



Computational Neurobiology

Lecture 3: Neuron models 1

Dmitriy Bozhko



Syllabus

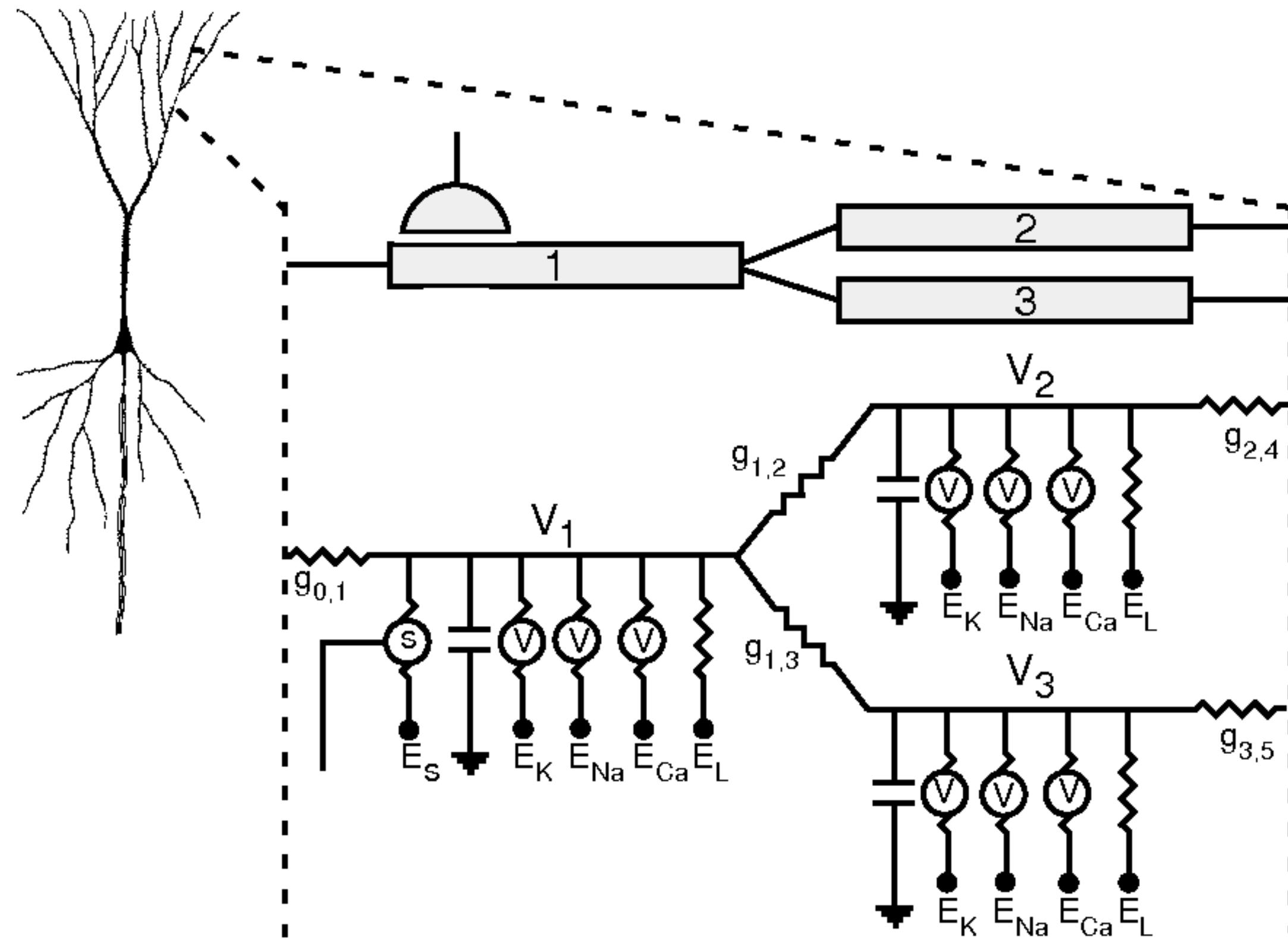
- Single-compartment models
- Integrate-and-fire models
- Voltage-dependent conductances
- The Hodgkin-Huxley model



Single-compartment models

- Retrospective of compartments
- Single-compartment model
- Membrane capacitance and resistance
- Relation between the membrane potential and charge
- Basic equation for all single-compartment models

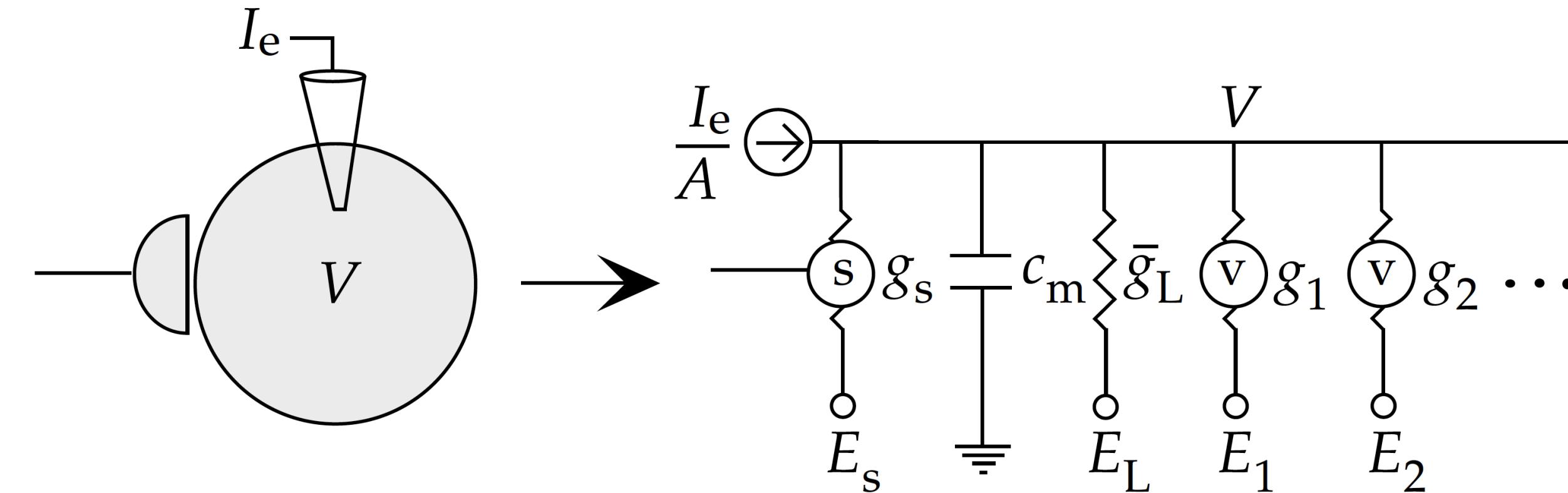
Retrospective of compartments



A multi-compartment model of a neuron. The expanded region shows three compartments at a branch point where a single cable splits into two.

Single-compartment model

Models that describe the membrane potential of a neuron by a single variable V are called **single-compartment models**.



The equivalent circuit for a one-compartment neuron model. The neuron is represented, at the left, by a single compartment of surface area A with a synapse and a current-injecting electrode.

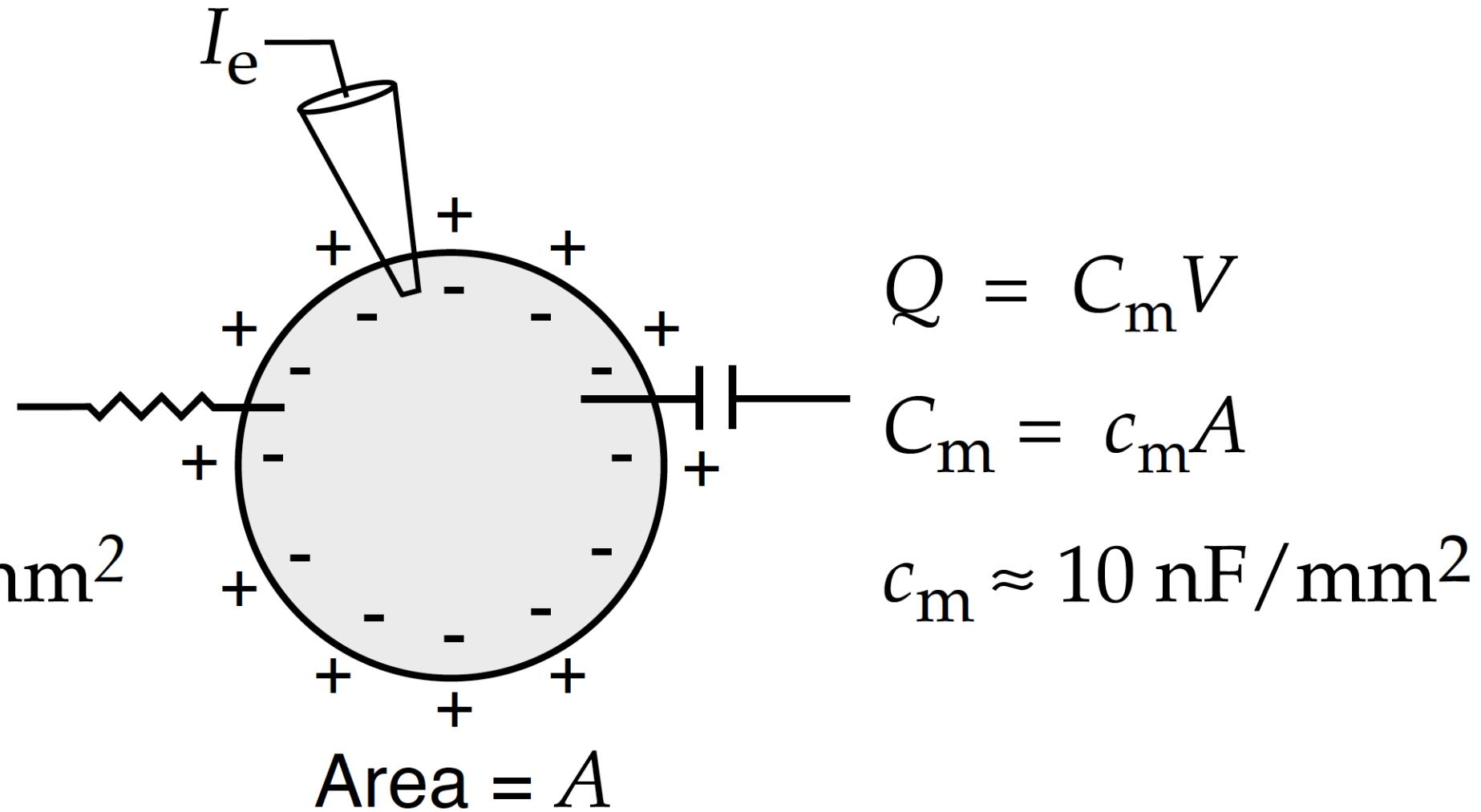


Membrane capacitance and resistance

$$\Delta V = I_e R_m$$

$$R_m = r_m / A$$

$$r_m \approx 1 \text{ M}\Omega \text{ mm}^2$$



The capacitance and membrane resistance of a neuron considered as a single compartment.



Membrane capacitance

$Q = C_m V$, where Q is charge, C_m is total capacitance, V is membrane potential

$$\frac{dQ}{dt} = C_m \frac{dV}{dt}, \text{ and}$$

$$\frac{dQ}{dt} = I_C - \text{current passing into the cell}$$

So the amount of current needed to change the membrane potential of a neuron with a total capacitance C_m at a rate $\frac{dV}{dt}$ is $C_m \frac{dV}{dt}$. For example, 1 nA will change the membrane potential of a neuron with a capacitance of 1 nF at a rate of 1 mV/ms.



Membrane resistance

Holding the membrane potential steady at a level different from its resting value also requires current, but this current is determined by the membrane resistance rather than by the capacitance of the cell.

$$\Delta V = I_R R_m \text{ - Ohm's law}$$

The restriction to small currents and small ΔV is required membrane because membrane resistances can vary as a function of voltage, whereas Ohm's law assumes R_m is constant over the range ΔV .



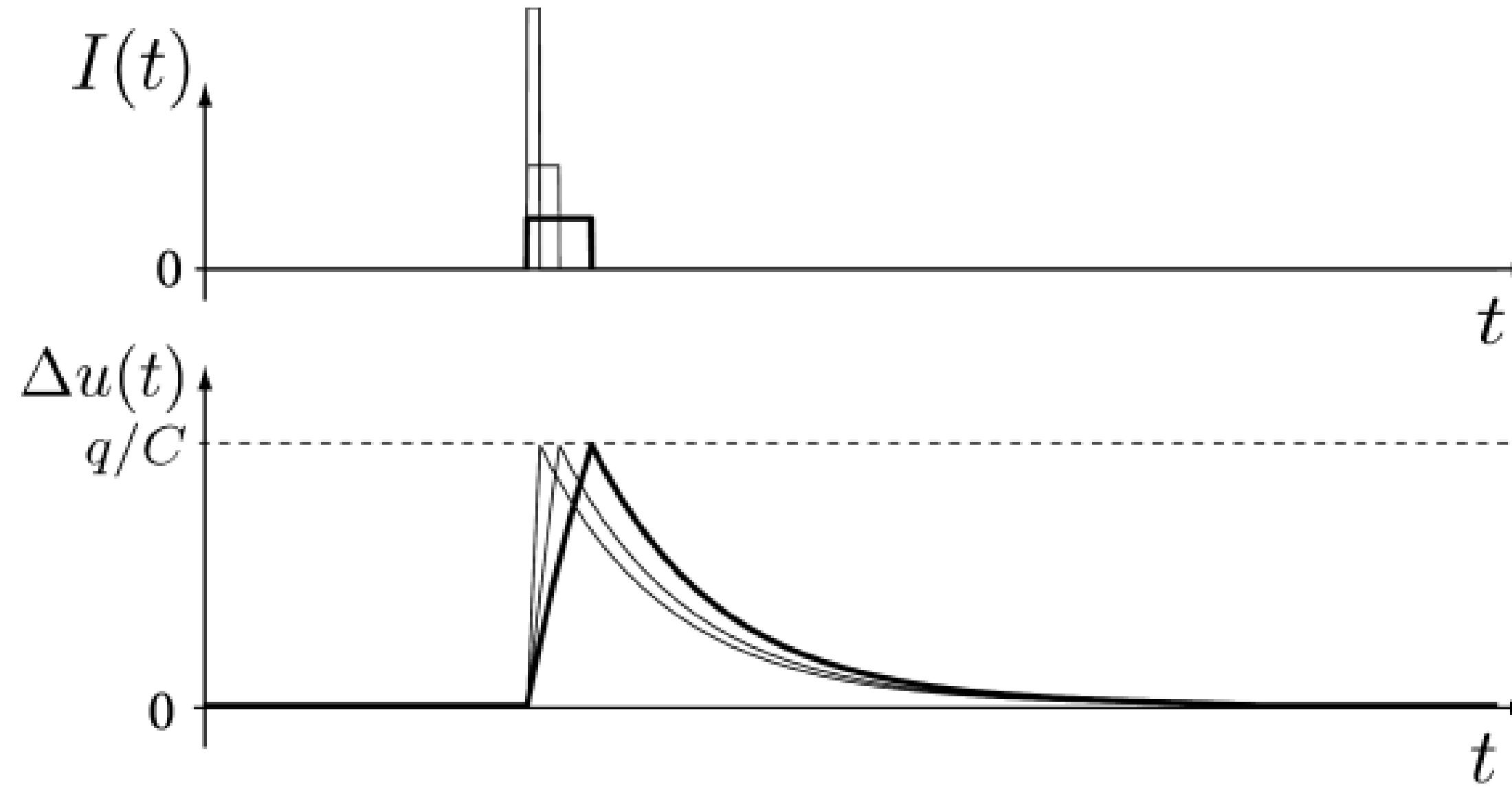
Passive membrane model

$$I_e = I_C + I_R \text{ - total current}$$

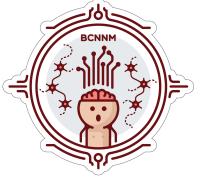
$$I_R = \frac{\Delta V}{R_m} \text{ - resistive current from Ohm's law}$$

$$I_e = C_m \frac{dV}{dt} + \frac{\Delta V}{R_m}$$

Pulse input



Short pulses and total charged delivered on the passive membrane. The amplitude of the voltage response (bottom) of a leaky integrator driven by a short current pulse $I(t)$ (top) depends only on the total charge $q = \int I(t)dt$, but not on the height of the current pulse.



Integrate-and-fire models

- Introduction to integrate-and-fire model
- Leaky and generalized models
- Firing rate of an integrate-and-fire model
- Spike-Rate Adaptation and Refractoriness

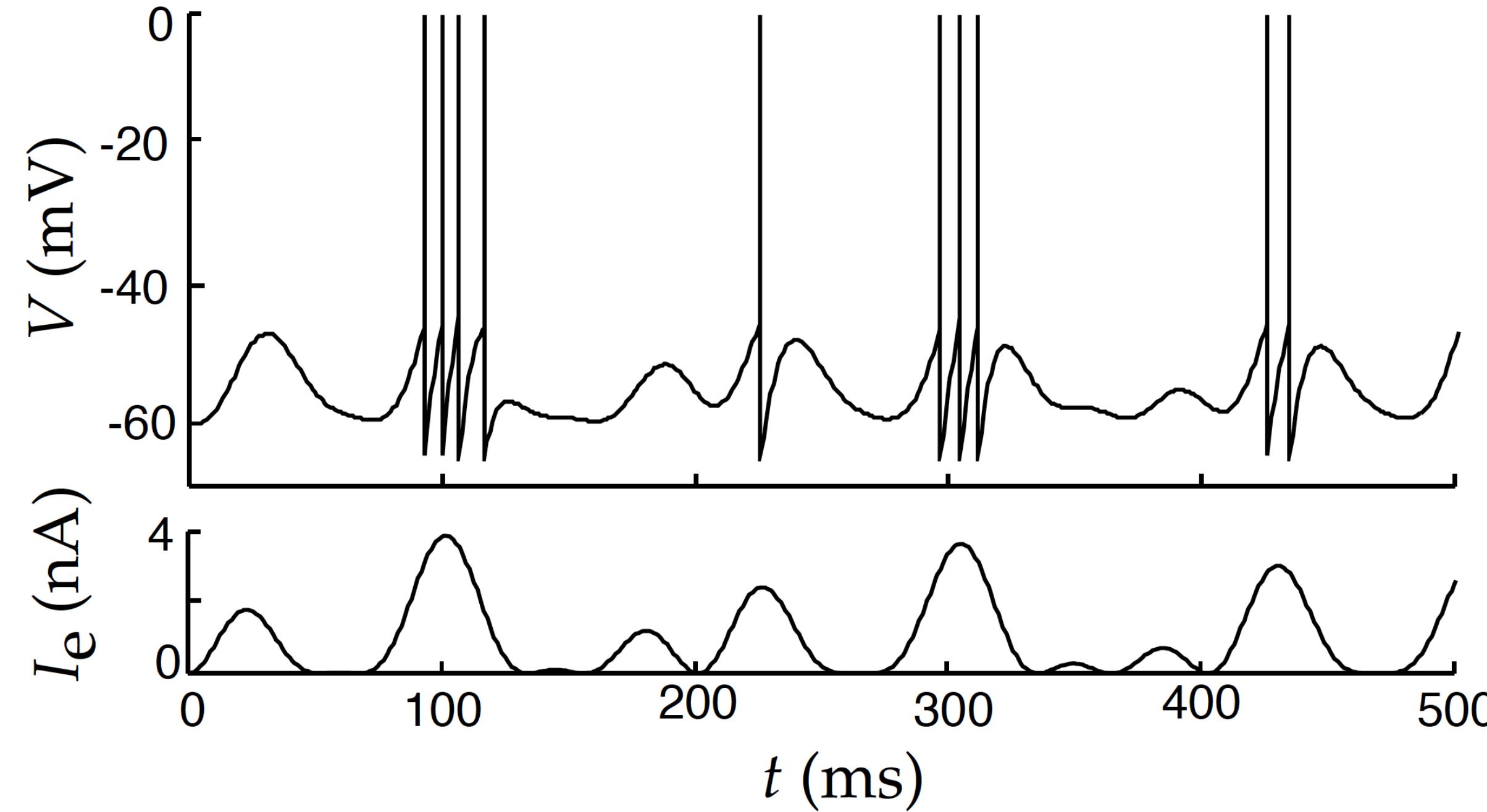


Introduction to integrate-and-fire model

- The basic integrate-and-fire model was proposed by Lapicquein 1907
- Neuron models can be simplified if the biophysical mechanisms are not explicitly included in the model
- Action potential occurs whenever the membrane potential reaches a threshold value V_{th}
- After the AP, the potential is reset to a value $V_{reset} < V_{th}$
- Modeling only subthreshold membrane potential dynamics



Passive integrate-and-fire model driven by a time-varying electrode current



A passive integrate-and-fire model. The upper trace is the membrane potential, and the bottom trace the driving current.



The basic equation of the passive or leaky integrate-and-fire models

$$I_e = C_m \frac{dV}{dt} + \frac{\Delta V}{R_m}$$

- relation between injected current and membrane potential

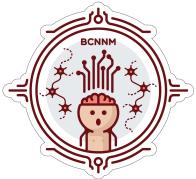
$$R_m C_m \frac{dV}{dt} = -\Delta V + R_m I_e$$

$$\tau_m \frac{dV}{dt} = E_L - V + R_m I_e, \text{ where}$$

$\tau_m = R_m C_m$ is time constant, sets the basic time scale for changes in the membrane potential and typically falls in the range between 10 and 100 ms.

E_L is the resting potential of the model cell.

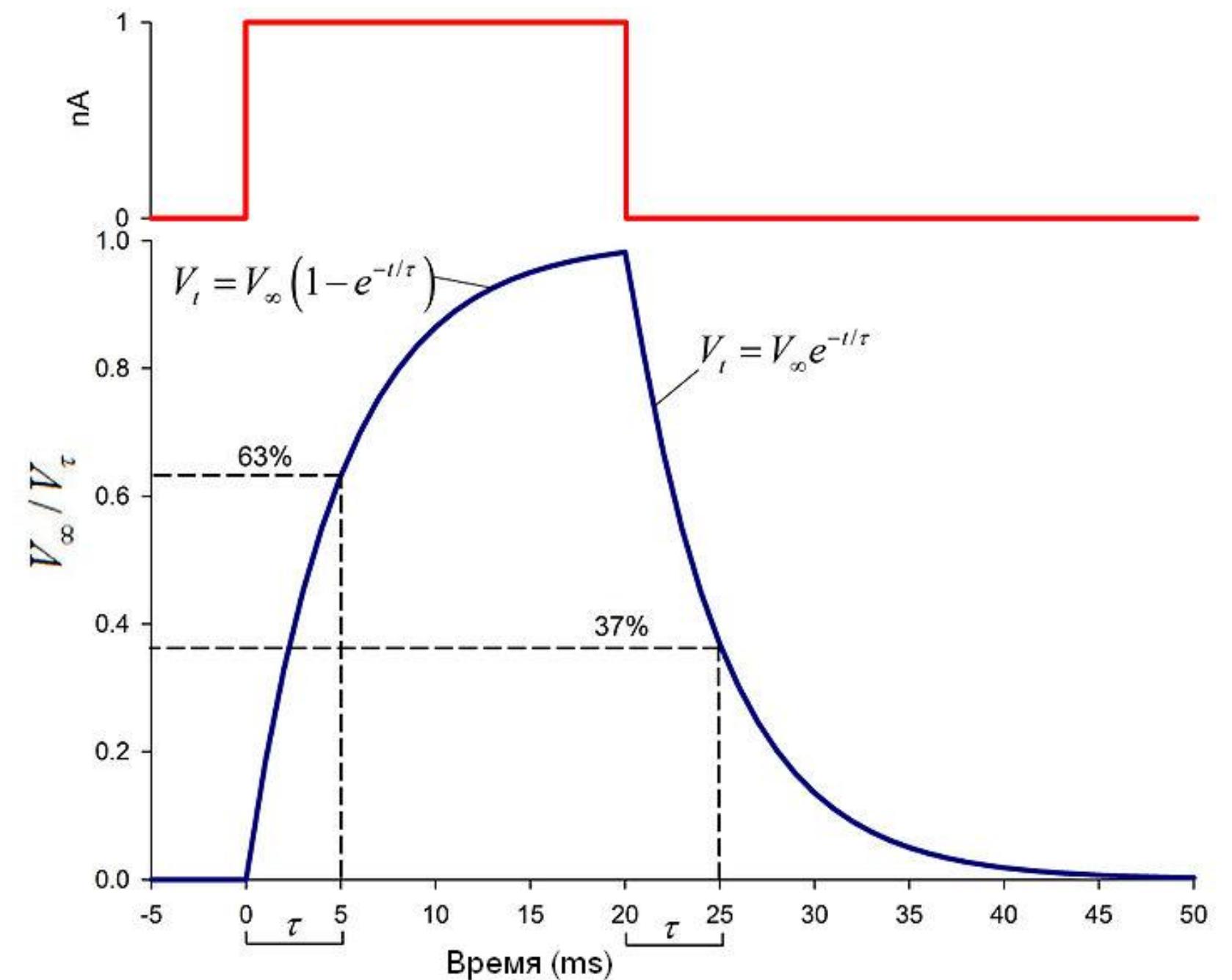
When $I_e = 0$, the membrane potential relaxes exponentially with time constant τ_m to $V = E_L$



BCNN



Time constant τ_m



Change of membrane potential from pulse input

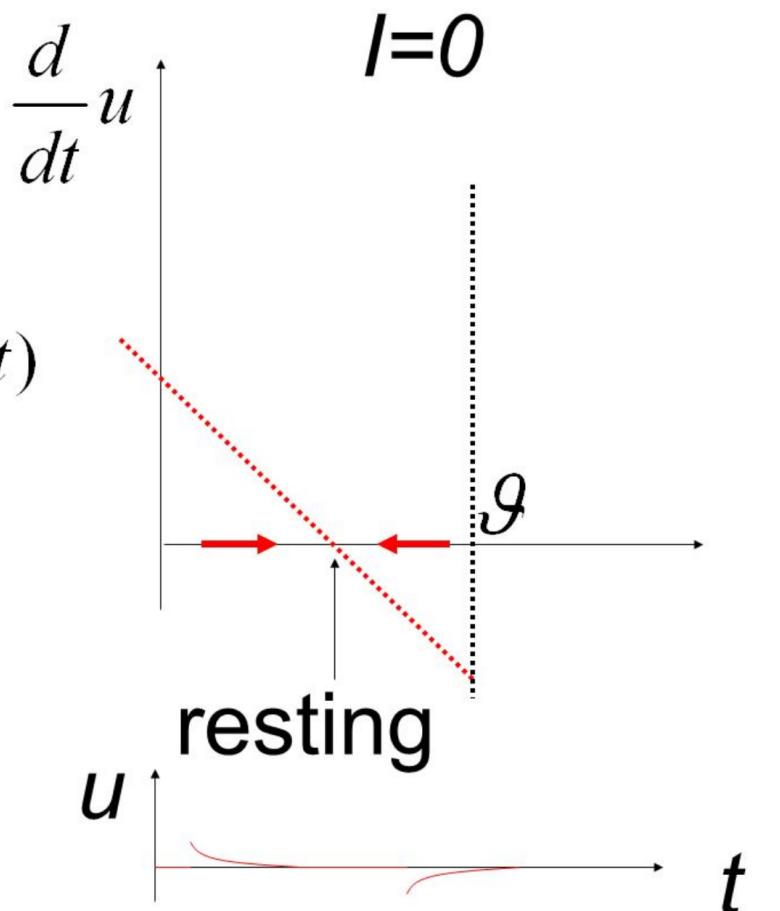


LIF

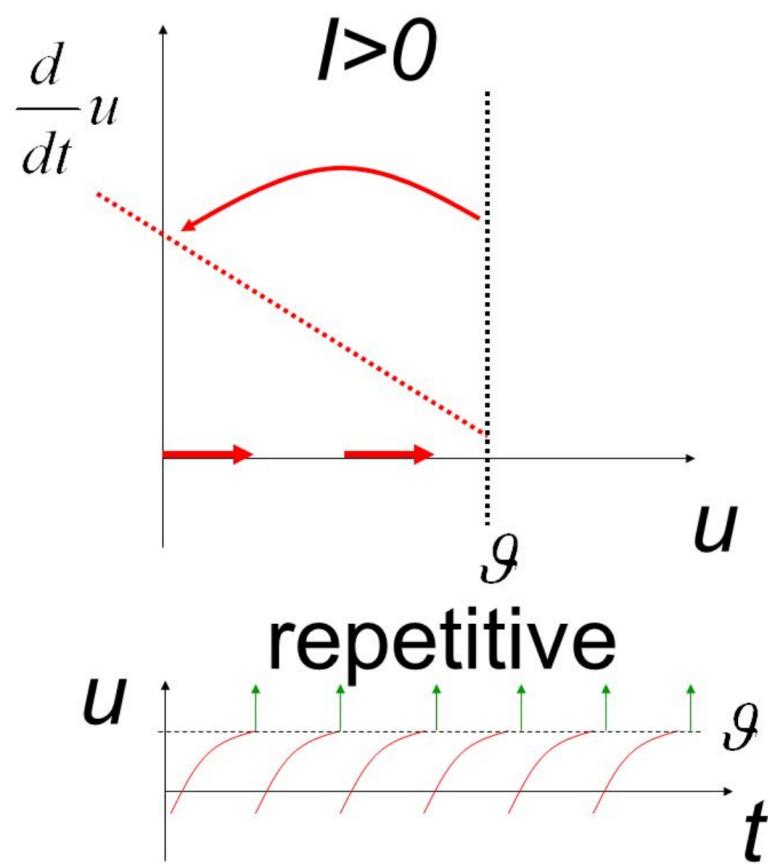
$$\tau \cdot \frac{d}{dt}u = -(u - u_{rest}) + RI(t)$$

If firing:

$$u \rightarrow u_r$$



$$I=0$$



$$I>0$$

repetitive



Firing rate of an integrate-and-fire model

When I_e is independent of time, the subthreshold potential $V(t)$ can easily be computed by

solving equation $\tau_m \frac{dV}{dt} = E_L - V + R_m I_e$:

$$V(t) = E_L + R_m I_e + (V(0) - E_L - R_m I_e) \exp(-t/\tau_m)$$

It is valid for the integrate-and-fire model only as long as V stays below the threshold. Suppose that at $V(t) = V_{reset}$ where $t = 0$, so the next AP will occur at $t = t_{isi}$ then:

$$V(t_{isi}) = V_{th} = E_L + R_m I_e + (V_{reset} - E_L - R_m I_e) \exp(-t_{isi}/\tau_m)$$

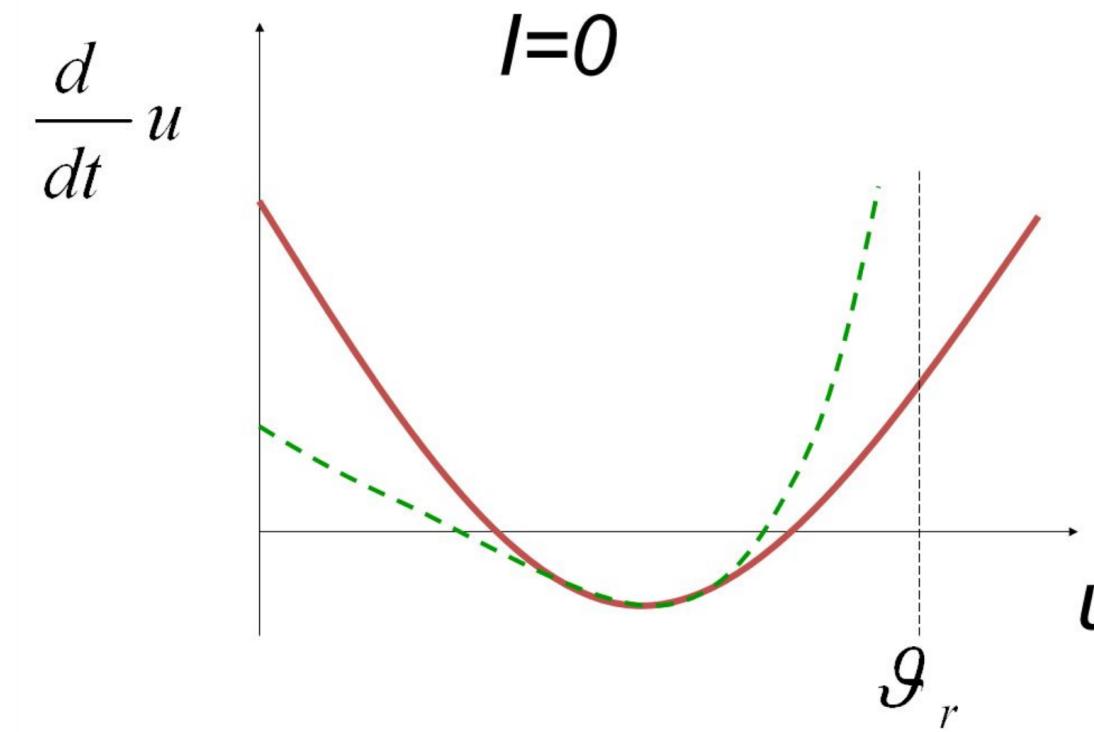
$$r_{isi} = \frac{1}{t_{isi}} = \left(\tau_m \ln \left(\frac{R_m I_e + E_L - V_{reset}}{R_m I_e + E_L - V_{th}} \right) \right)^{-1}$$

- the interspike-interval firing rate of the neuron.



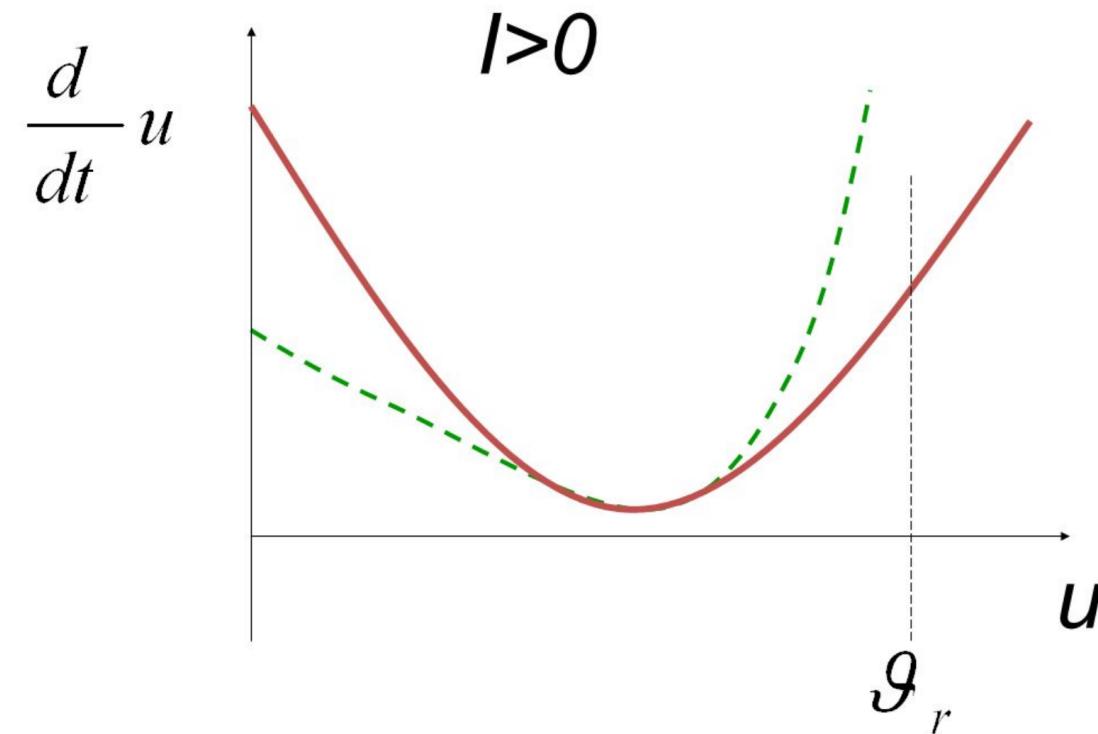
Generalized models

Nonlinear Integrate-and-fire Model



$$\tau \cdot \frac{d}{dt}u = F(u) + RI(t)$$

if $u(t) = \vartheta_r$ then Fire+reset



Quadratic I&F:

$$F(u) = c_2(u - c_1)^2 + c_0$$

exponential I&F:

$$F(u) = -(u - u_{rest}) + c_0 \exp(-|u - \vartheta|)$$

Quadratic and exponential IF models

Integrate-and-fire model vs cortical neuron

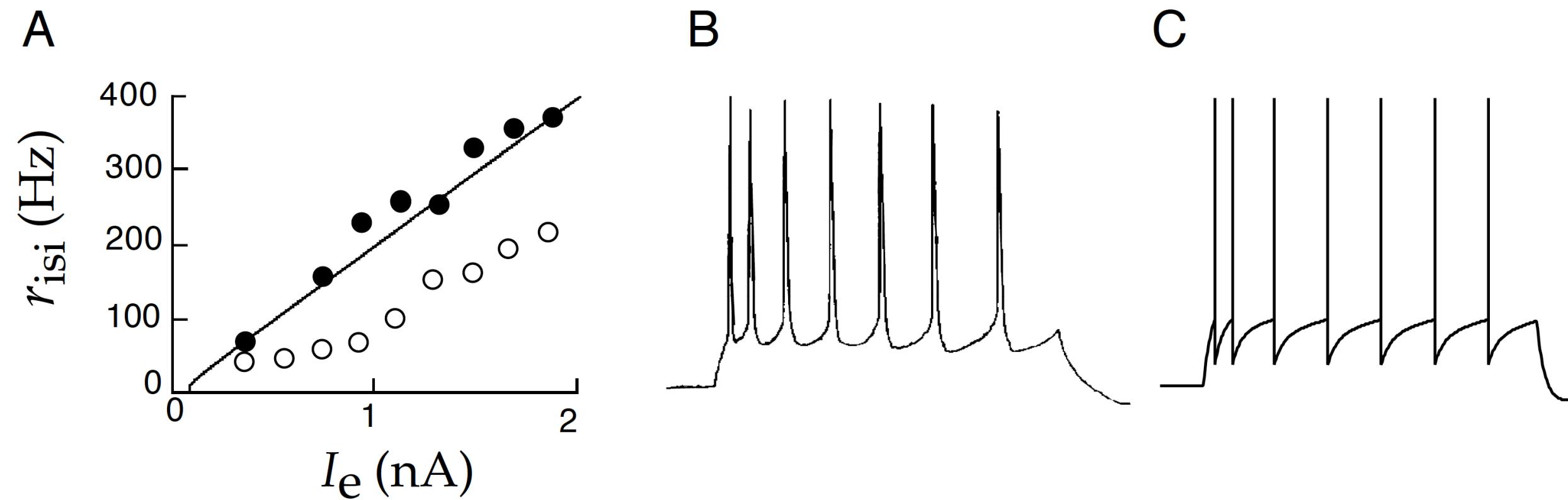


Figure of comparison of interspike-interval firing rates as a function of injected current for an integrate-and-fire model and a cortical neuron measure in vivo



Spike-Rate Adaptation and Refractoriness

- A highly simplified description of the action potential and a linear approximation for the total membrane current
- Refractory effect is not included in the basic integrate-and-fire model

What we can do?

- Add a condition to the basic threshold crossing rule that forbids firing for a period of time immediately after a spike
- Refractoriness can be incorporated in a more realistic way by adding a conductance similar to the spike-rate adaptation conductance
- Raise the threshold for action-potential generation following a spike and then allow it to relax back to its normal value



Spike-rate adaptation model

$$\tau_m \frac{dV}{dt} = E_L - V - r_m g_{sra}(V - E_K) + R_m I_e$$

The conductance g_{sra} relaxes exponentially to 0

$$\tau_{sra} \frac{dg_{sra}}{dt} = -g_{sra}$$

Whenever the neuron fires a spike, g_{sra} is increased

$$g_{sra} \rightarrow g_{sra} + \Delta g_{sra}$$

The spike-rate adaptation conductance g_{sra} has been modeled as a K^+ conductance so, when activated, it will hyperpolarize the neuron, slowing any spiking that may be occurring



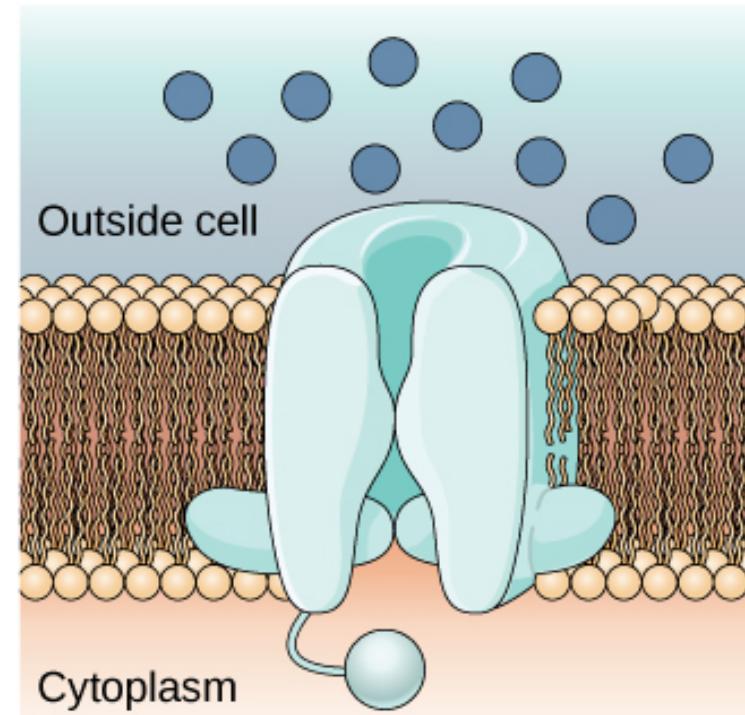
Voltage-dependent conductances

- Ion channels retrospective
- Ion channel fluctuations
- Persistent and transient conductances
- Hyperpolarization-activated conductances

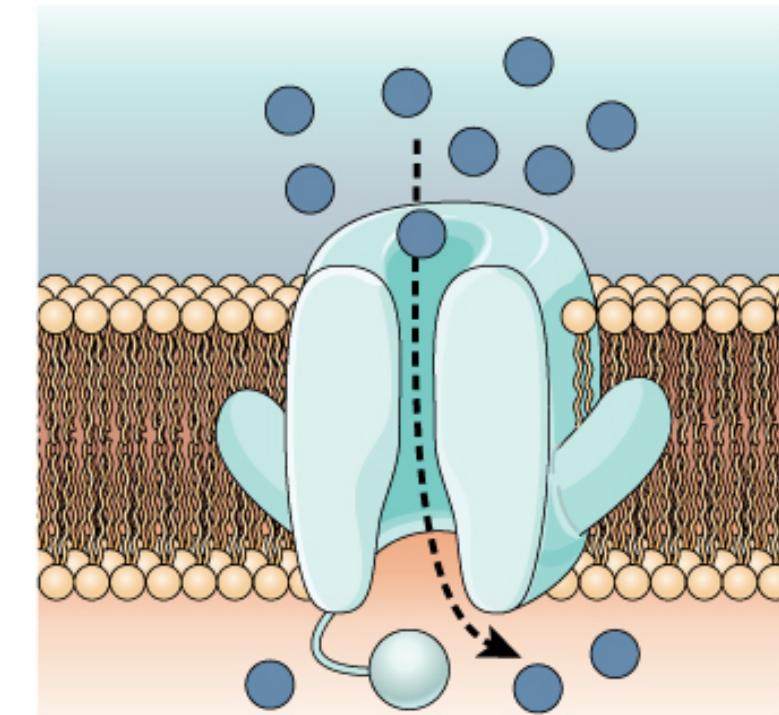


Ion channels retrospective

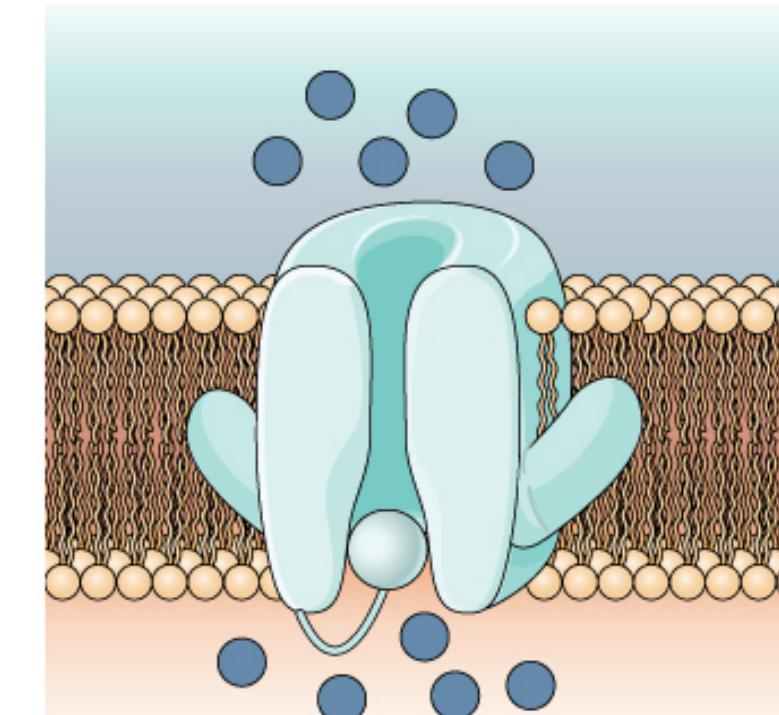
Voltage-gated Na^+ Channels



Closed At the resting potential, the channel is closed.



Open In response to a nerve impulse, the gate opens and Na^+ enters the cell.

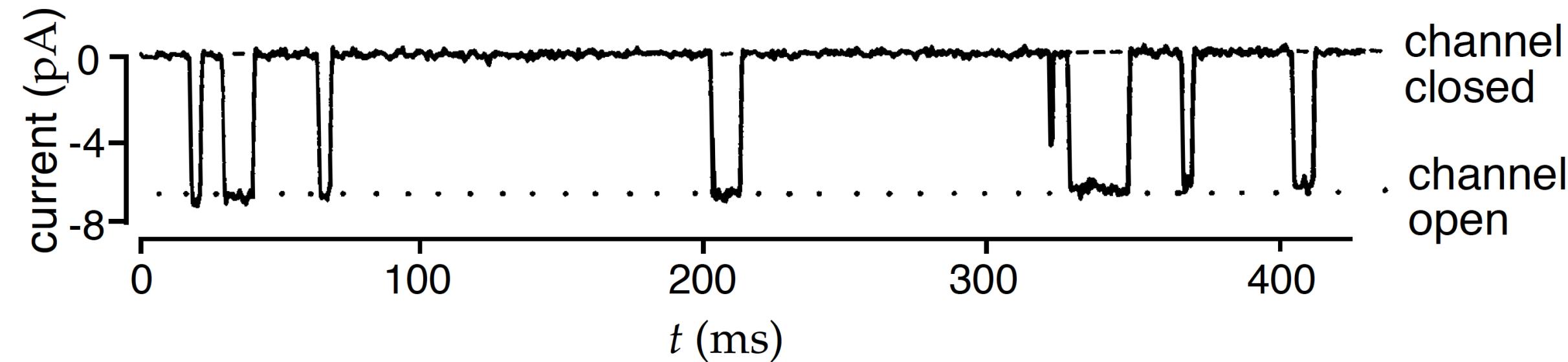


Inactivated For a brief period following activation, the channel does not open in response to a new signal.



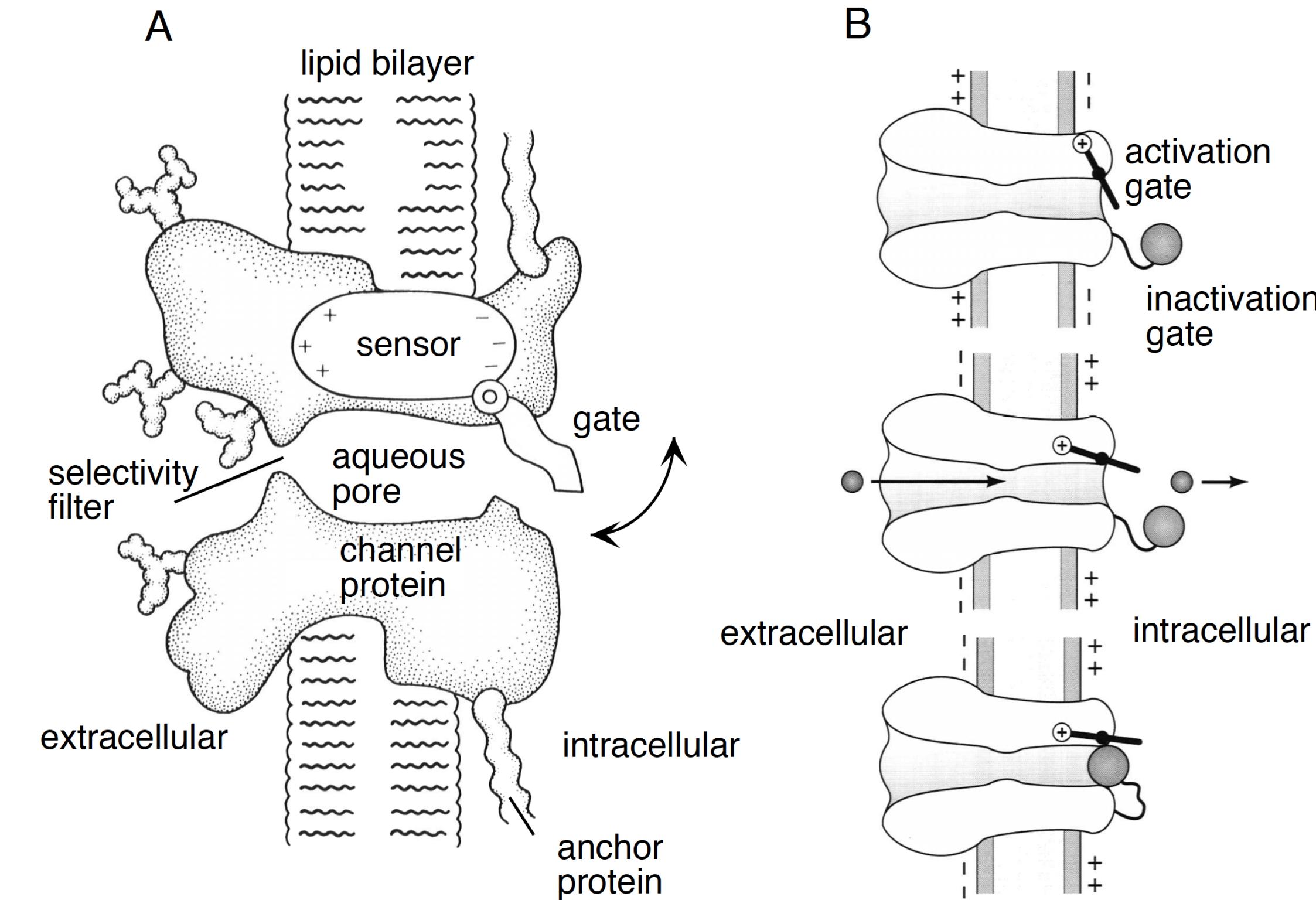
Single ion channel

Recordings of the current flowing through single channels indicate that channels fluctuate rapidly between open and closed states in a stochastic manner



This is a synaptic receptor channel sensitive to the neurotransmitter acetylcholine.

Persistent and transient conductances



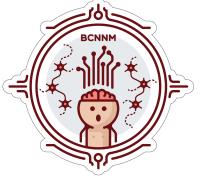
Gating of membrane channels. (A) Gating of a persistent conductance. (B) Gating of a transient conductance



Hyperpolarization-activated conductances

- Persistent currents act as if they are controlled by an activation gate
- Transient currents act as if they have both an activation and an inactivation gate
- Hyperpolarization-activated conductances behave as if they are controlled solely by an inactivation gate

They are thus persistent conductances, but they open when the neuron is hyperpolarized rather than depolarized

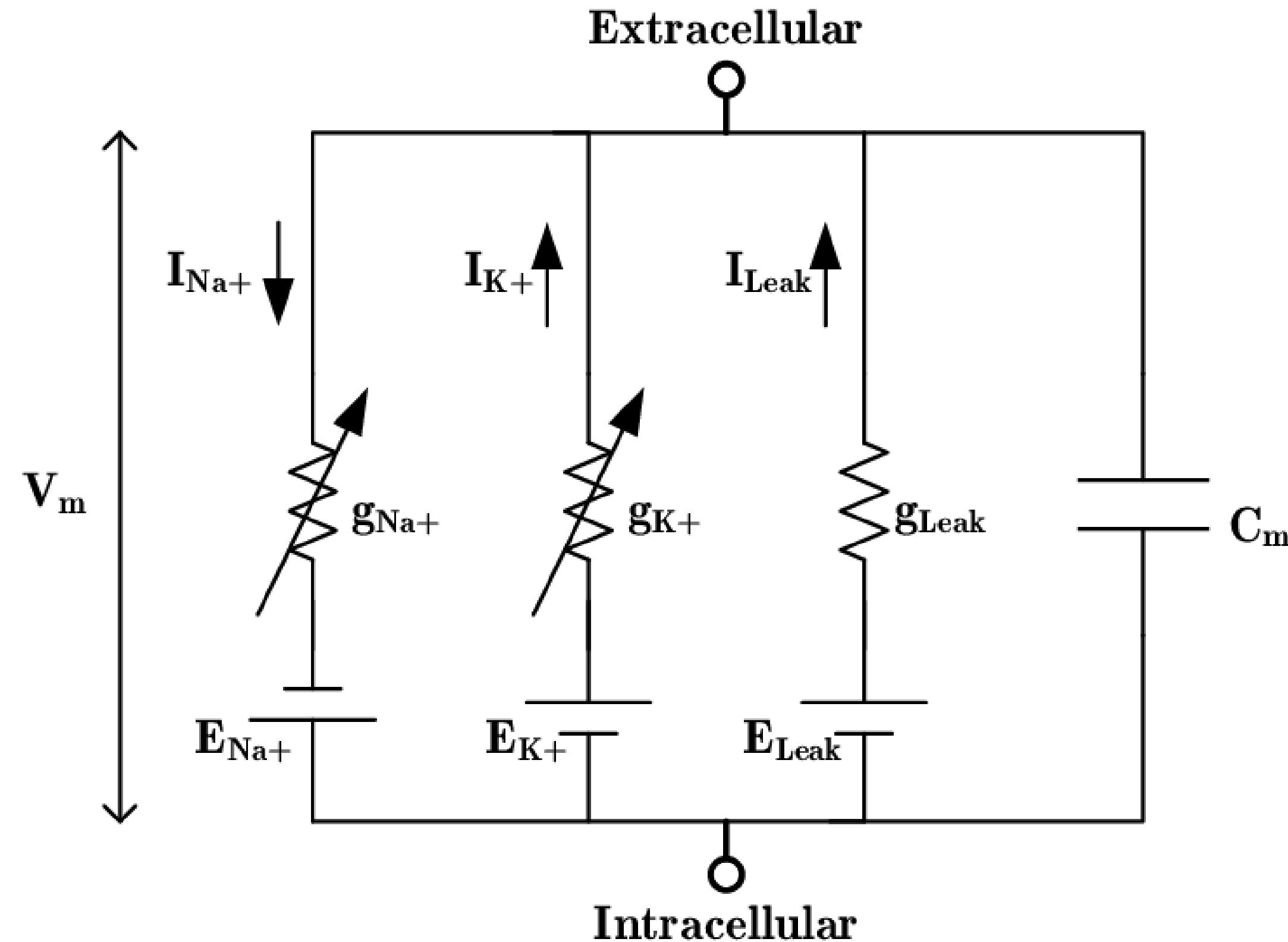


The Hodgkin-Huxley model

- Basic components
- Limitations



Equivalent circuit for Hodgkin-Huxley model





Currents in Hodgkin–Huxley model

$$I = I_c + \sum_{i=1}^k I_i \text{ - total current}$$

$$I_c = C_m \frac{dV_m}{dt} \text{ - capacitance current}$$

$$I_i = g_i(V_m - V_i) \text{ - current through a given ion channel}$$

Thus, for a cell with sodium and potassium channels, the total current through the membrane is given by:

$$I = C_m \frac{dV_m}{dt} + g_K(V_m - E_K) + g_{Na}(V_m - E_{Na}) + g_L(V_m - E_L)$$



Hodgkin–Huxley model

In voltage-gated ion channels, the channel conductance g_i is a function of both time and voltage ($g_n(t, V)$), while in leak channels g_i is a constant

$$I_e = C_m \frac{dV_m}{dt} + \bar{g}_K n^4 (V_m - E_K) + \bar{g}_{Na} m^3 h (V_m - E_{Na}) + \bar{g}_L (V_m - E_L)$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) - \beta_n(V_m)n$$

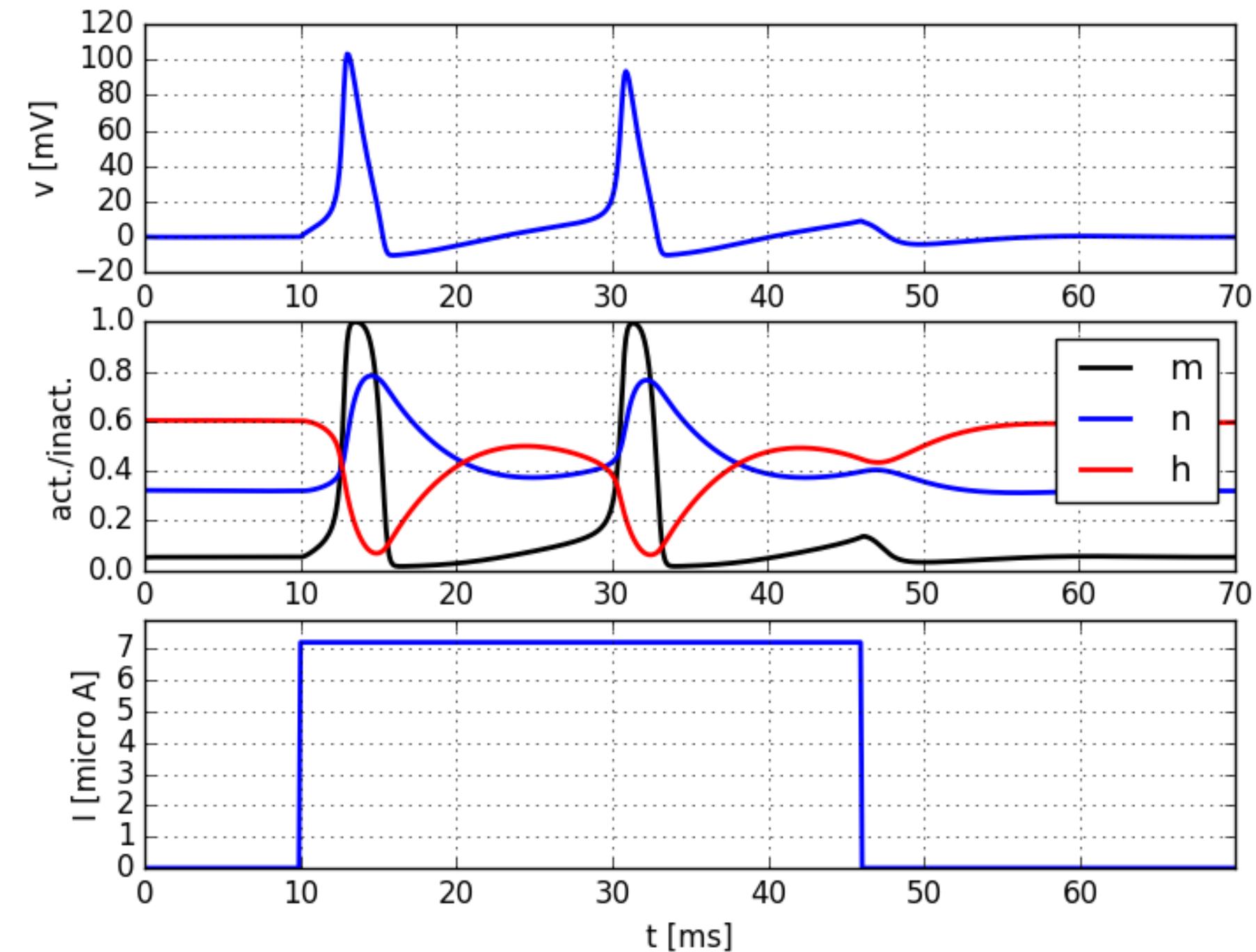
$$\frac{dm}{dt} = \alpha_m(V_m)(1 - m) - \beta_m(V_m)m$$

$$\frac{dh}{dt} = \alpha_h(V_m)(1 - h) - \beta_h(V_m)h$$

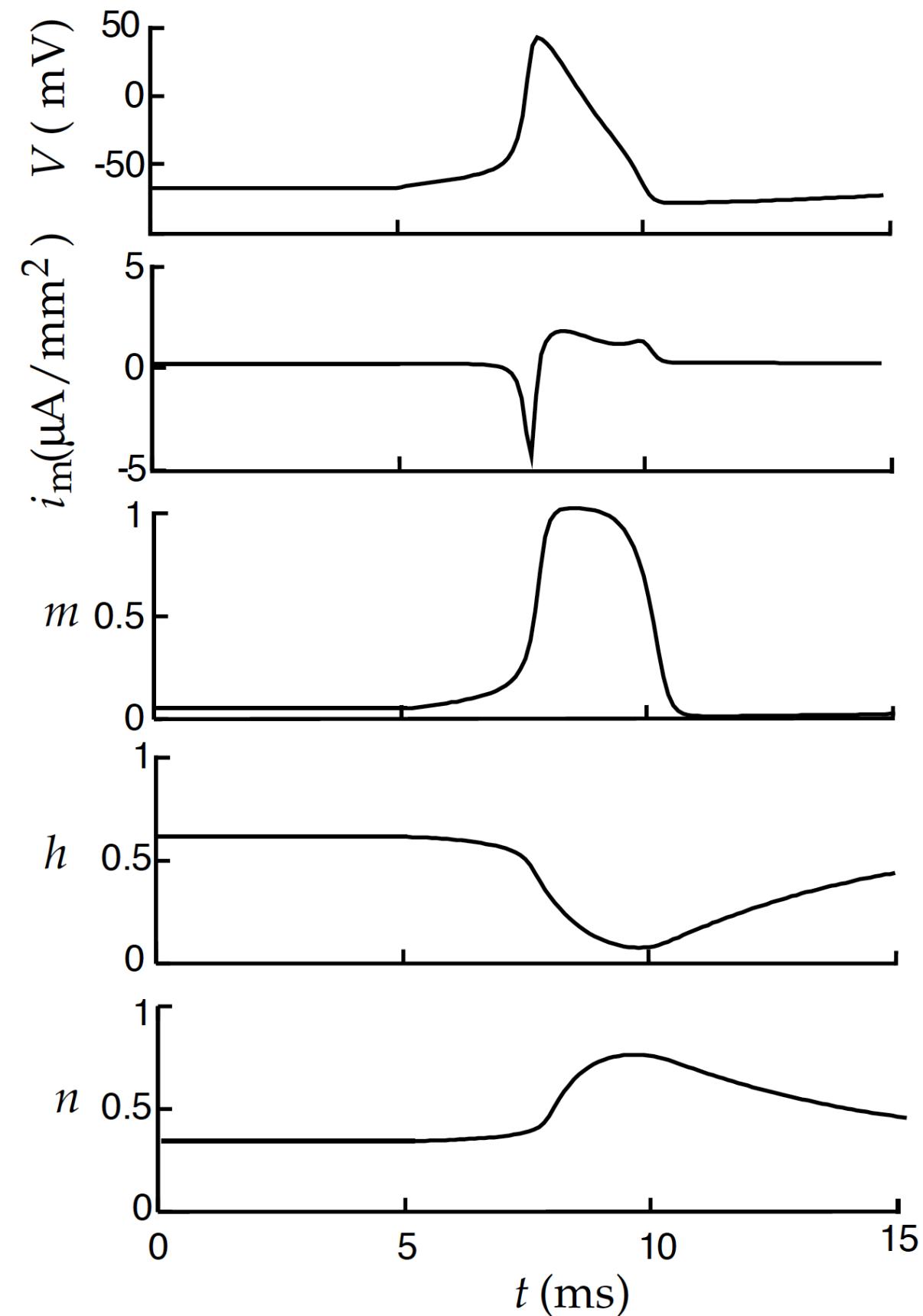
where I is the current per unit area, and α_i (closed → opened) and β_i (opened → closed) are voltage-dependent rates for the i -th ion channel, which depend on voltage but not time. \bar{g}_n is the maximal value of the conductance. n , m , and h are dimensionless gating variables between 0 and 1 that are associated with potassium channel activation, sodium channel activation, and sodium channel inactivation, respectively.



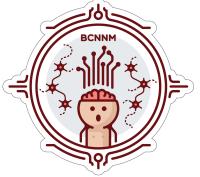
HH Neuron, step current



Step current injection into a Hodgkin-Huxley neuron

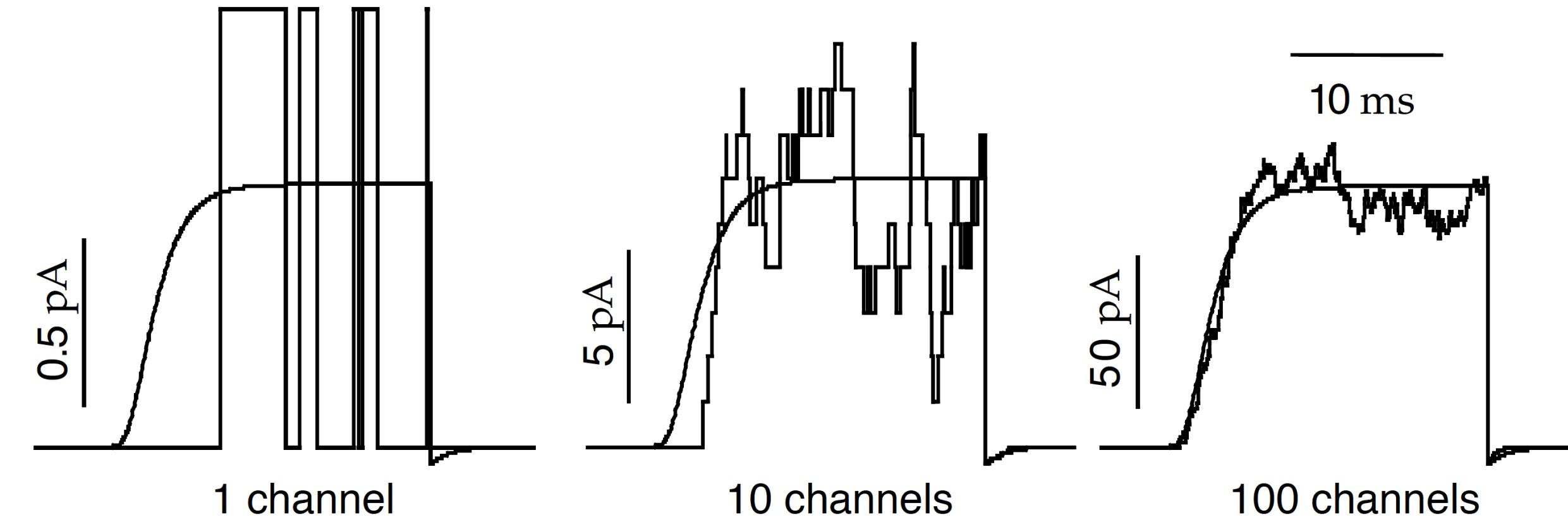


The dynamics of V , m , h , and n in the Hodgkin-Huxley model during the firing of an action potential

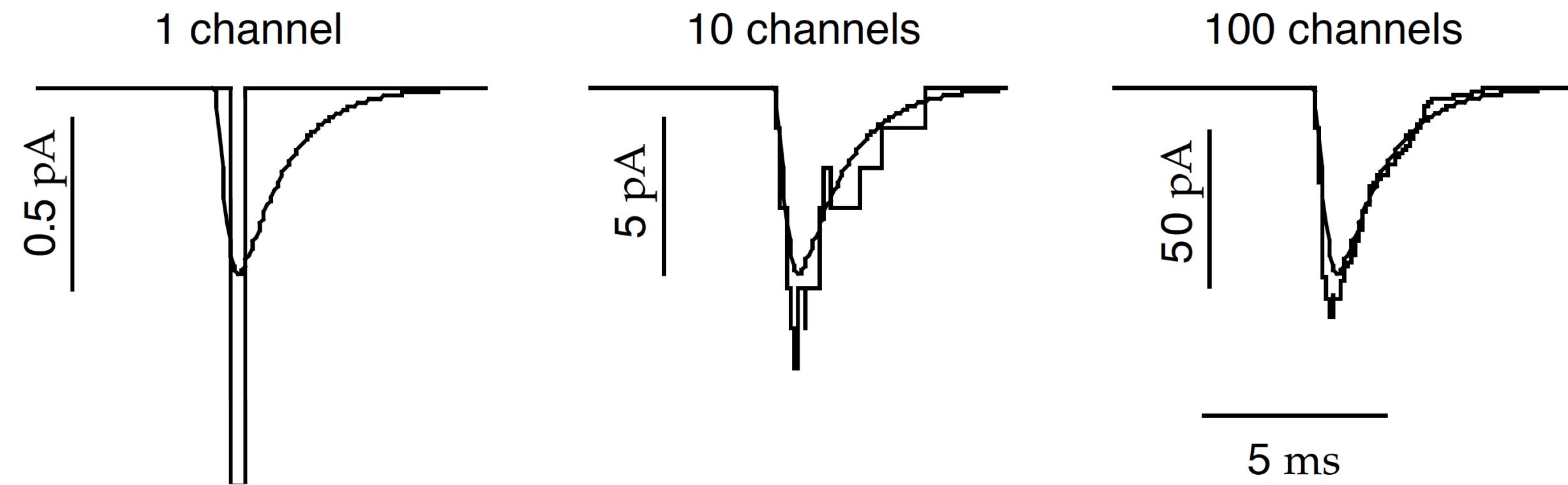


Limitations

- No minor ion channels (Cl^- , Ca^{2+})
- Leakage conductance is constant
- We don't simulate channels individually
- Only electrophysiology



Comparison of the Hodgkin-Huxley and individual channels simulation



A model of the fast Na^+ channel