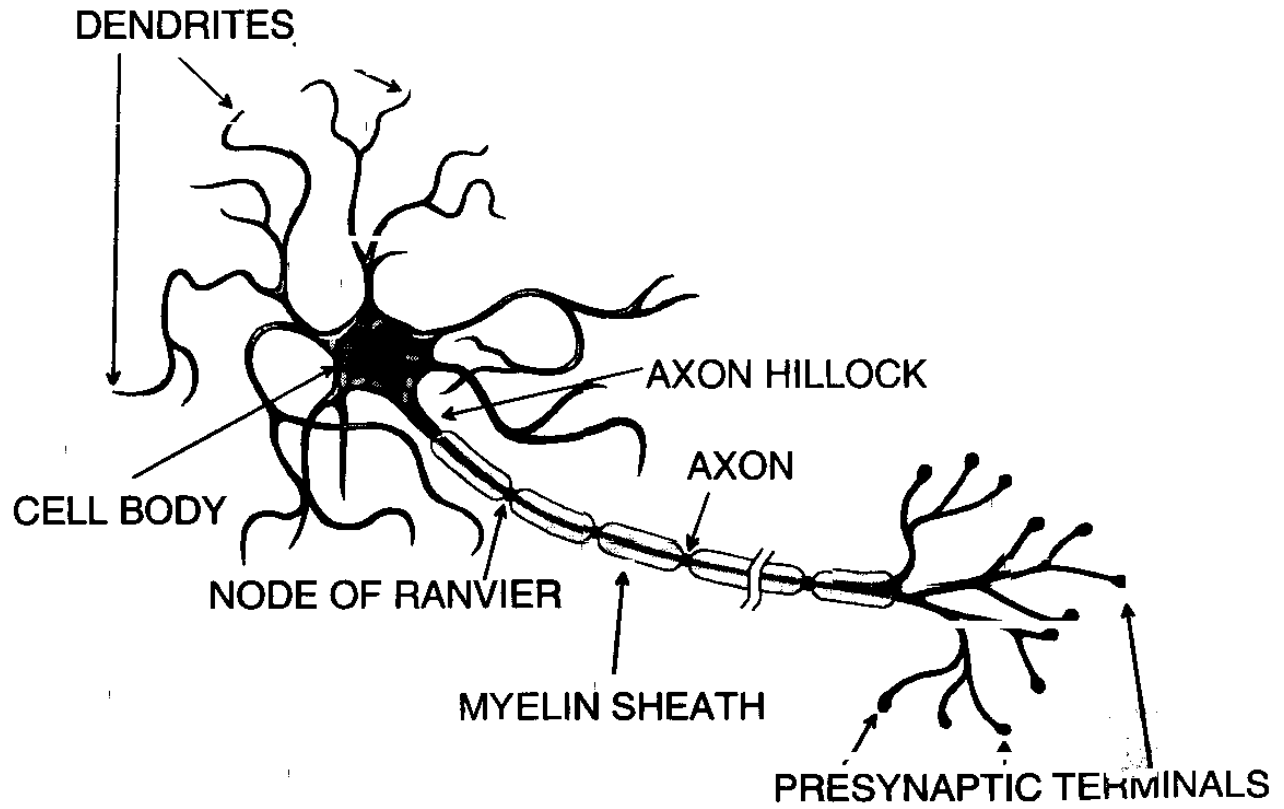
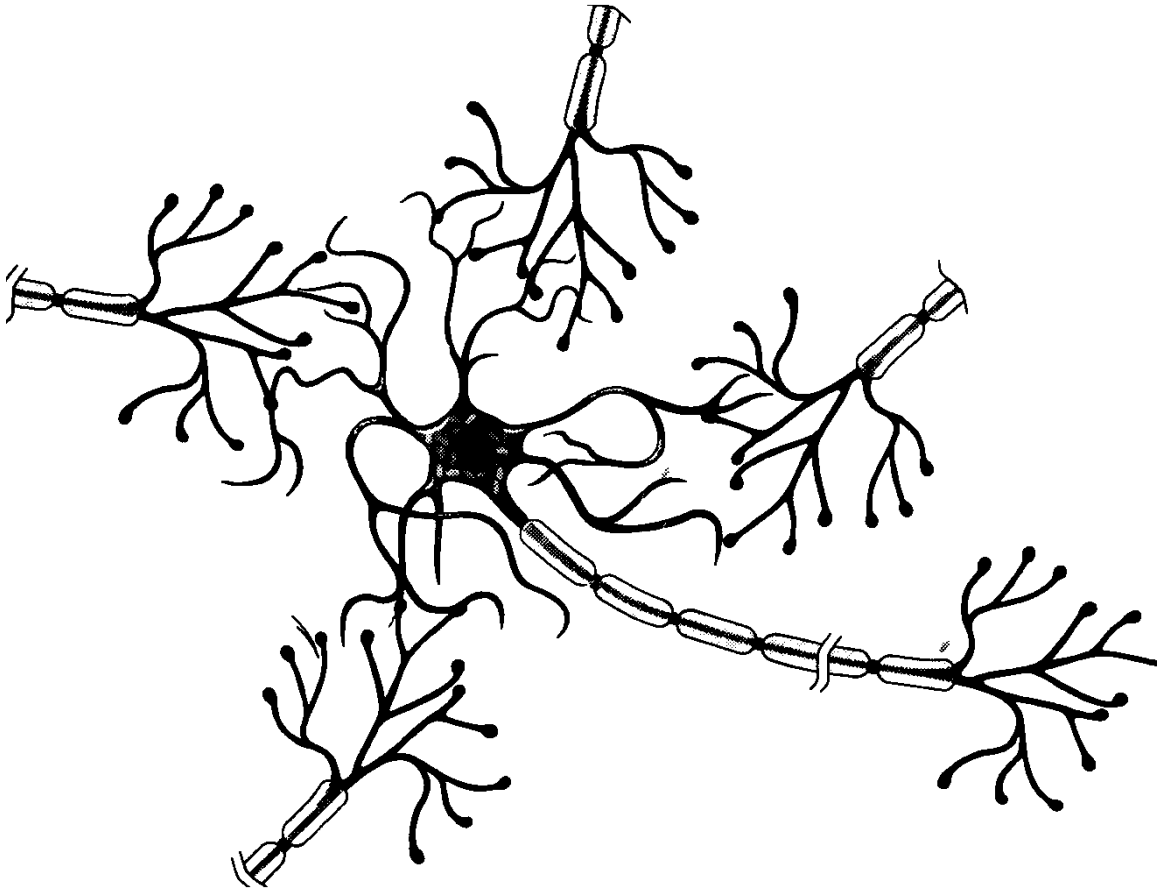


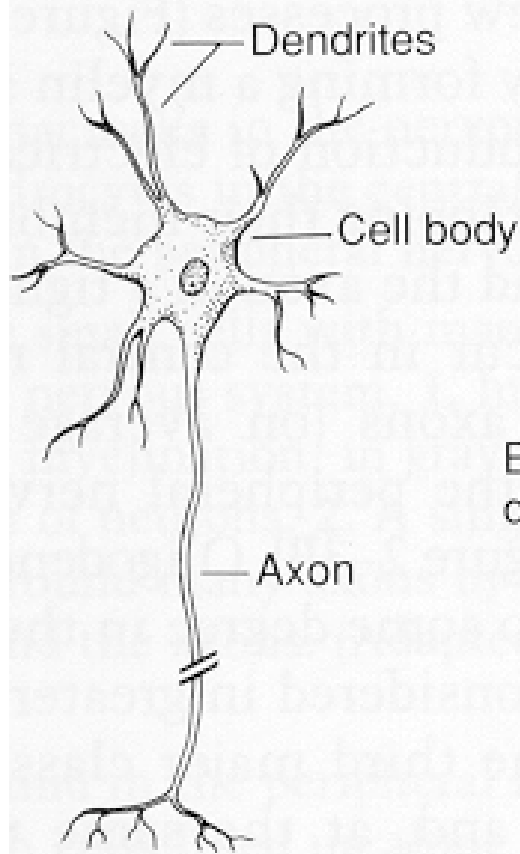
Neuron



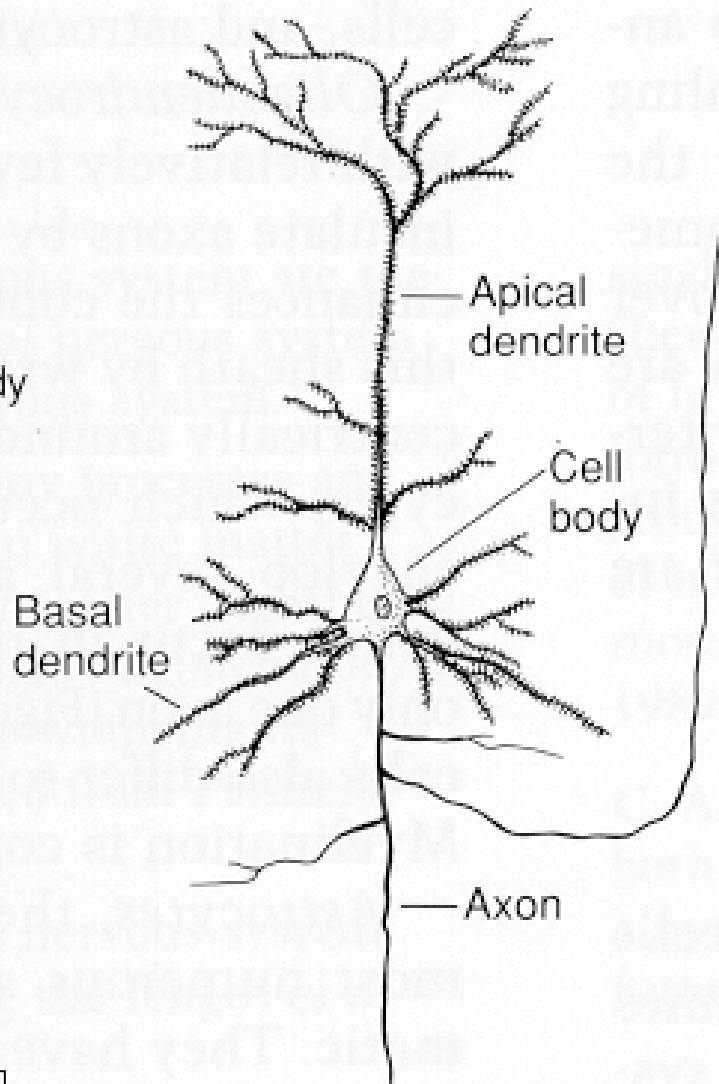
One neuron synapses with many neurons



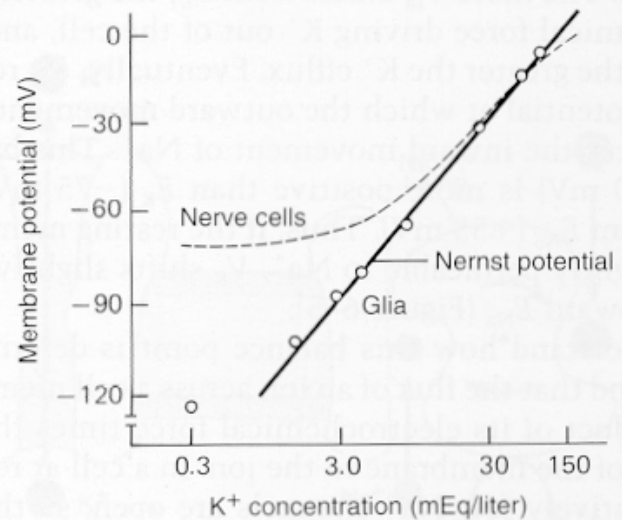
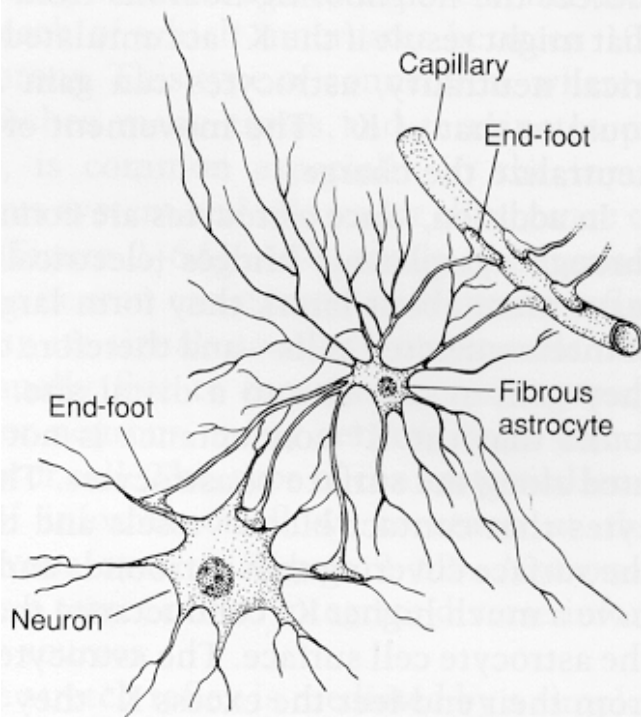
Non-pyramidal neuron



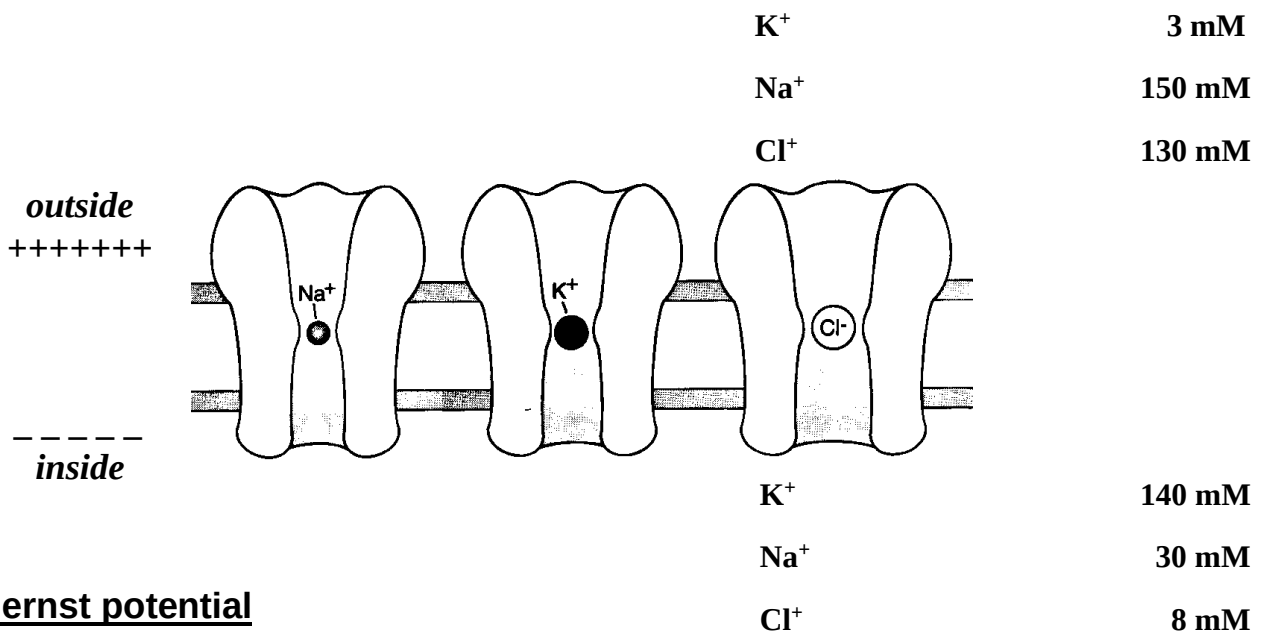
Pyramidal neuron



Neuronal-glial connection



Adapted from Orkland (1977) Glial cells in "Handbook of physiology" (Ed. E.R. Kandel), Bethesda, MD, p. 855-875



Nernst potential

$$E_p = (RT) / (Z_p F) \ln (C_{p,e} / C_{p,i}) \quad [10]$$

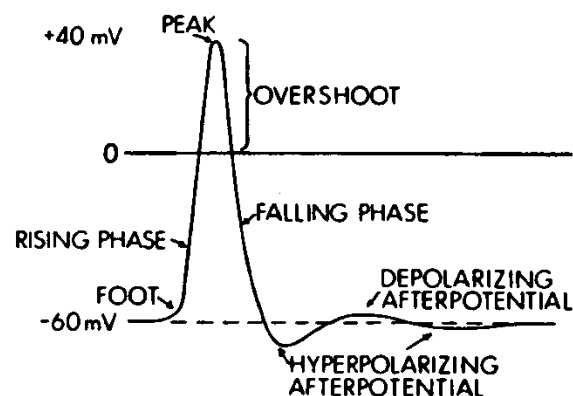
$$E_K = 25.8 \ln (3/140) = - 99.2 \text{ mV}$$

$$E_{Na} = 25.8 \ln (150/30) = + 41.5 \text{ mV}$$

$$E_{Cl} = - 25.8 \ln (130/8) = - 71.9 \text{ mV}$$

Goldmann equation

$$V_m = \frac{RT}{F} \ln \frac{P_K [K_e] + P_{Na} [Na_e] + P_{Cl} [Cl_i]}{P_K [K_i] + P_{Na} [Na_i] + P_{Cl} [Cl_e]} \quad [23]$$



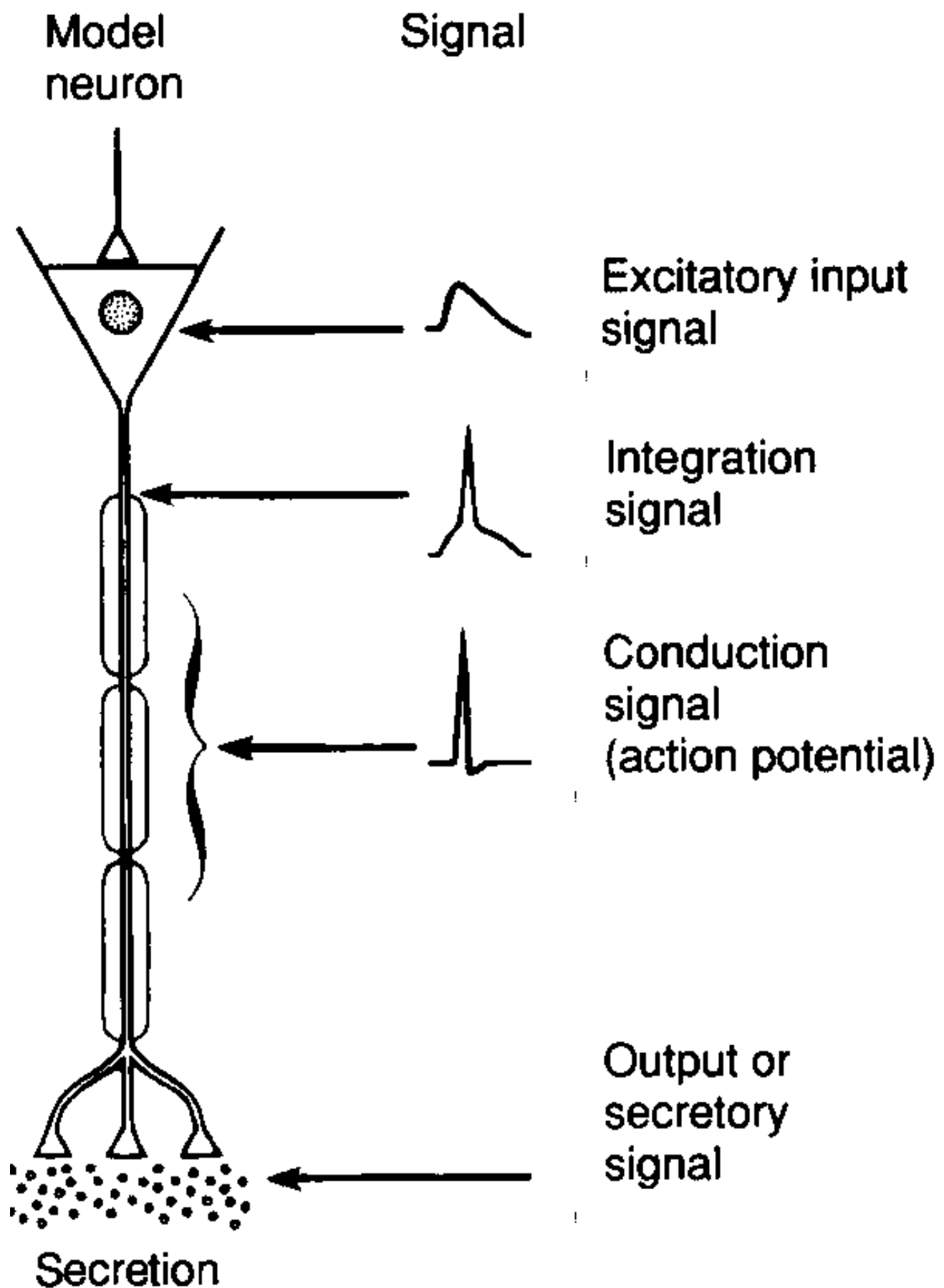
- $P_K : P_{Na} : P_{Cl} = 1.0 : 0.04 : 0.45$ for membrane at rest

- $P_K : P_{Na} : P_{Cl} = 1.0 : 10.0 : 0.45$ for active membrane

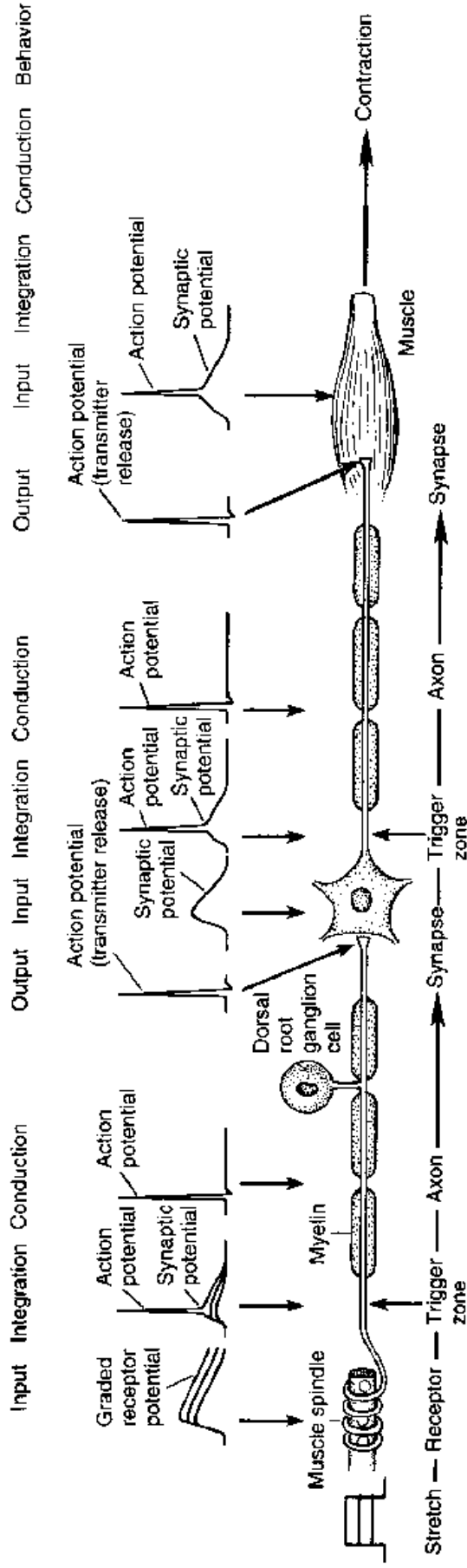
- at rest $V_m \approx E_K$

- at peak $V_m \approx E_{Na}$

Functional properties of a signaling neuron

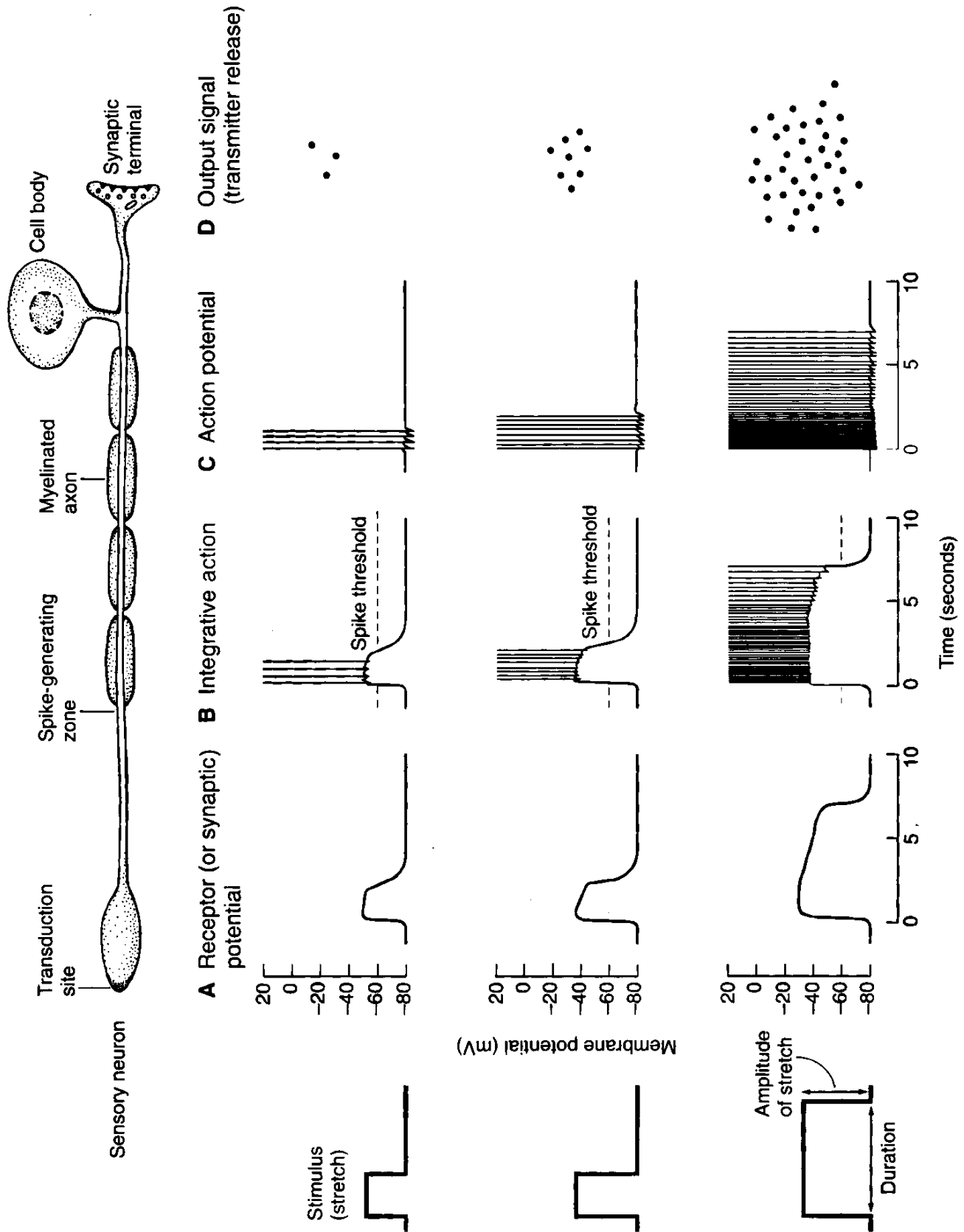


Receptor, synaptic, and action potentials

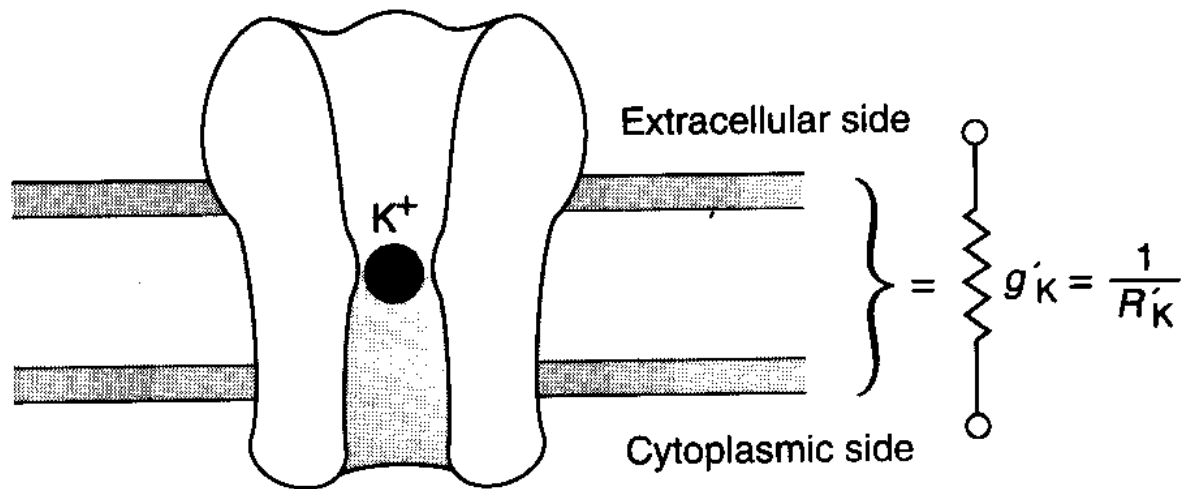


Feature	Receptor potential	Synaptic potential	Action potential
Amplitude	0.1 - 10 mV	0.1 - 10 mV	70 - 110 mV
Duration	5 - 100 ms	5 - 20 min	1 - 10 ms
Summation	graded	graded	all-or-none
Signal	hyper or depolarizing	hyper or depolarizing	depolarizing
Propagation	passive	passive	active

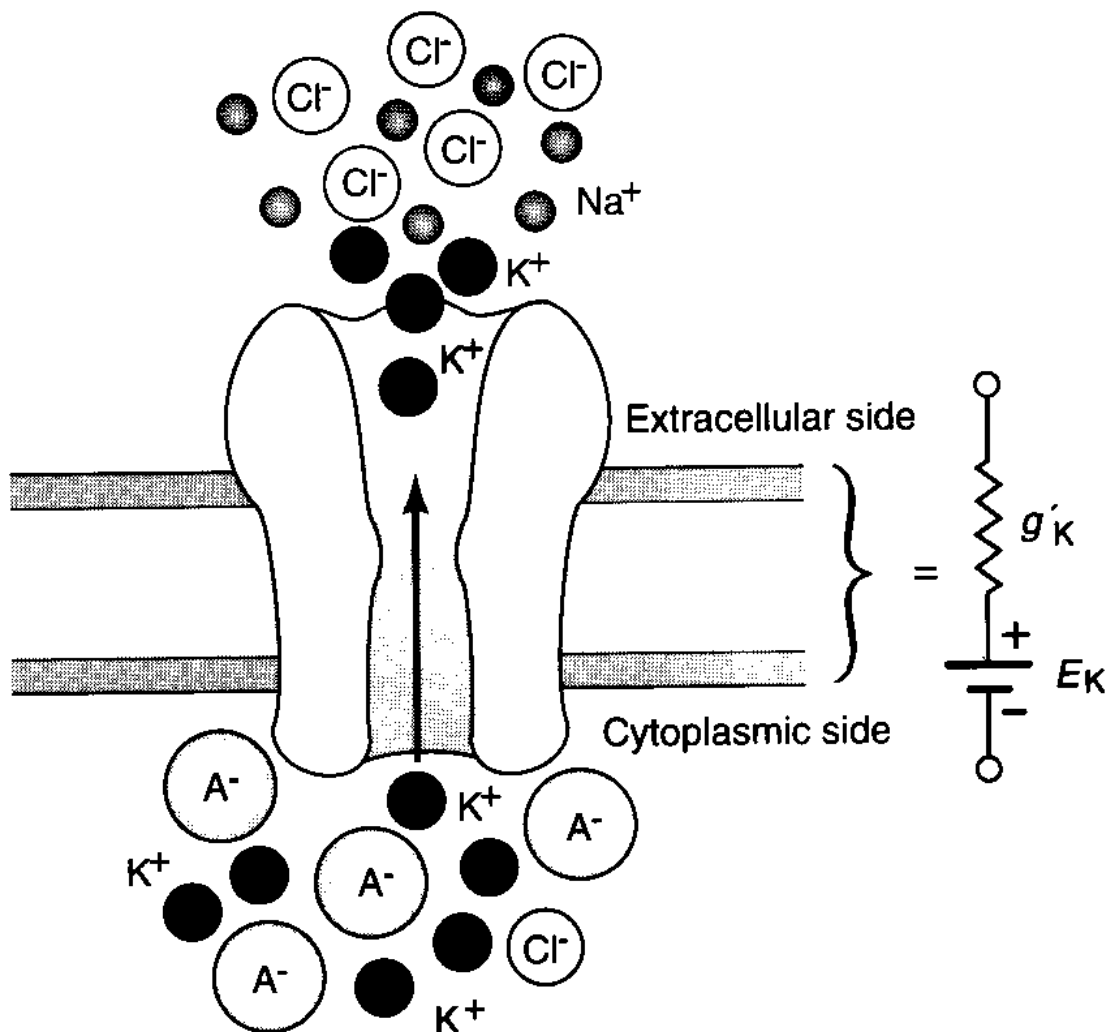
Transformation of information (from a stimulus) within a neuron



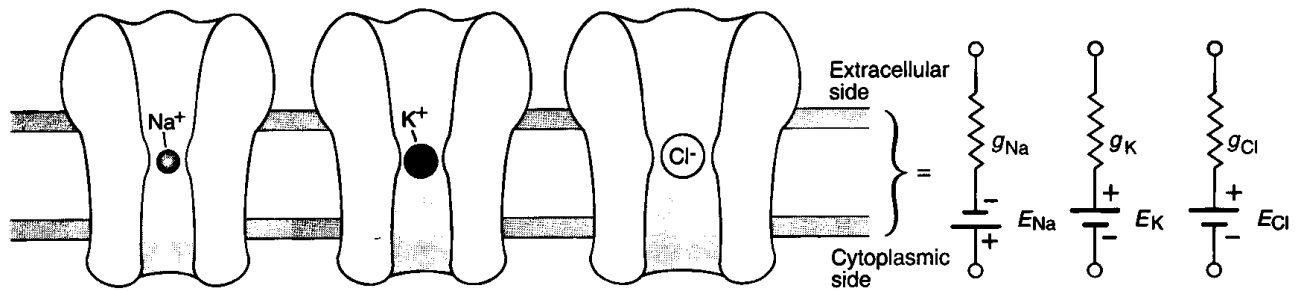
A single K channel can be represented by the electrical symbol for a conductor, g_K



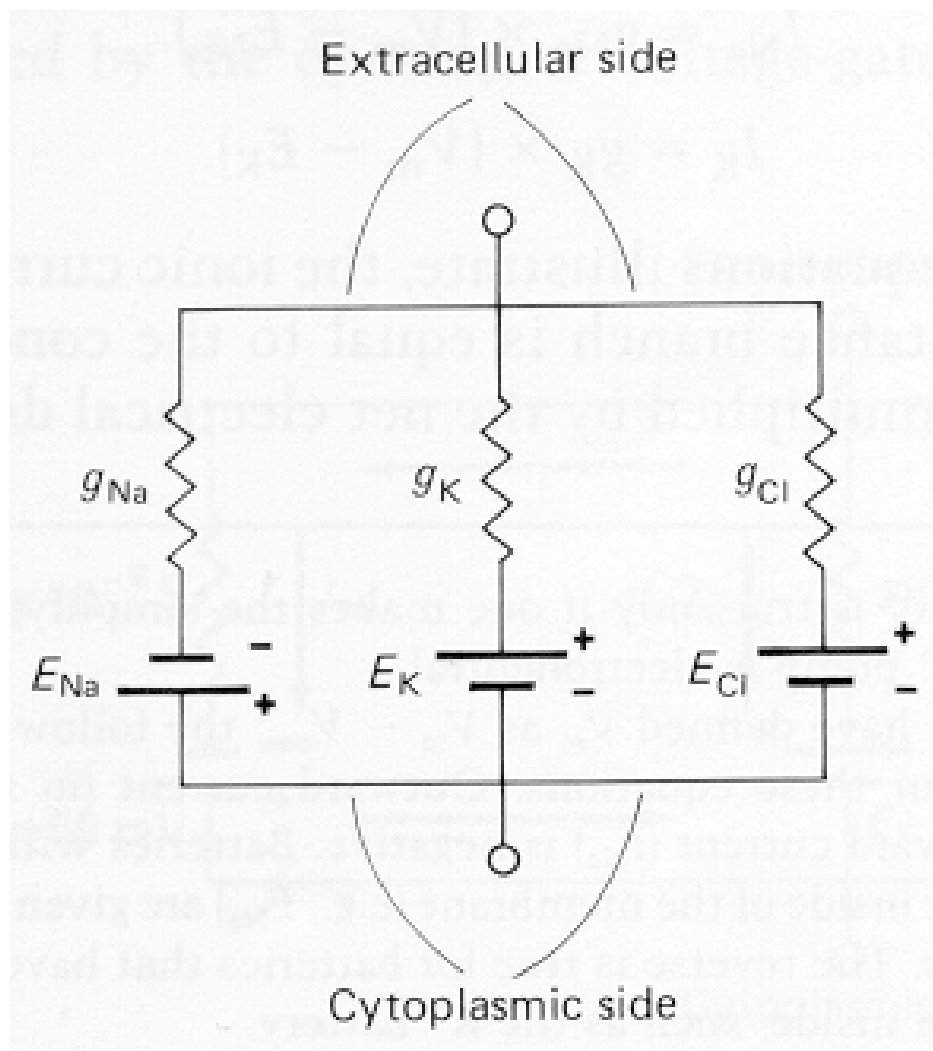
A channel selectively permeable to K ions gives rise to an electromotive force with a value equal to the K Ernst potential, which can be represented by a battery, E_K , in series with a conductor, g_K



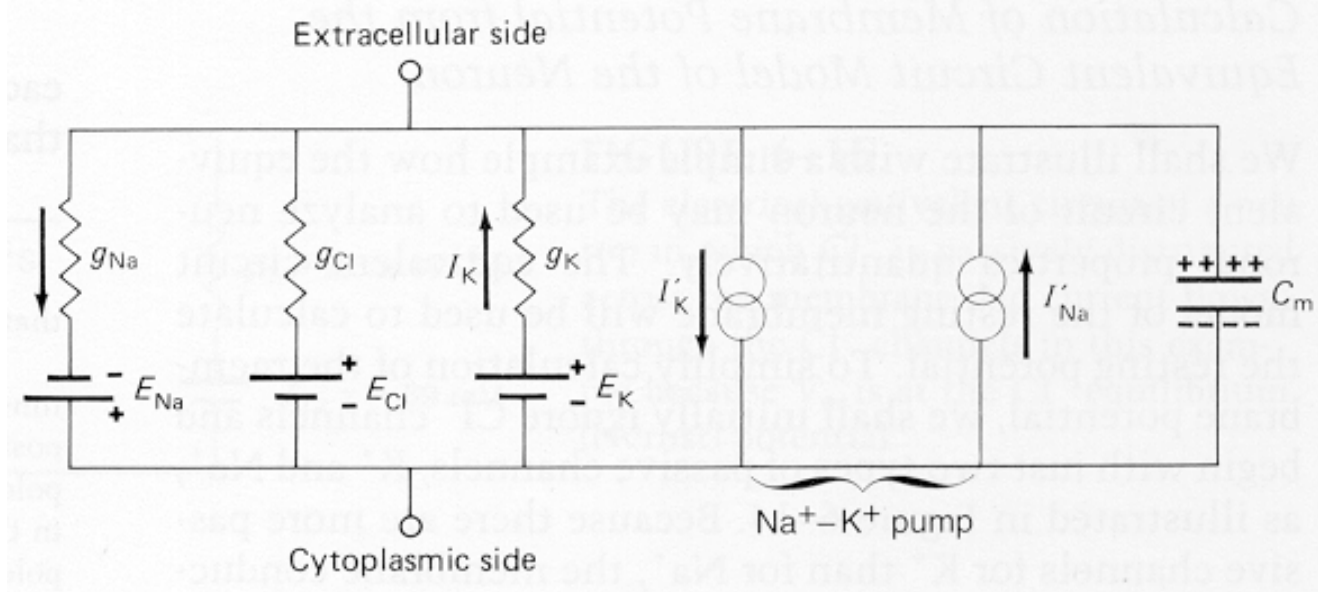
Each population of ion channels selective for Na, K, and Cl can be represented by a battery in series with a conductor



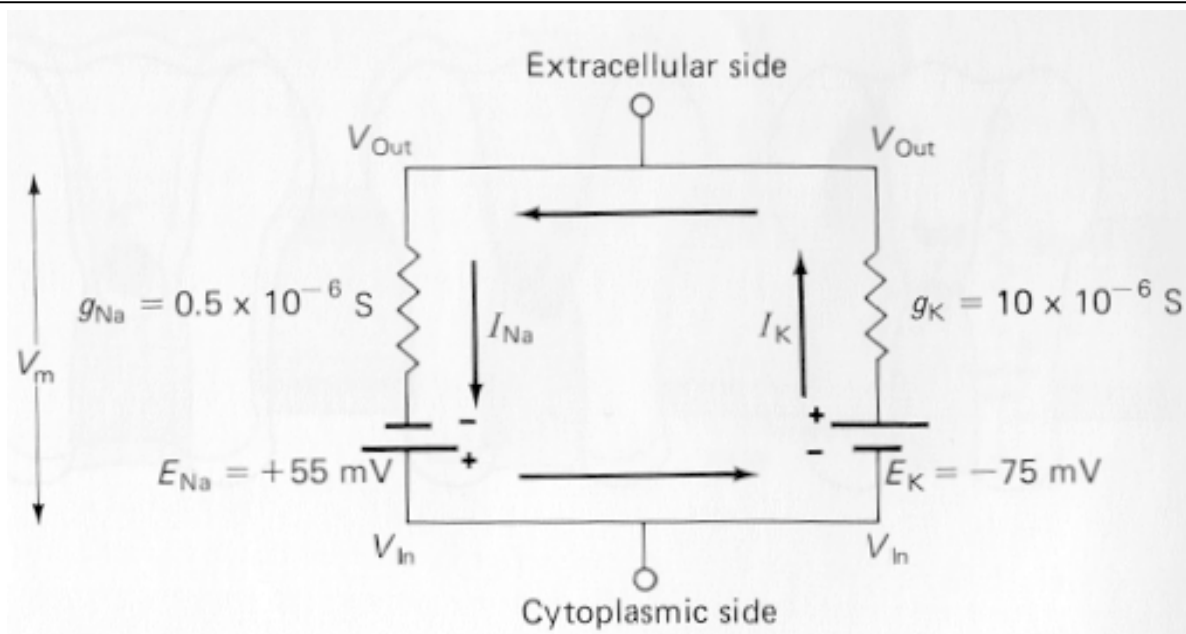
Current flow in a neuron can be modeled by an electrical equivalent circuit that includes elements representing the ion-selective membrane channels, and the short-circuit pathways provided by the cytoplasm and extracellular fluid



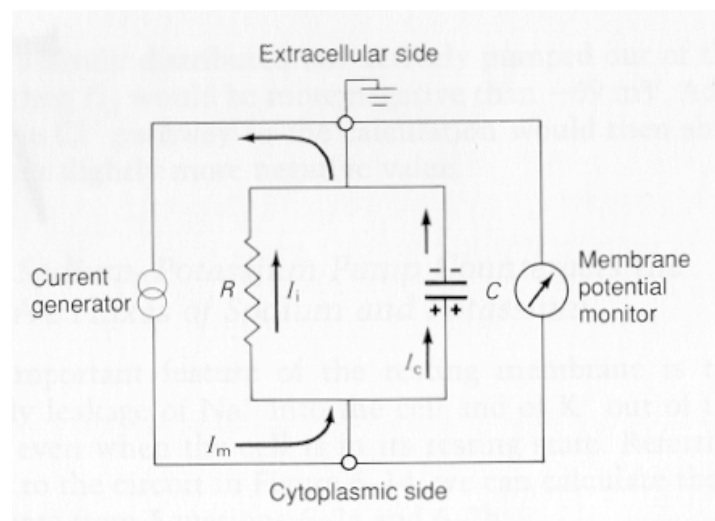
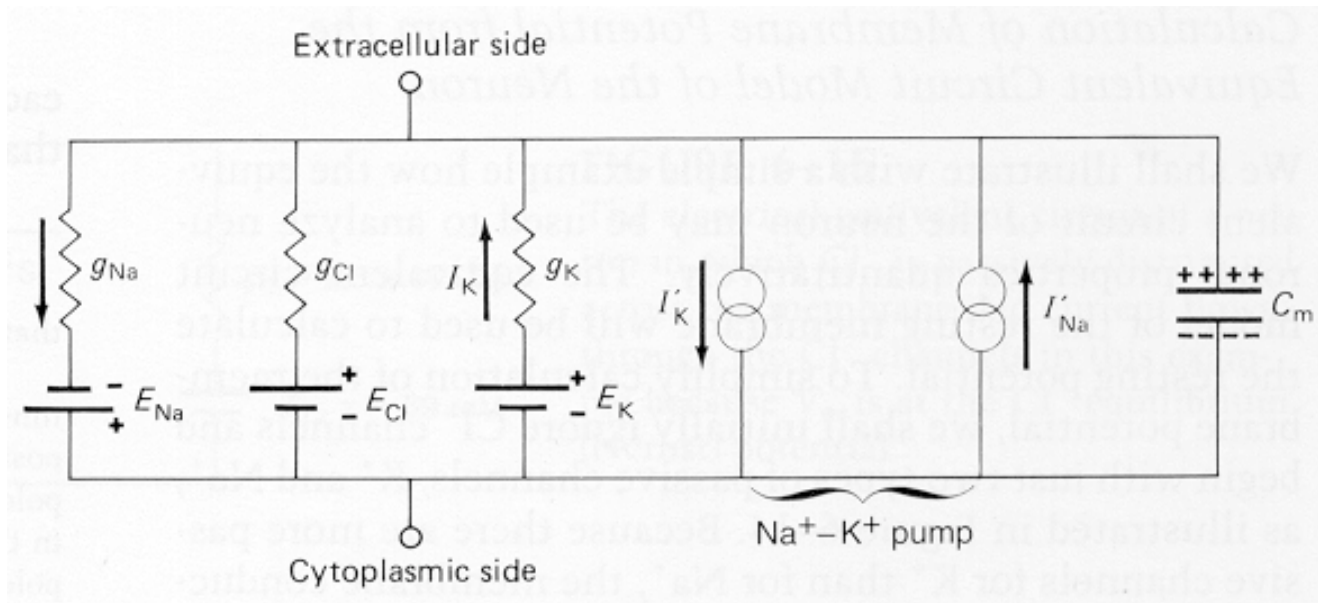
Electrical equivalent circuit of a neuron at rest includes the most abundant types of ion channels in parallel. Under steady-state conditions, Na and K currents resulting from passive diffusion through membrane channels are balanced by active Na and K fluxes (I'_{Na} and I'_{K}) driven by the Na-K pump. The lipid bilayer endows the membrane with electrical capacitance (C_m), where the charge (Q) build up is given by $C_m V_m$



Electrical equivalent circuit for calculating resting membrane potential omits the Cl pathways for simplicity. Note that since the value of g_K is much greater than g_{Na} , this indicates that there are more passive channels for K than for Na



Thevenin equivalent circuit



$$R_{Th} = 1/(g_{Na} + g_K + g_l)$$

$$V_{Th} = V_m$$

$$I_{Na} + I_K = 0$$

$$V_m = E_{Na} + I_{Na} / g_{Na}$$

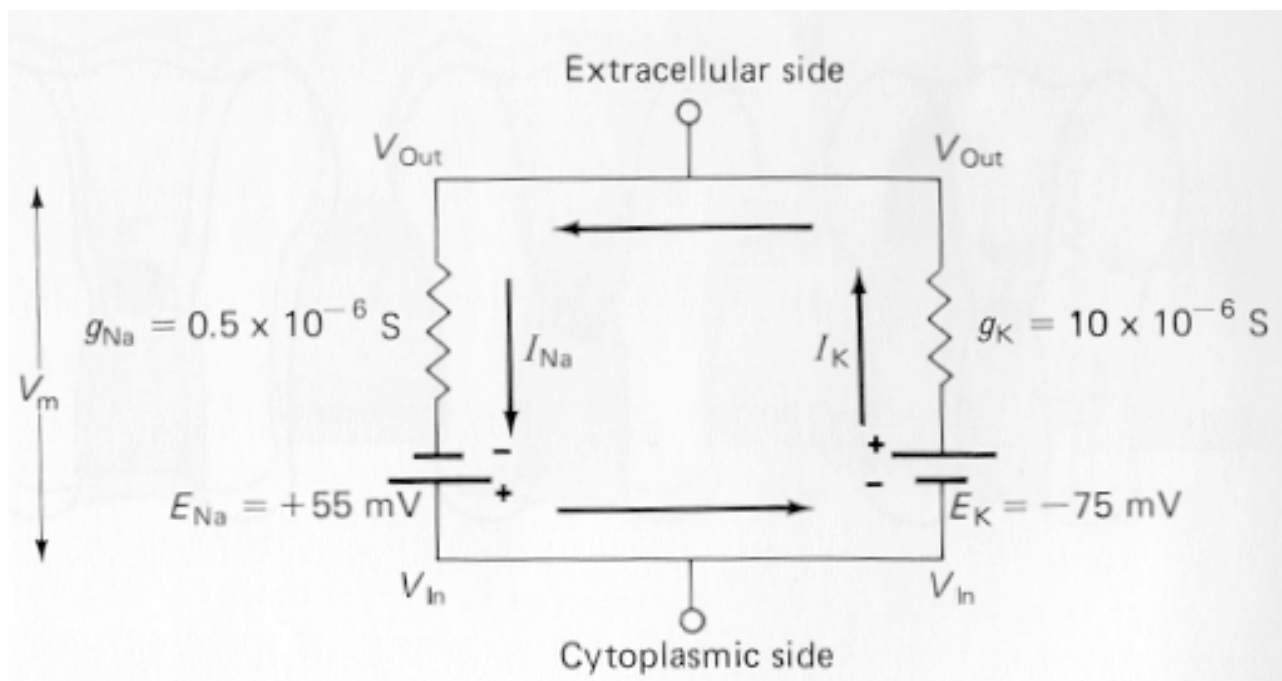
$$V_m = E_K + I_K / g_K$$

$$I_{Na} = g_{Na} (V_m - E_{Na})$$

$$I_K = g_K (V_m - E_K)$$

$$g_{Na} (V_m - E_{Na}) + g_K (V_m - E_K) = 0$$

$$V_m = \frac{(E_{Na} g_{Na}) + (E_K g_K)}{g_{Na} + g_K} = -69 \text{ mV}$$



$$I_{Na} + I_K + I_{Cl} = 0$$

$$V_m = E_{Na} + I_{Na} / g_{Na}$$

$$V_m = E_K + I_K / g_K$$

$$V_m = E_{Cl} + I_{Cl} / g_{Cl}$$

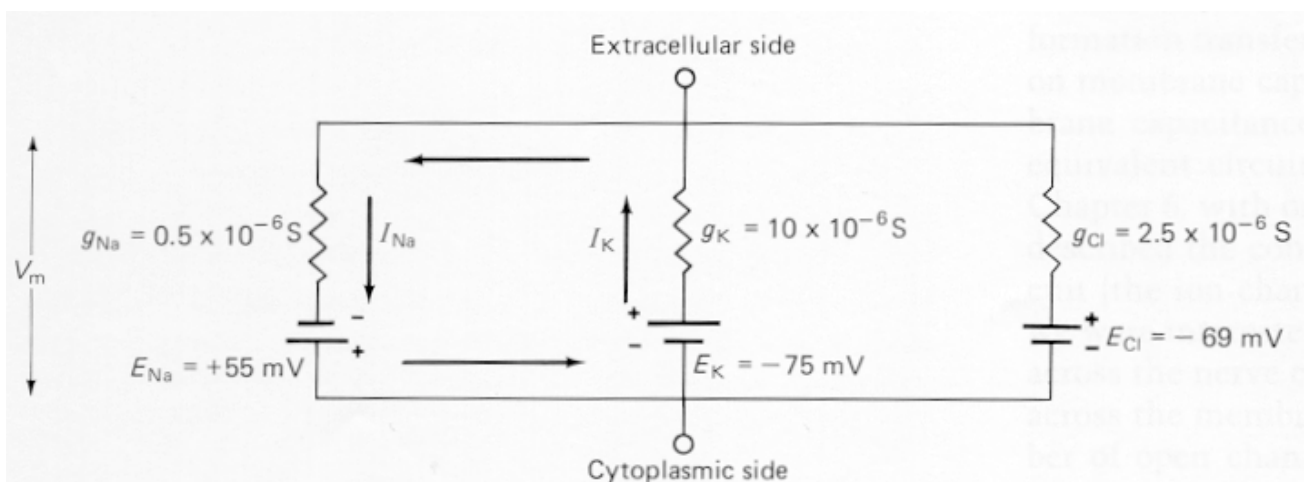
$$I_{Na} = g_{Na} (V_m - E_{Na})$$

$$I_K = g_K (V_m - E_K)$$

$$I_{Cl} = g_{Cl} (V_m - E_{Cl})$$

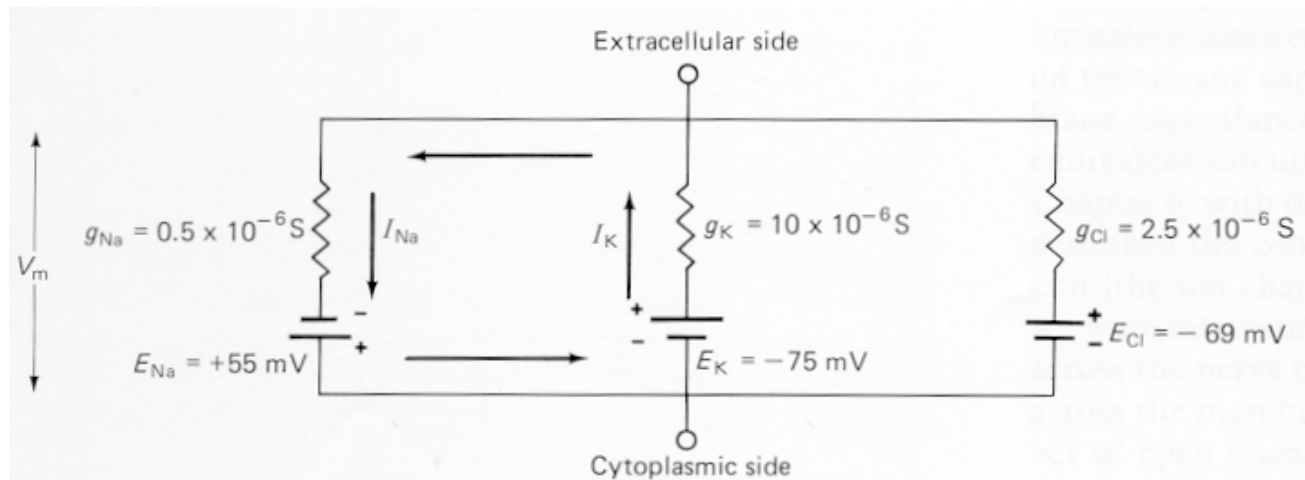
$$g_{Na} (V_m - E_{Na}) + g_K (V_m - E_K) = 0$$

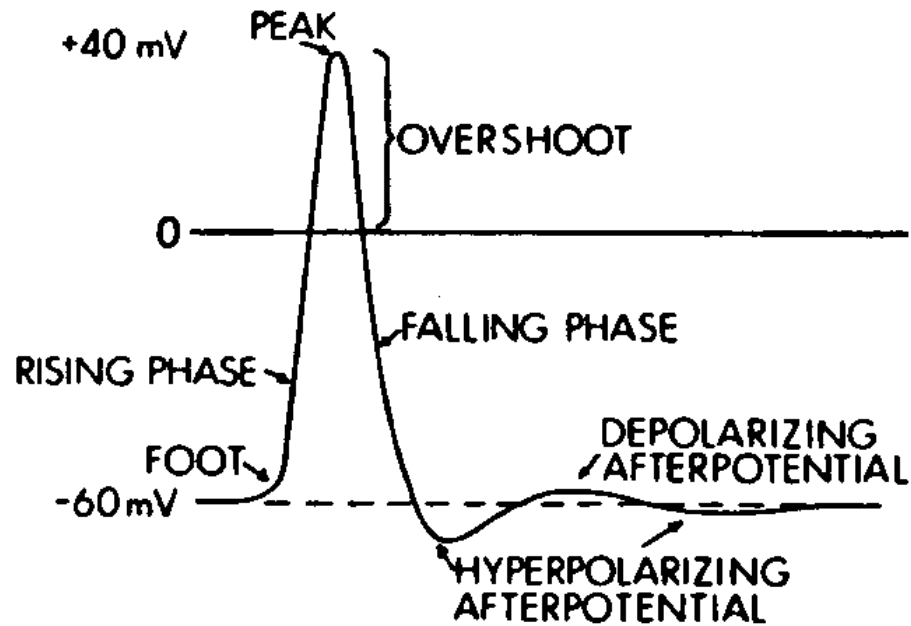
$$V_m = \frac{(E_{Na} g_{Na}) + (E_K g_K) + (E_{Cl} g_{Cl})}{g_{Na} + g_K + g_{Cl}} = -69 \text{ mV}$$



Giant squid axon (at rest)

	intra	extra	relative permeability	Nernst potential
K	400	20	1	- 74
Na	50	440	0.04	+55
Cl	52	560	0.45	- 60





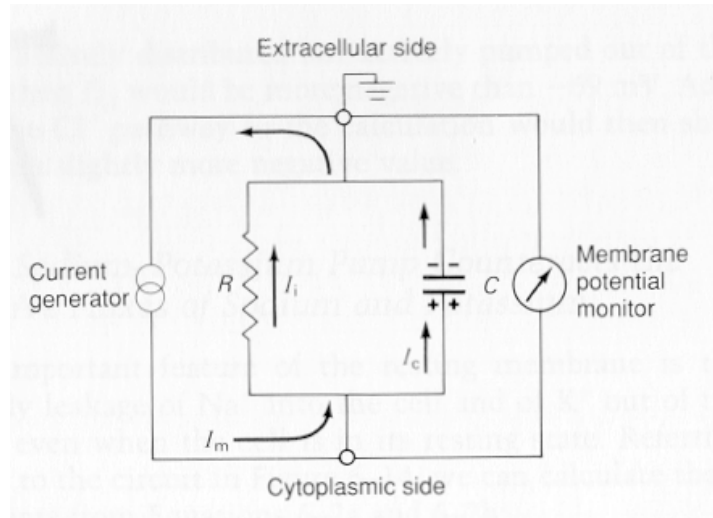
- from Hodgkin and Katz (1949) *J Physiol* 108:37 and Natsuk and Hodgkin (1950) *J Cell Comp Physiol* 35:39
- $P_K : P_{Na} : P_{Cl} = 1.0 : 0.04 : 0.45$ for membrane at rest
- $P_K : P_{Na} : P_{Cl} = 1.0 : 10.0 : 0.45$ for active membrane
- at rest $V_m \approx E_K$
- at peak $V_m \approx E_{Na}$

Ionic current (I_i), capacititive (I_c), and membrane (I_m) currents

$$I_m = I_i + I_c \text{ (Kirchhoff's law)}$$

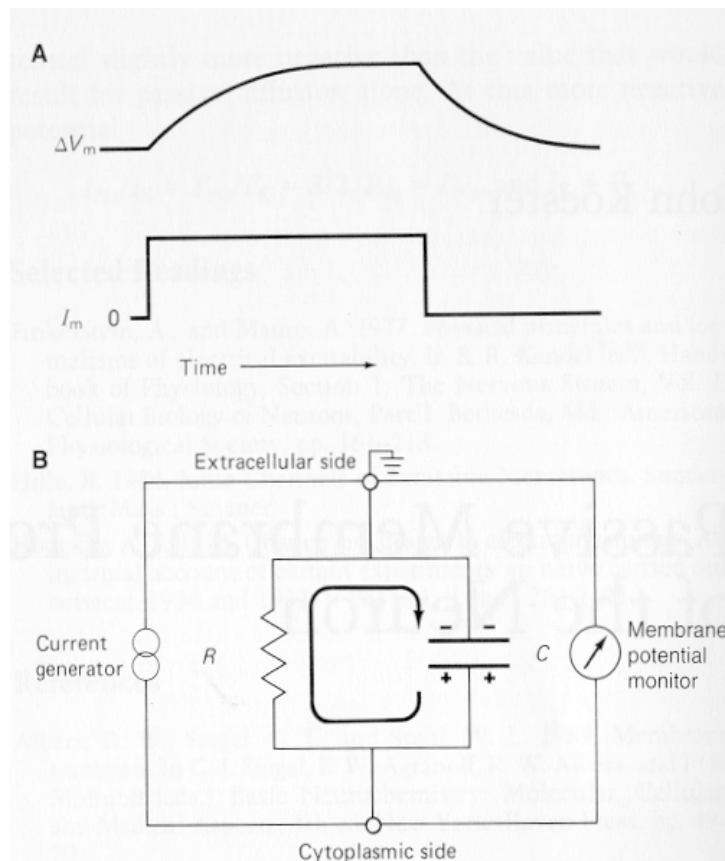
$$\text{where } I_c = C_m (dV_m/dt)$$

$$\text{and } I_i = I_K + I_{Na} + I_{Cl}$$



The rate of change of V_m slowed by C_m

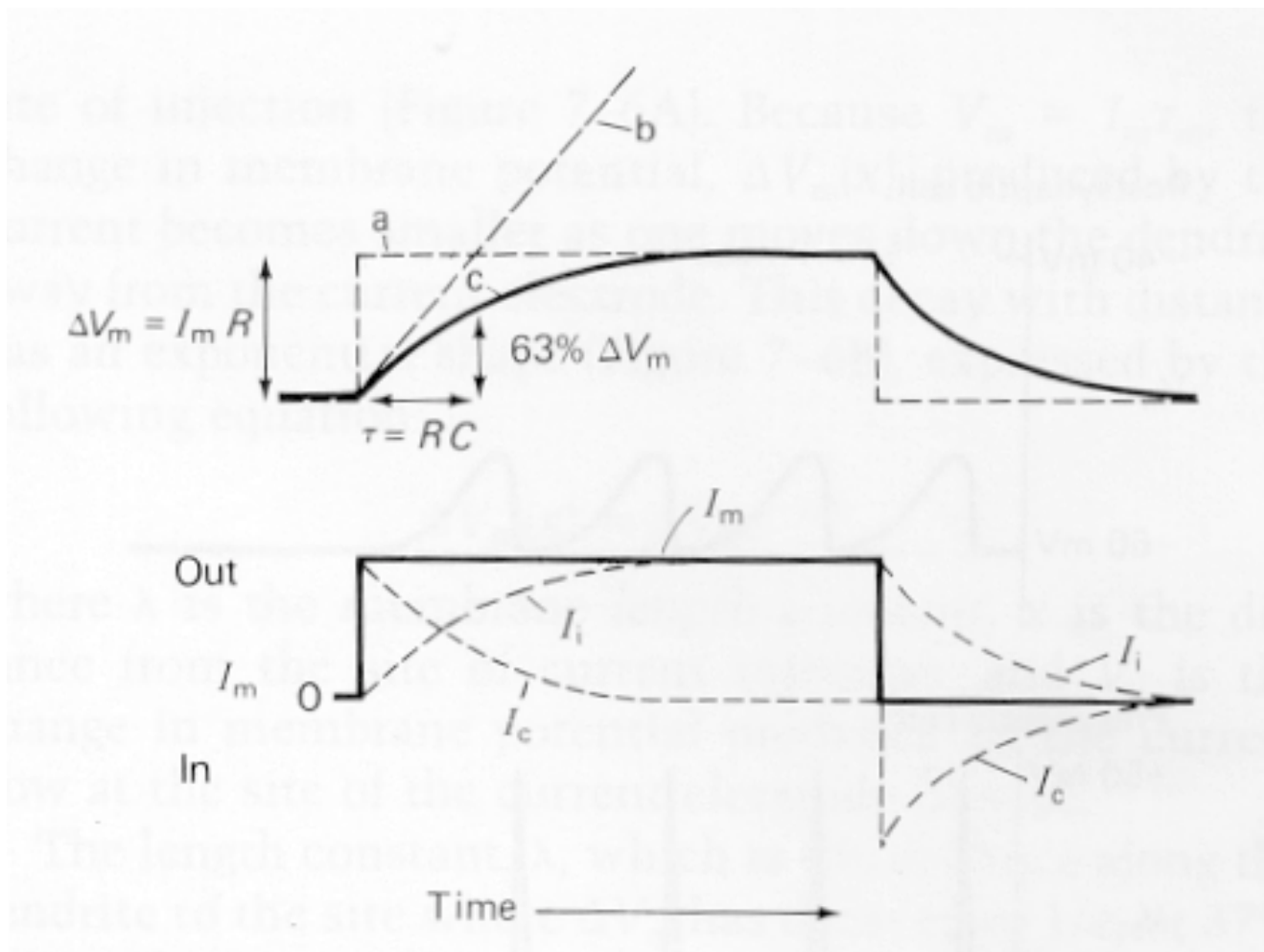
$$\Delta V_m = \Delta Q / C_m$$



Temporal dynamics of the change of V_m in response to a step function of current (i.e., stimulus) combines the features of a purely capacitative and a resistive element.

$$\Delta V_m(t) = I_m R (1 - \exp(-t/\tau))$$

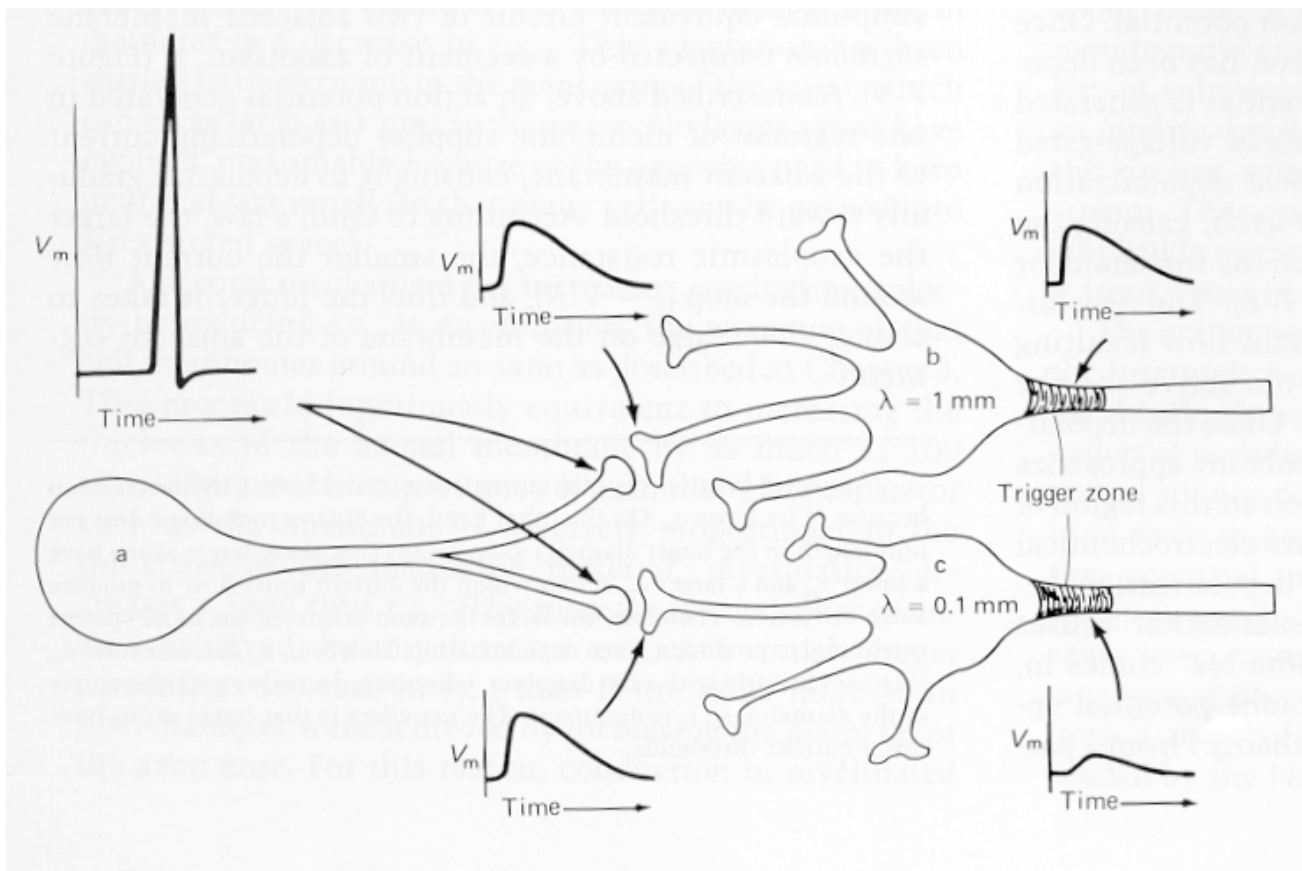
where τ is given by RC_m



Spatial dependence of the change of V_m in response to an action potential in the presynaptic terminal. An action potential in cell “a” elicits synaptic potentials in cells “b” and “c”. The sizes of the synaptic potentials in cells “b” and “c” are different because of the different values of λ .

$$\Delta V_m(x) = \Delta V_o \exp(-x/\lambda)$$

where λ is given by the ratio $\sqrt{r_m/r_a}$; r_m is the membrane resistance (units of $\Omega \text{ cm}$), r_a is the axial resistance (units of Ω/cm); typical values of λ ranges from 0.1- 1 mm; ΔV_o is the change in V_m at $x = 0$ (i.e., the site of stimulus electrode)



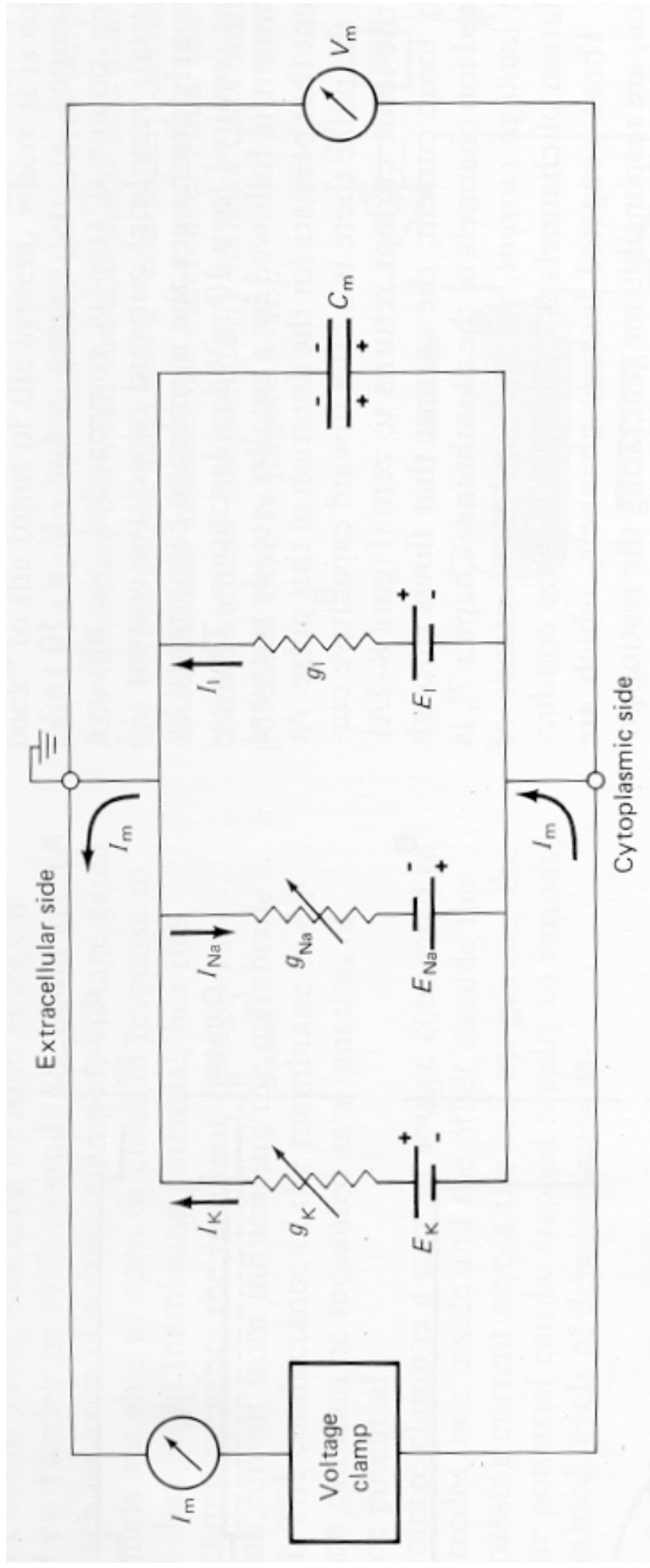
Voltage-clamp

The ionic battery of the passive leaky channels, E_l , is equal to V_m (recall the same idea of $E_{Cl} = V_m$), at rest.

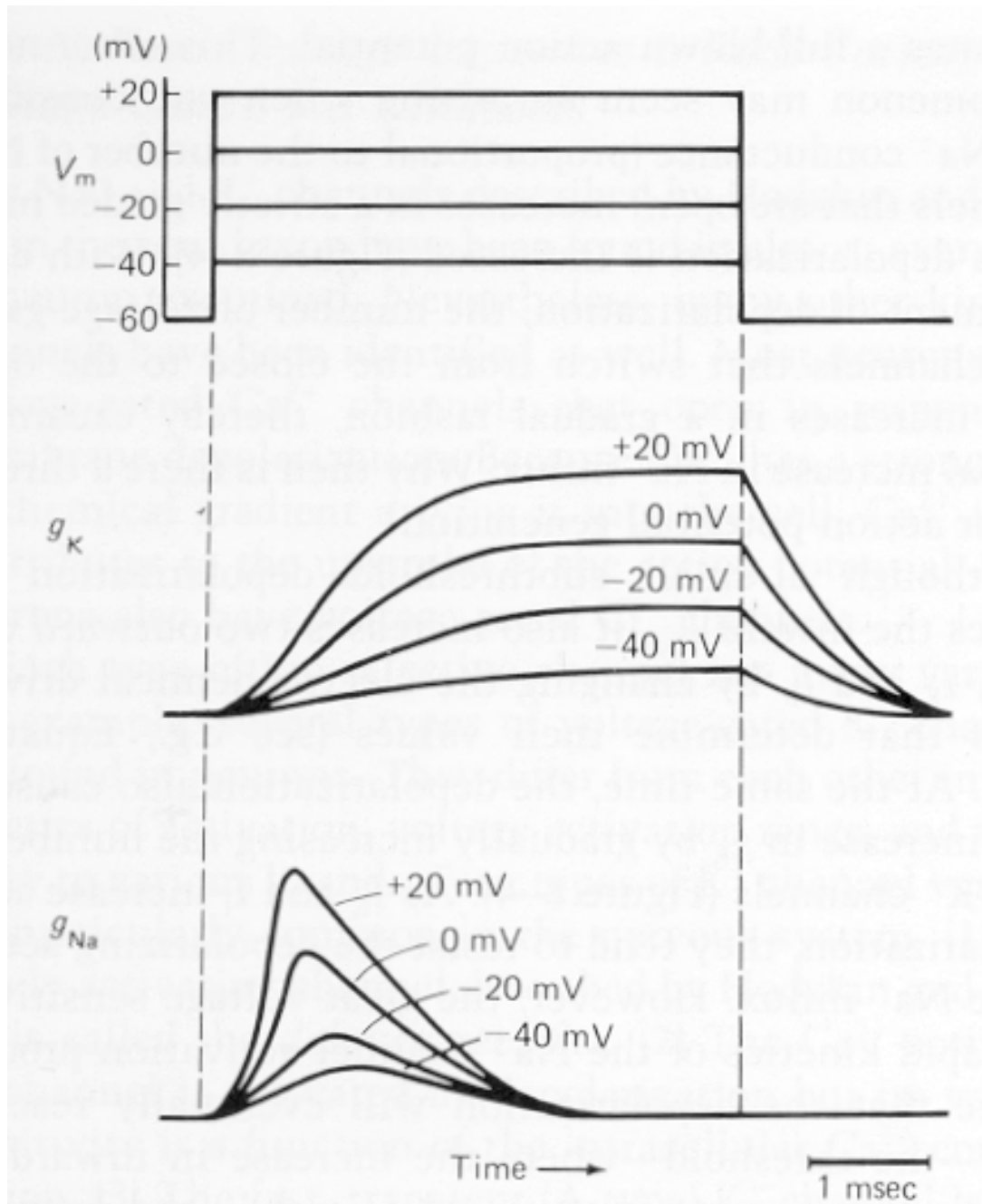
However, with stimulation

$$I_m = g_{Na} (V_m - E_{Na}) + g_K (V_m - E_K) + (V_m - E_l)/R_l + C_m (dV_m/dt)$$

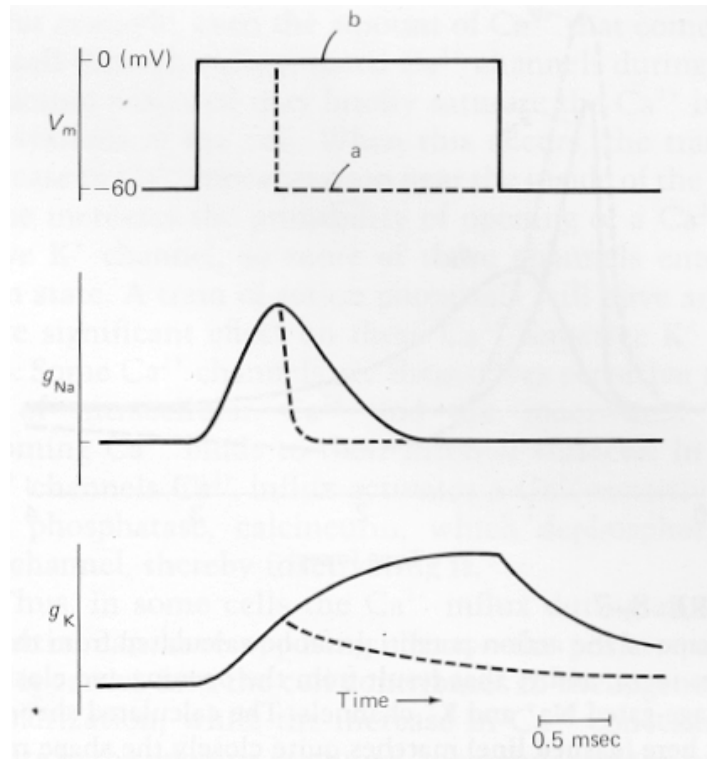
which is Kirchhoff's law



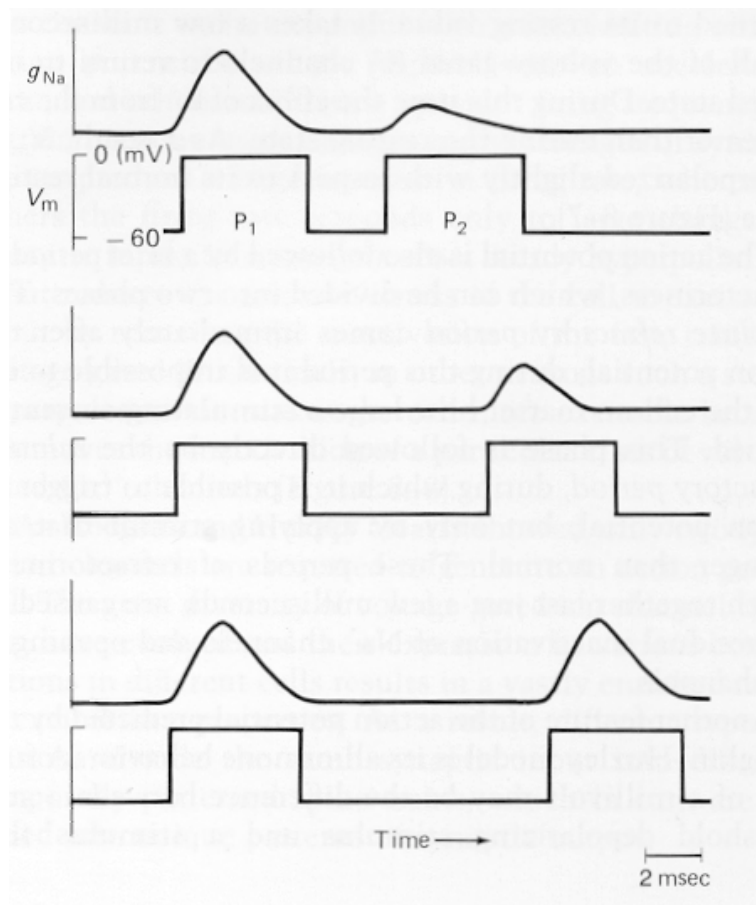
Voltage-clamp experiments show that g_{Na} turns on and off more rapidly than g_K over a wide range of V_m



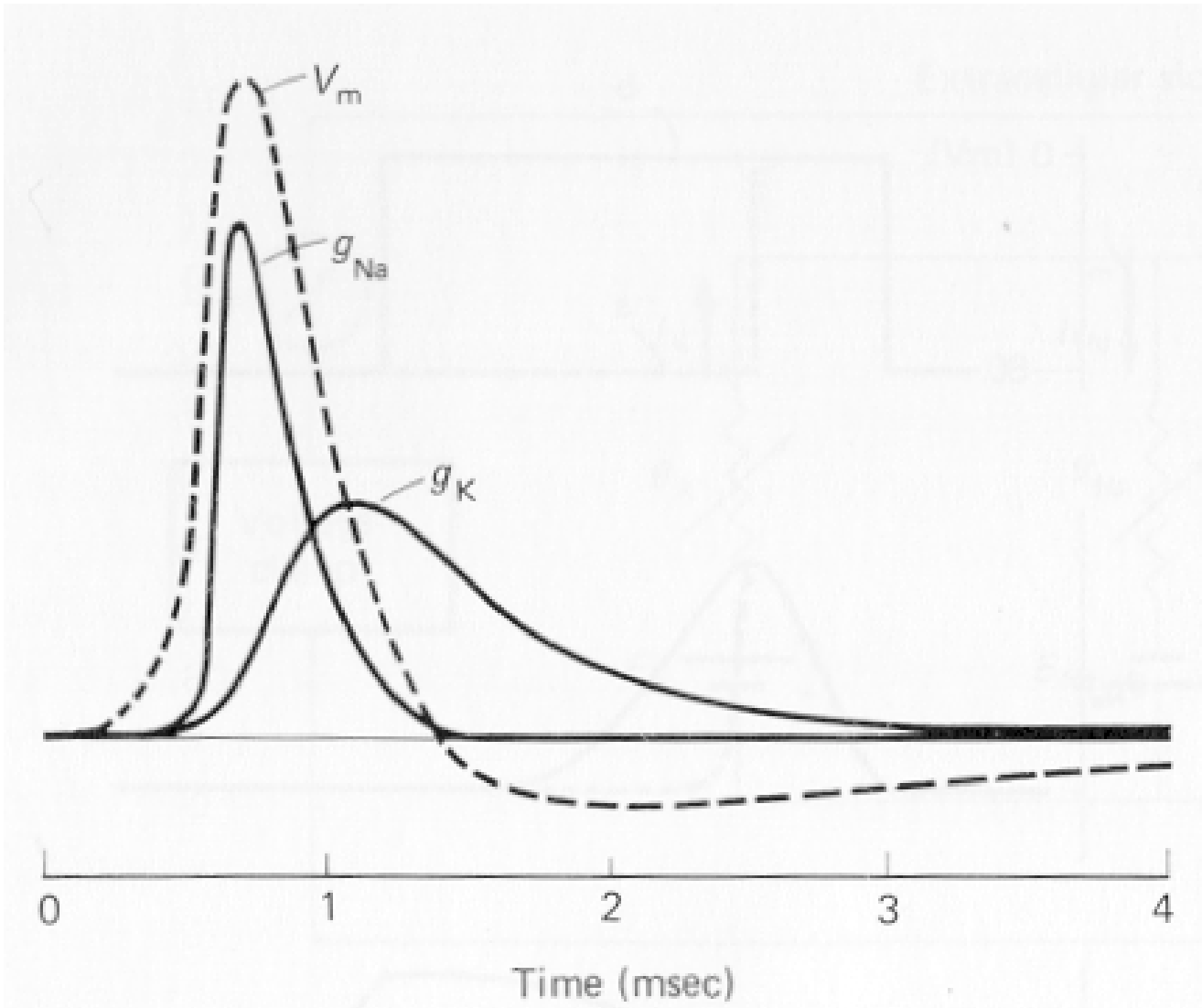
Brief (a) and long (b) depolarizing steps and the corresponding dynamics of g_{Na} and g_K



Neuronal refractory period demonstrated with two consecutive pulses



Typical time-course of V_m , g_K , and g_{Na}



$$g_K(t, \Delta V_m) = g_{K,o} n^4(t, \Delta V_m)$$

$$g_{Na}(t, \Delta V_m) = g_{Na,o} m^3(t, \Delta V_m) h(t, \Delta V_m)$$

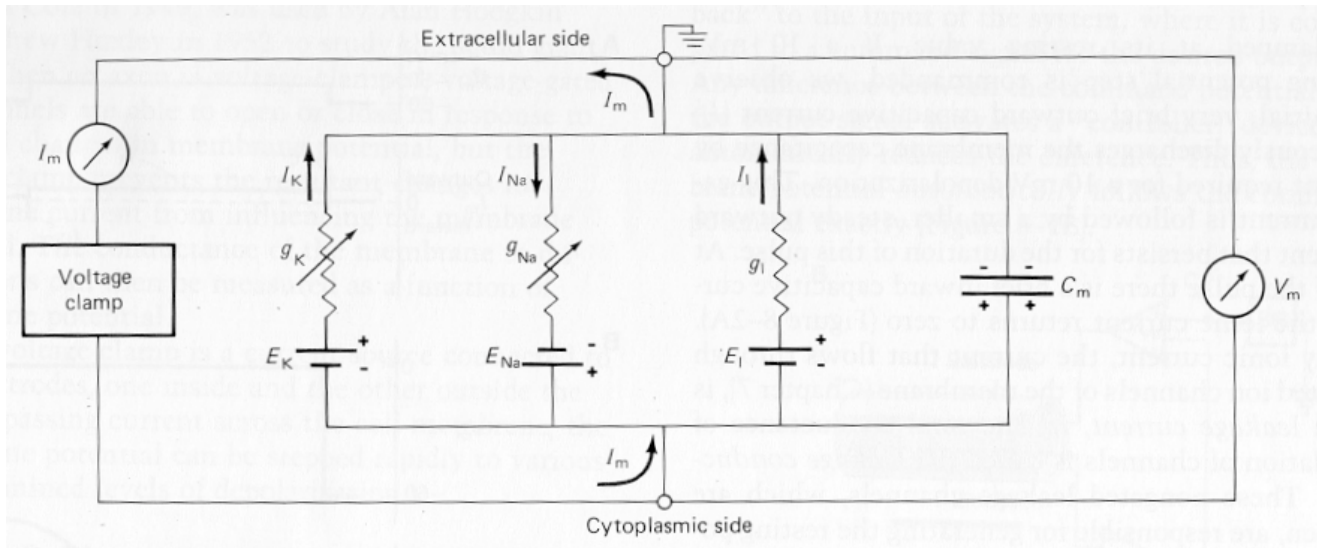
$$V_m(t) = V_{Th} + R_{Th} K \{1 - \exp(-(t-t_o)/(R_{Th}C))\} u(t) - R_{Th} K \{1 - \exp(-(t-t_o)/(R_{Th}C))\} u(t-t_o)$$

where K is the amplitude of I_m and $u(t)$ defines it in time

Hodgkin-Huxley model

- from Hodgkin and Huxley (1952) *J Physiol* 117:500-504

$$I_m = g_{Na} (V_m - E_{Na}) + g_K (V_m - E_K) + (V_m - E_l)/R_l + C_m (dV_m/dt)$$



- potassium

$$g_K(t, \Delta V_m) = g_{K,o} n^4(t, \Delta V_m)$$

where

$$g_{K,o} = 36 \text{ mS}$$

$$n_o \approx 0.31769$$

$$\alpha_n = 0.01 (10 - \Delta V_m) / [\exp((10 - \Delta V_m)/10) - 1]$$

$$\beta_n = 0.125 \exp(-\Delta V_m/80)$$

$$dn/dt = \alpha_n (1 - n) - \beta_n n$$

$$\Delta V_m = V_m(\text{stimulation}) - V_m(\text{rest})$$

Hodgkin-Huxley model (continued):

- sodium

$$g_{\text{Na}}(t, \Delta V_m) = g_{\text{Na},o} m^3(t, \Delta V_m) h(t, \Delta V_m)$$

where

$$g_{\text{Na},o} = 120 \text{ mS}$$

$$m_o = 0.05294$$

$$\alpha_m = 0.1 (25 - \Delta V_m) / [\exp((25 - \Delta V_m)/10) - 1]$$

$$\beta_m = 4 \exp(-\Delta V_m/18)$$

$$dm/dt = \alpha_m (1 - m) - \beta_m m$$

$$h_o = 0.59615$$

$$\alpha_h = 0.07 \exp(-\Delta V_m/18)$$

$$\beta_h = 1 / [\exp((30 - \Delta V_m)/10) + 1]$$

$$dh/dt = \alpha_h (1 - h) - \beta_h h$$

$$\Delta V_m = V_m(\text{stimulation}) - V_m(\text{rest})$$