Methods of Applied Mathematics II (Math451H): Neuronal Dynamics

The Hodgkin-Huxley equation

Hodgkin & Huxley (1949) demonstrated that:

- The resting membrane of a squid axon is 25 times more permeable to K^+ than to Na^+
- At the peak of an action potential the membrane is 20 times more permeable to Na^+ than to K^+.
- During after - hyperpolarization the membrane permeability to Na^+ is very low and that of K^+ is larger than at rest

Multi-ion electrochemical equilibrium

✓ Major ionic currents:

$I_K = g_K (V - E_K)$ $I_{Na} = g_{Na} (V - E_{Na})$ $I_{Ca} = g_{Ca} (V - E_{Ca})$ $I_{Cl} = g_{Cl} (V - E_{Cl})$

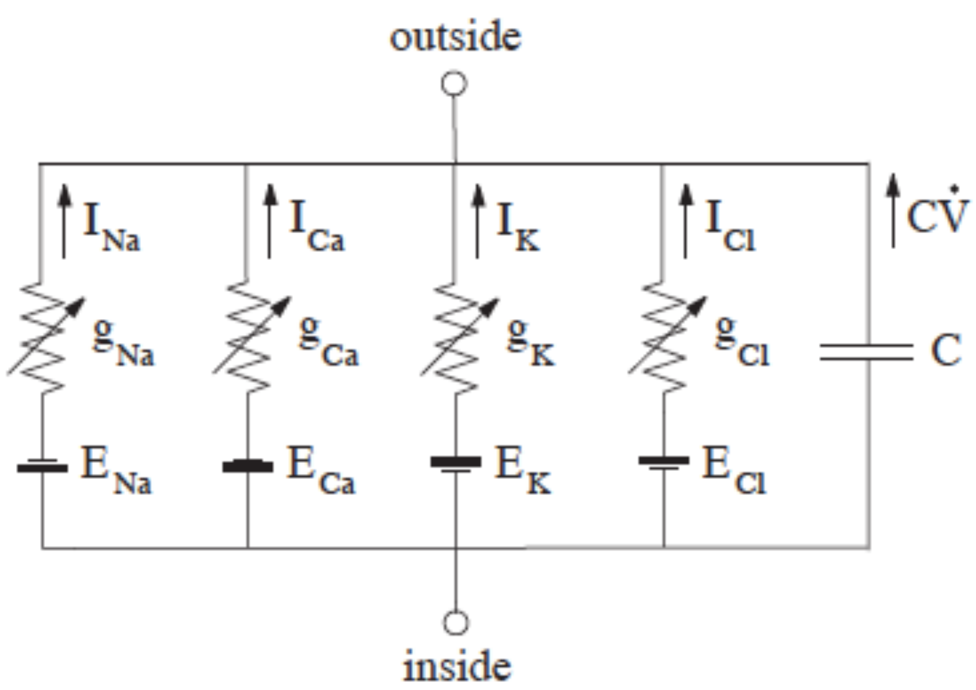


Figure 2.3: Equivalent circuit representation of a patch of cell membrane.

Multi-ion electrochemical equilibrium

Kirchhoff's current law: the total current flowing across a patch of cell membrane is the sum of the membrane capacitive current and all the ionic currents.

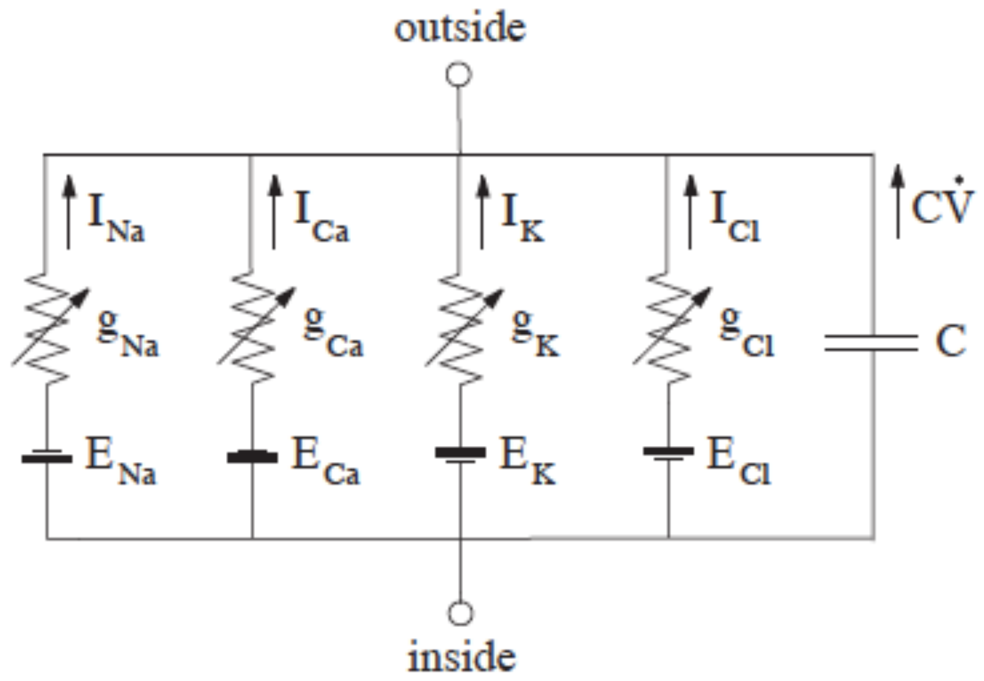


Figure 2.3: Equivalent circuit representation of a patch of cell membrane.

$$C\dot{V} = I - I_{\mathrm{Na}} - I_{\mathrm{Ca}} - I_{\mathrm{K}} - I_{\mathrm{Cl}}$$

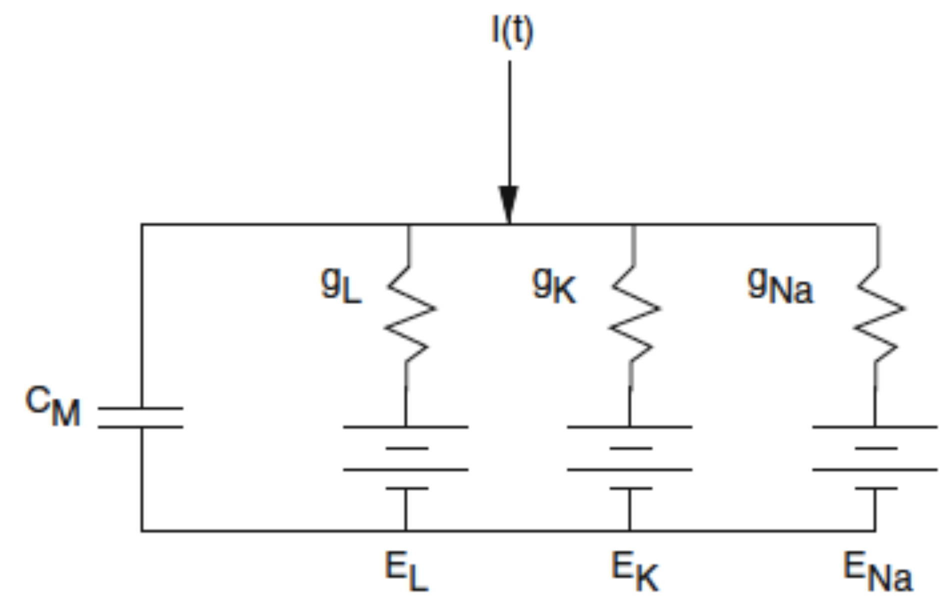
$$C\dot{V} = I - g_{\mathrm{Na}}\,(V - E_{\mathrm{Na}}) - g_{\mathrm{Ca}}\,(V - E_{\mathrm{Ca}}) - g_{\mathrm{K}}\,(V - E_{\mathrm{K}}) - g_{\mathrm{Cl}}\,(V - E_{\mathrm{Cl}})$$

Multi-ion electrochemical equilibrium

✓ Major ionic currents:

$$I_K = g_K (V - E_K) \qquad I_{Na} = g_{Na} (V - E_{Na})$$

Fig. 1.6 Equivalent circuit underlying the Hodgkin–Huxley equations



$$C \frac{dV}{dt} = I \quad -g_{Na}(V - E_{Na}) \quad - g_K(V - E_K) \quad - g_L(V - E_L)$$

Multi-ion electrochemical equilibrium

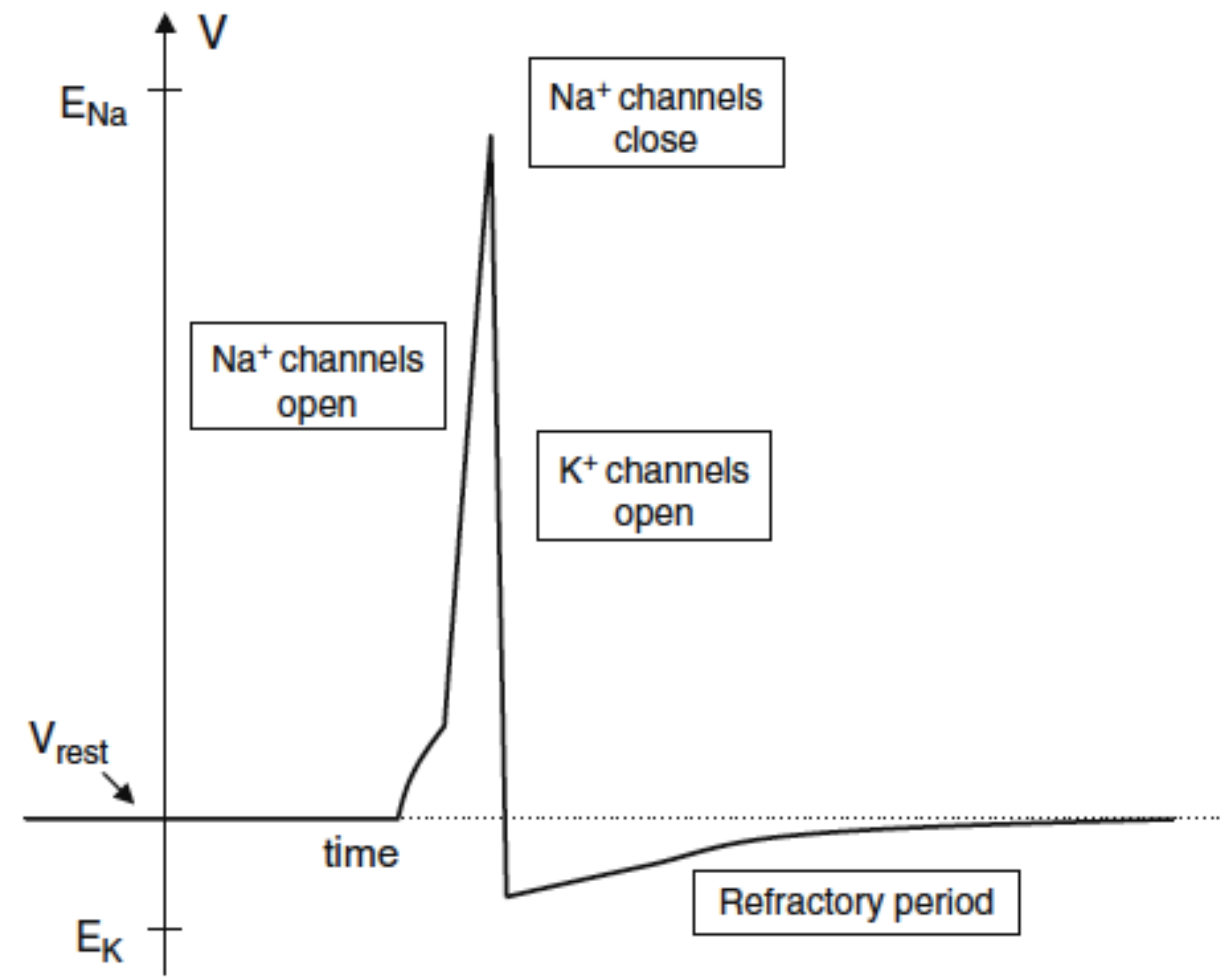


Fig. 1.7 The action potential. During the upstroke, Na^+ channels open and the membrane potential approaches the Na^+ Nernst potential. During the downstroke, Na^+ channels are closed, K^+ channels are open, and the membrane potential approaches the K^+ Nernst potential

$$C \frac{dV}{dt} = I \quad -g_{Na}(V - E_{Na}) \quad - g_K(V - E_K) \quad - g_L(V - E_L)$$

Multi-ion electrochemical equilibrium

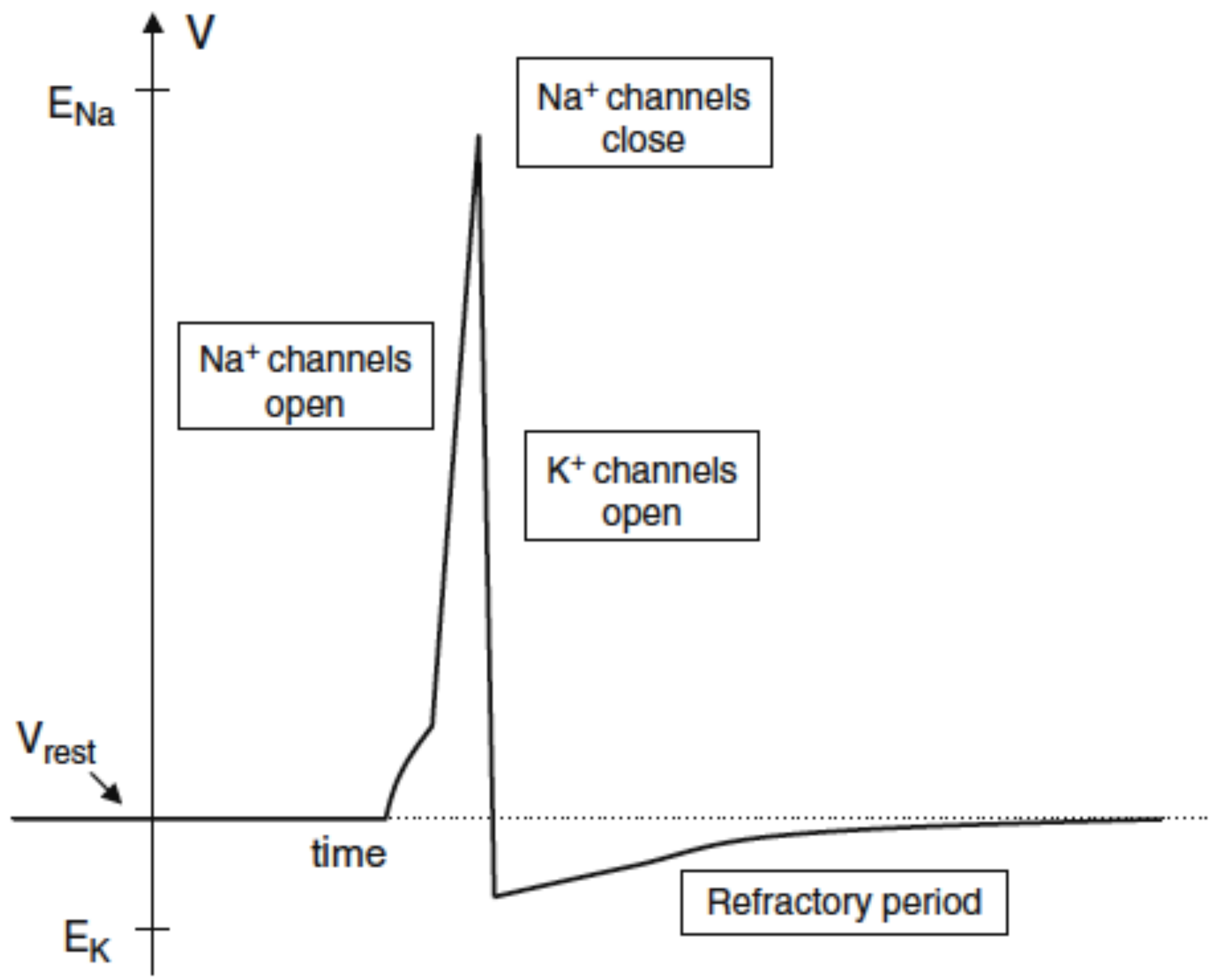
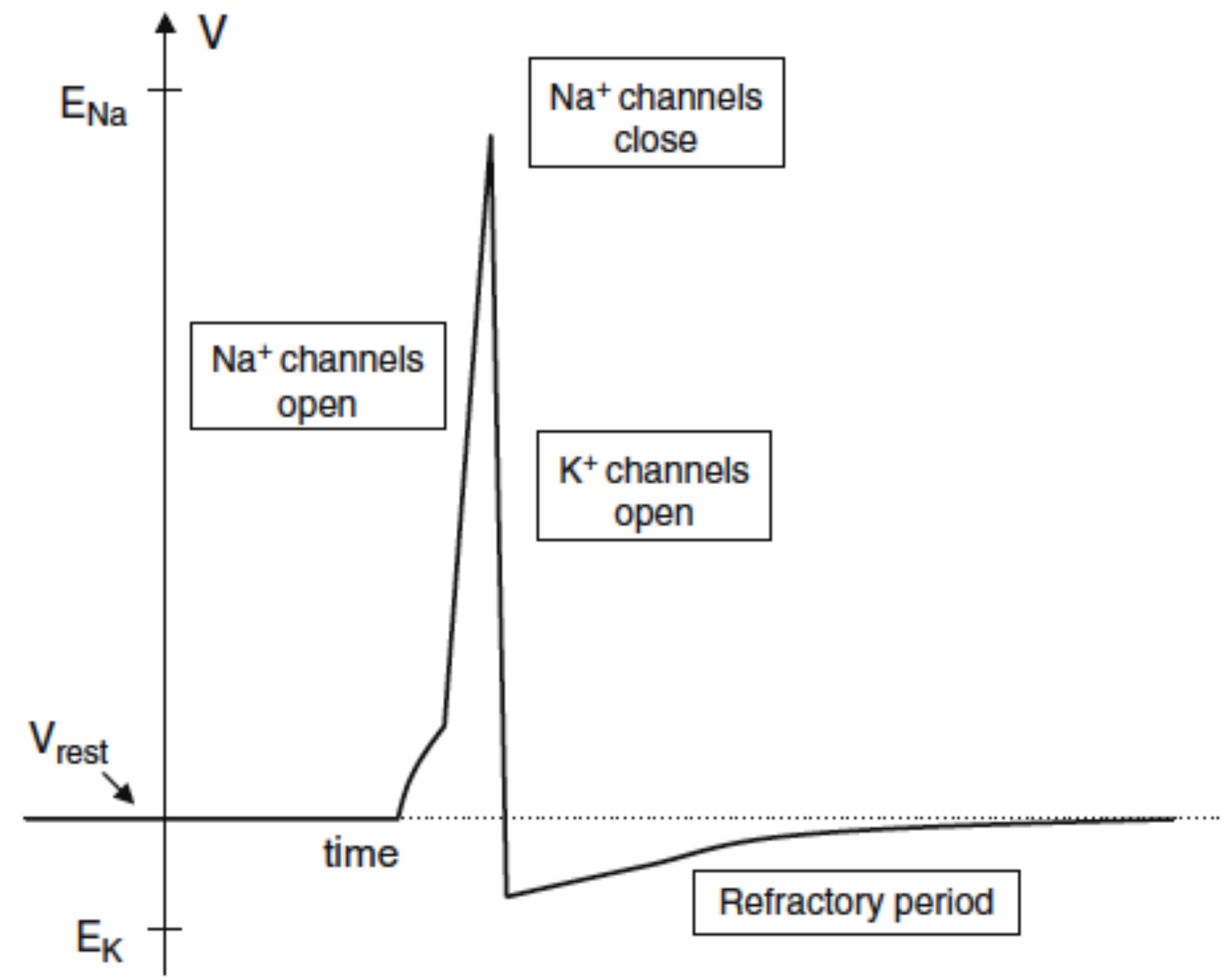


Fig. 1.7 The action potential. During the upstroke, Na^+ channels open and the membrane potential approaches the Na^+ Nernst potential. During the downstroke, Na^+ channels are closed, K^+ channels are open, and the membrane potential approaches the K^+ Nernst potential

$$C\frac{dV}{dt} = I \cancel{-g_{Na}(V - E_{Na})} \cancel{-g_K(V - E_K)} - g_L(V - E_L)$$

Multi-ion electrochemical equilibrium



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$$C\frac{dV}{dt} = I \quad -g_{Na}(V - E_{Na}) \quad - g_K(V - E_K) \quad - g_L(V - E_L)$$

Multi-ion electrochemical equilibrium

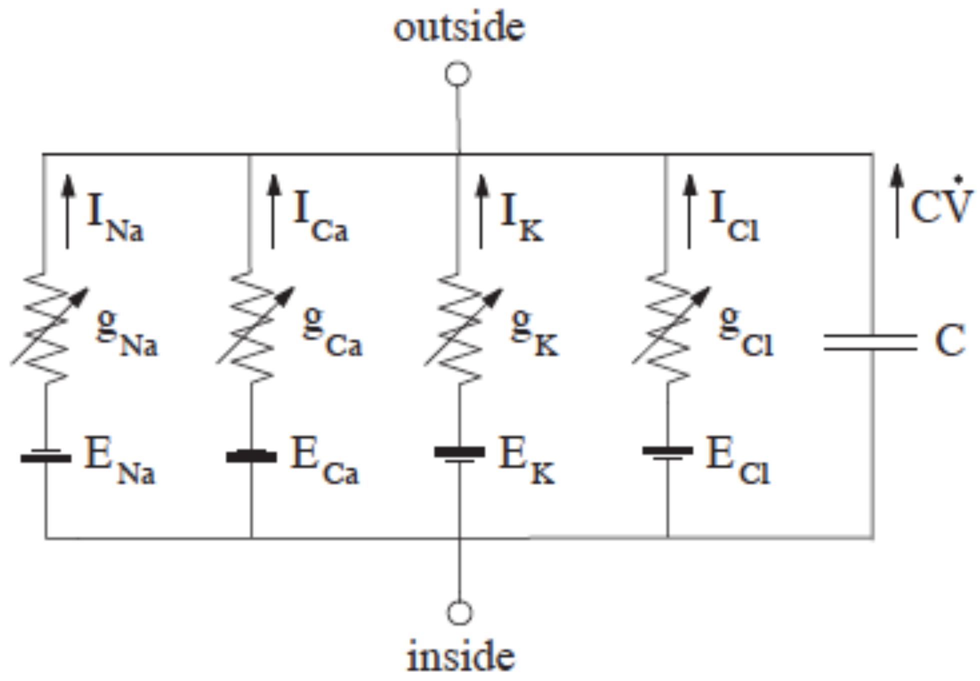


Figure 2.3: Equivalent circuit representation of a patch of cell membrane.

$$C\dot{V} = I - g_{\mathrm{Na}}\left(V - E_{\mathrm{Na}}\right) - g_{\mathrm{Ca}}\left(V - E_{\mathrm{Ca}}\right) - g_{\mathrm{K}}\left(V - E_{\mathrm{K}}\right) - g_{\mathrm{Cl}}\left(V - E_{\mathrm{Cl}}\right)$$

$$C\,\dot{V} = I - g_{\mathrm{inp}}(V - V_{\mathrm{rest}})$$

$$g_{\mathrm{inp}} = g_{\mathrm{Na}} + g_{\mathrm{Ca}} + g_{\mathrm{K}} + g_{\mathrm{Cl}}$$

$$V_{\mathrm{rest}} = \frac{g_{\mathrm{Na}}E_{\mathrm{Na}} + g_{\mathrm{Ca}}E_{\mathrm{Ca}} + g_{\mathrm{K}}E_{\mathrm{K}} + g_{\mathrm{Cl}}E_{\mathrm{Cl}}}{g_{\mathrm{Na}} + g_{\mathrm{Ca}} + g_{\mathrm{K}} + g_{\mathrm{Cl}}}$$

Multi-ion electrochemical equilibrium

$$C\dot{V} = I - g_{\mathrm{Na}}\,(V - E_{\mathrm{Na}}) - g_{\mathrm{Ca}}\,(V - E_{\mathrm{Ca}}) - g_{\mathrm{K}}\,(V - E_{\mathrm{K}}) - g_{\mathrm{Cl}}\,(V - E_{\mathrm{Cl}})$$

$$C\,\dot{V} = I - g_{\mathrm{inp}}(V - V_{\mathrm{rest}})$$

$$V_{\mathrm{rest}} = \frac{g_{\mathrm{Na}}E_{\mathrm{Na}} + g_{\mathrm{Ca}}E_{\mathrm{Ca}} + g_{\mathrm{K}}E_{\mathrm{K}} + g_{\mathrm{Cl}}E_{\mathrm{Cl}}}{g_{\mathrm{Na}} + g_{\mathrm{Ca}} + g_{\mathrm{K}} + g_{\mathrm{Cl}}}$$

$g_{\mathrm{inp}} = g_{\mathrm{Na}} + g_{\mathrm{Ca}} + g_{\mathrm{K}} + g_{\mathrm{Cl}}$ input conductance

$R_{\mathrm{inp}} = 1/g_{\mathrm{inp}}$ input resistance

measures the asymptotic sensitivity of the membrane potential to injected (applied) or intrinsic currents

$$V \to V_{\mathrm{rest}} + I R_{\mathrm{inp}}$$

Multi-ion electrochemical equilibrium

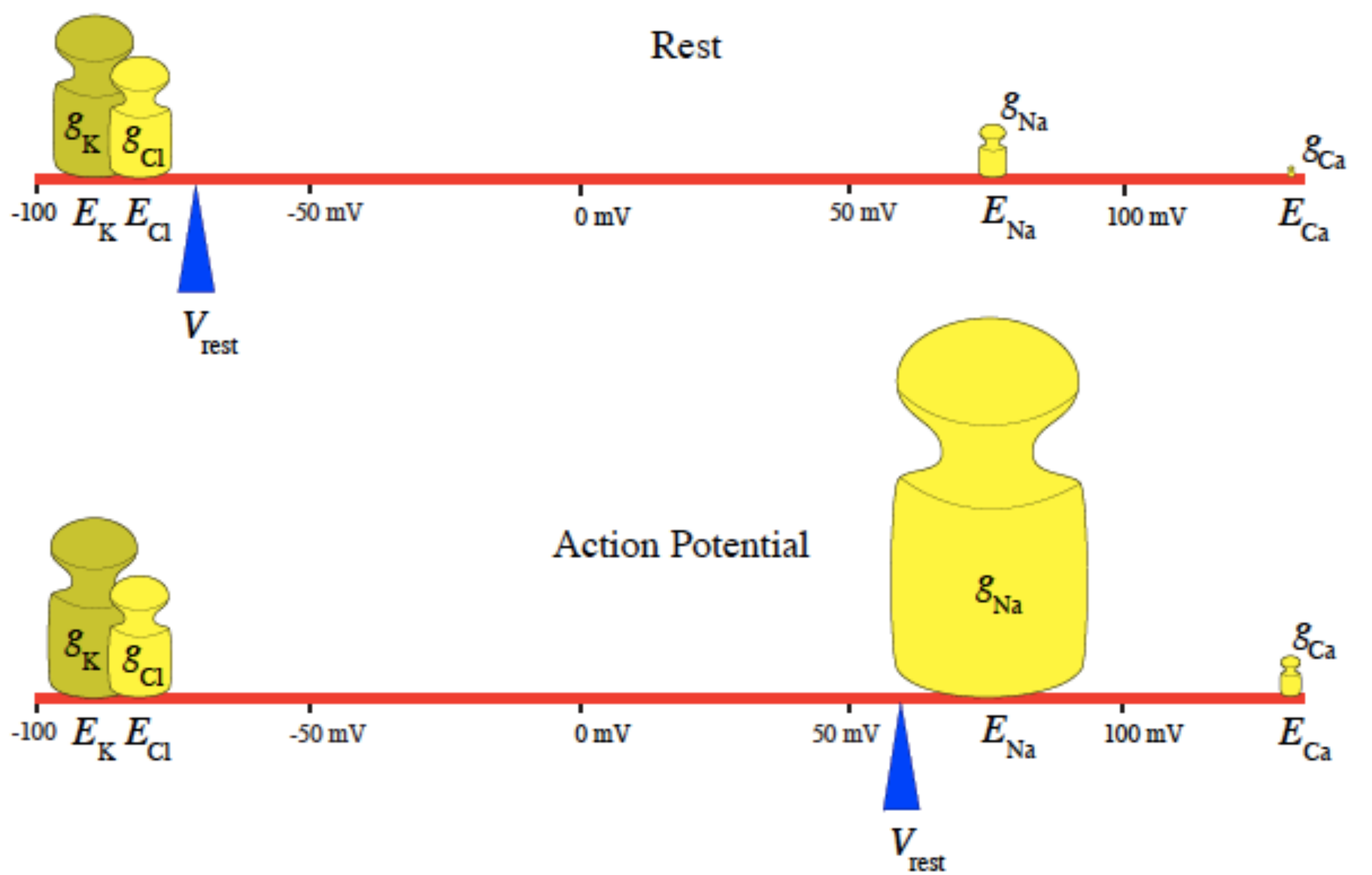


Figure 2.4: Mechanistic interpretation of the resting membrane potential (2.4) as the center of mass. Na^+ conductance increases during the action potential.

Hodgkin-Huxley equations

Ionic channels:

- Transitions between open and closed states in individual channels are stochastic

- However, the net current I generated by a large population or ensemble of identical channels can be reasonably be described by

$$I = G_X \, p \, (V - E_X)$$

p: average proportion of channels in the open state →
G_X: maximal conductance of the population
E_X: reversal potential of the current (potential at which the current reverses its direction)

If the channels are selective for a single ionic species

reversal potential = Nernst potential for that ionic species

Hodgkin-Huxley equations

Ionic channels:

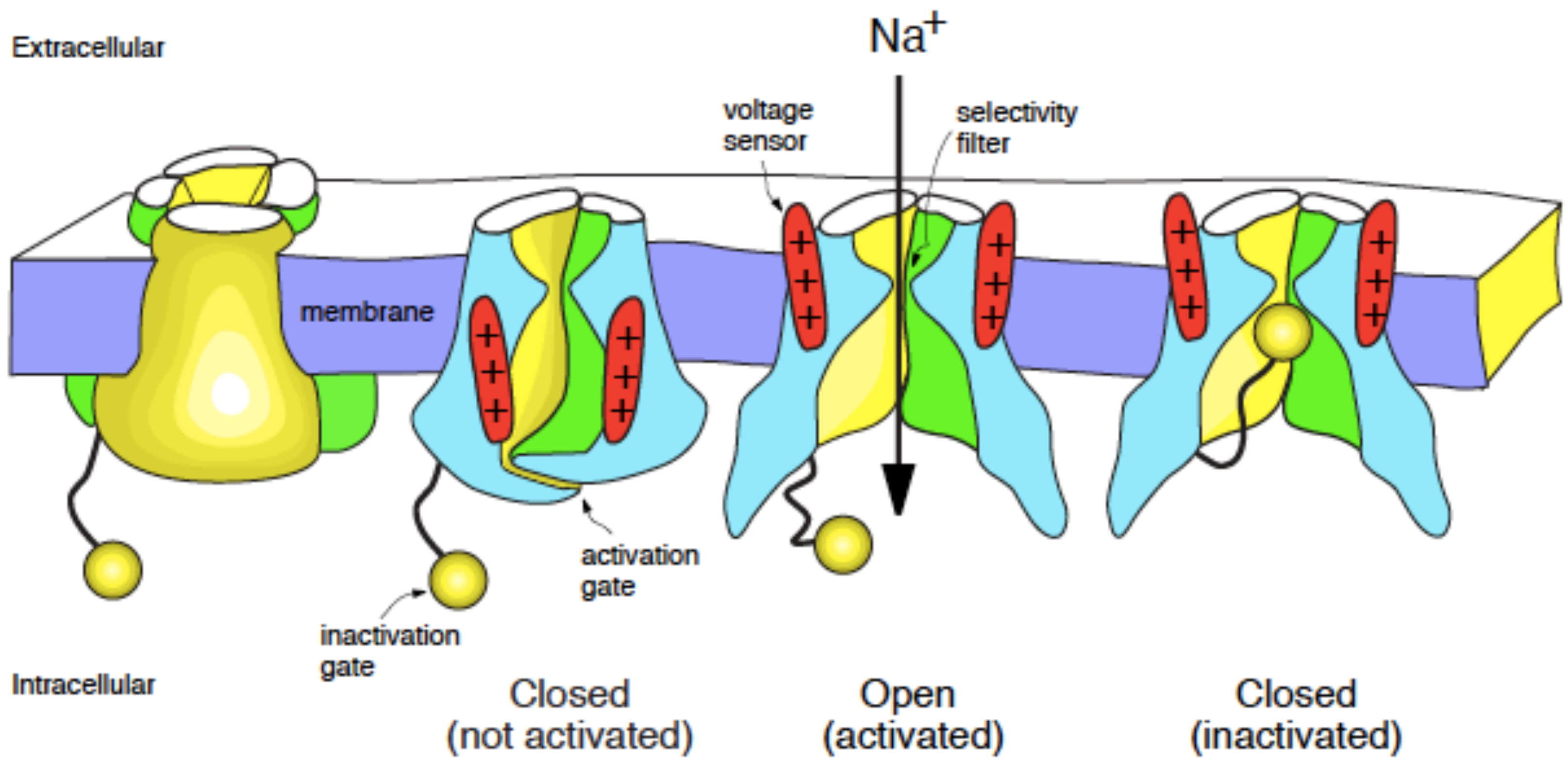


Figure 2.8: Structure of voltage-gated ion channels. Voltage sensors open activation gate and allow selected ions to flow through the channel according to their electrochemical gradients. The inactivation gate blocks the channel (modified from Armstrong and Hille 1998).

Hodgkin-Huxley equations

Voltage-gated ionic channels:

- Activating gates: open the channels
- Inactivating gates: close the channels

$$I = G_X\, p\, (V - E_X)$$

$$p = m^a h^b$$

- $m = 1$: activated
- $m = 0$: deactivated (not activated)
- $h = 1$: inactivated
- $h = 0$: deinactivated (released from inactivation)

Hodgkin-Huxley equations

Voltage-gated ionic channels:

- Activating gates: open the channels
- Inactivating gates: close the channels

$$I = G_X\, p\, (V - E_X)$$

$$p = m^a h^b$$

- persistent currents: do not inactivate (b = 0)
- transient currents: do inactivate

Hodgkin-Huxley equations

Voltage-gated ionic channels: diagram

$$C \underset{\beta(V)}{\overset{\alpha(V)}{\rightleftarrows}} O$$

C: closed states

O: open states

$\alpha(V)$: rate constant at which the gate goes from the closed to the open states

$\beta(V)$: rate constant at which the gate goes from the open to the closed states

Hodgkin-Huxley equations

Voltage-gated ionic channels: diagram

$$C \underset{\beta(V)}{\overset{\alpha(V)}{\rightleftharpoons}} O$$

m: fraction of open gates

1-m: fraction of closed states

$$\frac{dm}{dt} = \alpha(V)(1-m) - \beta(V)m$$

$$\frac{dm}{dt} = (m_\infty(V) - m)/\tau(V)$$

$$m_\infty(V) = \frac{\alpha(V)}{\alpha(V)+\beta(V)} \qquad \tau(V) = \frac{1}{\alpha(V)+\beta(V)}$$

Hodgkin-Huxley equations

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= \alpha_n(V)(1-n) - \beta_n(V) n \\
\dot{m} &= \alpha_m(V)(1-m) - \beta_m(V) m \\
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V) h \, ,
\end{aligned}
$$

$$\alpha_n(V) = 0.01 \frac{10 - V}{\exp(\frac{10-V}{10}) - 1}$$

$$\alpha_m(V) = 0.1 \frac{25 - V}{\exp(\frac{25-V}{10}) - 1}$$

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

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

$$\beta_m(V) = 4 \exp\left(\frac{-V}{18}\right)$$

$$\beta_h(V) = \frac{1}{\exp(\frac{30-V}{10}) + 1}$$

Hodgkin-Huxley equations

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= (n_\infty(V) - n)/\tau_n(V)\,, \\
\dot{m} &= (m_\infty(V) - m)/\tau_m(V)\,, \\
\dot{h} &= (h_\infty(V) - h)/\tau_h(V)\,,
\end{aligned}
$$

$$
\begin{aligned}
n_\infty &= \alpha_n/(\alpha_n + \beta_n)\,, & \tau_n &= 1/(\alpha_n + \beta_n)\,, \\
m_\infty &= \alpha_m/(\alpha_m + \beta_m)\,, & \tau_m &= 1/(\alpha_m + \beta_m)\,, \\
h_\infty &= \alpha_h/(\alpha_h + \beta_h)\,, & \tau_h &= 1/(\alpha_h + \beta_h)
\end{aligned}
$$

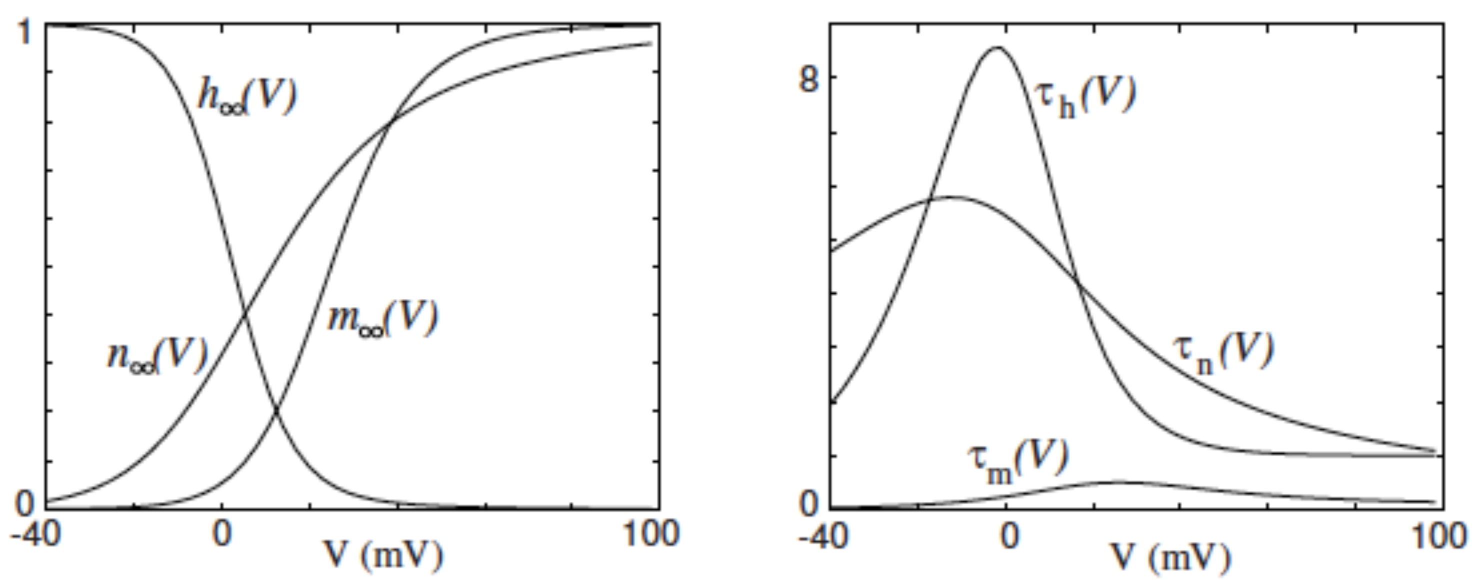


Figure 2.13: Steady-state (in)activation functions (left) and voltage-dependent time constants (right) in the Hodgkin-Huxley model.

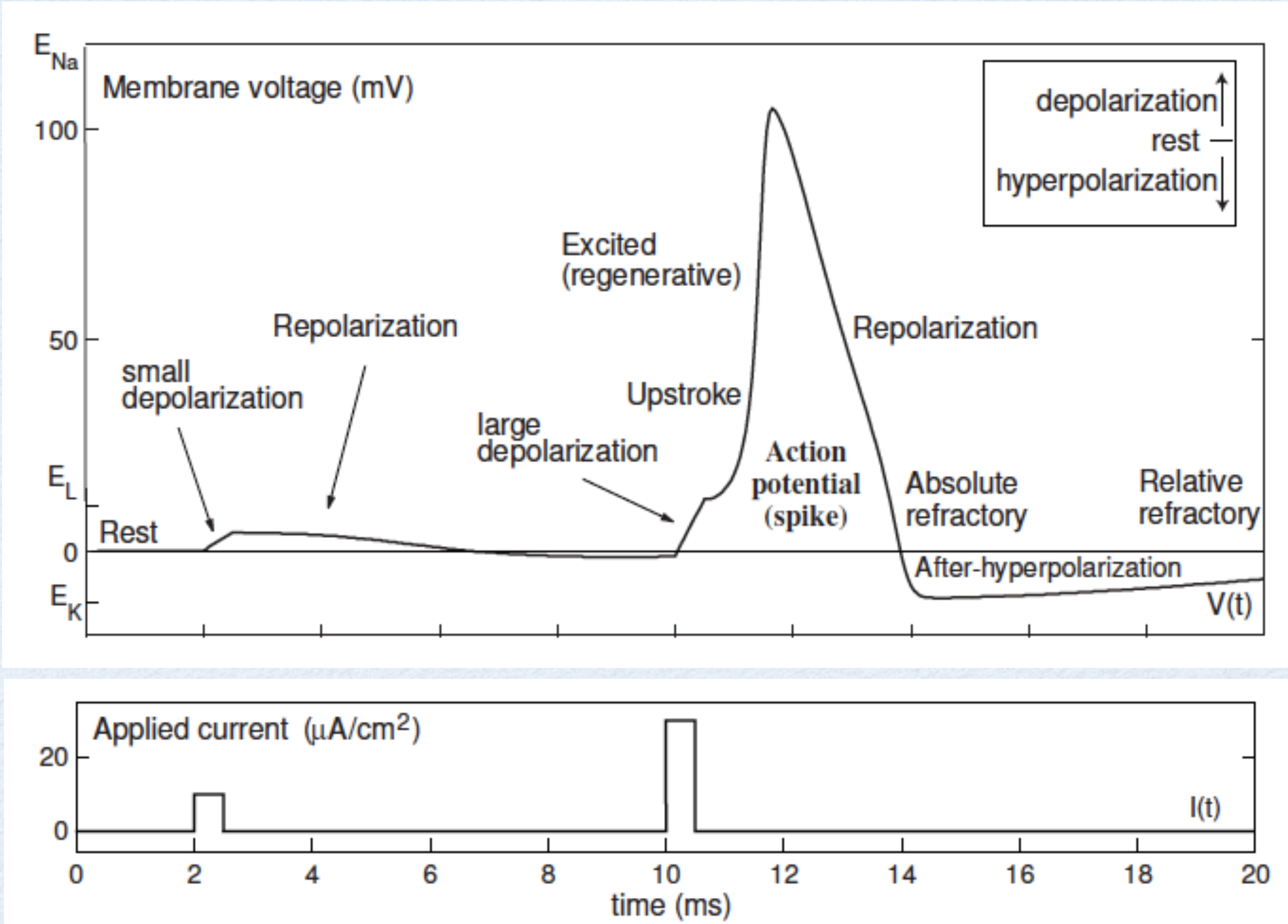
Hodgkin-Huxley equations

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}} (V - E_{\mathrm{L}})}^{I_{\mathrm{L}}} \\
\dot{n} &= \alpha_n(V)(1-n) - \beta_n(V) n \\
\dot{m} &= \alpha_m(V)(1-m) - \beta_m(V) m \\
\dot{h} &= \alpha_h(V)(1-h) - \beta_h(V) h \,,
\end{aligned}
$$

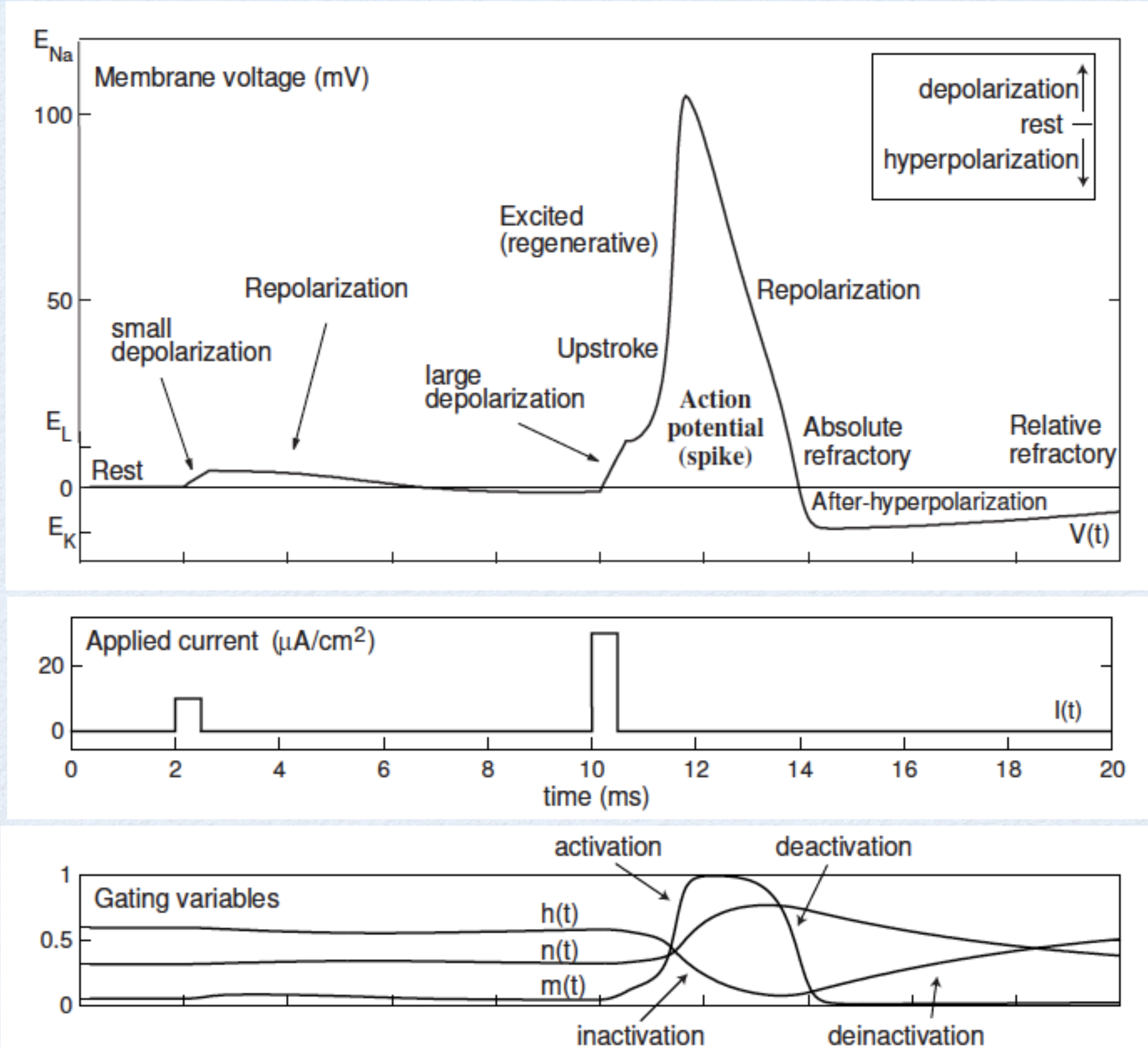
$E_{\mathrm{K}} = -12\ \mathrm{mV}$ $\quad$ $E_{\mathrm{Na}} = 120\ \mathrm{mV}$ $\quad$ $E_{\mathrm{L}} = 10.6\ \mathrm{mV}$

$\bar{g}_{\mathrm{K}} = 36\ \mathrm{mS/cm^2}$ $\quad$ $\bar{g}_{\mathrm{Na}} = 120\ \mathrm{mS/cm^2}$ $\quad$ $g_{\mathrm{L}} = 0.3\ \mathrm{mS/cm^2}$

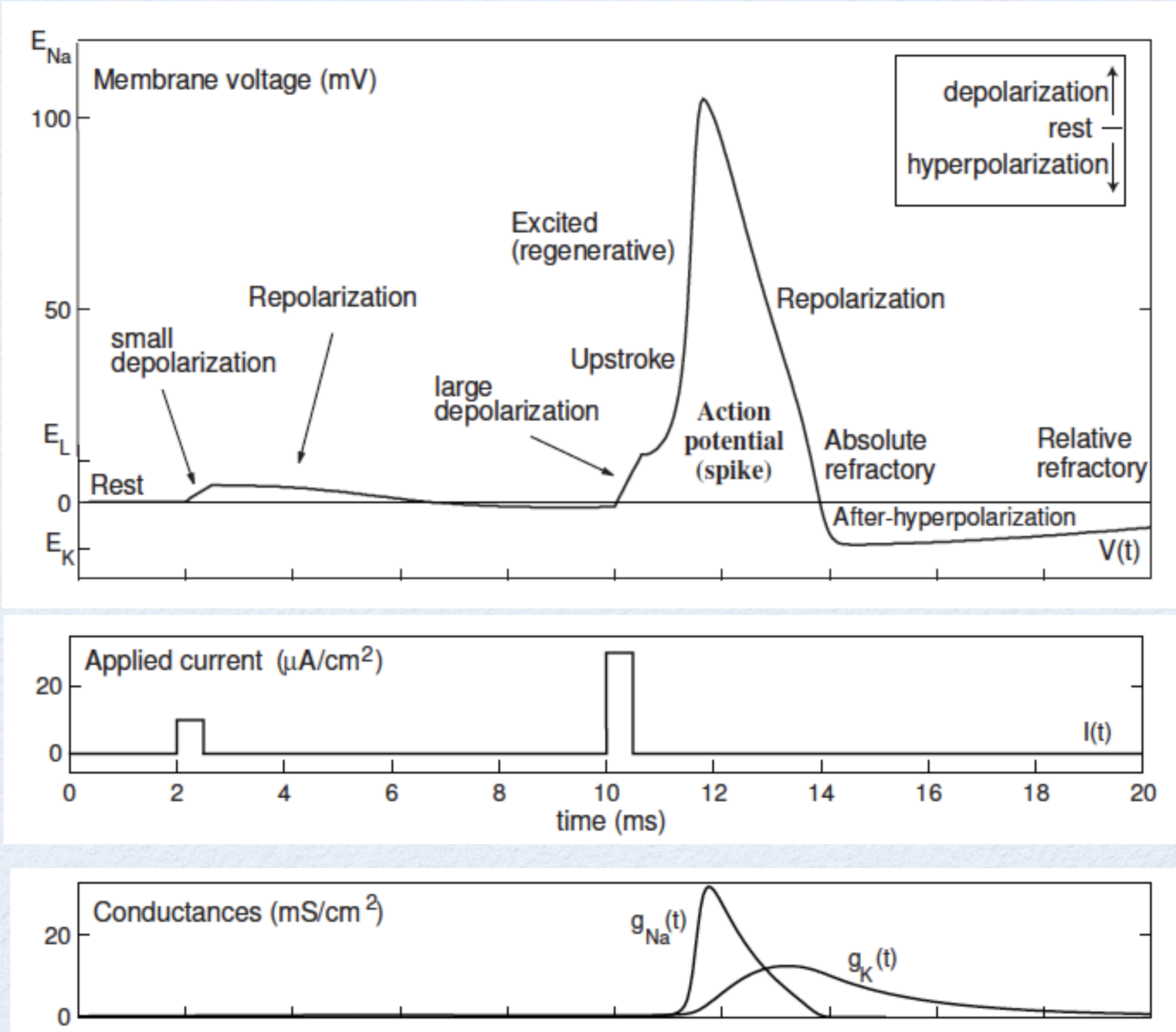
Hodgkin-Huxley equations



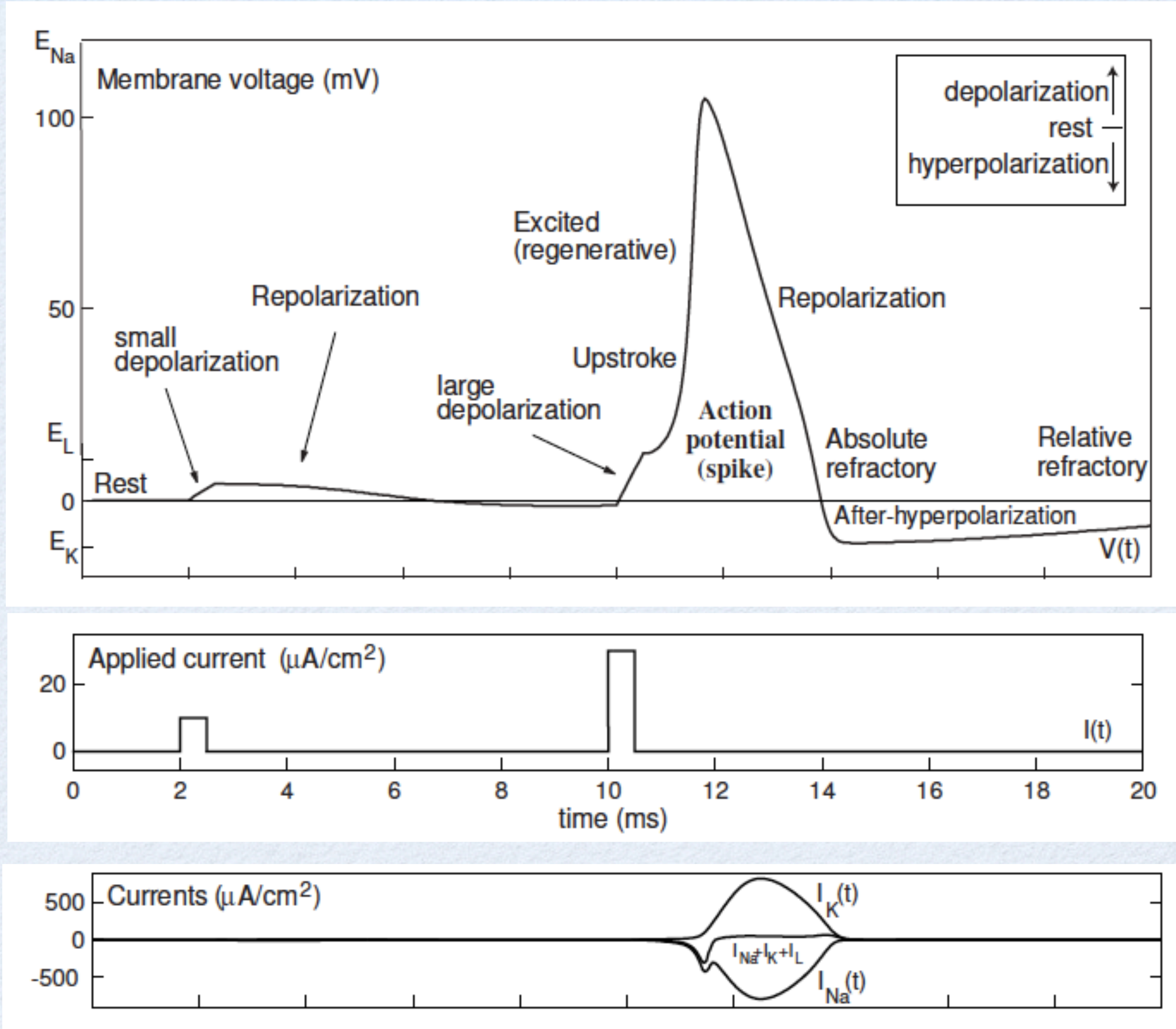
Hodgkin-Huxley equations



Hodgkin-Huxley equations

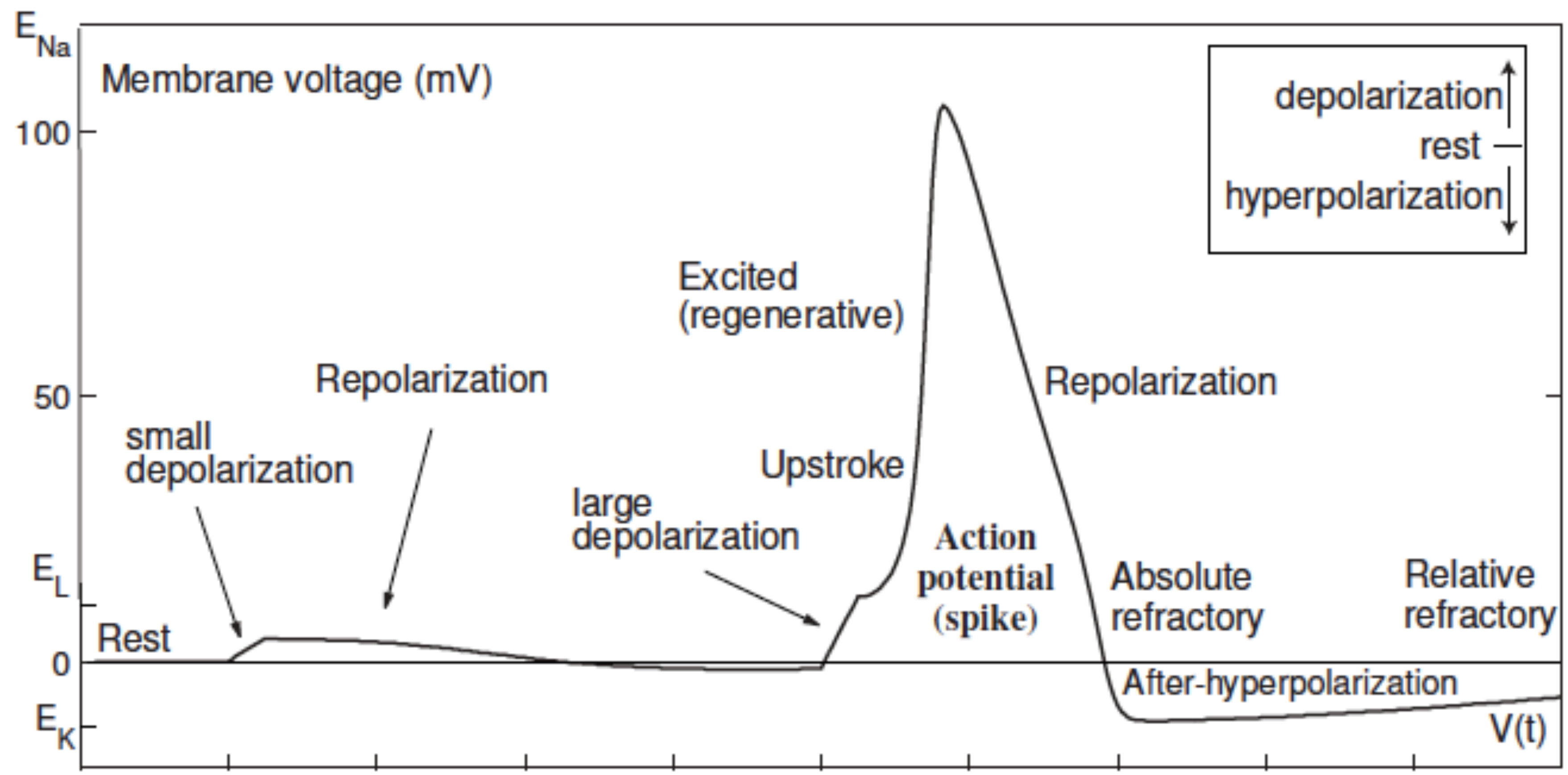


Hodgkin-Huxley equations



Hodgkin-Huxley equations

Action potential:



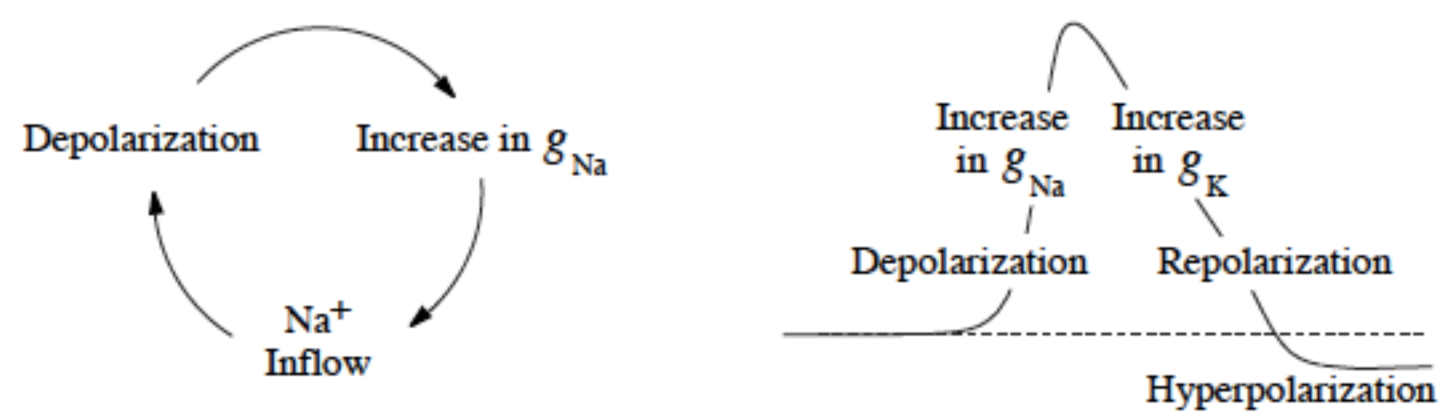


Figure 2.16: Positive and negative feedback loops resulting in excited (regenerative) behavior in neurons.