Signaling within Neurons:Electrical properties of Neurons and Action Potentials

神经元中的信号：神经元电学性质和动作电位

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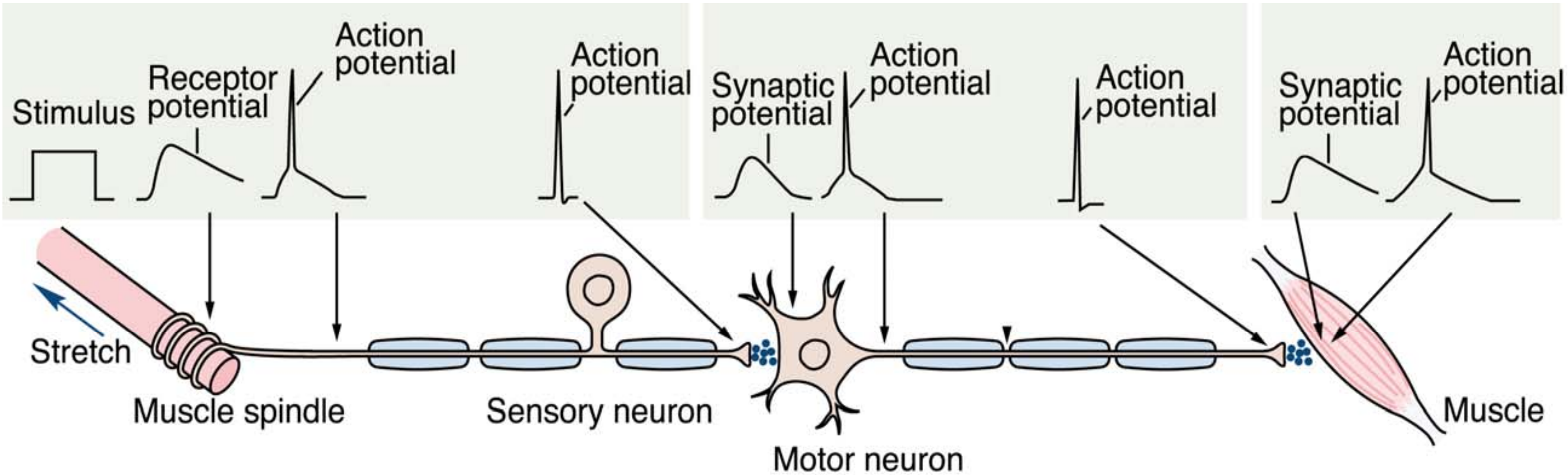
April 19, 2016

2015/9/28

Diagram of information transfer in the nervous system
神经系统中的信息传递



Generator Potentials, Synaptic Potentials and Action Potentials All Can Be Described by the <u>Equivalent Circuit Model</u> of the Membrane

引发电位，突触电位和动作电位的影响都可以通过膜的等效电路模型来描述

PNS, Fig 2-11

Logics

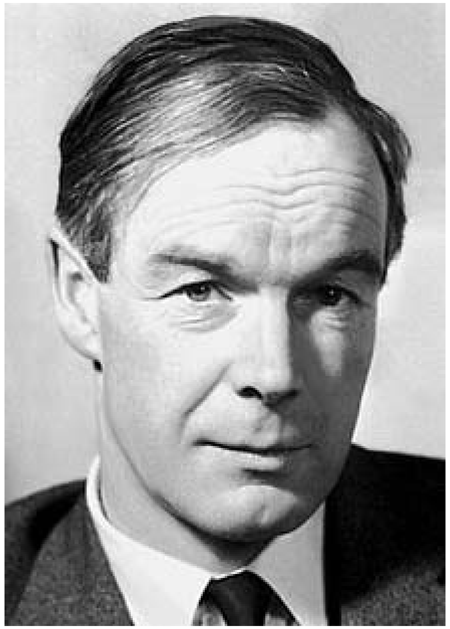
Illustrate the mechanism of AP generation and propogation.

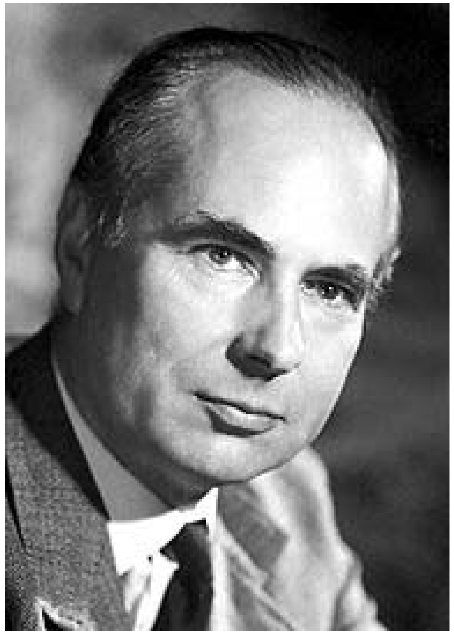
↓

Identification (cloning) of ion channel genes.

↓

Illustrate the structure basis of ion channel function.





Sir Alan Lloyd Hodgkin   Sir Andrew Huxley

1963 Nobel Prize in Physiology or Medicine

- 1982 Nature

Primary structure of α-subunit precursor of *Torpedo californica* acetylcholine receptor deduced from cDNA sequence

Masaharu Noda[*], Hideo Takahashi[*], Tsutomu Tanabe[*], Mitsuyoshi Toyosato[*], Yasuji Furutani[*], Tadaaki Hirose[†], Michiko Asai[†], Seiichi Inayama[†], Takashi Miyata[‡] & Shosaku Numa[*]

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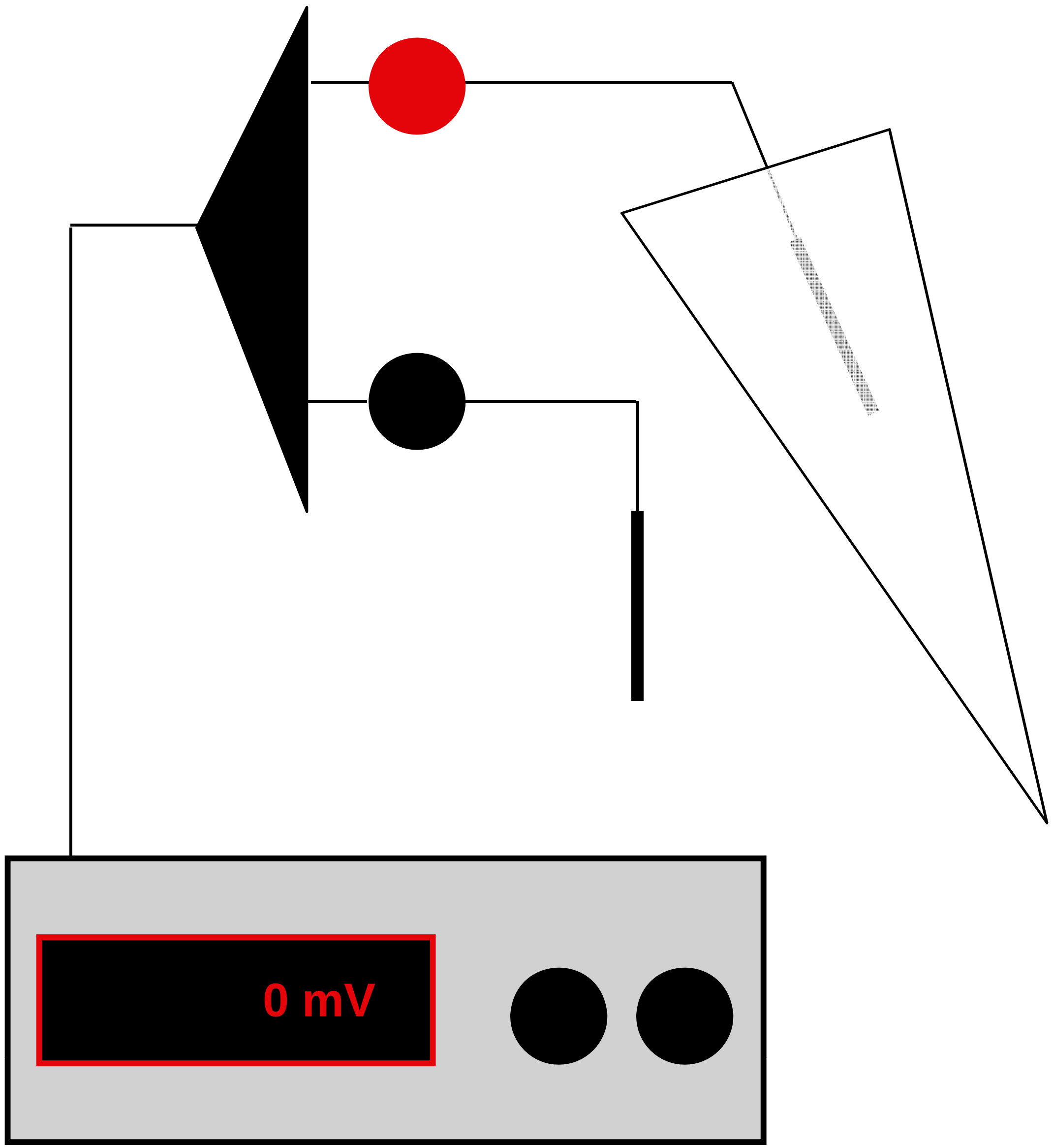
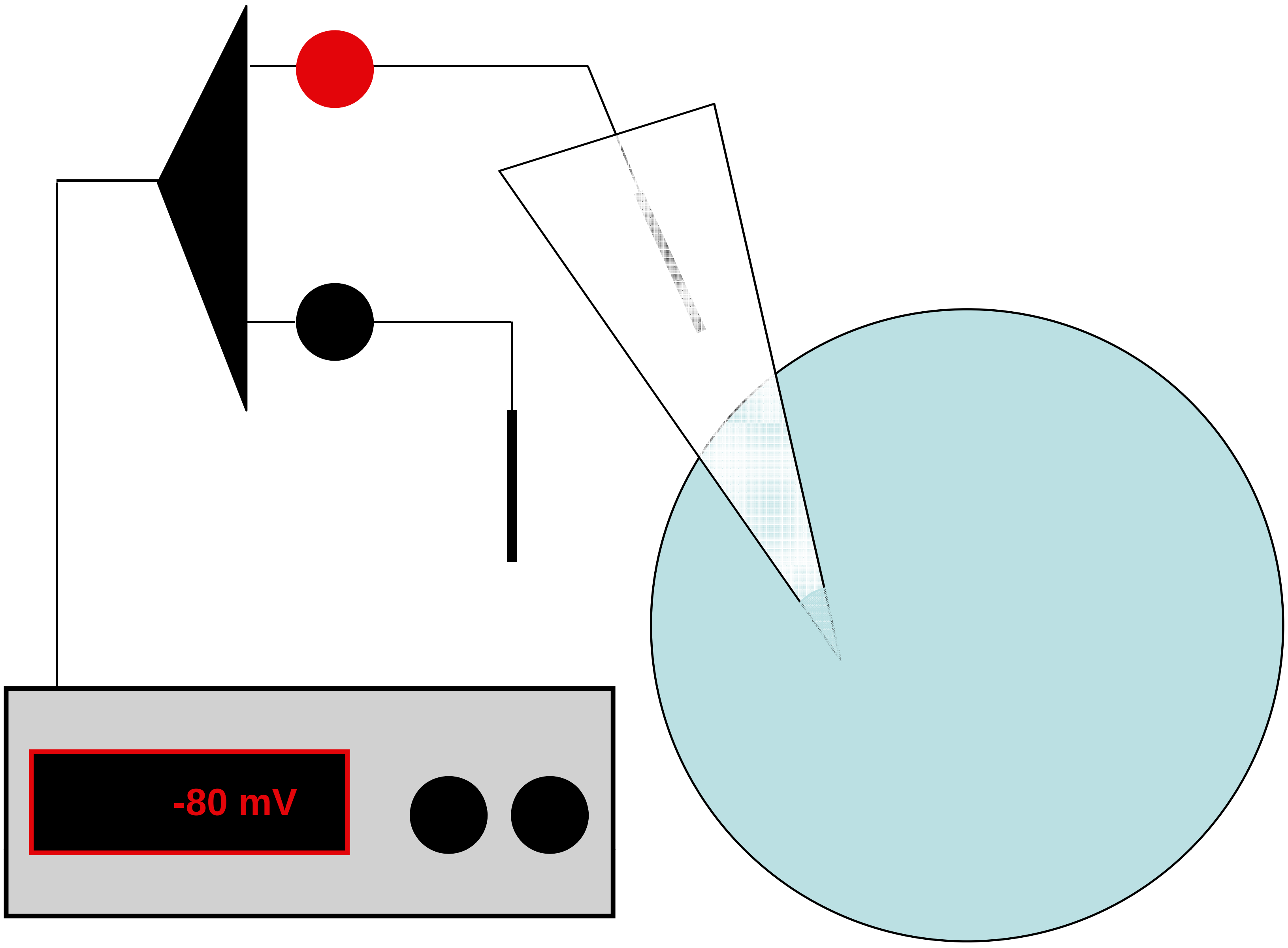
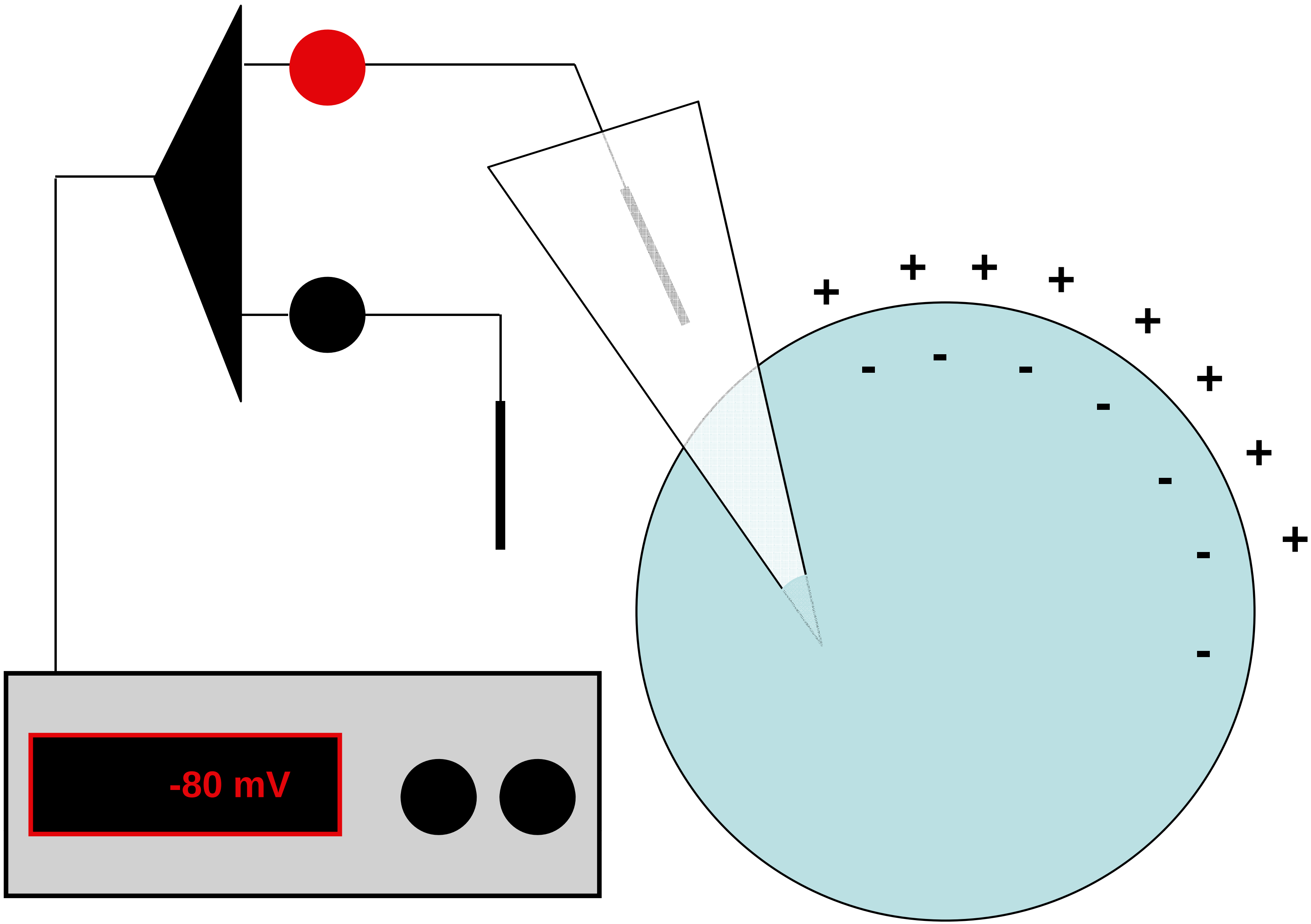
- Shosaku Numa

Outlines

- 1. Ohm’ s law R=V/I
- 2. Resting membrane potential
- 3. Nernst equation: chemical energy vs. electrical energy; GHK equation
- 4. cell membrane (capacitance, resistance/conductance, membrane potential/reversed potential, ion channels).
- 5. Hodgin-Huxeley model


0 mV


-80 mV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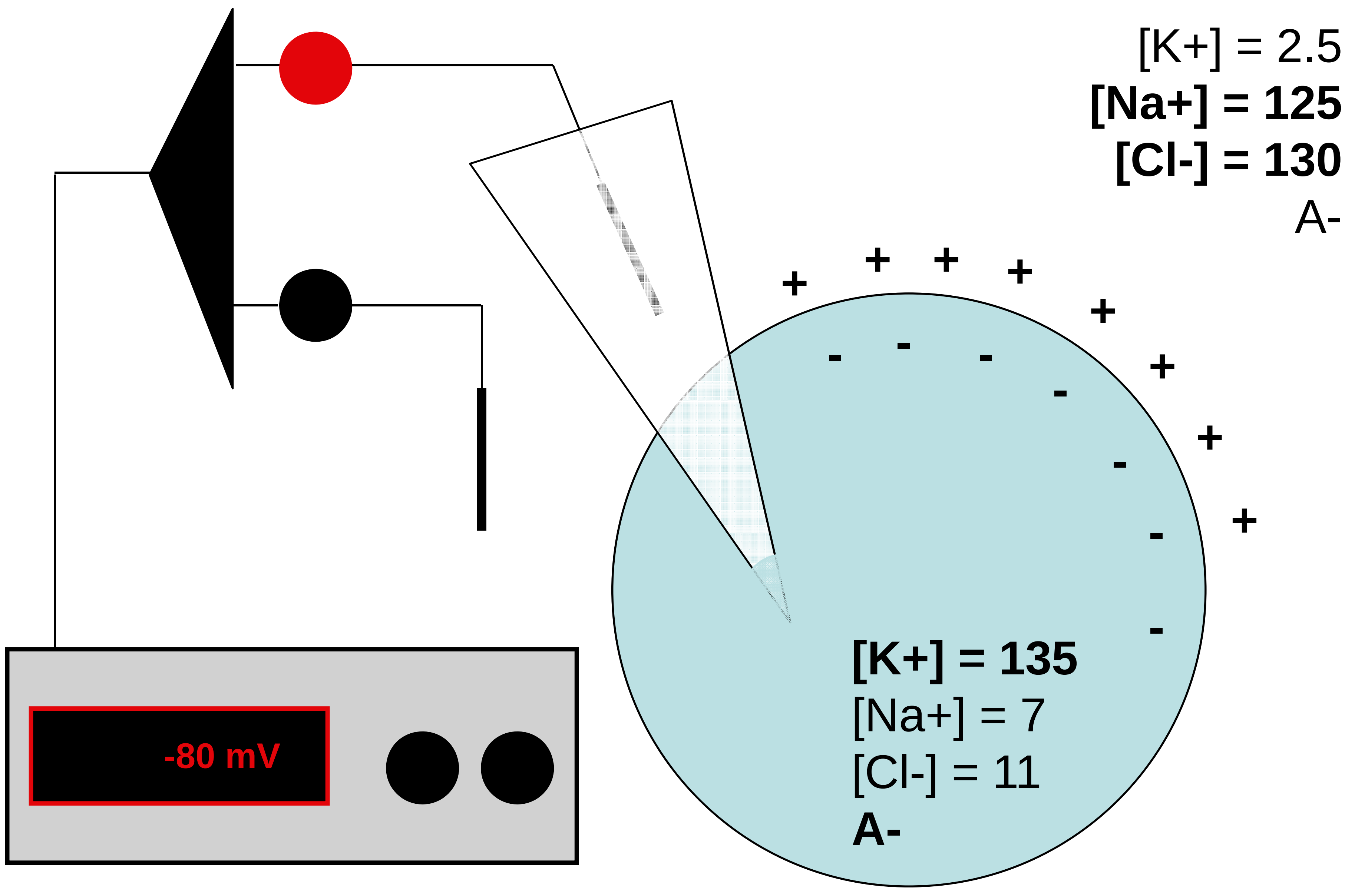


[K+] = 2.5
[Na+] = 125
[Cl-] = 130
A-
[K+] = 135
[Na+] = 7
[Cl-] = 11
A-
-80 mV

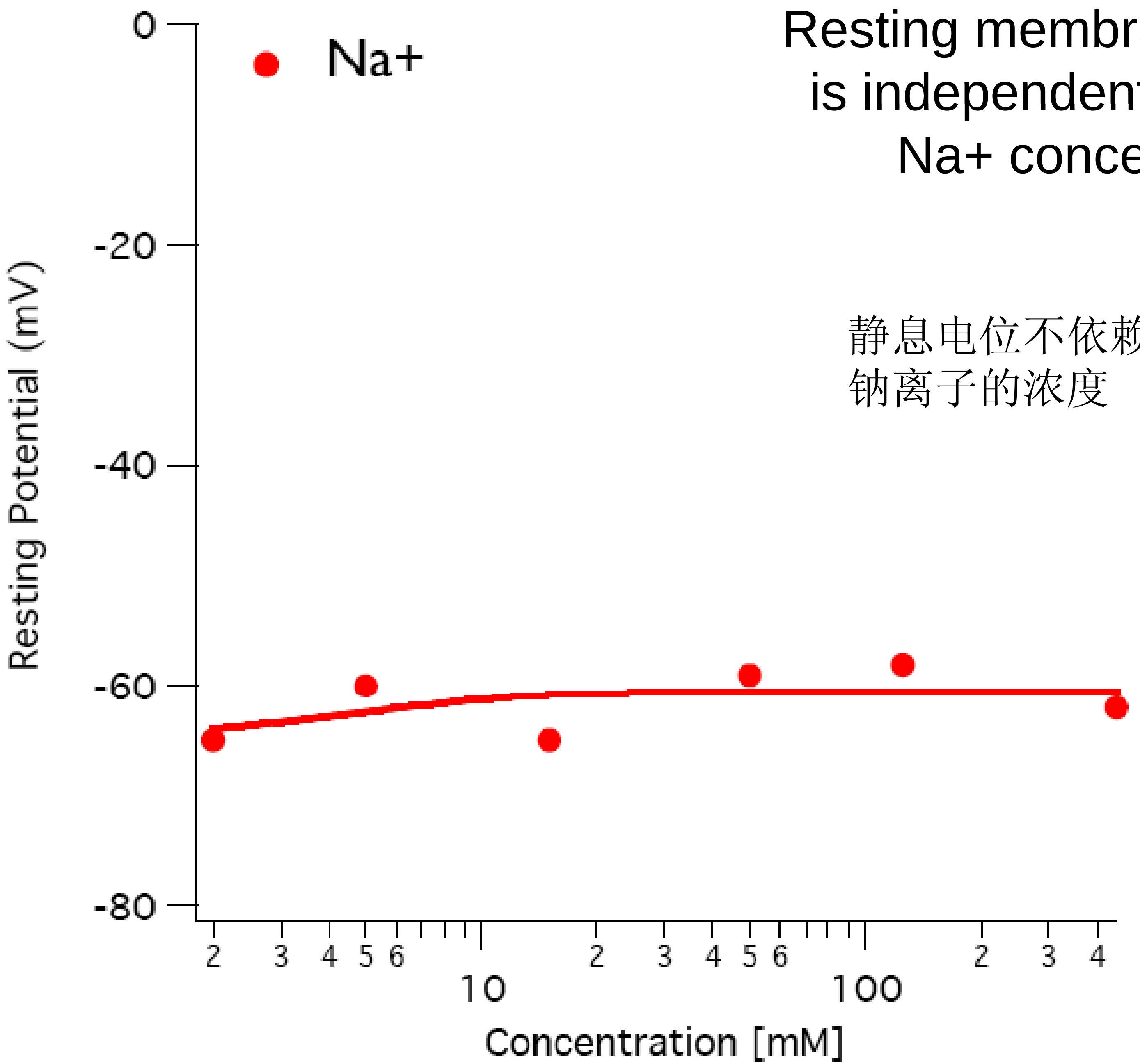
Julius Berstein
German scientist

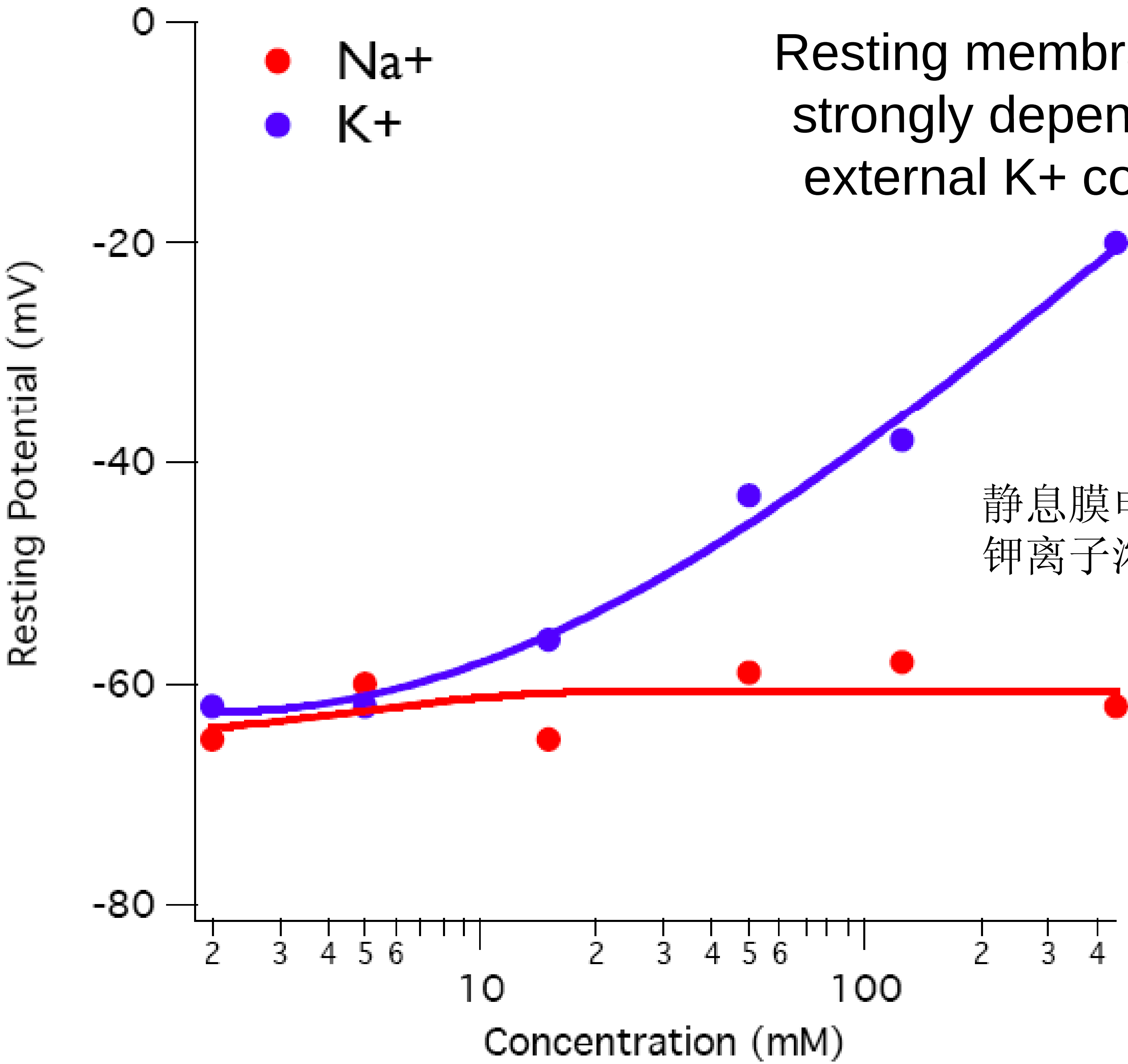
Bernstein (1902, 1912) correctly proposed that excitable cells are surrounded by a membrane selectively permeable to K+ ions at rest and that during excitation the membrane ″membrane breakdown “ to be permeable to other ions.

伯恩斯坦(1902, 1912)最先正确提出，静息时细胞膜只对钾离子有通透性，由于细胞内外钾离子浓度不同，因此两侧出现内负外正的电位差。当细胞受到刺激而兴奋时，细胞膜暂时失去对离子的选择性，所有离子都能通过。

Resting membrane potential is independent of external Na+ concentration

静息电位不依赖于细胞外钠离子的浓度



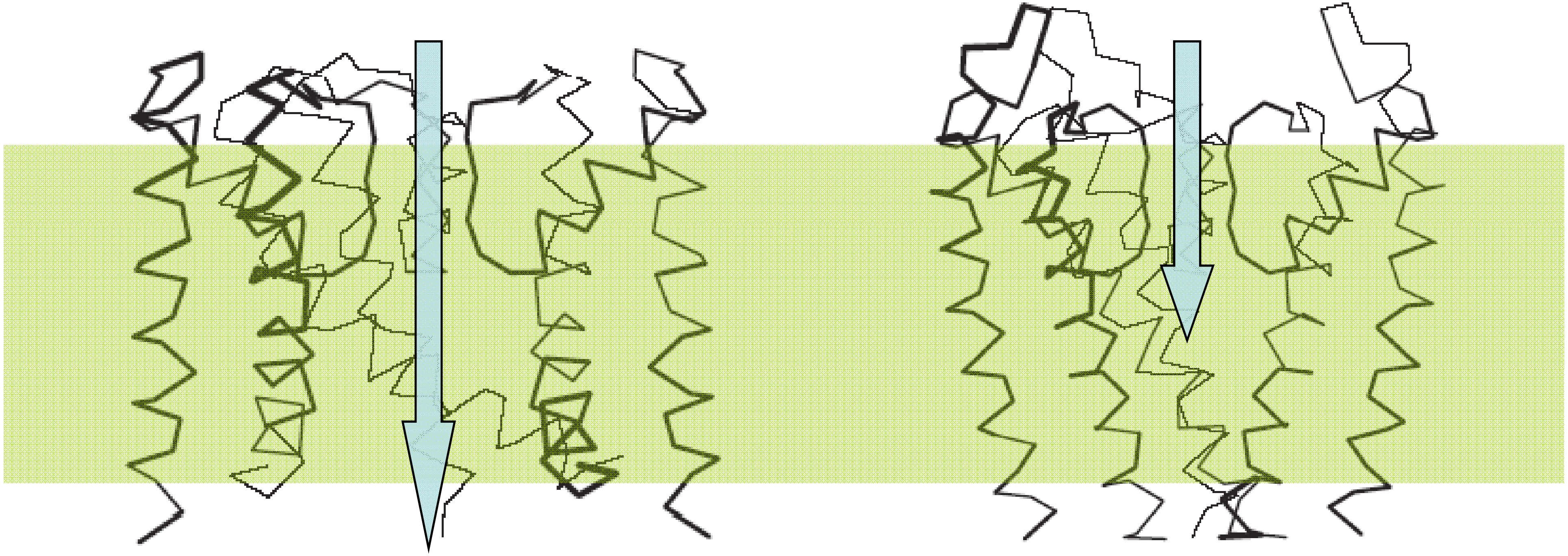


Resting membrane potential strongly depends upon the external K+ concentration

静息膜电位依赖于细胞外钾离子浓度

Why is the resting potential altered by changes in one ion (K+) but not another (Na+)?

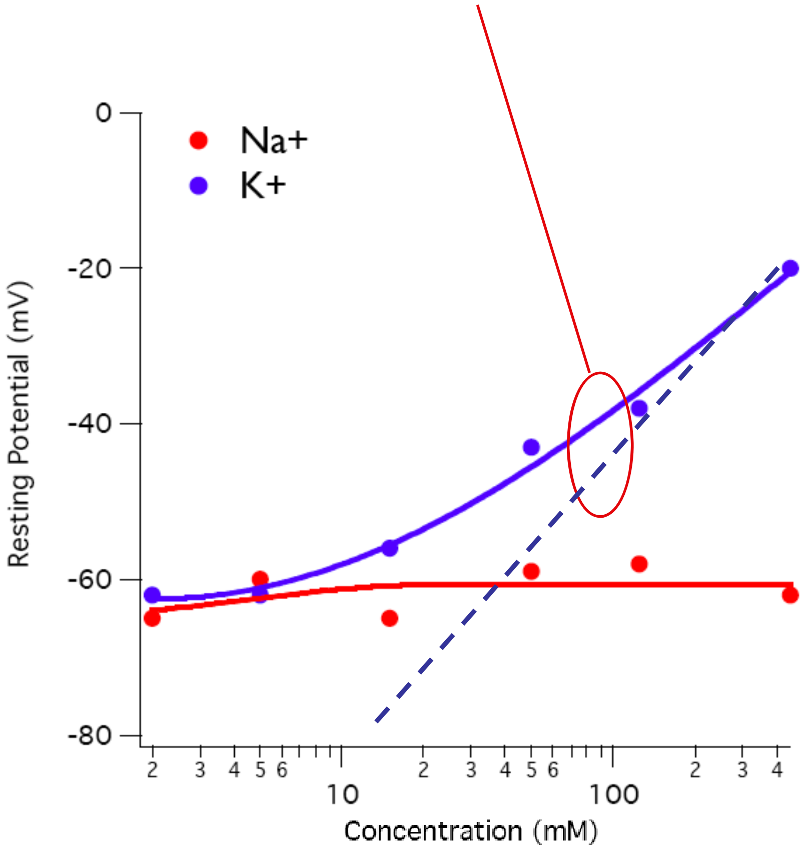
It depends upon the number and type of ion channels that are open at rest



Can we quantify how the resting membrane potential depends upon changes in ion concentration?

Some things to think about

What is the slope of this line?



1. What happens to these considerations during the action potential?

   动作电位的具体过程

2. Why are the ions collected close to the membrane? What does this mean for the polarization of the bulk solution?

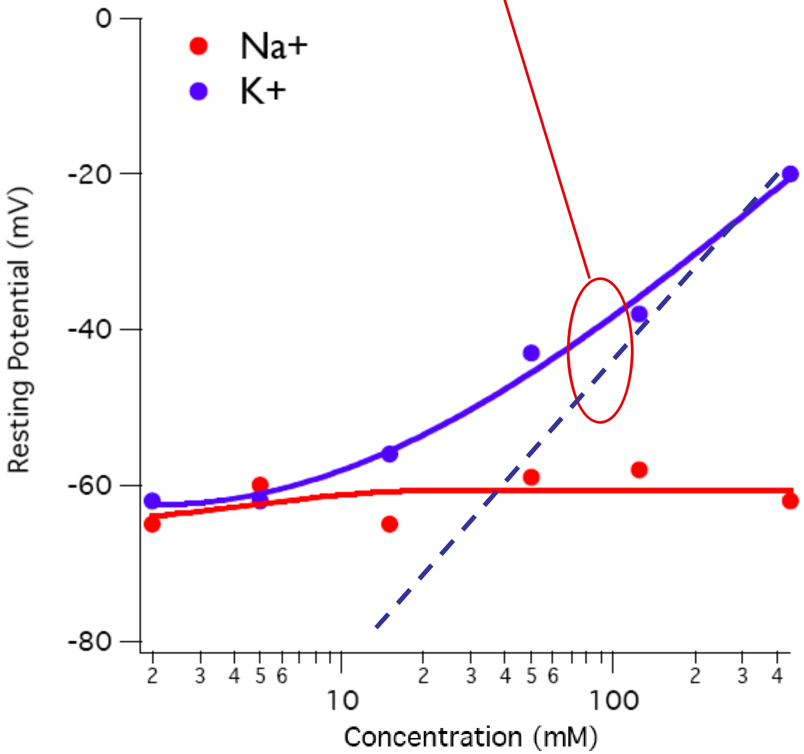
   离子为何靠近膜附近？这对于极化有什么意义？

3. How many ions are moving across the membrane?

   有多少离子进行了跨膜运输

Some things to think about

What is the slope of this line?



4. Why is the membrane impermeant to ions?

细胞膜为何对离子不通透?

5. If the membrane is impermeant to ions it means that there is a large energetic barrier that must be overcome. How do ion channels overcome this energetic barrier?

如果细胞膜对离子不通透，这意味着首先需要克服一个大的能量障碍。离子通道是如何克服这个能量障碍?

So far…

The resting potential is the result of an unequal distribution of ions across the membrane.

The resting potential is sensitive to ions in proportion to their ability to permeate the membrane.

Forget the membrane and consider what factors determine the movement of ions in solution.

到目前为止

静息电位的产生是由于细胞膜两侧不同的离子分布导致的。

静息电位对离子的特异性与该离子相对于细胞膜的通透性成正比。

忽略细胞膜，有哪些因素会决定离子的移动。

Aqueous diffusion

-and-

Electrophoretic movement

水扩散

和

电泳运动

First aqueous diffusion

Diffusion is just the result of thermal agitation.

We can formalize diffusion as:

$$M_s' = -D_s \frac{dc_s}{dx}$$

It is tempting to think of diffusion as a force, however, Einstein demonstrated that it is merely a statistical property of a collection of molecules.

Now electrophoresis

Electrophoresis can be formalized in an analogous fashion.

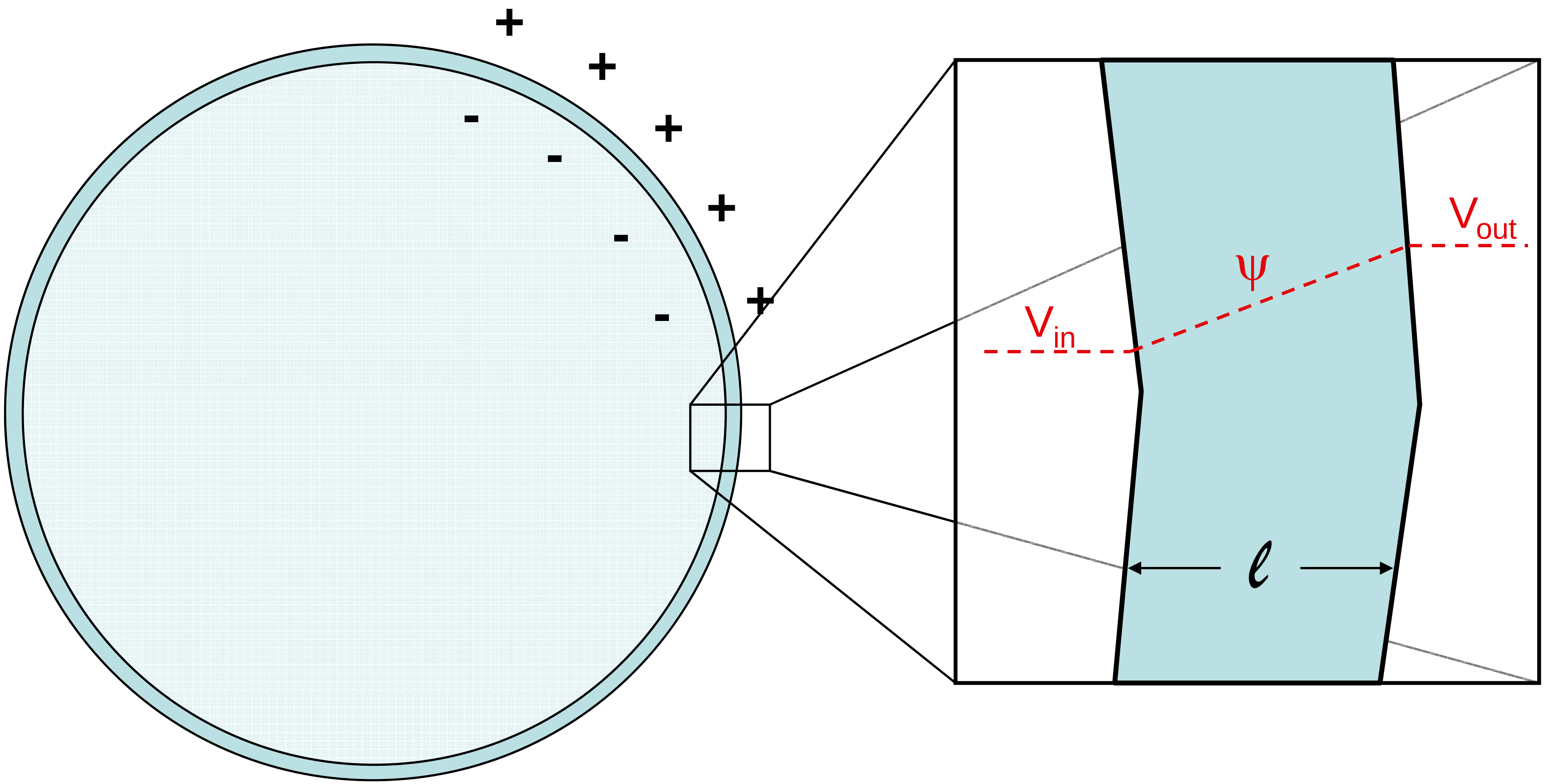
We can formalize electrophoresis as:

$$M_s' = -u_s c_s \frac{d\psi}{dx}$$

In both diffusion and electrophoresis the rate of movement of molecules, or the flux, is determined by friction with the surrounding solution.

Combining diffusion and electrophoresis we get:

$$M_s = -D_s \frac{dc_s}{dx} - u_s c_s \frac{d\psi}{dx}$$



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$$M_s = -D_s \frac{dc_s}{dx} - u_s c_s \frac{d\psi}{dx}$$

Two important relationships

Nernst-Einstein

$$D_s = \frac{u_s RT}{z_s F}$$

Faraday's constant

$$I_s = M_s z_s F$$

What we care about for membrane potential is the current across the membrane

$$I_s = -z_s F D_s \frac{dc_s}{dx} - z_s F \frac{D_s z_s F}{RT} c_s \frac{d\psi}{dx}$$

That oh so famous Nernst-Planck Relationship

$$I_s = -z_s F D_s \left[\frac{dc_s}{dx} + \frac{z_s F}{RT} c_s \frac{d\psi}{dx} \right]$$

But, we care about equilibrium state. When are we at equilibrium

When $I_s = 0$ then, $\frac{d\psi}{dx} = -\frac{RT}{z_s F} \frac{1}{c_s} \frac{dc_s}{dx}$

Finally, if we integrate across the membrane we arrive at the Nernst Equation

$$\psi_i - \psi_o = \frac{RT}{z_s F} \ln \frac{[s]_o}{[s]_i}$$

A little bit more about the Nernst Equation

The general form of the equation in your textbook:

$$E_x = \frac{RT}{zF} \ln \frac{[X]_o}{[X]_i}$$

What is the meaning of E_x?

E_x is the potential at which the flux due to diffusion is equal and opposite to the flux due to electrophoresis

What is E_K for the cell we showed at the beginning?

$$E_K = \frac{58mV}{z} \log \frac{[K]_o}{[K]_i} = \frac{58mV}{\log} \frac{2.5}{135} \cong -100mV$$

In our cell why was the resting potential -80mV if E_K = -100mV?

This cell, as in many other cells in the nervous system, is permeable to more than one ionic species at rest

How can we quantify the contribution of multiple ionic species?

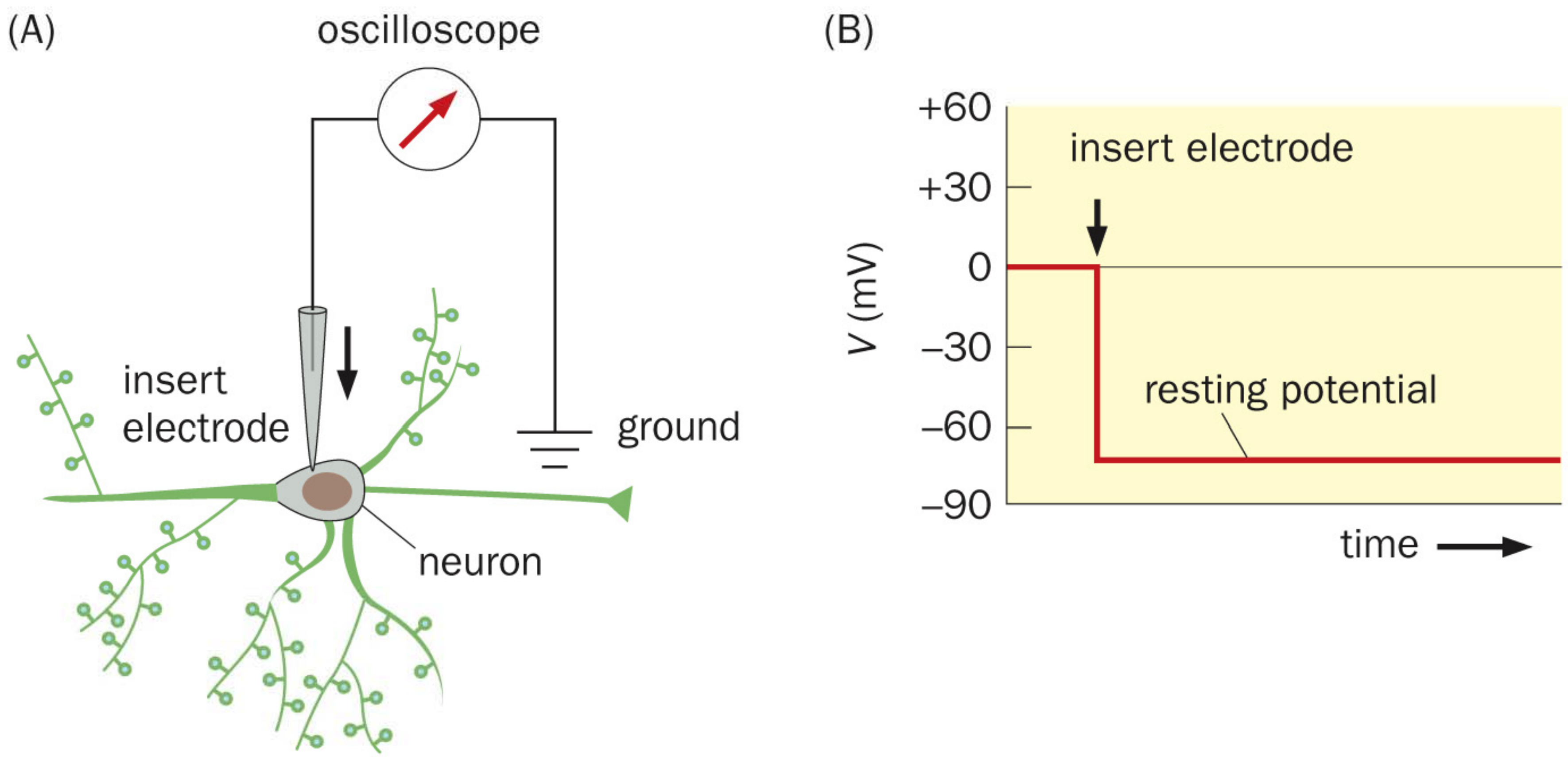
The Goldman Equation (or the GHK Equation)

$$V_m = \frac{RT}{F} \ln \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

Some important details:

- Derives from the Nernst-Planck equation and a few assumptions
- Uses permeabilities rather than conductances
- Cl- is flipped to account for a -1 valence

2.5 Neurons are electrically polarized at rest because of ion concentration differences across the plasma membrane and differential ion permeability
由于细胞膜两侧离子通透性和离子浓度的不同，静息状态下的神经元具有电学极性



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CELL BIOLOGICAL AND ELECTRICAL PROPERTIES OF NEURONS

2.4 Channels and transporters move solutes passively or actively across neuronal membranes

神经元的细胞生物学及电学性质

2.4通道和转运体通过被动或主动运输的方式跨膜转运溶质

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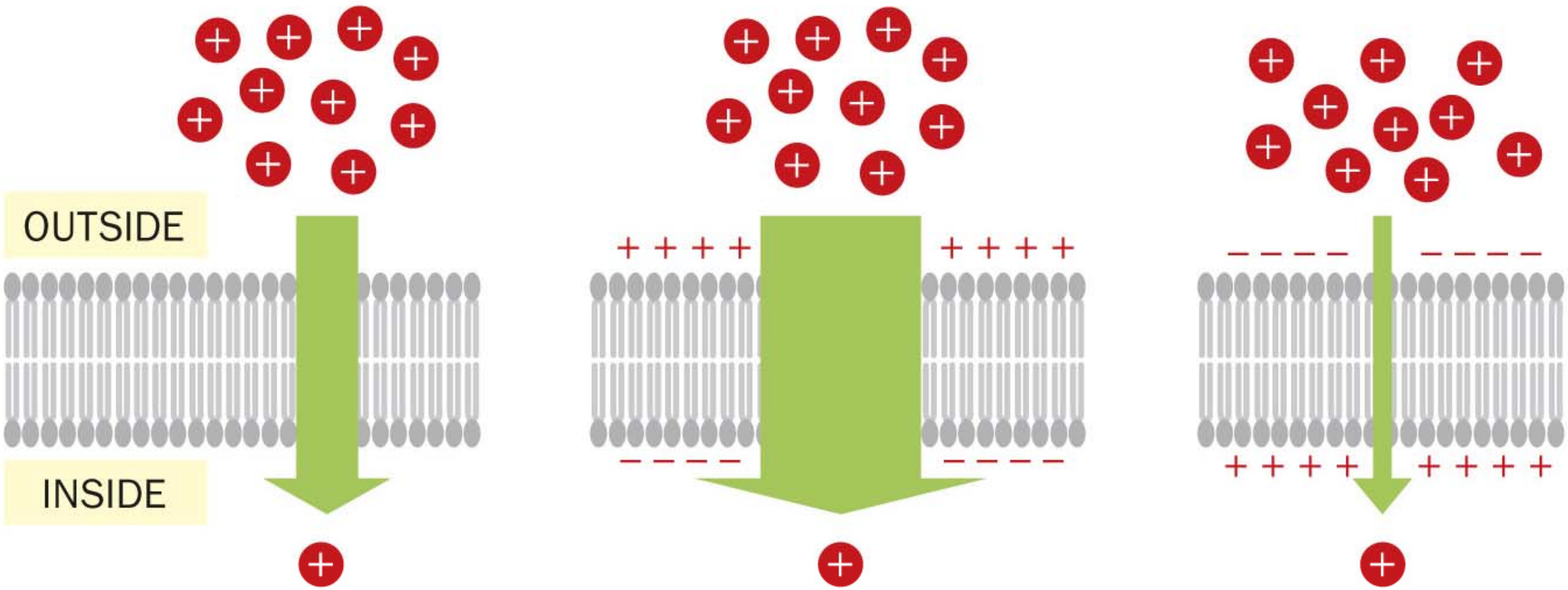

chemical gradient alone; no membrane potential

只有化学梯度，无膜电势

chemical gradient and electrical gradient driving ion movement in the same direction

化学梯度和电学梯度驱动离子同向移动

chemical gradient and electrical gradient driving ion movement in opposing directions

化学梯度和电学梯度驱动离子反向移动

Albert B, Johnson A, Lewis J et al. [2015] Molecular biology of the cell, 6th

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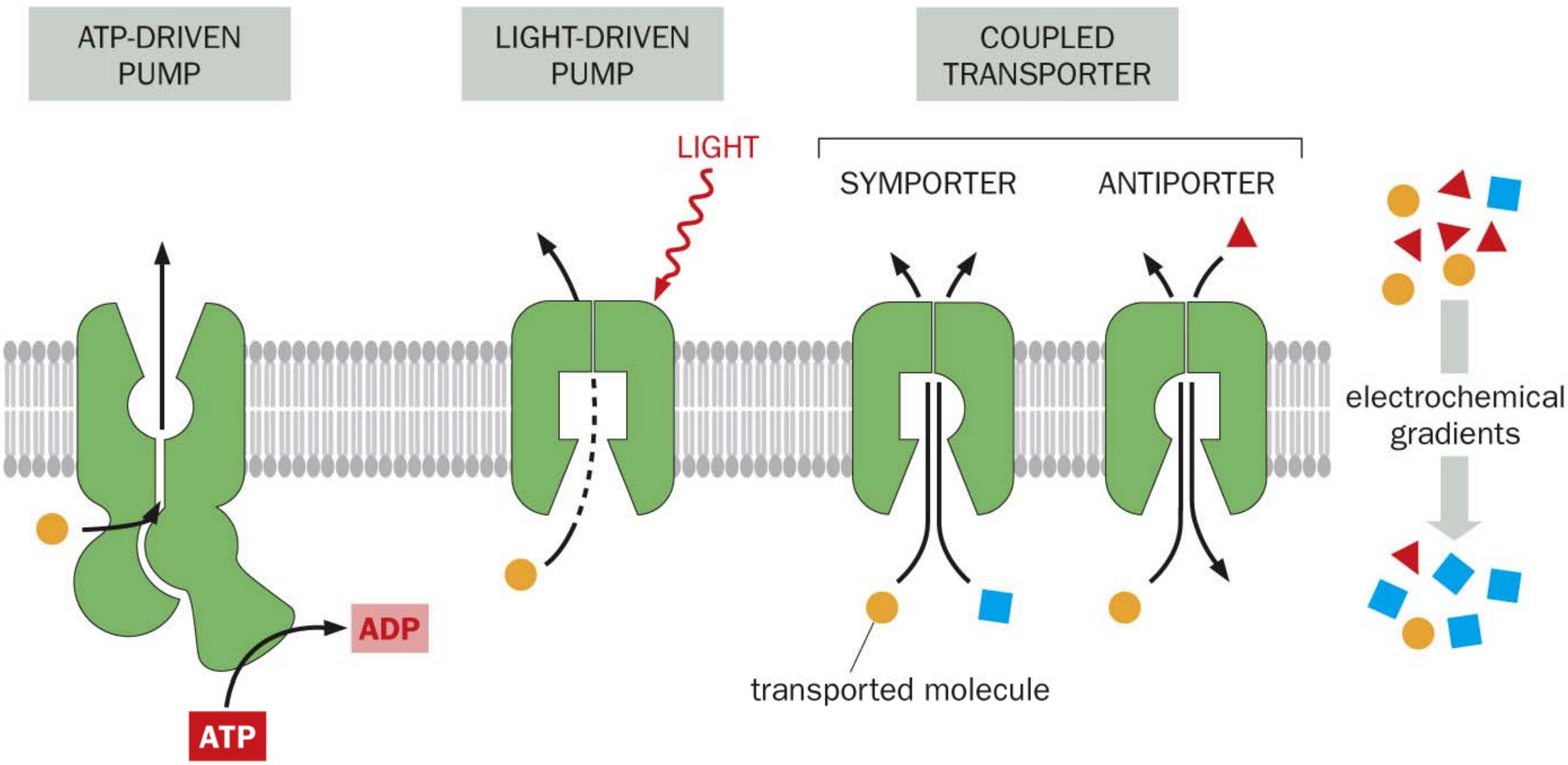

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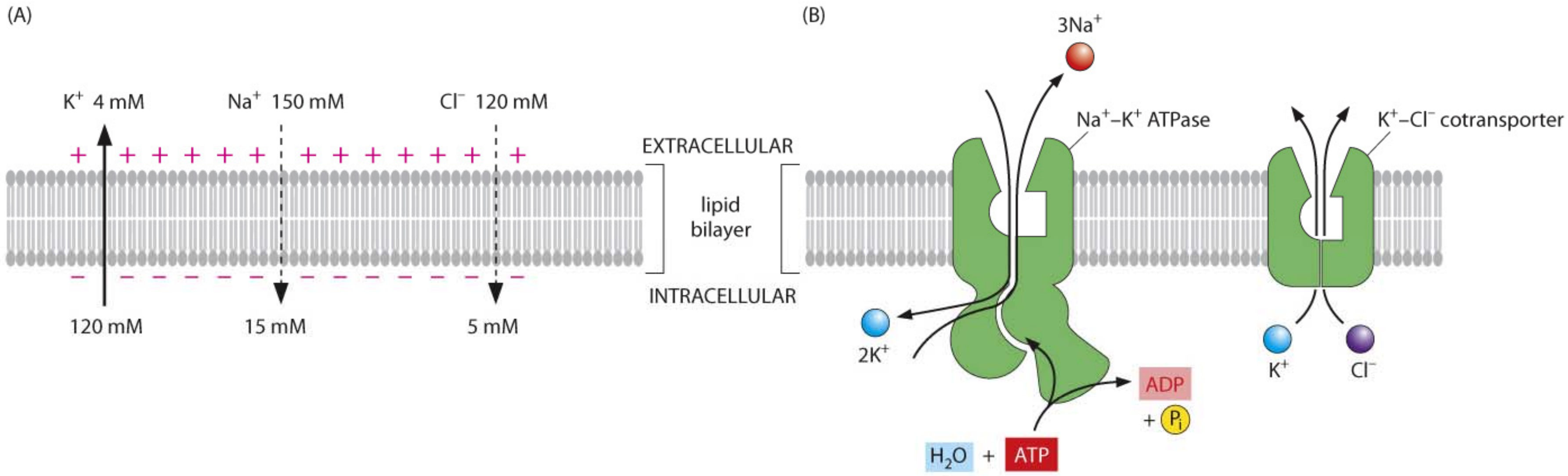

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CELL BIOLOGICAL AND ELECTRICAL PROPERTIES OF NEURONS

2.6 Neuronal plasma membrane can be described in terms of electrical circuits

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2.6神经元细胞膜的电路

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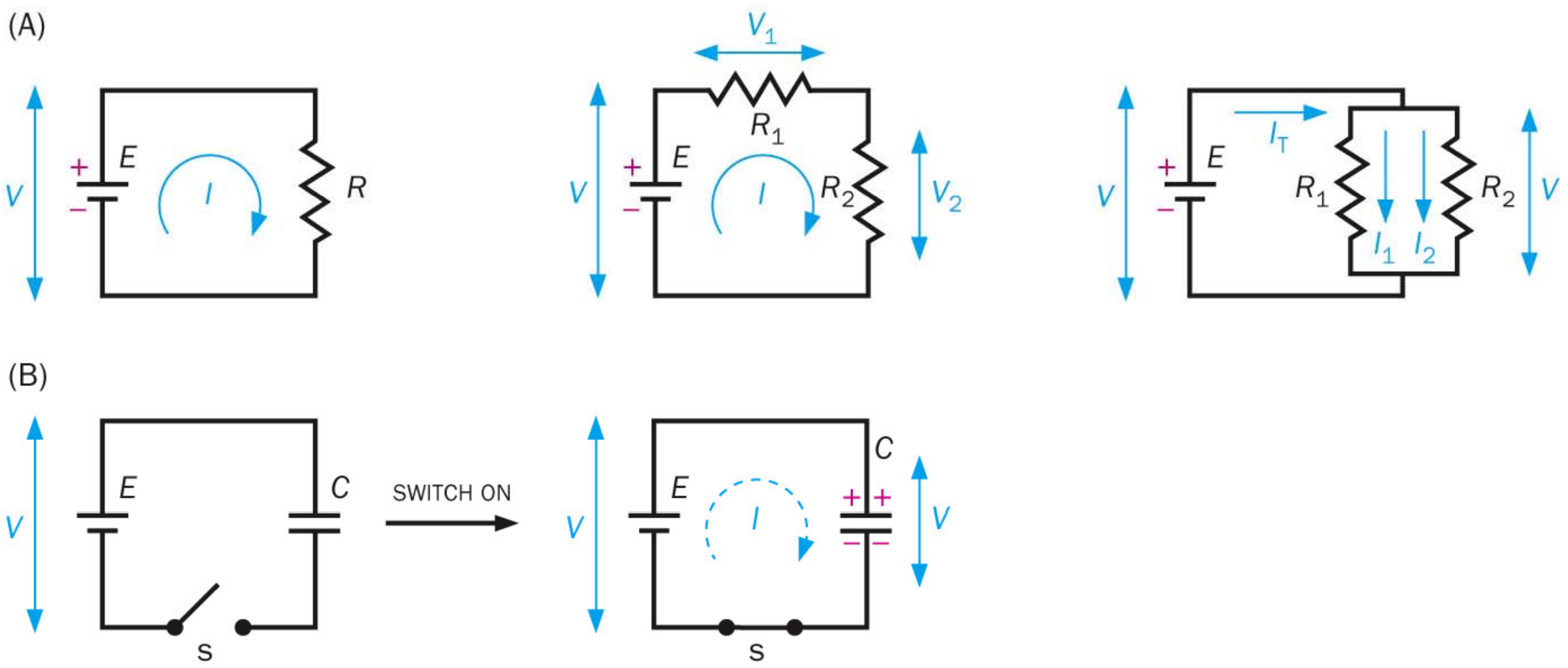

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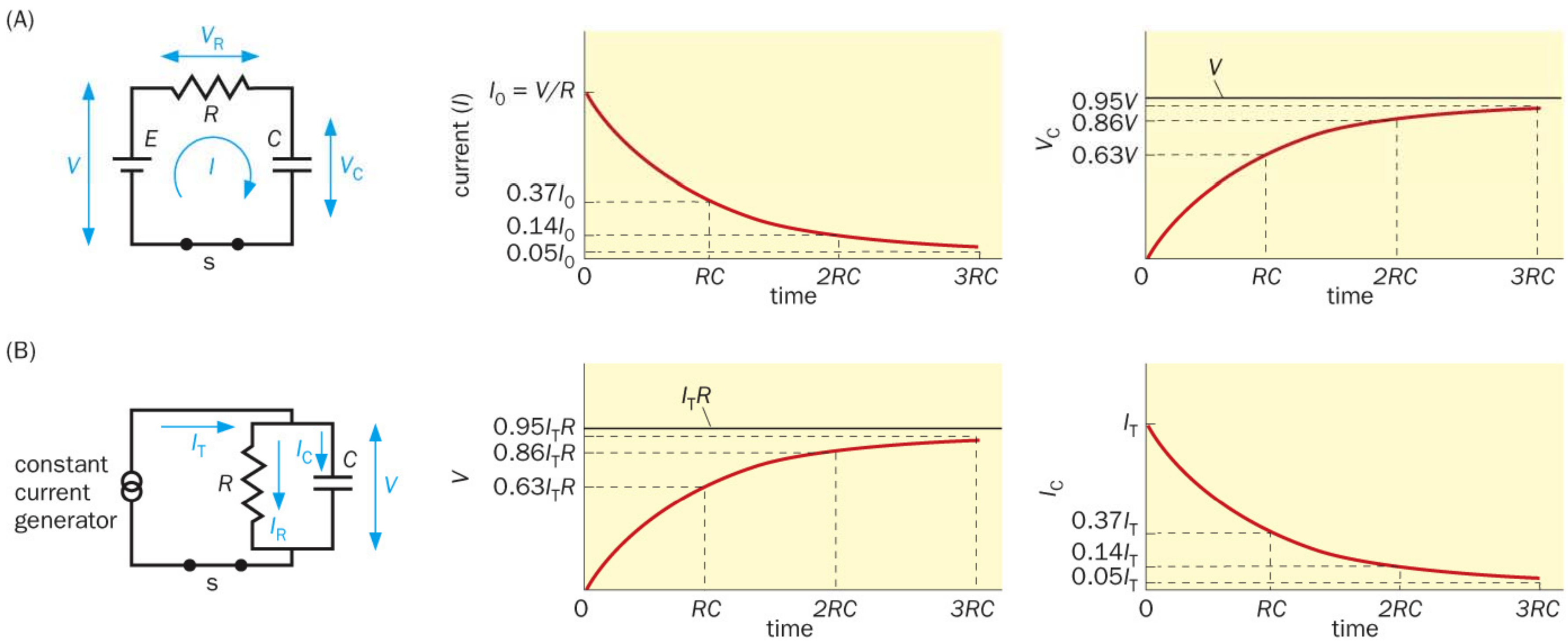

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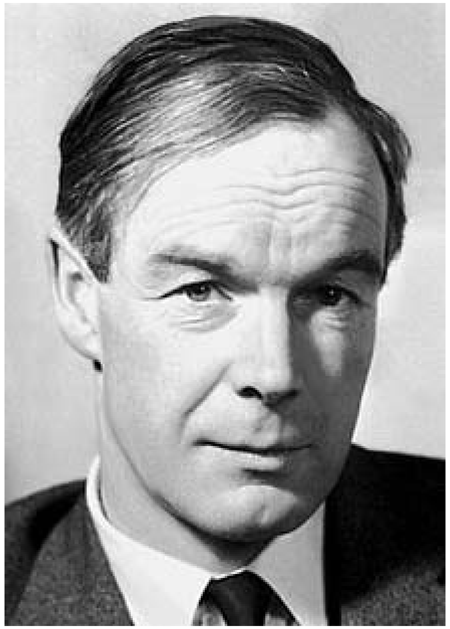
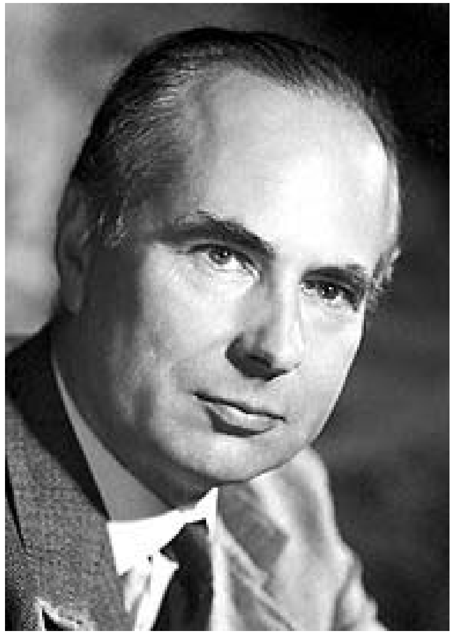
CELL BIOLOGICAL AND ELECTRICAL PROPERTIES OF NEURONS

2.7 Electrical circuit models can be used to analyze ion flows across glial and neuronal plasma membrane

神经元的细胞生物学及电学性质

2.7利用电路模型分析神经元和神经胶质细胞跨膜离子流动





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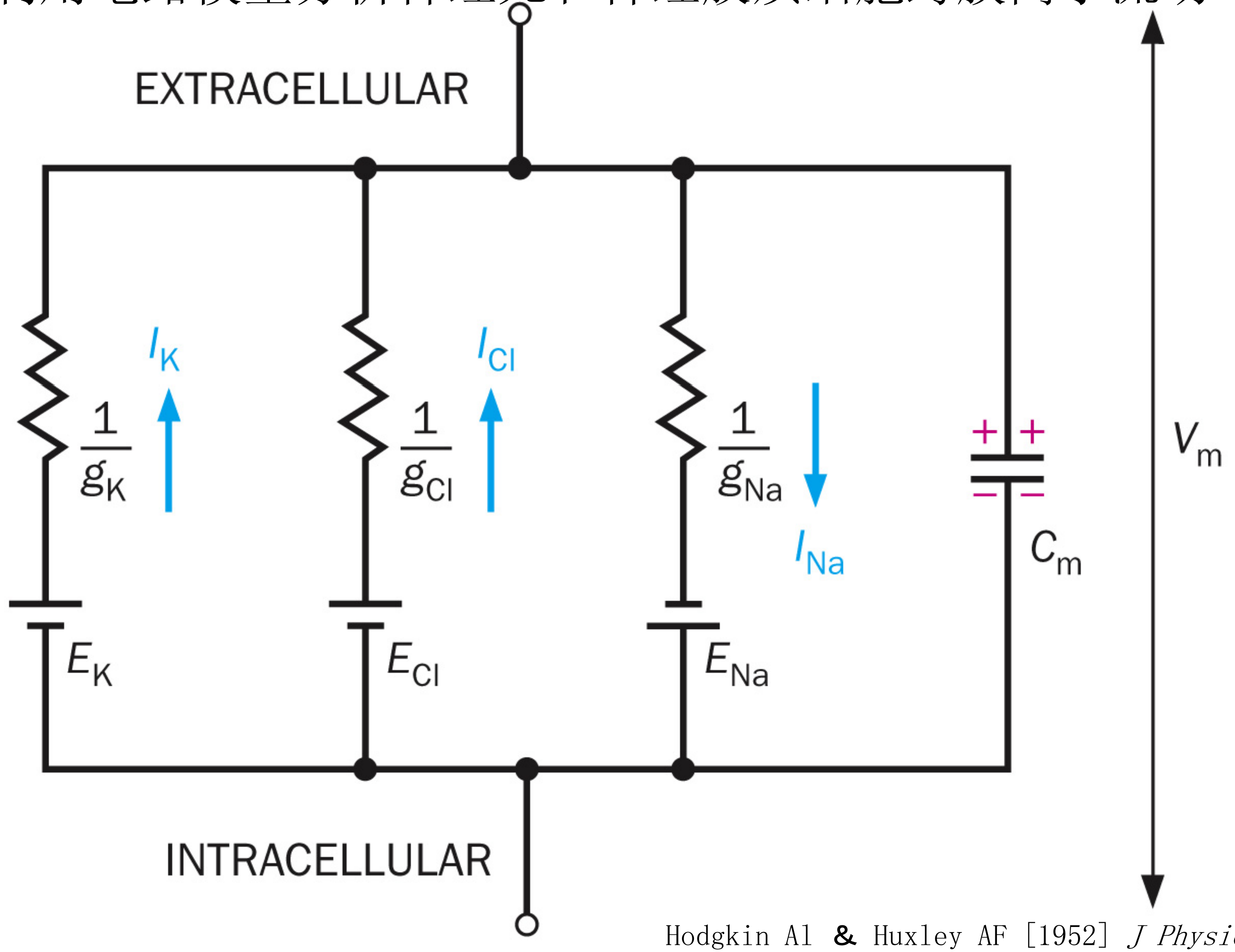

Hodgkin Al & Huxley AF [1952] *J Physiol* 117:500

CELL BIOLOGICAL AND ELECTRICAL PROPERTIES OF NEURONS

2.8 Passive electrical properties of neurons: electrical signals evolve over time and decay across distance

神经元的细胞生物学及电学性质

2.8 神经元的被动电学性质：电信号沿细胞膜进行传导并随距离远离而衰弱。

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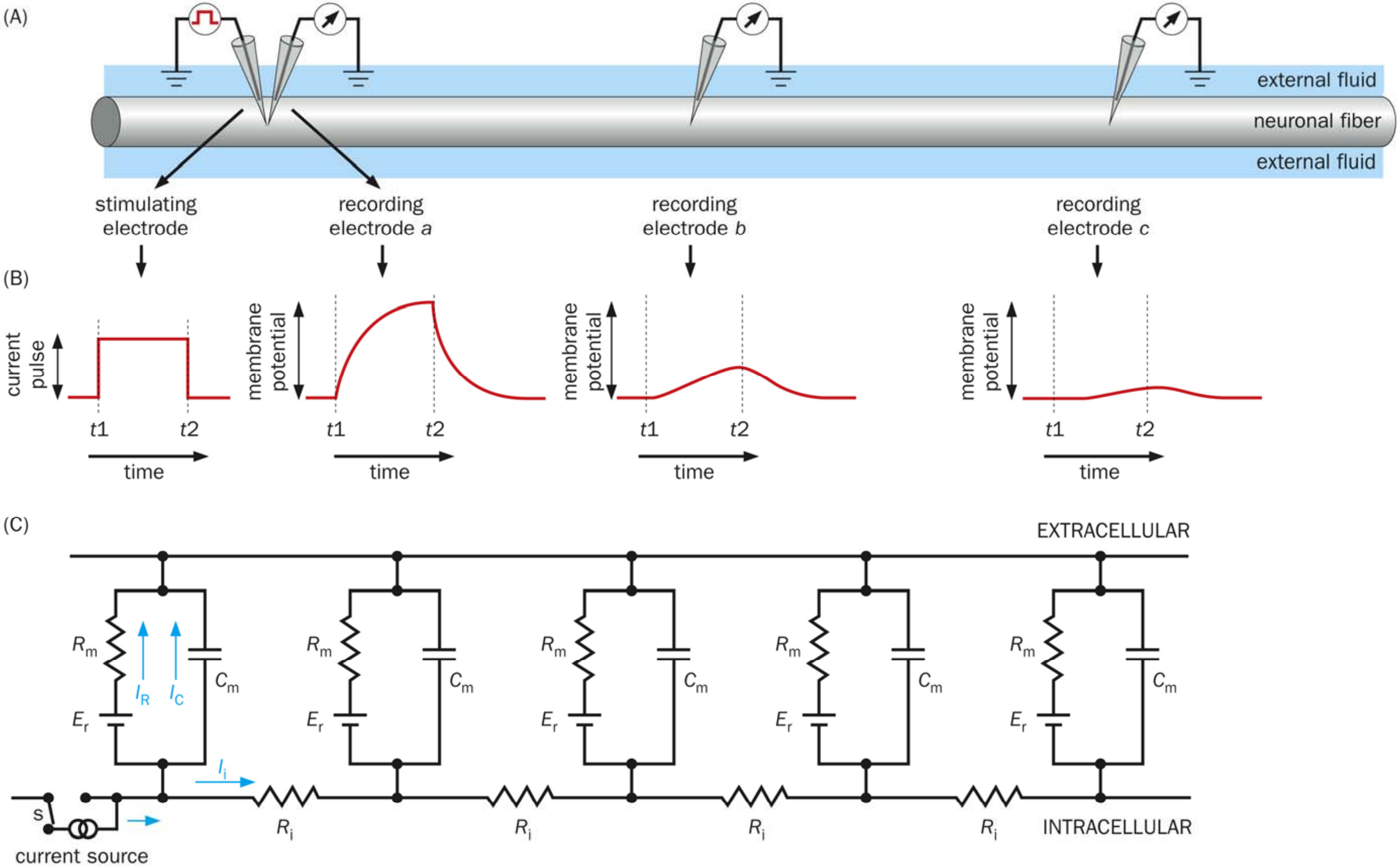

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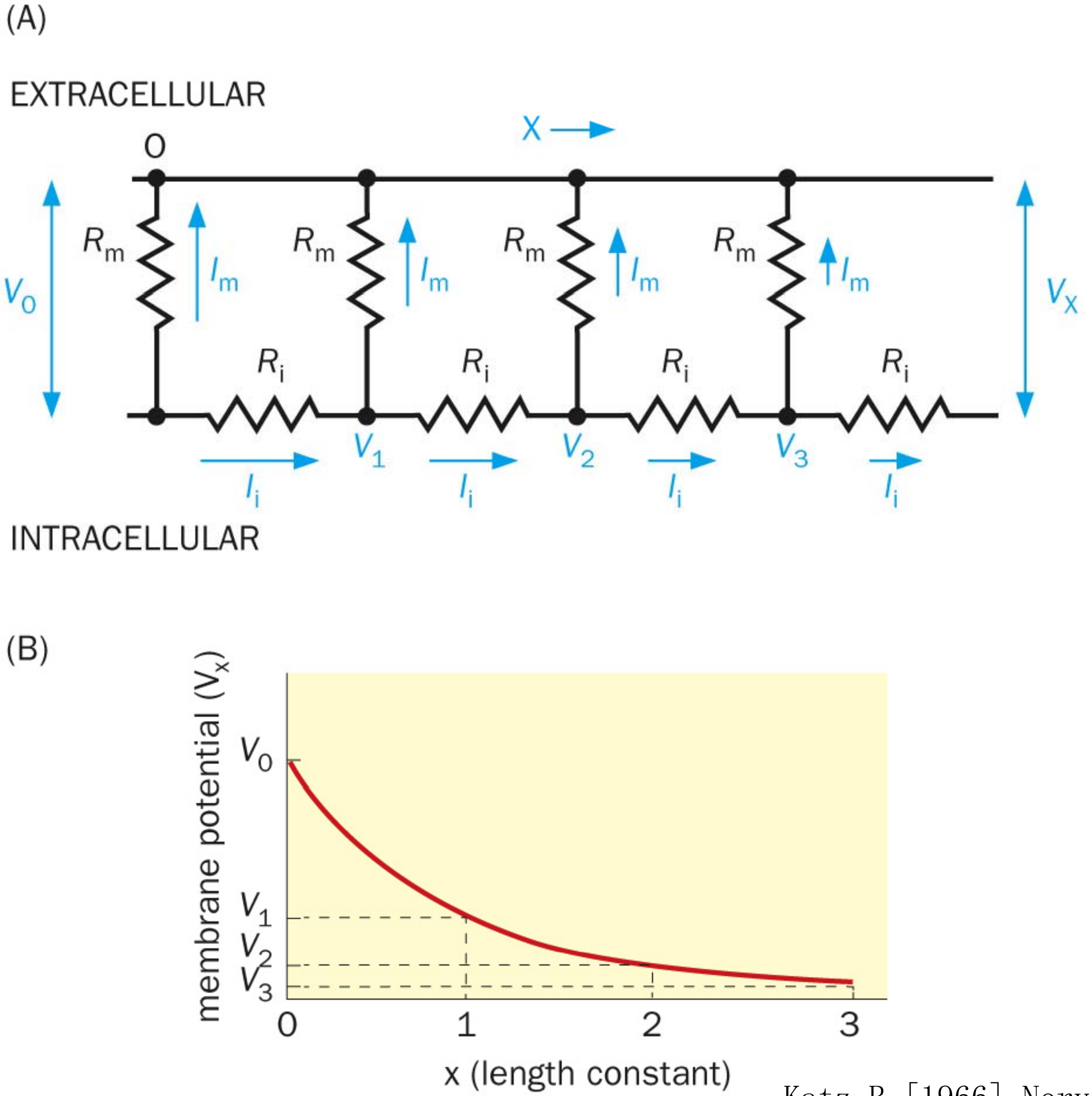

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Table 2–1: Time and length constants of axons, dendrites, and muscle cell

Fiber	Diameter (μm)	Length constant (mm)	Time constant (ms)
Squid giant axon[1]	500	5	0.7
Lobster nerve[1]	75	2.5	2
Frog muscle[1]	75	2	24
Apical dendrite of mammalian cortical pyramidal neuron[2]	3	1	~20

[1]Data from Katz B (1966) Nerve, Muscle, and Synapse. McGraw-Hill; length constants were measured in large extracellular volume.

[2]Data from Stuart G, Spruston N & Hausser M (1999) Dendrites. Oxford University Press.

CELL BIOLOGICAL AND ELECTRICAL PROPERTIES OF NEURONS

2.9 Active electrical properties of neurons: depolarization above a threshold produces action potentials

神经元的细胞生物学及电学性质

2.9 神经元的主动电学性质：阈上去极化导致动作电位的产生

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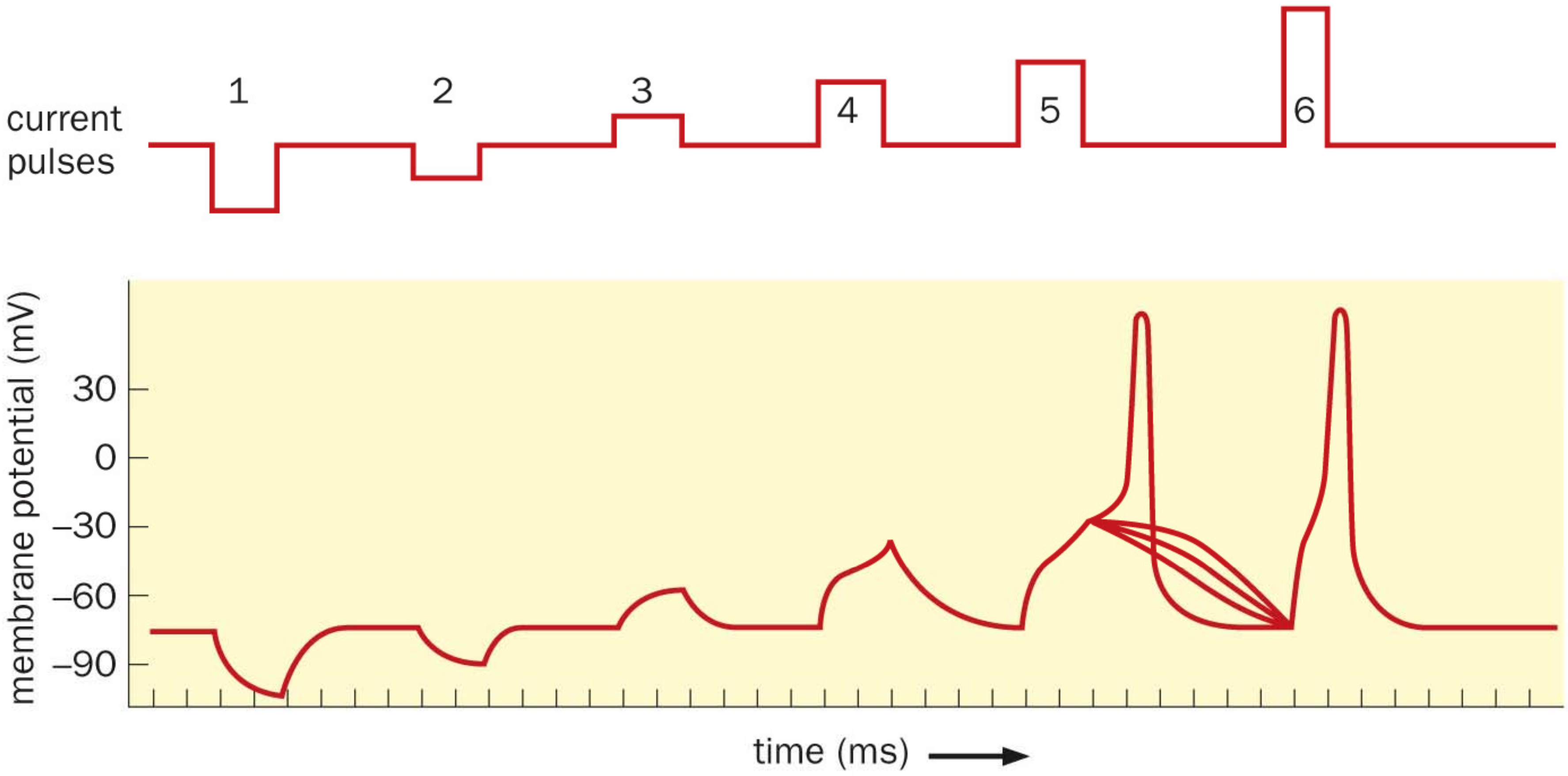

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HOW DO ELECTRICAL SIGNALS PROPAGATE FROM THE NEURONAL CELL BODY TO ITS AXON TERMINALS?

2.10 Action potentials are initiated by depolarization-induced inward flow of Na^+

电信号如何从神经元细胞胞体向轴突末梢传播

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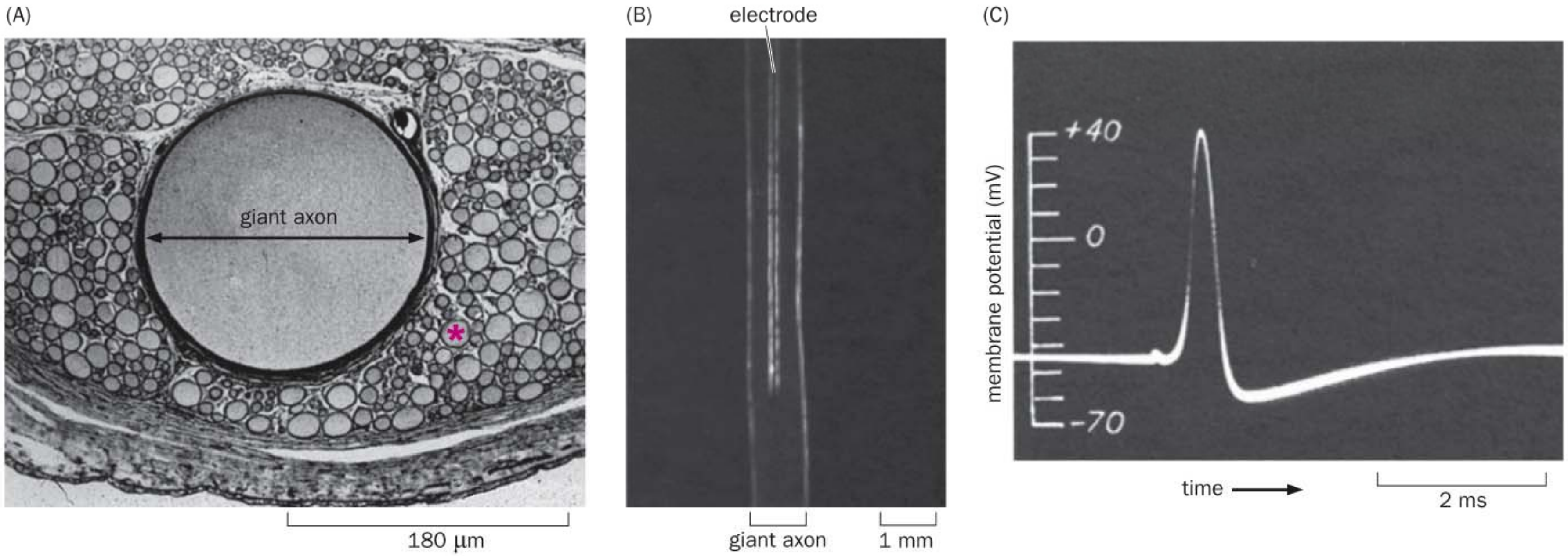

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2.11 Sequential, voltage-dependent changes in Na^+ and K^+ conductances account for action potentials

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2. 11动作电位是通过电压依赖的钠钾离子电导的先后改变而产生

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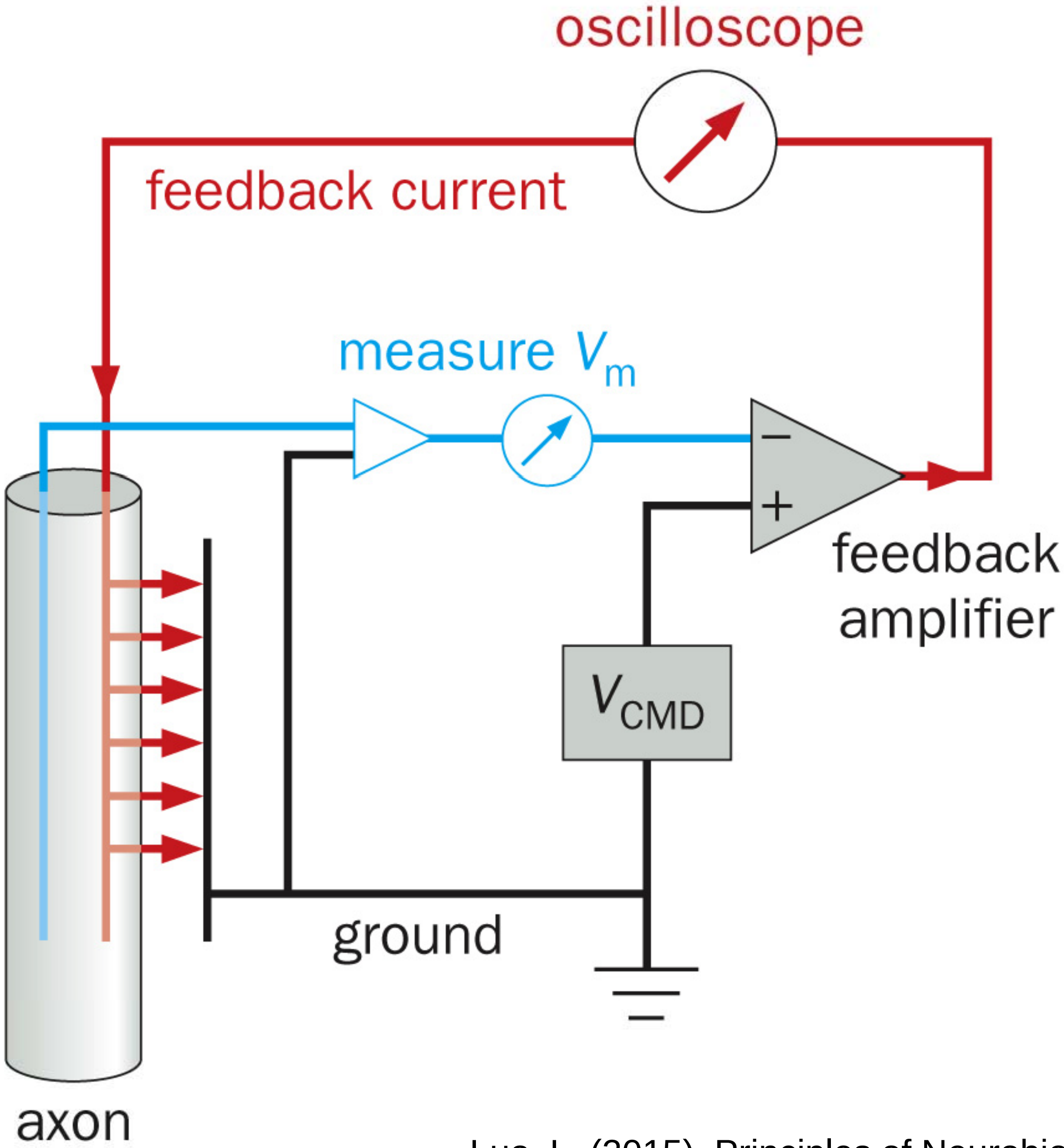

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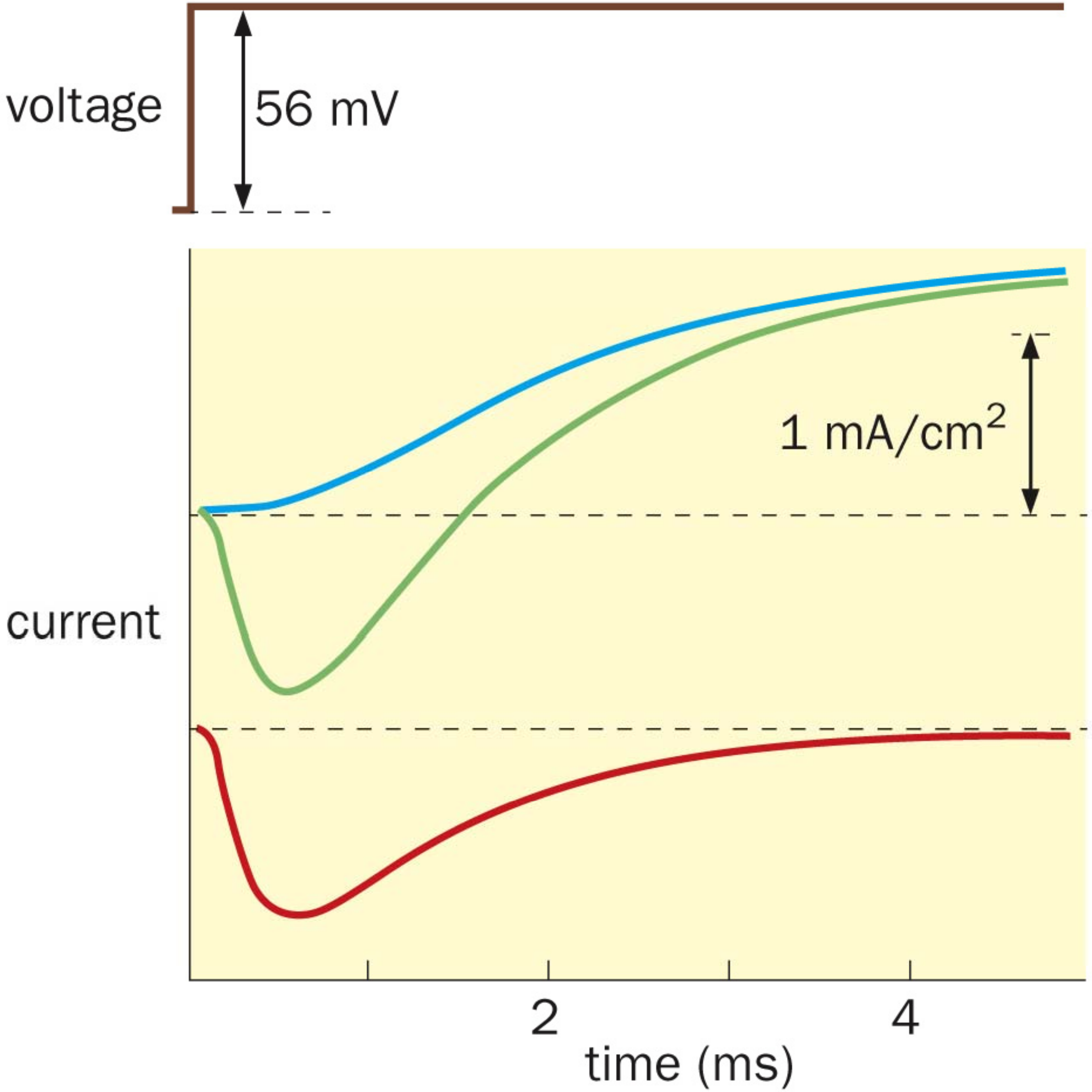

Hodgkin Al & Huxley AF [1952] *J Physiol* 116:44

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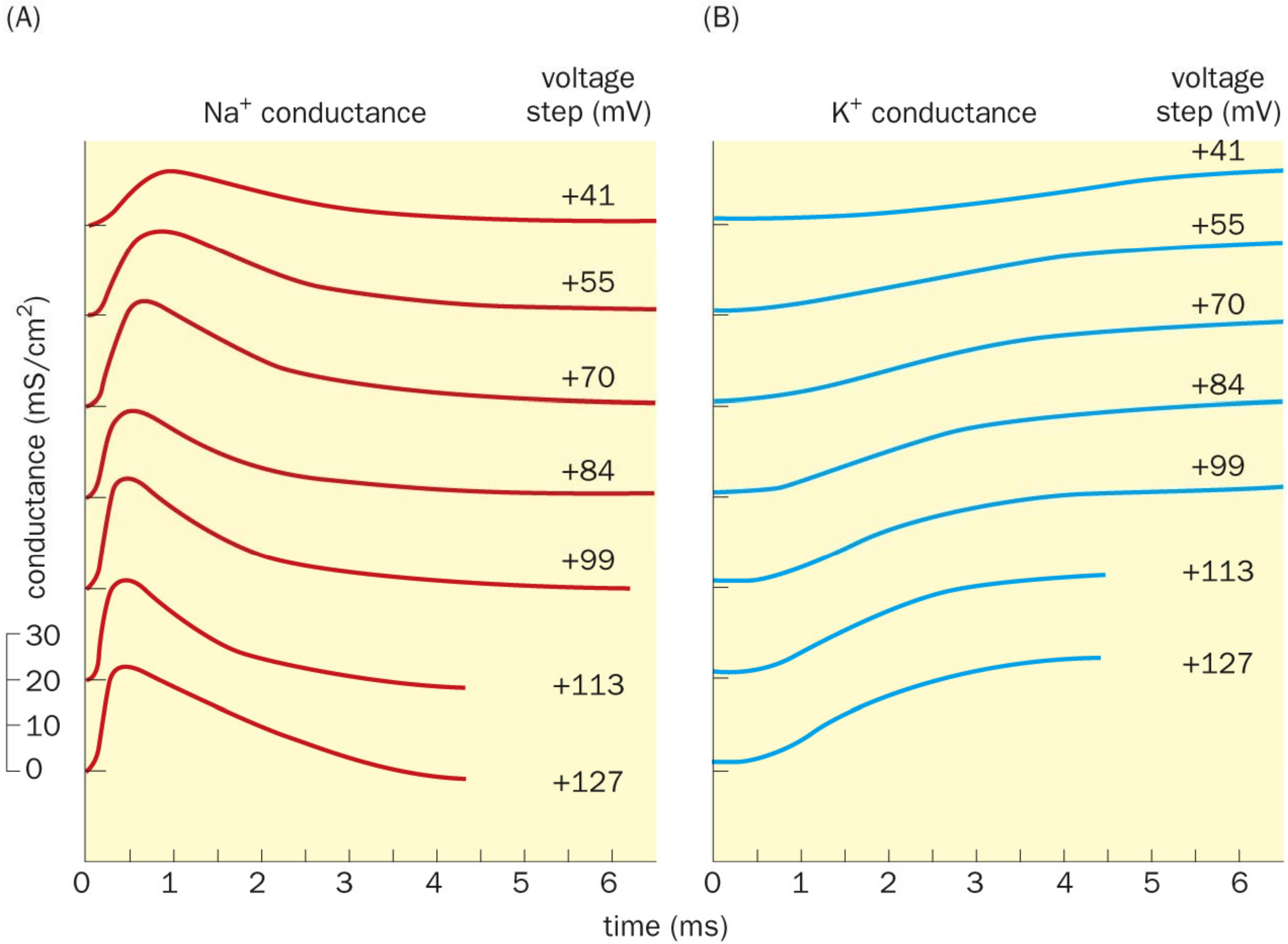

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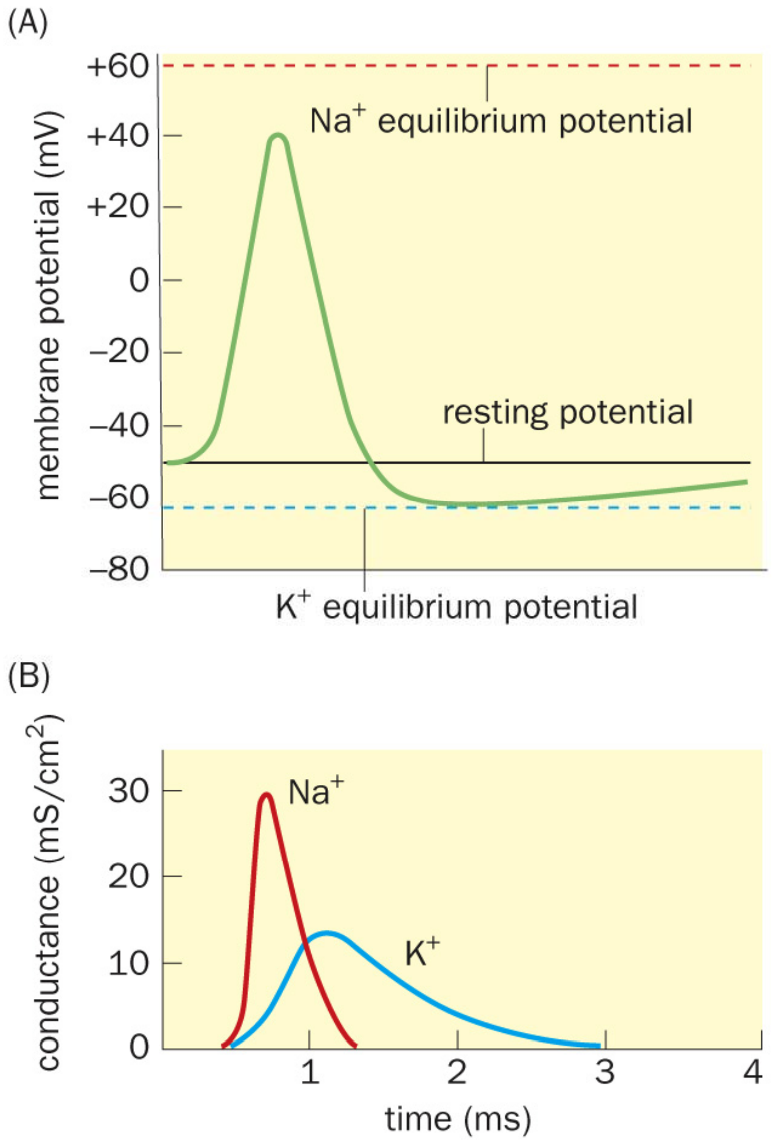

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2.12 Action potentials are all-or-none, are regenerative, and propagate unidirectionally in the axon

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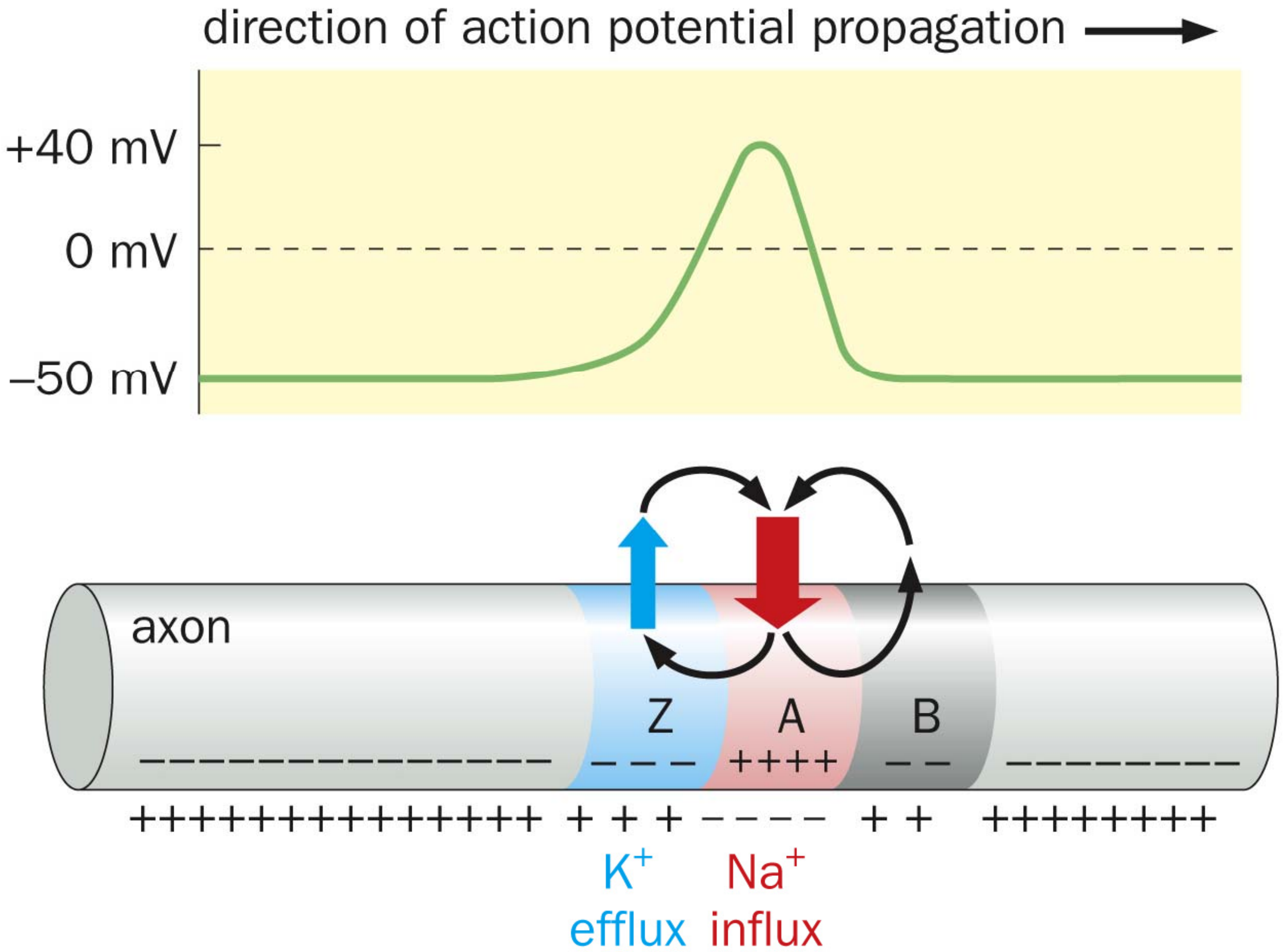
2.12 Action potentials are all-or-none, are regenerative, and propagate unidirectionally in the axon

2.12 动作电位是全或无的，可再生的，沿着轴突单向传播



Luo, L. (2015). Principles of Neurobiology. Garland Science.

HOW DO ELECTRICAL SIGNALS PROPAGATE FROM THE NEURONAL CELL BODY TO ITS AXON TERMINALS?

2.13 Action potentials propagate more rapidly in axons with larger diameters and in myelinated axons

电信号如何从神经元细胞胞体向轴突末梢传播

2.13 动作电位在大直径轴突中及髓鞘包裹的轴突中传播的更快

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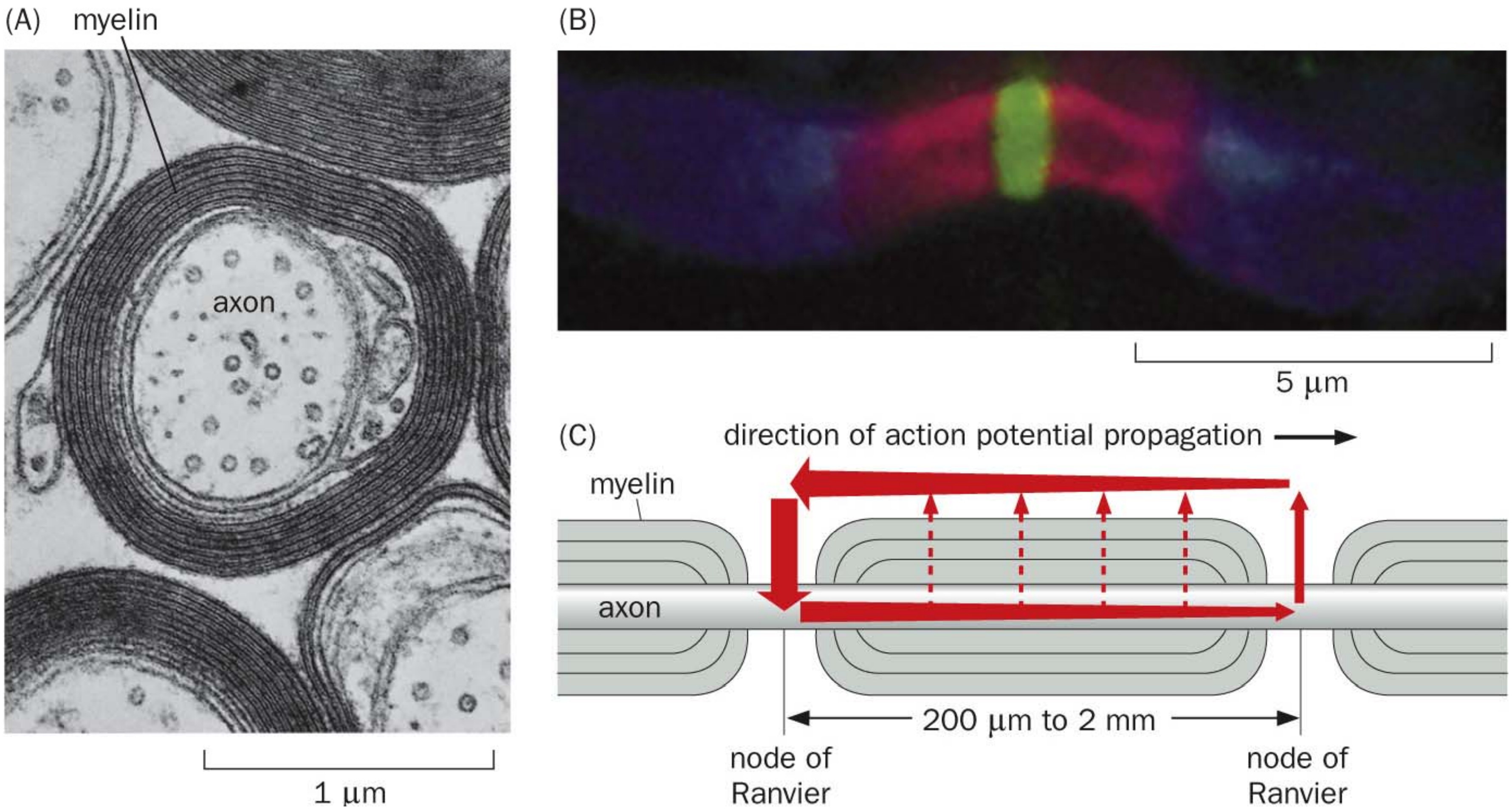

Courtesy of Cedric Raine.

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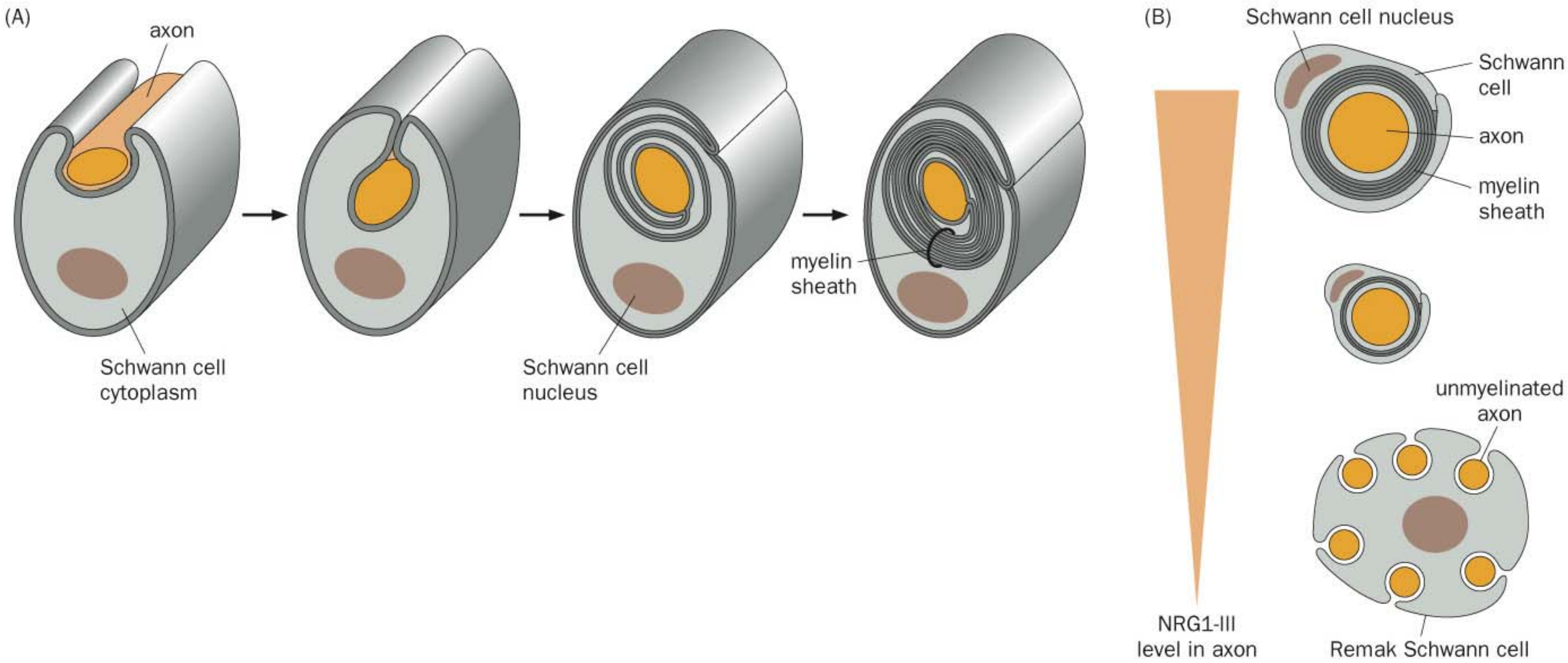

Nave KA & Salzer JL [2006] *Curr Opin Neurobio* 16:492

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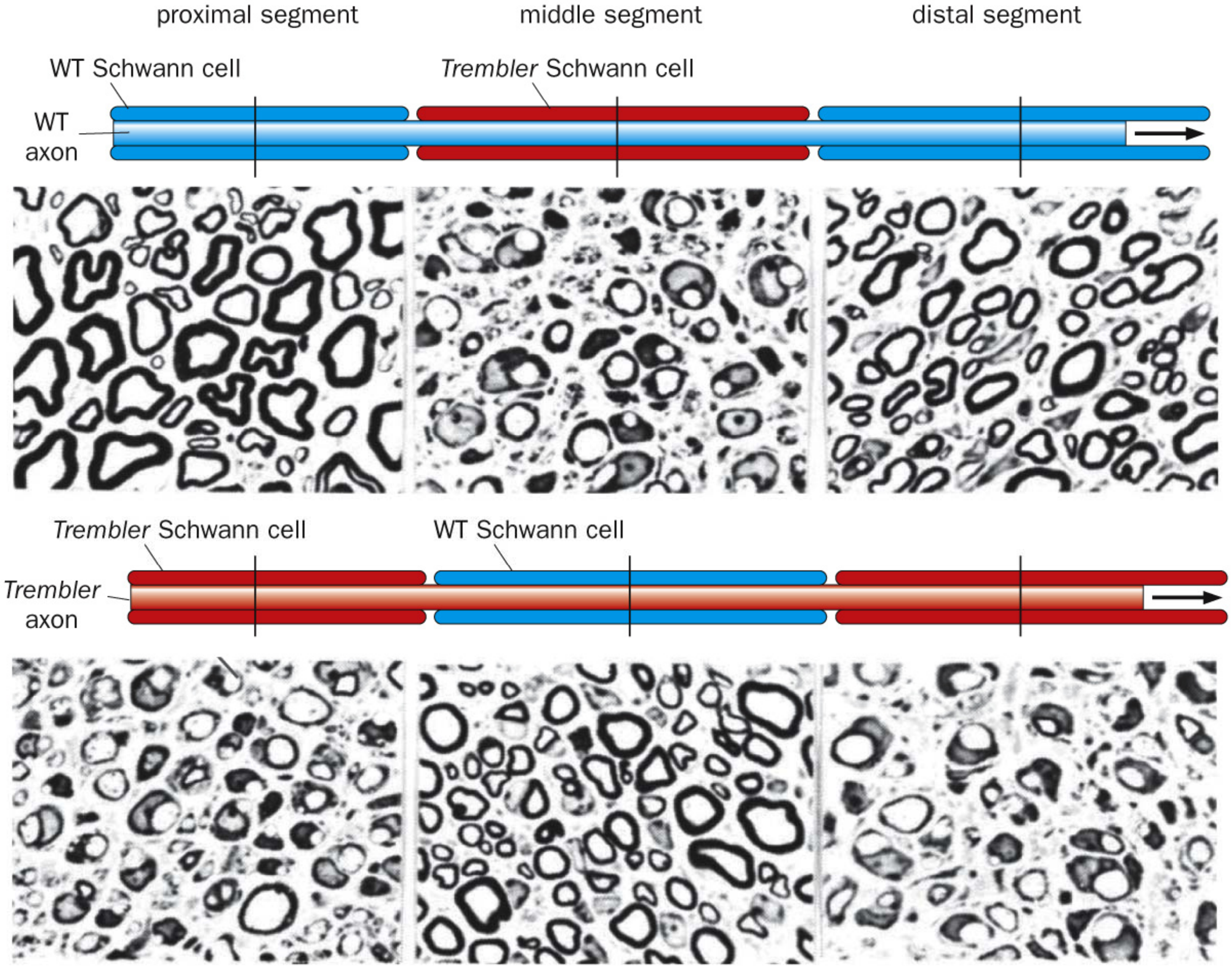
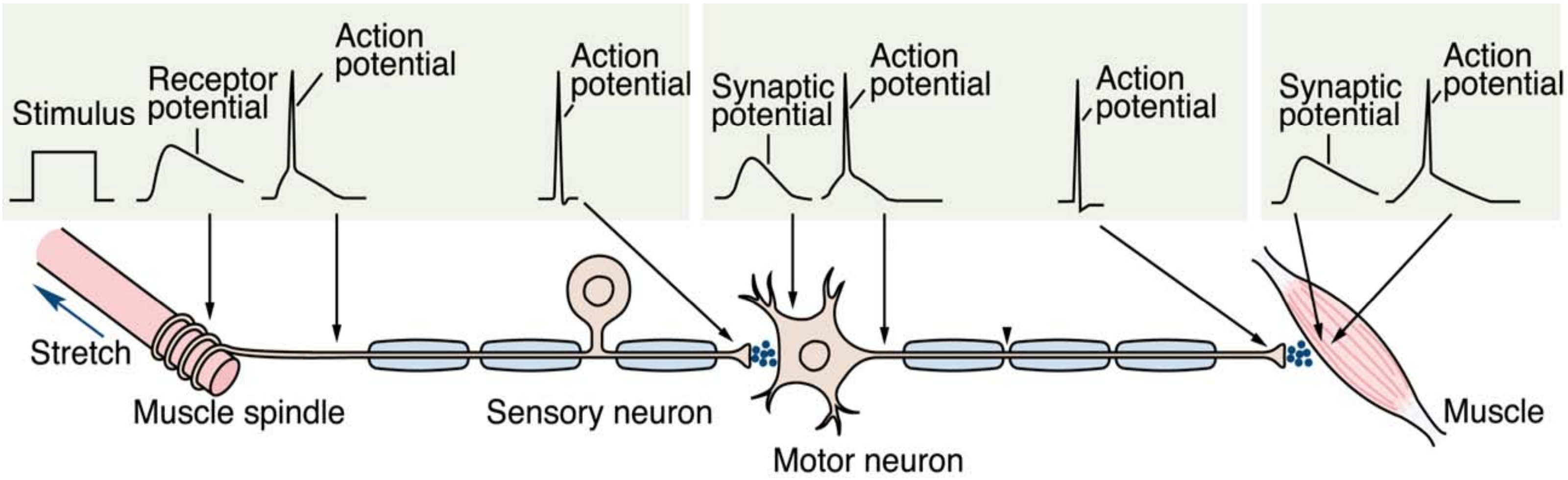


Aguayo AJ, Attiwell M, Trecarten J et al. [1977] *Nature*

Diagram of information transfer in the nervous system

神经系统中的信息传递



PNS, Fig 2-11

HOW DO ELECTRICAL SIGNALS PROPAGATE FROM THE NEURONAL CELL BODY TO ITS AXON TERMINALS?

2.14 Patch clamp recording enables the study of current flow across individual ion channels

电信号如何从神经元细胞胞体向轴突末梢传播

2.14 利用膜片钳研究通过单个离子通道的电流

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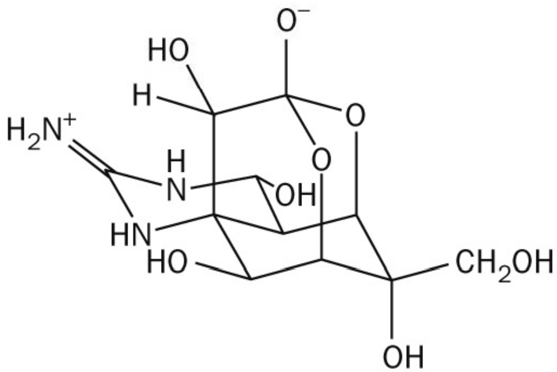

Image Courtesy of Brochen Inaglory/Wikipedia.

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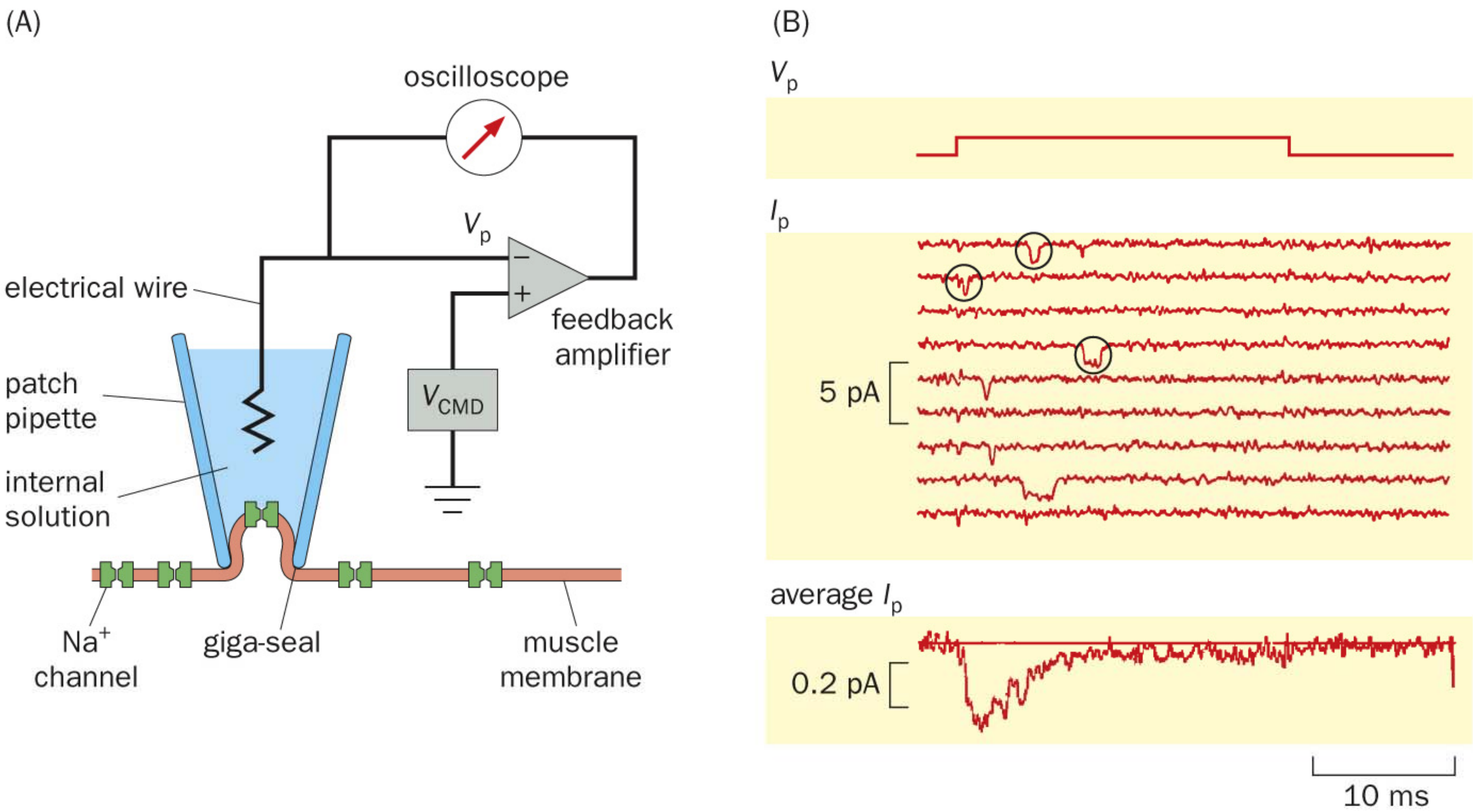

HOW DO ELECTRICAL SIGNALS PROPAGATE FROM THE NEURONAL CELL BODY TO ITS AXON TERMINALS?

2.15 Cloning of genes that encode ion channels allows their structure–function relationship to be studied

电信号如何从神经元细胞胞体向轴突末梢传播

2.15通过克隆编码离子通道的基因研究其结构-功能之间的关系

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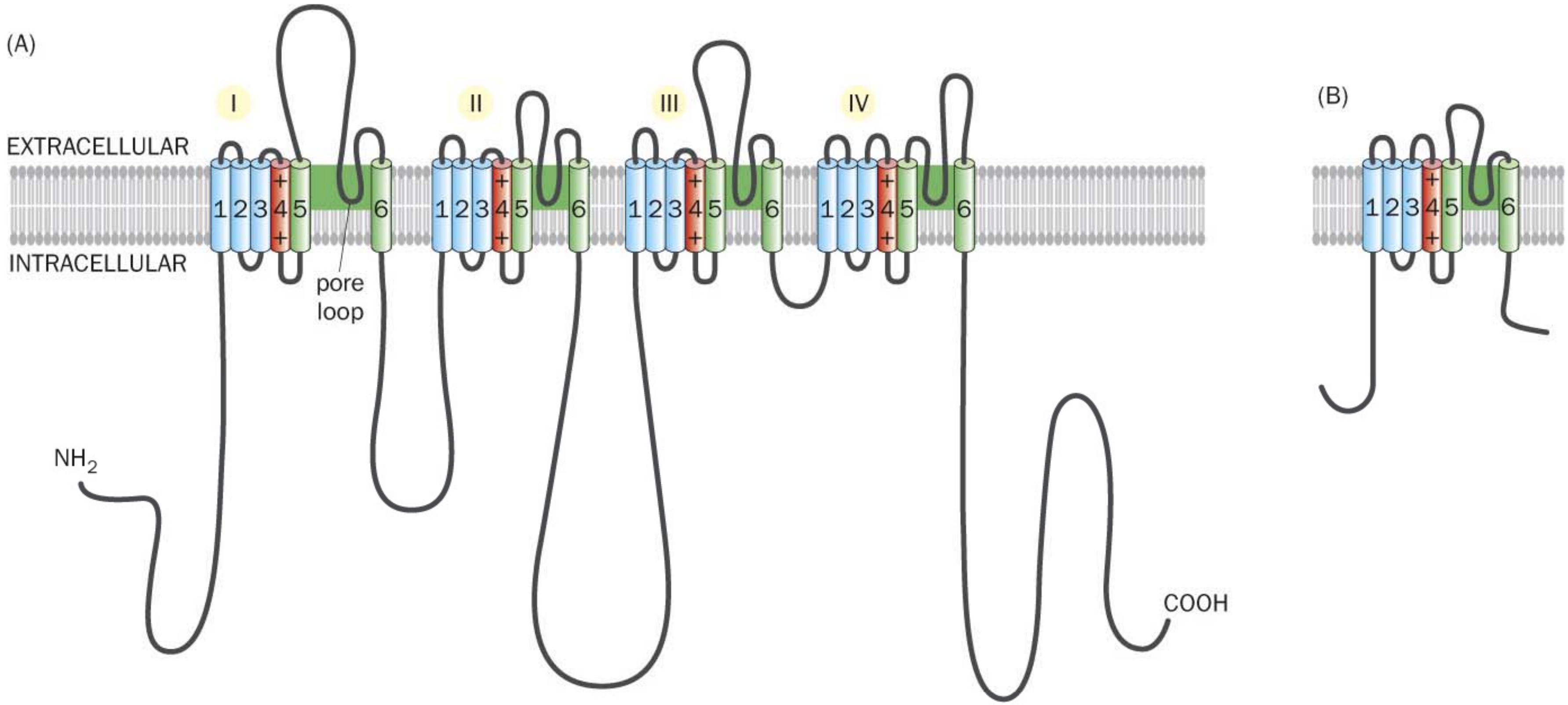

Yu FH & Catterall WA [2004] *Science* STKE 253:re15.

Sato C, Ueno Y, Asai K et al. [2001] *Nature* 409:1

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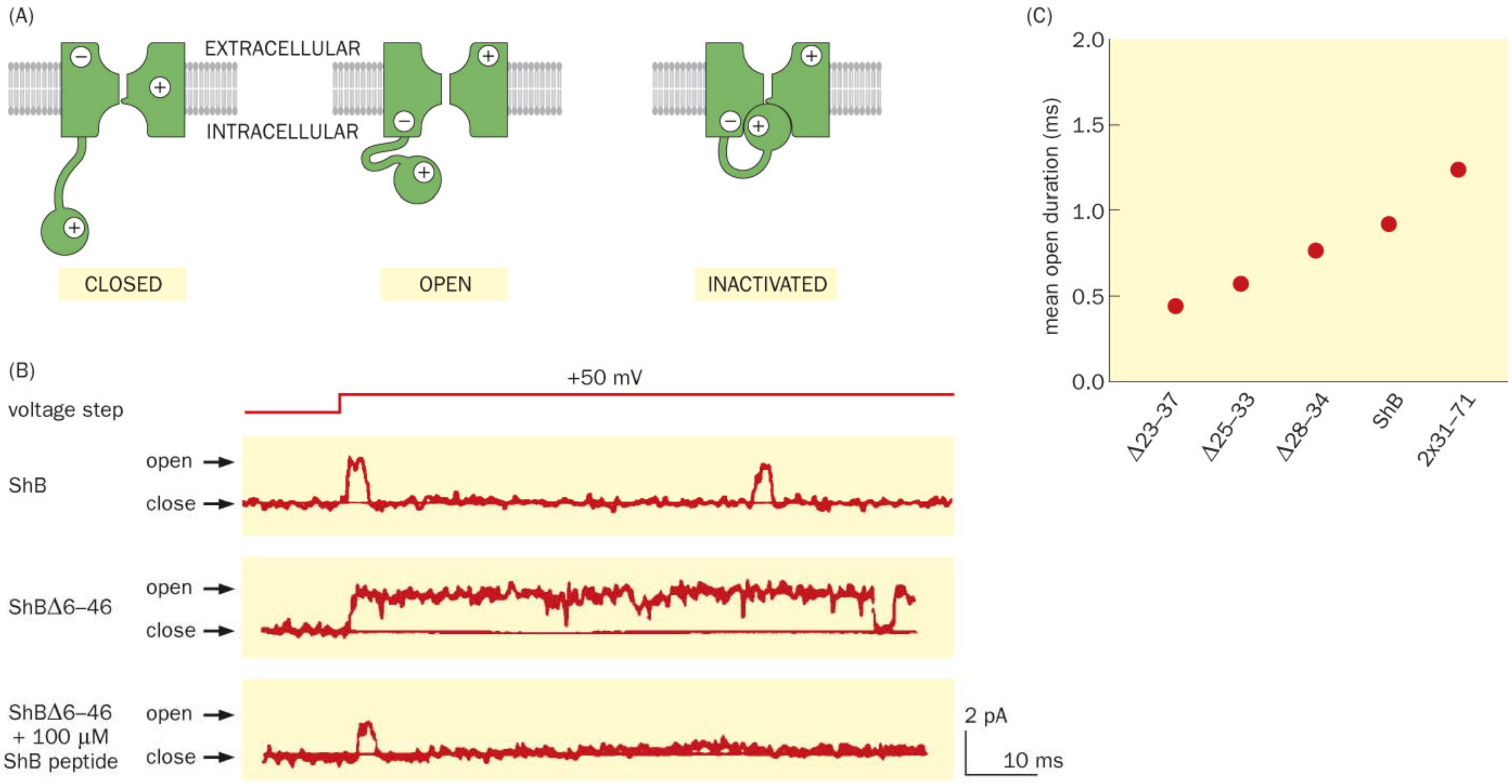

HOW DO ELECTRICAL SIGNALS PROPAGATE FROM THE NEURONAL CELL BODY TO ITS AXON TERMINALS?

2.16 Crystal structures reveal the atomic bases of ion channel properties

电信号如何从神经元细胞胞体向轴突末梢传播

2.16 晶体结构揭示了离子通道性质的原子基础

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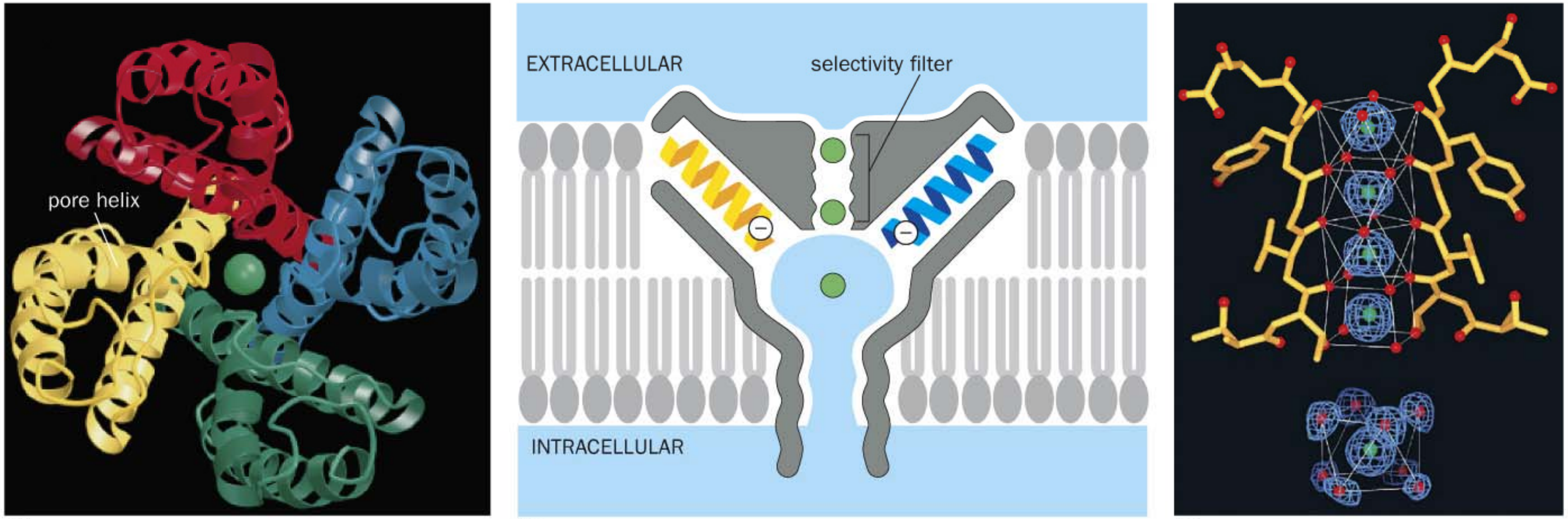


(A) (B) (C)

2.16 Crystal structures reveal the atomic bases of ion channel properties

2.16 晶体结构揭示离子通道性质的原子基础

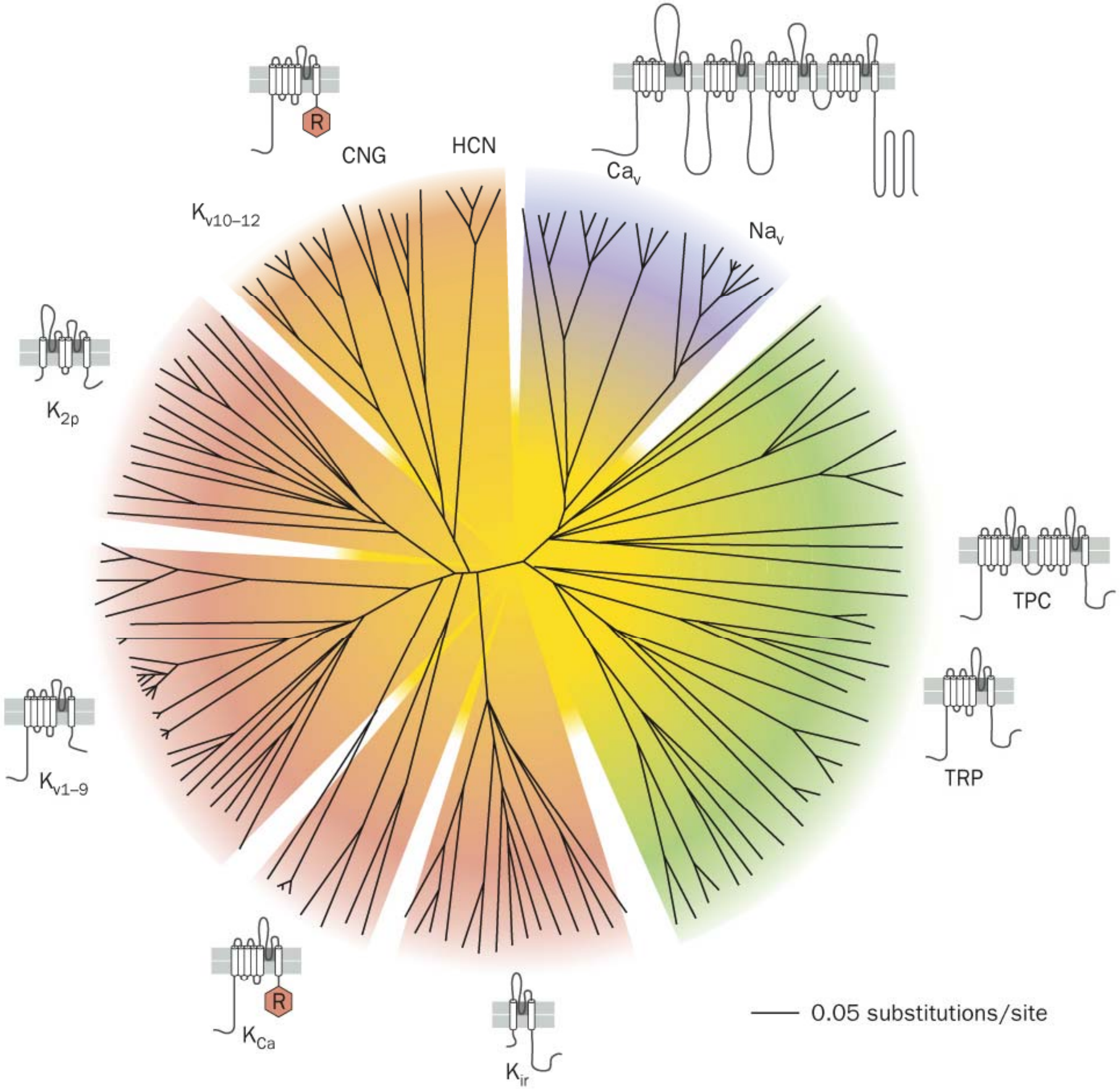
Table 2–2: Number of genes encoding ion channels in the human genome

Channel type	Gene number
K^+ channels	78
Voltage-gated K^+ channels	40
Inward-rectifier K^+ channels	15
Two-pore K^+ channels	15
Ca^{2+}-activated K^+ channels	8
Na^+/Ca^{2+} channels	27
Voltage-gated Na^{2+} channels	9
Voltage-gated Ca^{2+} channels	10
Other Ca^{2+} channels	8
Cl^- channels	9
TRP channels	28
Cyclic-nucleotide-gated and HCN channels	10
Neurotransmitter-gated channels	70

Data from the IUPHAR (International Union of Basic and Clinical Pharmacology) database (www.iuphar-db.org).
Abbreviations: TRP, transient receptor potential; HCN, hyperpolarization-activated cyclic-nucleotide-gated.
This table does not include all discovered ion channels.

2.16 Crystal structures reveal the atomic bases of ion channel properties

2.16 晶体结构揭示离子通道性质的原子基础



Yu FH & Catterall WA [2004] *Science STKE* 253

Summary

1. The membrane conducts ions very poorly and allows the separation of ionic species. This results is a potential difference between the outside and the inside of the membrane.

   细胞膜对不同离子的通透性不同导致跨细胞膜的离子选择。细胞膜内外电势的不同是这一现象的原因

2. The magnitude of the resting potential is determined by the selective permeability of the membrane to ionic species.

   静息电位的大小由膜对不同离子选择通透性决定。

3. We can quantify the the magnitude of the resting potential by considering both the **diffusive** and **electrophoretic** properties.

   我们可以通过同时考虑扩散和电泳特性量化静息电位的幅度

4. In order to understand the time dependence and individual contributions of ionic species to the membrane potential it is convenient to use an electrical equivalent circuit.

   电等效电路的使用使得研究不同种类离子对膜电势的贡献及时间依赖性更方便。

Question 1:

Consider a hypothetical two-compartment system separated by a membrane permeable to K^+ and Cl^-, but not to A^-. No active pump is involved.

	I	II
A^-	100	0
K^+	150	150
Cl^-	50	150

(in mM)

a. Is the system in electrochemical equilibrium (ECE)?

b. If not, in what direction will each ion move? What are the final equilibrium levels each ion will reach in I and II?

c. If the membrane is permeable to water, which direction water will flow.

问题1：

假设细胞膜两侧存在两个不同的系统，该细胞膜对钾离子氯离子通透，但对A阴离子不通透。不存在其他活性泵。

A：请问该系统是否处于电化学平衡状态？
B：如果不是，各离子将向什么方向移动？最终各离子将达到怎样的平衡？
C：如果细胞膜对水通透，水会向什么方向移动？

	I	II
A^-	100	0
K^+	150	150
Cl^-	50	150

(in mM)

Question 2:

A large dissociated neuron (with $[K^+]_{in} = 150$ mM, $[Na^+]_{in} = 10$ mM, $[Cl^-]_{in} = 50$ mM, anions $[A^-]_{in} = 110$ mM, $[Ca^{2+}]_{in} = 10^{-4}$ mM) is placed in a chamber containing a small volume (about the same volume as that of the neuron) of culture medium (which consists of 150 mM K^+, 90 mM Na^+, 250 mM Cl^-, and 5 mM Ca^{2+}. The permeability ratio of the plasma membrane of the neuron at rest is $P_K : P_{Na} : P_{Cl} : P_A : P_{Ca} = 1:0:1:0:0$.

(a) Is the neuron in electrochemical equilibrium (ECE) immediately after it is placed in the culture medium? Explain concisely. What are the final equilibrium intracellular and extracellular concentrations of K^+, Na^+, Cl^-, A^-, and Ca^{2+}? What is the resting potential of this neuron in the culture medium after reaching equilibrium?

(b) After reaching equilibrium, immediately after the onset of a sustained stimulus, $P_K : P_{Na} : P_{Cl} : P_A : P_{Ca} = 1:10:1:0:0$. Two seconds after the stimulus onset, $P_K : P_{Na} : P_{Cl} : P_A : P_{Ca} = 1:10:10:0:0$. Draw the voltage response of this neuron to the sustained stimulus (> 5 sec). Label the membrane voltage at rest, immediately after the stimulus onset, and at steady state with appropriate values and units.

问题2：

假设有一个神经元（细胞内钾离子浓度150毫摩，钠离子10毫摩，氯离子50毫摩，阴离子A 110毫摩，钙离子10^{-4}毫摩）置于一个容器中。容器中钾离子浓度150毫摩，钠离子90毫摩，氯离子250毫摩，钙离子5毫摩。细胞膜对各种离子的通透性比例如下：

$P_K:P_{Na}:P_{Cl}:P_A:P_{Ca}=1:0:1:0:0$

(1)　　这个神经元被放在这个容器的瞬间电化学平衡会不会改变，为什么？各种离子在达到平衡时的浓度分别是多少？达到平衡后，这个神经元的静息膜电位是多少？

(2)　　在达到平衡后，迅速给这个神经元施加一个持续的刺激，使细胞膜对各种离子的通透性变为$P_K:P_{Na}:P_{Cl}:P_A:P_{Ca}=1:10:1:0:0$，两秒钟后通透性变为$P_K:P_{Na}:P_{Cl}:P_A:P_{Ca}=1:10:10:0:0$.请画出该神经元对该刺激的响应曲线（大于5秒），并标出静息膜电位，刺激时的膜电位，以及达到稳定后膜电位

Question 3:

All cell membrane has similar capacitance, which is 1 uF/cm^2 and the concentration of ions inside and outside the cell are about 0.1M. Please calculate the fraction of uncompensated ions on each side of the membrane required to produce 100 mV

a) Across a 1 cm^2 patch of membrane (fraction of 1 cm^3 cytoplasm);

b) In a spherical cell (10 um radius);

c) In a cylindrical cell (1 um radius, 100 um long).

问题3：

假设所有细胞膜有相似的电容，1 uF/cm2，细胞膜两侧的离子浓度大约0.1摩尔。求计算，在以下几种条件下，细胞膜两侧未补偿的离子分别多少时才能产生100毫幅电势。

A: 1平方厘米膜面积
B：一个圆形细胞，半径10微米
C：一个圆柱形细胞，1微米半径，100微米长