulation with piece-wise I(t)

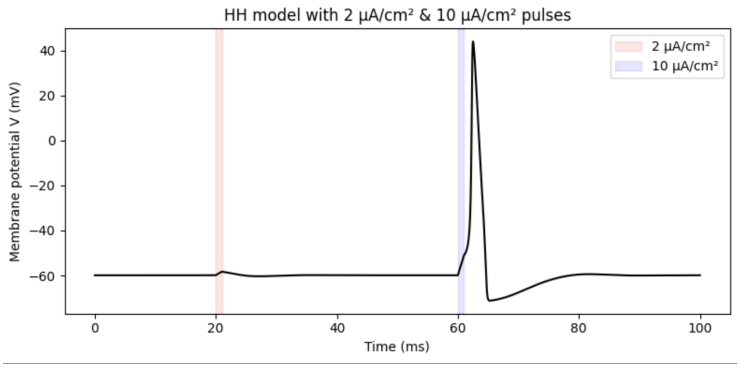

Figure 1: Membrane potential $V(t)$ in response to a $2\mu A/cm^2$ pulse at 20–21ms (shaded red) and a $10\mu A/cm^2$ pulse at 60–61ms (shaded blue).

Interpretation

The simulation in Figure 1 illustrates two qualitatively distinct responses of the Hodgkin–Huxley model:

1. Subthreshold response ($2\mu A/cm^2$ pulse). When a $2\mu A/cm^2$ current is injected from 20 to 21ms, the membrane depolarizes only slightly from its resting potential (about $-60\,\mathrm{mV}$), reaching roughly $-55\,\mathrm{mV}$ but *not* crossing the threshold for regenerative sodium entry. Because

$$m_\infty(V) \;=\; \frac{\alpha_m(V)}{\alpha_m(V)+\beta_m(V)}$$

remains low and $n_\infty(V)$ and $h_\infty(V)$ change only modestly, the resulting sodium conductance $g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}}\, m^3\, h$ fails to dominate leak and potassium currents. Thus the membrane simply "bumps up" and passively returns to rest.

2. Suprathreshold response (10µA/cm^2 pulse). In contrast, the 10µA/cm^2 step at 60–61ms depolarizes V beyond the critical threshold (near $-55\,\mathrm{mV}$), triggering the positive-feedback loop:

(i) $m_\infty(V)\uparrow \Longrightarrow\ g_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}}\, m^3\, h$ rises sharply,

(ii) large Na^+ influx overwhelms K^+ and leak currents $\Longrightarrow$ rapid upstroke,

(iii) h-inactivation and delayed n-activation $\Longrightarrow$ peak inactivation of Na^+ conductance and rise of K^+ condu

(iv) repolarization and after-hyperpolarization via K^+ efflux,

(v) return of (m, n, h) toward their resting steady states.

This all-or-none spike exemplifies how the nonlinear gating kinetics of the Hodgkin–Huxley equations convert a sufficiently large depolarization into a full action potential, whereas smaller currents produce only passive, subthreshold deflections.

Problem 2: Effect of Leak Conductance on Excitability

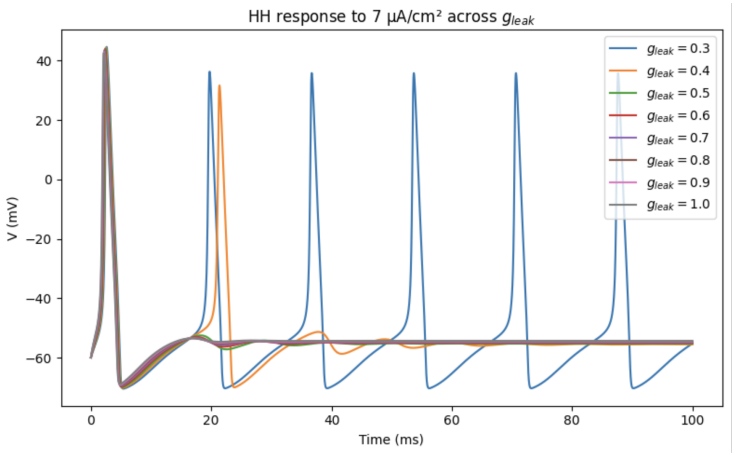

Figure 2: Membrane potential responses to a constant $I_{\mathrm{app}} = 7\ \mu\mathrm{A/cm}^2$ for varying leak conductance $g_{\mathrm{leak}} \in [0.3, 1.0]\,\mathrm{mS/cm}^2$.

As g_{leak} increases, the passive leak current

$$I_{\mathrm{leak}} \;=\; g_{\mathrm{leak}}\,\big(V - E_{\mathrm{leak}}\big)$$

grows proportionally, so more of the injected current is *shunted* away. From the membrane equation

$$C\frac{dV}{dt} = I_{\mathrm{app}} - I_K - I_{\mathrm{Na}} - I_{\mathrm{leak}},$$

at the threshold voltage V_{th} (–55 mV) one can estimate the *rheobase* current by setting $dV/dt = 0$ and neglecting transients:

$$I_{\text{rheo}} \approx g_{\text{leak}}\,(V_{\text{th}} - E_{\text{leak}}) + \underbrace{g_K(V_{\text{th}} - E_K) + g_{\text{Na}}(V_{\text{th}} - E_{\text{Na}})}_{\text{small at rest}}.$$

Thus I_{rheo} grows linearly with g_{leak}.

- For low $g_{\text{leak}} = 0.3$, the fixed drive $7\,\mu\text{A/cm}^2 > I_{\text{rheo}}$ and the cell fires repetitively.
- As g_{leak} rises (0.4–0.5), I_{rheo} approaches $7\mu\text{A/cm}^2$, lengthening the inter-spike interval or aborting later spikes.
- Beyond a critical $g_{\text{leak}} \approx 0.6$, we have $7\,\mu\text{A/cm}^2 < I_{\text{rheo}}$, so no action potential can be generated.

Hence increasing g_{leak} strongly *decreases excitability* by raising the threshold current required for spike initiation.

Problem 3: Firing Period and Spike Amplitude vs. Constant Drive

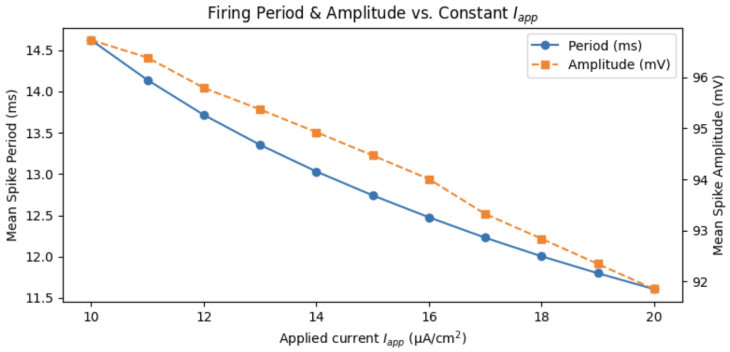

Figure 3: Mean inter-spike period T (blue circles, left axis) and mean spike amplitude A (orange squares, right axis) as functions of constant applied current I_{app}.

We varied the constant drive I_{app} from 10 to 20 $\mu\text{A/cm}^2$ and measured:

- The *mean inter-spike period*

$$T(I_{\text{app}}) = \langle t_{k+1} - t_k \rangle,$$

Table 1: Measured firing period T and spike amplitude A for $I_{\text{app}} = 10$–$20\ \mu\text{A/cm}^2$.

I_{app} (μA/cm^2)	T (ms)	A (mV)
10	14.62	96.73
11	14.14	96.39
12	13.72	95.80
13	13.35	95.37
14	13.03	94.93
15	12.74	94.47
16	12.48	94.01
17	12.23	93.32
18	12.01	92.84
19	11.80	92.35
20	11.61	91.85

which decreases monotonically with I_{app} (Fig. 3, left axis). Equivalently, the firing rate $f = 1/T$ increases nearly linearly, mimicking a classic *f–I curve*.

- The *mean spike amplitude*

$$A(I_{\text{app}}) = \left\langle V_{\text{peak}} \right\rangle - V_{\text{rest}},$$

which shows a modest decline as I_{app} increases (Fig. 3, right axis), due to partial sodium-channel inactivation at higher steady depolarizations.

Thus, with stronger constant drive, the neuron not only fires more rapidly but also exhibits slightly smaller peak deflections—quantitative hallmarks of Hodgkin–Huxley excitability under tonic current injection.

Problem 4: Spontaneous Spiking under Maximal Conductance Variations

Sodium-conductance sweep (Fig. 4). At low $\bar{g}_{\text{Na}}$ (190–192mS/cm^2) the cell shows only a single transient depolarization before settling back to rest. Once $\bar{g}_{\text{Na}}$ exceeds approximately 193mS/cm^2, the net inward sodium current at rest,

$$I_{\text{Na}} \;=\; \bar{g}_{\text{Na}}\, m_\infty^3(V_{\text{rest}})\, h_\infty(V_{\text{rest}})\, (V_{\text{rest}} - E_{\text{Na}}),$$

outweighs the outward potassium plus leak currents, and the membrane crosses threshold repeatedly: it enters a regime of *autonomous, rhythmic spiking* without any external drive.

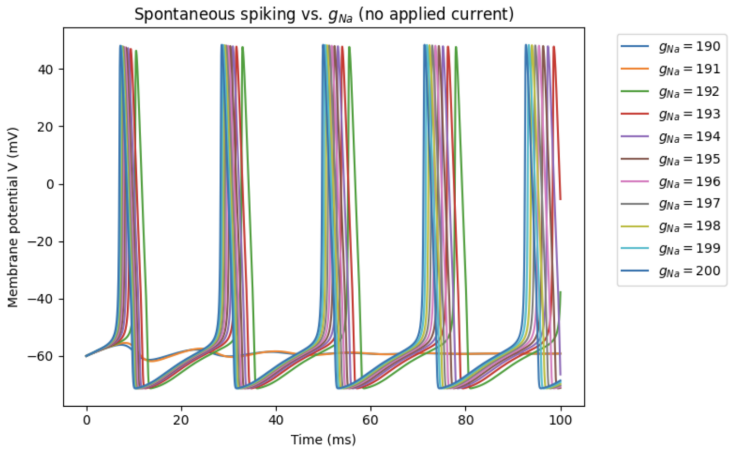

Figure 4: Membrane potential with $I_{\text{app}} = 0$, as maximal sodium conductance $\bar{g}_{\text{Na}}$ is stepped from 190 to 200mS/cm^2.

Potassium-conductance sweep (Fig. 5). With high $\bar{g}_K$ (30–28mS/cm^2) the outward K^+ current

$$I_K \;=\; \bar{g}_K \, n_\infty^4(V_{\text{rest}}) \, (V_{\text{rest}} - E_K)$$

is large enough to clamp the cell at rest. As $\bar{g}_K$ falls below about 27mS/cm^2, this stabilizing outward current weakens so much that small fluctuations push the membrane above threshold. The result is again *spontaneous, repetitive firing* in the absence of applied current.

Biological interpretation. The Hodgkin–Huxley model rests on a balance of inward sodium and outward potassium (plus leak) currents at the resting potential. Increasing $\bar{g}_{\text{Na}}$ amplifies the inward "recruitment" current, while decreasing $\bar{g}_K$ reduces the stabilizing outward conductance. In both cases, the cell's net current–voltage balance at rest becomes unstable to any small depolarization, triggering the positive-feedback loop of sodium-channel activation and thus generating *spontaneous* action potentials without any external stimulus.

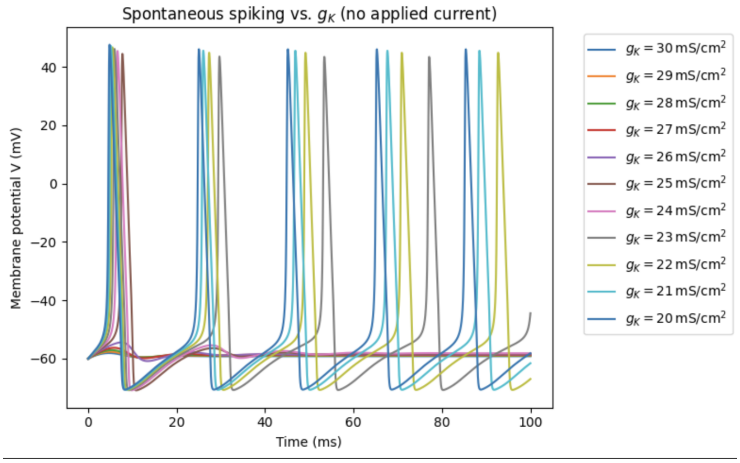

Figure 5: Membrane potential with $I_{\text{app}} = 0$, as maximal potassium conductance $\bar{g}_K$ is stepped from 30 to 20mS/cm^2.

Problem 5: Activation vs. Inactivation Dynamics of Na^+ Channels(under settings of problem1)

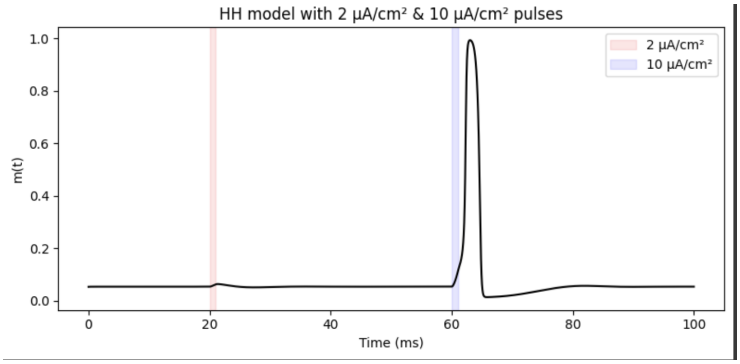

Figure 6: Time-course of the activation gate $m(t)$ under the two brief current injections ($2\mu A/cm^2$ at 20–21ms, $10\mu A/cm^2$ at 60–61ms).

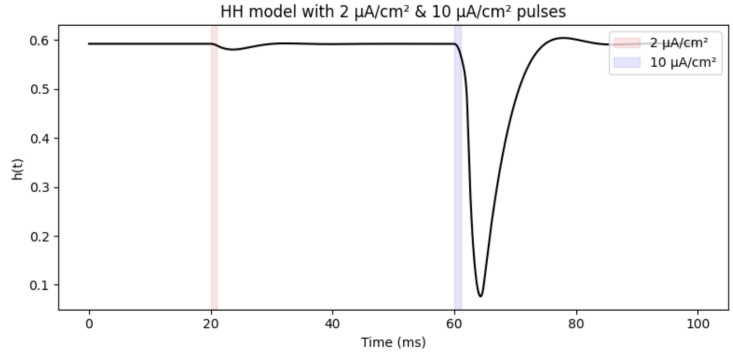

Figure 7: Time-course of the inactivation gate $h(t)$ under the same stimulus protocol.

Outside of the rapid upstroke and downstroke of the action potential, $m(t)$ remains near its low resting value $m_\infty(V_{\text{rest}})$ while $h(t)$ stays near its high resting value $h_\infty(V_{\text{rest}})$. Because the sodium conductance is

$$g_{\text{Na}}(t) \;=\; \bar{g}_{\text{Na}}\, m^3(t)\, h(t)\,,$$

the product m^3h stays vanishingly small at rest. During the spike, $m(t)$ quickly rises toward 1 and $h(t)$ simultaneously falls, so m^3h transiently peaks—driving the inward Na^+ current. Thus, except for that narrow window of spike initiation and repolarization, activation and inactivation gates effectively "cancel" each other, preventing sodium current between spikes.

Problem 6: Temporal Ordering of Sodium and Potassium Currents

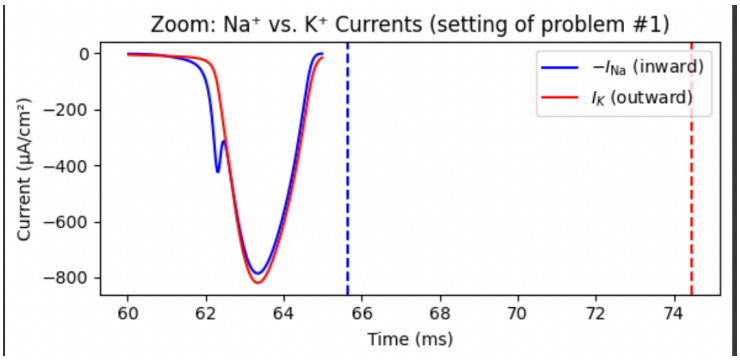

Figure 8: Zoomed view of the inward sodium current $-I_{\mathrm{Na}^+}(t)$ (blue) and outward potassium current $I_{K^+}(t)$ (red) during the action potential triggered by the $10\mu\mathrm{A/cm}^2$ pulse. Vertical dashed lines mark the peak times of each current.

Analysis of Figure 8 yields

$$t_{\mathrm{Na\ peak}} = 65.640 \text{ ms}, \qquad t_{\mathrm{K\ peak}} = 74.460 \text{ ms},$$

so that the potassium current lags the sodium current by

$$\Delta t = t_{\mathrm{K\ peak}} - t_{\mathrm{Na\ peak}} = 8.820 \text{ ms}.$$

This confirms the biophysical sequence of the action potential:

1. A rapid, inward sodium flux (I_{Na^+}) initiates the upstroke.
2. After a brief delay Δt, the slower potassium conductance activates, producing the outward potassium current (I_{K^+}) that repolarizes the membrane.

Thus the HH model faithfully reproduces the textbook ordering of ionic currents during spike generation.

Problem 7: Steady-State Values and Time Constants from $\alpha(V)$ and $\beta(V)$

The gating variables $n(t)$, $m(t)$, and $h(t)$ each satisfy an ordinary differential equation of the form

$$\frac{dx}{dt} \;=\; \alpha_x(V)\big[1 - x(t)\big] \;-\; \beta_x(V)\, x(t),$$

where $x \in \{n, m, h\}$. We now show that this can be written in the equivalent "x_∞–τ_x" form

$$\frac{dx}{dt} \;=\; \frac{x_\infty(V) - x}{\tau_x(V)},$$

with

$$x_\infty(V) \;=\; \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)}, \qquad \tau_x(V) \;=\; \frac{1}{\alpha_x(V) + \beta_x(V)}.$$

(i) Steady-state value x_∞. At equilibrium $dx/dt = 0$, so

$$0 = \alpha_x(V)\big[1 - x_\infty\big] - \beta_x(V)\, x_\infty \;\;\Longrightarrow\;\; \alpha_x(V) - \big[\alpha_x(V) + \beta_x(V)\big]\, x_\infty \;=\; 0 \;\;\Longrightarrow\;\; x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)}.$$

(ii) Time constant τ_x. Factor the right-hand side of the original ODE:

$$\frac{dx}{dt} = \alpha_x(V) - \big[\alpha_x(V) + \beta_x(V)\big]\, x = \big[\alpha_x(V) + \beta_x(V)\big]\, \Big[\tfrac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)} - x\Big].$$

Recognizing x_∞ in the bracket and defining

$$\tau_x(V) \;=\; \frac{1}{\alpha_x(V) + \beta_x(V)},$$

we obtain

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)},$$

which shows that $x(t)$ relaxes *exponentially* to $x_\infty(V)$ with time-constant $\tau_x(V)$.

(iii) Role of α and β.

- $\alpha_x(V)$ is the *opening rate* (per ms) driving the gate variable upward.
- $\beta_x(V)$ is the *closing rate* (per ms) driving the gate variable downward.
- Their *ratio* $x_\infty(V) = \dfrac{\alpha_x}{\alpha_x + \beta_x}$ fixes the equilibrium fraction of open gates at voltage V.
- Their *sum* $\alpha_x + \beta_x = \tau_x^{-1}$ determines how fast $x(t)$ approaches that equilibrium.

By carrying out the same steps for $n(t)$, $m(t)$, and $h(t)$, we can recover the textbook expressions for n_∞, m_∞, h_∞ and τ_n, τ_m, τ_h. This mathematical structure underlies the HH model's ability to capture both equilibrium gating probabilities and their voltage-dependent kinetics.