Single Neuron Model (1):

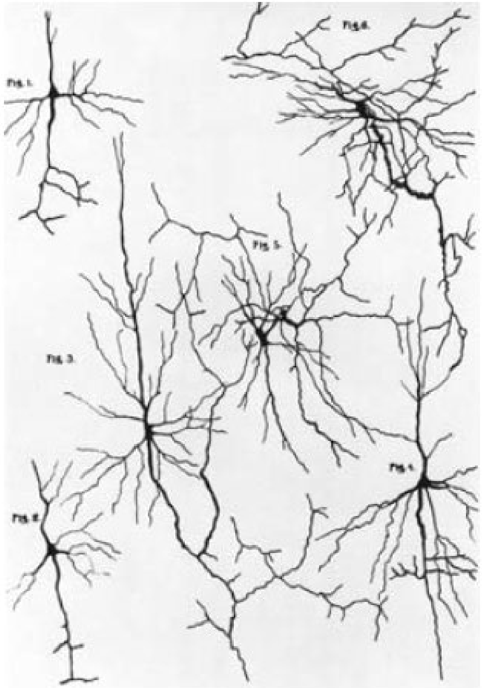
Hodgkin-Huxley neuron model

Neuron models	HH neuron model
	LIF neuron model
	Exponential IF model
Synapse models	AMPA/GABA/NMDA synapse
	Exponential synapse
Network Models	E/I balance network
	Continuous attractor network
	Working memory model
	Decision making model

Single Neuron

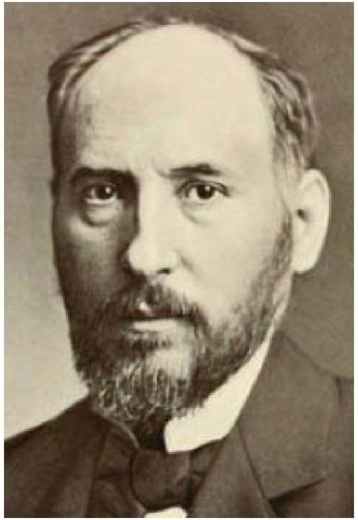
神经元是大脑信息处理的基本单元

a

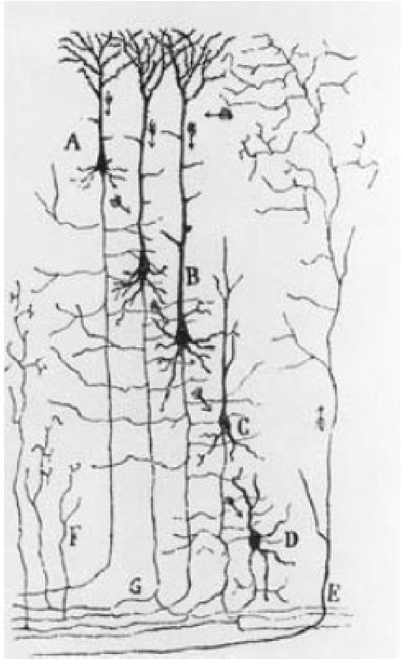


b

FIGURE 1.10 **(a)** Camillo Golgi (1843–1926), cowinner of the Nobel Prize in 1906. **(b)** Golgi's drawings of different types of ganglion cells in dog and cat.



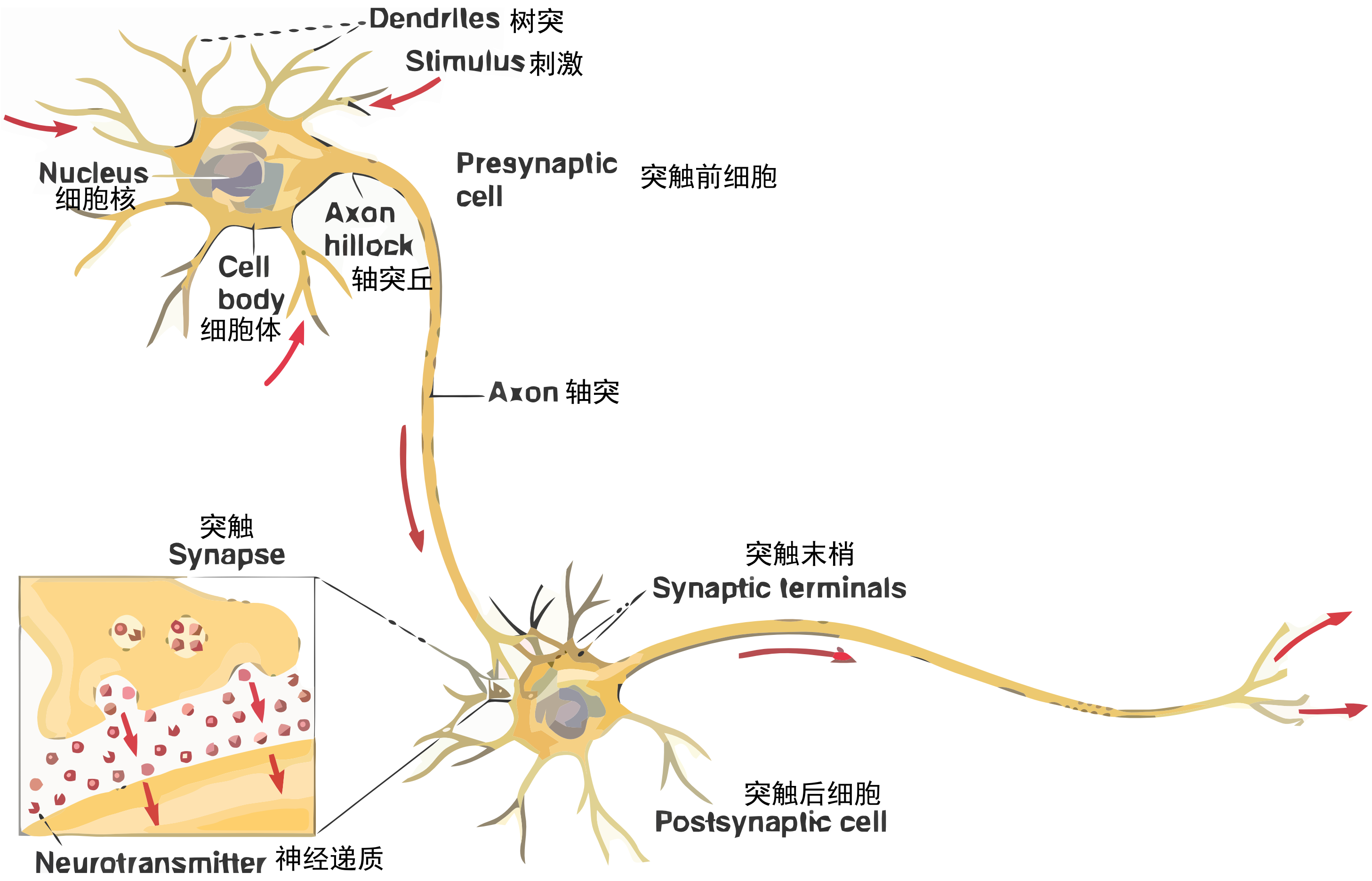
a

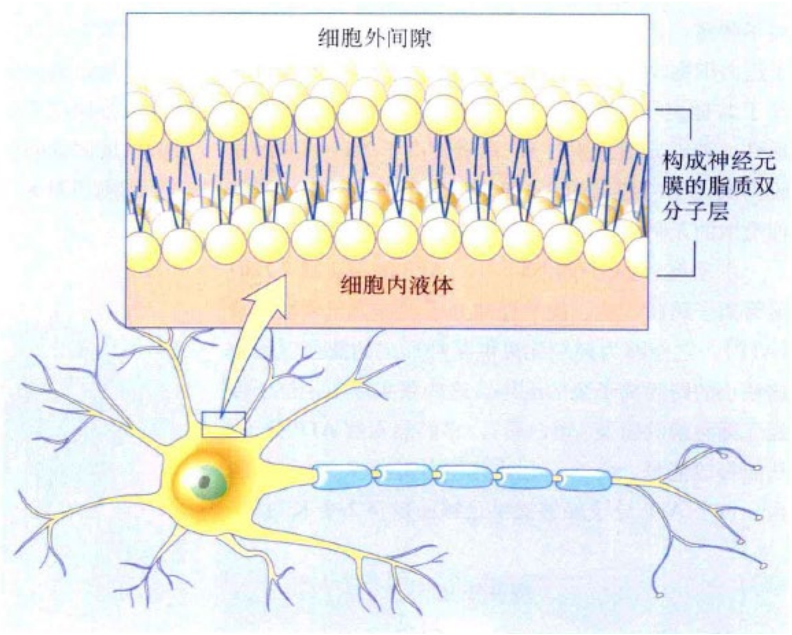


b

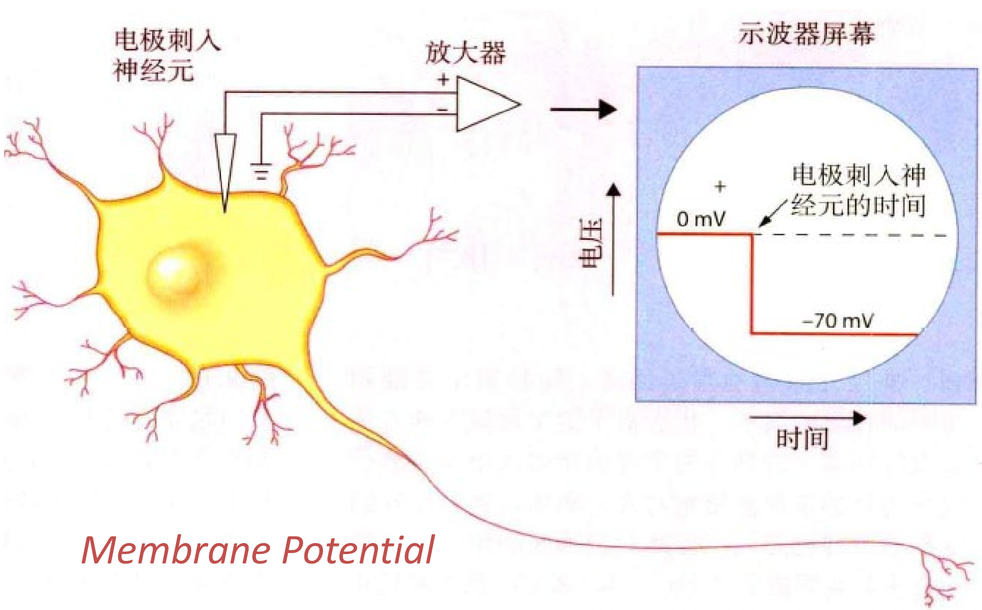
FIGURE 1.11 **(a)** Santiago Ramón y Cajal (1852–1934), cowinner of the Nobel Prize in 1906. **(b)** Ramón y Cajal's drawing of the afferent inflow to the mammalian cortex.

神经元是大脑信息处理的基本单元

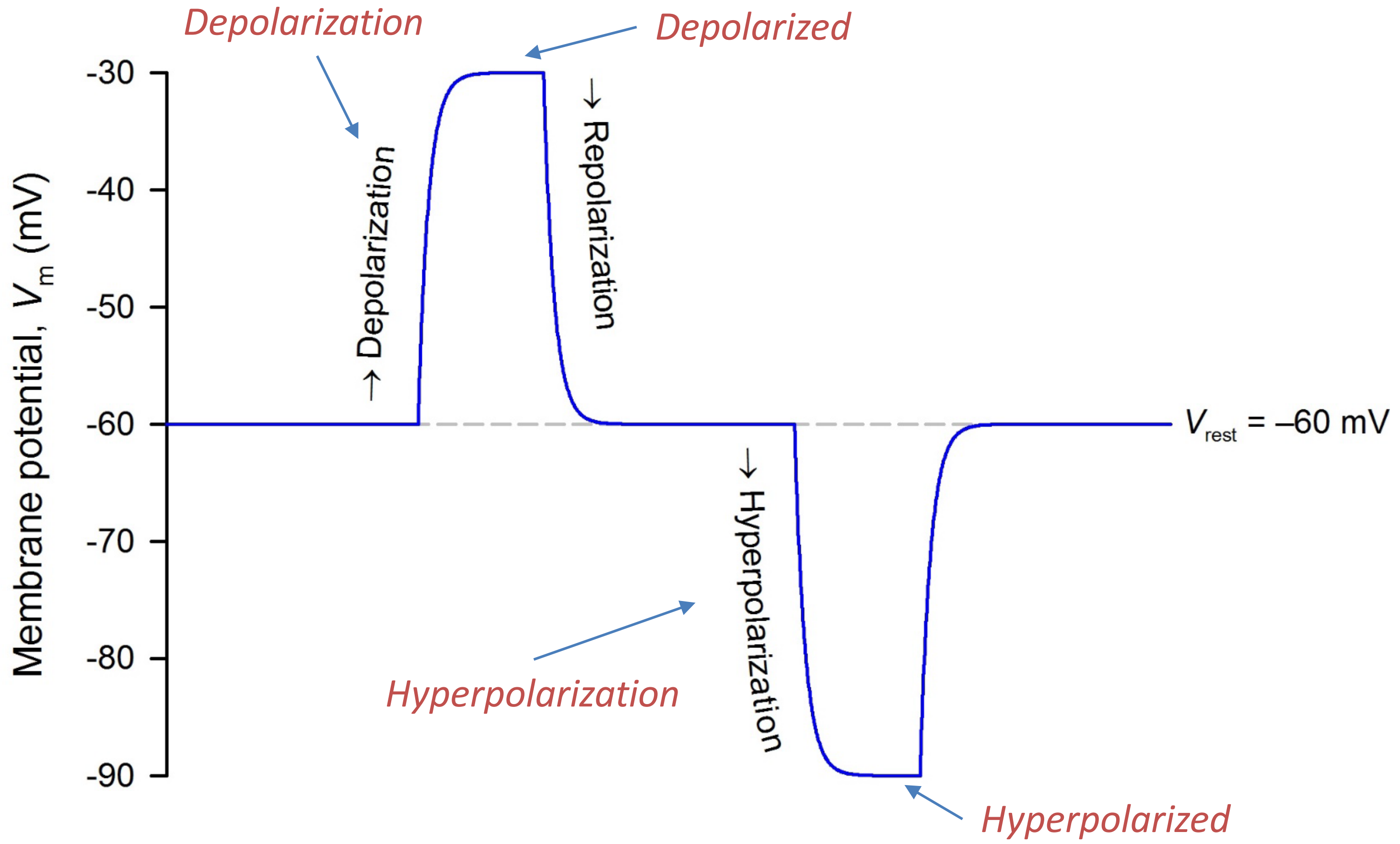



细胞外间隙
构成神经元膜的脂质双分子层
细胞内液体

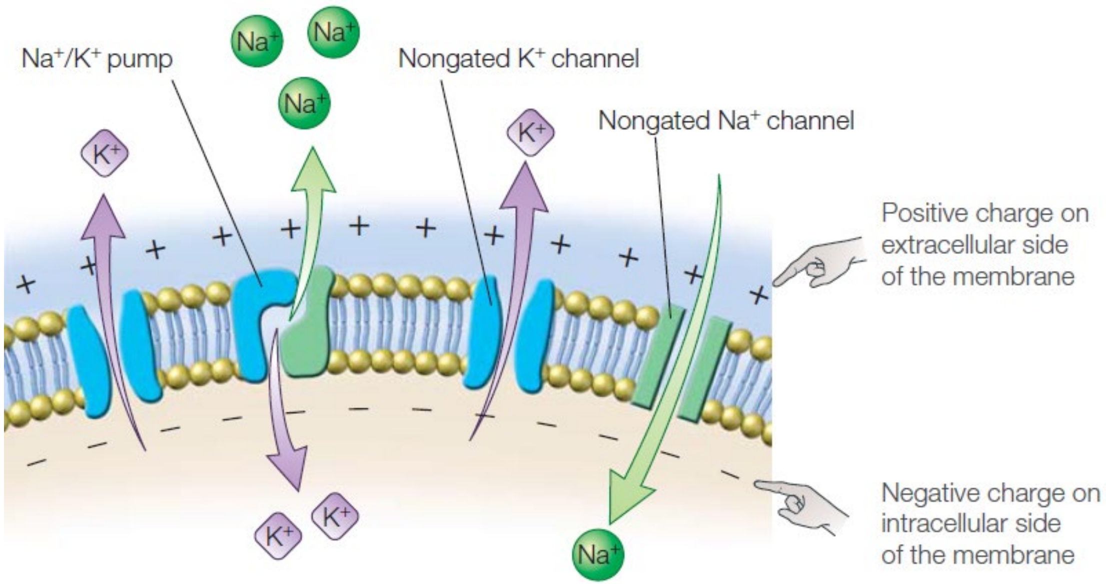
神经元细胞膜


电极刺入神经元
放大器
+
–
示波器屏幕
电压
+
0 mV
电极刺入神经元的时间
–70 mV
时间
Membrane Potential

胞内记录



Depolarization
Depolarized
-30
-40
-50
-60
-70
-80
-90
Membrane potential, V_m (mV)
→ Depolarization
→ Repolarization
→ Hyperpolarization
V_{rest} = –60 mV
Hyperpolarization
Hyperpolarized



Voltage-gated channels

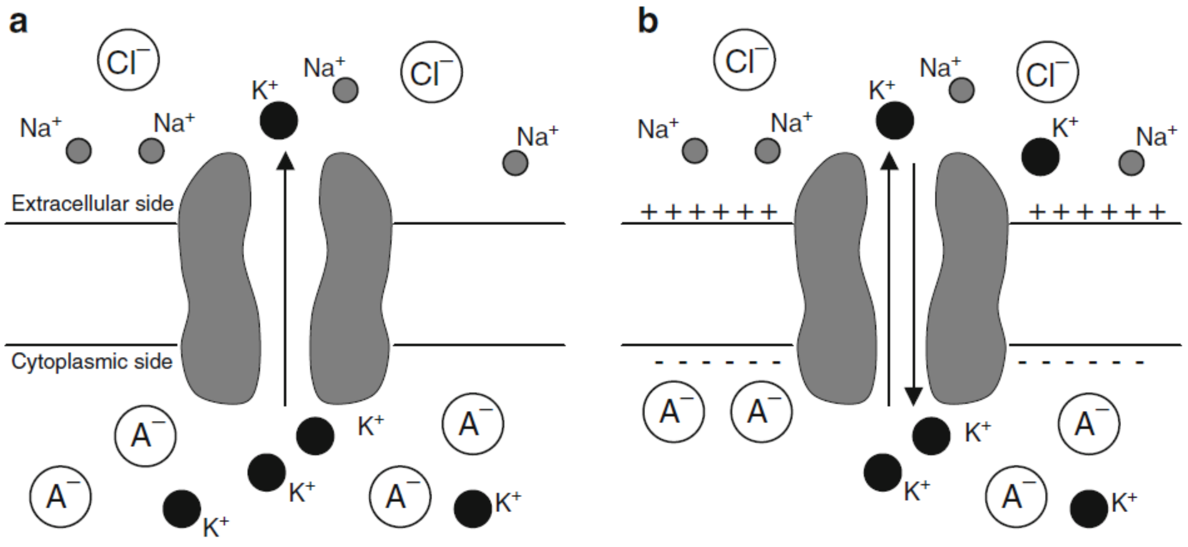
Outward current ➔ hyperpolarization

Inward current ➔ depolarization

Permeability

- The membrane's selective permeability to some ions.
- Most gated channels are closed at rest.
- Hence, the non-gated ion channels are primarily responsible for establishing the resting potential.

The K^+ flux is determined by both the K^+ concentration gradient and the electrical potential across the membrane.



Reversal potential *Nernst equation*

$$E_K = -\frac{RT}{zF} \ln \frac{[K^+]_{in}}{[K^+]_{out}}$$

- R is the gas constant
- T is the absolute temperature in kelvin
- z is the valence of K^+
- F is Faraday's constant
- $[K^+]_{in}$ is concentration of K^+ ions outside
- $[K^+]_{out}$ is concentration of K^+ ions inside

Exercise

$T = 309.15\,^{o}K$ $\quad R = 8.31441\, J/(mol^{o}K)$ $\quad F = 96489\, C/mol$

$$\boxed{E_K = -\frac{RT}{zF}\ln\frac{[K^+]_{in}}{[K^+]_{out}}}$$

Na^+	K^+	Cl^-	Ca^+
$[Na^+]_{in}$ = 12 mM	$[K^+]_{in}$ = 155 mM	$[Cl^-]_{in}$ = 4 mM	$[Ca^{2+}]_{in}$ = 2.4e^{-4} mM
$[Na^+]_{out}$ = 145 mM	$[K^+]_{out}$ = 4 mM	$[Cl^-]_{out}$ = 120 mM	$[Ca^{2+}]_{out}$ = 2 mM
⇩	⇩	⇩	⇩
$E_{Na} = 66.38\, mV$	$E_K = -97.42\, mV$	$E_{Cl} = -90.61\, mV$	$E_{Ca} = 120.25\, mV$

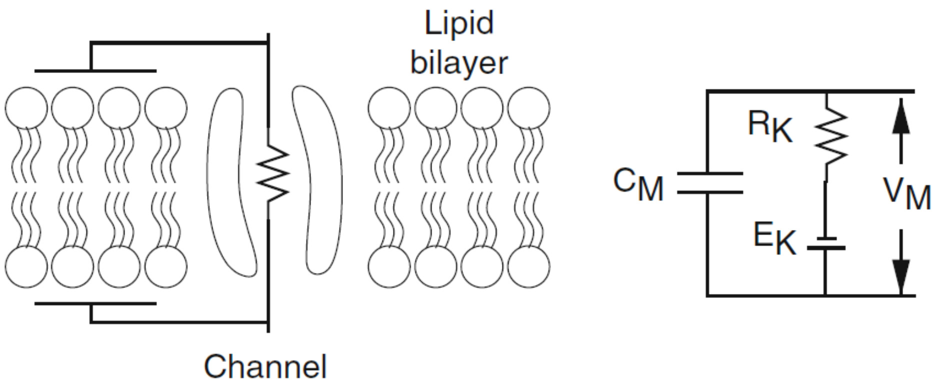
Typical ion concentrations in cells

Ion	Inside (mM)	Outside (mM)	Equilibrium potential (mV), $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
Frog muscle			$T = 20°C$
K^+	124	2.25	$58 \log \frac{2.25}{124} = -101$
Na^+	10.4	109	$58 \log \frac{109}{10.4} = +59$
Cl^-	1.5	77.5	$-58 \log \frac{77.5}{1.5} = -99$
Ca^{2+}	10^{-4}	2.1	$29 \log \frac{2.1}{10^{-4}} = +125$
Squid axon			$T = 20°C$
K^+	400	20	$58 \log \frac{20}{400} = -75$
Na^+	50	440	$58 \log \frac{440}{50} = +55$
Cl^-	40–150	560	$-58 \log \frac{560}{40-150} = -66 \text{ to } -33$
Ca^{2+}	10^{-4}	10	$29 \log \frac{10}{10^{-4}} = +145$
Mammalian cell			$T = 37°C$
K^+	140	5	$62 \log \frac{5}{140} = -89.7$
Na^+	5–15	145	$62 \log \frac{145}{5-15} = +90 - (+61)$
Cl^-	4	110	$-62 \log \frac{110}{4} = -89$
Ca^{2+}	10^{-4}	2.5–5	$31 \log \frac{2.5-5}{10^{-4}} = +136 - (+145)$

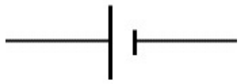
Single Neuron Modeling

Neuron as an electric circuit

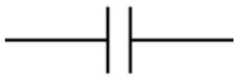
Can we describe an equivalent circuit to calculate the change in membrane potential V by considering the ion channels?



Differences in ion concentration → Batteries →



Cell membrane → Capacitor →

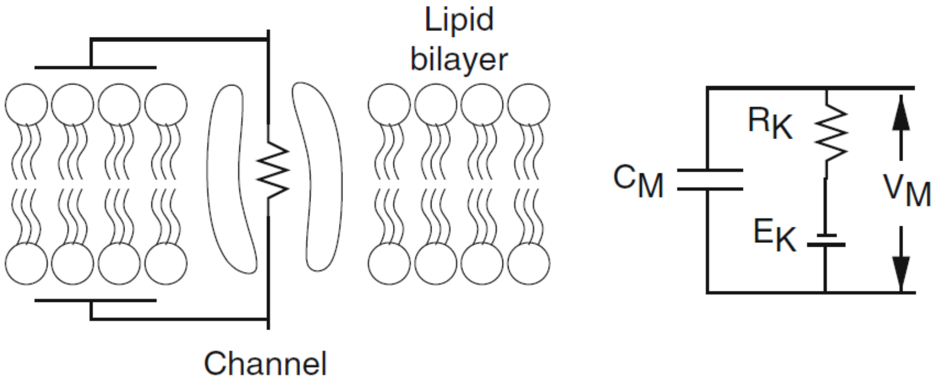


Ionic channels → Resistors →

The relationship between the charge stored and the potential is given by:

$$q = C_M V_M,$$

the total charge q is proportional to the potential V with a proportionality constant C.



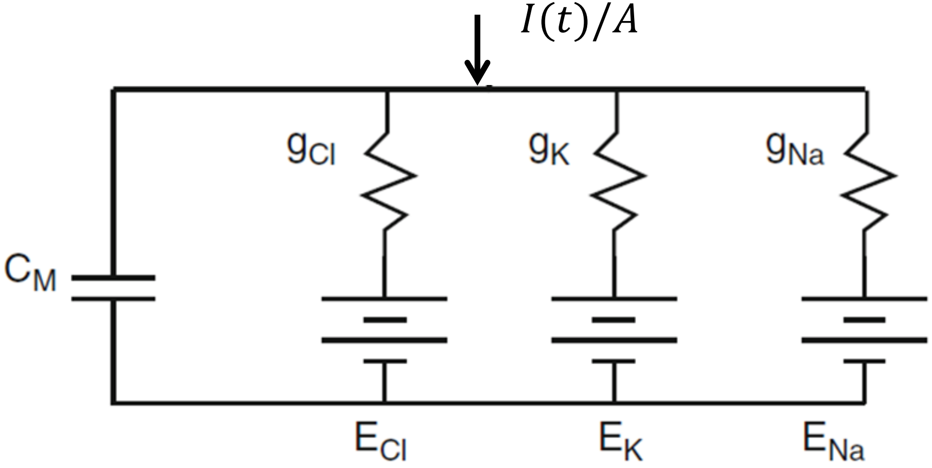
Differentiate q by time t

Kirchoff's law: the total current flowing across the cell membrane is the sum of the capacitive current and the ionic currents.

$$I = C_M \frac{dV_M}{dt}$$

$$I = I_K = \frac{E_K - V_M}{R_K} = g_K(E_K - V_M)$$

$$C_M \frac{dV_M}{dt} = -g_K(V_M - E_K)$$



$$I_{ion} = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na})$$

$$\Downarrow$$

$$C_M \frac{dV_M}{dt} = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na})$$

$$\Downarrow$$

$$C_M \frac{dV_M}{dt} = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na}) + \frac{I(t)}{A}$$

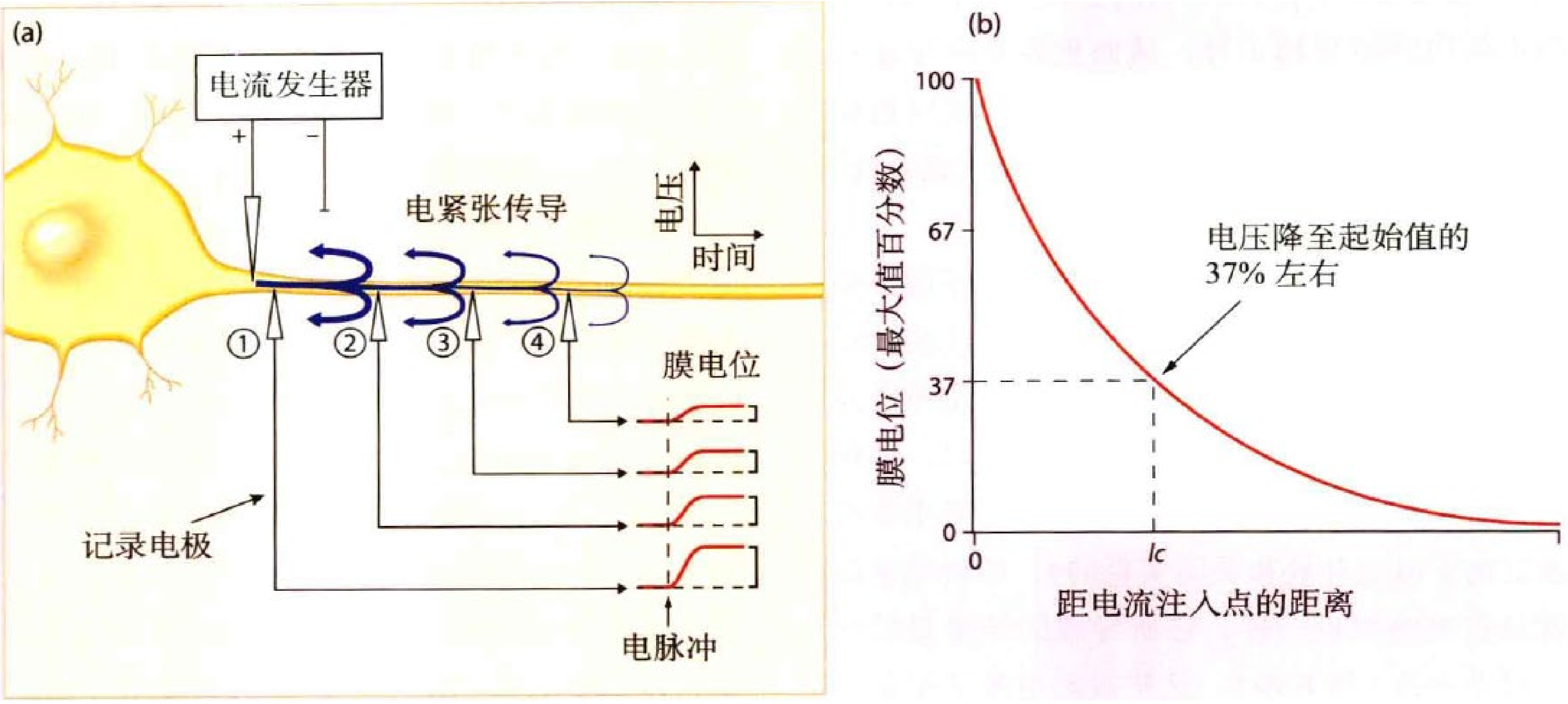
Solving resting potential

$$0 = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na}) + \frac{I(t)}{A}$$

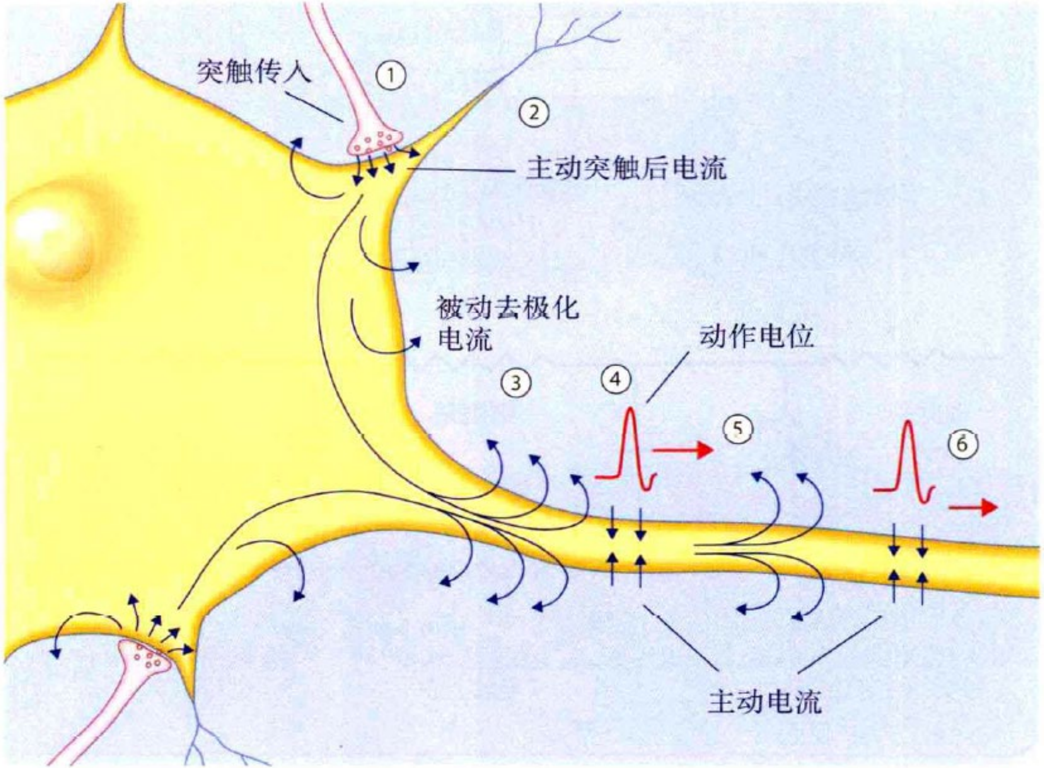
$$\Downarrow$$

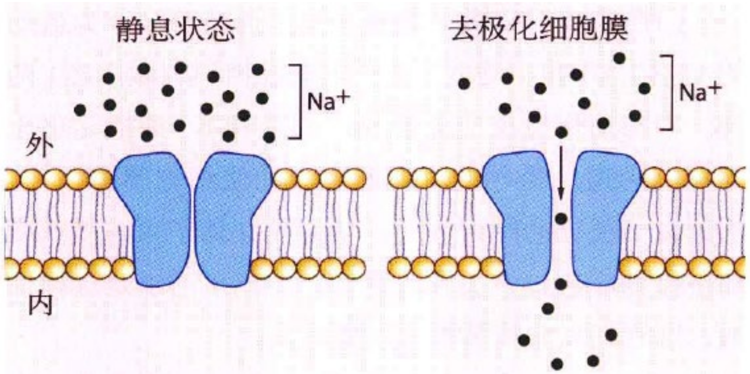
$$V_{SS} = \frac{g_{Cl}E_{Cl} + g_K E_K + g_{Na}E_{Na} + \frac{I(t)}{A}}{g_{Cl} + g_{Na} + g_K} \qquad \text{(steady state)}$$

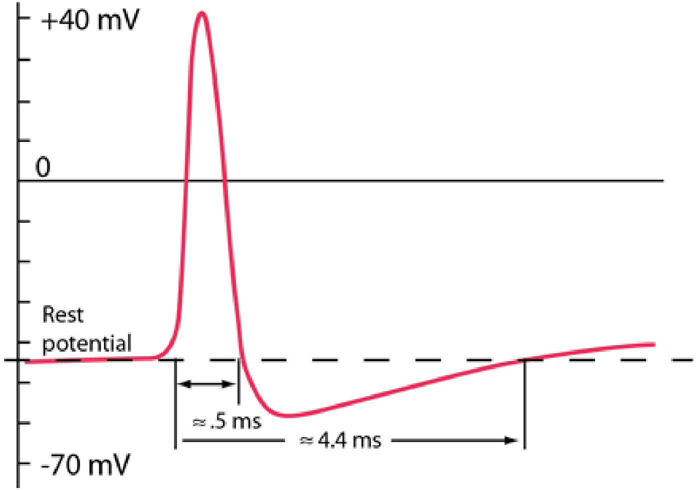
How electrical signal propagates through the axon?



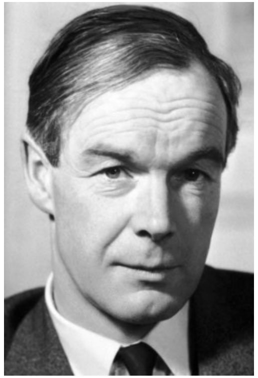
Solution: Voltage-gated Channels & Action Potential!



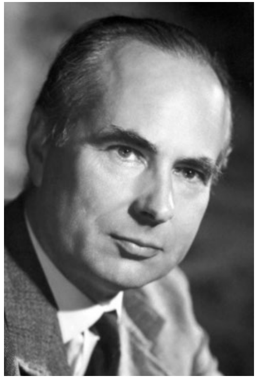




Hodgkin-Huxley neuron model: quantitative model for action potential generation



Alan Lloyd Hodgkin



Andrew Fielding Huxley

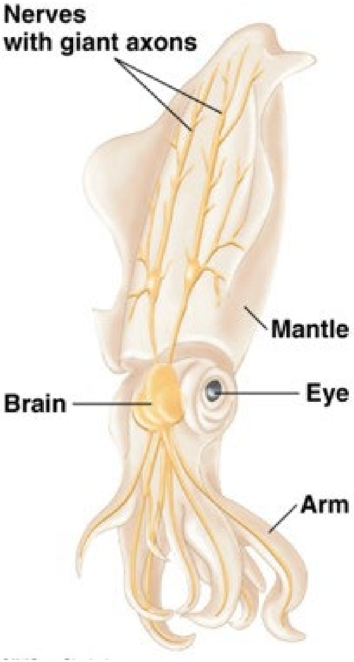
J. Physiol. (1952) 117, 500–544

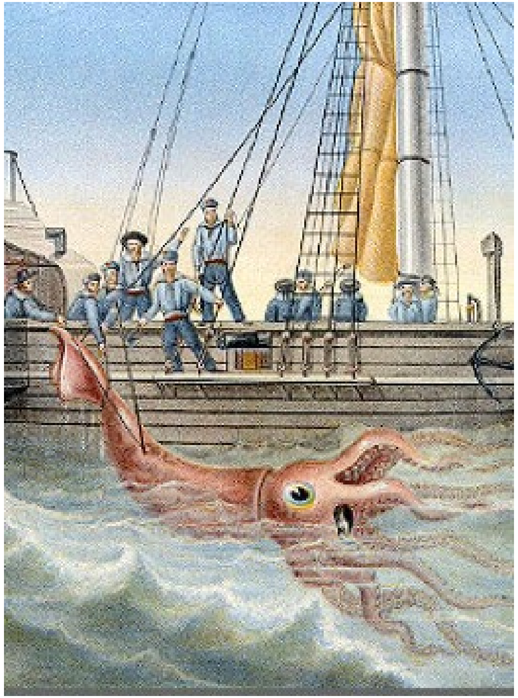
A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

By A. L. HODGKIN and A. F. HUXLEY
From the Physiological Laboratory, University of Cambridge

(*Received* 10 *March* 1952)

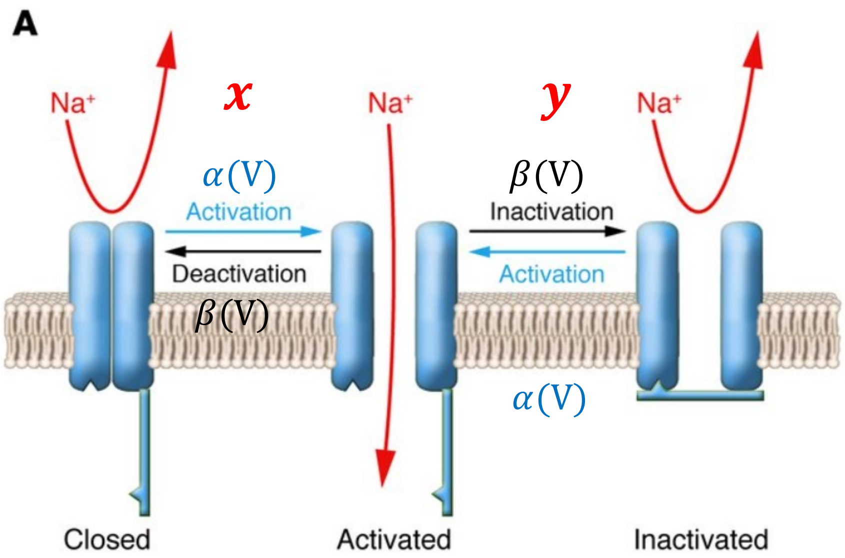
Nobel Prize in Medicine or Physiology in 1963





Made their experiments on the squid giant axon!

$$C\frac{dV}{dt} = -g_{Cl}(V - E_{Cl}) - g_K(V)(V - E_K) - g_{Na}(V)(V - E_{Na}) + \frac{I(t)}{A}$$



- The channel has activation and inactivation pores

$$g_X(V) = g_{max} x^p(V) y^q(V)$$

- The pores have gates that can be either open or closed;
- The probability that a gate is open or closed depends on the membrane potential.

$$C \underset{\alpha(V)}{\overset{\beta(V)}{\leftarrow\!\!\!\rightarrow}} O$$

where

- $\alpha(V)$ and $\beta(V)$ are the voltage-dependent rate constants
- C and O correspond to the closed and open states

Let x be the fraction of open gates, then $1-x$ is the fraction of closed gates.

$$C \underset{\alpha(V)}{\overset{\beta(V)}{\longleftarrow\!\!\longrightarrow}} O$$

$$\frac{dx}{dt} = \alpha(V)(1-x) - \beta(V)x$$

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}, \quad \left\{ \begin{array}{l} x_\infty(V) = \dfrac{\alpha(V)}{\alpha(V)+\beta(V)} \\ \tau_x(V) = \dfrac{1}{\alpha(V)+\beta(V)} \end{array} \right.$$

In conclusion

$$g_X(V) = g_{max} x^p(V) y^q(V)$$

$$\frac{dx}{dt} = \alpha_x(V)(1-x) - \beta_x(V)x$$

$$\frac{dy}{dt} = \alpha_y(V)(1-y) - \beta_y(V)y$$

- $\alpha(V), \beta(V), x_\infty(V), \tau_x(V)$ should be derived by fitting the data.
- $\alpha(V) = A_\alpha \exp(-B_1 V)$
- $\beta(V) = A_\beta \exp(-B_2 V)$

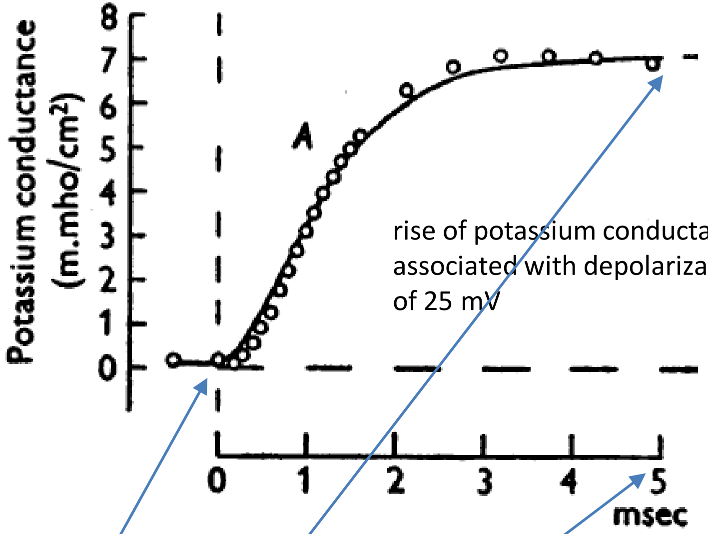
Fit functions best match the experimental data

Step 1

$x_0\ (t = 0),\ x_\infty;$ $\quad x(t) = \boldsymbol{x_\infty(V)} + (x_0 - \boldsymbol{x_\infty(V)})e^{-t/\boldsymbol{\tau(V)}}$

Step 2

For potassium conductance,

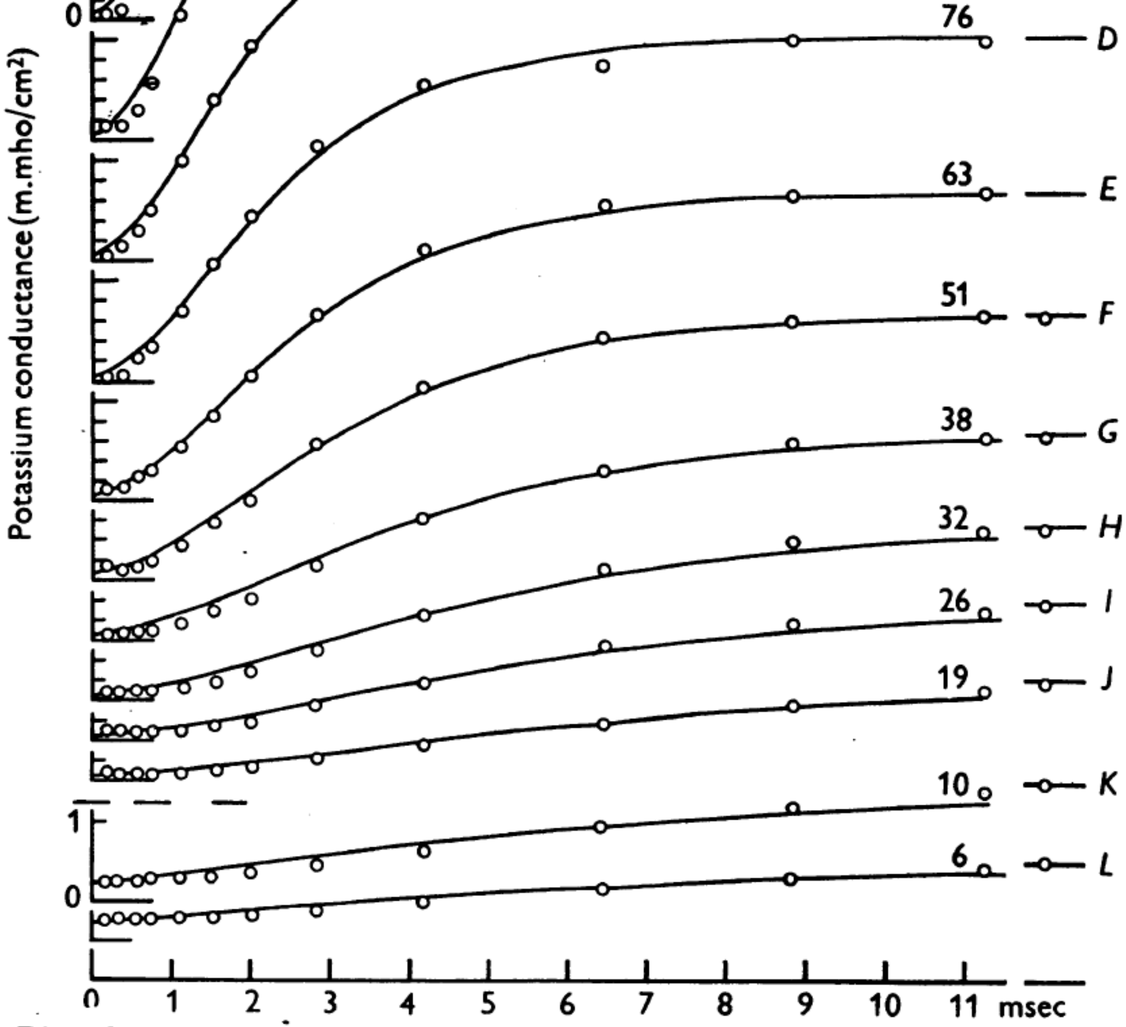


rise of potassium conductance associated with depolarization of 25 mV

$$g_K = g_{max} n^4$$

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

$$g_K(t) = g_{max}\left(\frac{g_{K\infty}}{g_{max}}^{\frac{1}{4}} + \left(\frac{g_{K0}}{g_{max}}^{\frac{1}{4}} - \frac{g_{K\infty}}{g_{max}}^{\frac{1}{4}}\right)e^{-\frac{t}{\tau(V)}}\right)^4$$



The number on each curve gives the depolarization in mV.

Fig. 3. Rise of potassium conductance associated with different depolarizations. The circles are

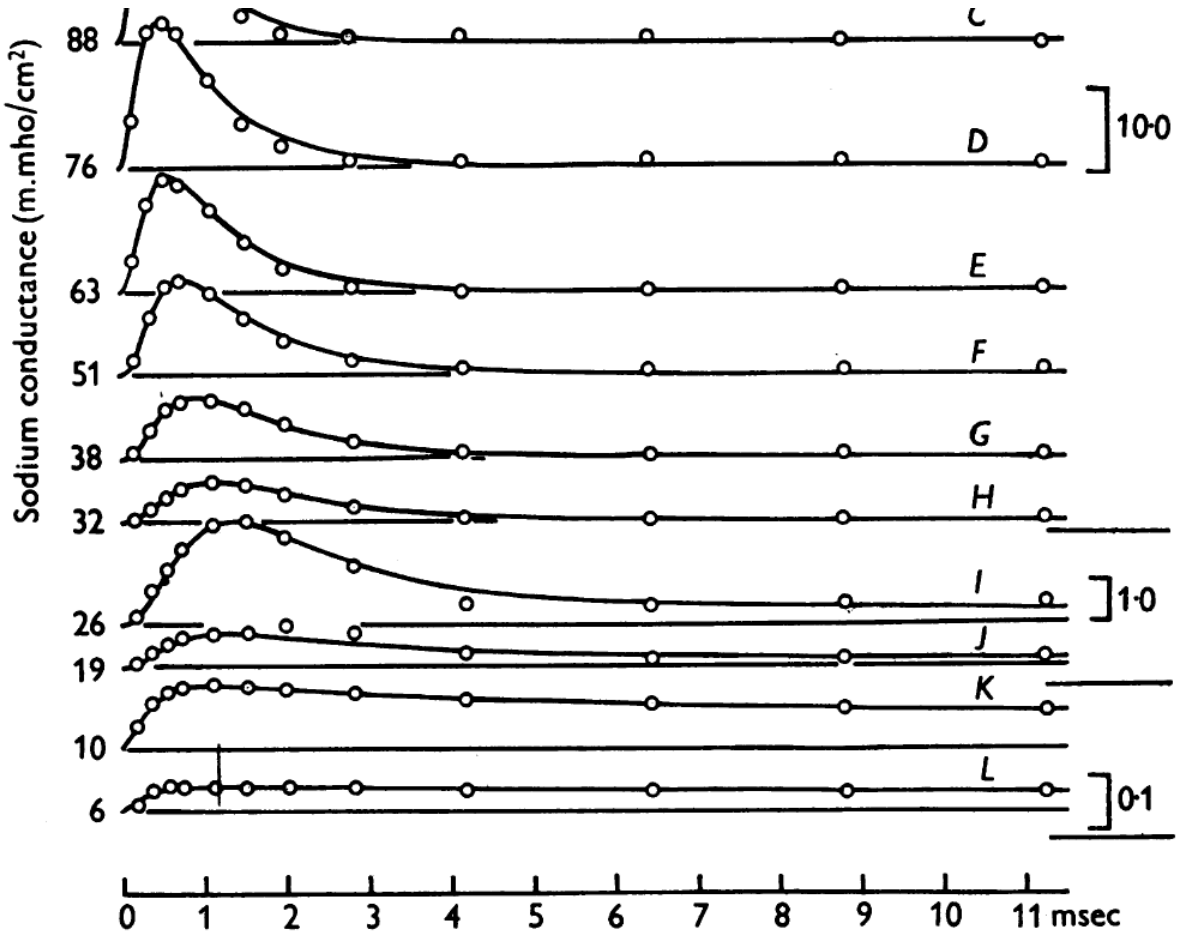


Fig. 6. Changes of sodium conductance associated with different depolarizations. The circles

Step 3

For sodium conductance,

$$g_{Na} = g_{max} m^3 h$$

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

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

1. In the resting state the sodium conductance is very small, We therefore neglect m_0 if the depolarization is greater than 30 mV.

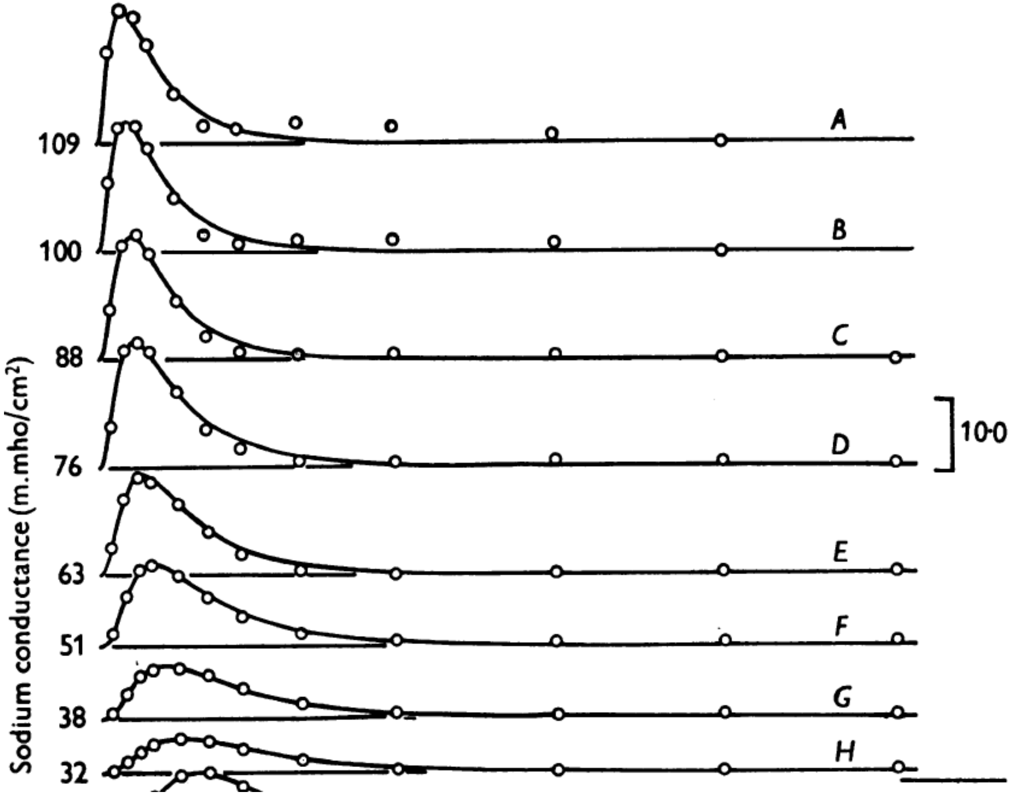
2. Inactivation is very nearly complete if V > 30 mV so that h_∞ may also be neglected.

$$\mathrm{m}(t) = \boldsymbol{m_\infty(V)} + (m_0 - \boldsymbol{m_\infty(V)})e^{-t/\boldsymbol{\tau(V)}}$$

$$\mathrm{h}(t) = \boldsymbol{h_\infty(V)} + (h_0 - \boldsymbol{h_\infty(V)})e^{-t/\boldsymbol{\tau(V)}}$$

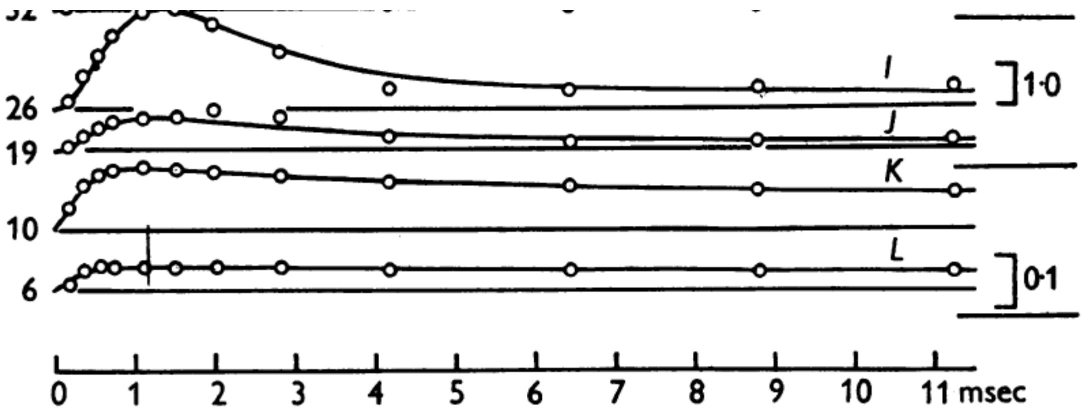
$$g_{Na} = \boldsymbol{g_{max}} \left[1 - \exp\left(-\frac{t}{\boldsymbol{\tau_m}}\right)\right]^3 \exp(-t/\boldsymbol{\tau_h})$$

Fitting curves A to H in to get $\boldsymbol{g_{max}}, \boldsymbol{\tau_m}, \boldsymbol{\tau_h}$



$$g_{Na} = g_{max}\left[\boldsymbol{m_\infty(V)} + (m_0 - \boldsymbol{m_\infty(V)})\exp\left(-\frac{t}{\tau_m}\right)\right]^3 [\boldsymbol{h_\infty(V)} + (h_0 - \boldsymbol{h_\infty(V)})\exp(-t/\tau_h)]$$

Fitting curves I to L in to get $\boldsymbol{m_\infty}$, $\boldsymbol{h_\infty}$



Step 4

Finally, n_∞, τ_n, m_∞, τ_m, h_∞, τ_h

$$\alpha_x = x_\infty/\tau_x$$

$$\beta_x = (1 - x_\infty)/\tau_x$$

The full Hodgkin-Huxley neuron model

$$C\frac{dV}{dt} = -\left(\bar{g}_{Na} m^3 h (V - E_{Na}) + \bar{g}_K n^4 (V - E_K) + g_{leak}(V - E_{leak})\right) + I(t)$$

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

$$\alpha_m = 0.1(V + 40) / \left[1 - \exp\left(\frac{-(V+40)}{10}\right)\right]$$

$$\beta_m = 4.0 \exp\left(\frac{-(V+65)}{18}\right)$$

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

$$\alpha_h = 0.07 exp\left(\frac{-(V+65)}{20}\right)$$

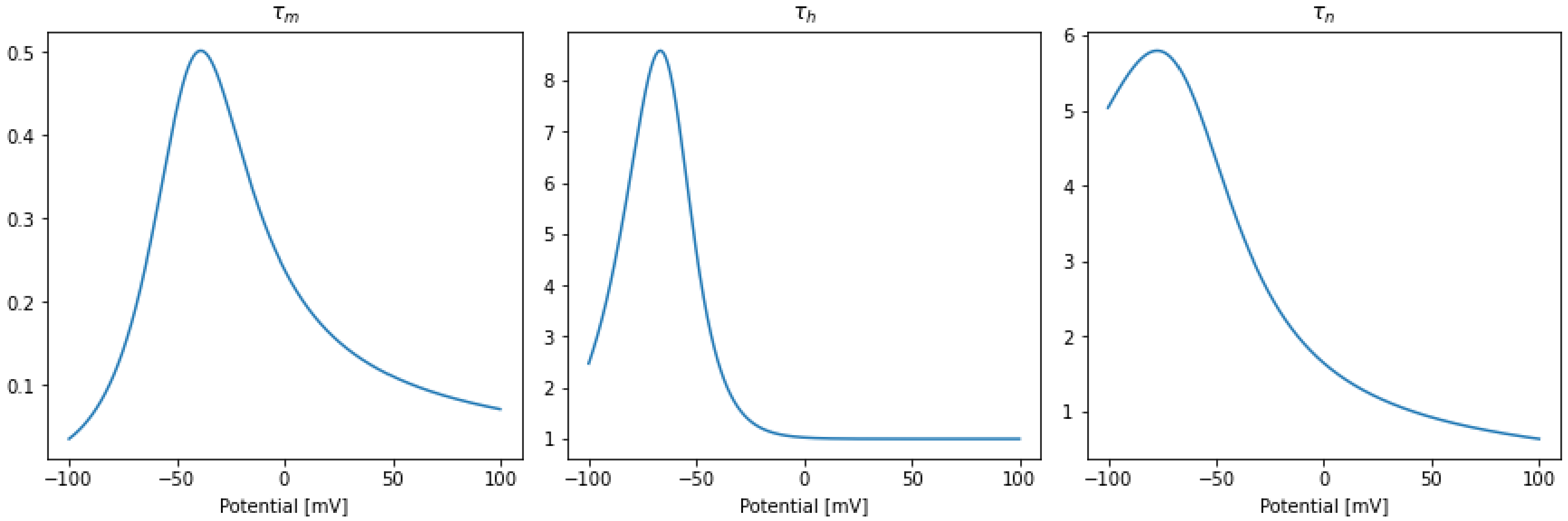
$$\beta_h = 1 / \left[1 + exp\left(\frac{-(V+35)}{10}\right)\right]$$

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

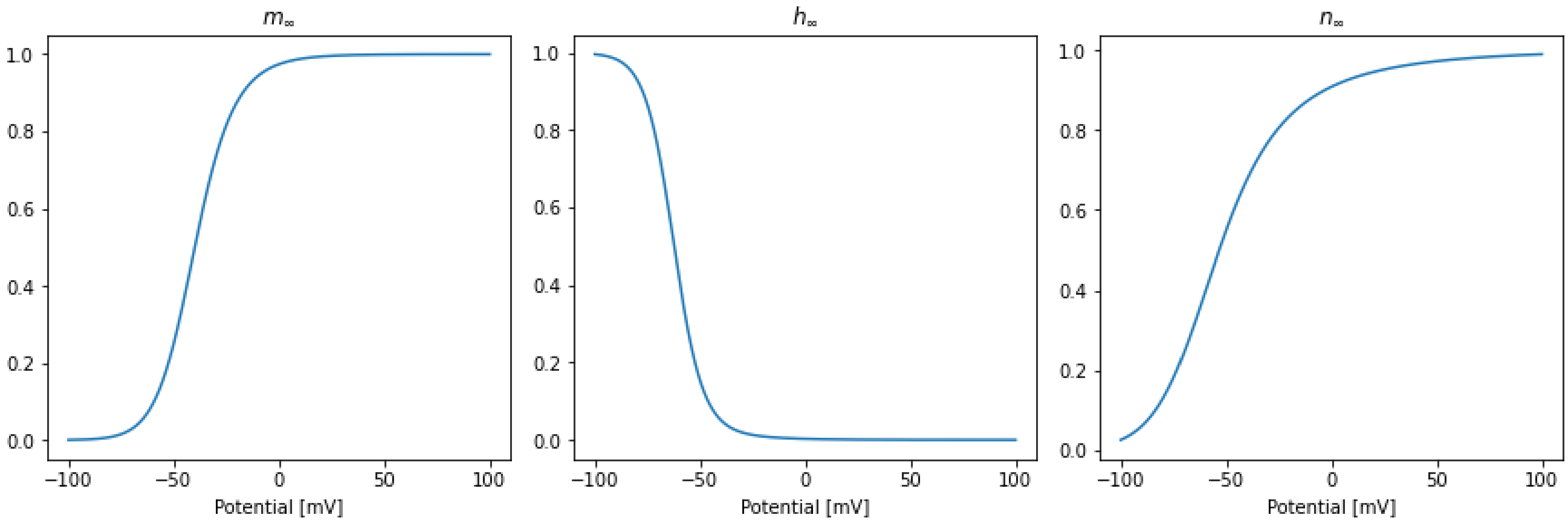
$$\alpha_n = 0.01(V + 55) / [1 - exp(-(V + 55)/10)]$$

$$\beta_n = 0.125 exp\left(\frac{-(V+65)}{80}\right)$$

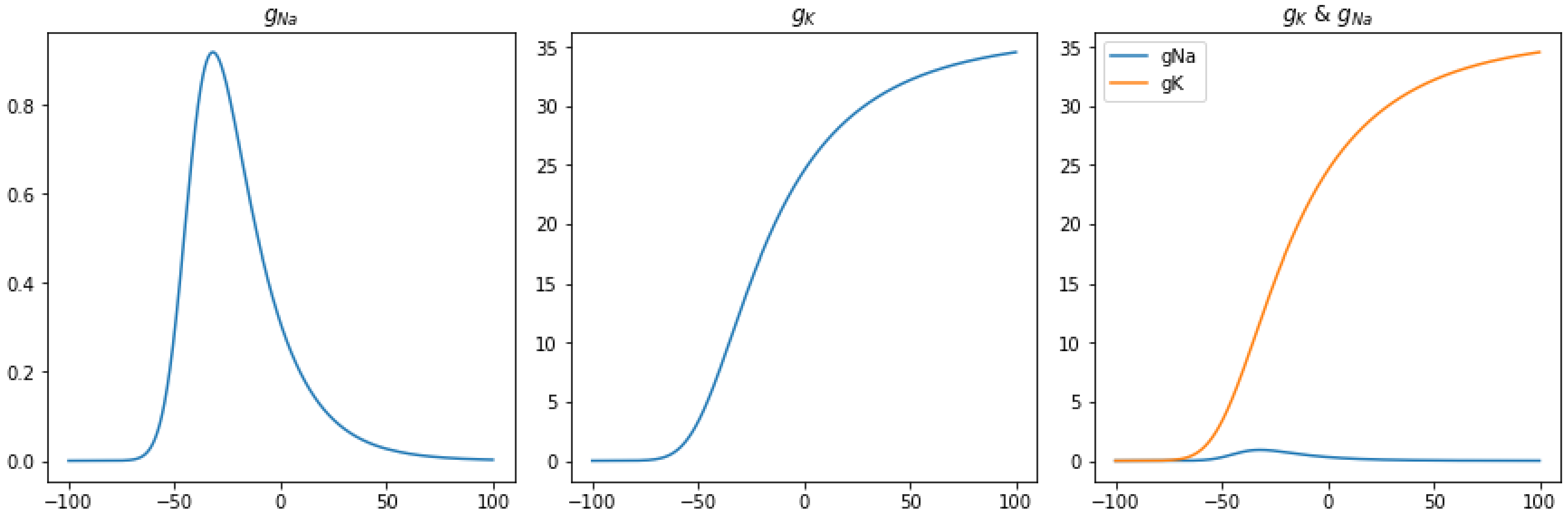
Time Constants



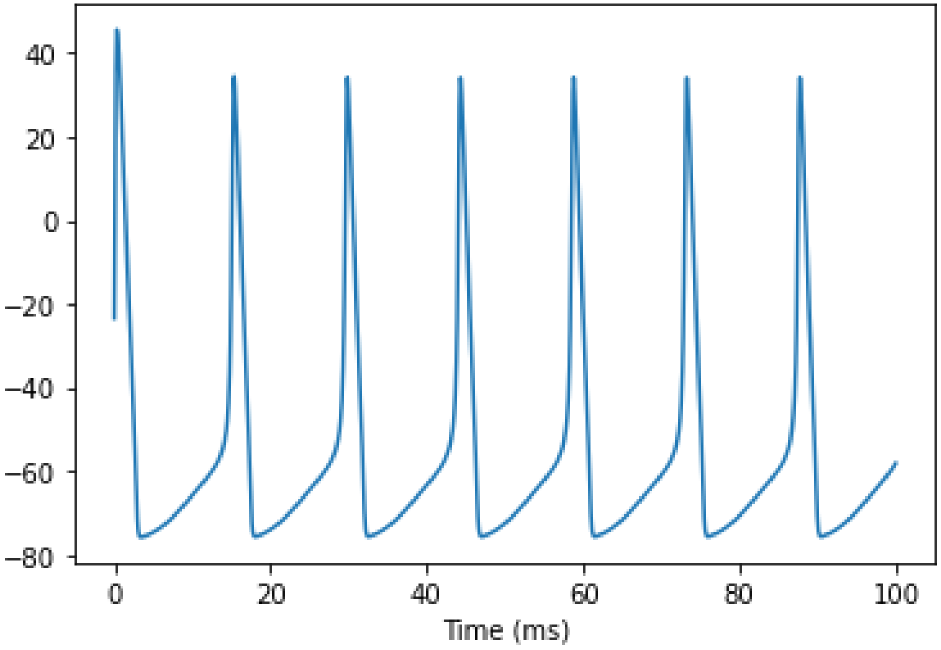
Steady States



Conductance



Membrane potential



The mechanism underlying action potential