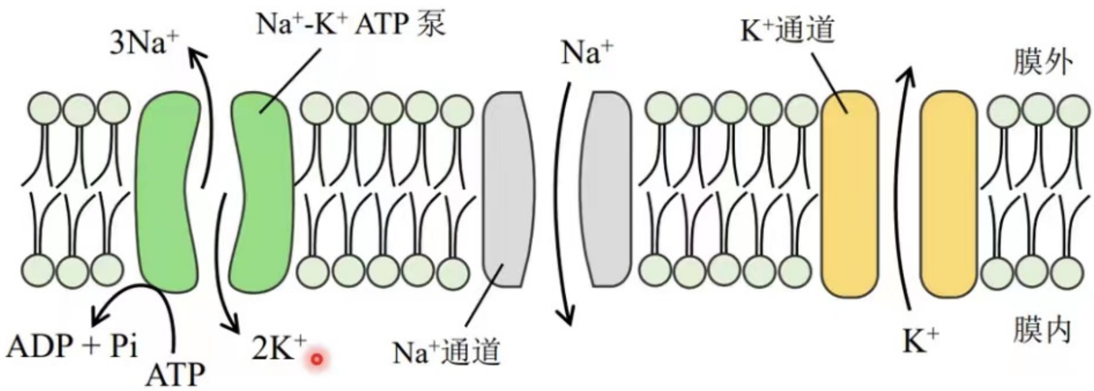
Single Neuron Modeling: Conductance-Based models

Neuronal structure,resting potential,and equivalent circuits

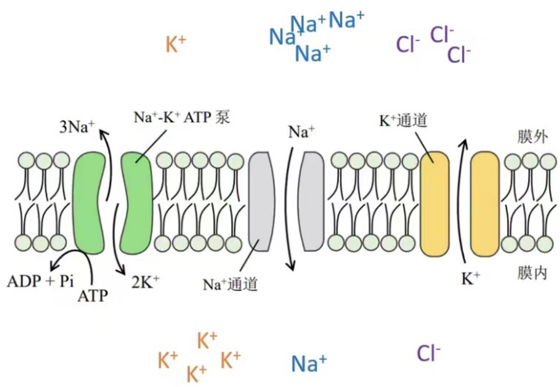
- Components pf a neuron
  - cell body/soma
  - Synapse
  - Axon
  - Dendrite
- Resting potential
  - Ion channels
  - Ion pumps
  - 

  - Ion concentration difference → chemical gradient → electrocal gradient
    - Nernst Equation:

$$E = \frac{RT}{zF} \ln \frac{[\text{ion}]_{\text{out}}}{[\text{ion}]_{\text{in}}}$$

    - Goldman-Hodgkin-Katz (GHK) Equation:

$$V_m = \frac{RT}{F} \ln \left(\frac{P_{\text{Na}}[\text{Na}^+]_{\text{out}} + P_{\text{K}}[\text{K}^+]_{\text{out}} + P_{\text{Cl}}[\text{Cl}^-]_{\text{in}}}{P_{\text{Na}}[\text{Na}^+]_{\text{in}} + P_{\text{K}}[\text{K}^+]_{\text{in}} + P_{\text{Cl}}[\text{Cl}^-]_{\text{out}}} \right)$$

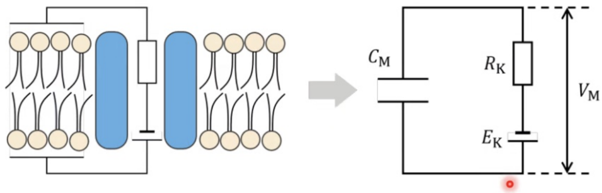
  - 

- Equivalent circuits
  - components of an equivalet circuit
    - battery(离子浓度差)
    - Capacitor(细胞膜)
    - Resisitor(离子通道)

Considering the potassium channel **ONLY**:

$$0 = I_{\text{cap}} + I_K = c_M \frac{dV_M}{dt} + \frac{V_M - E_K}{R_K},$$

$$c_M \frac{dV_M}{dt} = -\frac{V_M - E_K}{R_K} = -g_K(V_M - E_K).$$



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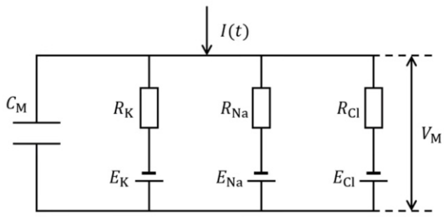
Considering the Na⁺, K⁺, and Cl⁻ channels and the external current $I(t)$:

$$\frac{I(t)}{A} = c_M \frac{dV_M}{dt} + i_{\text{ion}}$$

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



Steady-state membrane potential given a constant current input I:

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

$$V_{ss} = \frac{g_{\text{Cl}}E_{\text{Cl}} + g_K E_K + g_{\text{Na}}E_{\text{Na}} + I/A}{g_{\text{Cl}} + g_K + g_{\text{Na}}} \xrightarrow{I=0} V_{ss,I=0} = E_R = \frac{g_{\text{Cl}}E_{\text{Cl}} + g_K E_K + g_{\text{Na}}E_{\text{Na}}}{g_{\text{Cl}} + g_K + g_{\text{Na}}}$$

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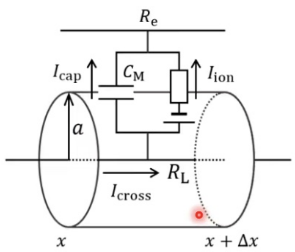
Cable Theory & passive conduction

- Cable theory
  - How electrical signals are transmitted along a single neuron(an axon)

Considering the axon as a long cylindrical cable:

$$\boxed{I_{\text{cross}}(x,t)} = \boxed{I_{\text{cross}}(x+\Delta x,t)} + \boxed{I_{\text{ion}}(x,t)} + \boxed{I_{\text{cap}}(x,t)}$$



$$V(x+\Delta x,t) - V(x,t) = -I_{\text{cross}}(x,t)R_L = -I_{\text{cross}}(x,t)\frac{\Delta x}{\pi a^2}\rho_L$$

$$\boxed{I_{\text{cross}}(x,t)} = -\frac{\pi a^2}{\rho_L}\frac{\partial V(x,t)}{\partial x}$$

$$\boxed{I_{\text{ion}}} = (2\pi a \Delta x) i_{\text{ion}}$$

$$\boxed{I_{\text{cap}}(x,t)} = (2\pi a \Delta x) c_M \frac{\partial V(x,t)}{\partial t}$$

$$(2\pi a \Delta x) c_M \frac{\partial V(x,t)}{\partial t} + (2\pi a \Delta x) i_{\text{ion}} = \frac{\pi a^2}{\rho_L}\frac{\partial V(x+\Delta x,t)}{\partial x} - \frac{\pi a^2}{\rho_L}\frac{\partial V(x,t)}{\partial x}$$

$$c_M \frac{\partial V(x,t)}{\partial t} = \frac{a}{2\rho_L}\frac{\partial^2 V(x,t)}{\partial x^2} - i_{\text{ion}}$$

Cable Equation

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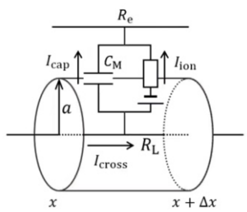
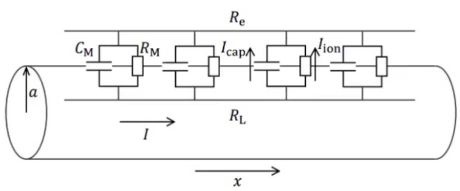
Passive conduction: ion currents are caused by leaky channels exclusively

$$i_{\text{ion}} = V(x,t)/r_M \Rightarrow c_M \frac{\partial V(x,t)}{\partial t} = \frac{a}{2\rho_L}\frac{\partial^2 V(x,t)}{\partial x^2} - \frac{V(x,t)}{r_M}$$

$$\tau \frac{\partial V(x,t)}{\partial t} = \lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2} - V(x,t) \qquad \lambda = \sqrt{0.5 a r_M/\rho_L}$$



If a constant external current is applied to $x = 0$
the steady-state membrane potential $V_{ss}(x)$ is



$$\lambda^2 \frac{d^2 V_{ss}(x)}{dx^2} - V_{ss}(x) = 0 \xrightarrow{I_{\text{cross}}(0,t) = I_0} V_{ss}(x) = \frac{\lambda \rho_L}{\pi a^2} I_0 e^{-x/\lambda}$$

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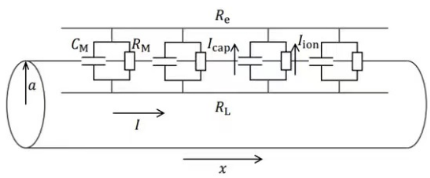
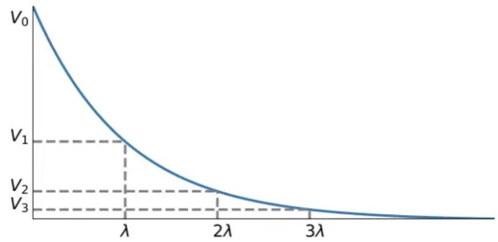
Passive conduction: ion currents are caused by leaky channels exclusively

$$V_{ss}(x) = \frac{\lambda \rho_L}{\pi a^2} I_0 e^{-x/\lambda}$$





Action potential & active transport

- How to transmit electrical signal with less or no decay
- Steps of an action potential:
  - Depolaritzation
  - Repolarization
  - Hyperpolarization
  - resting
- Charactertics:
  - All or none
  - Fixed shape
  - Active electrical property
- Action potential
  - mechanism:voltage-gated ion channels
    - 去极化(Na离子通道变多)，过极化(钾离子通道变多)
- Nodes of Ranvier
  - Saltatory conduction with a much higher speed and less energy consumption

The Hodgkin-Huxley model

- modeling of ion channels
  - modeling of each channel:$g_m = \bar{g}_m m^x$
  - Modeling of each ion gate:

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

(closed) (open)

$1 - m$ m

Gating variable

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

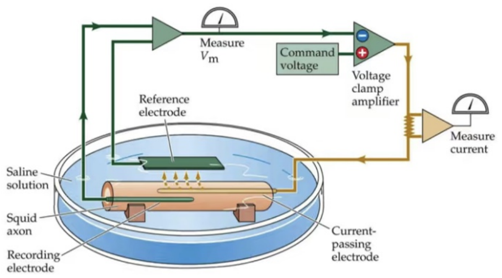
$$m_\infty(V) = \frac{\alpha(V)}{\alpha(V)+\beta(V)}$$

$$\tau_m(V) = \frac{1}{\alpha(V)+\beta(V)}$$

If V is constant: $m(t) = m_\infty(V) + (m_0 - m_\infty(V))e^{-t/\tau_m(V)}$

  - Voltage clamp(快速改变并稳定膜电位)

$$\frac{I(t)}{A} = c_M \frac{dV_M}{dt} + i_{ion}$$
$$\Rightarrow \quad c_M \frac{dV_M}{dt} = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na}) + \frac{I(t)}{A}$$



- The membrane potential is kept constant
- The current from capacitors is excluded
- Currents must come from leaky/voltage-gated ion channels

$$I_{cap} = c\frac{dV}{dt} = 0$$
$$I_{fb} = \quad i_{ion} = g_{Na}(V - E_{Na}) + g_K(V - E_K) + g_L(V - E_L)$$

- leaky channels

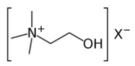
  Hyperpolarization → the sodium and potassium channels are closed

$$I_{fb} = g_{Na}(V - E_{Na}) + g_K(V - E_K) + g_L(V - E_L)$$
$$\Downarrow$$
$$I_{fb} = g_L(V - E_L)$$

$$g_L = 0.3\,\mathrm{mS/cm^2},\ E_L = -54.4\,\mathrm{mV}$$

- Potassium and sodium channels

  Potassium channels: Use choline to eliminate the inward current of Na^+
  Na^+ current: $I_{fb} - I_K$



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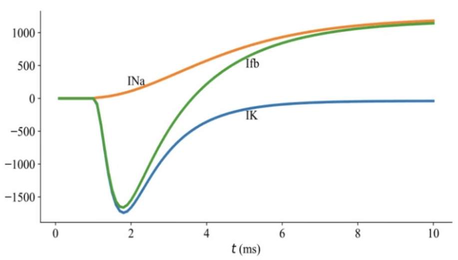
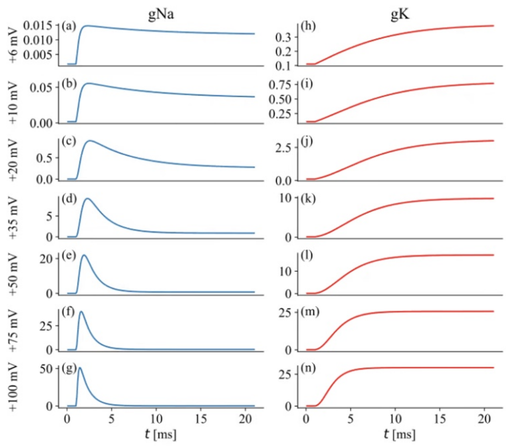




Potassium channels

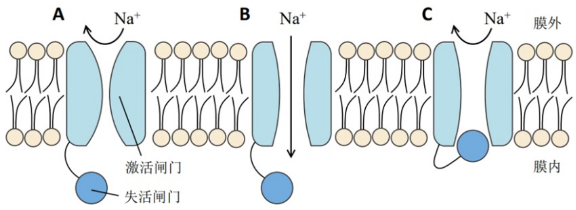
- Resting state (gate closed)
- Activated state (gate open)

Activation gate: $g_K = \bar{g}_K n^x$

Sodium channels

- Resting state (gate closed)
- Activated state (gate open)
- Inactivated state (gate blocked)

Activation gate + inactivation gate: $g_{Na} = \bar{g}_{Na} m^3 h$



The gates of sodium channels

Modeling of each ion gate:

$$g_K = \bar{g}_K n^x$$
$$g_{Na} = \bar{g}_{Na} m^3 h$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n$$
$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m$$
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

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

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

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

- HH model

The Hodgkin-Huxley (HH) Model

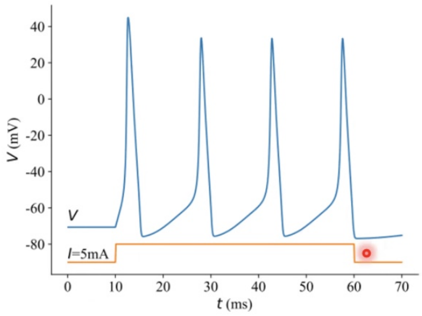
$$c_M \frac{dV_M}{dt} = -g_{Cl}(V_M - E_{Cl}) - g_K(V_M - E_K) - g_{Na}(V_M - E_{Na}) + \frac{I(t)}{A}$$

$$\begin{cases} c\dfrac{dV}{dt} = -\bar{g}_{Na} m^3 h\,(V - E_{Na}) - \bar{g}_K n^4\,(V - E_K) - \bar{g}_L\,(V - E_L) + I_{ext}, \\ \dfrac{dn}{dt} = \phi\,[\alpha_n(V)(1-n) - \beta_n(V)n] \\ \dfrac{dm}{dt} = \phi\,[\alpha_m(V)(1-m) - \beta_m(V)m], \\ \dfrac{dh}{dt} = \phi\,[\alpha_h(V)(1-h) - \beta_h(V)h], \end{cases}$$

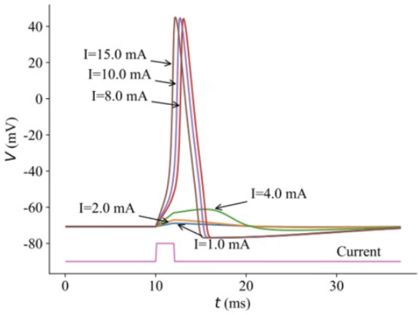
$$\alpha_n(V) = \frac{0.01(V+55)}{1-\exp\left(-\frac{V+55}{10}\right)}, \quad \beta_n(V) = 0.125\exp\left(-\frac{V+65}{80}\right),$$
$$\alpha_h(V) = 0.07\exp\left(-\frac{V+65}{20}\right), \quad \beta_h(V) = \frac{1}{\left(\exp\left(-\frac{V+35}{10}\right)+1\right)},$$
$$\alpha_m(V) = \frac{0.1\,(V+40)}{1-\exp(-(V+40)/10)}, \quad \beta_m(V) = 4\exp(-(V+65)/18).$$

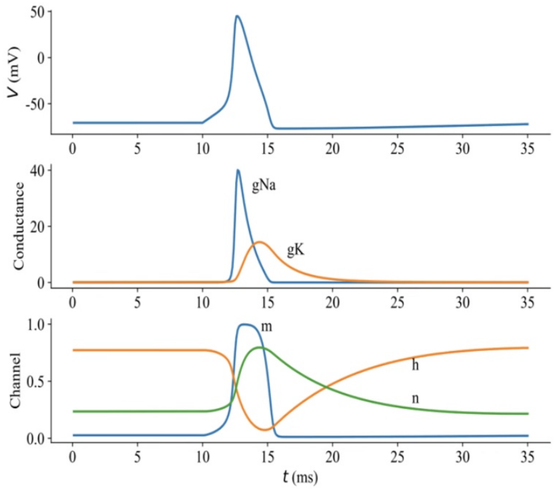
$$\phi = Q_{10}^{(T-T_{base})/10}$$

陈啸宇的屏幕共享



Response to a constant input





Change of ion channel conductance and gating variables

- All-or-none characteristics
- 钾离子激活和钠离子抑制时间常数速率差不多不过都比钠离子激活慢（在去极化过程钾离子失活通道不明显 ）

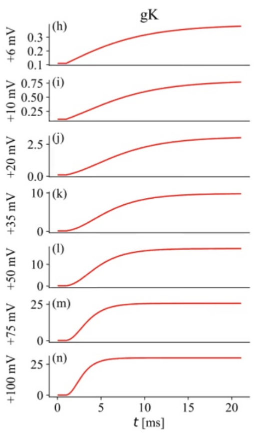
- How to fit each gatinng variables

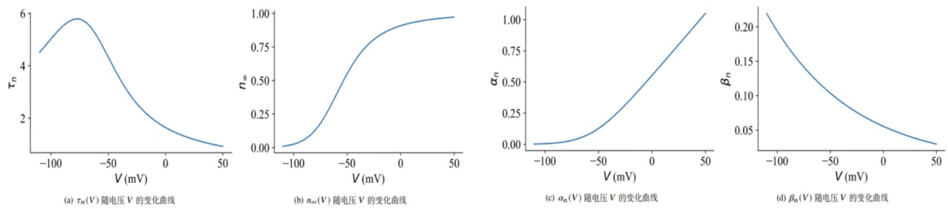
Fitting n: $g_K = \bar{g}_K n^x$ $\quad m(t) = m_\infty(V) + (m_0 - \boxed{m_\infty(V)})e^{-t/\boxed{\tau_m(V)}}$

$$g_K(V,t) = \bar{g}_K\left[n_\infty(V) - (n_\infty(V) - n_0(V))e^{-\frac{t}{\tau_n(V)}}\right]^x$$

$$g_{K\infty} = \bar{g}_K n_\infty^x, g_{K0} = \bar{g}_K n_0^x$$

$$g_K(V,t) = \left[g_{K\infty}^{1/x} - (g_{K\infty}^{1/x} - g_{K0}^{1/x})e^{-\frac{t}{\tau_n(V)}}\right]^x$$



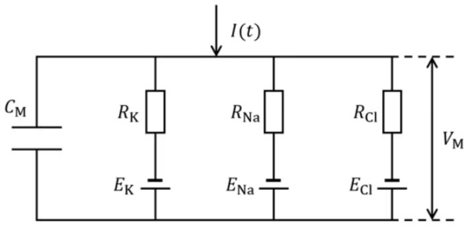


Summary

- Equivalent circuits:

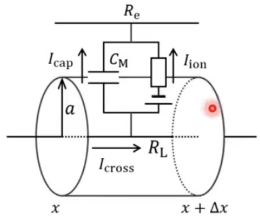
$$\frac{I(t)}{A} = c_{\mathrm{M}} \frac{\mathrm{d}V_{\mathrm{M}}}{\mathrm{d}t} + i_{\mathrm{ion}}$$

$$\Rightarrow \quad c_{\mathrm{M}} \frac{\mathrm{d}V_{\mathrm{M}}}{\mathrm{d}t} = -g_{\mathrm{Cl}}(V_{\mathrm{M}} - E_{\mathrm{Cl}}) - g_{\mathrm{K}}(V_{\mathrm{M}} - E_{\mathrm{K}}) - g_{\mathrm{Na}}(V_{\mathrm{M}} - E_{\mathrm{Na}}) + \frac{I(t)}{A}$$



- Cable theory: $$c_{\mathrm{M}} \frac{\partial V(x,t)}{\partial t} = \frac{a}{2\rho_{\mathrm{L}}} \frac{\partial^2 V(x,t)}{\partial x^2} - i_{\mathrm{ion}}$$

- Passive conductance



- Action potential

Mechanism: voltage-gated ion channels $\quad g_{\mathrm{Na}} \rightarrow g_{\mathrm{Na}}(V) \quad\quad g_{\mathrm{K}} \rightarrow g_{\mathrm{K}}(V)$

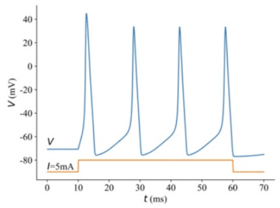
- The Hodgkin-Huxley Model
- Voltage clamp

$$c\frac{\mathrm{d}V}{\mathrm{d}t} = -\bar{g}_{\mathrm{Na}} m^3 h\,(V - E_{\mathrm{Na}}) - \bar{g}_{\mathrm{K}} n^4\,(V - E_{\mathrm{K}}) - \bar{g}_{\mathrm{L}}\,(V - E_{\mathrm{L}}) + I_{\mathrm{ext}},$$

$$\frac{\mathrm{d}n}{\mathrm{d}t} = \phi\,[\alpha_n(V)(1-n) - \beta_n(V)n]$$

$$\frac{\mathrm{d}m}{\mathrm{d}t} = \phi\,[\alpha_m(V)(1-m) - \beta_m(V)m]\,,$$

$$\frac{\mathrm{d}h}{\mathrm{d}t} = \phi\,[\alpha_h(V)(1-h) - \beta_h(V)h]\,,$$



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$$\phi = Q_{10}^{(T-T_{\mathrm{base}})/10}$$