Feb 24 2024

中研院高中生培育計畫

生物的電現象

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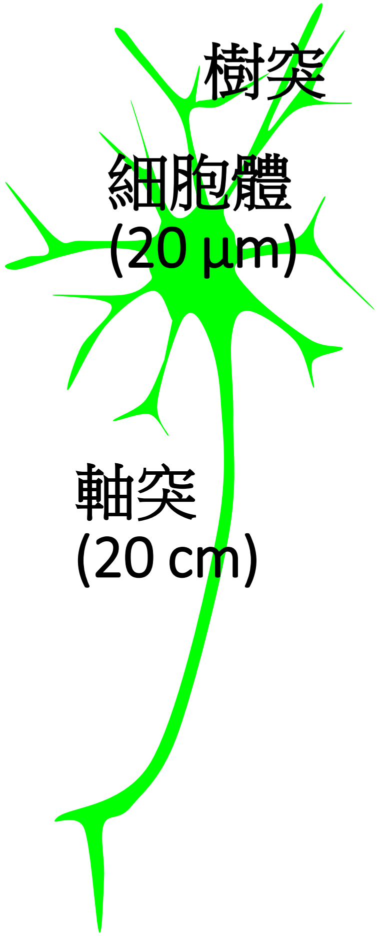
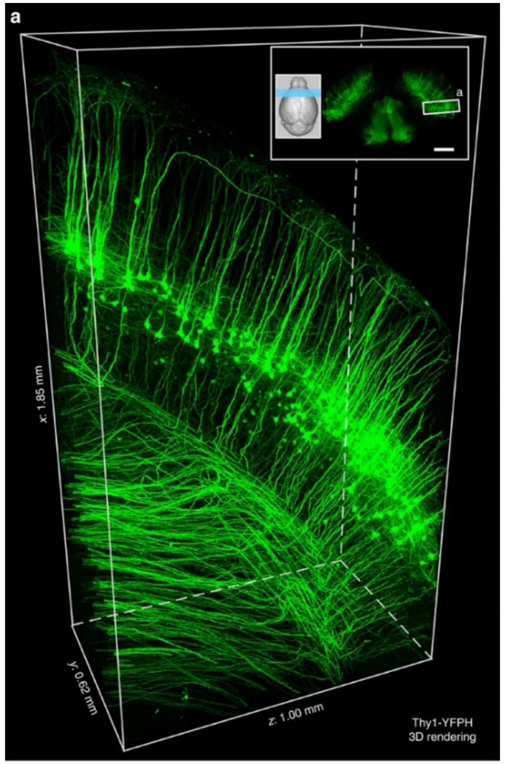
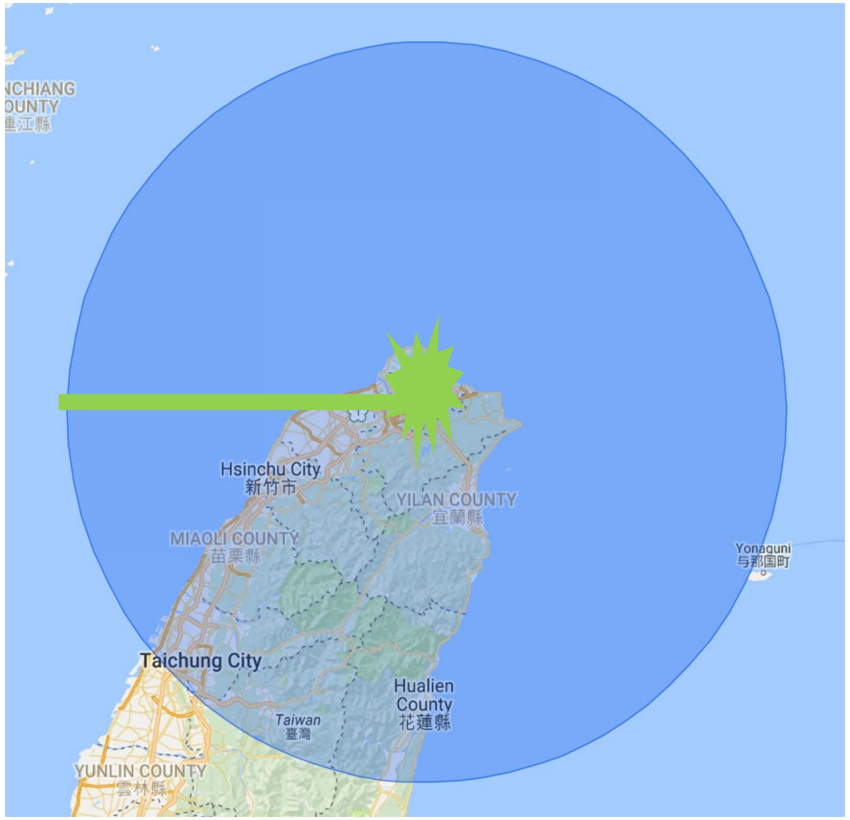
Institute of Biomedical Sciences, Academia Sinica

教科書上的神經元





如果神經元的細胞體(20 µm) 跟成人的身高一樣(~1.5 m)

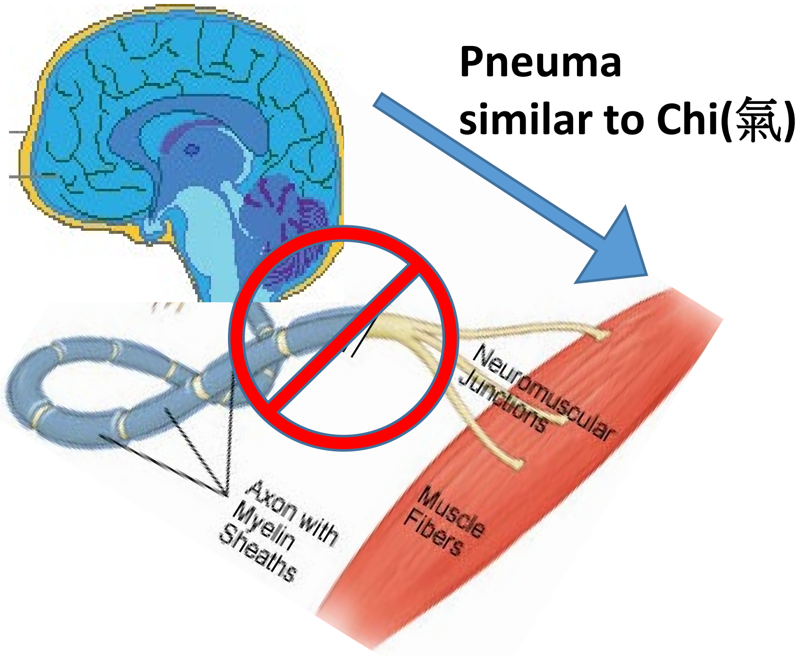


神經細胞如何傳遞長距離的訊號?

神經生理之氣球學說

古時候的生理學家只用剪刀鑷子做出來的觀察結果:

- 腦室中儲存“氣”.
- 肌肉的收縮膨脹，是由”氣“引導的.
- 神經是”氣“的傳導管路，當神經截斷，氣的傳導受阻，肌肉則無法收縮.



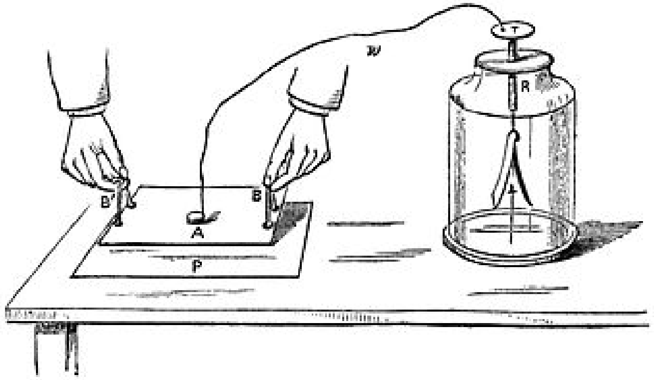
蓋倫 (~200AD)
Aelius Galenus (Galen of Pergamon)

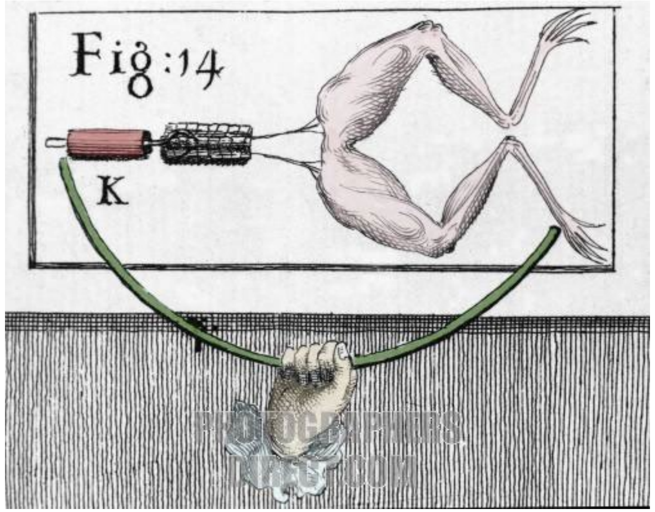
生物的電現象

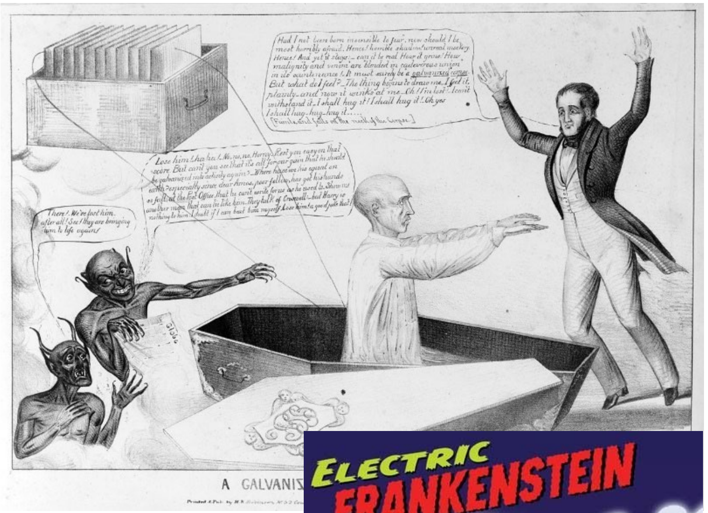
伽伐尼Galvani (~1800):

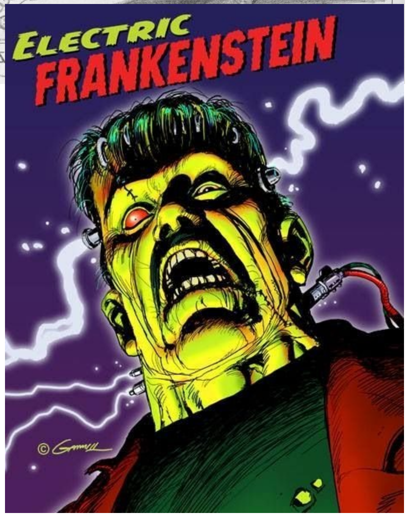
- 掛在鐵欄杆晾乾的蛙腿，會自主產生收縮.
- “電溶液”由脊隨產生，傳遞到腿部.

Luigi Galvani



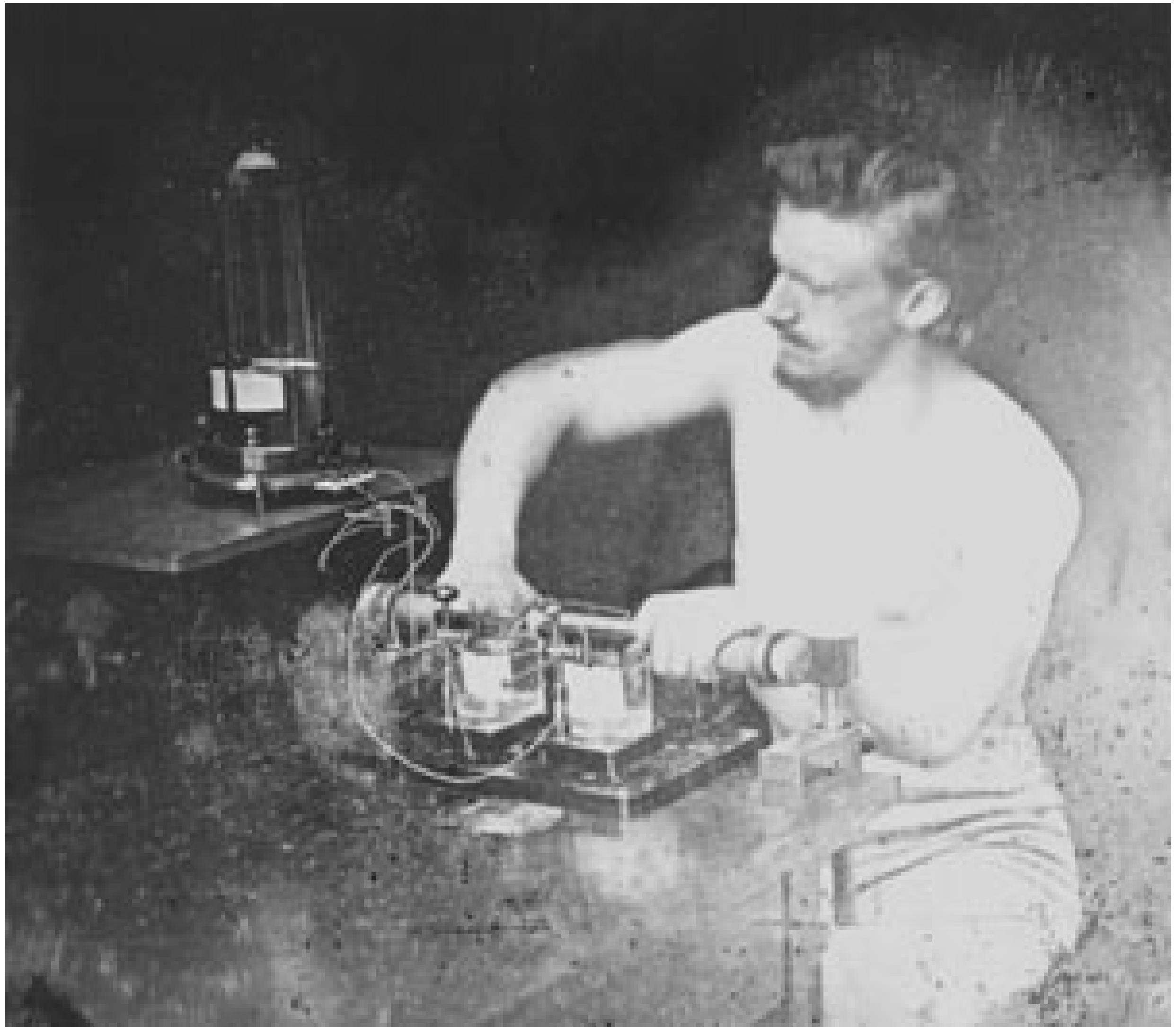






動作電位的產生:

~1850: 杜布瓦-雷蒙 **du Bois-Reymond** 認為所有生物現象皆能用物理化學數學的概念來描述。他偵測到肌肉收縮前，會有激烈的電位變化，由中樞向四肢傳遞。



綱要:

- 生物學家的電子元件:
- 膜電位的生理學基礎:
- 動作電位產生的機制:
- 動作電位的傳遞:

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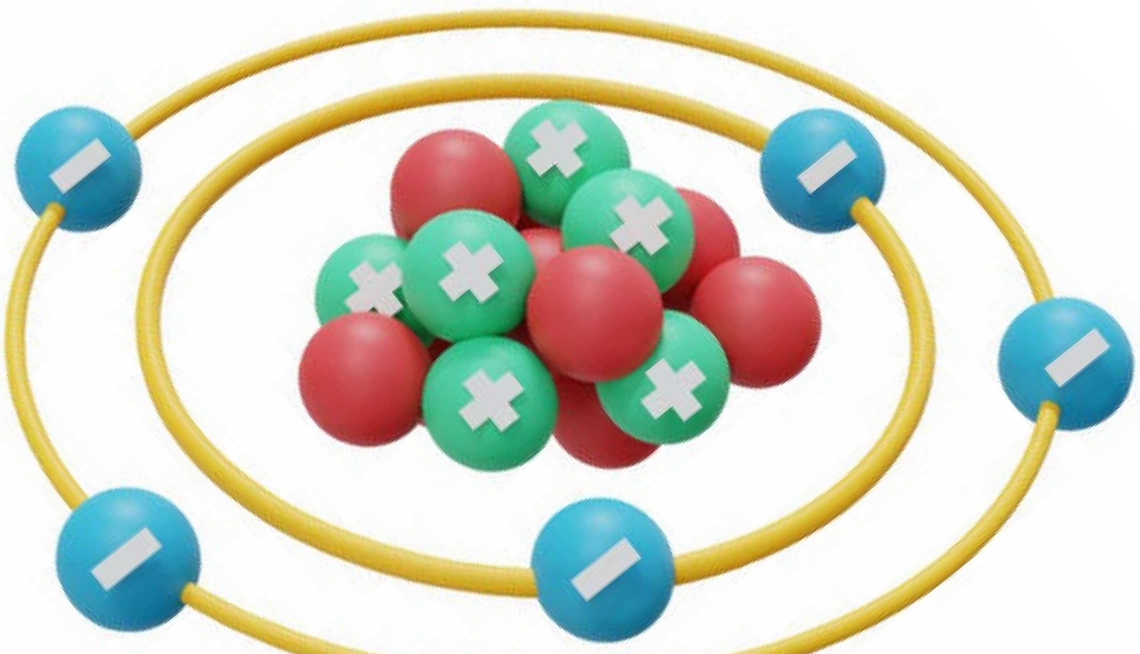
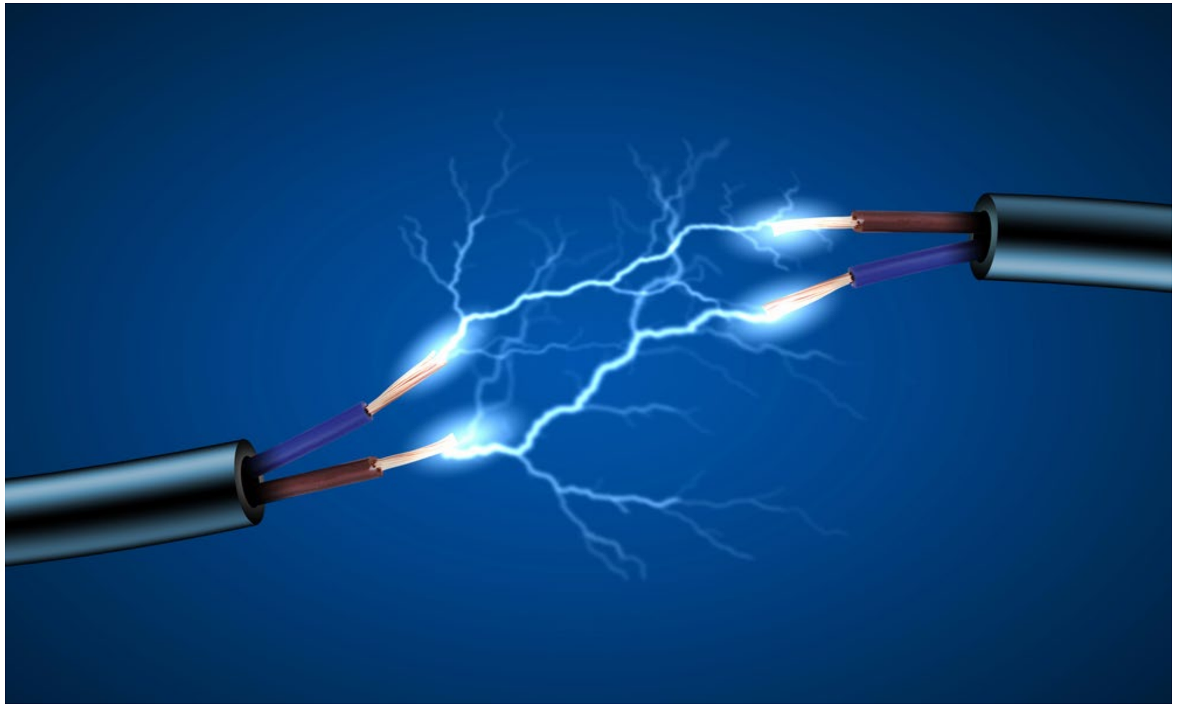
什麼是電?

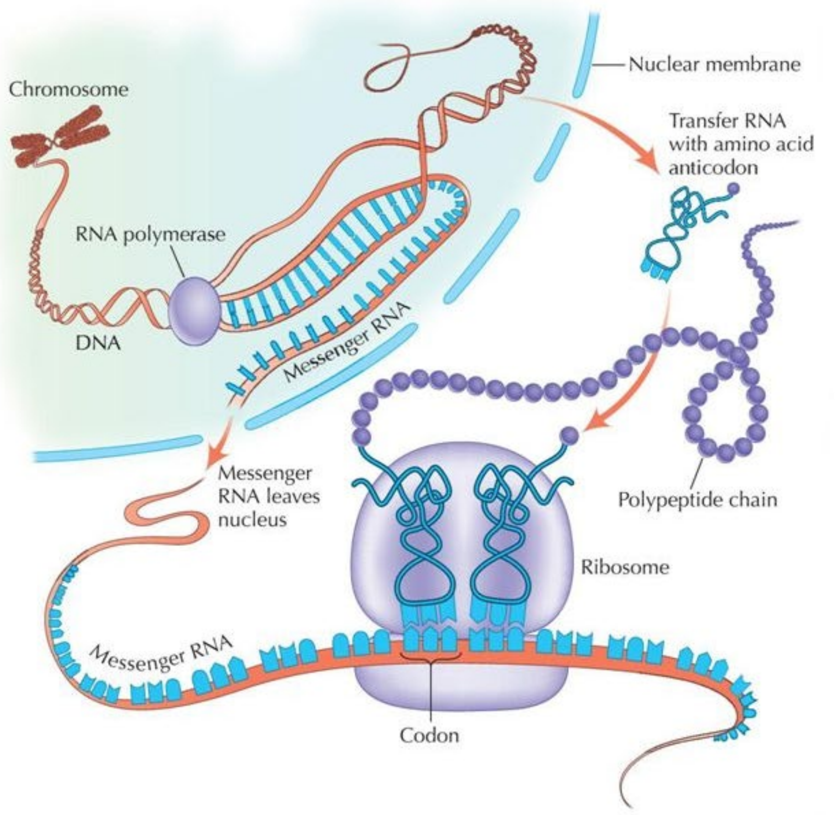
電是粒子?



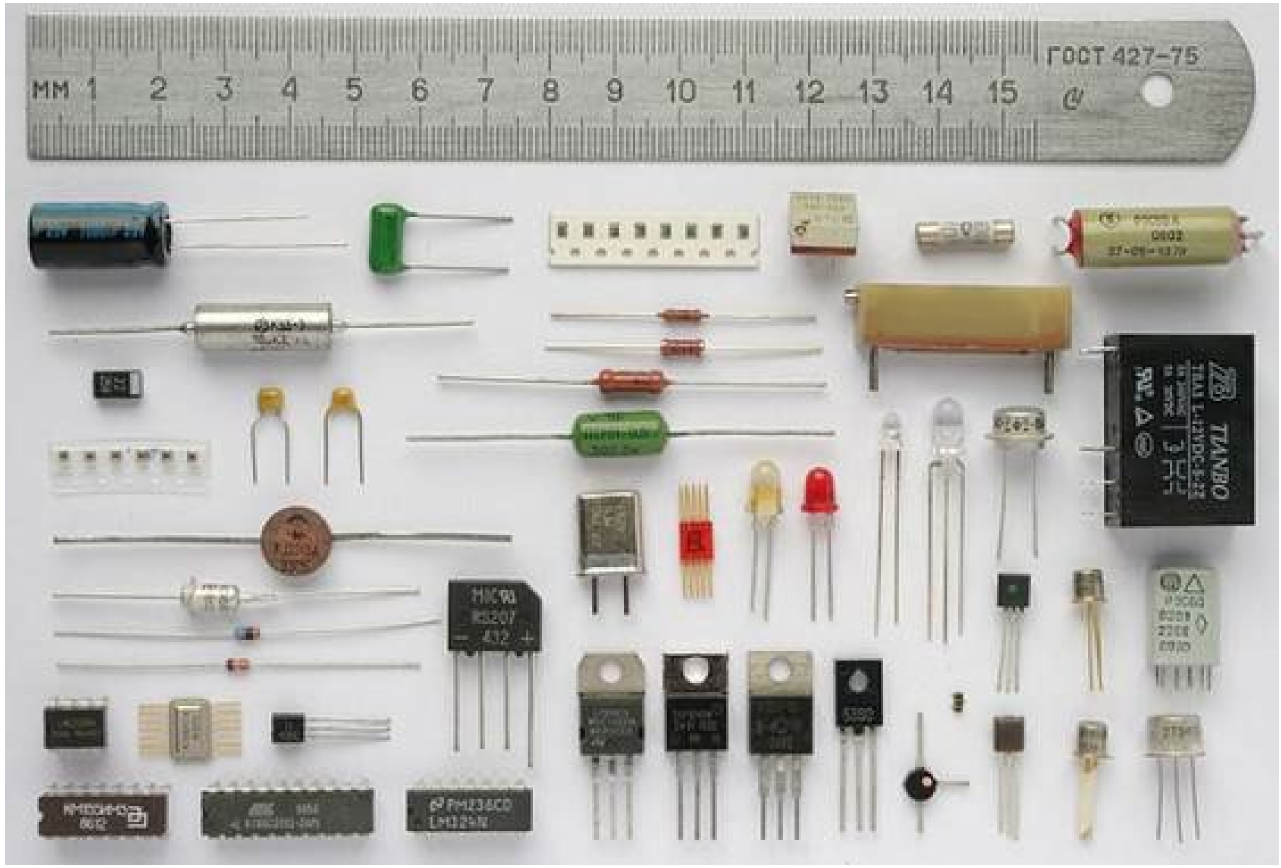
電是能量?



這堂課需要用到的基本物理學概念:
電阻，電容，電池



DNA
↓
RNA
↓
PROTEIN

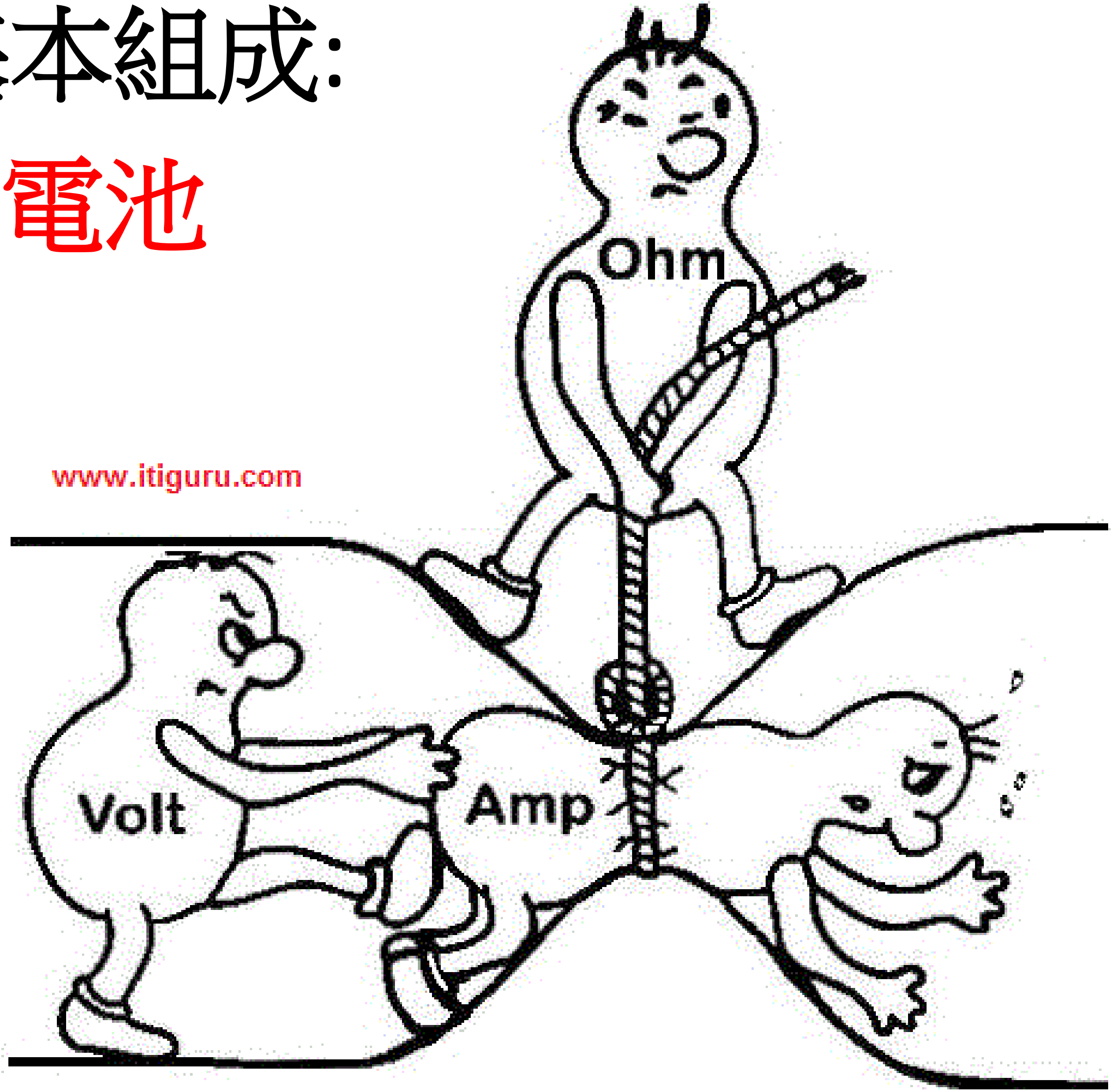


生物電子學的基本組成:

電阻，電容，電池

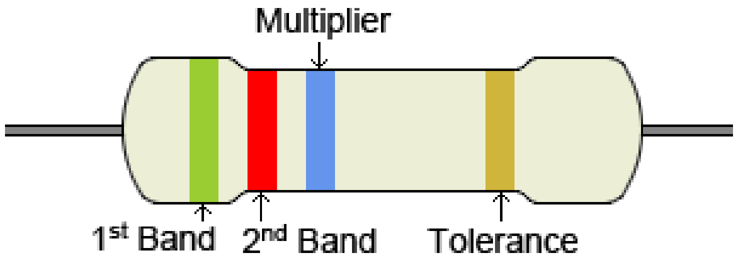
歐姆定律:

V=IR

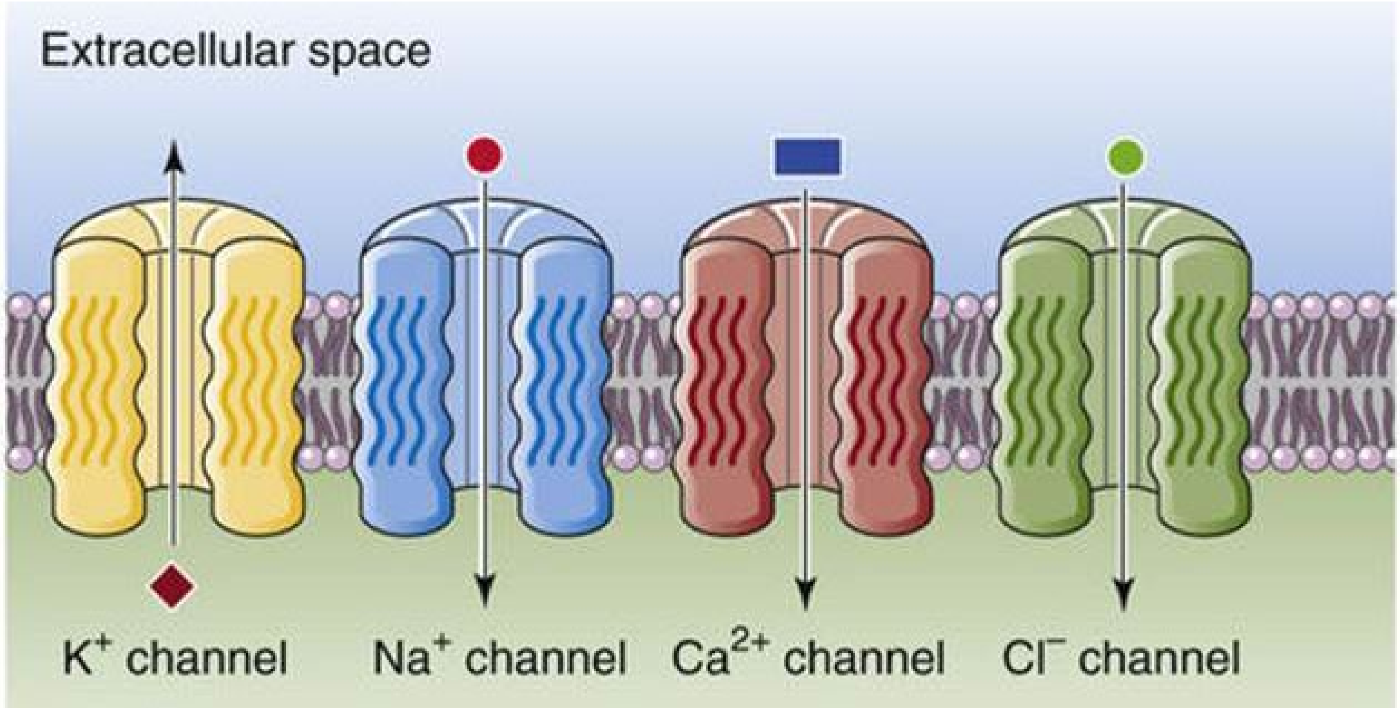


電阻，電容，電池

膜蛋白中的離子通道為基本電阻元件



Color	1st, 2nd Band Significant Figures	Multiplier	Tolerance
Black	0	× 1	
Brown	1	× 10	±1% (F)
Red	2	× 100	±2% (G)
Orange	3	× 1K	±0.05% (W)
Yellow	4	× 10K	±0.02% (P)
Green	5	× 100K	±0.5% (D)
Blue	6	× 1M	±0.25% (C)
Violet	7	× 10M	±0.1% (B)
Grey	8	× 100M	±0.01% (L)
White	9	× 1G	
Gold		× 0.1	±5% (J)
Silver		× 0.01	±10% (K)



電阻，電容，電池

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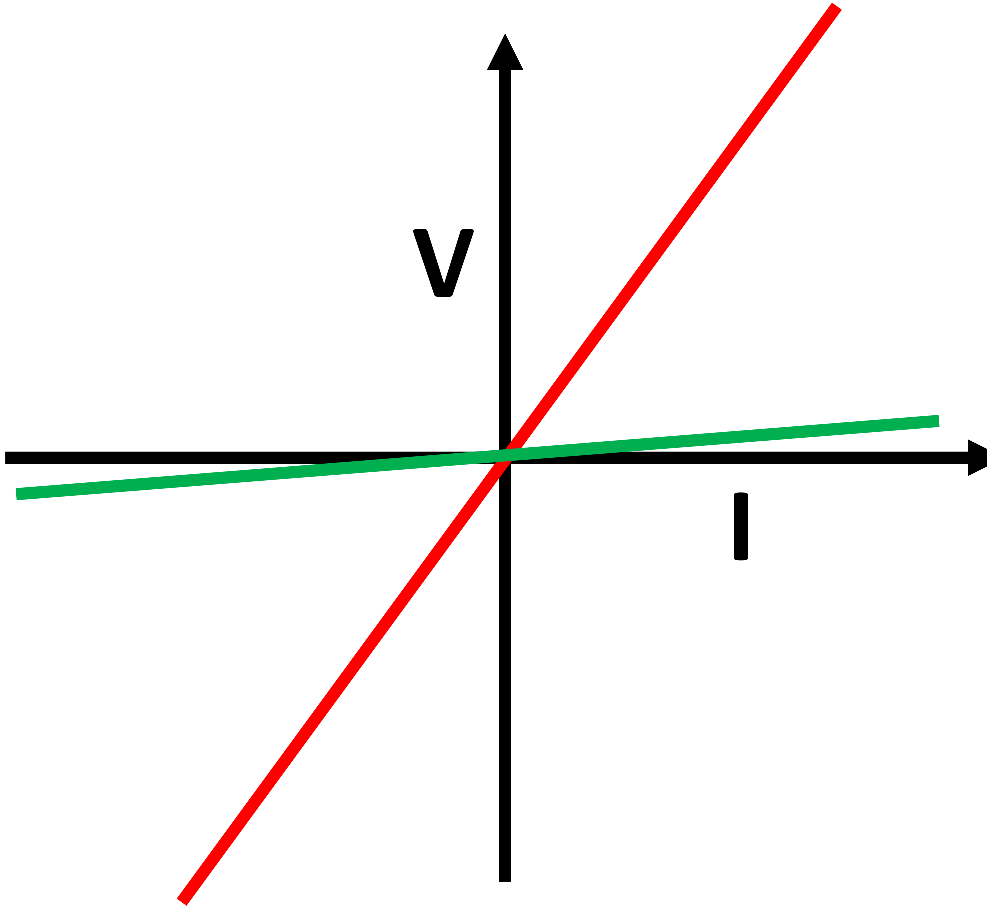
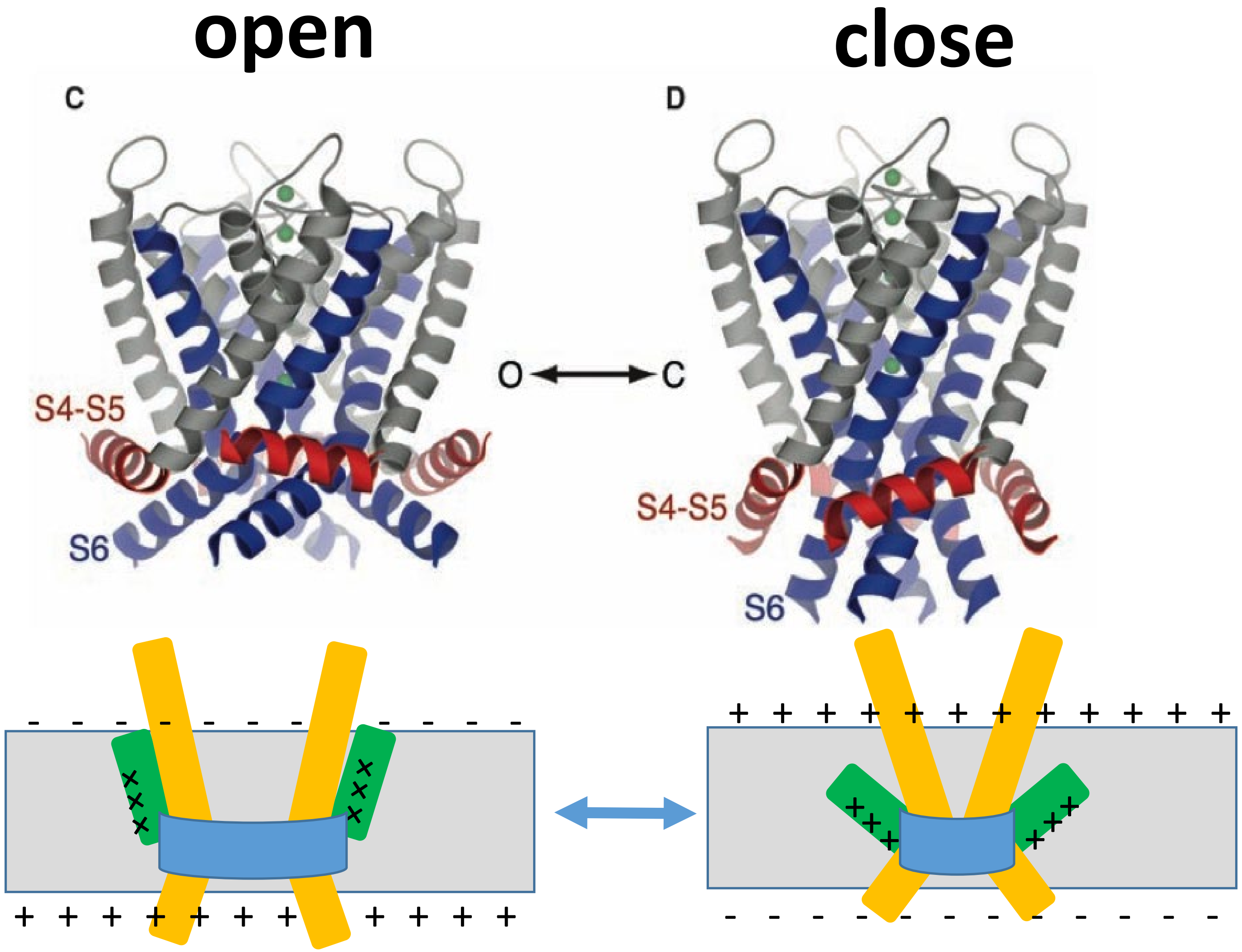
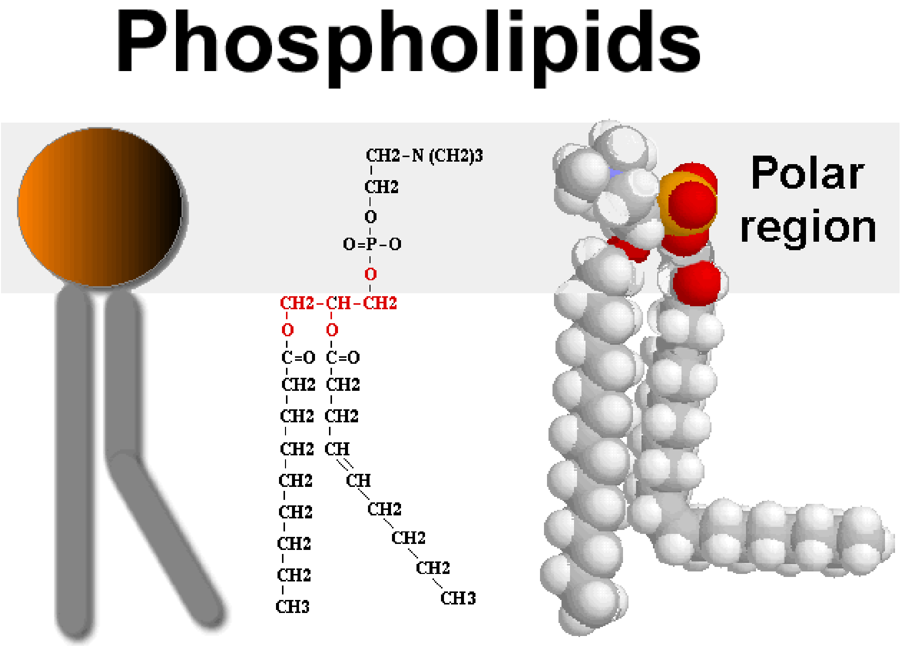
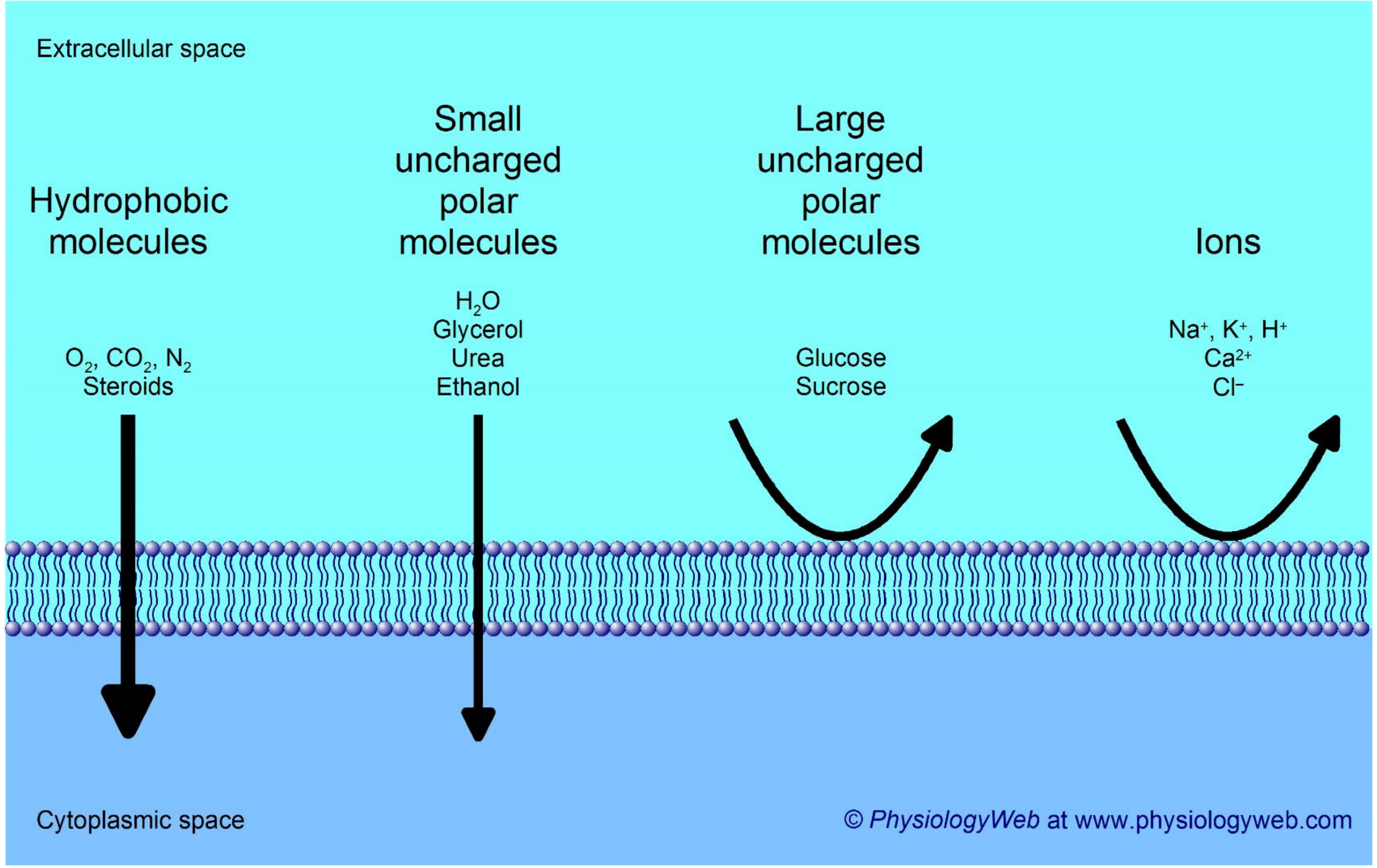




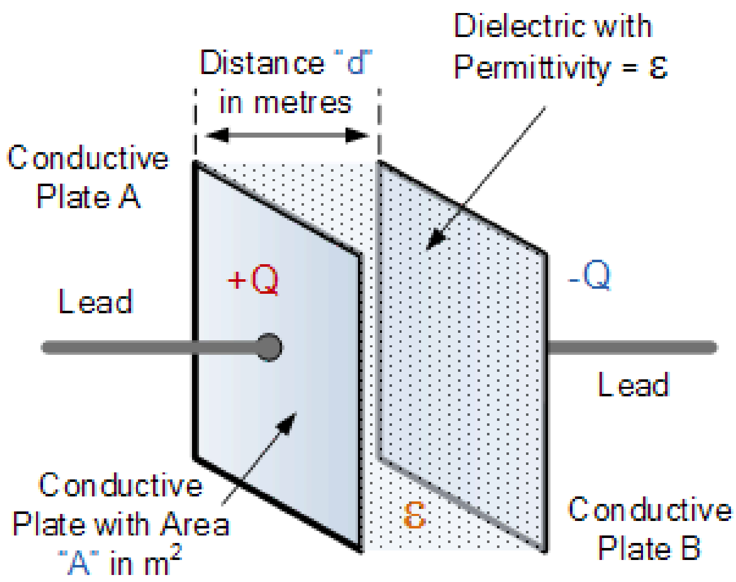
電阻，電容，電池

細胞膜是對水性分子有很強的阻隔能力。





電阻，電容，電池



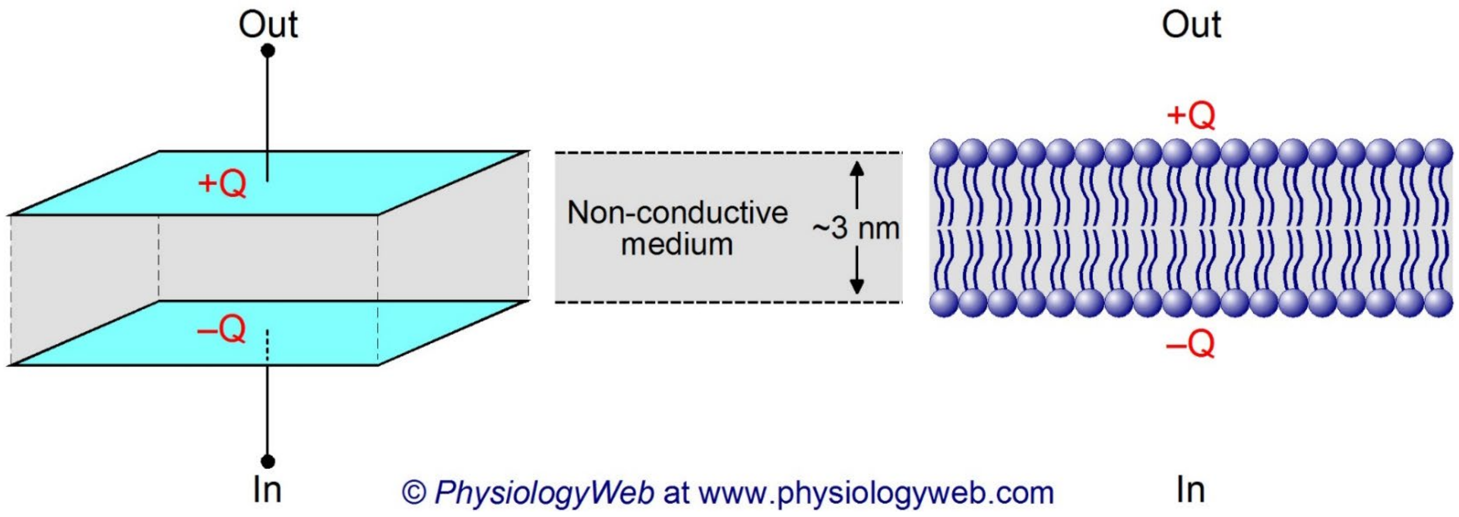
C= Q/V

C: Farad

Q: Coulomb

V: Volt

細胞膜為良好的電容



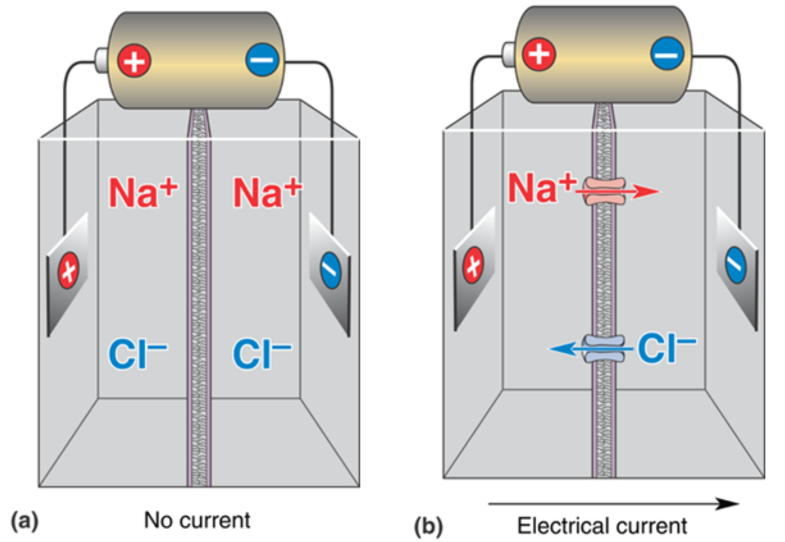
電容為0.5 μF/ cm²

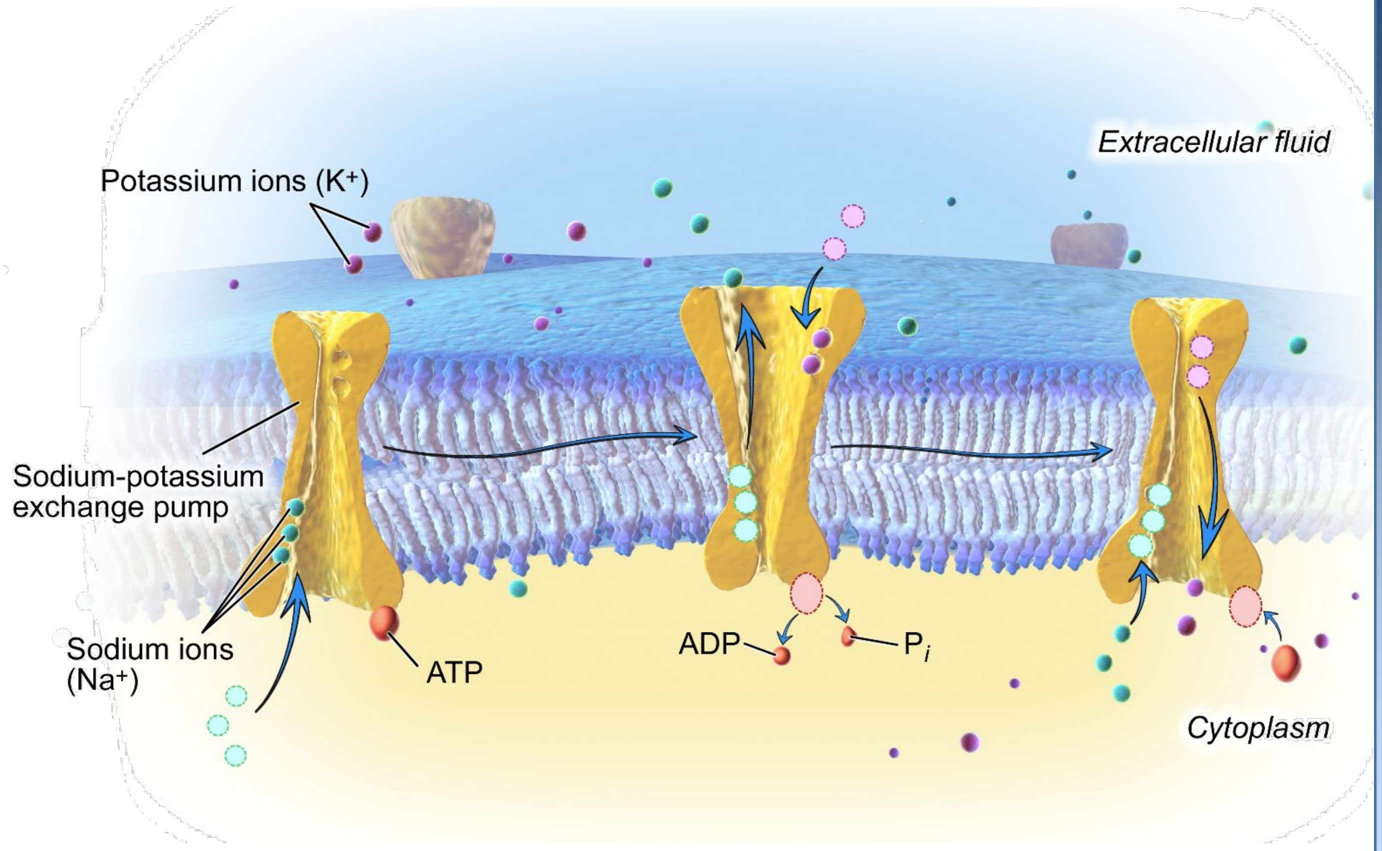
一般大小的細胞，在細胞膜上的帶電粒子數量為:

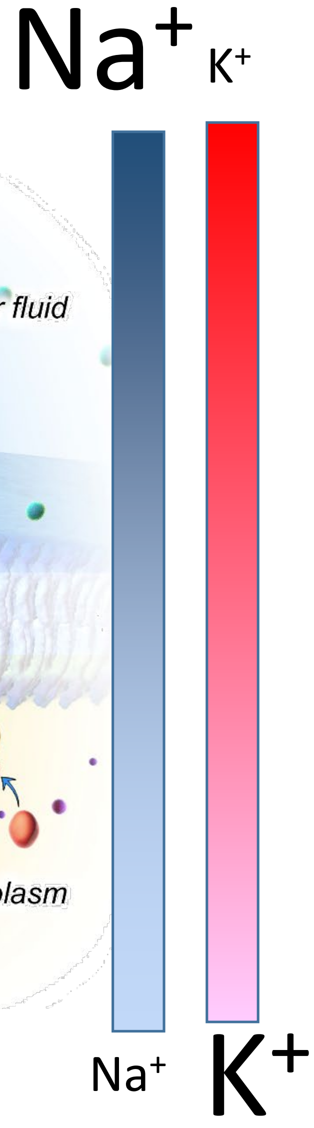
1X10⁸ e

電阻，電容，電池

鈉鉀幫浦:分子電池，藉由消耗ATP產生化學電位



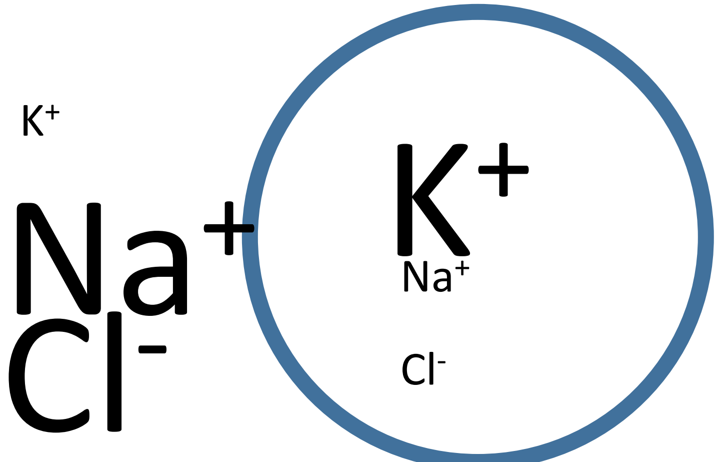




電阻，電容，電池

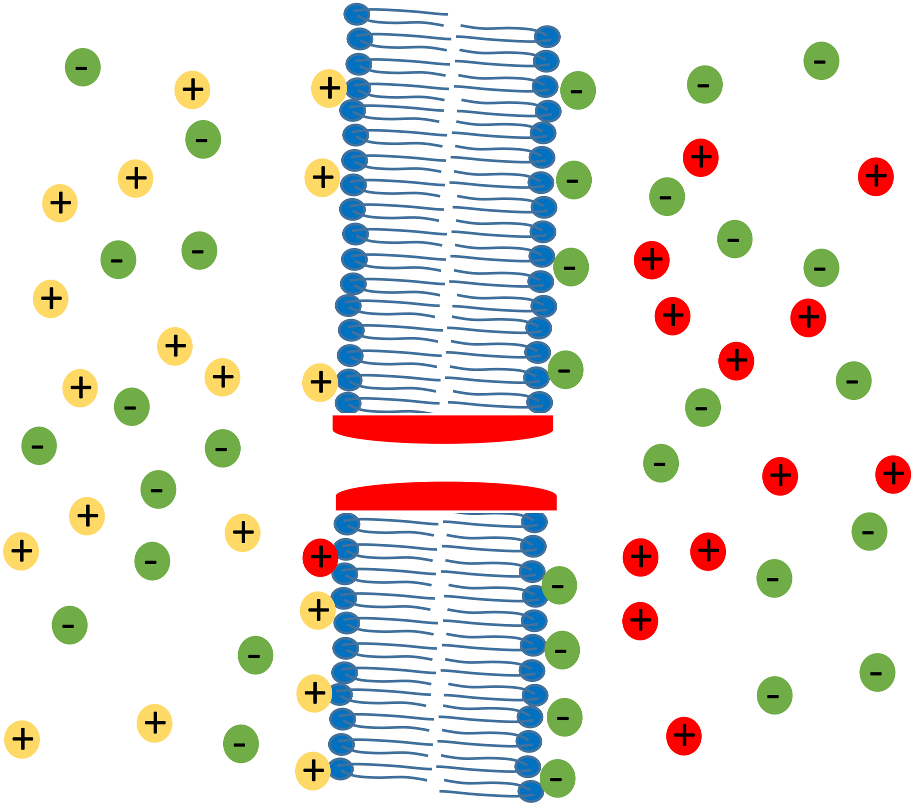
細胞內外的離子分布不均勻:

Ion	Concentration outside (in mM)	Concentration inside (in mM)	Ratio Out : In	E_{ion} (at 37°C)
K^+	5	100	1 : 20	−80 mV
Na^+	150	15	10 : 1	62 mV
Ca^{2+}	2	0.0002	10,000 : 1	123 mV
Cl^-	150	13	11.5 : 1	−65 mV



電阻，電容，電池

化學平衡電位可以下列算式估計:



Nernst equation:

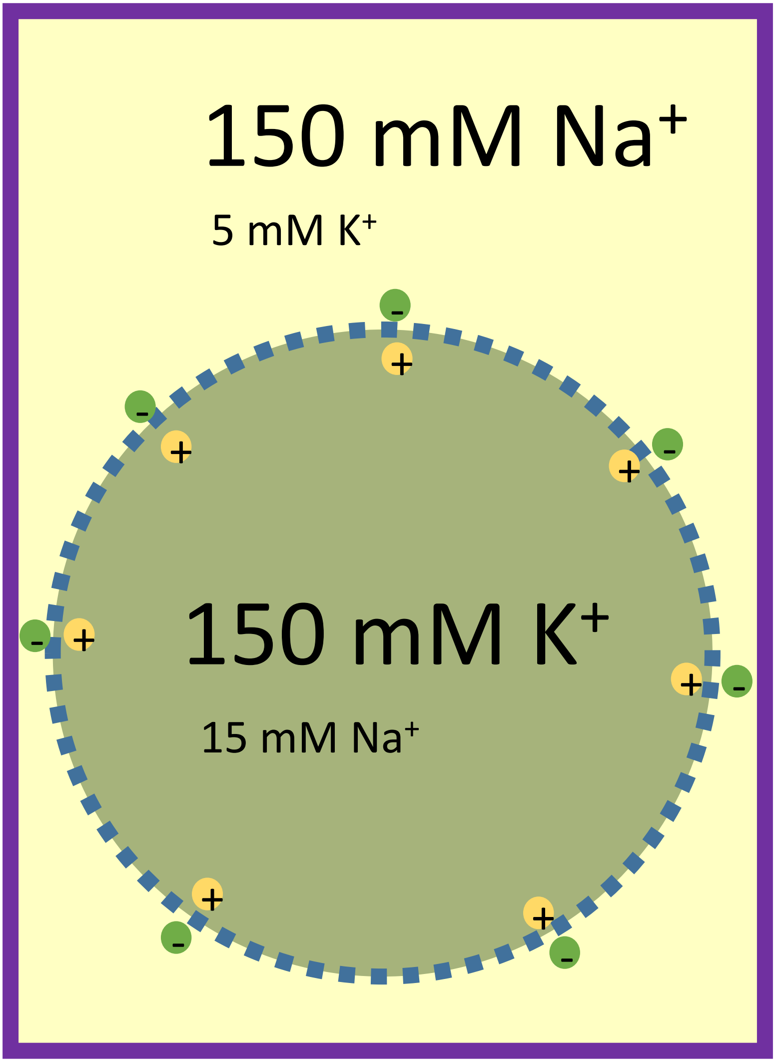
$$E_x = 2.303\frac{RT}{zF}\log\frac{[X]_{out}}{[X]_{in}}$$

R is the universal gas constant, ~ 8.3 $J.K^{-1}.mol^{-1}$ (Joules per Kelvin per mole).
T is the temperature in Kelvin (K = °C + 273).
z is the valence of the ionic species. z is +1 for Na^+ and K^+.
F is the Faraday's constant, ~96000 $C.mol^{-1}$ (Coulombs per mole).

電阻，電容，電池

E_{Na+} = ?

E_{K+} = ?



- $E_x = 2.303\frac{RT}{zF}\log\frac{[X]_{out}}{[X]_{in}}$

Volt = Joule/Coulomb.

R is the universal gas constant, ~ 8.3 $J.K^{-1}.mol^{-1}$ (Joules per Kelvin per mole).

T is the temperature in Kelvin (K = °C + 273).

z is the valence of the ionic species. z is +1 for Na^+ and K^+.

F is the Faraday's constant, ~96000 $C.mol^{-1}$ (Coulombs per mole).

[X]*out* and **[X]*in*** are the ion X concentrations outside and inside of the cell

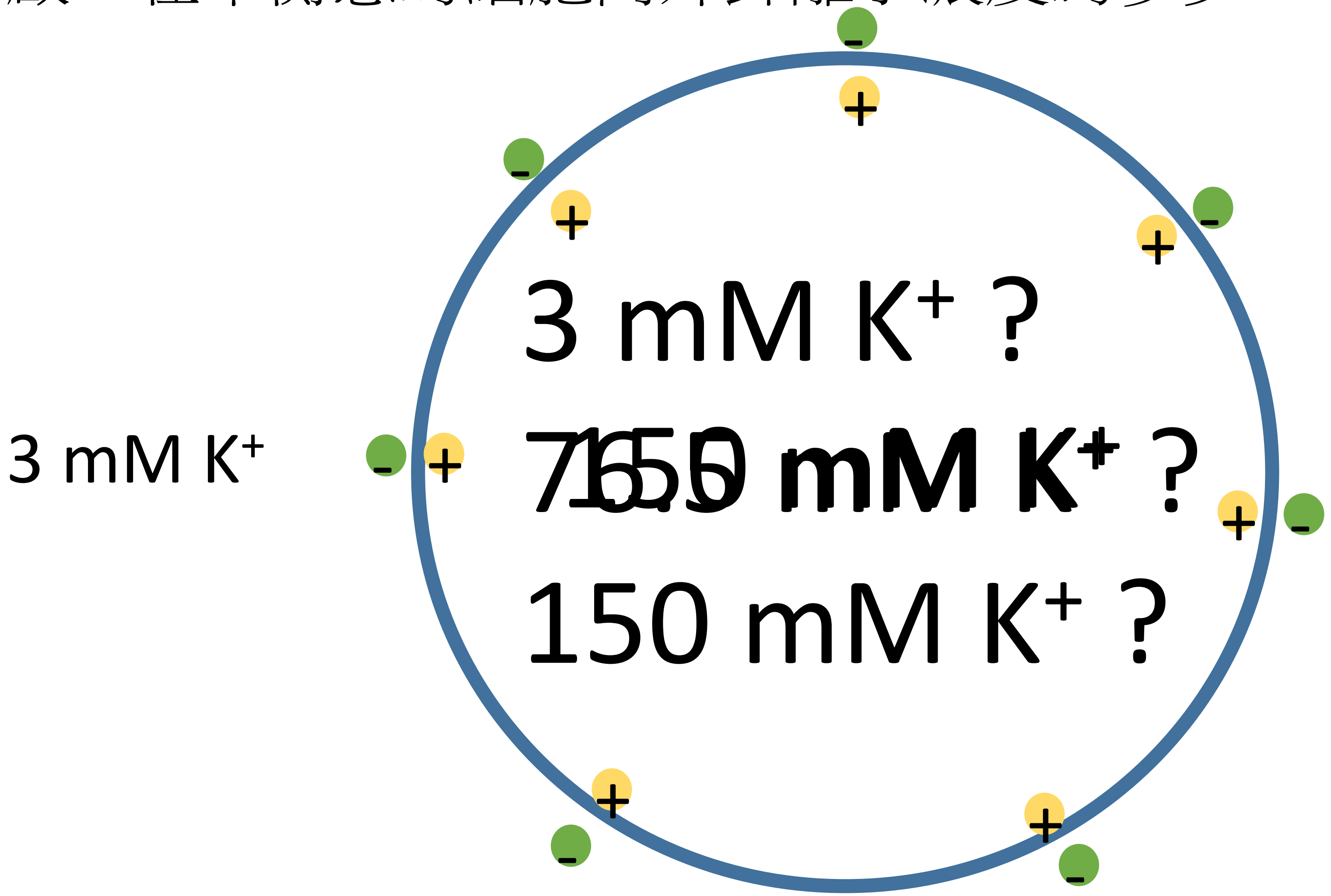
For your own convenience, the log values are provided in the table below.

Log (15/5)	Log (5/15)	Log (5/150)	Log (150/5)	Log (15/150)	Log (150/15)
0.48	-0.48	-1.48	1.48	-1	1

電阻，電容，電池

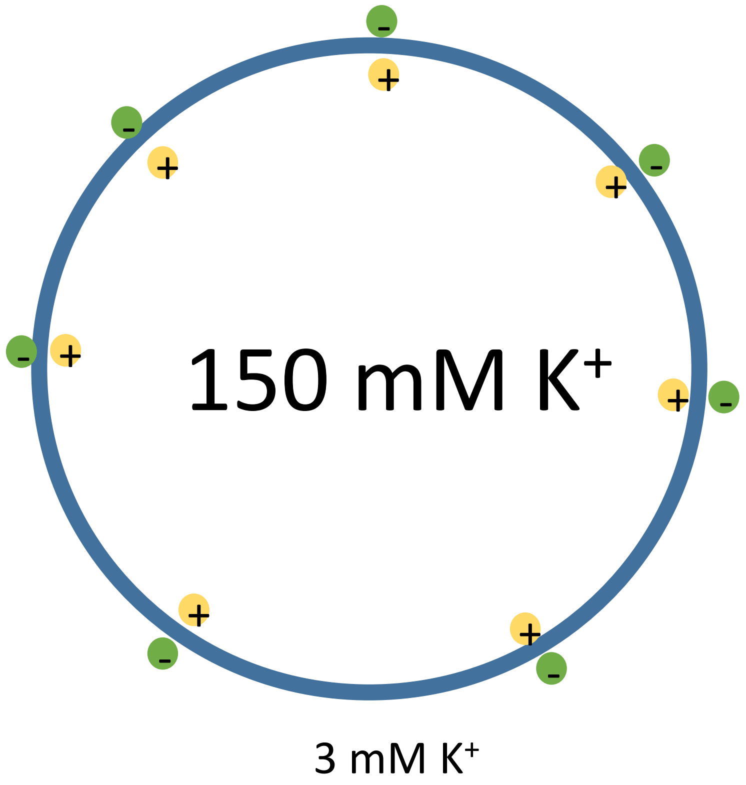
如果細胞內的[K$^+$] 是 150 mM,細胞外的[K$^+$] 是 3 mM.

當鉀離子通道開啟，在平衡態的細胞內外鉀離子濃度為多少?



電阻，電容，電池

At the electrochemical equilibrium state:



Cell diameter ~ 20 µm: Cell volume = 4200 μm^3

Number of K^+ in the cell

150 mM~$6X10^{11}$ K^+

Assuming the cell surface is 20 pF

E_K=-100 mV

Ions relocated for establishing equilibrium potential:

1 X 10^8 K^+

Redistributed ions: 1 X 10^8 / 6 X 10^{11} ~ 0.016%

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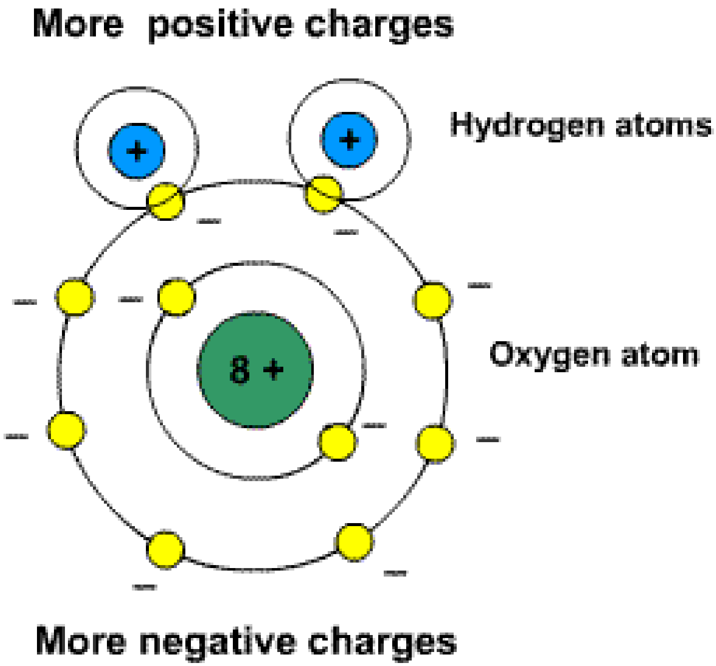
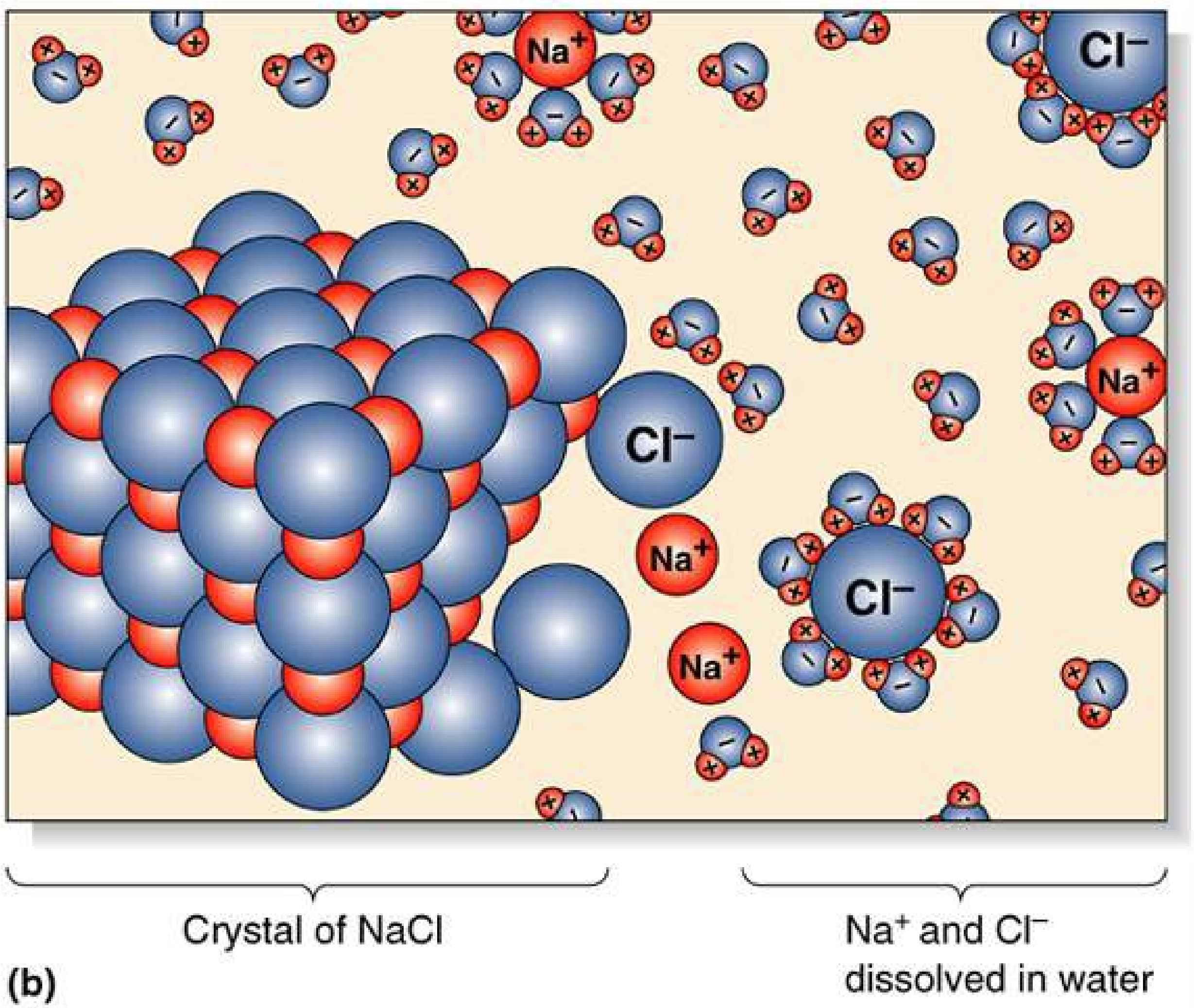
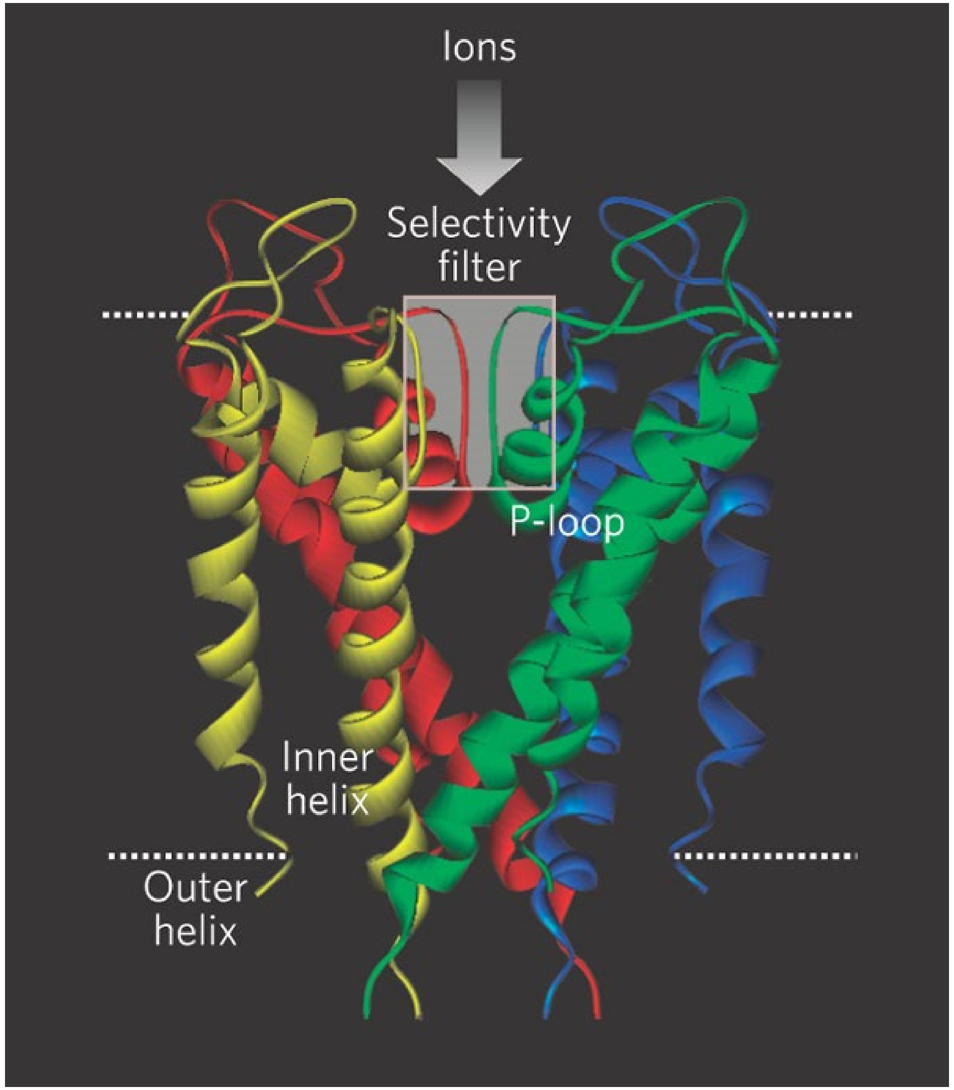
水為極性分子

- 水分子與其他水溶性分子形成氫鍵



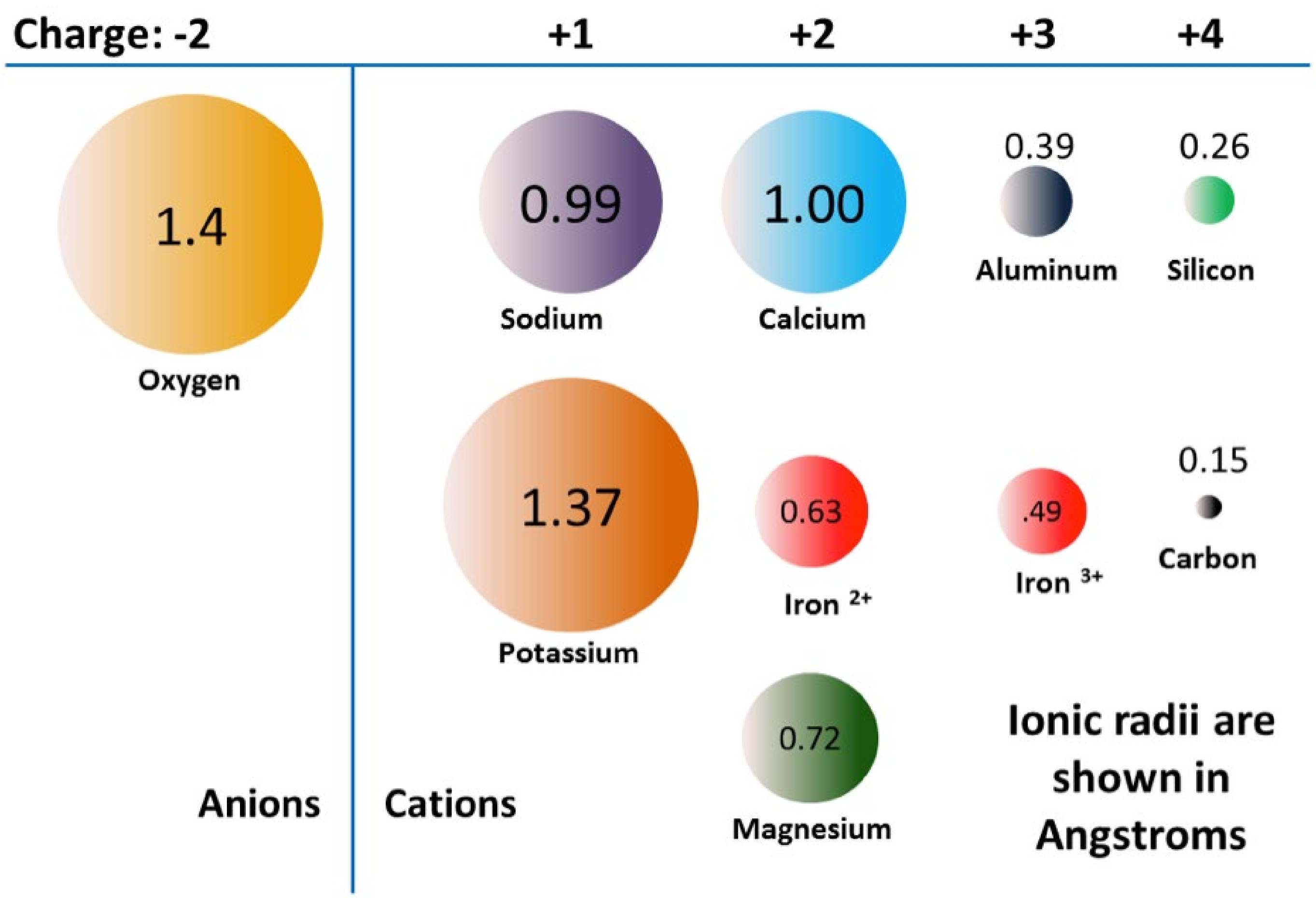


離子通道有高度選擇性(K : Na = 1000 : 1)
但通透速度接近擴散(~10^6 ion/sec)

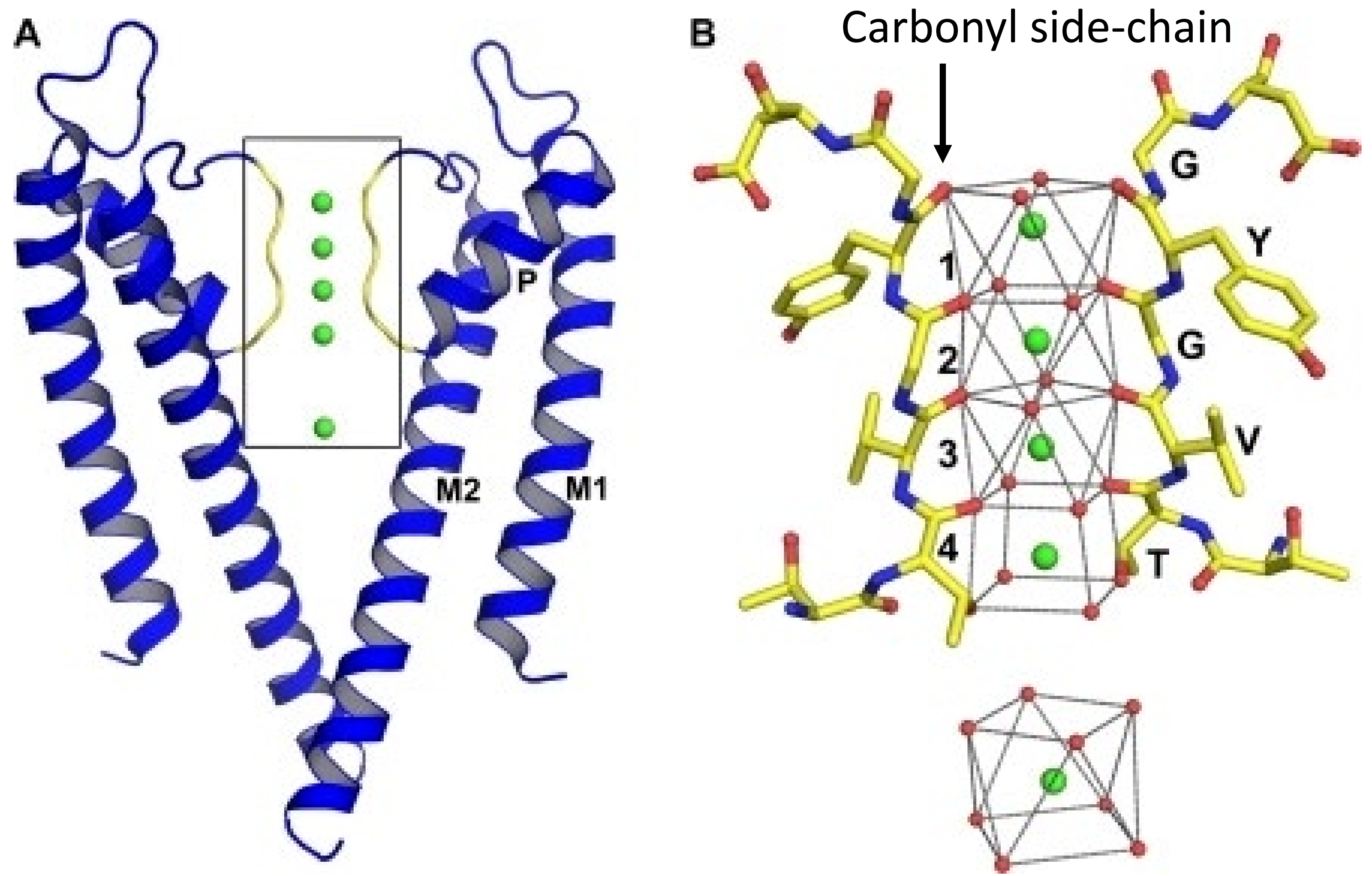


Science,1998 Apr 3;280(5360):69-77

離子通道的選擇性:
分子篩可藉由電價以及離子大小選擇

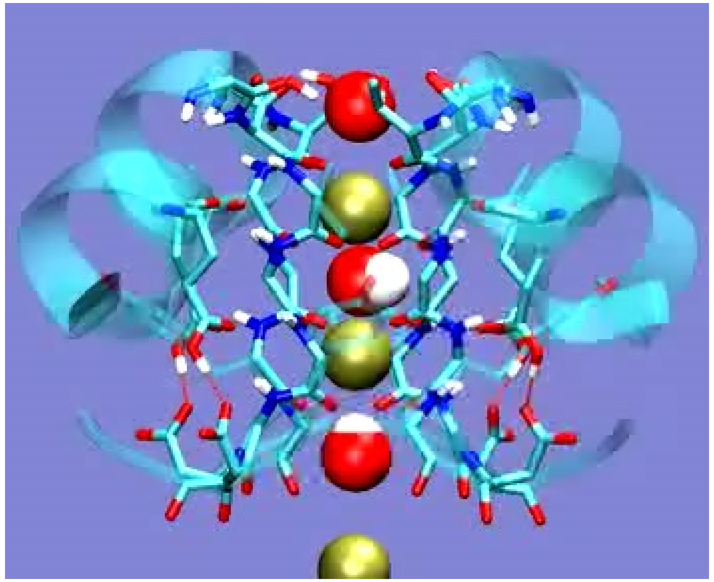


鉀離子通道的原子結構

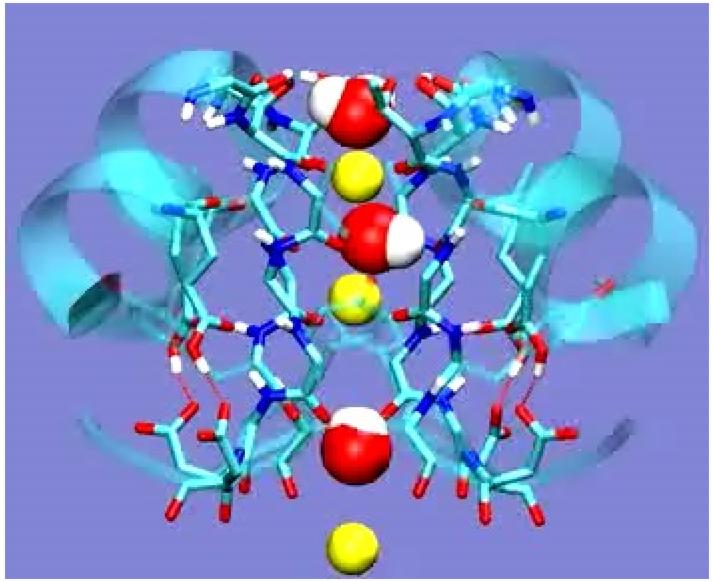


鉀離子通道如何選擇讓較大的鉀離子通過，但卻阻隔較小的鈉離子?

K^+ in K channel

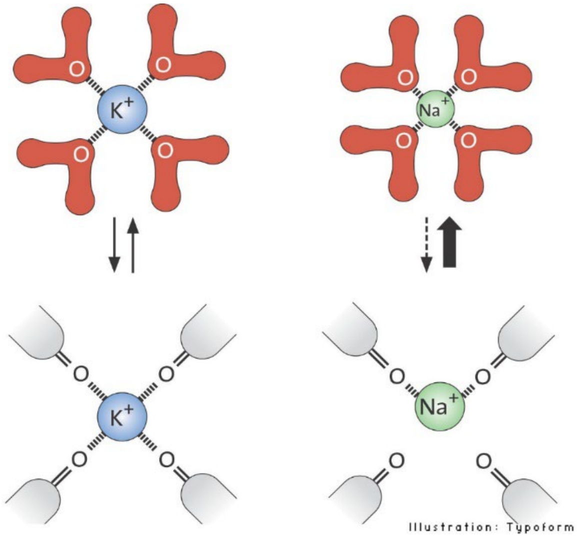


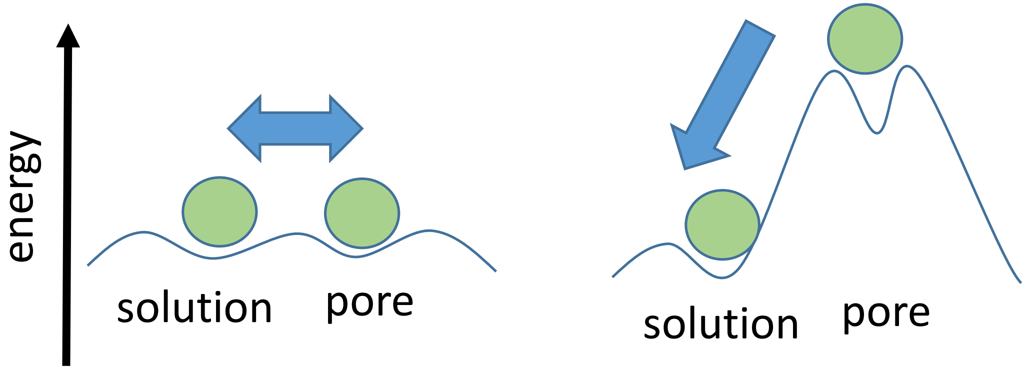
Na^+ in K channel



Hydration shell

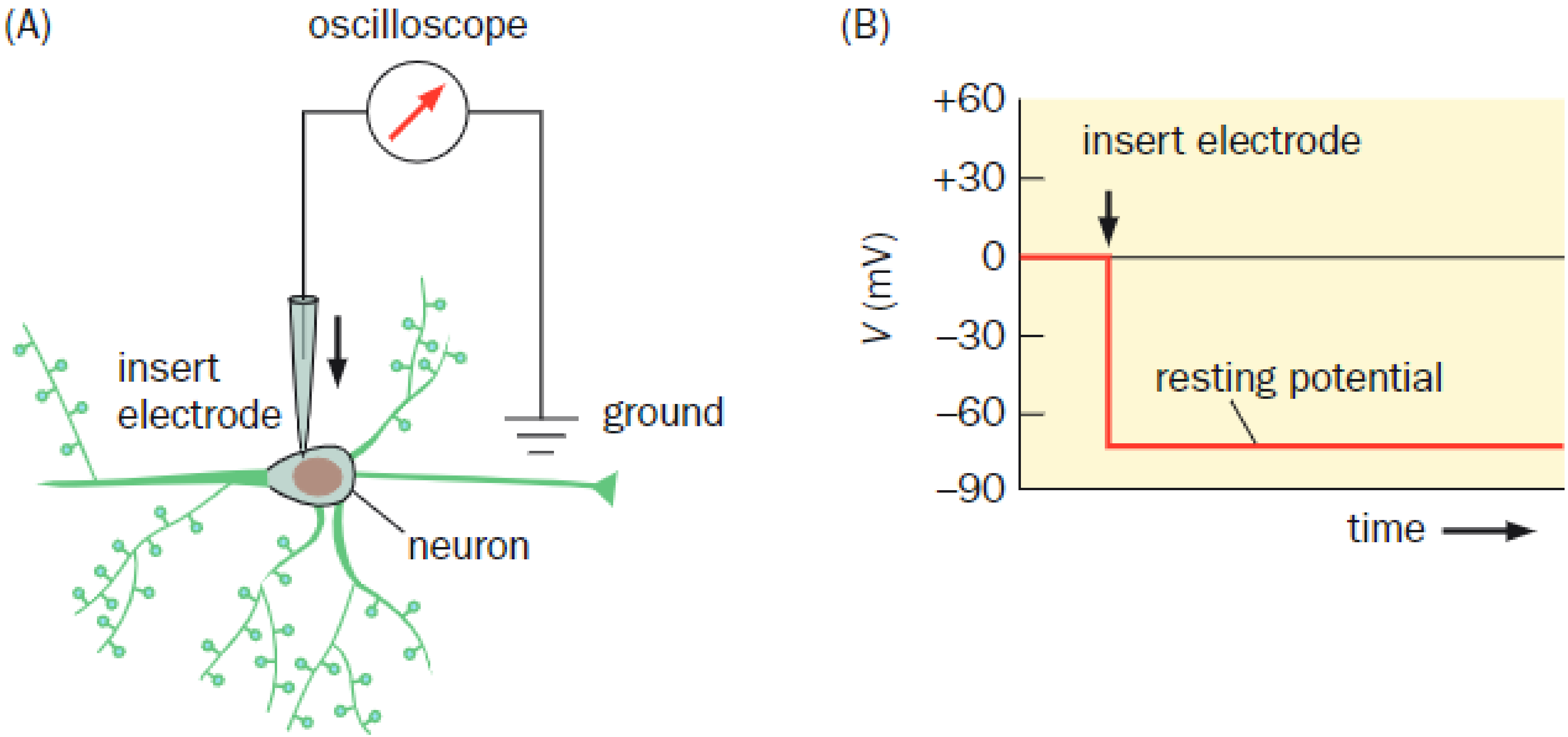
pore





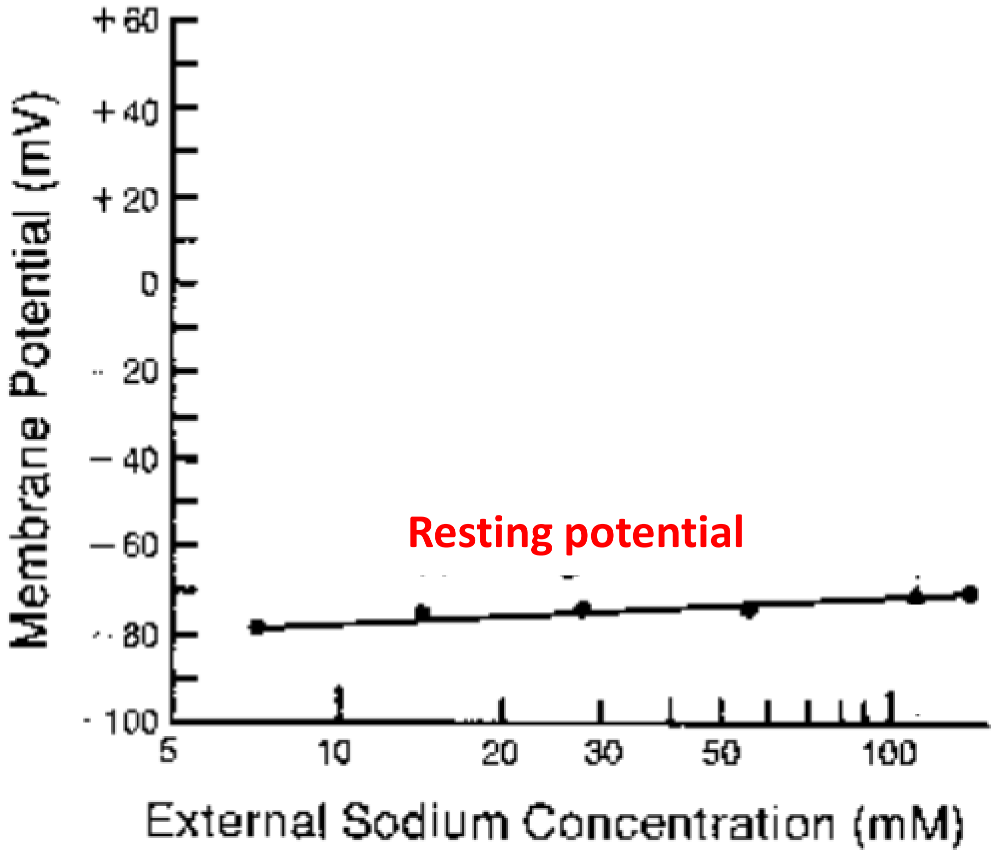
電阻，電容，電池

細胞內的電位比細胞外低

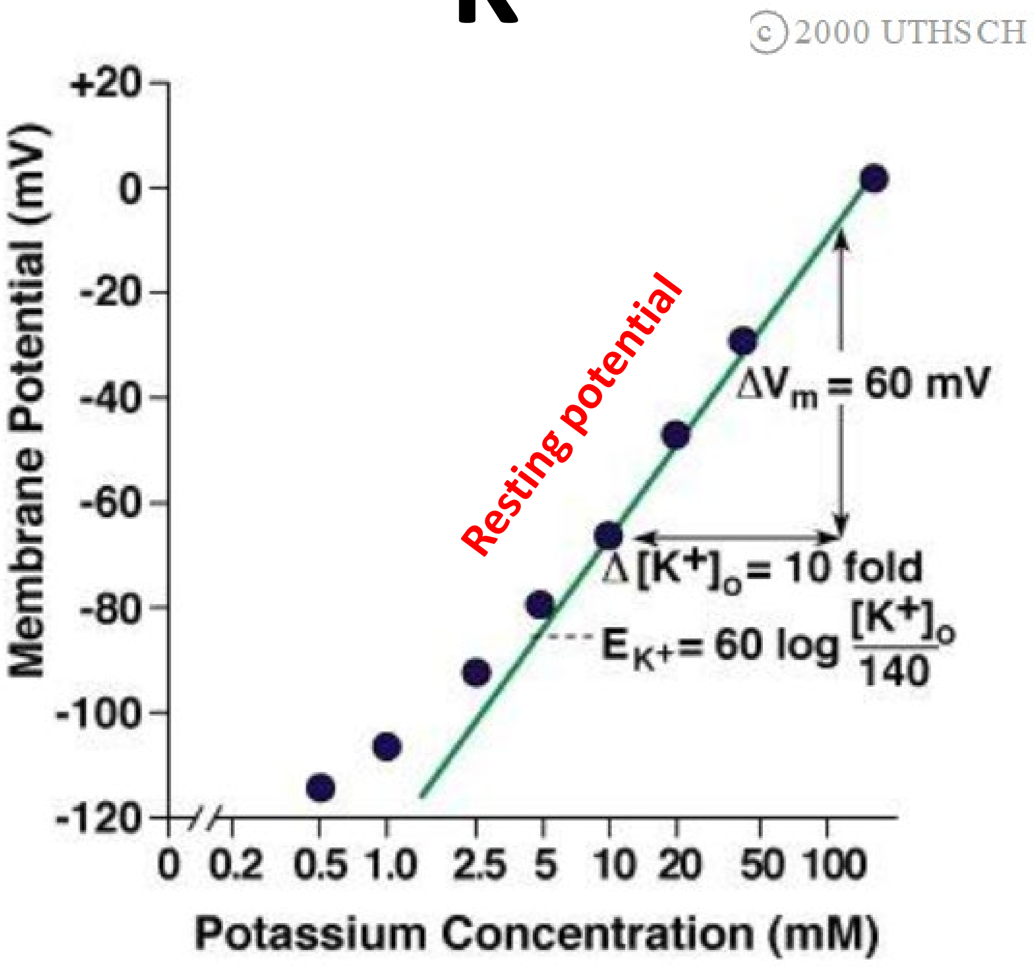


在休息狀態下，細胞膜對鉀離子有高度通透性

Na^+



K^+



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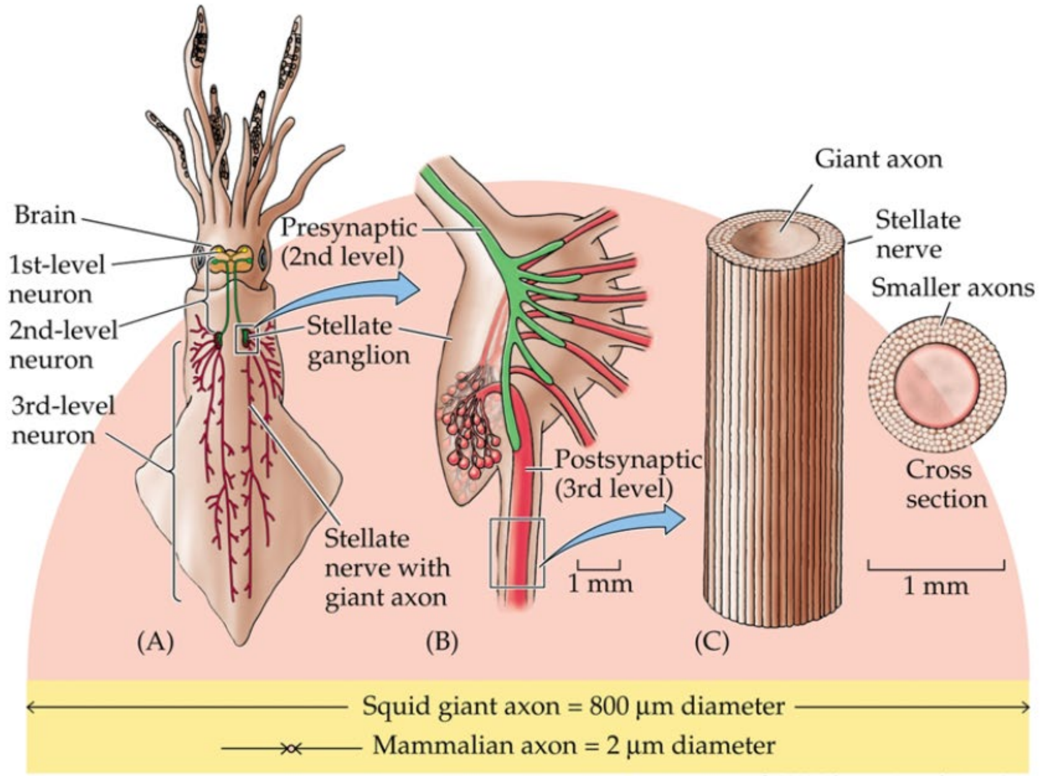
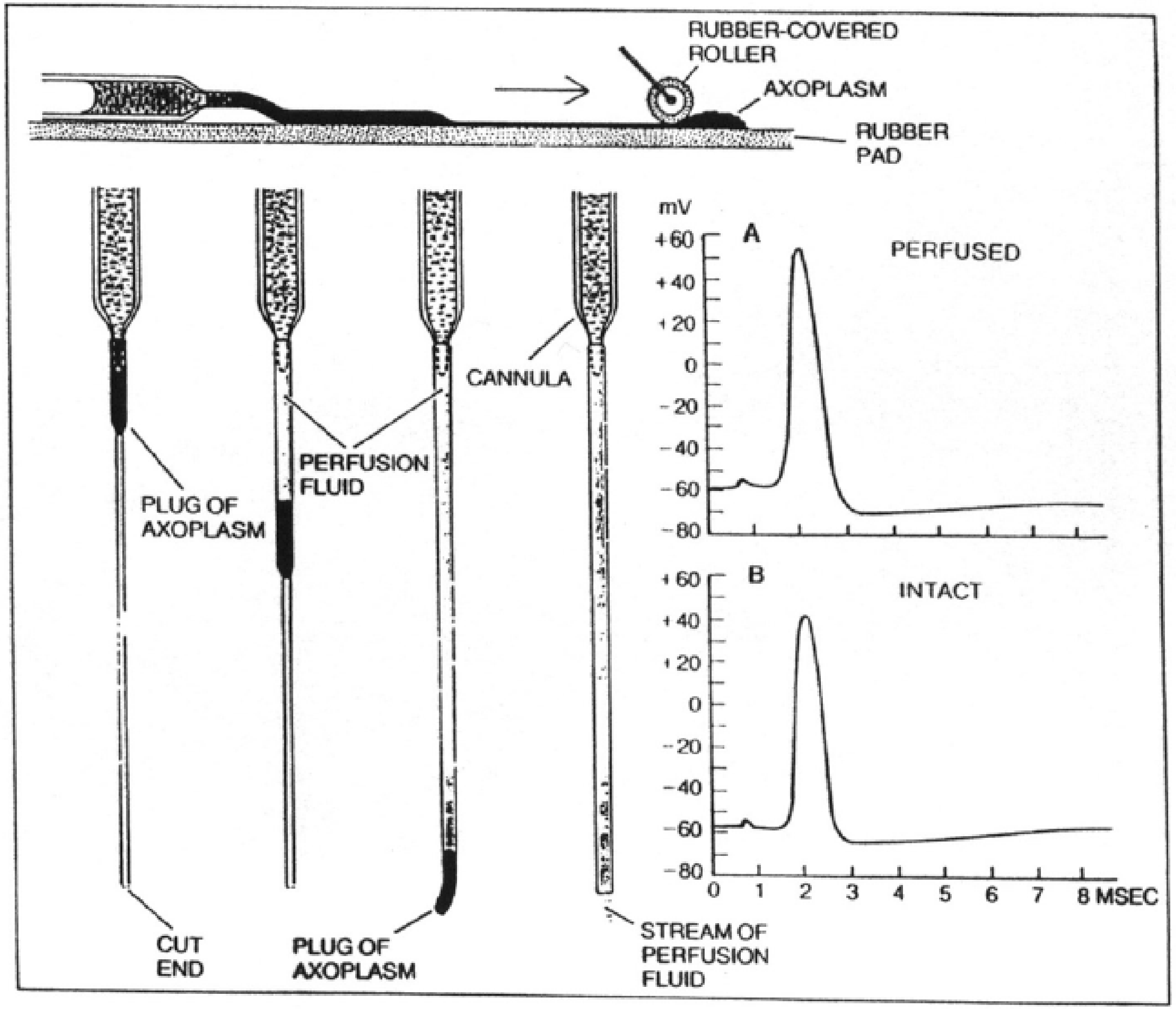
烏賊的巨大軸突



Brain
1st-level neuron
2nd-level neuron
3rd-level neuron
Presynaptic (2nd level)
Stellate ganglion
Stellate nerve with giant axon
Postsynaptic (3rd level)
1 mm
Giant axon
Stellate nerve
Smaller axons
Cross section
1 mm
(A)
(B)
(C)
Squid giant axon = 800 μm diameter
Mammalian axon = 2 μm diameter

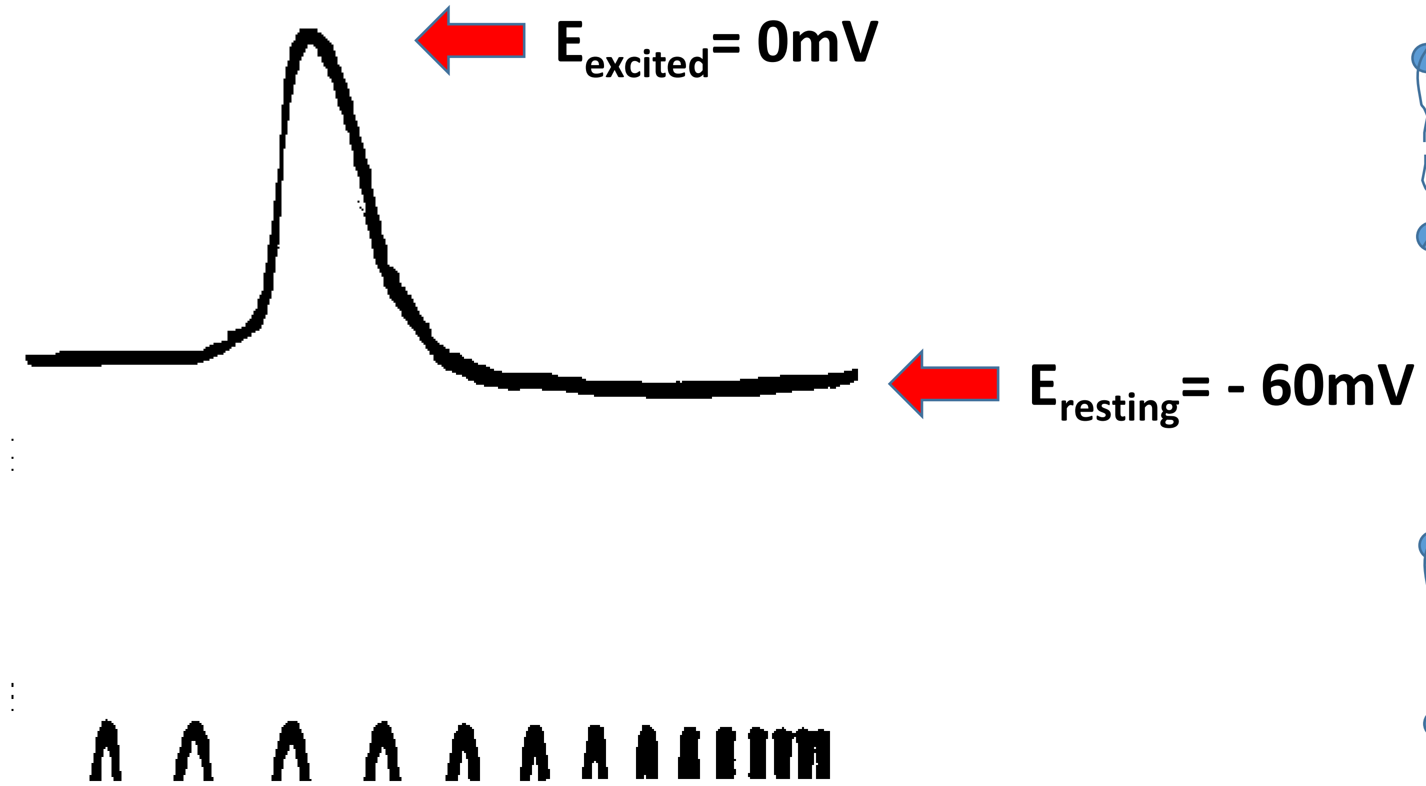


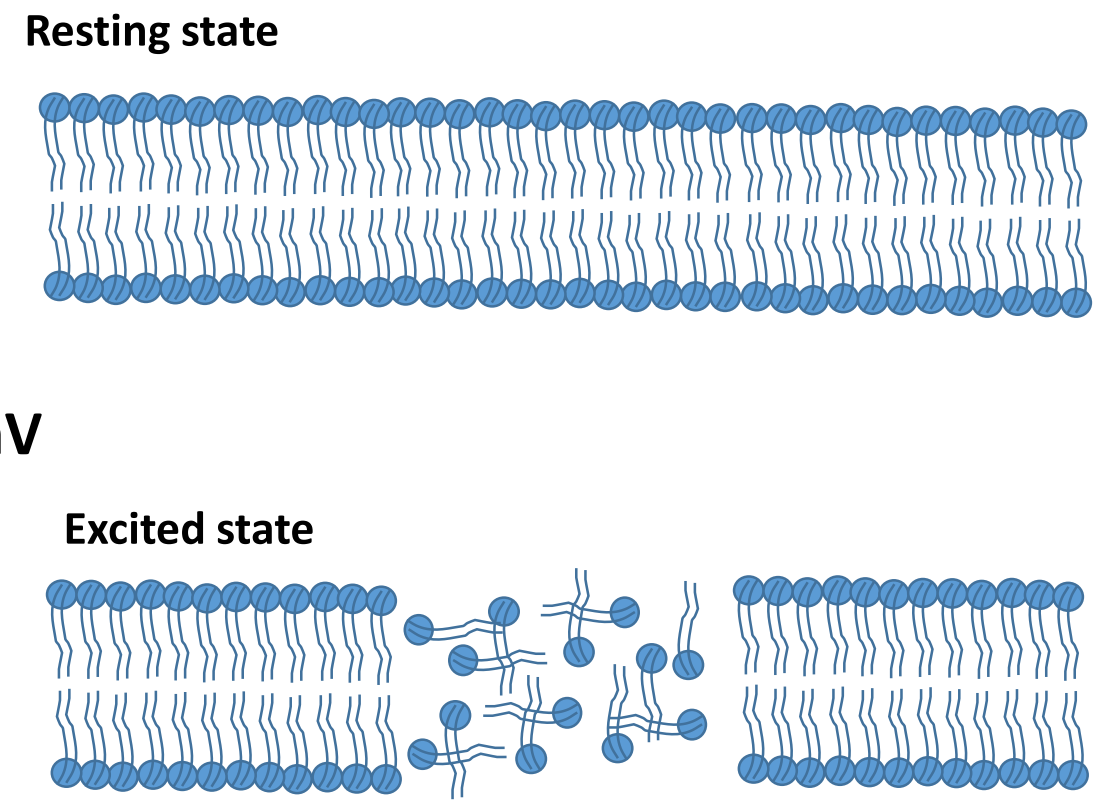
RUBBER-COVERED ROLLER
AXOPLASM
RUBBER PAD
PLUG OF AXOPLASM
CUT END
PERFUSION FLUID
PLUG OF AXOPLASM
CANNULA
STREAM OF PERFUSION FLUID
mV
A
PERFUSED
+60
+40
+20
0
-20
-40
-60
-80
B
INTACT
0
1
2
3
4
5
6
7
8 MSEC

動作電位:

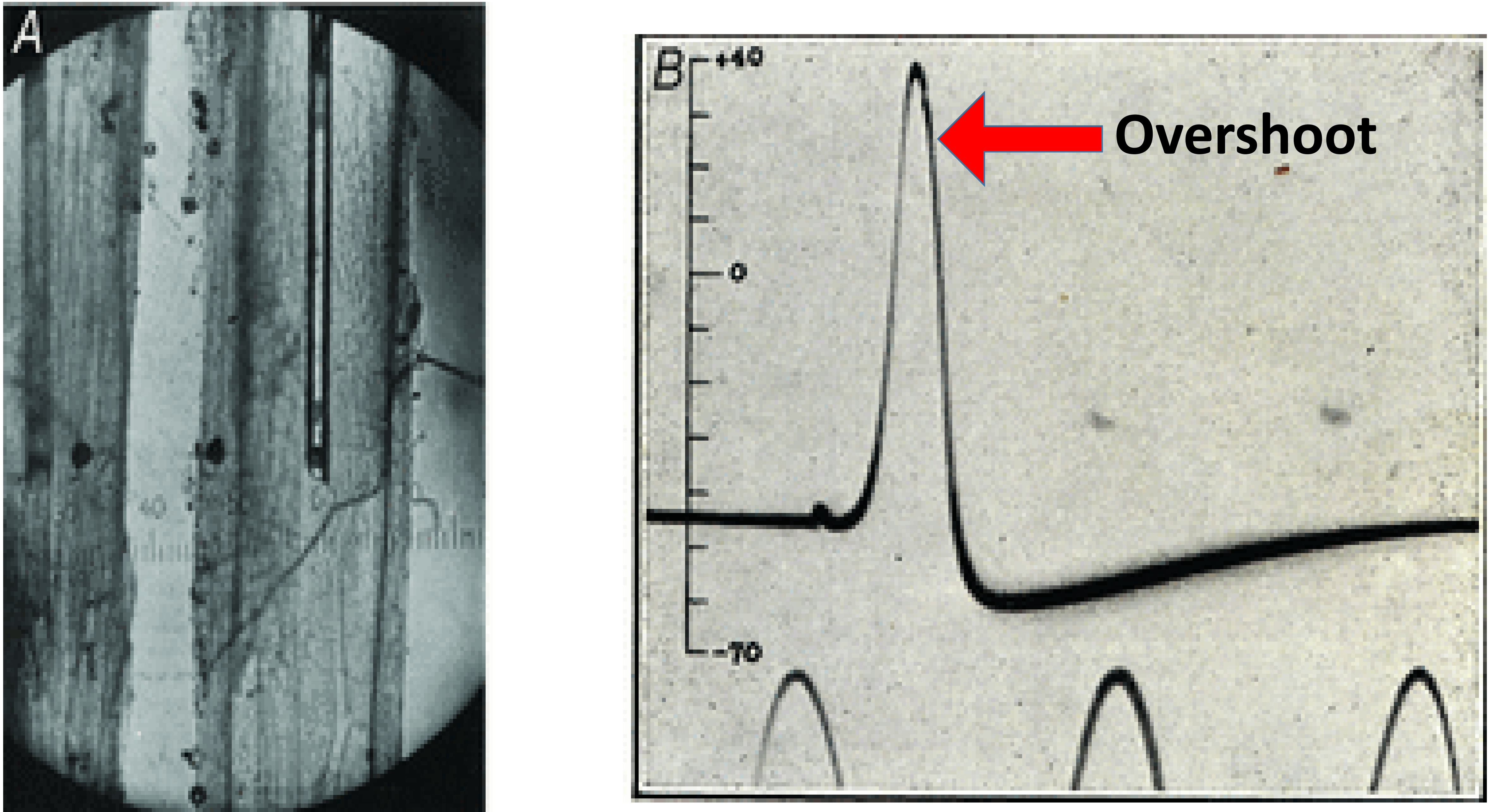
~1890 Julius Bernstein 細胞內的電位為-60 mV.

~1920 Cole and Curtis 動作電位產生時，可達到0 mV，推測細胞膜有破損。



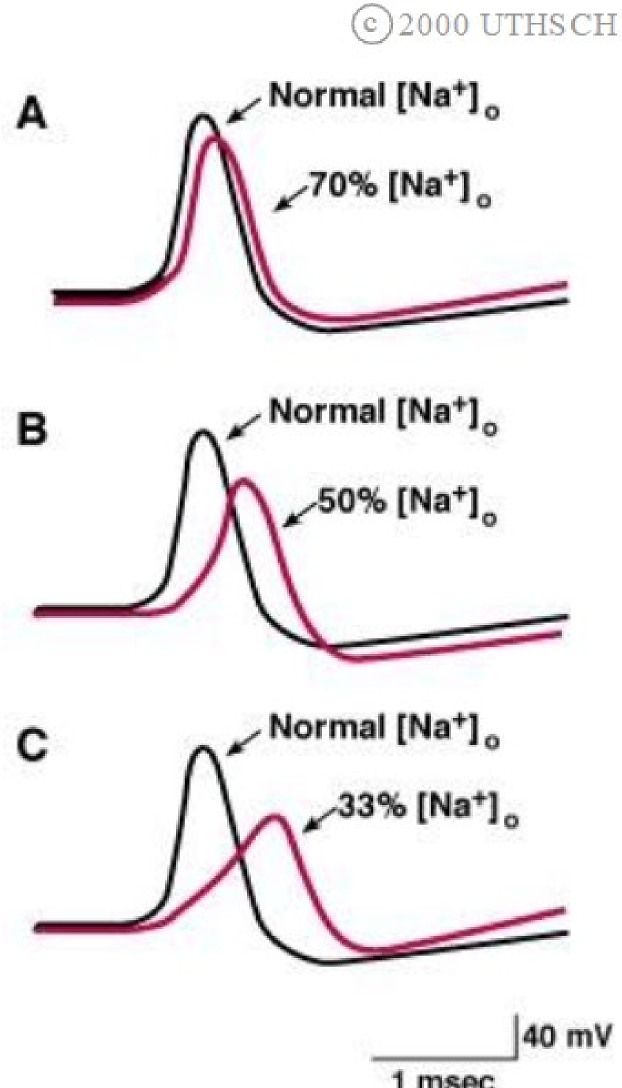


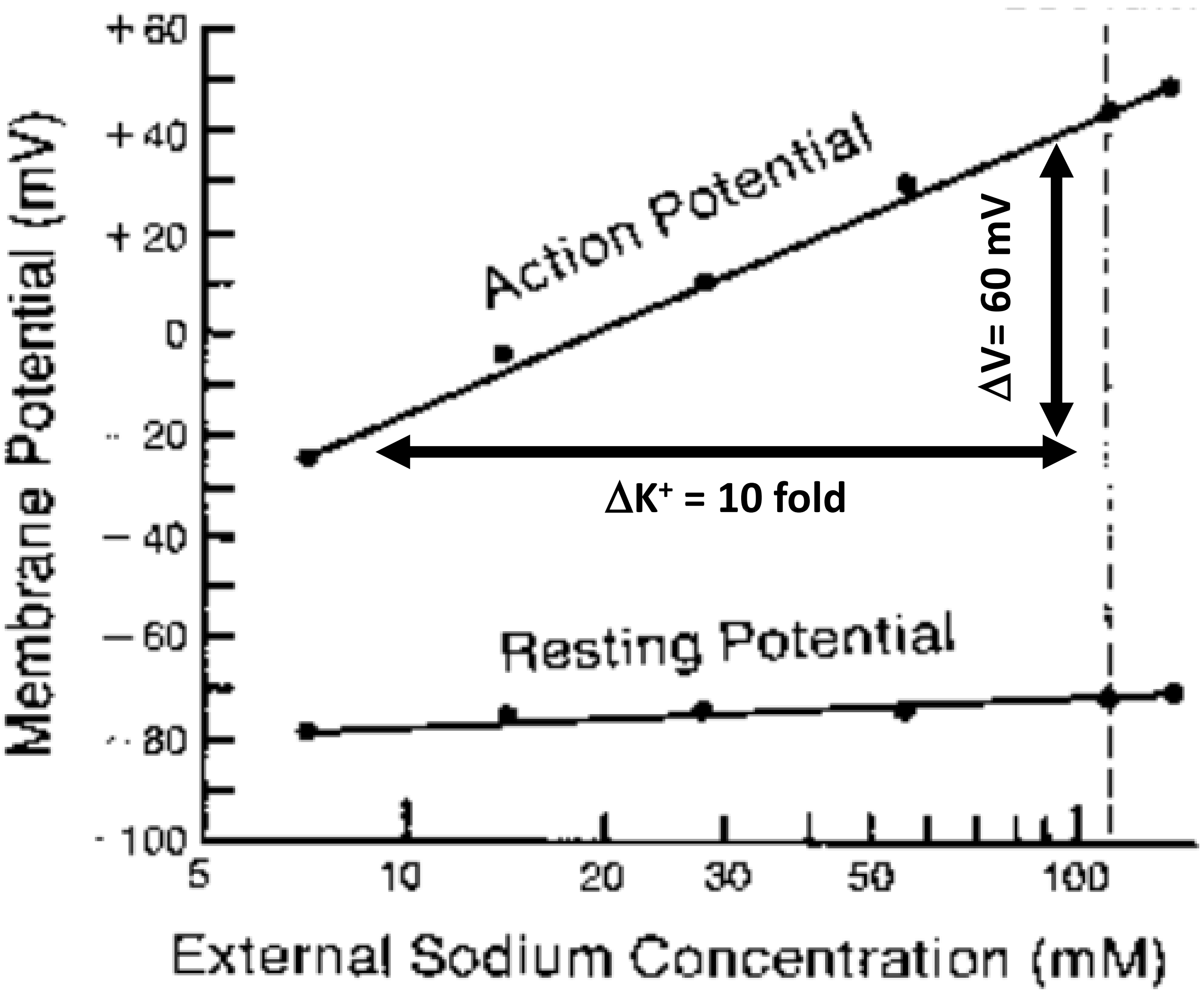
Action Potential: An overshoot of the action potential in squid giant axon



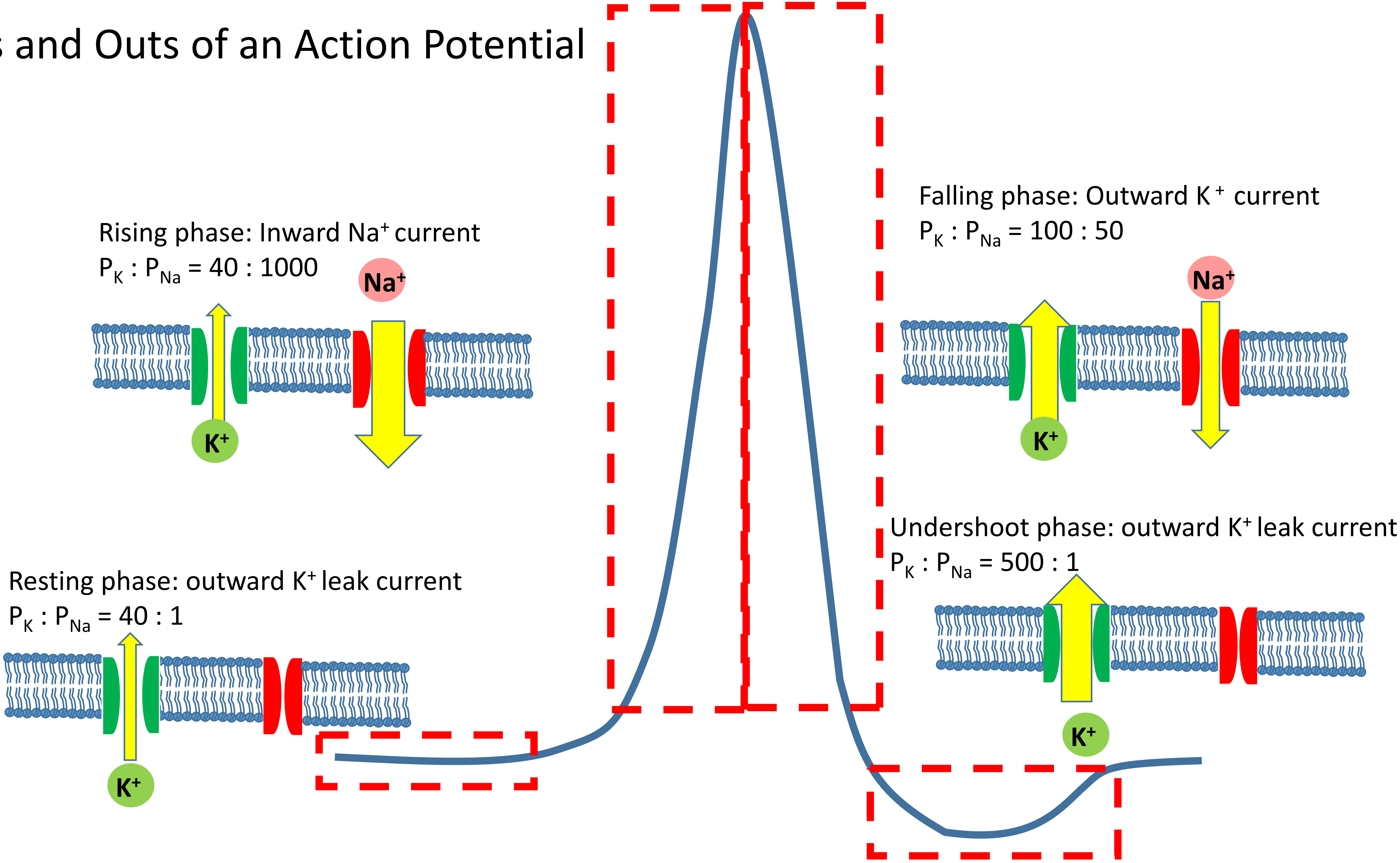
動作電位的數學模型:

動作電位的峰值由鈉離子

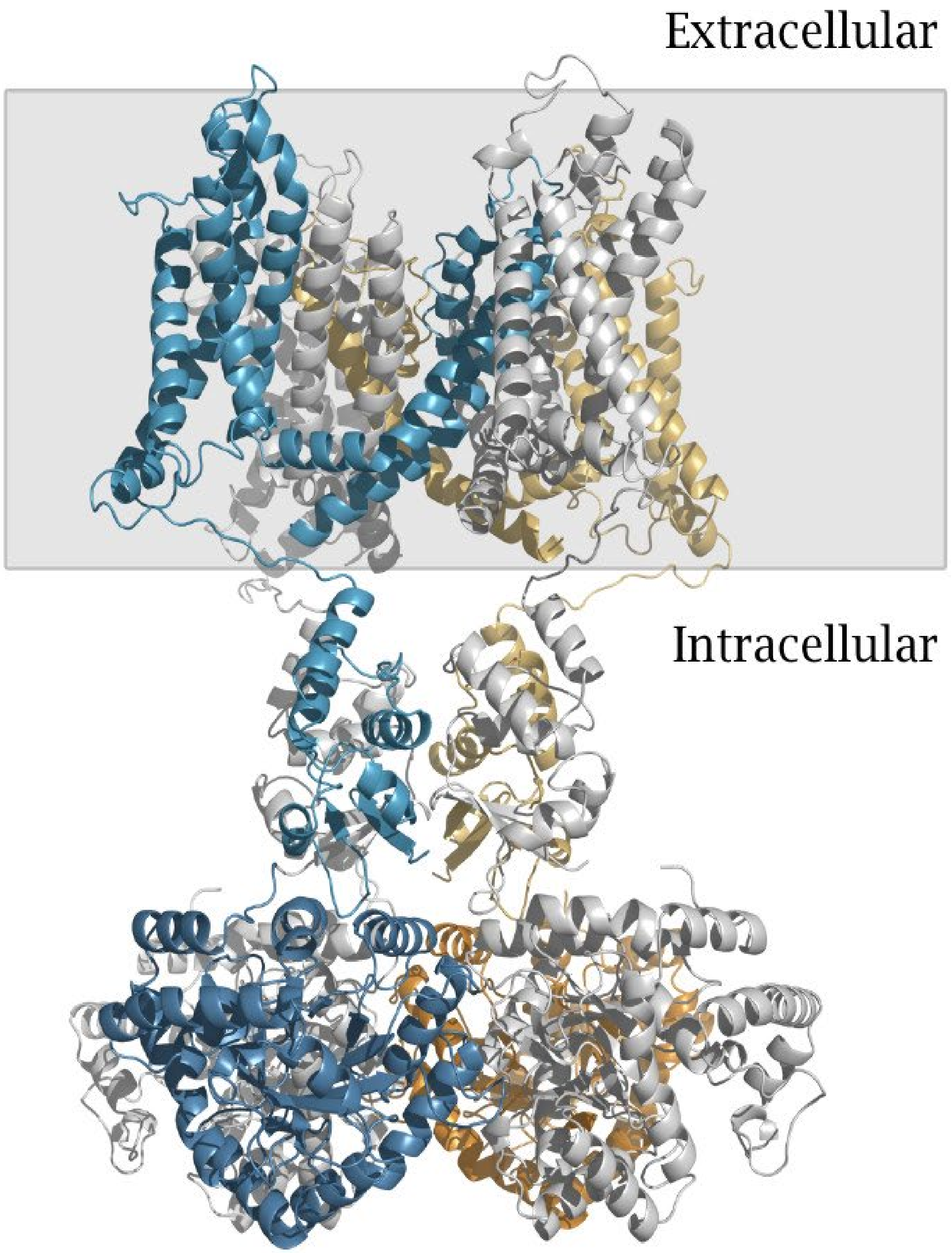


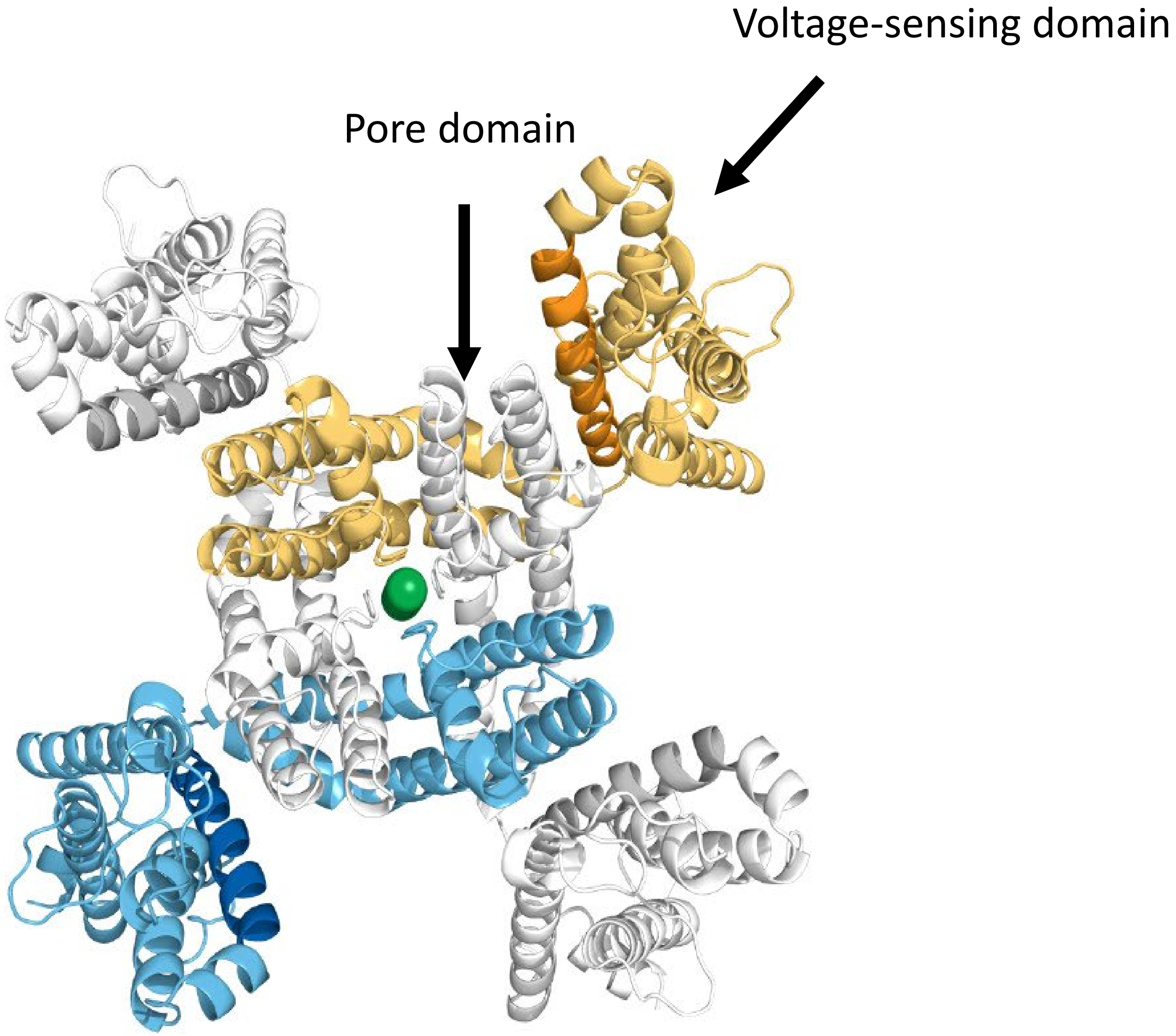


The Ins and Outs of an Action Potential

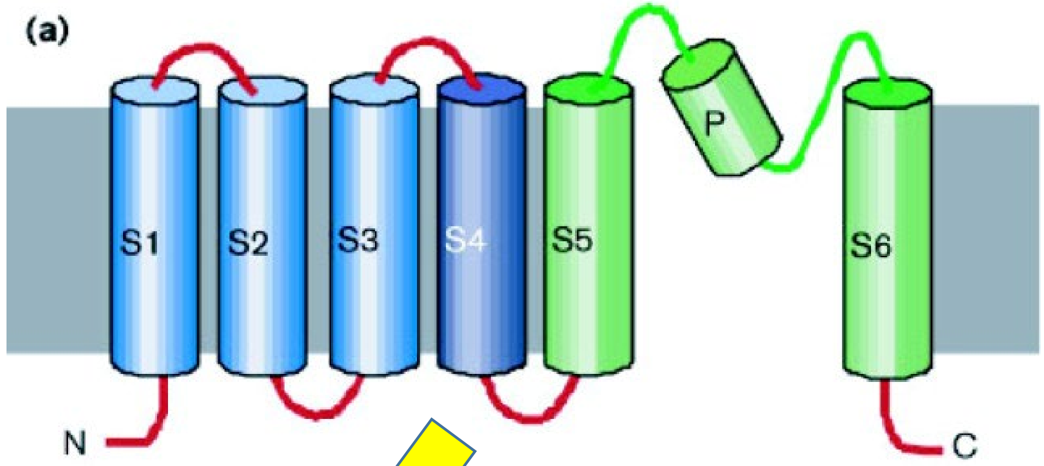


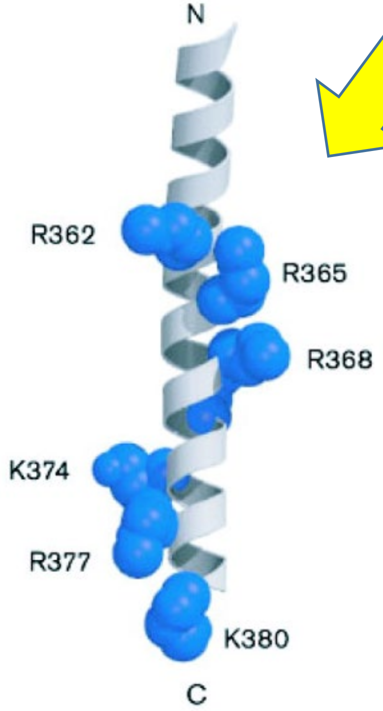
電壓控制鉀離子通道


Extracellular
Intracellular


Voltage-sensing domain
Pore domain

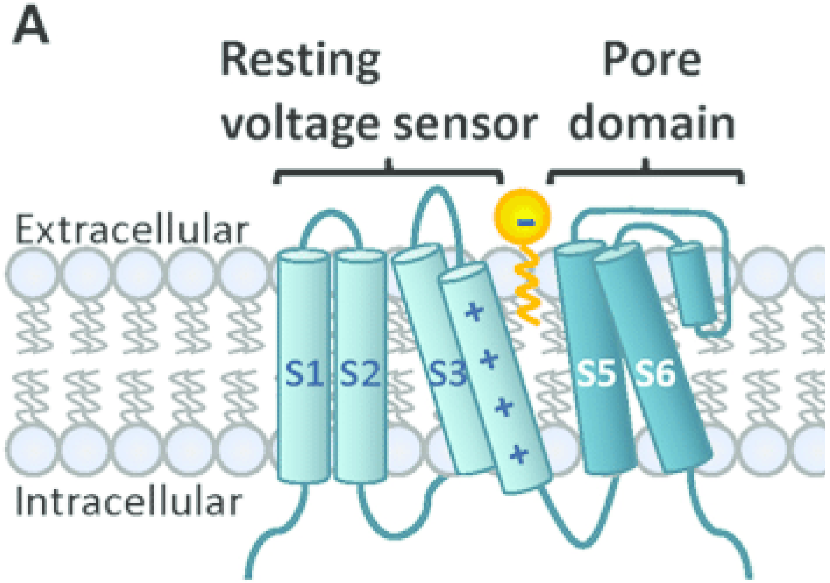
離子通道如何感受膜電位的變化?

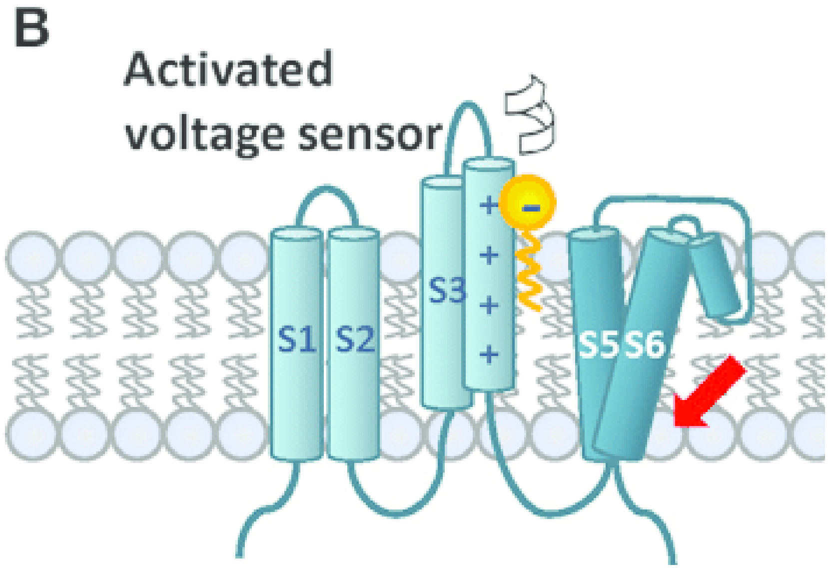




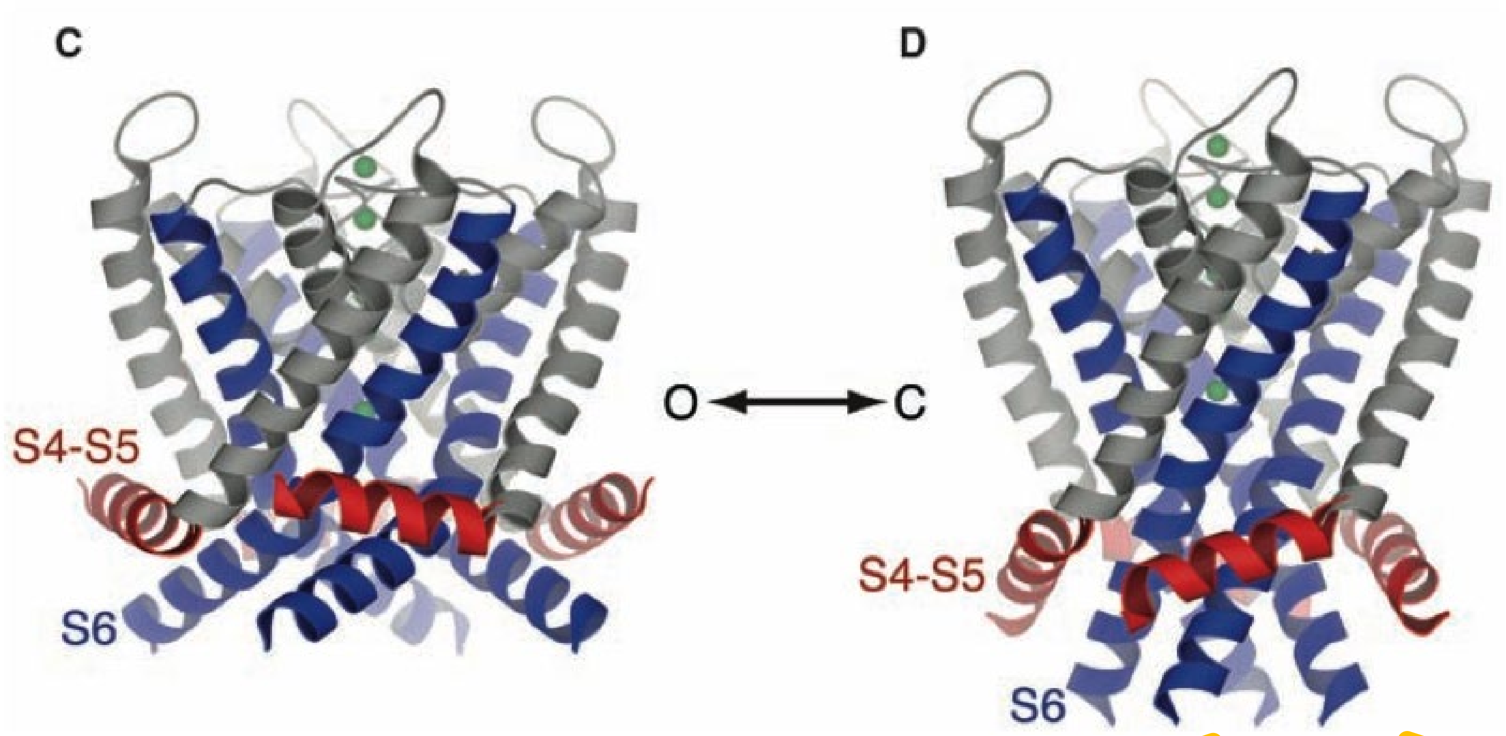
S4

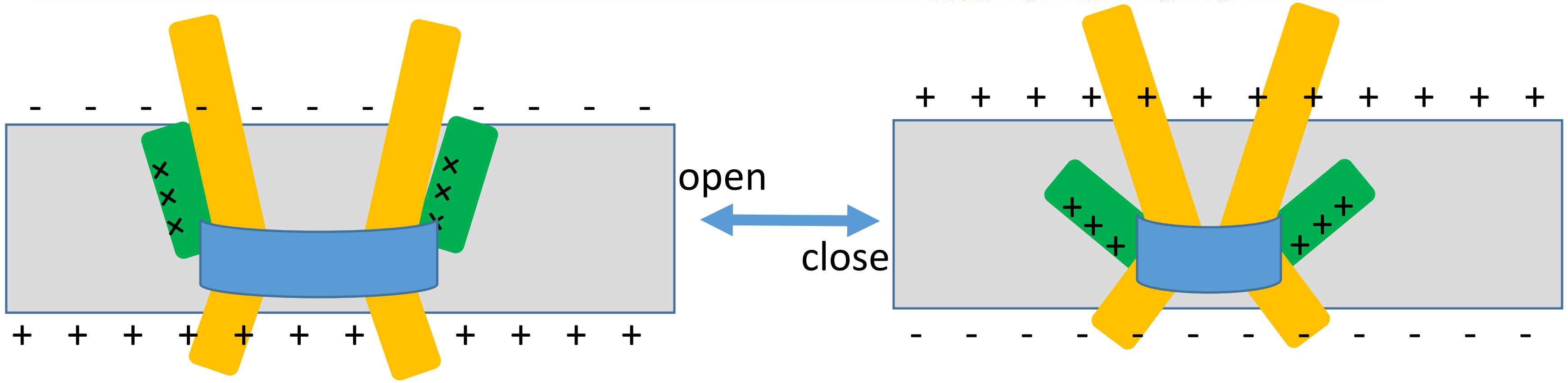
		R1	R2	R3	R4	K5	R6
Shaker	359	A I L R V I	R L V	R V F	R I F	K L S	R H S
NtKv3.2	322	D V I H V F	R I F	G I L	R V F	K I L	R H Y
NtKv3.1	300	R T L R G L	R I I	R V L	R M F	K L M	K H Y
RatKv1.2	291	A I L R V I	R L V	R V F	R I F	K L S	R H S
RatNa$_V$1.2II	845	G L - S V L	R S F	R L L	R V F	K L A	K S W
RatNa$_V$1.4II	658	G L - S V L	R S F	R L L	R V F	K L A	K S W





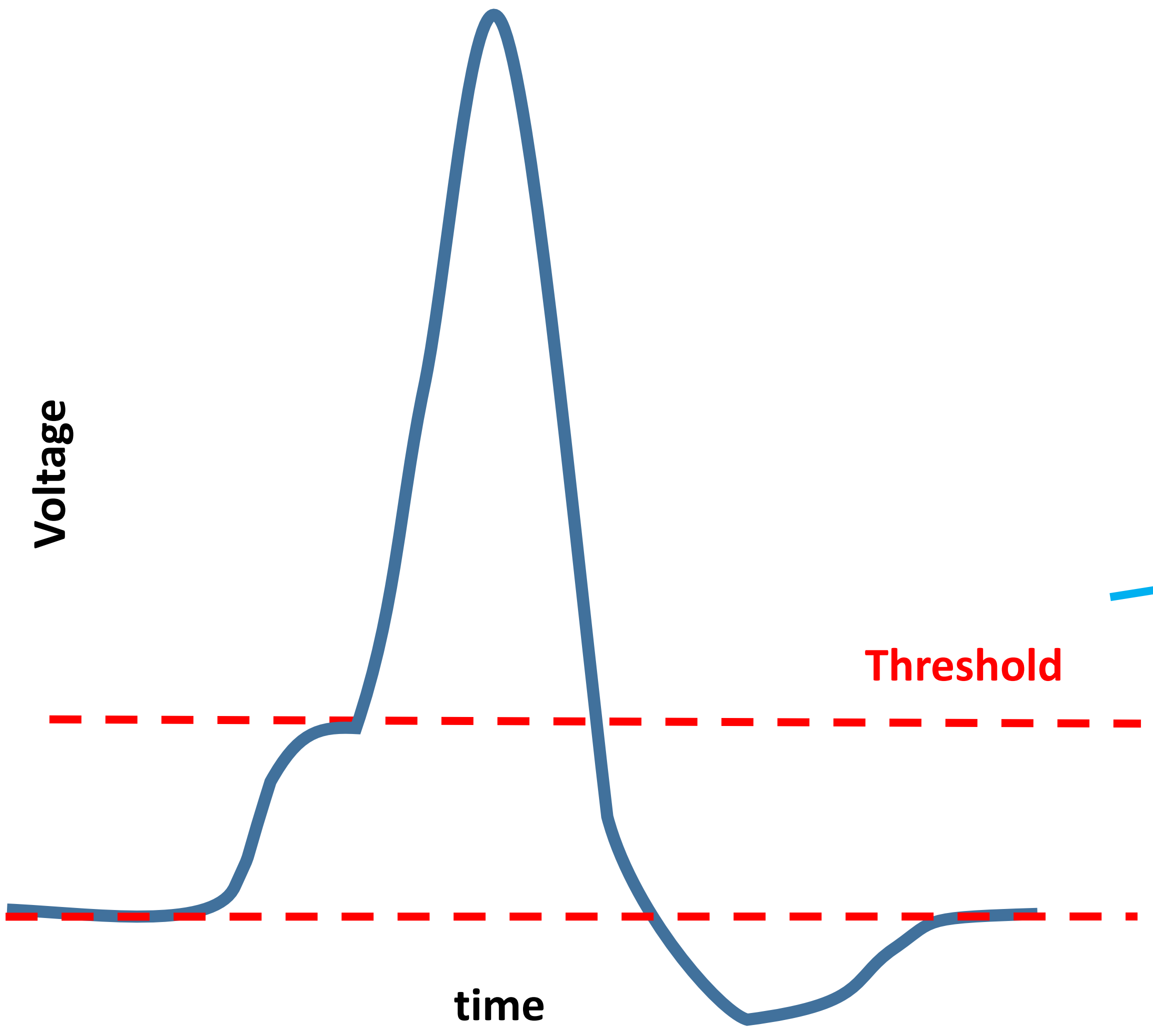
離子通道怎麼開關?

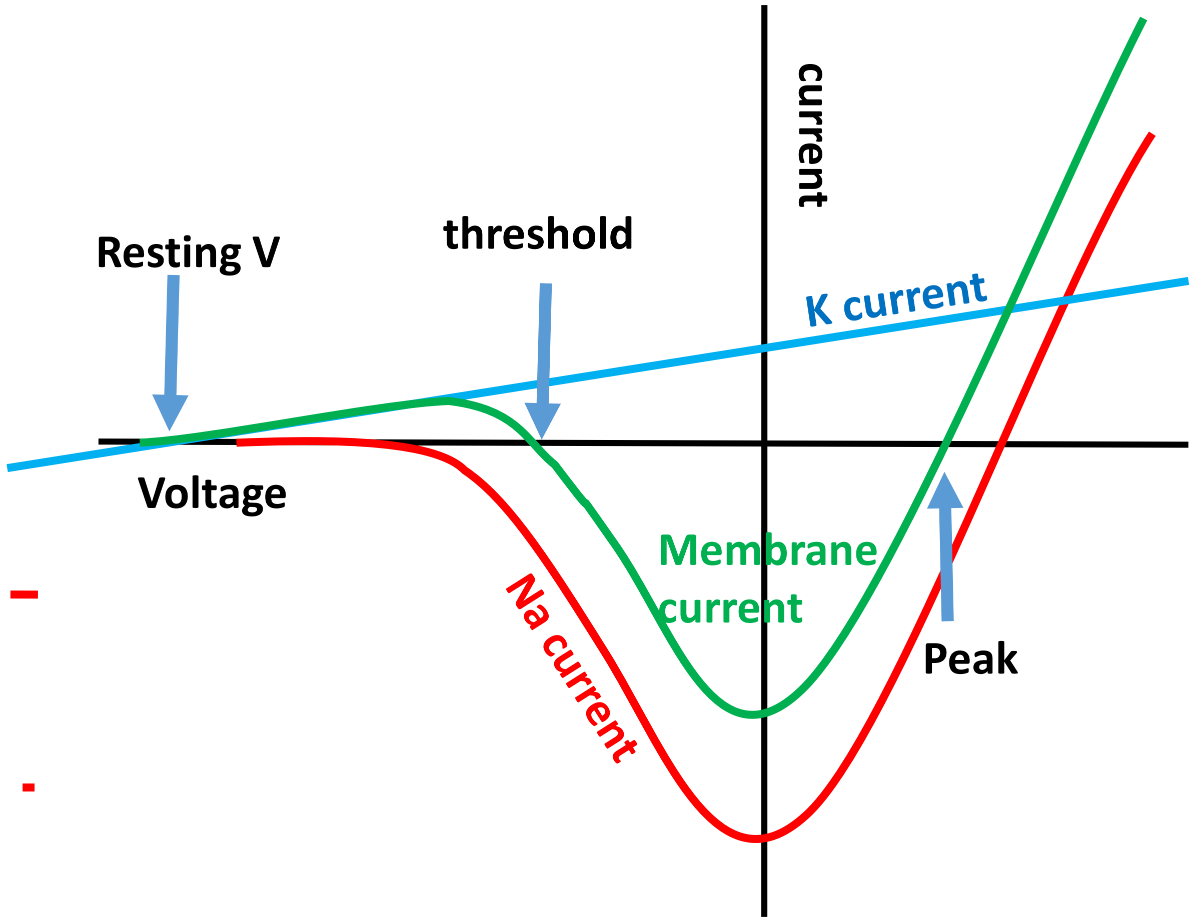




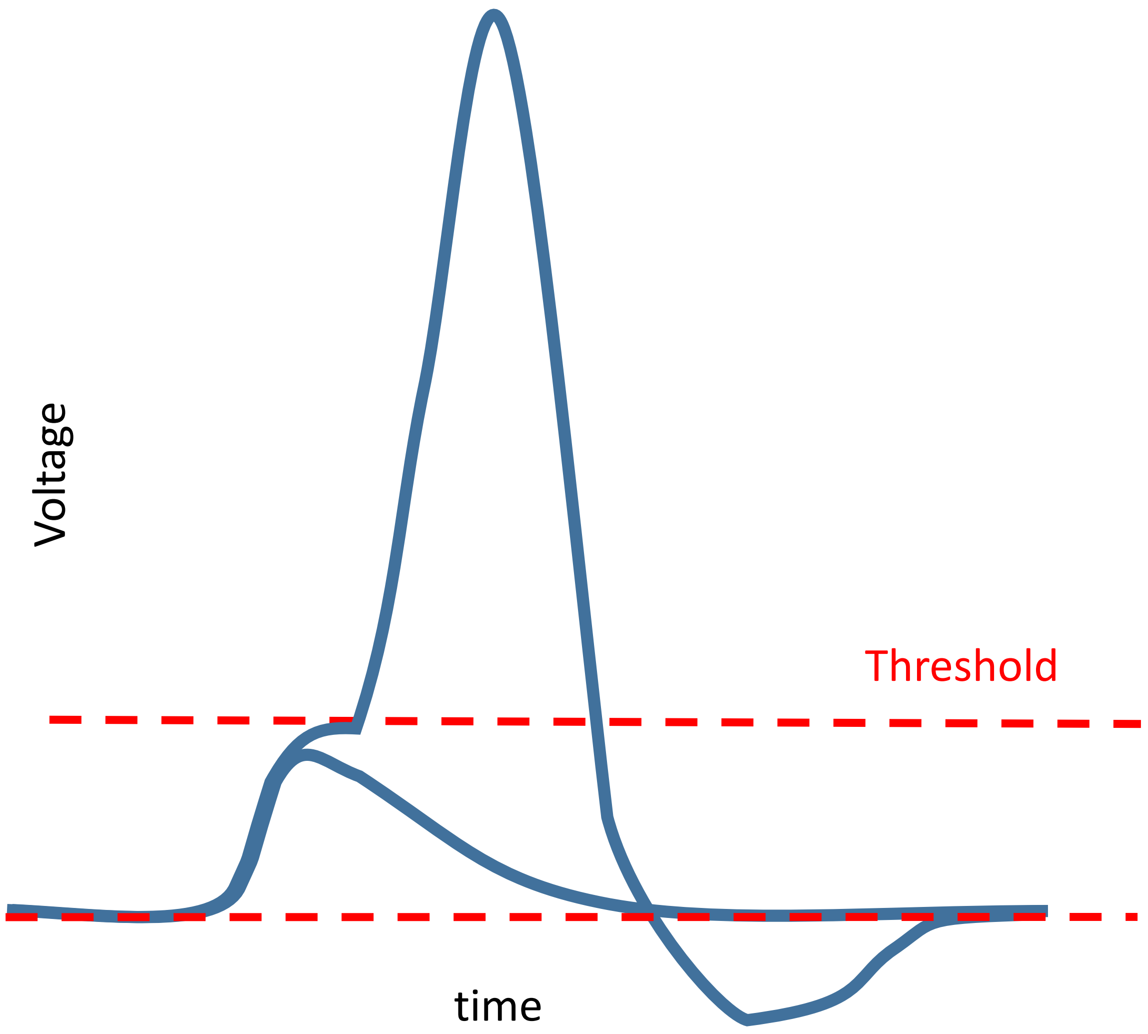
動作電位的產生:

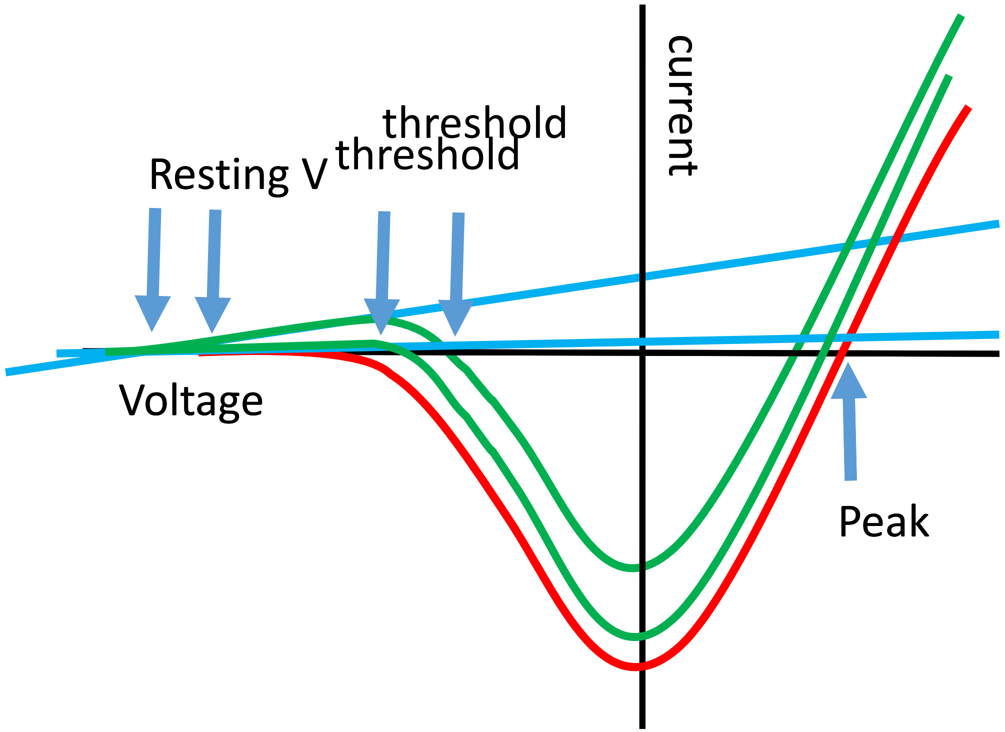
全有全無律: 膜電位超過閾值則可產生動作電位





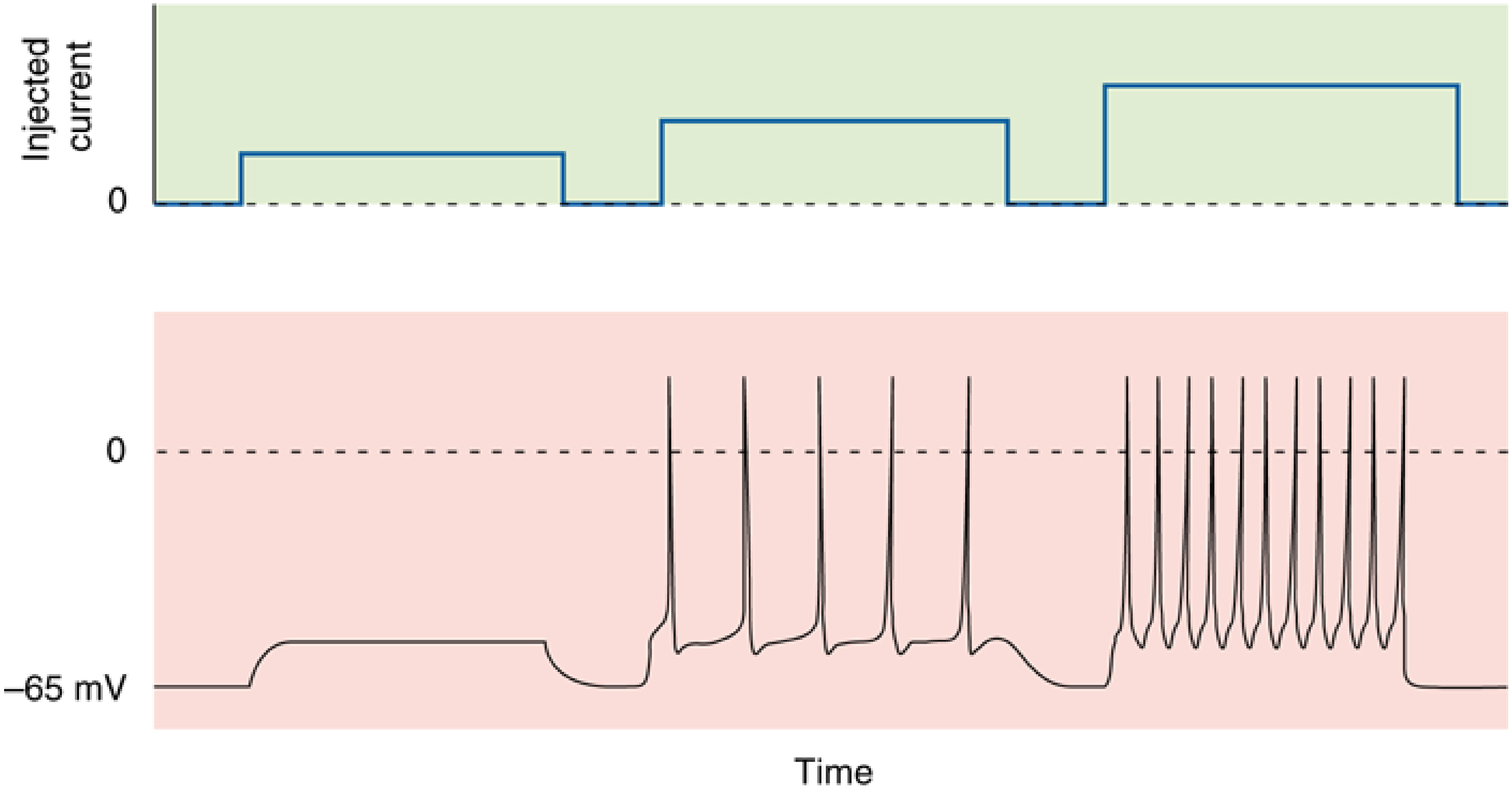
閾值可被調節


Voltage
Threshold
time


current
threshold
threshold
Resting V
Voltage
Peak

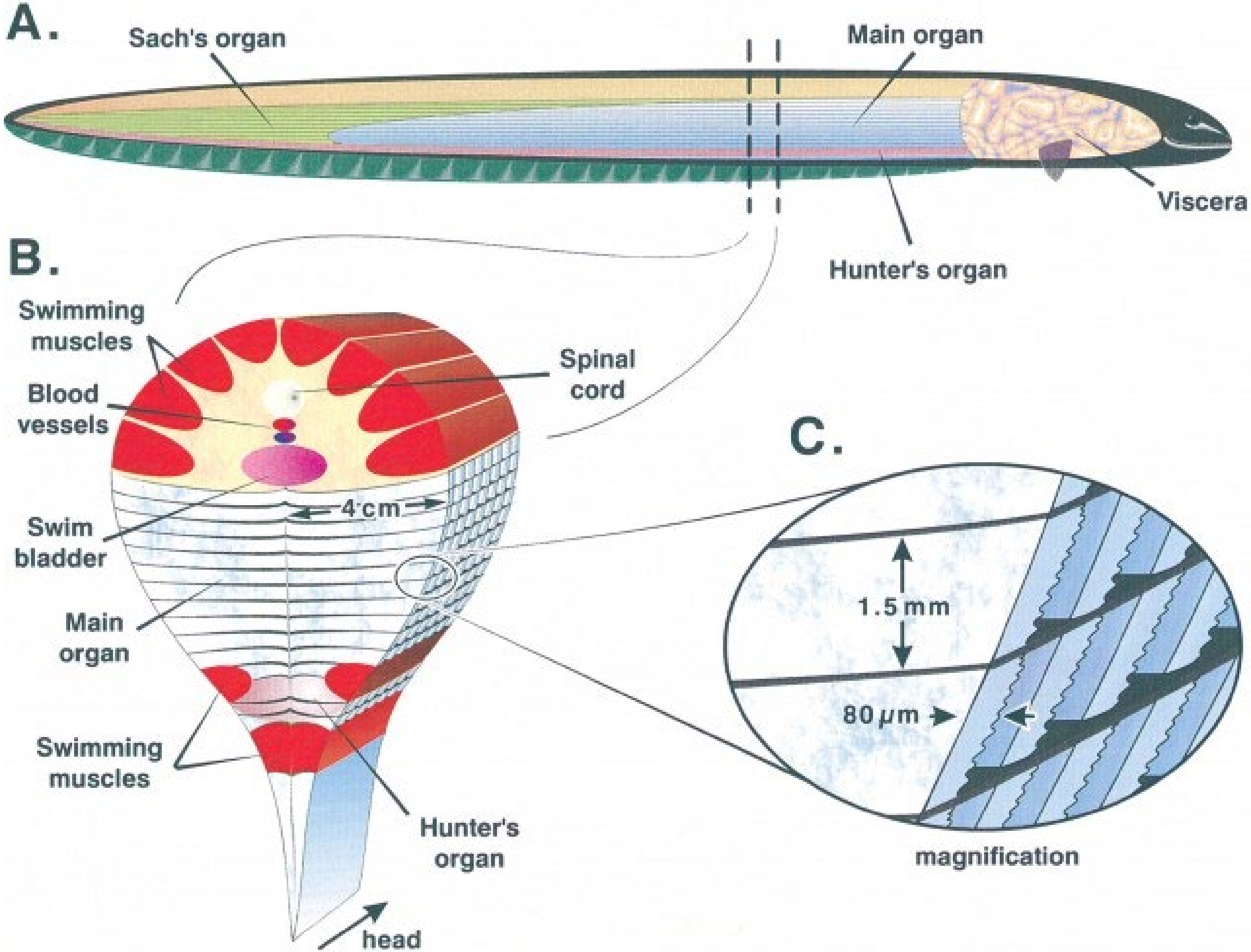
如果動作電位為全有全無，那神經的訊號怎麼產生?

動作電位的頻率決定神經訊號的內容



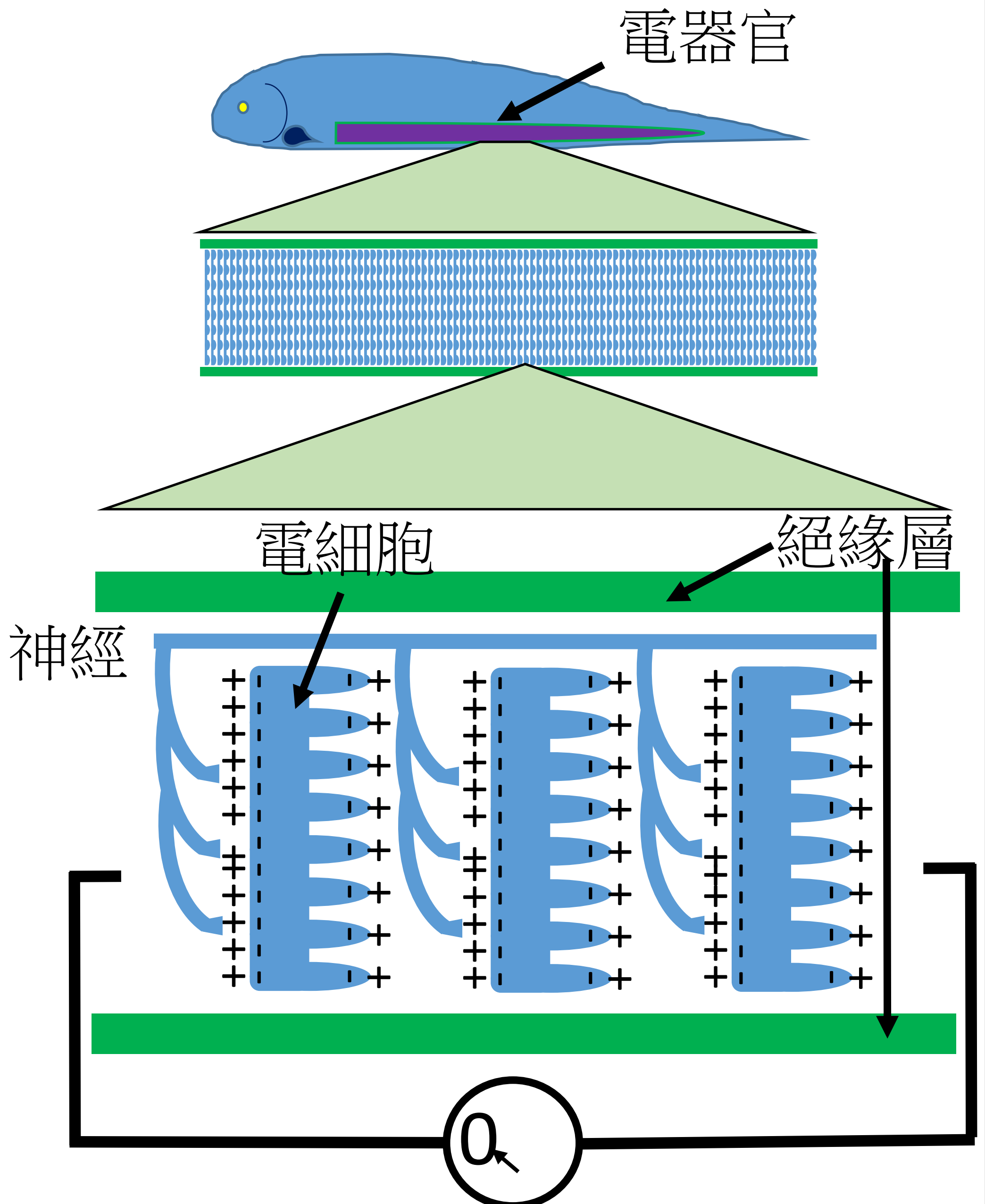
Mimicking EPSC

電鰻怎麼發電的?

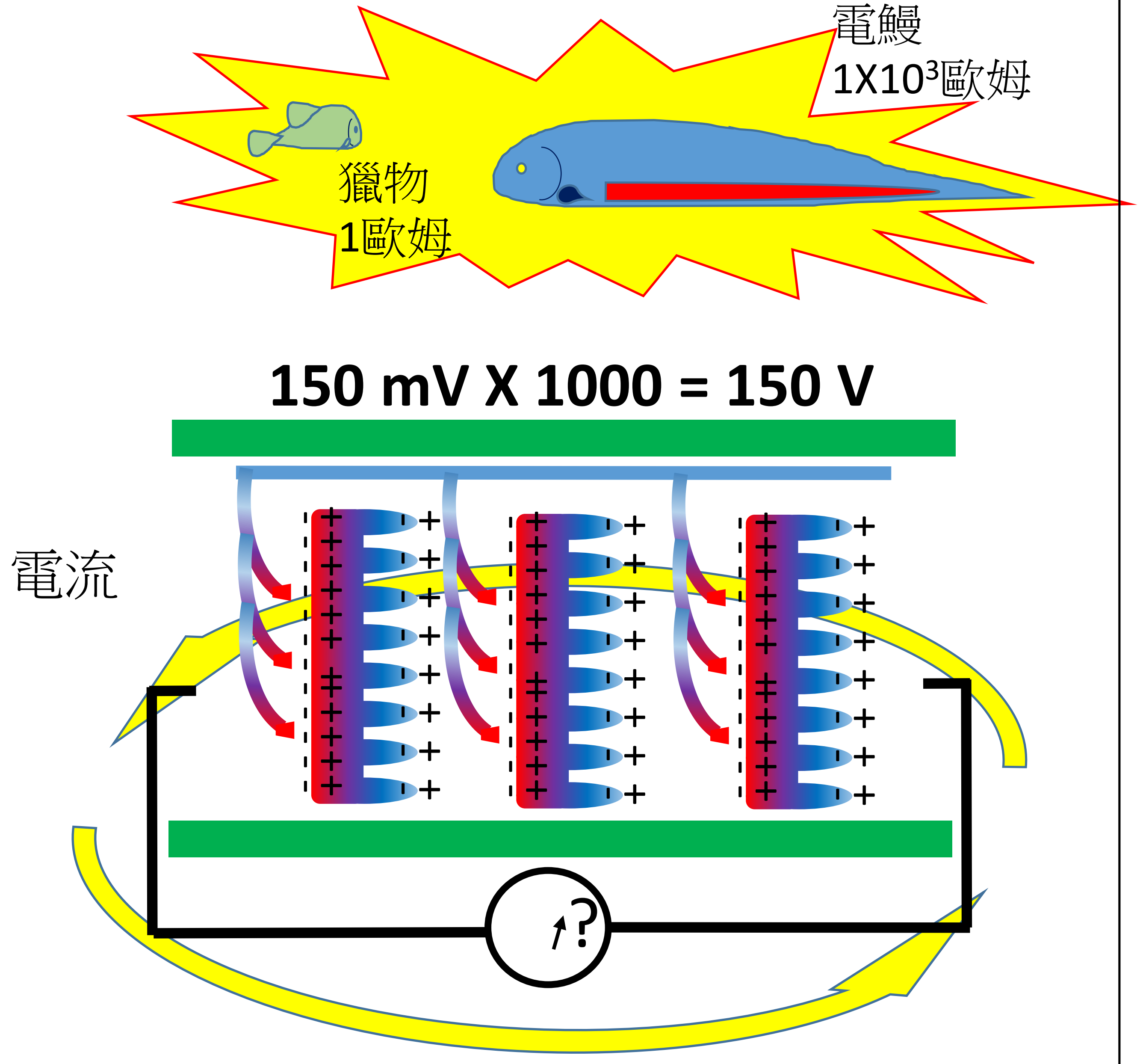


A.
Sach's organ
Main organ
Viscera
Hunter's organ
B.
Swimming muscles
Blood vessels
Spinal cord
Swim bladder
4 cm
Main organ
Swimming muscles
Hunter's organ
head
C.
1.5 mm
80 μm
magnification

靜止狀態



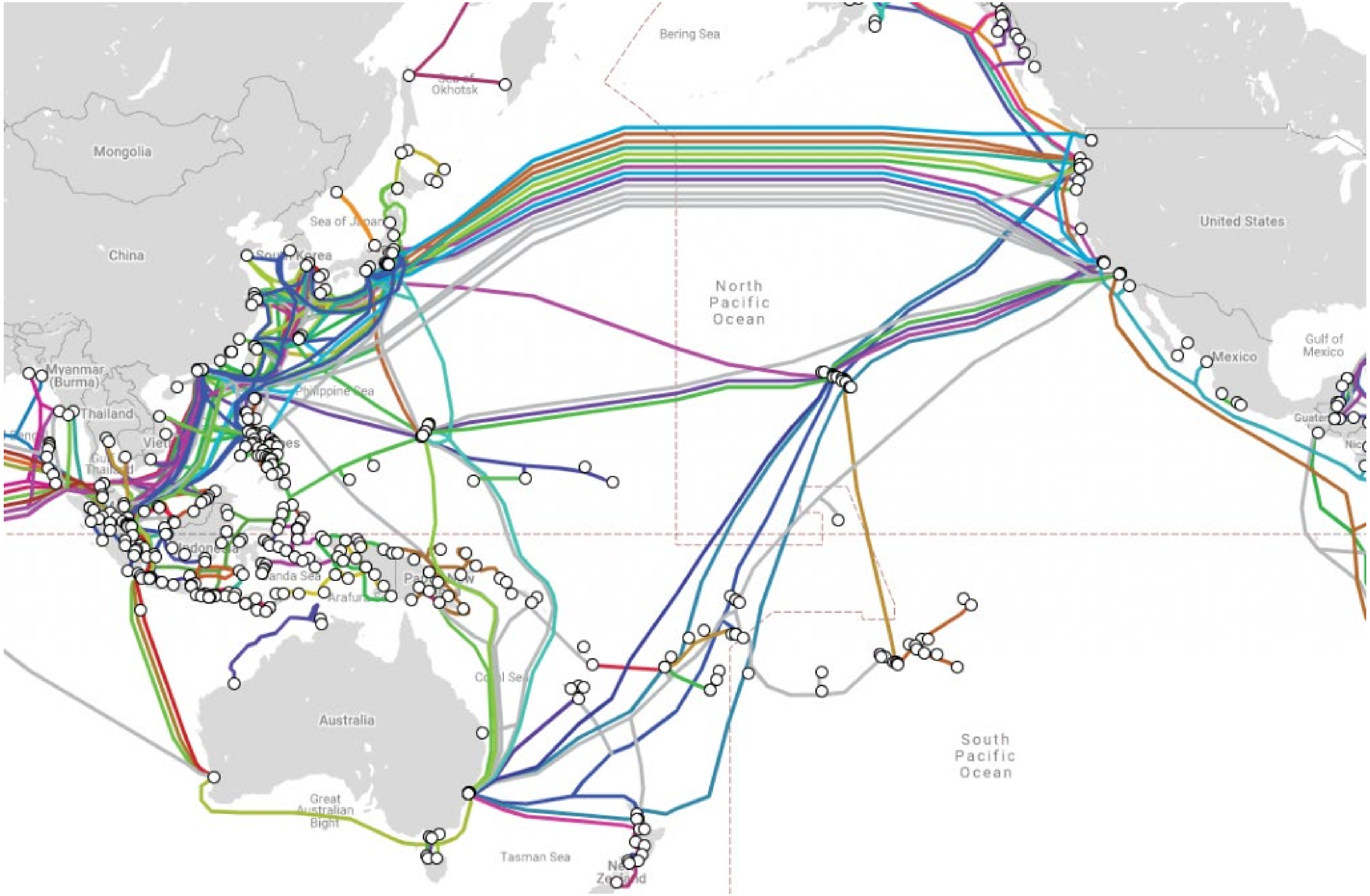
發電



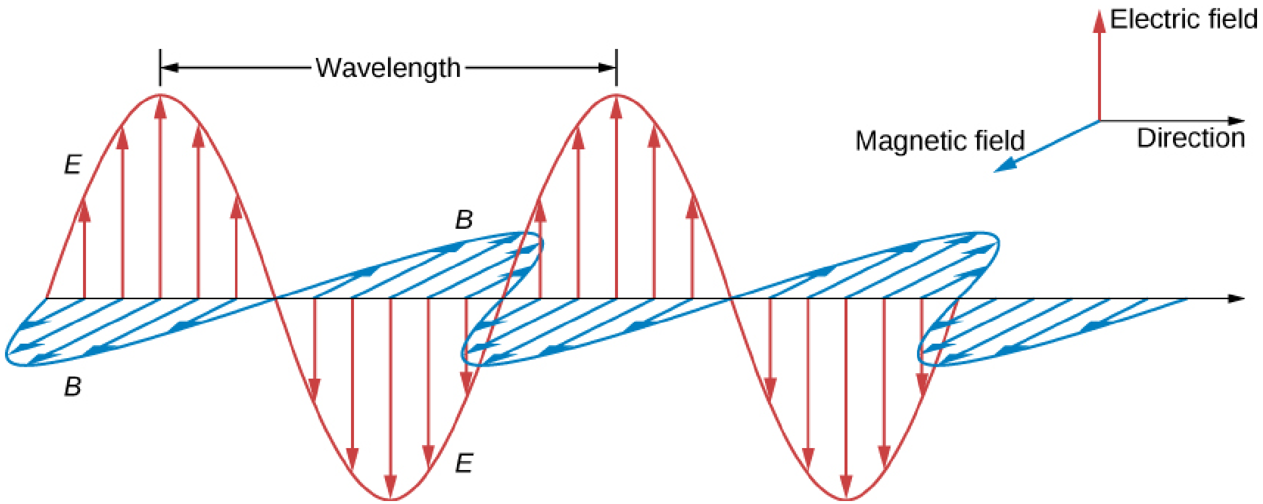
綱要:

- 生物學家的電子元件:
- 膜電位的生理學基礎:
- 動作電位產生的機制:
- 動作電位的傳遞:

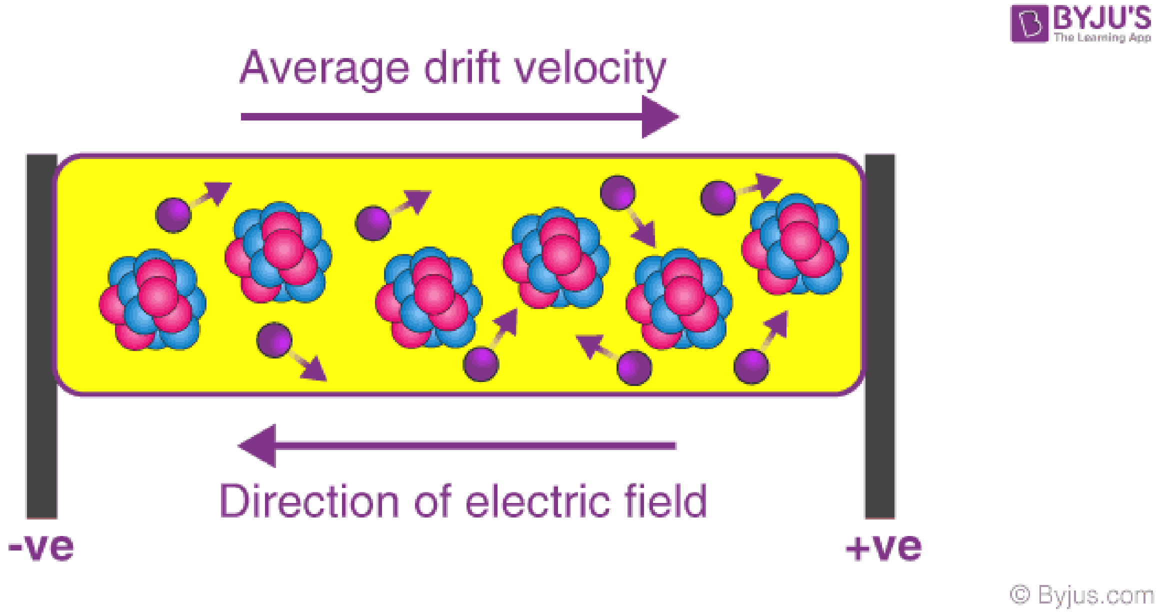
電磁訊號的傳遞速度為多少?



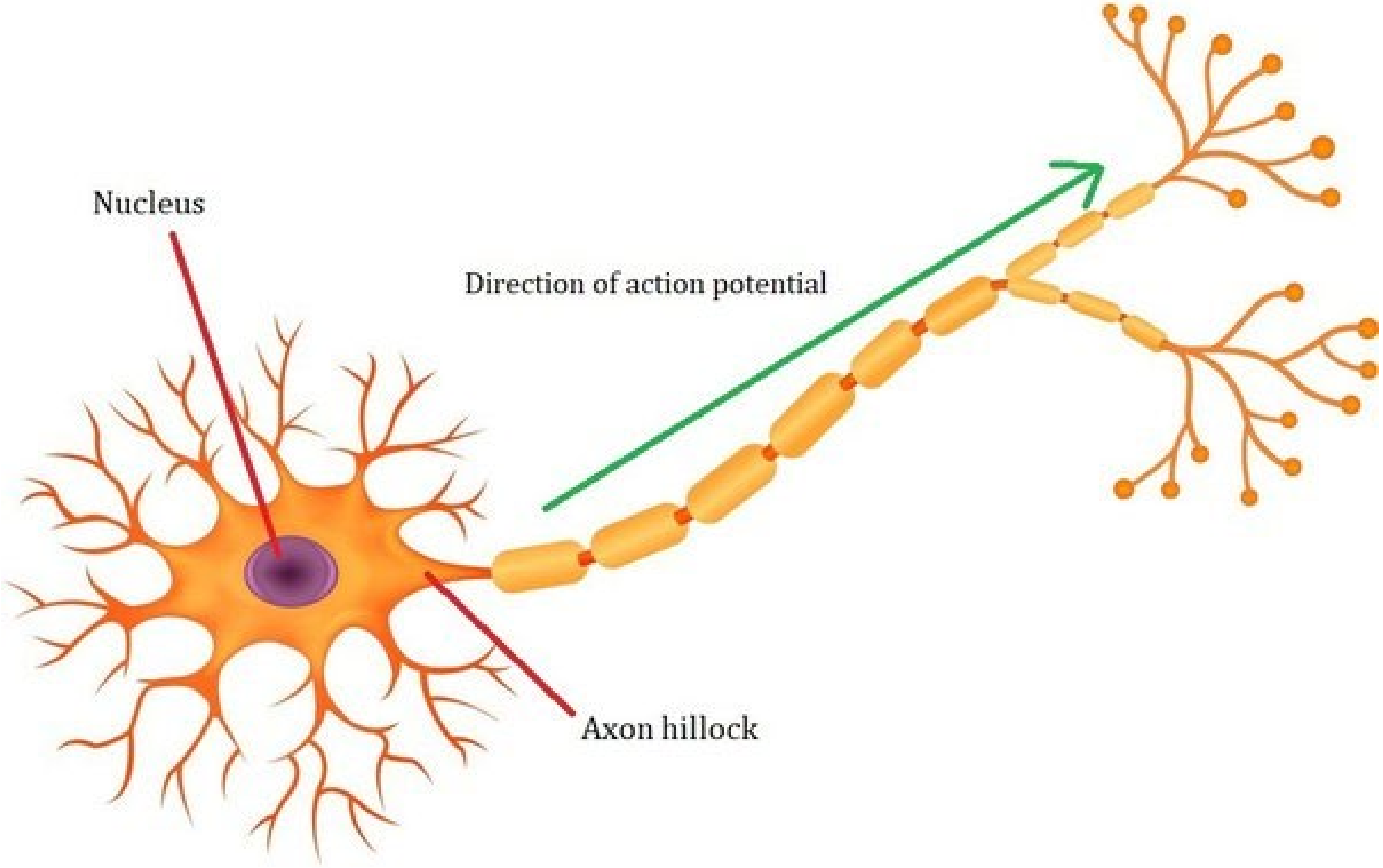
電磁波的傳遞速度: 50–99% 光速.



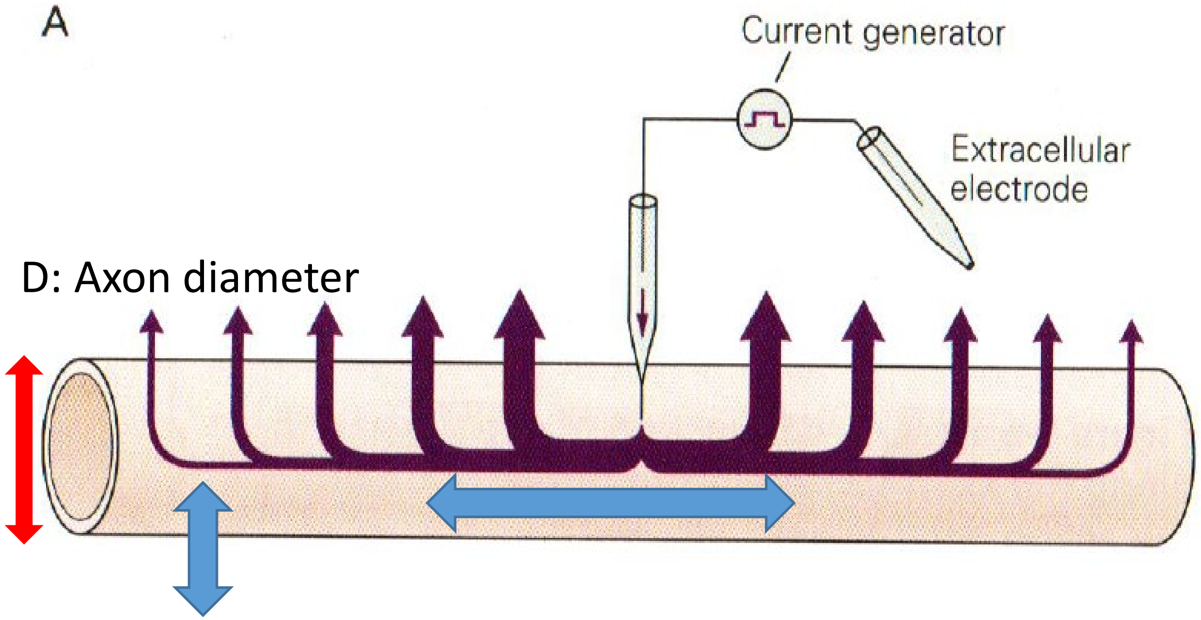
電子傳遞速度: ~ drift velocity and electron mobility.



神經動作電位傳導的速度?



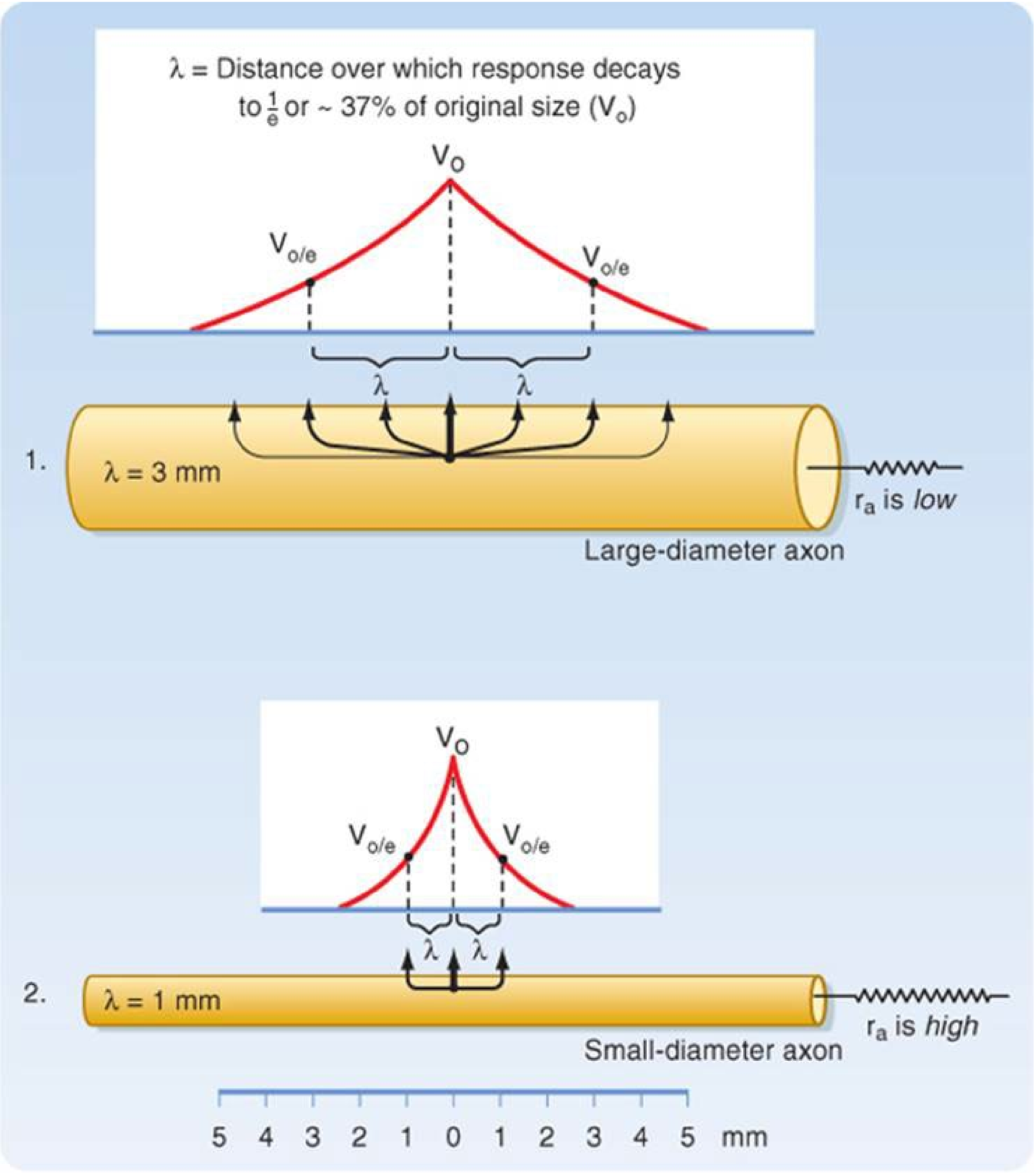
Action potential propagation speed is depending on the ion channel density and axon diameter



D: Axon diameter

R_m: membrane resistance /unit area (ion channel density)

R_i: axial resistance / unit volume

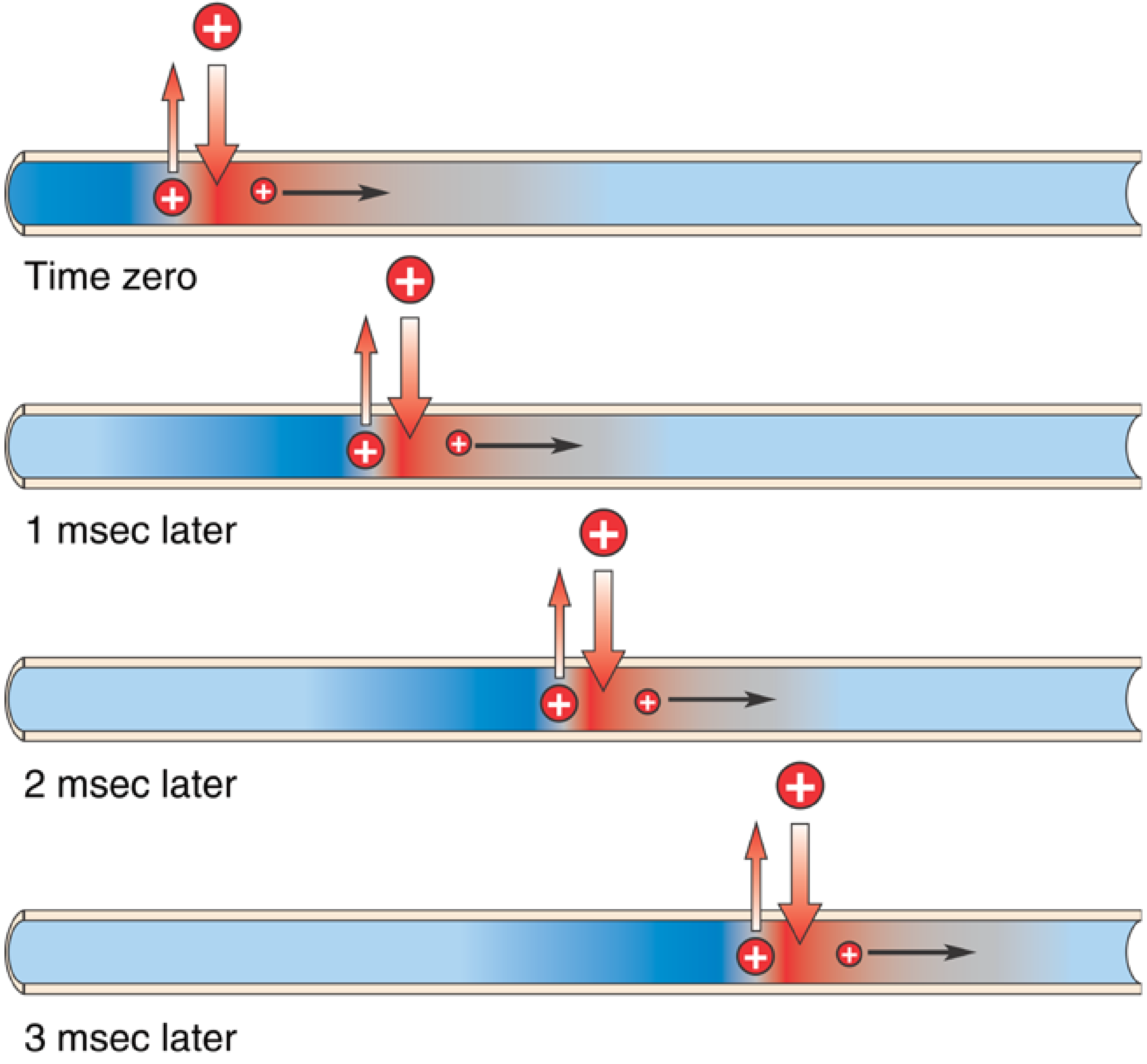


神經動作電位傳導的速度?

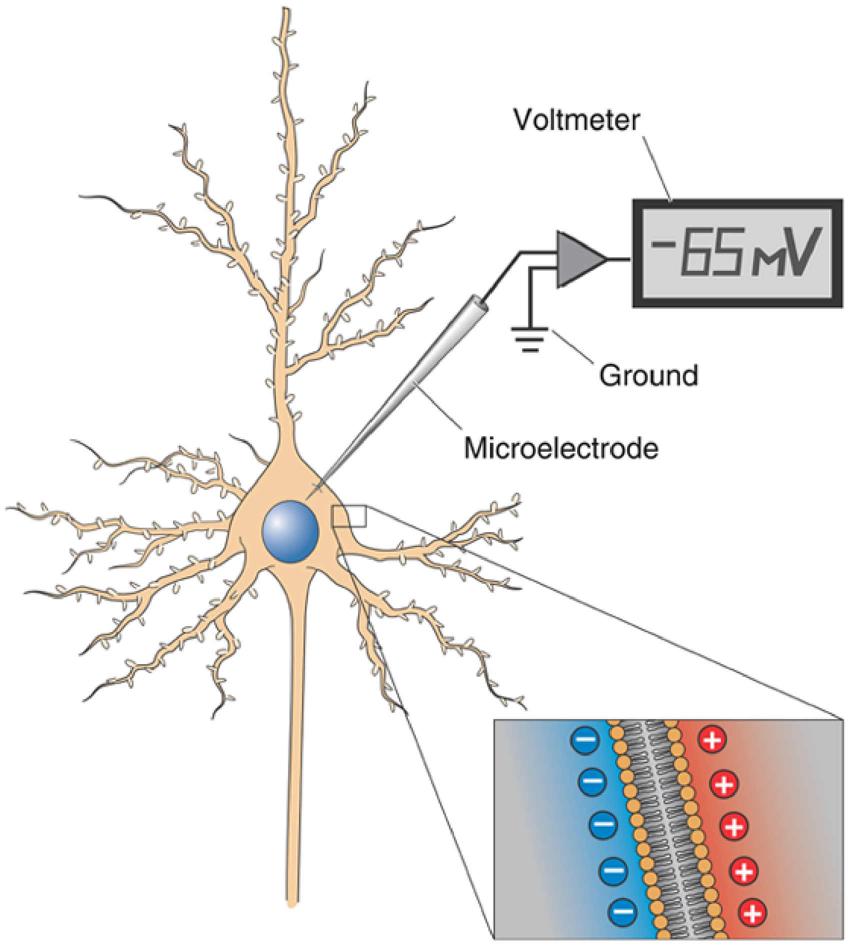
Typical conduction velocity: 10 m/sec

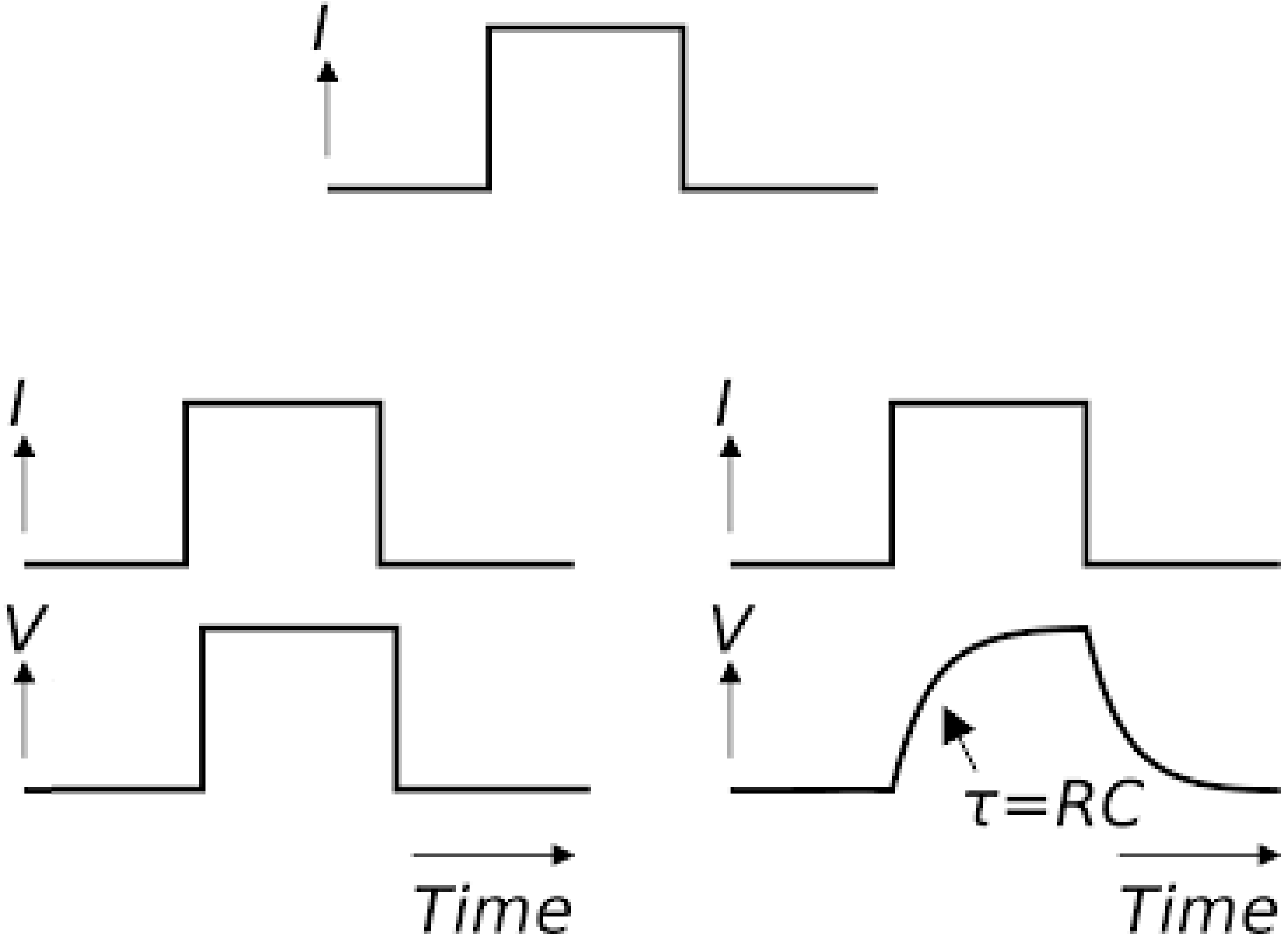
Length of action potential: 2 msec

Each action potential: ~2 cm

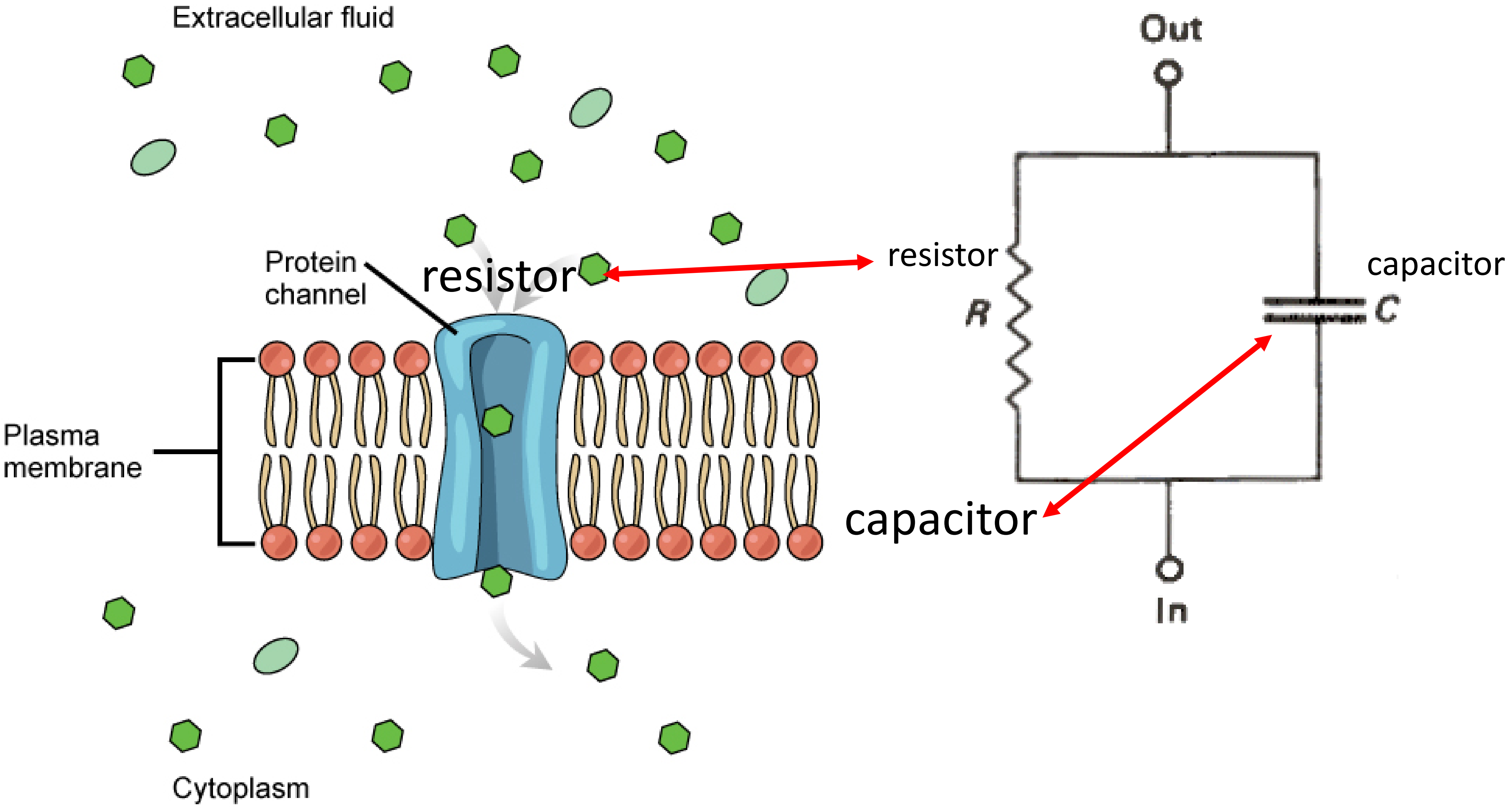


細胞膜有電阻以及電容:



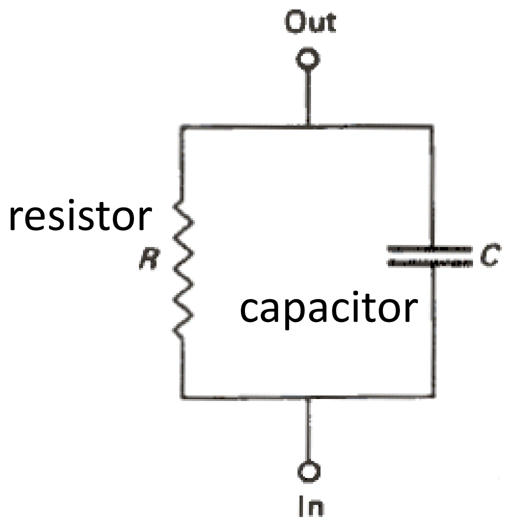


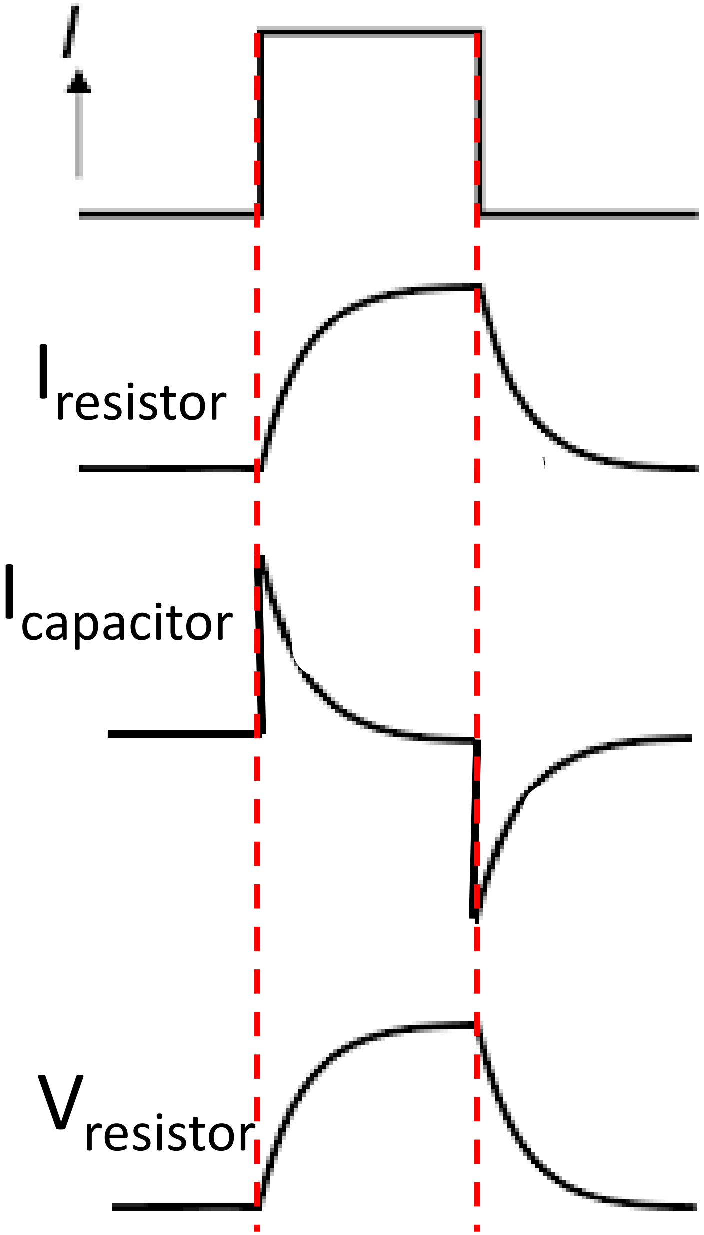
細胞膜有電阻以及電容:



Extracellular fluid
Protein channel
resistor
Plasma membrane
Cytoplasm
Out
resistor
R
capacitor
C
capacitor
In

Cell membrane as a RC circuit Time Constant





$$I_R = I_0(1 - e^{-\frac{t}{RC}})$$

$$I_c = I_0(e^{-\frac{t}{RC}})$$

$$As\ V = IR,$$

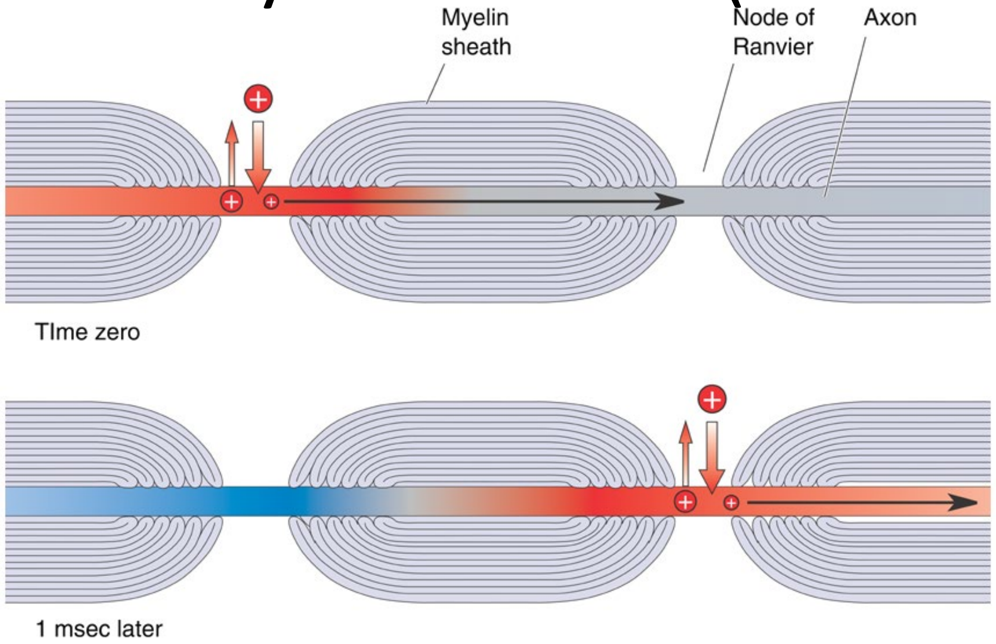
$$V(t) = R\, I_0(1 - e^{-\frac{t}{RC}})$$

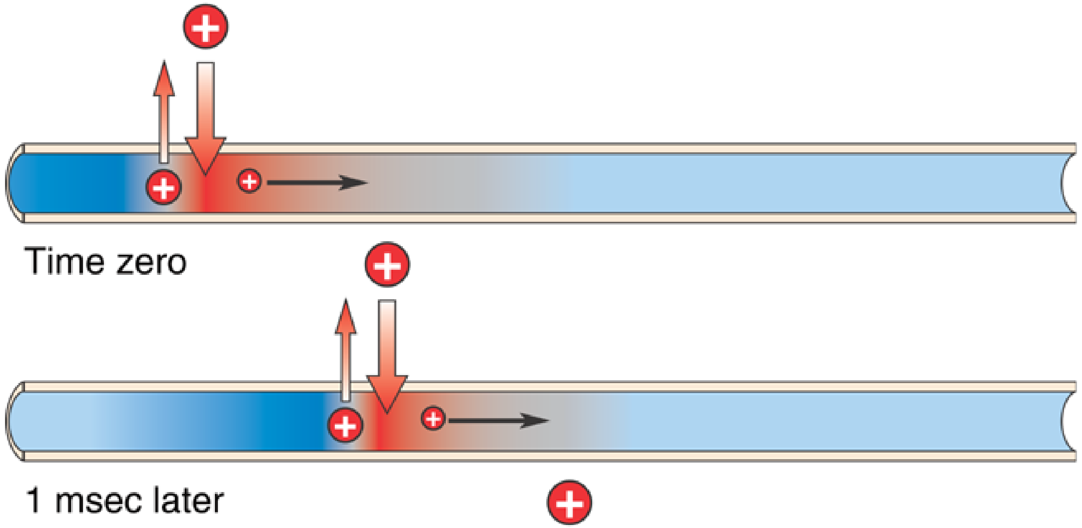
髓鞘可增加動作電位傳導速度

Un-myelinated axon: leaky pipe

Using myelin “tape” to fix it

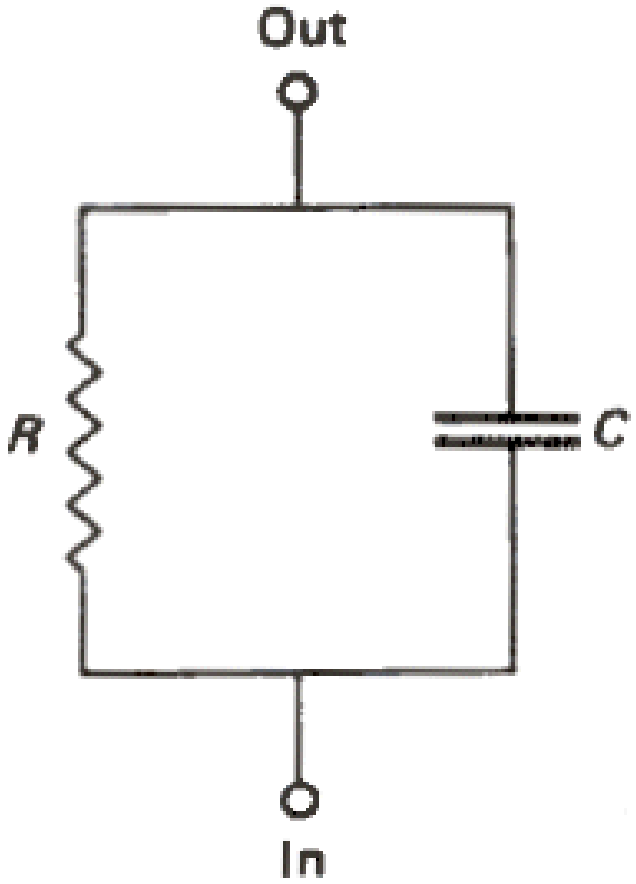
Saltatory conduction (Schwann cell)



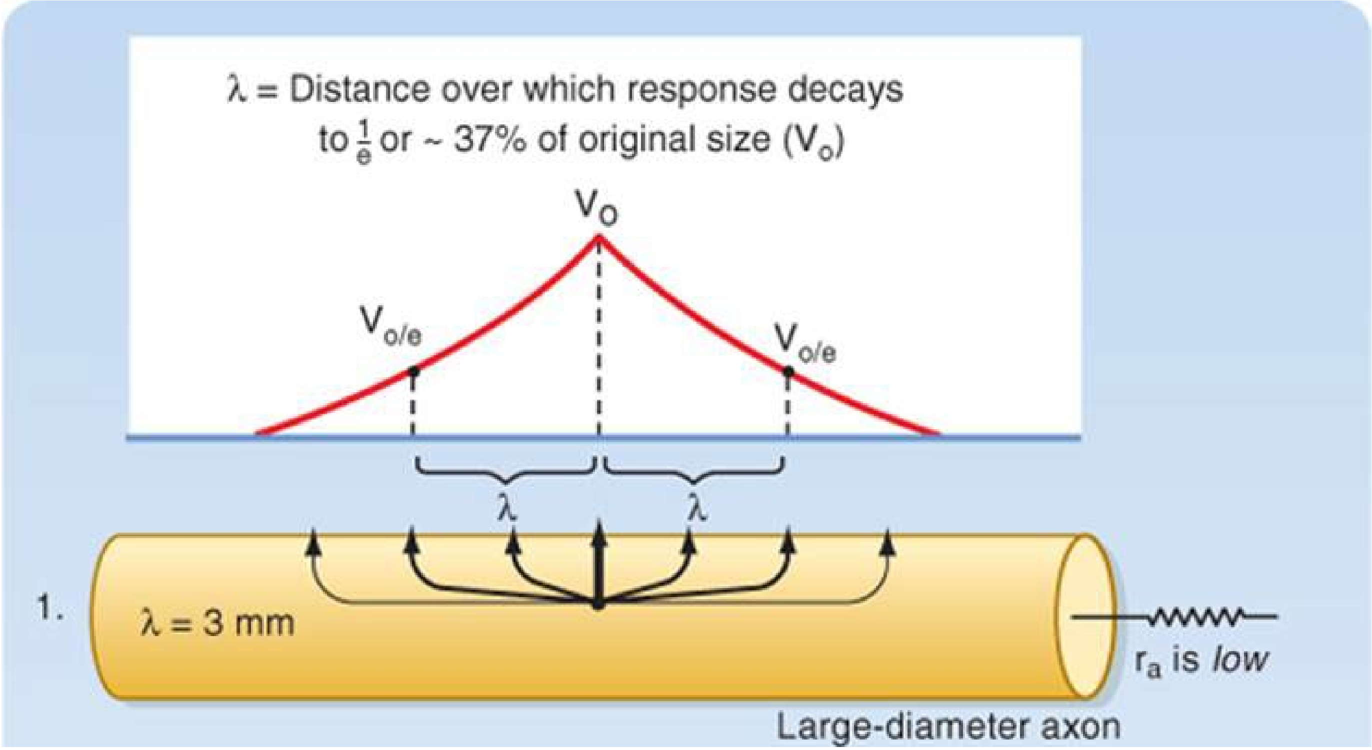


Myelination helps action potential propagation

Time constant: RC



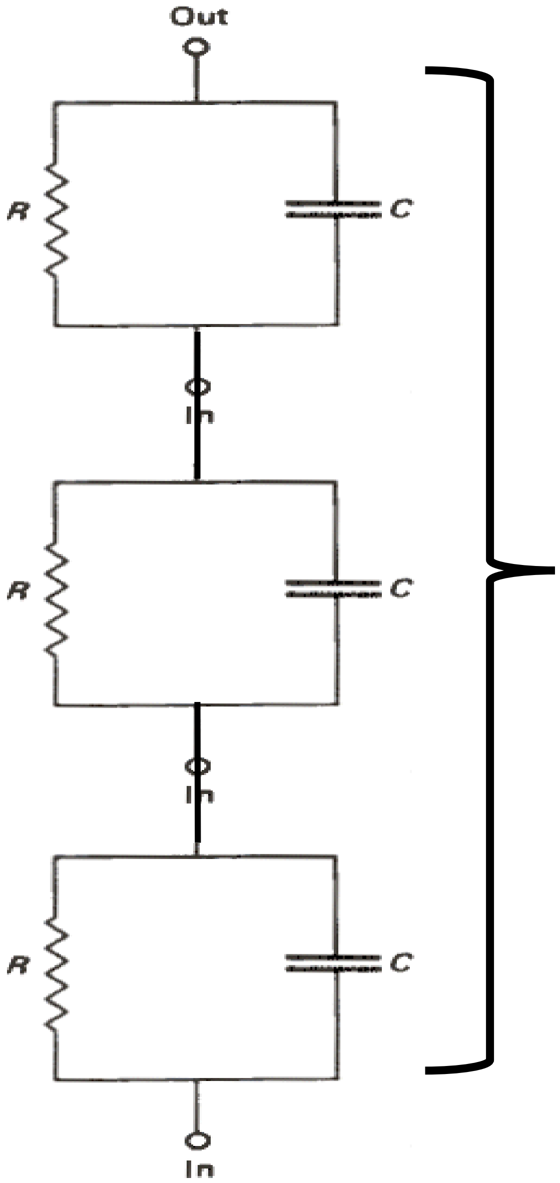
$Length\ constant$: $\mathrm{D}Rm/Ri$

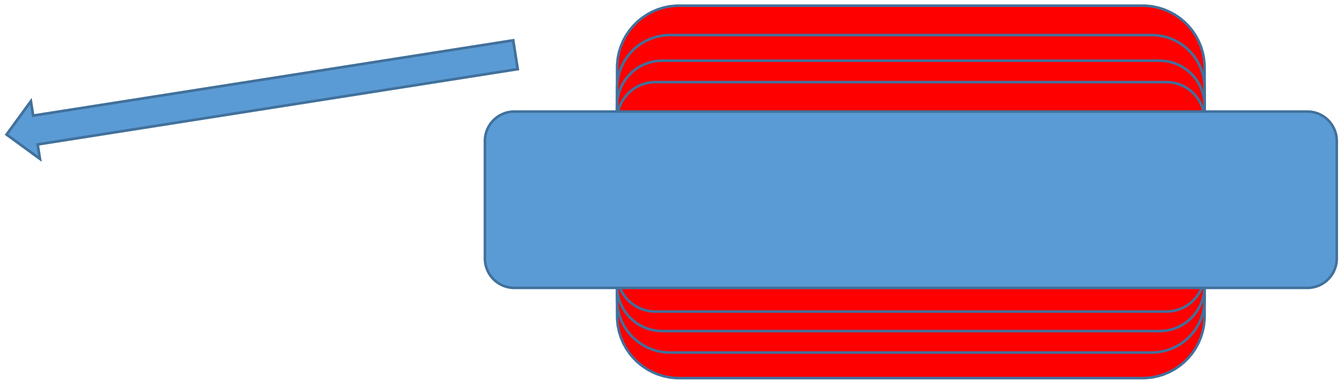


$$\mathbf{V}(t) = \mathbf{R\,I_0}(\mathbf{1} - \mathbf{e}^{-\frac{t}{RC}})$$

$$\mathbf{V}(x) = \mathbf{V_0 e}(^{-}\frac{x}{2\sqrt{DRm/Ri}})$$

Myelination helps action potential propagation





n layers of myelin

$$Time\ constant = nR\left(\frac{C}{n}\right) = RC$$

$$Length\ constant\!: \ \mathrm{D}\ n\frac{R_m}{R_i}$$

結論:

- 細胞的電阻電容以及電池:
- 離子通道產生電位變化
- 動作電位的全有全無律
- 髓鞘可增加傳導速度

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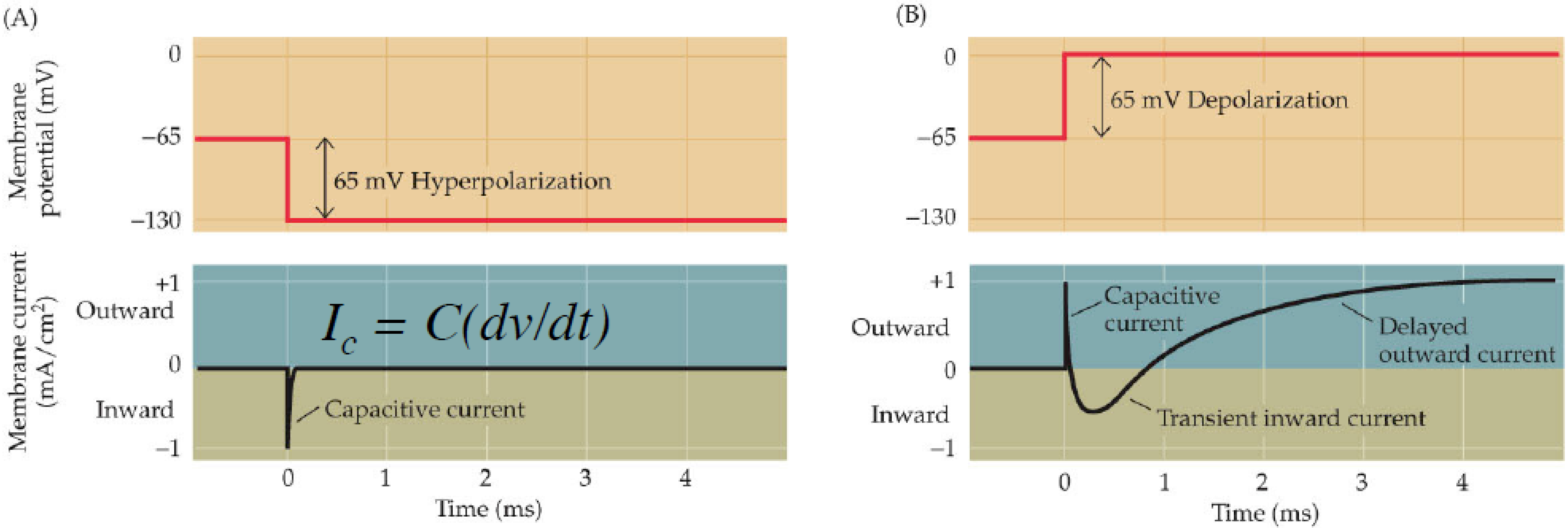
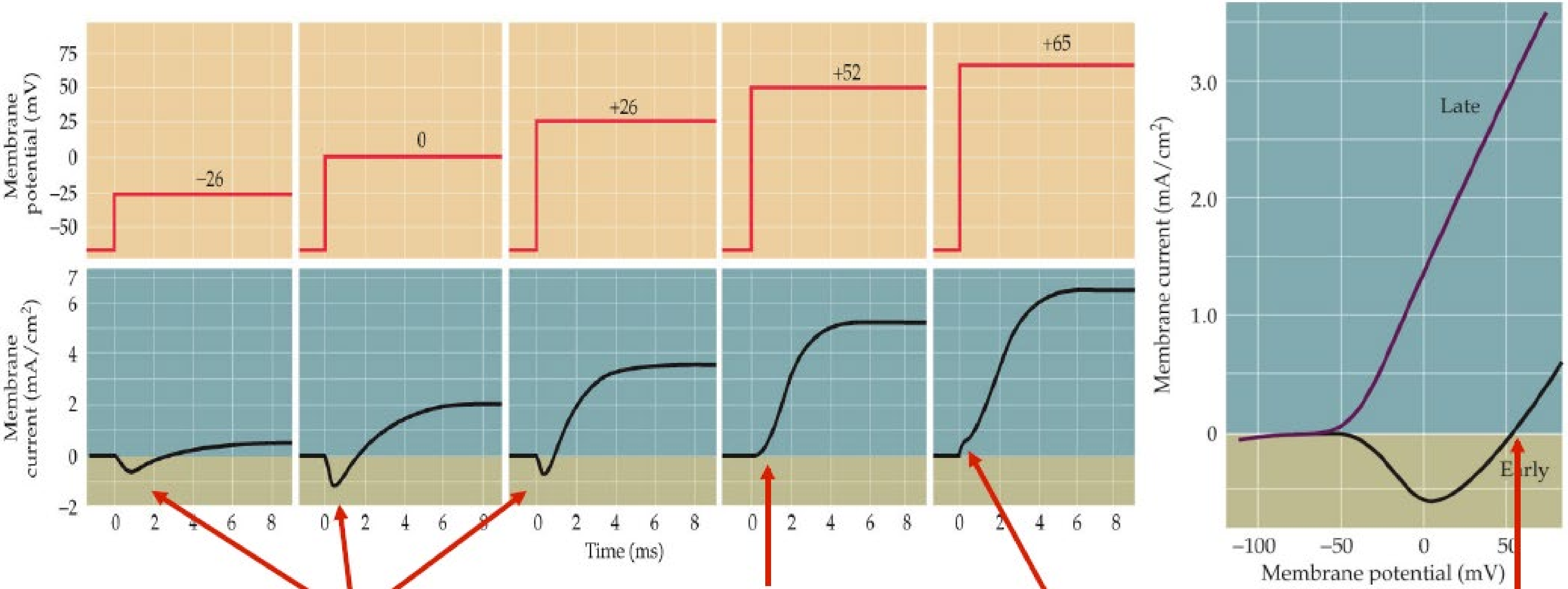
N701, Institute of Biomedical Sciences, Academia Sinica
sbyang@ibms.sinica.edu.tw
(02)26526532

Currents are activated upon membrane depolarization



Various currents are generated at different Vm



early component gets bigger then smaller

(G_{Na} activation, driving force large, then small, and G_{Na} inactivation)

No early component

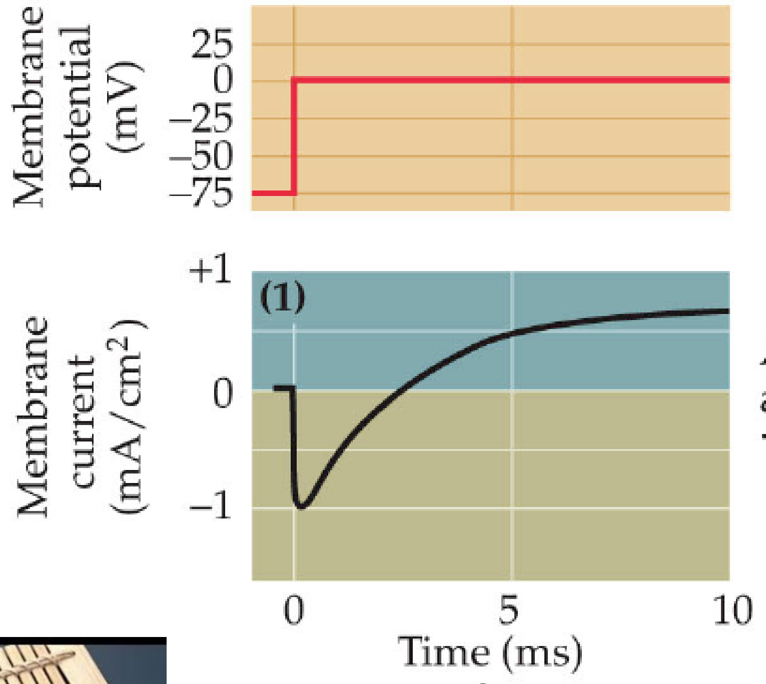
(at E_{Na})

early component now outward!

(past E_{Na})

Early component reverses close to E_{Na+}

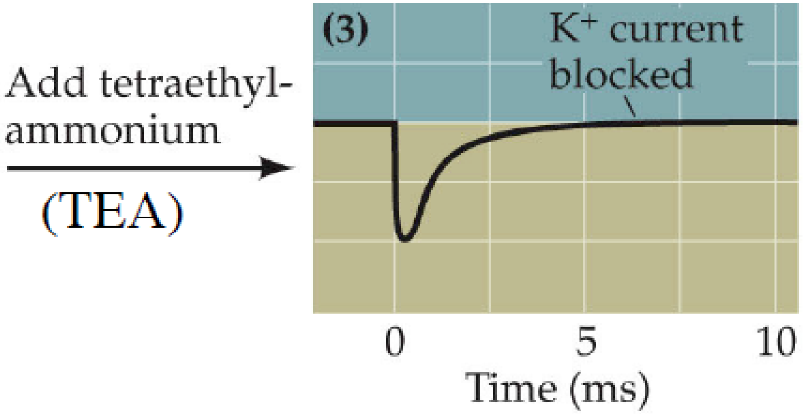
Pharmacological isolation of various currents

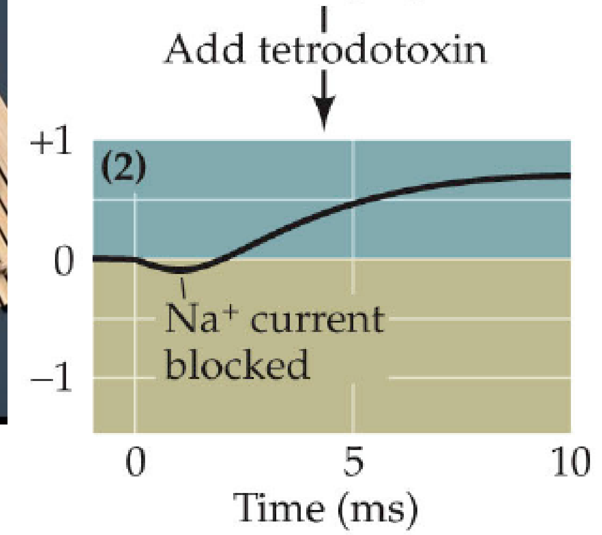


Inward current

-fast activating

-inactivating

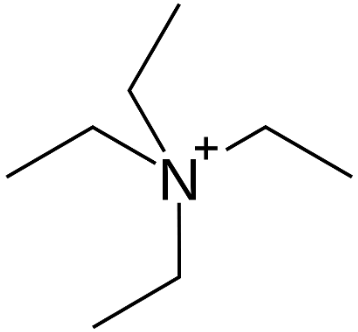




Outward current

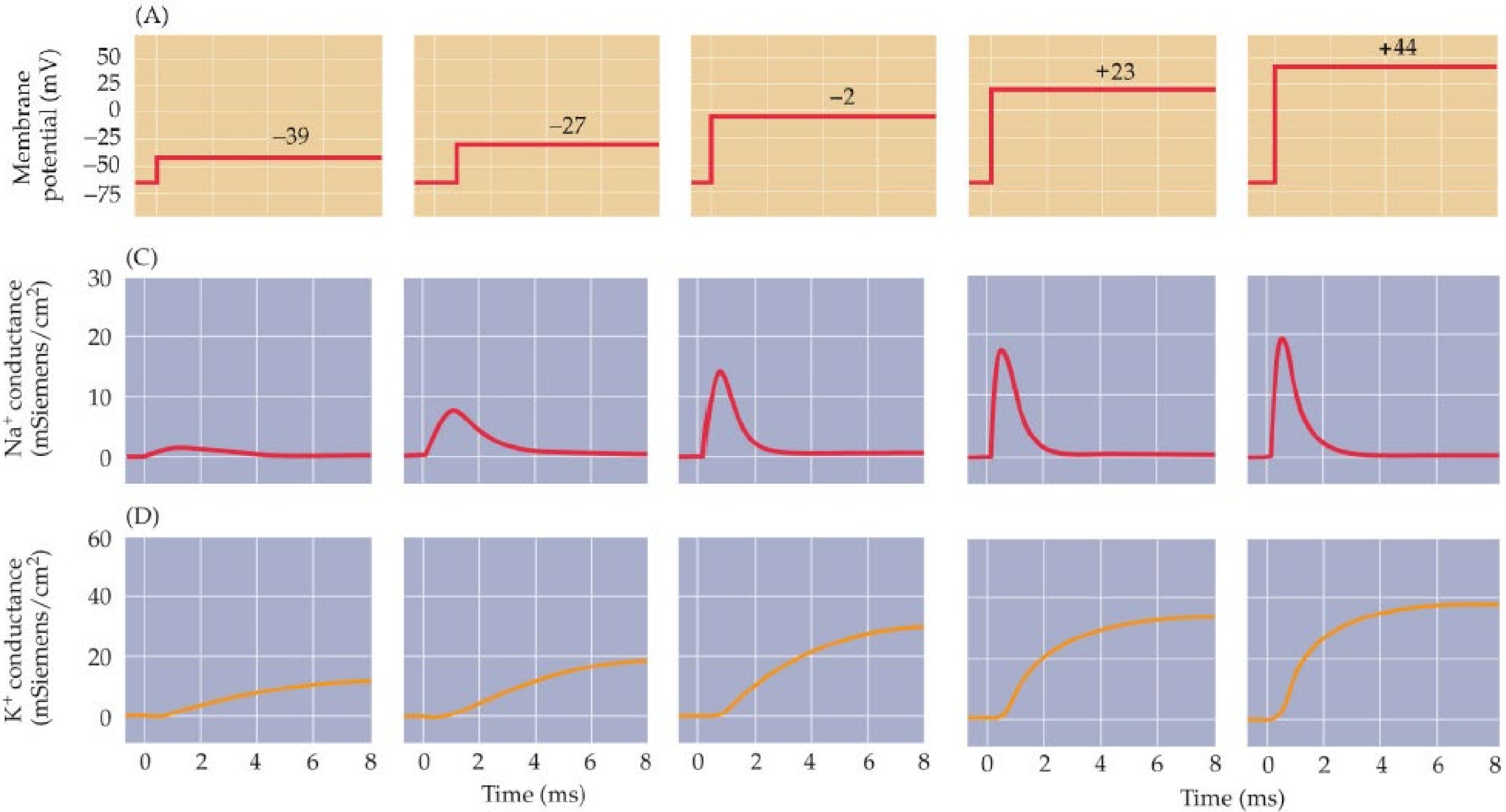
- slow activating

- non-inactivating



Tetraethylammonium

Isolation of Na^+ and K^+ currents



Spike-initiation zone

- Sensory nerve endings

Sensory Recetors

- Axon hillock

(initial segment)

High density of Na channel