Computational Cardiology Lecture 9

# Membrane current balance and voltage-dependent gates

Zan Ahmad

Fall 2024

# Membrane charge balance

$$C\dot{V} = I_{\text{stim}} - \sum_j g_j(V - E_j).$$

# Membrane charge balance

$$C\dot{V} = I_{\text{stim}} - \sum_j g_j(V - E_j).$$

Outward ionic current is positive; applied inward current is positive.

# Densities and total current

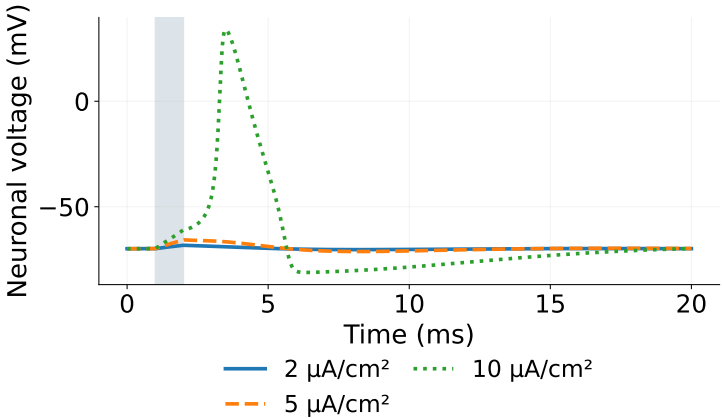
$$I_{\text{density}} = I_{\text{total}}/A.$$

# Densities and total current

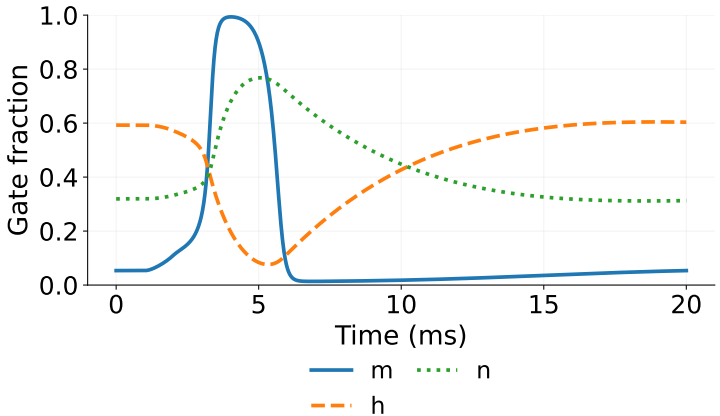
$$I_{\text{density}} = I_{\text{total}}/A.$$

$$(\mu\text{F/cm}^2)(\text{mV/ms}) = \mu\text{A/cm}^2.$$

# Equal-duration neuronal pulses



# Bounded gate fractions



# Voltage driving forces and conductances

$$g_{Na} = 120m^3h, \qquad g_K = 36n^4, \qquad g_L = .3.$$

# Voltage driving forces and conductances

$$g_{Na} = 120m^3h, \qquad g_K = 36n^4, \qquad g_L = .3.$$

$$(E_{Na}, E_K, E_L) = (45, -82, -59) \text{ mV}.$$

# The gate equation

$$\dot{s} = \alpha_s(V)(1 - s) - \beta_s(V)s.$$

# The gate equation

$$\dot{s} = \alpha_s(V)(1 - s) - \beta_s(V)s.$$

$$s_\infty = \frac{\alpha_s}{\alpha_s + \beta_s}, \qquad \tau_s = \frac{1}{\alpha_s + \beta_s}.$$

# Bounds of the continuous gate

At $s = 0$, $\dot{s} = \alpha_s \geq 0$. At $s = 1$, $\dot{s} = -\beta_s \leq 0$.

# Bounds of the continuous gate

At $s = 0$, $\dot{s} = \alpha_s \geq 0$. At $s = 1$, $\dot{s} = -\beta_s \leq 0$. The vector field points into the admissible interval.

# The removable rate singularity

$$f(z) = \frac{z}{1 - e^{-z}}, \qquad f(0) = 1.$$

# The removable rate singularity

$$f(z) = \frac{z}{1 - e^{-z}}, \qquad f(0) = 1.$$

$$f(z) = 1 + z/2 + z^2/12 - z^4/720 + O(z^6).$$

# Two activation rates

$$\alpha_m = f((V+45)/10), \qquad \alpha_n = .1f((V+60)/10).$$

# Two activation rates

$$\alpha_m = f((V+45)/10), \qquad \alpha_n = .1f((V+60)/10).$$

At $V = -45$ and $-60$ mV, the respective rates are $1$ and $.1\ \mathrm{ms}^{-1}$.

# An exact frozen-voltage gate step

For $k_s = \alpha_s + \beta_s > 0$,

$$s^{n+1} = s_\infty + (s^n - s_\infty)e^{-k_s \Delta t}.$$

# An exact frozen-voltage gate step

For $k_s = \alpha_s + \beta_s > 0$,

$$s^{n+1} = s_\infty + (s^n - s_\infty)e^{-k_s \Delta t}.$$

This is a convex combination of $s^n$ and $s_\infty$ for nonnegative rates.

# The zero-rate limit

If $\alpha_s = \beta_s = 0$, then $\dot{s} = 0$ and $s^{n+1} = s^n$.

# The zero-rate limit

If $\alpha_s = \beta_s = 0$, then $\dot{s} = 0$ and $s^{n+1} = s^n$. No equilibrium fraction needs to be formed by division by zero.

# Freeze conductances after the gate step

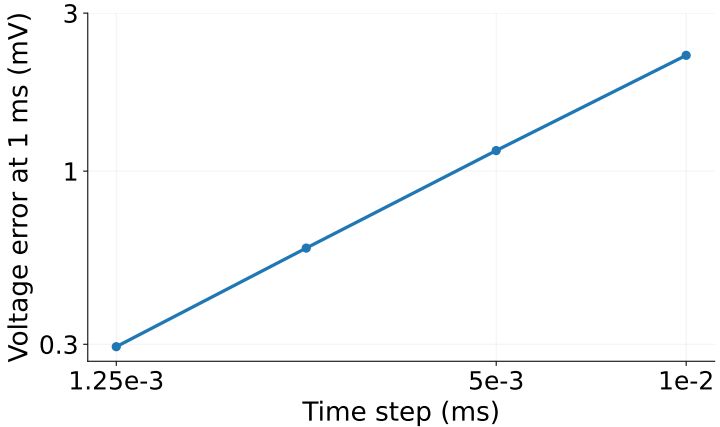
$$G = \sum_j g_j, \qquad B = \sum_j g_j E_j + I.$$

# Freeze conductances after the gate step

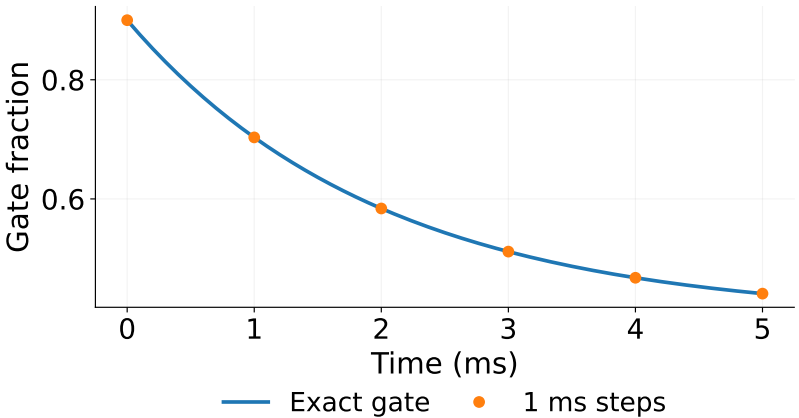
$$G = \sum_j g_j, \qquad B = \sum_j g_j E_j + I.$$

$$C\dot{V} = B - GV, \qquad V_\infty = B/G.$$

# First-order coupled error



# Frozen-rate gate check



# An exact frozen-conductance voltage step

$$V^{n+1} = V_\infty + (V^n - V_\infty)e^{-G\Delta t/C}.$$

# An exact frozen-conductance voltage step

$$V^{n+1} = V_\infty + (V^n - V_\infty)e^{-G\Delta t/C}.$$

The two exact substeps form a first-order coupled method.

# The coupled rest equation

$$\mathcal{I}(V) = \sum_j g_j(s_\infty(V))(V - E_j) = 0.$$

# The coupled rest equation

$$\mathcal{I}(V) = \sum_j g_j(s_\infty(V))(V - E_j) = 0.$$

Resting gates and zero net current must hold at the same voltage.

# Current cancellation at rest

Individual ionic currents can remain nonzero while their sum vanishes.

# Current cancellation at rest

Individual ionic currents can remain nonzero while their sum vanishes. The companion recomputes the equilibrium from its exact rate constants, near $-69.89767$ mV.

# Excitation depends on the protocol

Pulse amplitude, duration, initial voltage and initial gates jointly determine the response.

# Excitation depends on the protocol

Pulse amplitude, duration, initial voltage and initial gates jointly determine the response. A zero-crossing distinction for one pulse does not define a universal excitation threshold.

# Model identity

These neuronal kinetics describe a specific $V, m, h, n$ system.

# Model identity

These neuronal kinetics describe a specific $V, m, h, n$ system. A reduced cardiac model changes both the variables and the equations; it is not obtained by relabeling a neuronal trace.