Single Neuron Models

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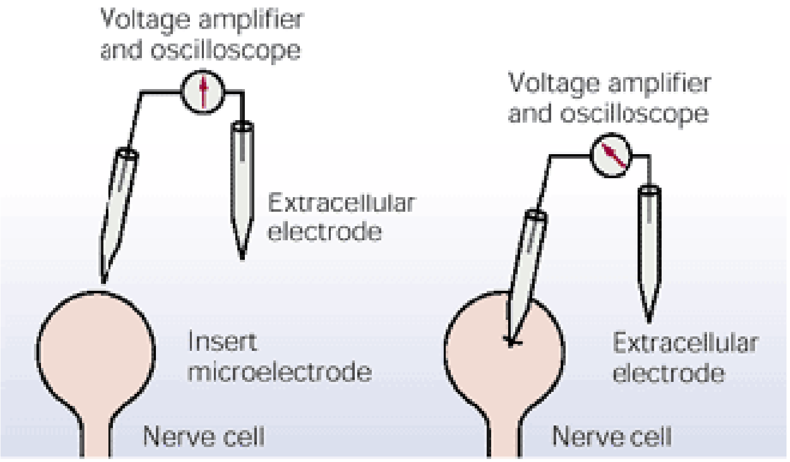
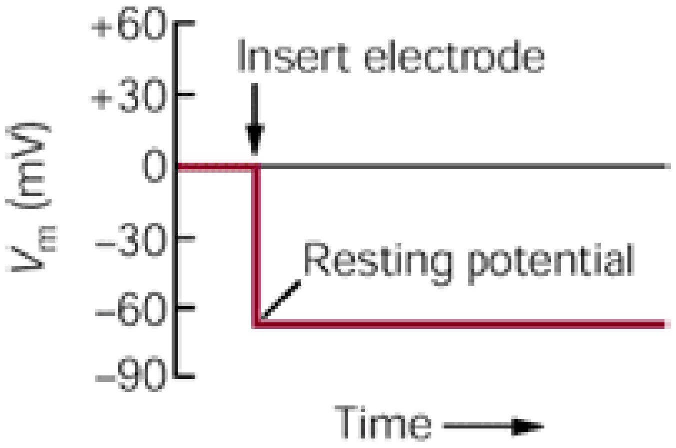
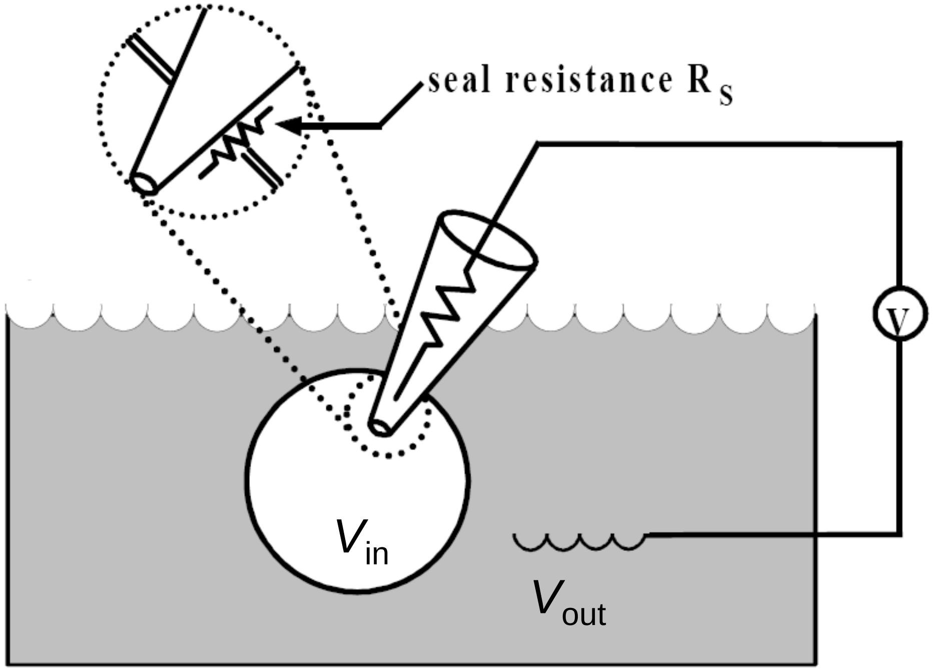
Neuronal state: Membrane potential

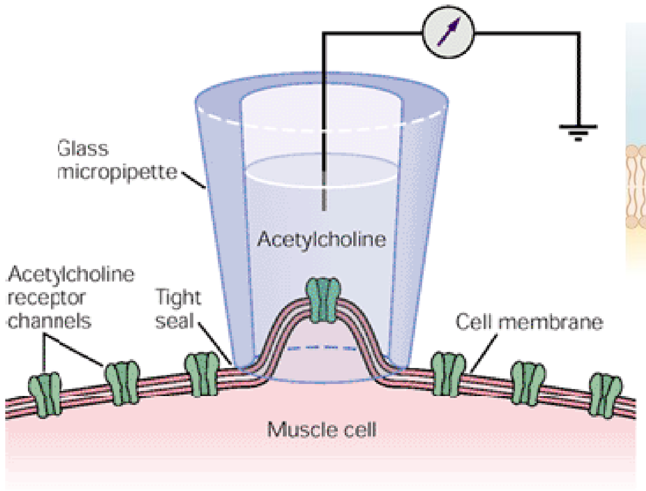


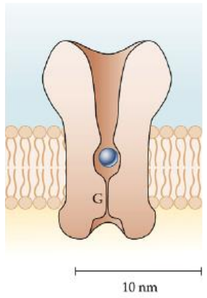


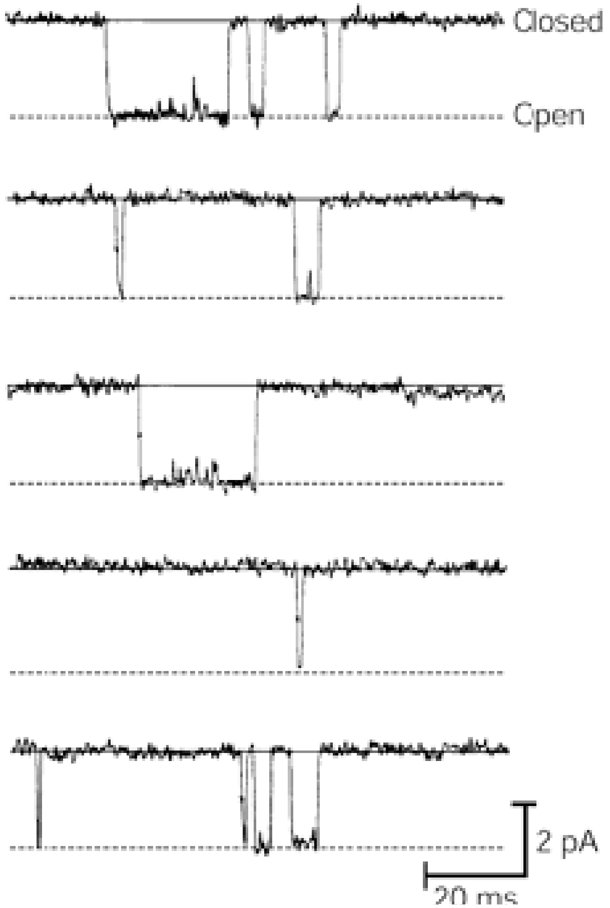


$$V_m = V_{in} - V_{out}$$

Dynamics of single Ion channels





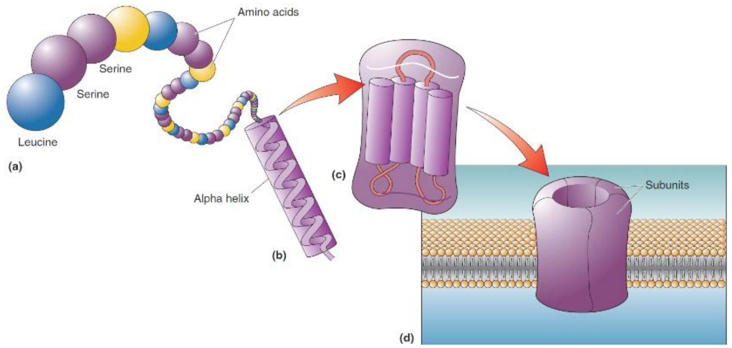


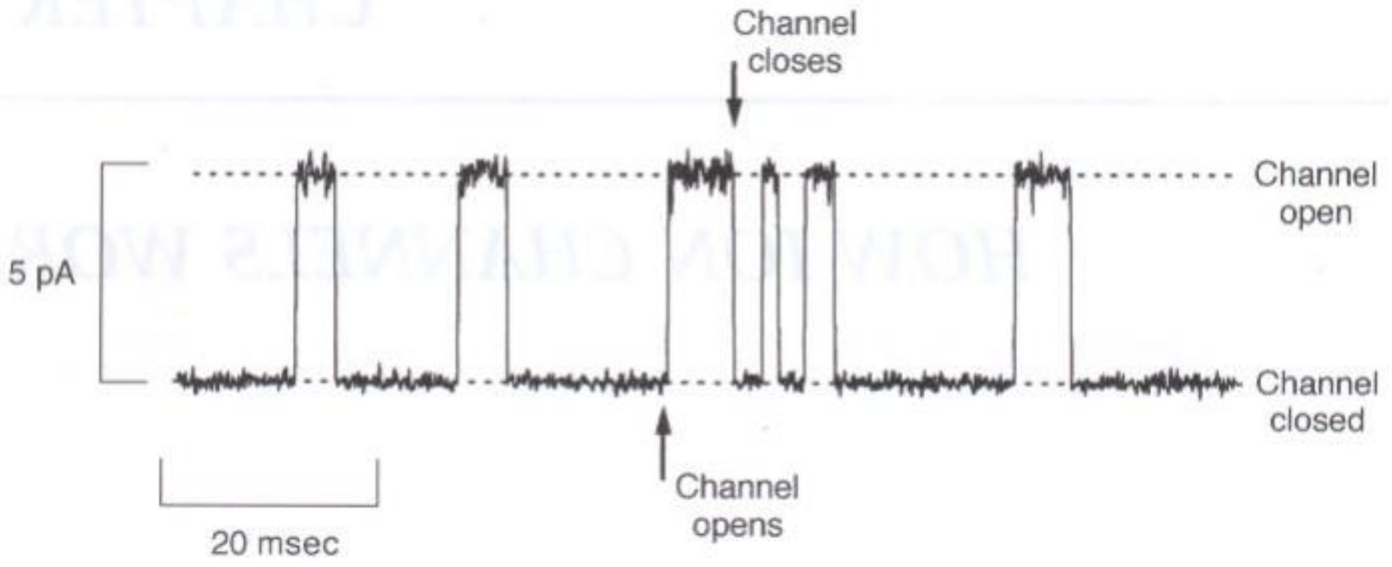
The Patch Clamp: Recording Current Flow in Single Ion Channels

Properties of Ion Channels

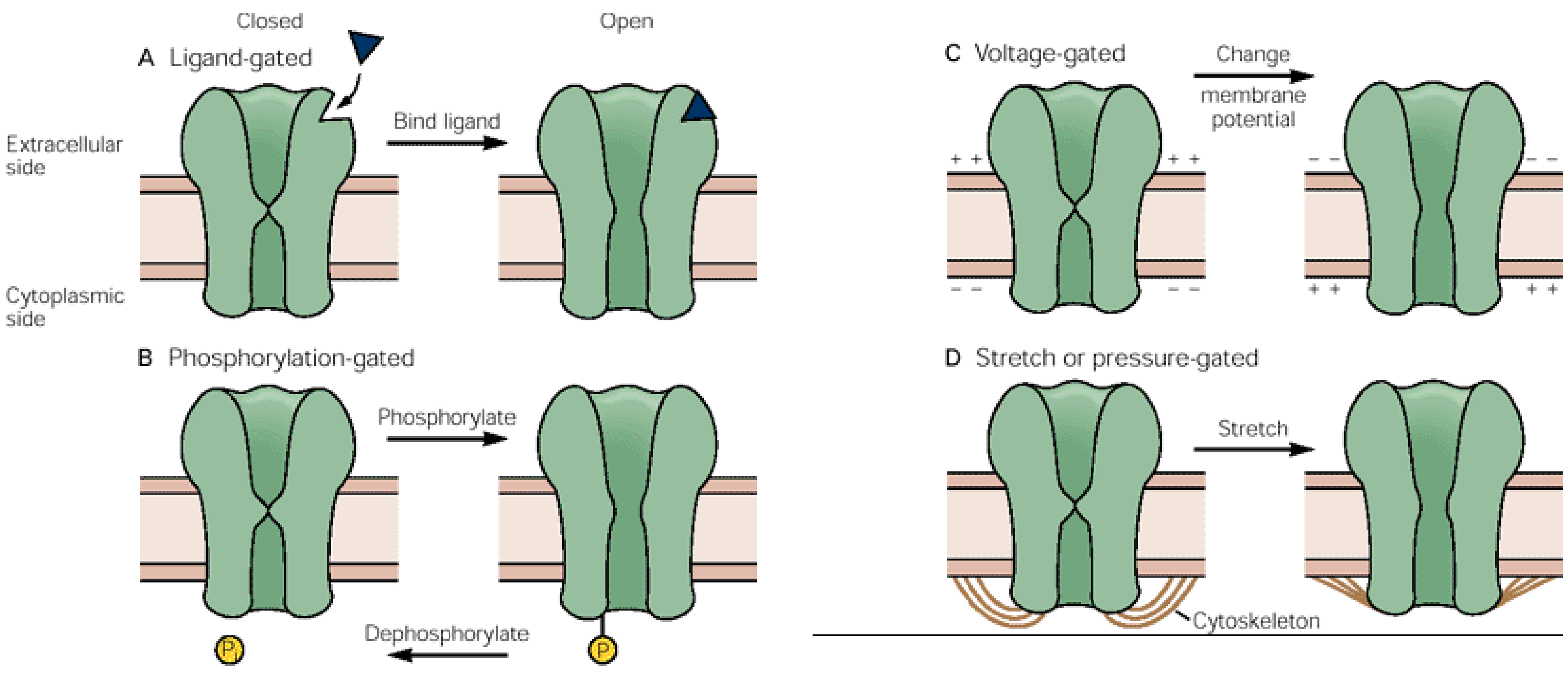
单个离子通道的开放特性:

1) All-or-none 全或无
2) small current 微小电流
3) stochastic 开放概率
4) ion permeation 通透的离子选择性
5) Gating 门控开关



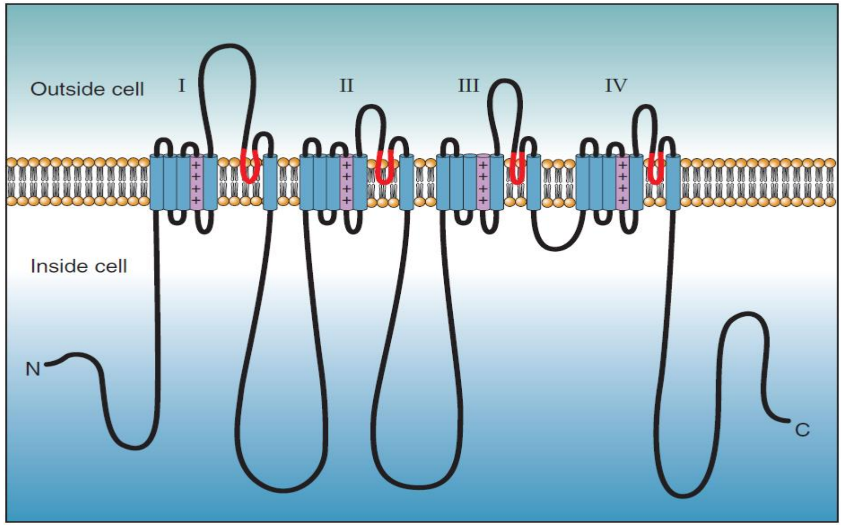


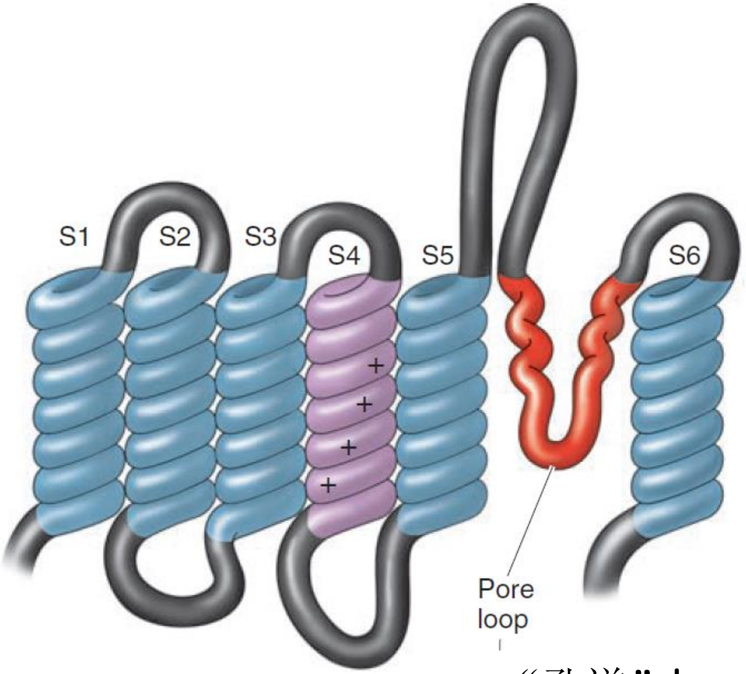
Types of Ion Channels



A) 电压门控 Voltage-gated channel : K+, Na+, Ca2+, Cl-, HCN channels
B) 配基（递质）门控 Ligand-gated channel : glutamate/GABA receptor channels;
C) 蛋白（磷酸化）修饰门控 Phosphorylation-gated channel
D) 机械张（压）力门控 Pressure-gated channel

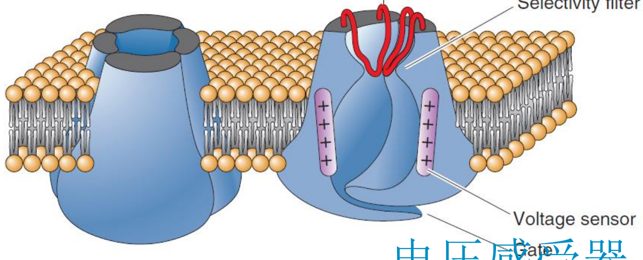
Voltage-gated Na+ channel





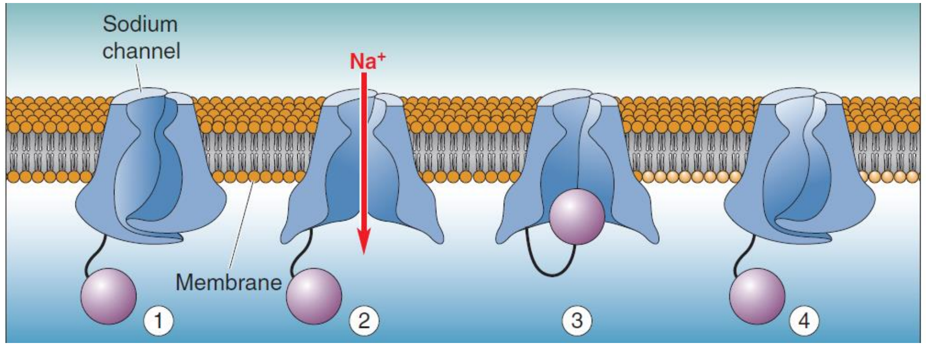
“孔道” loop

离子选择“筛”



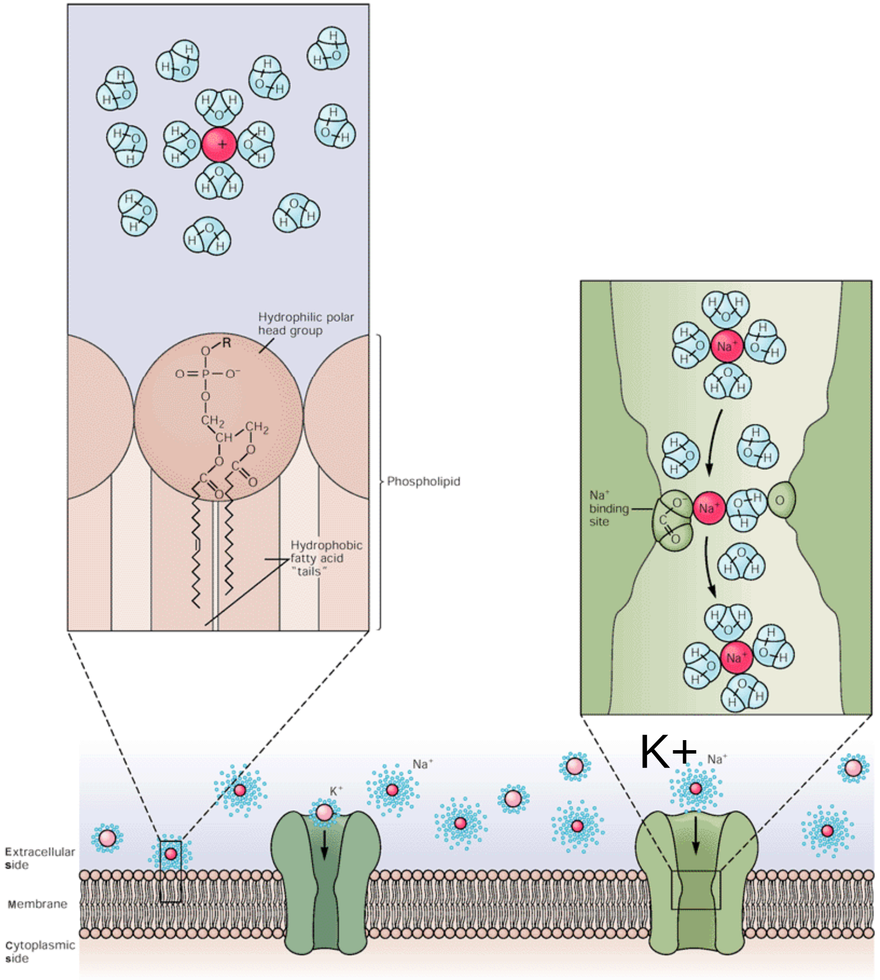
电压感受器

关闭 → 激活(开放) → 失活 → 去失活



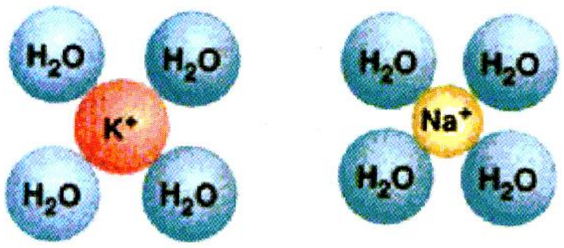
Ion selectivity of channels

1）合适的通过孔道和水合离子的大小
2）孔道壁上相反的弱电荷氨基酸
3）疏水性氨基酸



K^+ channels are 100-fold more permeable to K^+ than to Na^+.

Na^+ channels are 10~20-fold more permeable to Na^+ than to K

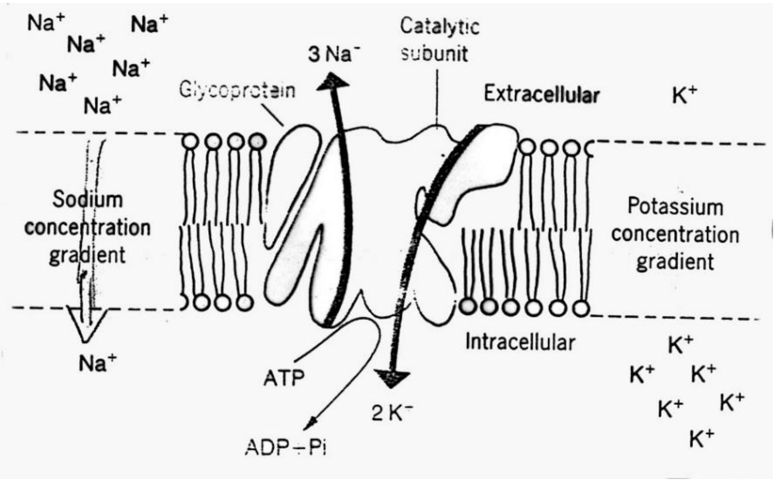


Water-filled pore:

R_K: 0.133 nm
R_{Na}: 0.095 nm

Speciality of Membrane

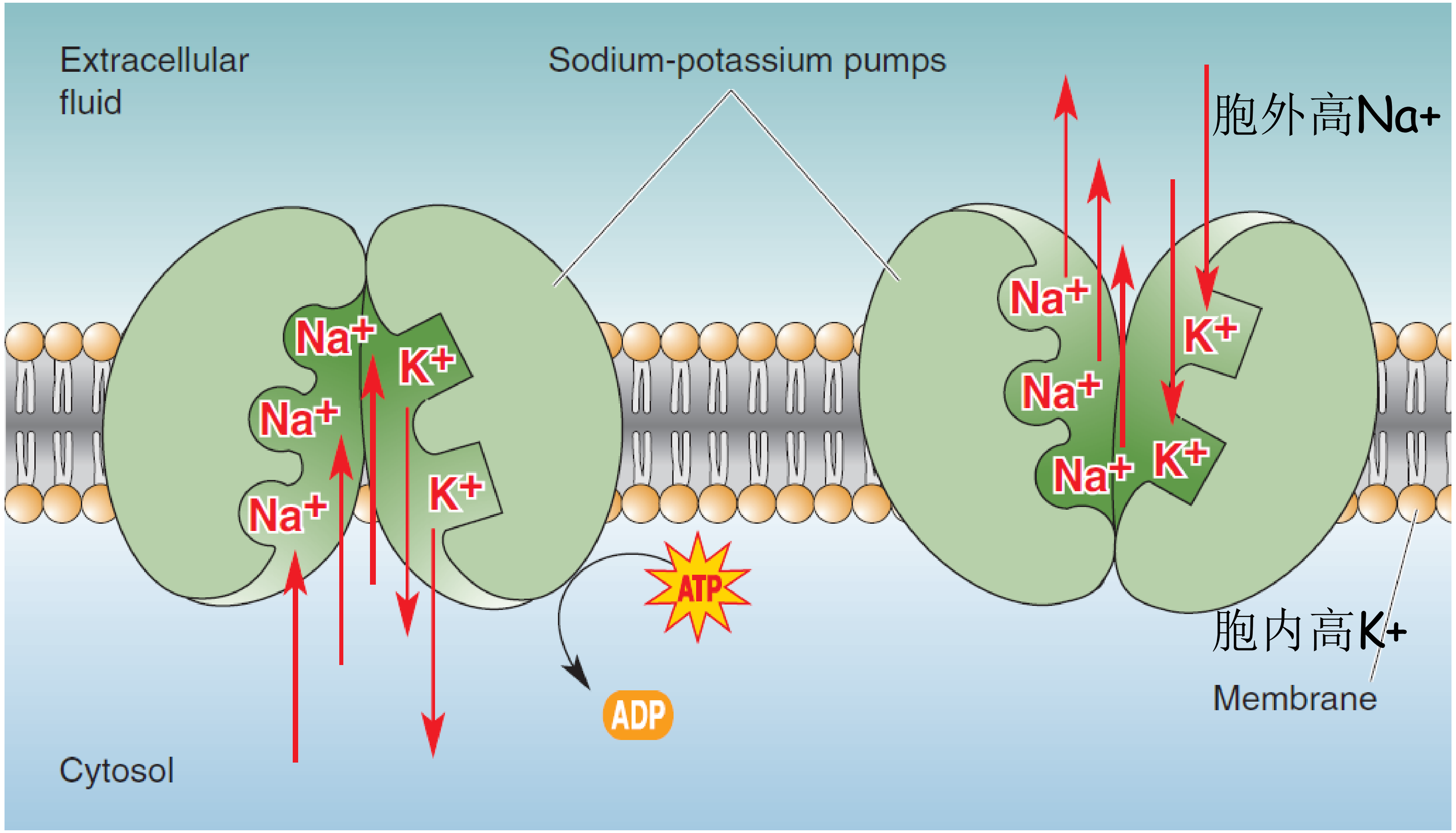
- Permeability of the membrane
- Ions types: Potassium, Sodium, Calcium and Chloride
- Ion channel types:
  - Leakage channel: always open
  - Voltage-gated channel: sensitive to the magnitude of membrane potentials
  - Neurotransmitter -gated channel: sensitive to neurotransmitters
  - Ion bump : generating concentration difference for ions within and outside the cell
  - And others



Resting membrane potential

静息膜电位

Ion gradient results from the activity of ion transporters



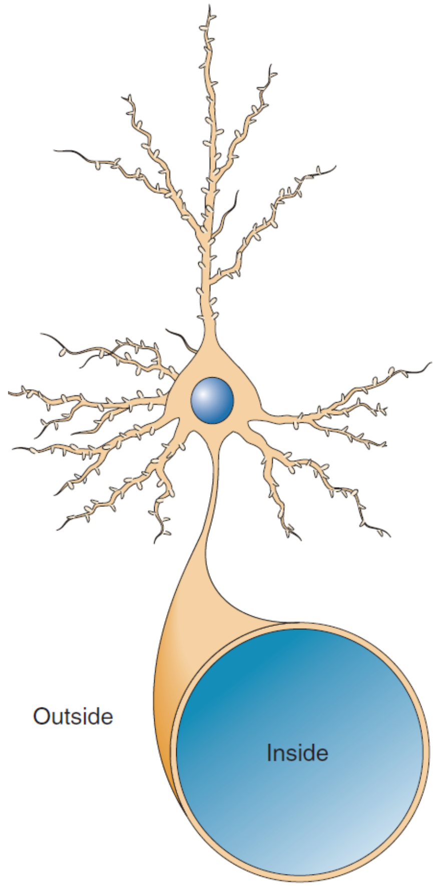
The Na+-K+ pump (ATPase，Na-K ATP泵)
Na-K-Cl-pump (NKCC1, NKCC2)

Segregation of ions by the cell membrane

Electrochemical gradient

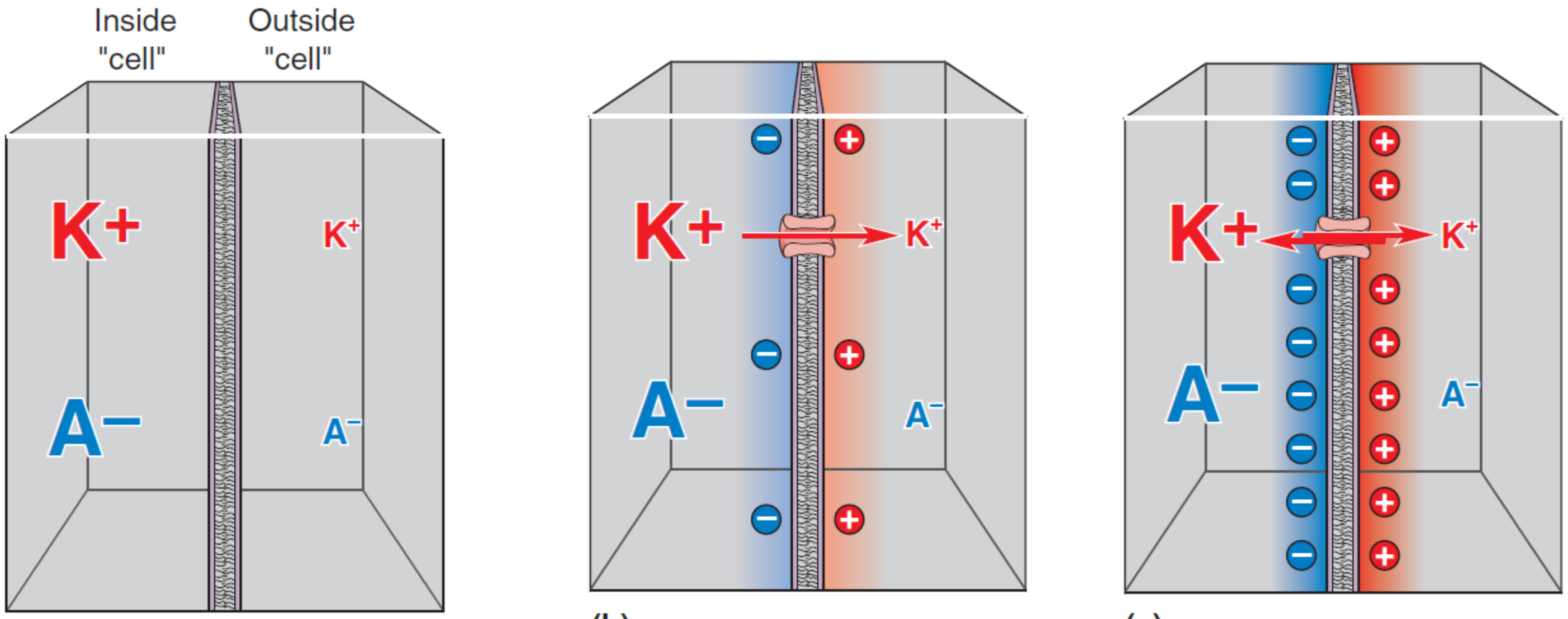
电化学梯度 （电化学势）

Ion	Concentration outside (in mM)	Concentration inside (in mM)	Ratio Out : In
K^+	5	100	1 : 20
Na^+	150	15	10 : 1
Ca^{2+}	2	0.0002	10,000 : 1
Cl^-	150	13	11.5 : 1



Equilibrium potential: 平衡电位

Resulting from a selectively permeable membrane



(a)

(b)

(c)

K+，带负电的蛋白质A：
内>外

胞内K+与带负电的蛋白质浓度 >> 细胞外浓度；静息时膜只对K+通透
→K+顺浓度差由胞内移到细胞外，负电的蛋白质离子不能透出细胞，
→K+外移造成膜内变负而膜外变正，
→“外正内负”的状态可随K+的外移而增加，同时，K+外移形成的电势差阻碍K+的进一步外移，
→达到一种因浓度差和电势差的平衡，使K+内外移动量相同，无净电流。

Equilibrium potential: 平衡电位

平衡电位
Nernst Equation:

RT/F = 25 mV at 25 °C, and the constant for converting from $\log_{10}$ to $\log_2$ is 2.3:

$$Ex = \frac{RT}{zF} \ln \frac{[X]o}{[X]i}$$

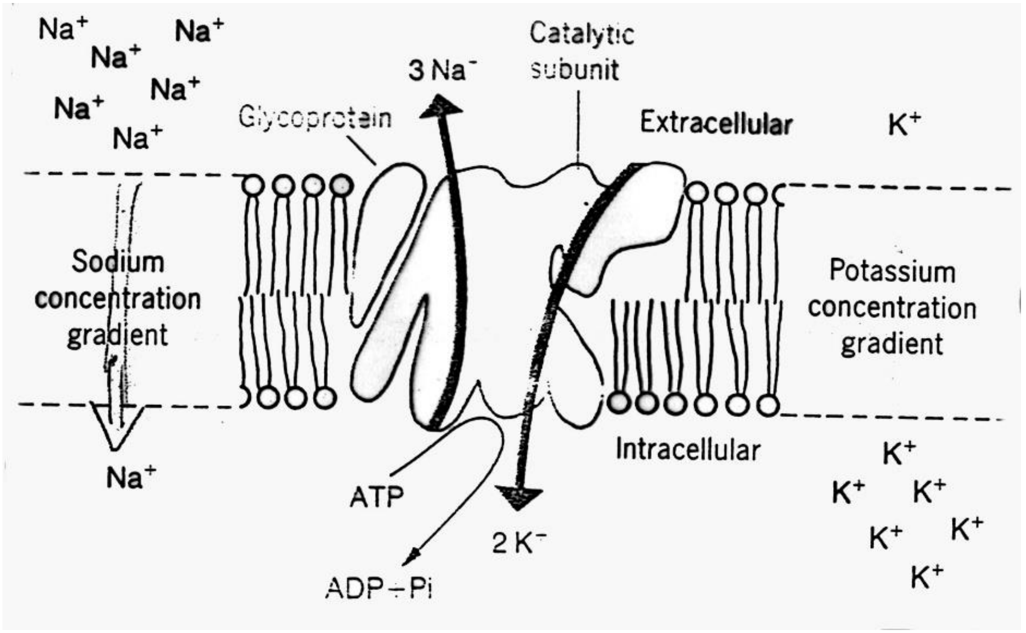
$$Ex = \frac{58\ mV}{z} \log \frac{[X]o}{[X]i}$$

R: 气体常数; T: 绝对温度; F: 法拉第常数; z: 离子电荷数

例： $E_k = \frac{58\ mV}{1} \log \frac{2.5}{140} = -101\ mV$

Resting membrane potential

• Ion pump generates concentration difference of ions; Under natural force, ions diffuse from high to low concentrations
•Positive charged ions (cations) leak through leakage channels, but the membrane is not permeable to the anions binding to cations; A electrical potential is generated.
•A balance is reached between the electrical and the diffusion forces

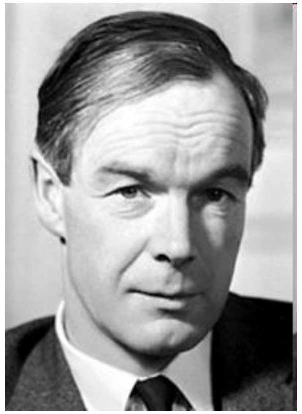


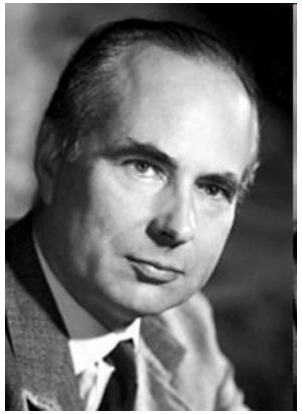
Action potential

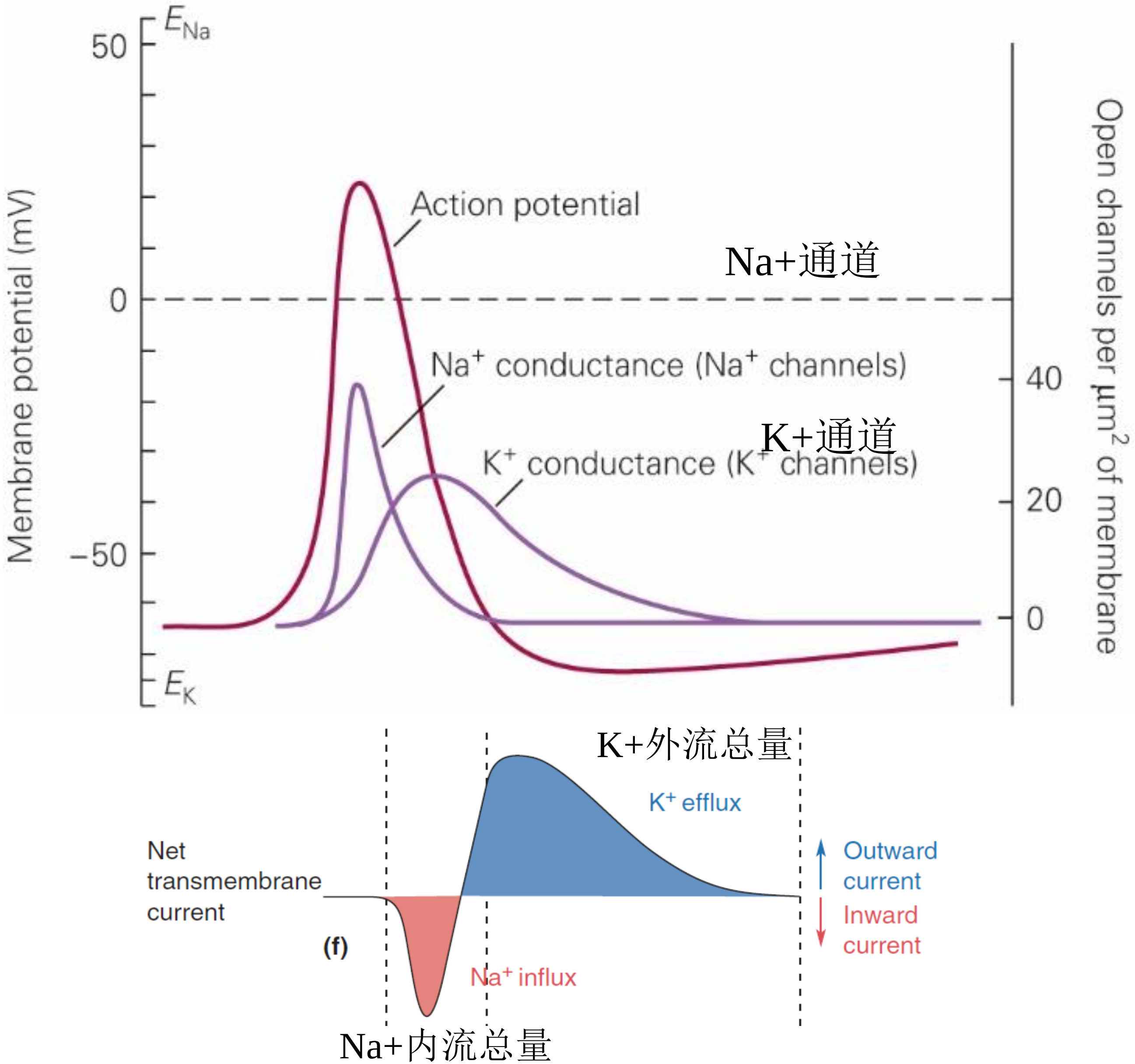
动作电位

Action potential recorded

ION channel dynamics of Spike

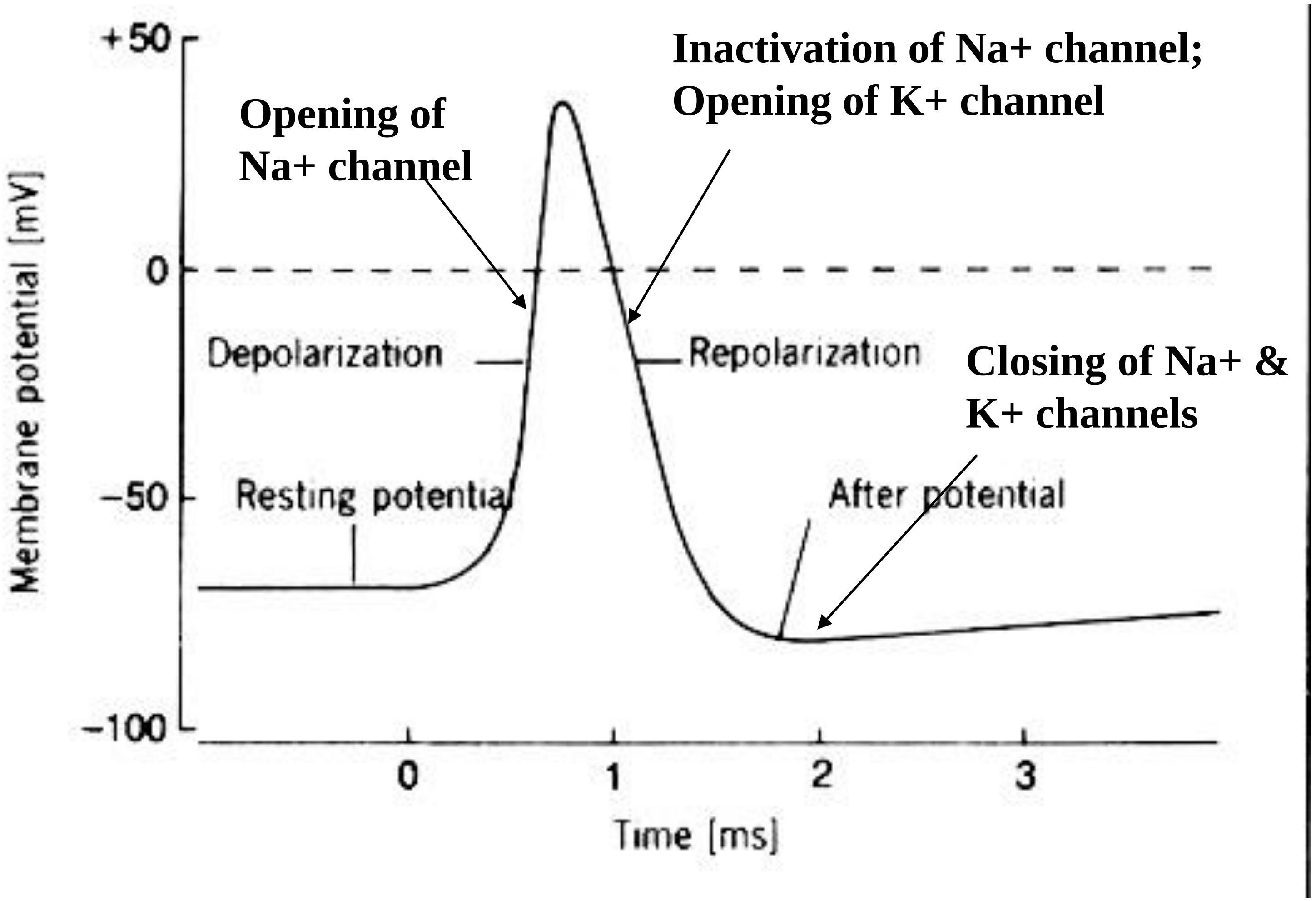






Hodgkin & Huxley revealed the ionic mechanisms for action potential.

The Status of Channels



The Minimal Mechanism of Spiking

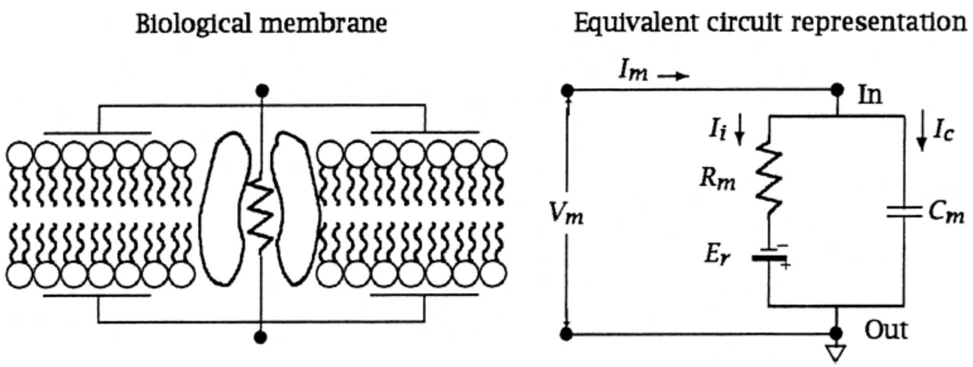
- Depolarization Phase:
  - The membrane voltage change triggers the opening of voltage-gated sodium channels
  - The influx of sodium depolarizes the neuron (up to V=+65mV)
- Hyper-polarization Phase:
  - The sodium channels become inactive at around 1ms after their opening
  - Meanwhile, the potassium channels open—the efflux of potassium ions overshoots the resting potential (down to V=-80mV).
- Re-setting phase
  - The hyper-polarization causes the close of potassium and sodium channels
  - Ion bump may be called to retain the concentration gradients of

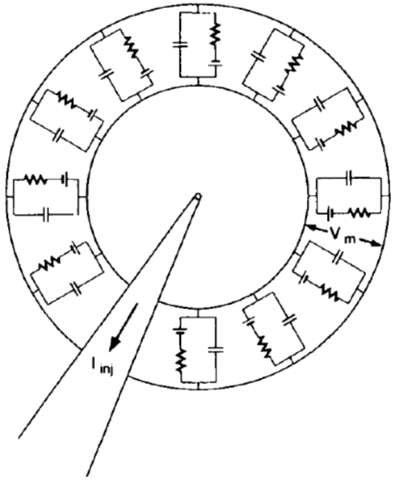
    potassium and sodium ions

HH Model (1)

- Neuron as a capacitor: the membrane potential V, the capacitance C, the excess internal charge Q: Q=CV.
- The reversal potential E_i (i index the ion type): the equilibrium potential that balance the diffusion force.

  (K+: -70~-90mV, Na+: 50mV)
- The membrane current I_i: the net movement of ion i across the membrane due to the opening of voltage-gated channels.
- The electrical conductance g_i (the inverse of resistance): reflecting the number of opening channels for the ion i (sensitive to voltage).





HH model (2)

- For ion i: $I_i = g_i(V - E_i)$
- The leakage current (g_L constant): $I_L = g_L(V - E_L)$
- The dynamics of the membrane potential:

$$C\frac{dV}{dt} = -\sum_i g_i(V - E_i) - g_L(V - E_L) + I(t)$$

where I(t) represents the external current, e.g., the current from the neurotransmitter-gated channels.

Dynamics of HH Model

- The Hodgkin-Huxley equation:

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

- The voltage-sensitive conductance

$$g_k = \bar{g}_k \cdot n^4$$

$$g_{Na} = \bar{g}_{Na} \cdot m^3 h$$

$\bar{g}_k, \bar{g}_{Na}$: the maxium conductances

n, m & h are time variables

n^4 : the activation of K^+ channels

m^3 : the activation of Na^+ channels

h : the inactivation of Na^+ channels

Eg: The dynamics of g_K

- The channel activation is determined activities of 4 independent subunit gates. The probability of each subunit open is n.

Thus $g_k = \bar{g}_k \cdot n^4$

- Consider the opening and closing rates of one subunit gate are $\alpha(V)$ and $\beta(V)$, respectively,

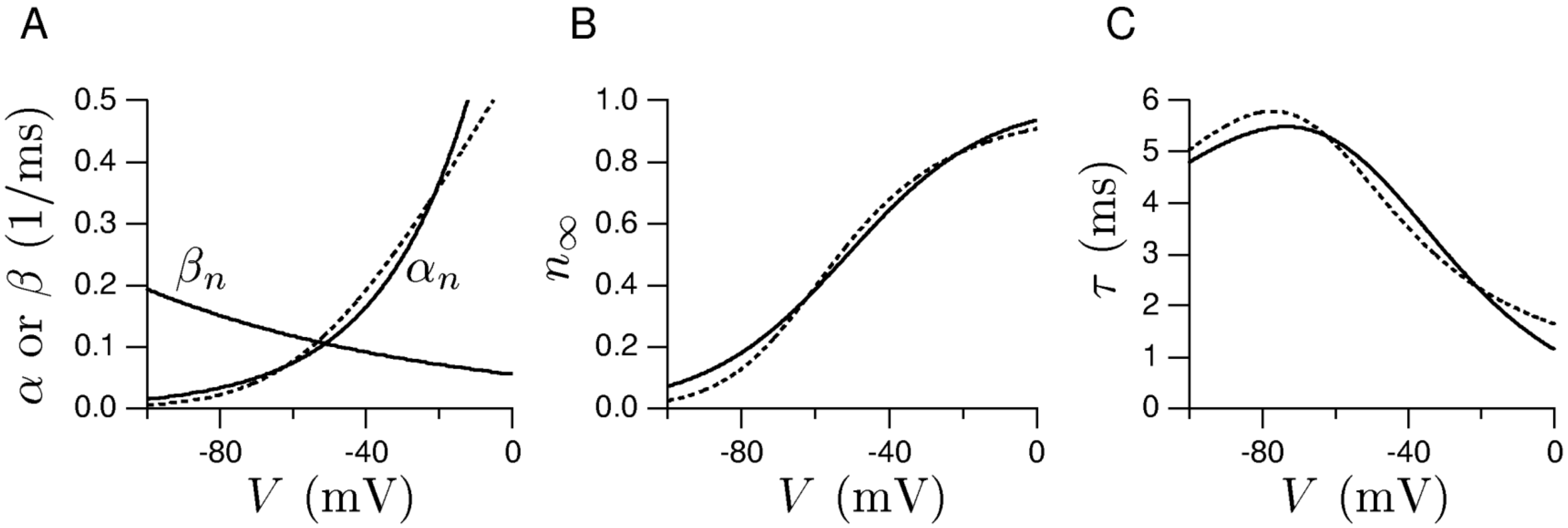
$$\frac{dn}{dt} = \alpha(V)(1-n) - \beta(V)n$$

$$\tau_n \frac{dn}{dt} = -[n - n_\infty(V)]$$

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

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

$\alpha(V), \beta(V), n_\infty$ *and* τ_n



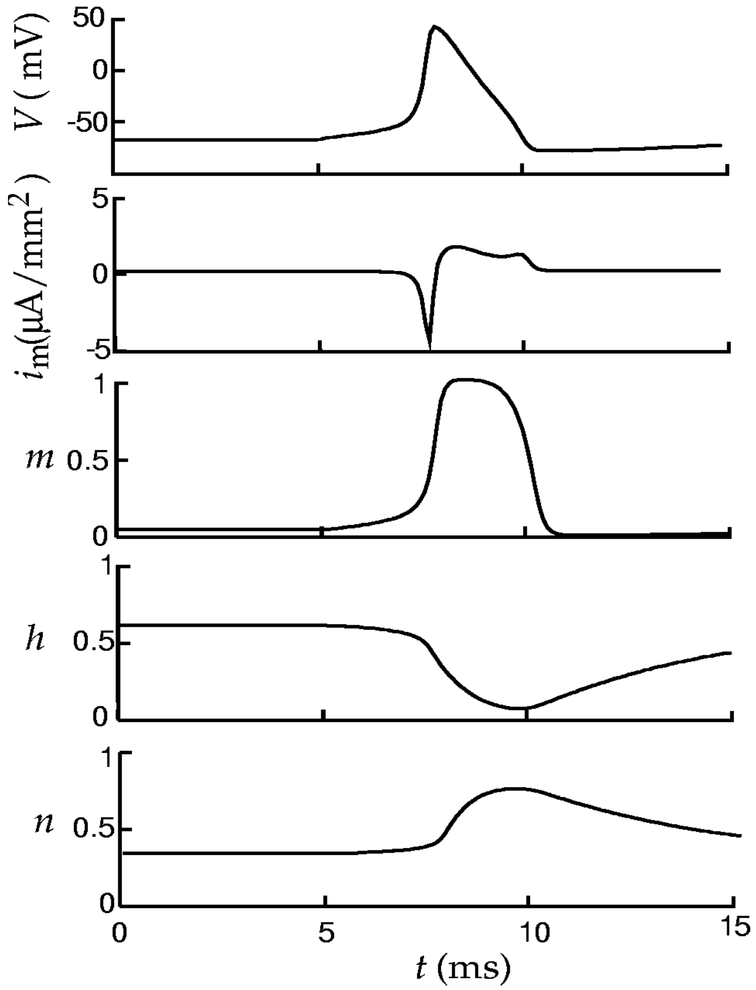
The dynamics of n,m,h

$$\tau_n \frac{dn}{dt} = -[n - n_\infty(V)]$$

$$\tau_m \frac{dm}{dt} = -[m - m_\infty(V)]$$

$$\tau_h \frac{dh}{dt} = -[h - h_\infty(V)]$$

Predictions of the HH model



•The membrane potential. External input was initiated at t=5ms

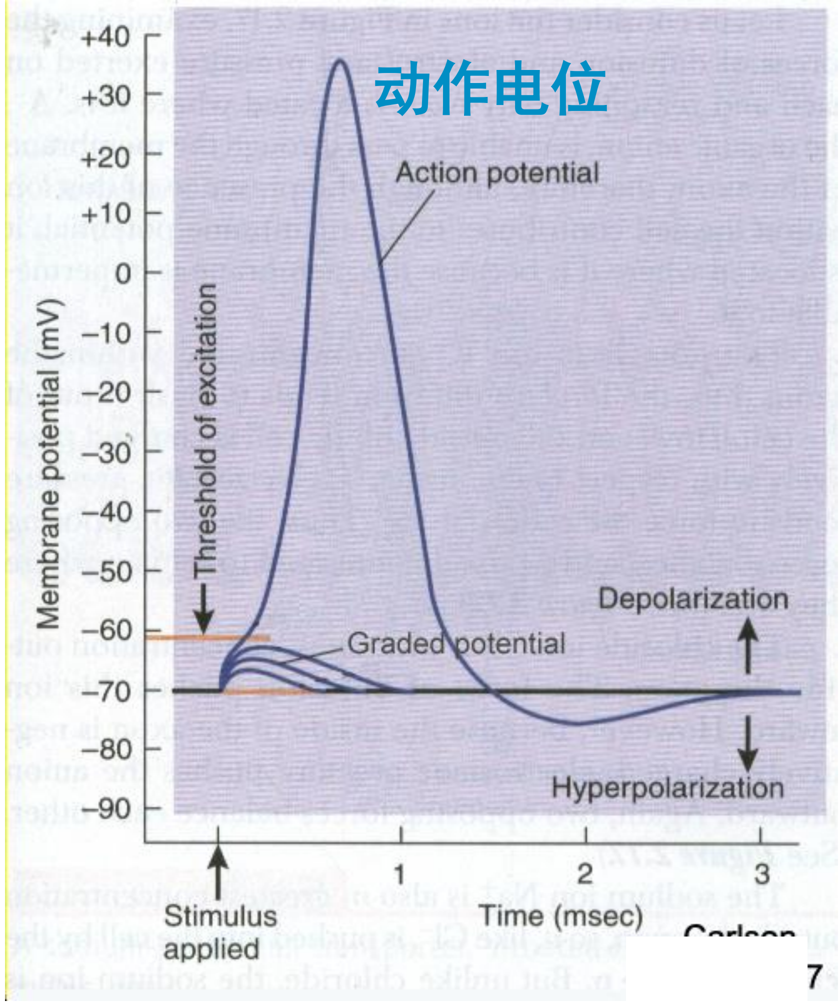
•The membrane current (the summation of Na+ and K+ currents)

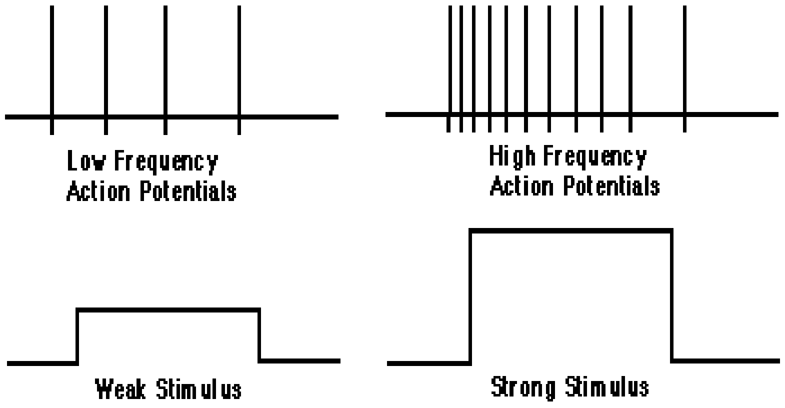
•The dynamics of m

•The dynamics of h

•The dynamics of n

Stereo-typed action potential





动作电位: (1 或 0)

The Simplified Integrate-and-Firing Model

- The simplest I & F model $$\tau \frac{dV}{dt} = -V + I(t)$$

V: the membrane potential

$I(t)$: the external input

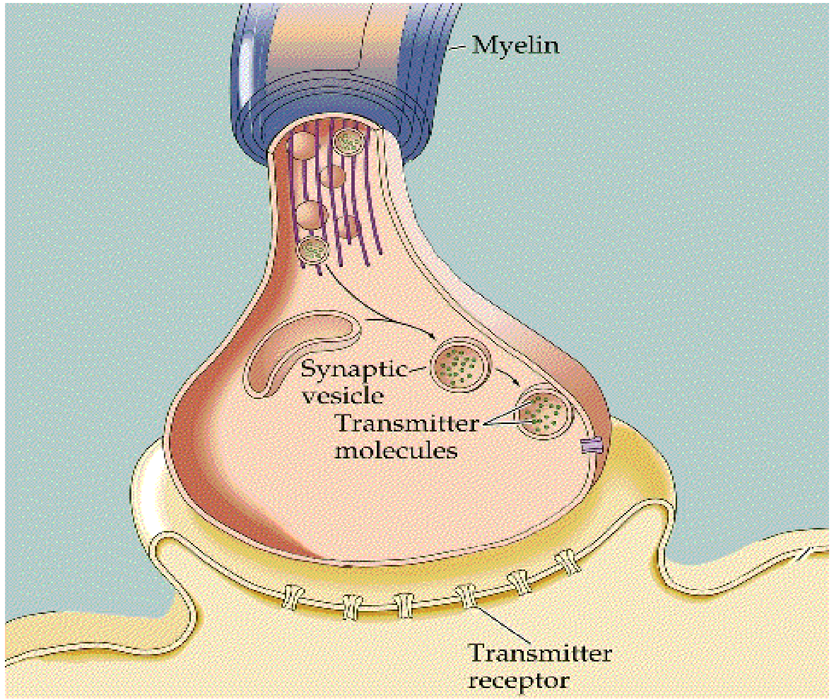
τ: the time constant

the term $(-V)$ represents the leaky effect

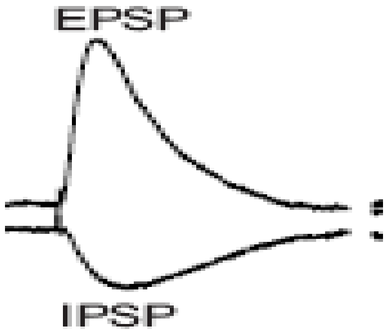
If $V > V_{threshold}$

the neuron fires, sending out a signal to connected neurons, and V is reset to be 0.

The Synapse

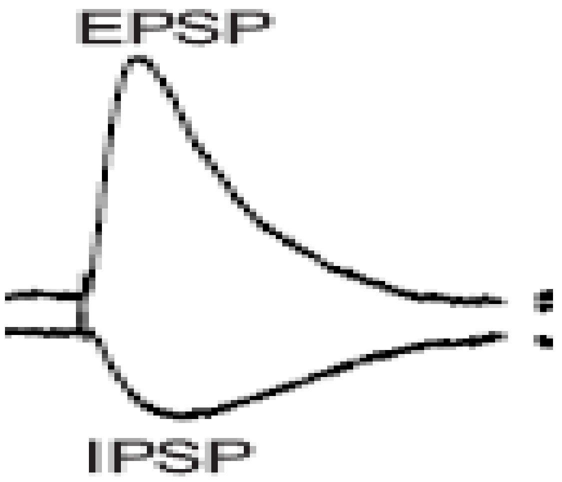


- Chemical Synapse: Action potential triggers the release of neurotransmitter
- Neurotransmitters diffuse across the synaptic cleft
- Neurotransmitter-gated channels open, generating postsynaptic potential
- Dependent on the sign of PSP, synapses are clarified as excitatory and inhibitory ones.



Synaptic current

$$\tau \frac{dV}{dt} = -V + w \sum \delta(t - t_i)$$



Synapse Efficacy=Connection Weight