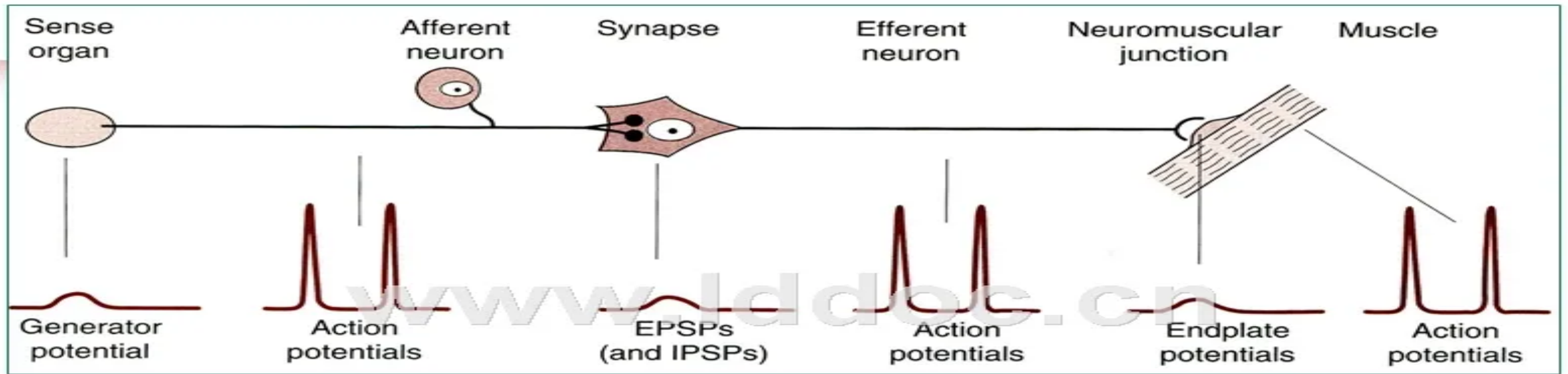


# 神经生物学第五讲：突触传递与受体之一



第一节、化学突触与电突触

第二节、化学突触传递过程

第三节、主要神经递质及受体

# 第一节、化学突触与电突触

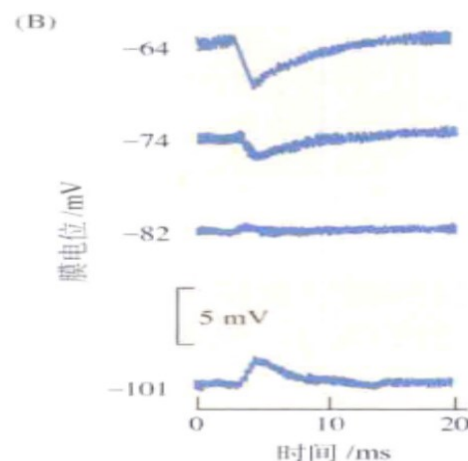
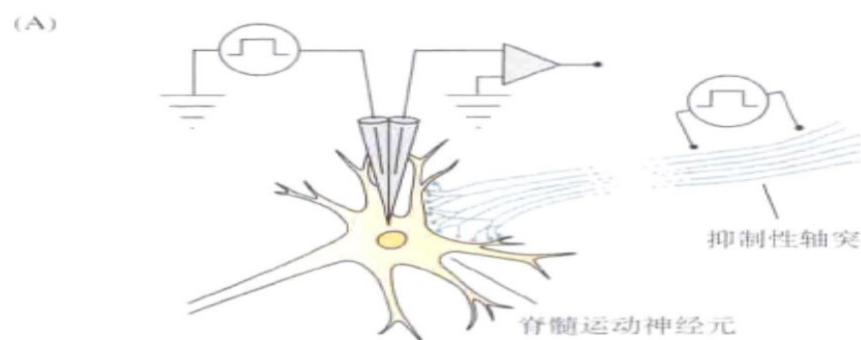
- 神经元之间信息的传递媒介的争论：a war of sparks or soups（电信号？化学分子？）
- 1849年 Claude Bernard 箭毒的对肌肉的作用
- 1904年，Thomas Elliott 肾上腺素引起剥离神经后的肌肉收缩，首先提出
- 1921年，Otto Loewi 蛙心灌流实验—决定性证据
- 1936年，Dale提示神经肌肉活动规律

贝（1811年） -  
马（1823）定律  
穆勒（德国1832）

突触一词首先由英国神经生理学家C.S.谢灵顿于1897年研究脊髓反射时引入生理学

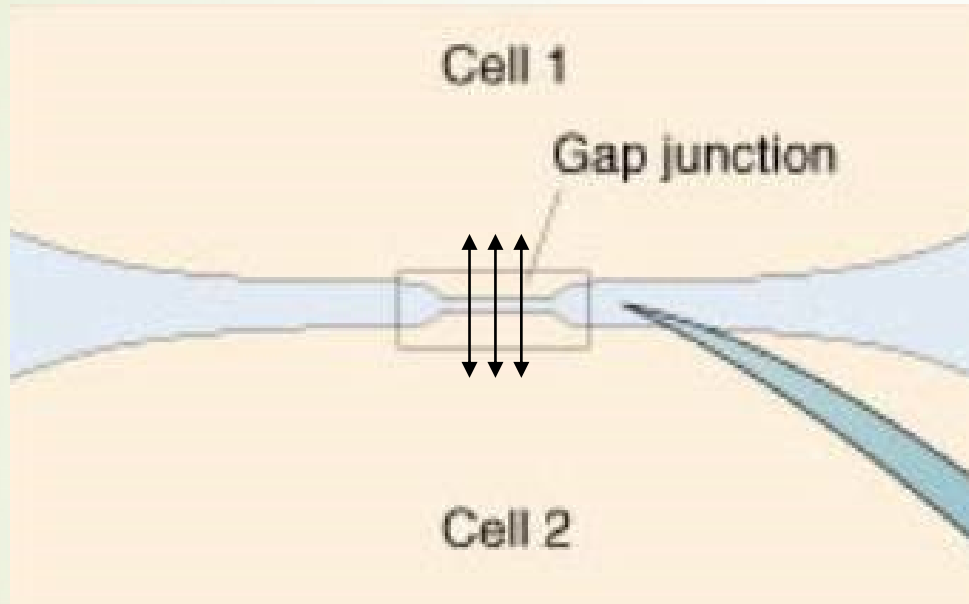
John Carew Eccles

第一个神经递质是什么？



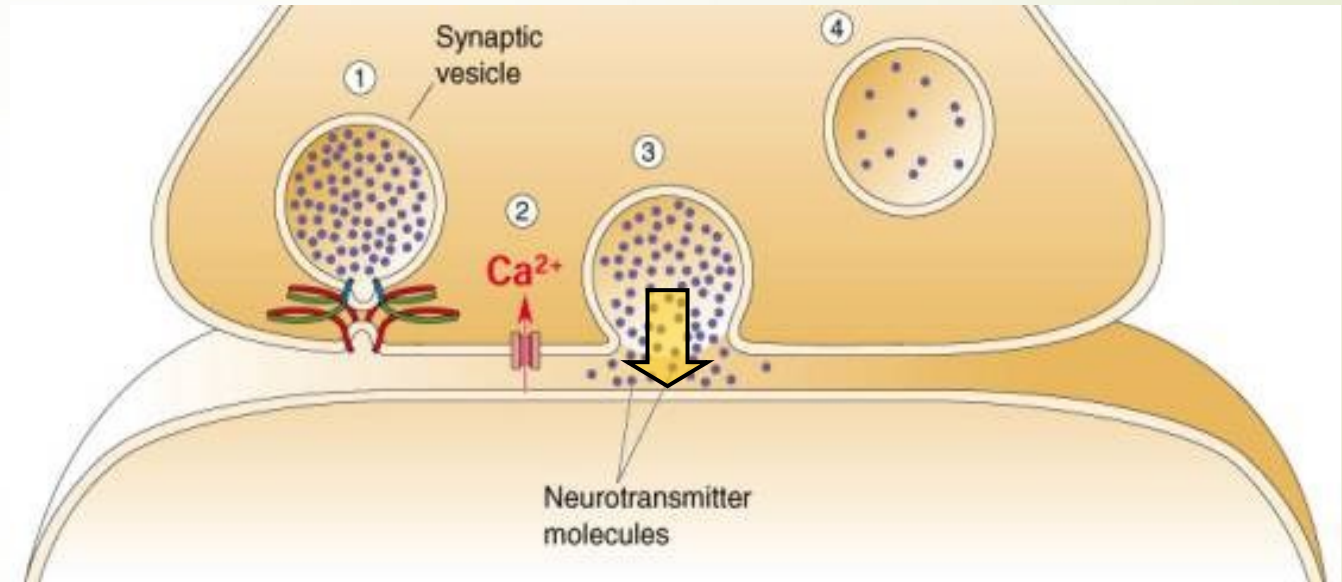
# Types of Synapses

## 电突触



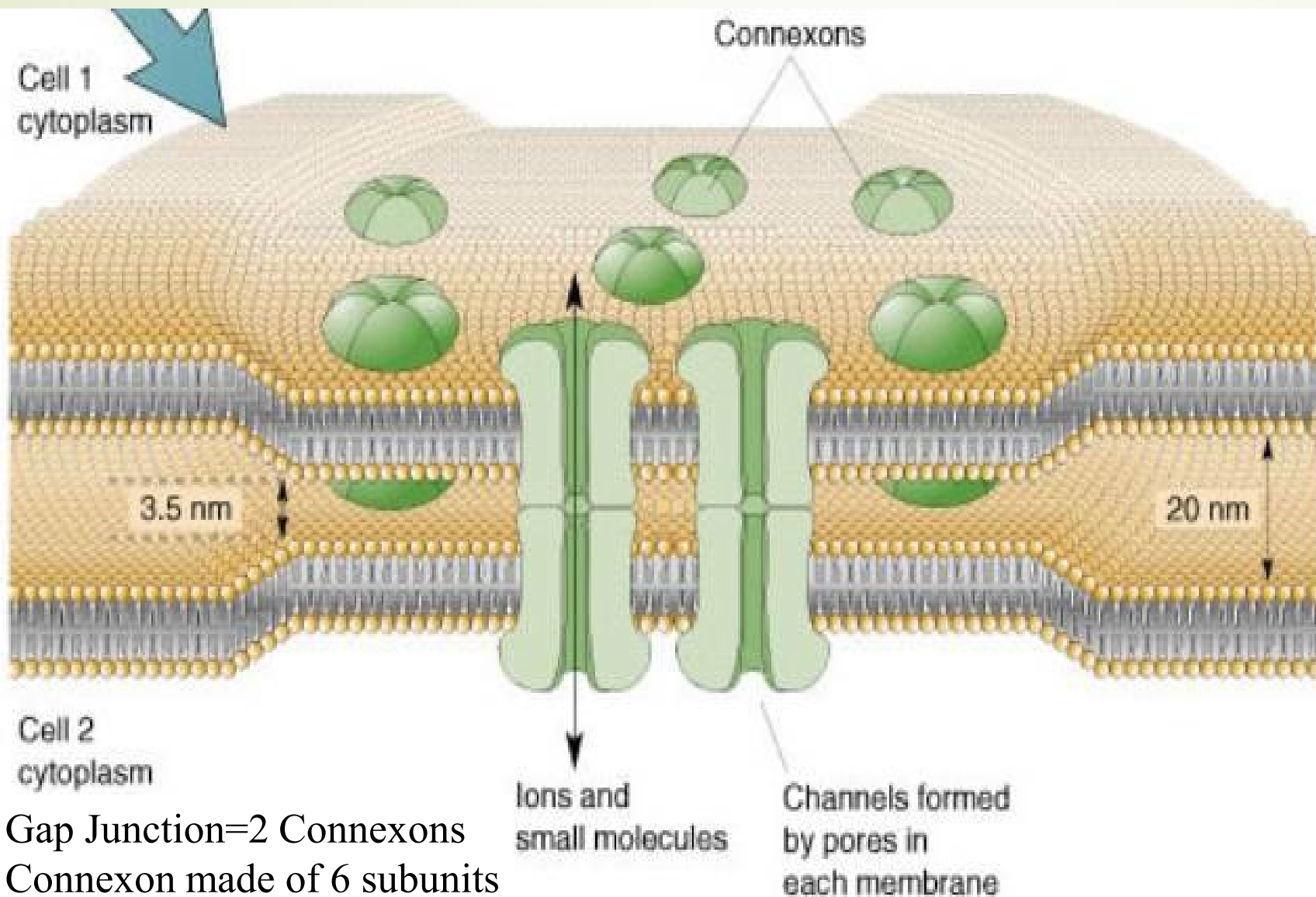
- Found in: escape reflex neurons (invertebrates)
- Epithelial cells (gut)
- Cardiac muscle cells (heart)

## 化学突触



- Found in: Almost all mammalian neurons

# 一、电突触

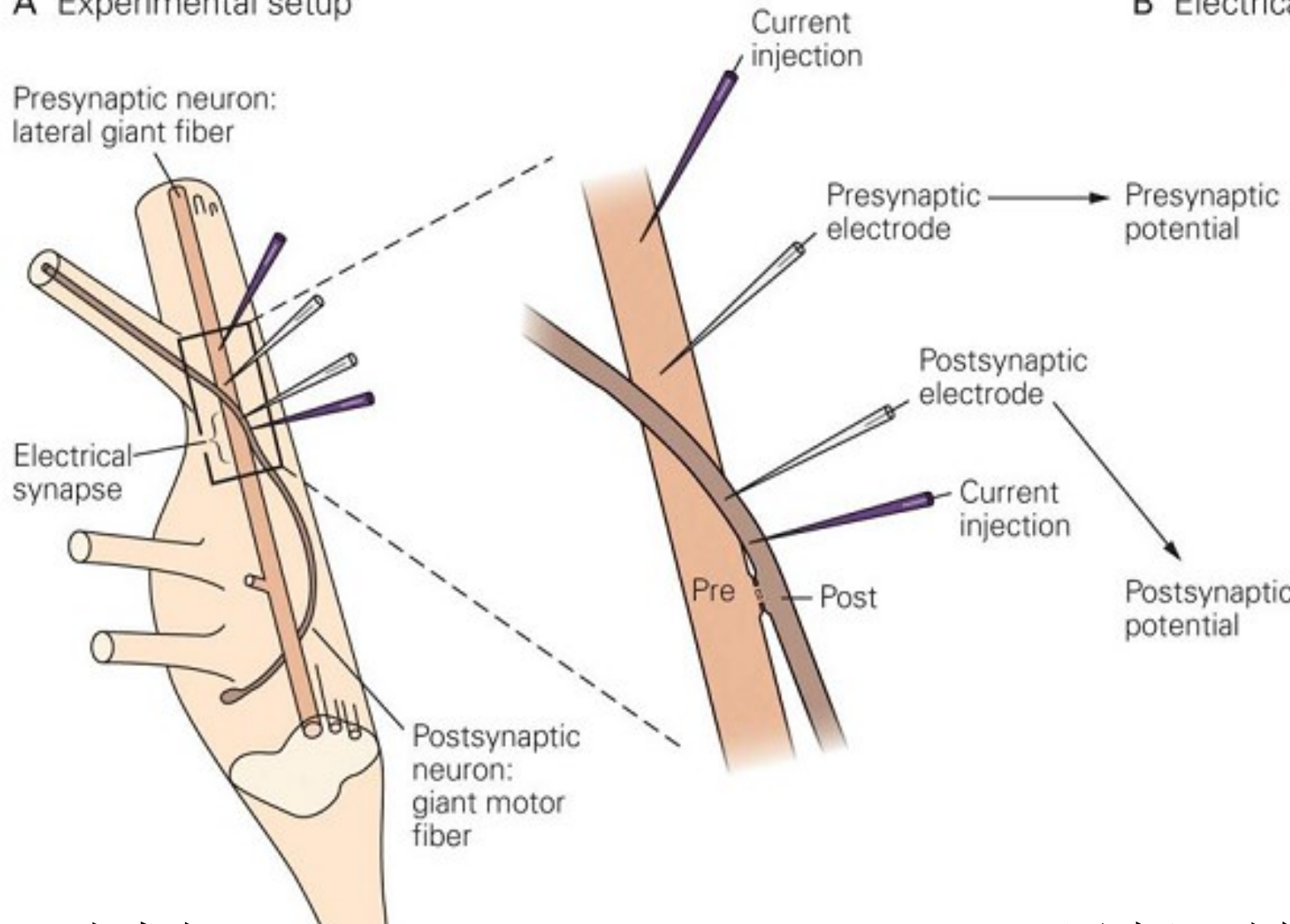


每个连接子  
connexon由六个  
连接蛋白connexin构  
成， connexin是一  
个很大的蛋白家族，  
在人类的基因组中已  
发现21种连接蛋白基  
因。

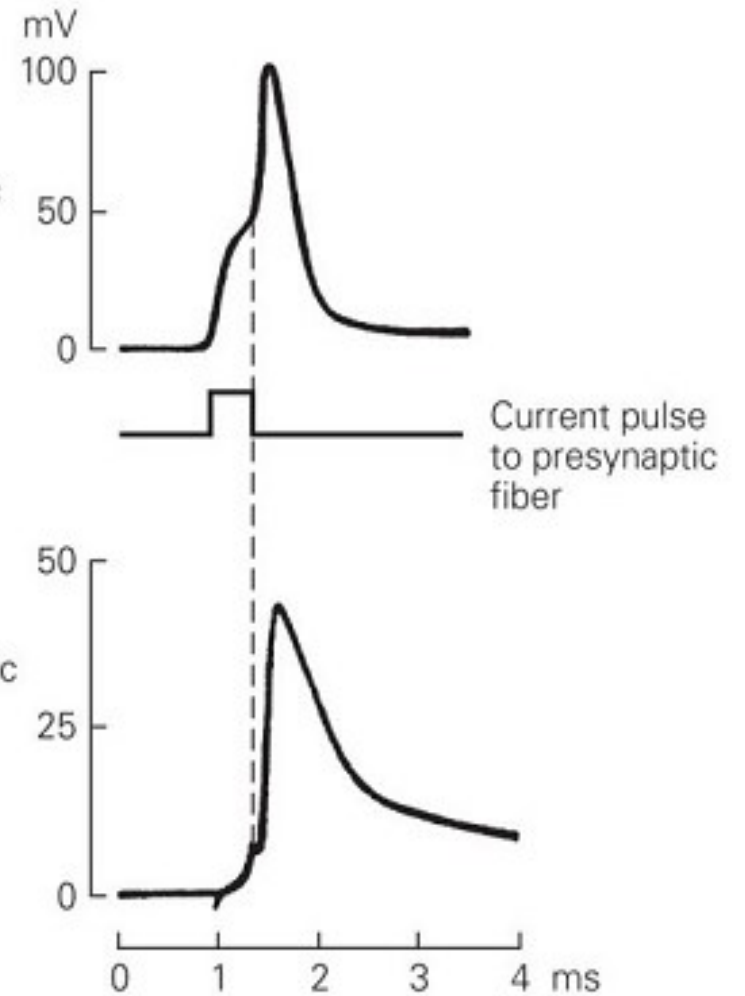
Cx45/Cx43

# 电突触传递：几乎没有突触延搁

A Experimental setup



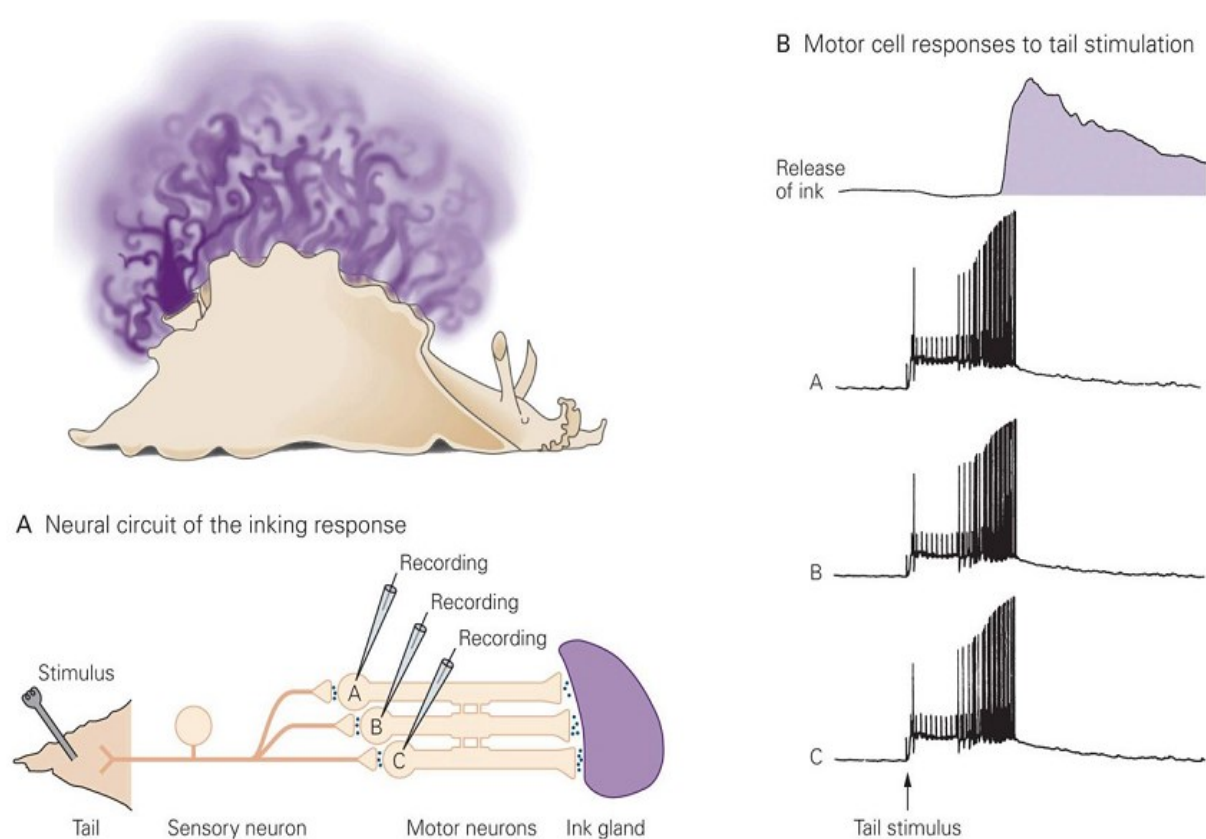
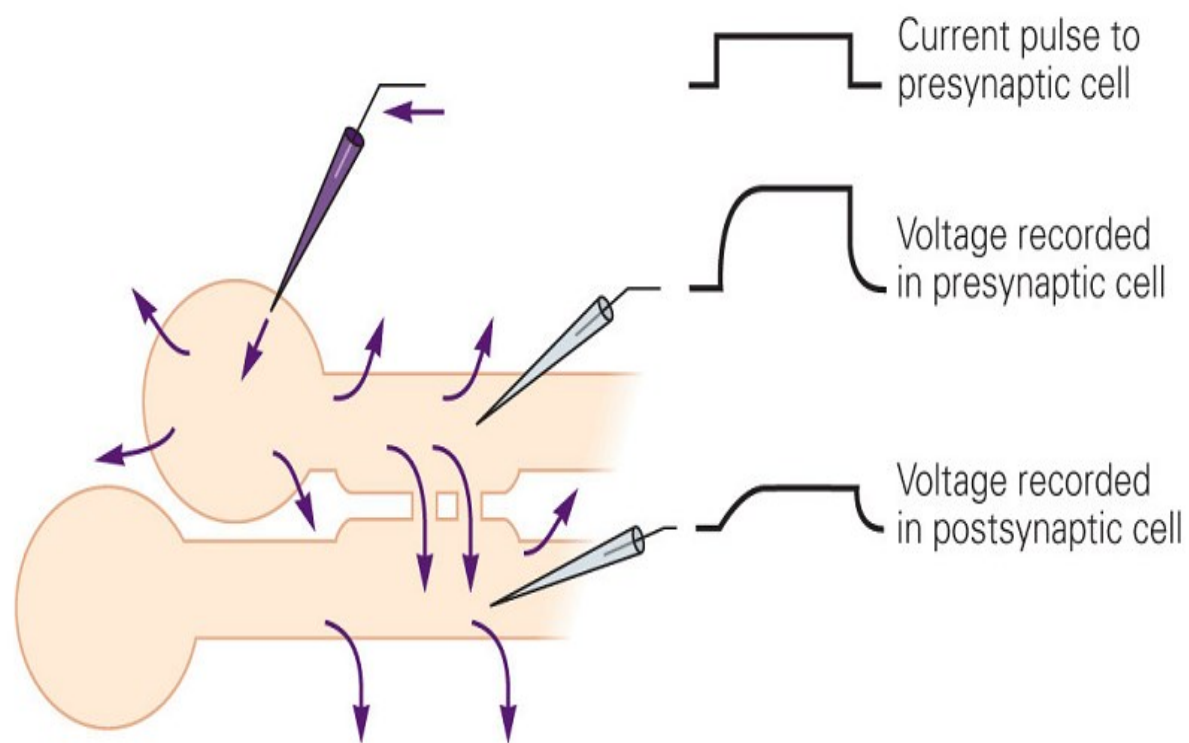
B Electrical synaptic transmission



小龙虾 (Crayfish) giant motor synapse (巨大运动轴突), 1957

# 电突触传递： 突触后电位形状大小与突触前电位相关

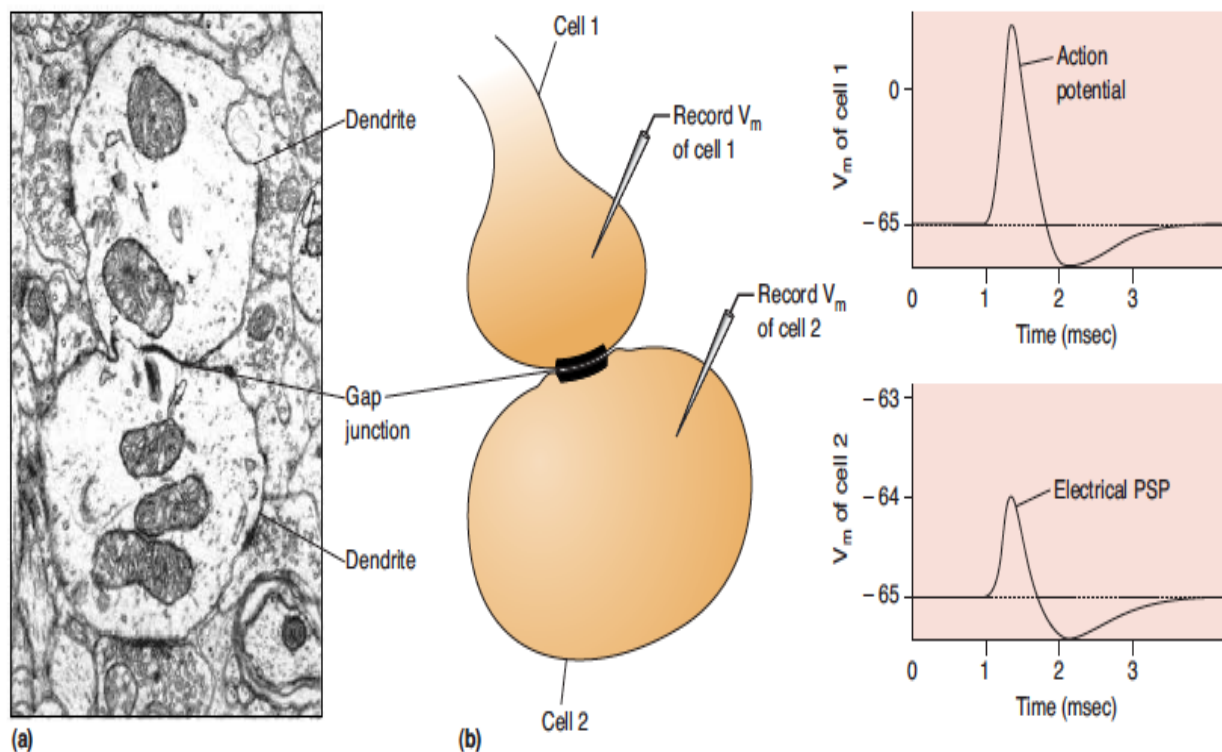
在阈值之下的电位也可以引起传导！



例子：海兔（Aplysia）喷墨反应

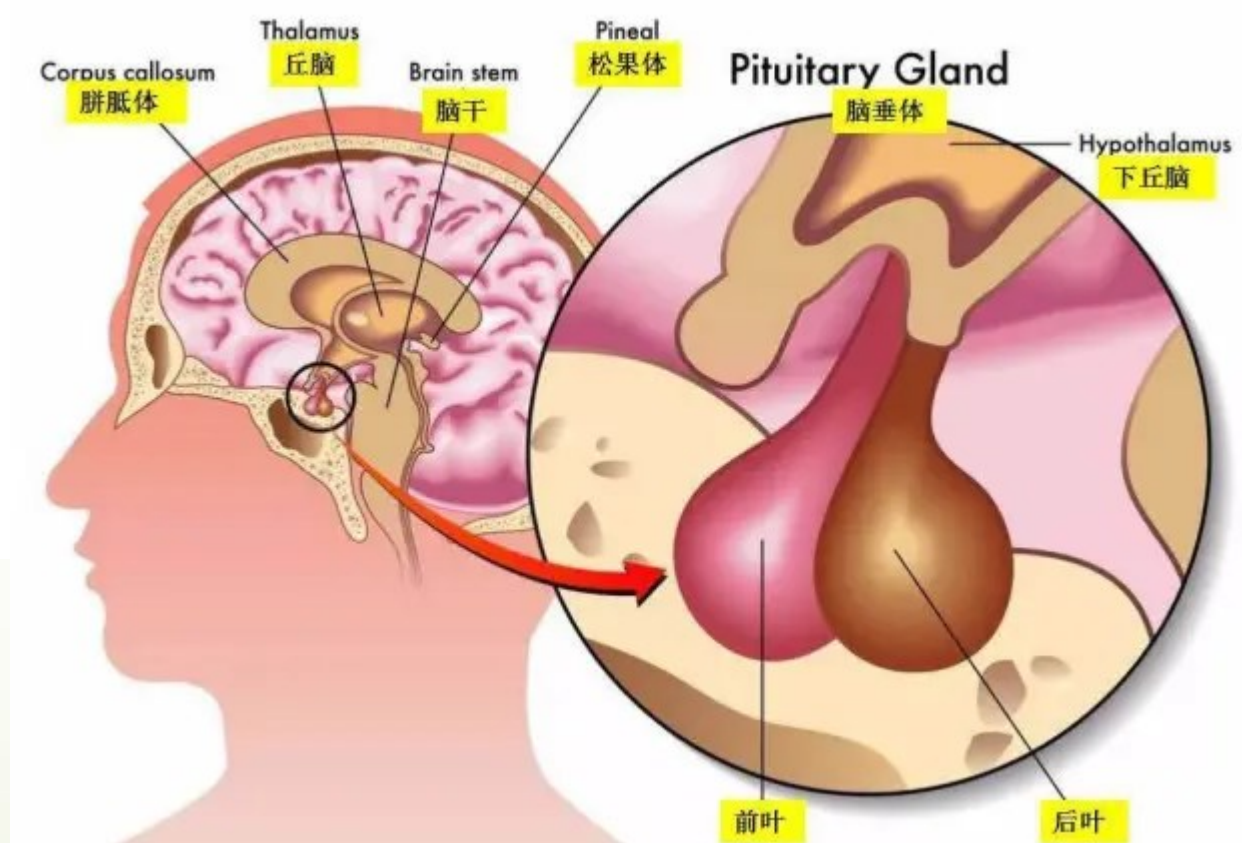
尾部刺激-感觉神经元-三个运动神经元同步去极化-肌肉收缩-喷墨

# 高等动物的电突触 电突触的作用：同步性

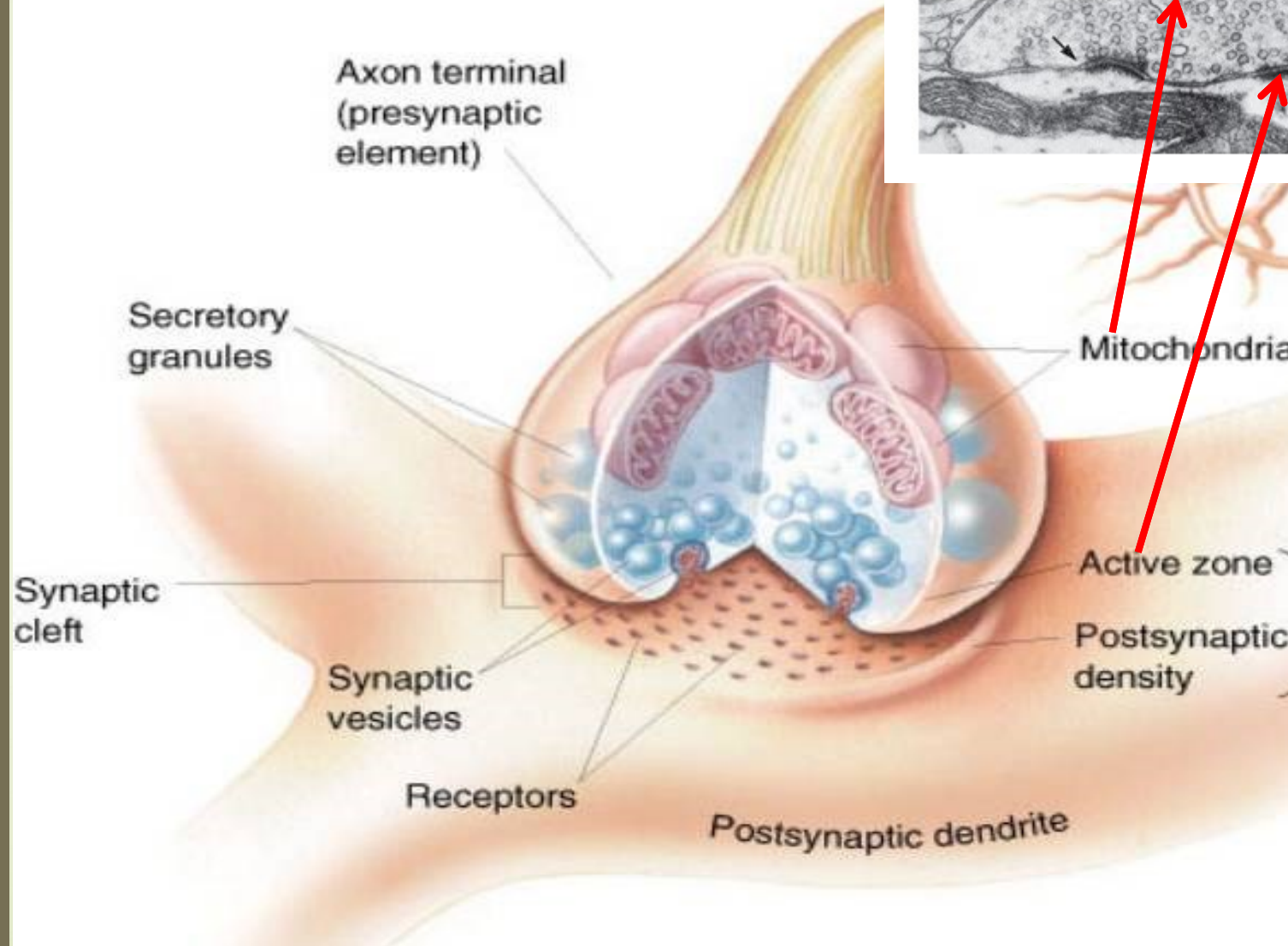


细胞1产生动作电位，  
细胞2同时产生突触后电位

脑核团的同步放电  
催产素的释放

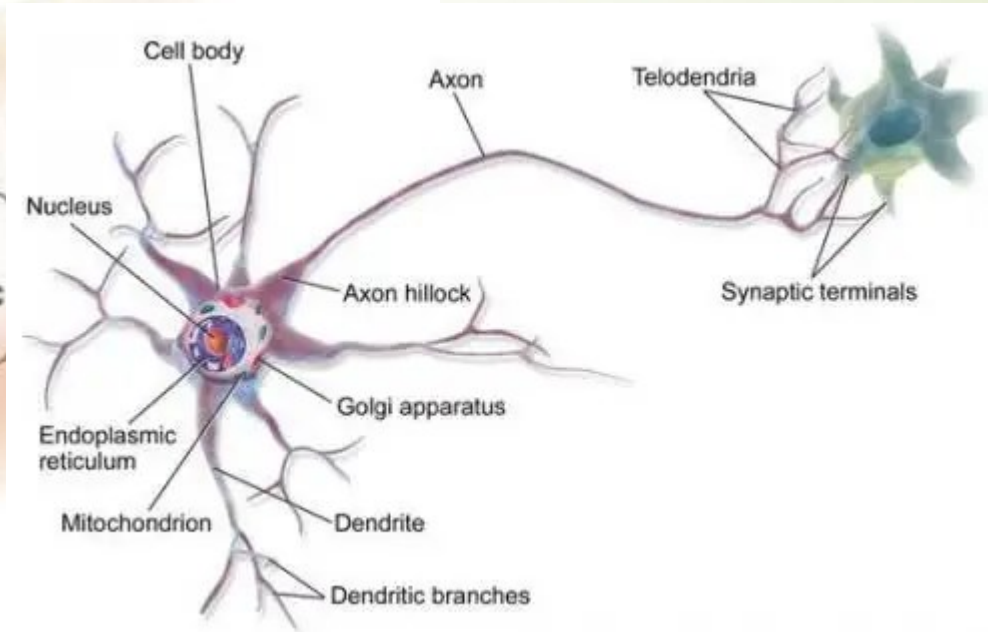


## 二、化学突触



囊泡

突触前膜  
突触间隙  
突触后膜

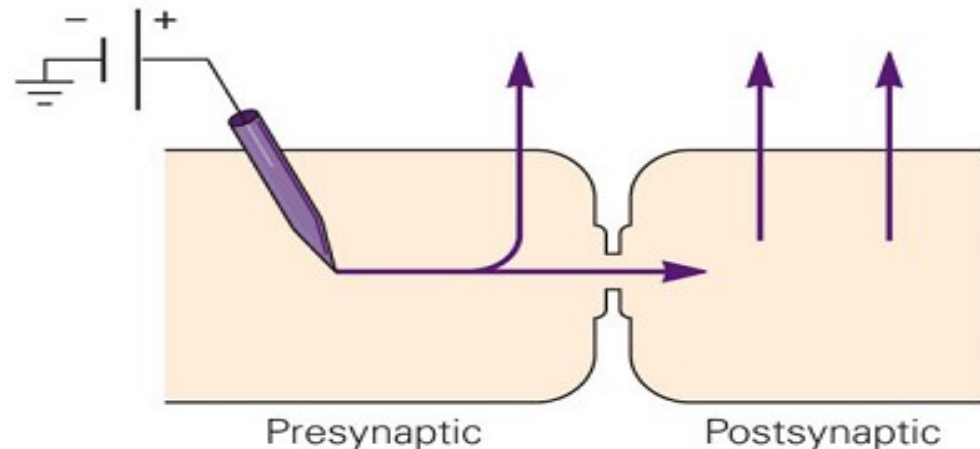


# 化学突触和电突触比较

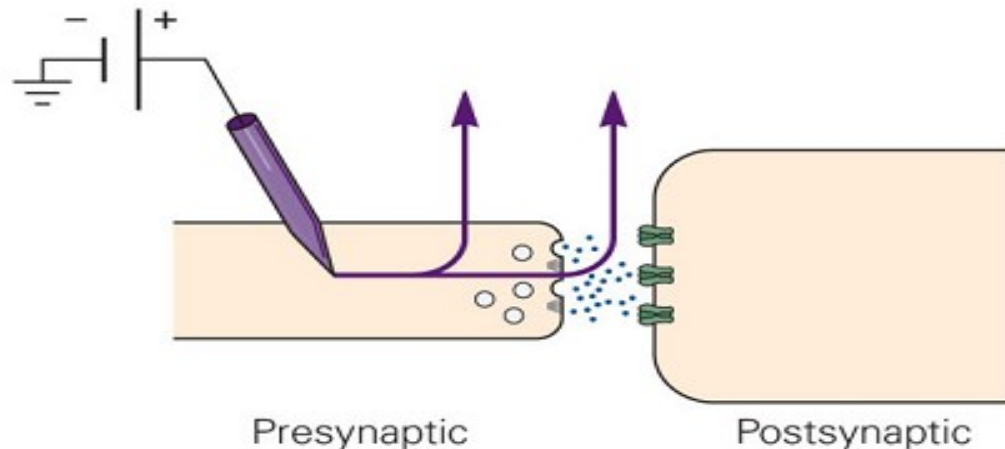
**Table 8-1** Distinguishing Properties of Electrical and Chemical Synapses

Type of synapse	Distance between pre- and postsynaptic cell membranes	Cytoplasmic continuity between pre- and postsynaptic cells	Ultrastructural components	Agent of transmission	Synaptic delay	Direction of transmission
Electrical	4 nm	Yes	Gap-junction channels	Ion current	Virtually absent	Usually bidirectional
Chemical	20–40 nm	No	Presynaptic vesicles and active zones; postsynaptic receptors	Chemical transmitter	Significant: at least 0.3 ms, usually 1–5 ms or longer	Unidirectional

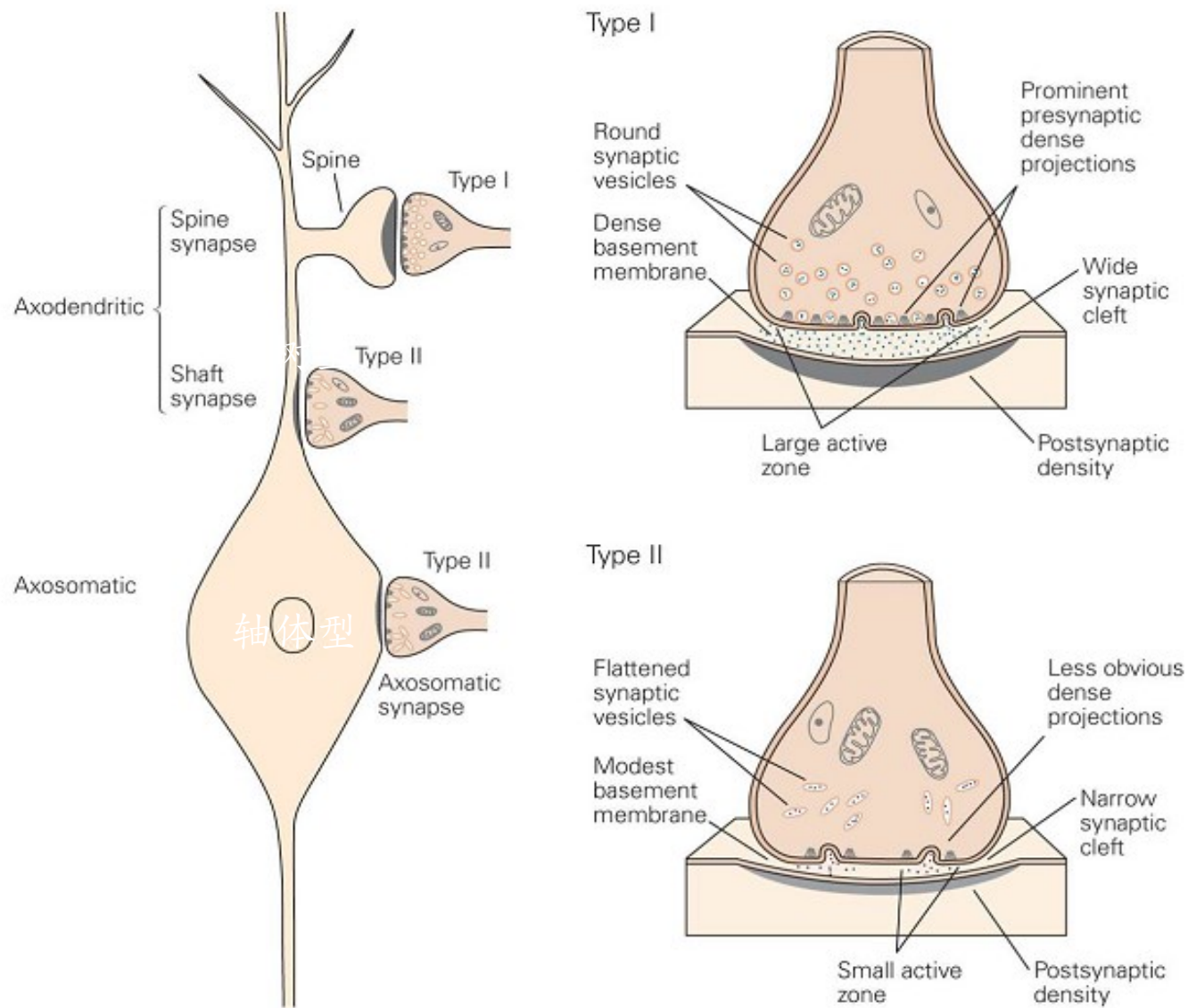
**A** Current pathways at electrical synapses



**B** Current pathways at chemical synapses



# 化学突触分类



➤ 中枢神经系统最常见两种:

**Gray I型突触: 兴奋性**

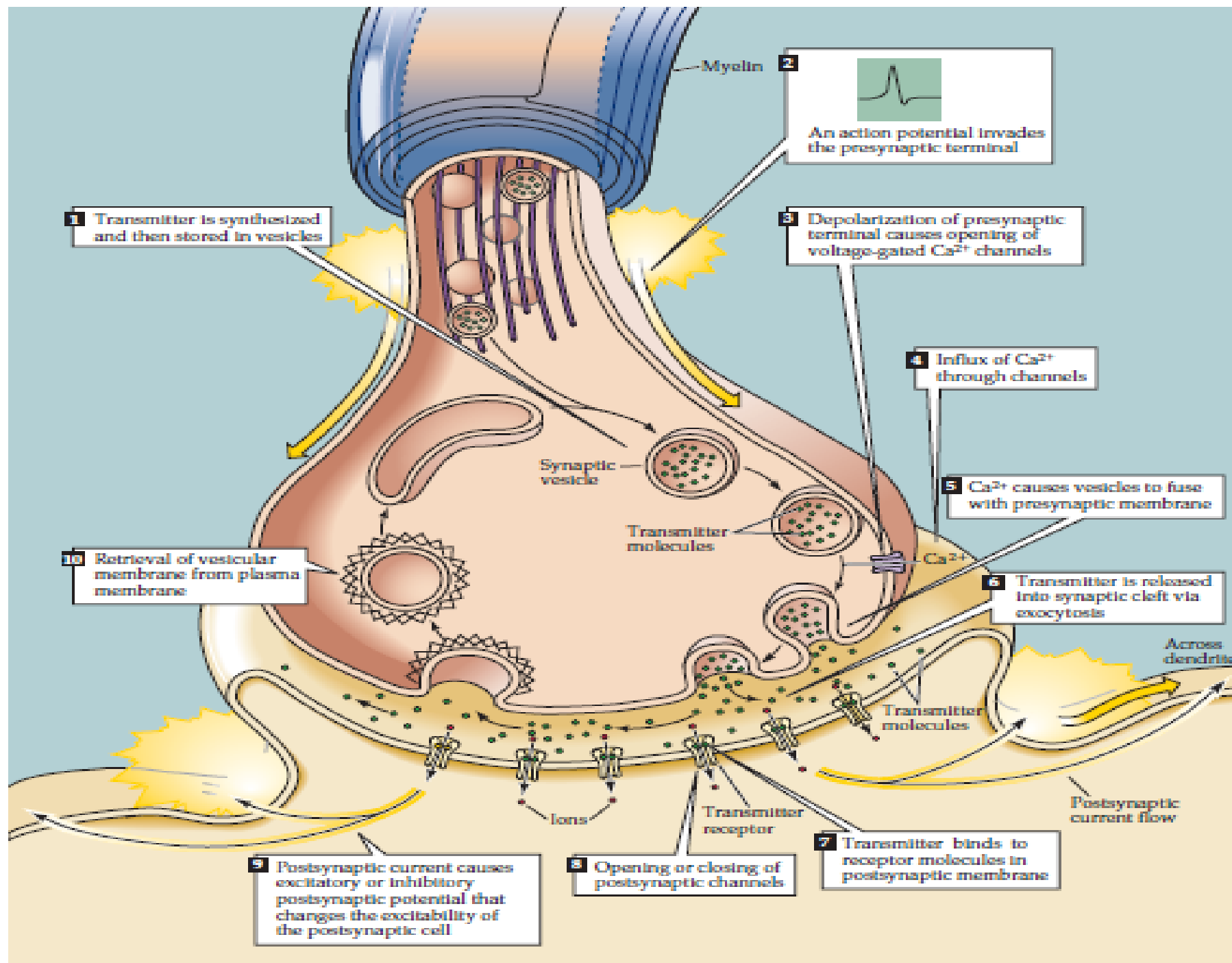
**Gray II型突触: 抑制性**

➤ 形态结构上差异

## 第二节 化学突触的传递过程

Transmitting  
传送 1-6

Receptive  
接收:7-9

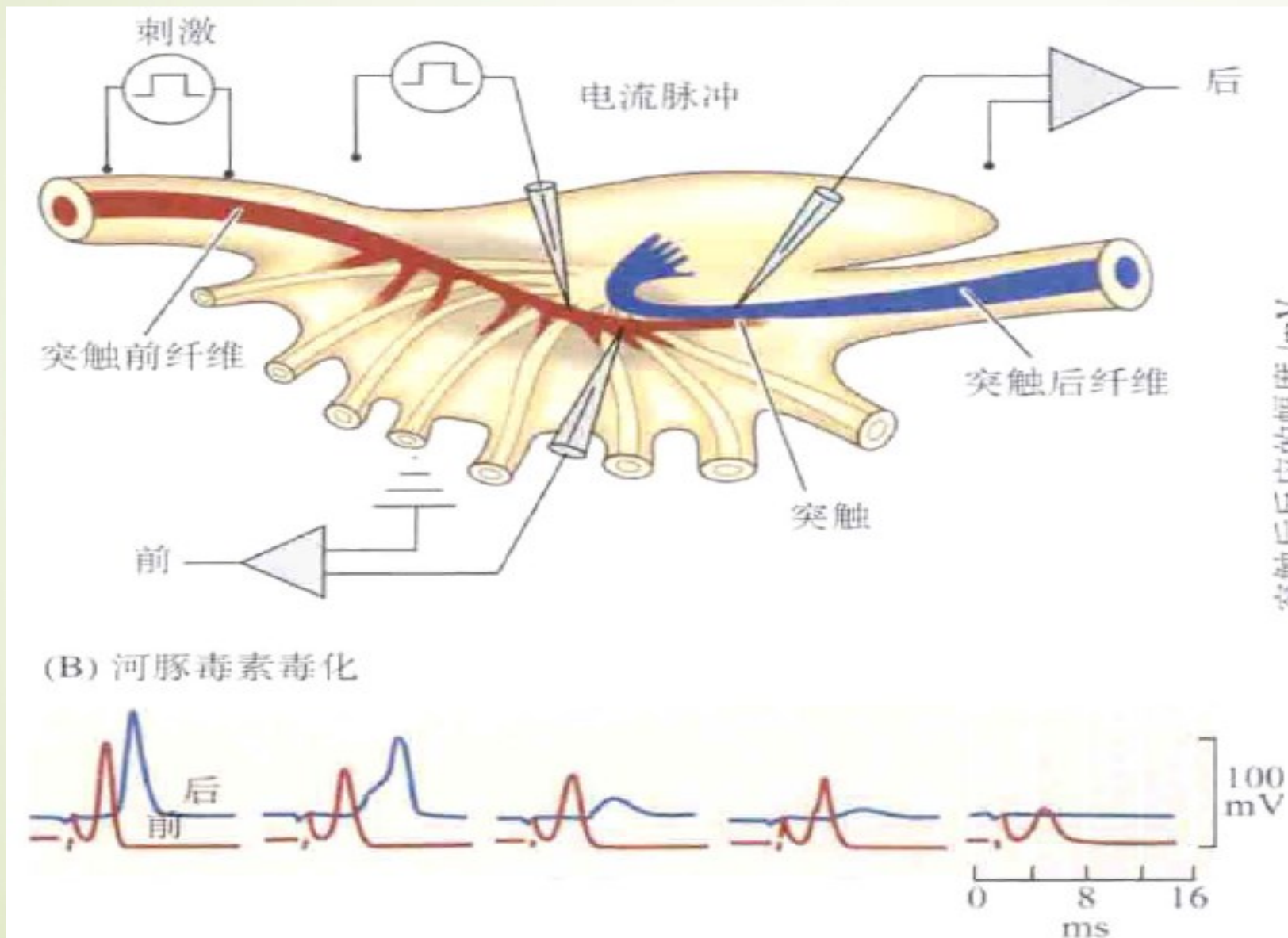


怎么知道突触传递过程各步骤的机制？

主要有哪些问题？

- 动作电位怎样驱动化学物质释放？
- 化学物质怎样释放？
- 突触传递延迟是怎样产生的？
- 化学物质怎样引起突触后膜的电反应？

# 1、突触后电反应与突触前电反应相关

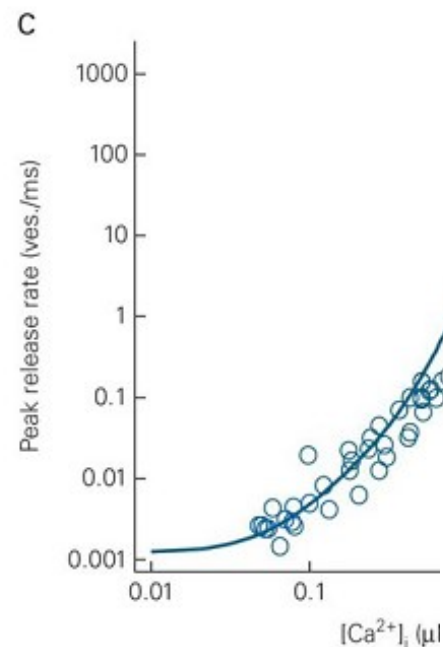
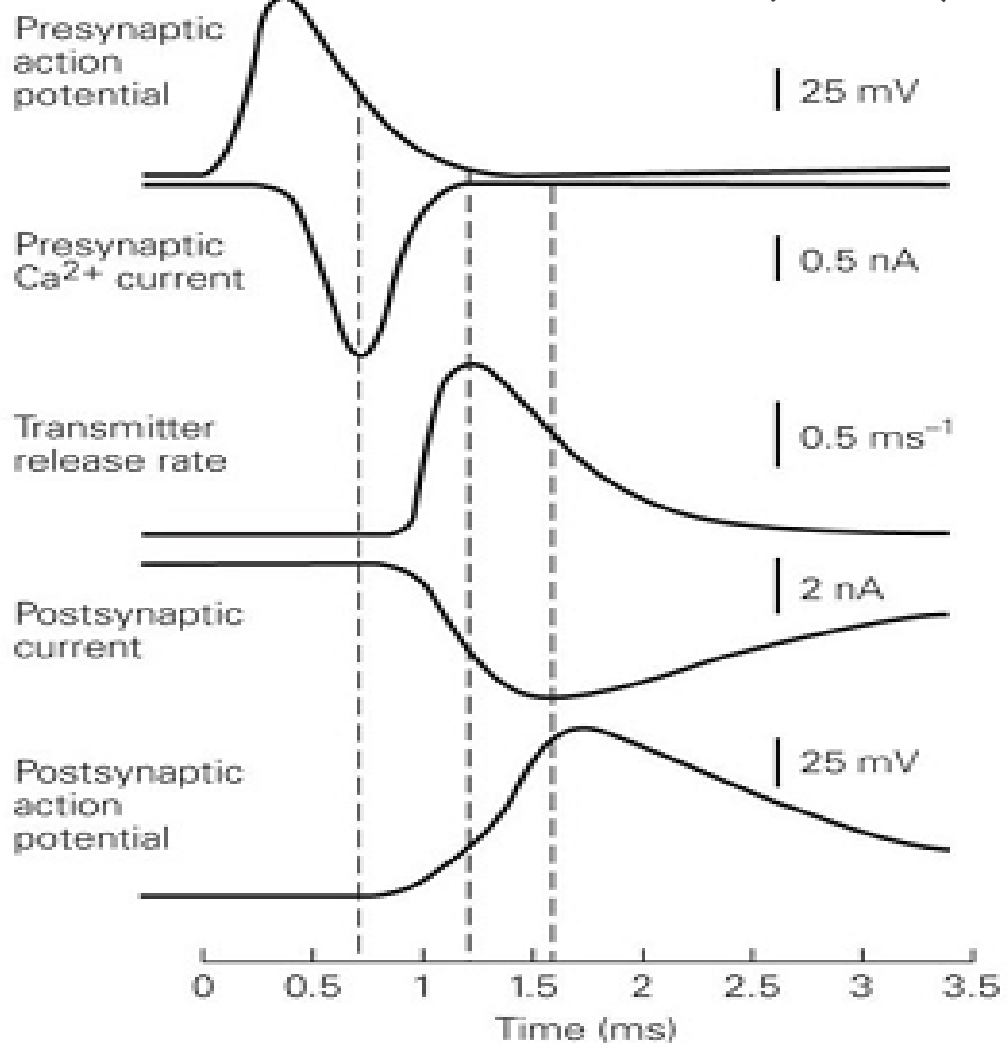


- 明显有一个传递的延迟，这可能是物质释放过程的机制
- 延迟时间与温度负相关

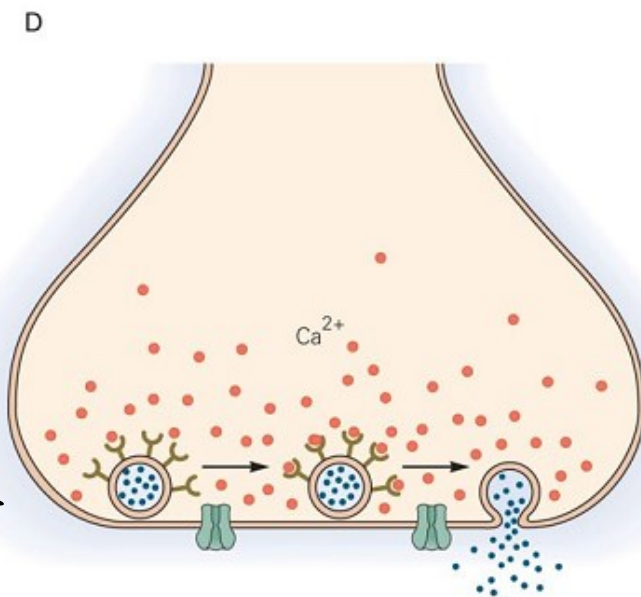
## 2、突触传递需要钙离子参与

神经递质释放需要结合多个钙离子  
哺乳动物听性脑干Calyx of Held (谷氨酸突触)

B ➡ 钙进入先于递质释放



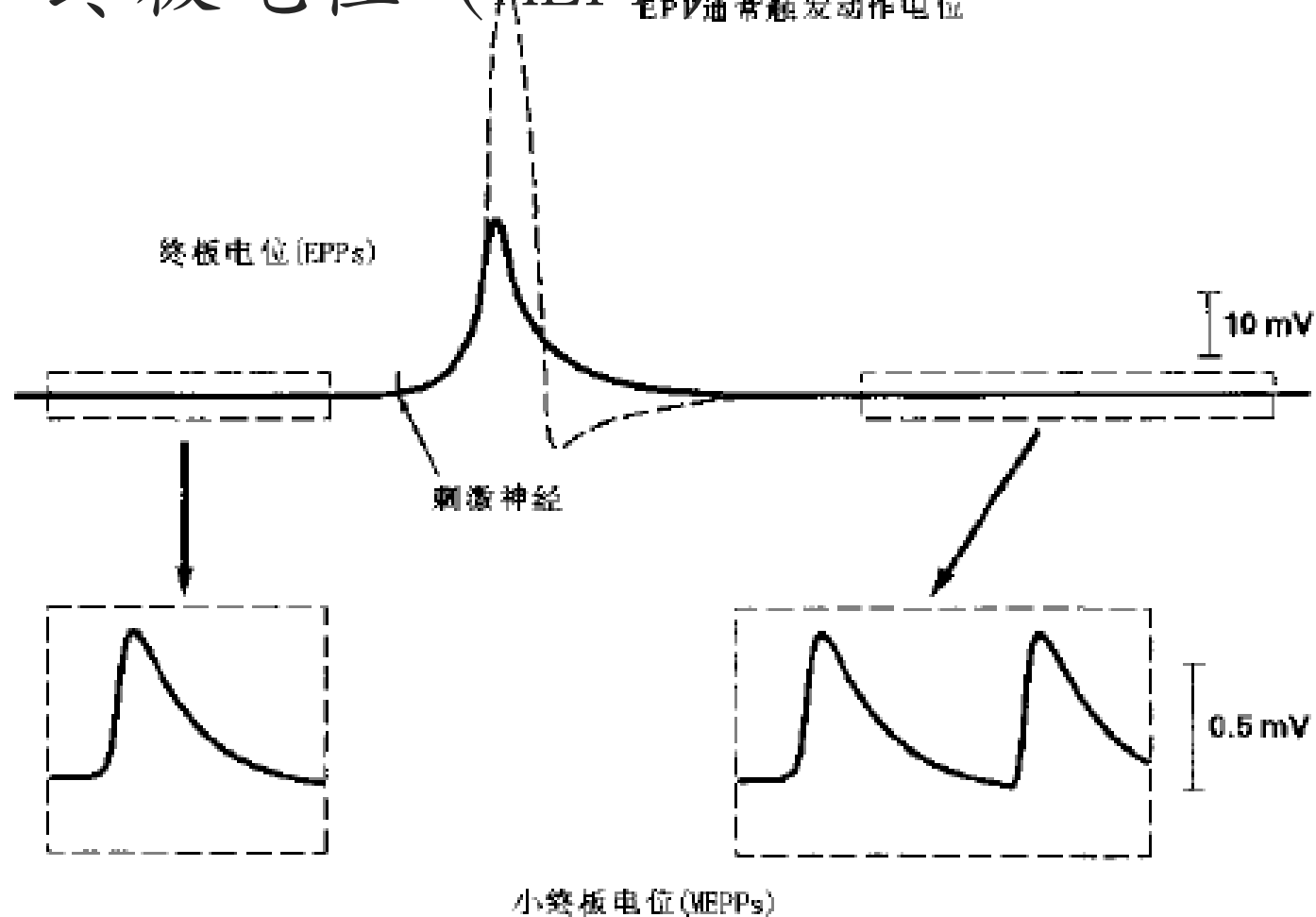
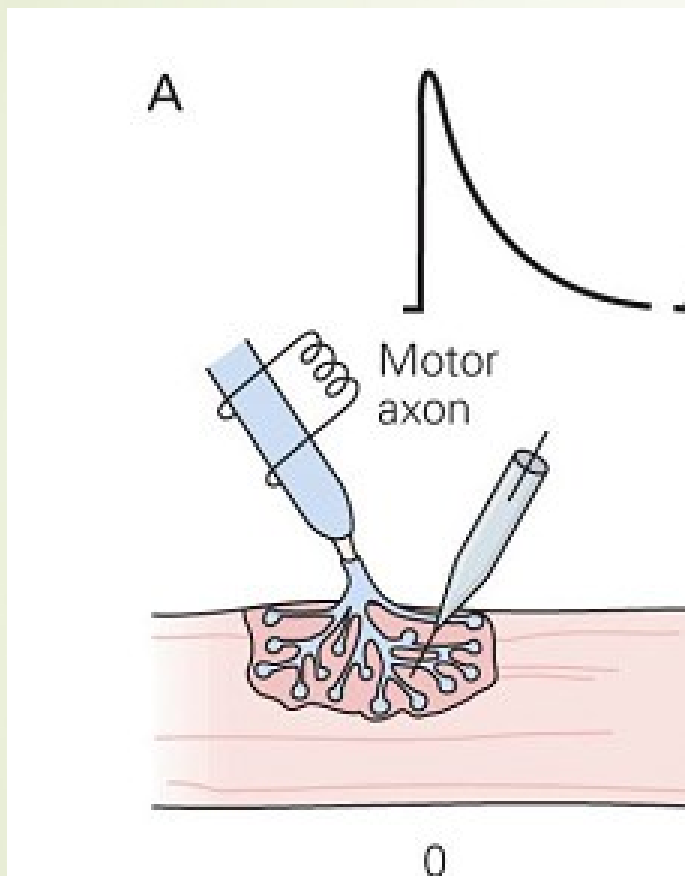
递质释放需要  
结合5个钙离子



### 3、递质的量子释放:

#### 终板电位 (EPP) 和小终板电位 (MEPP)

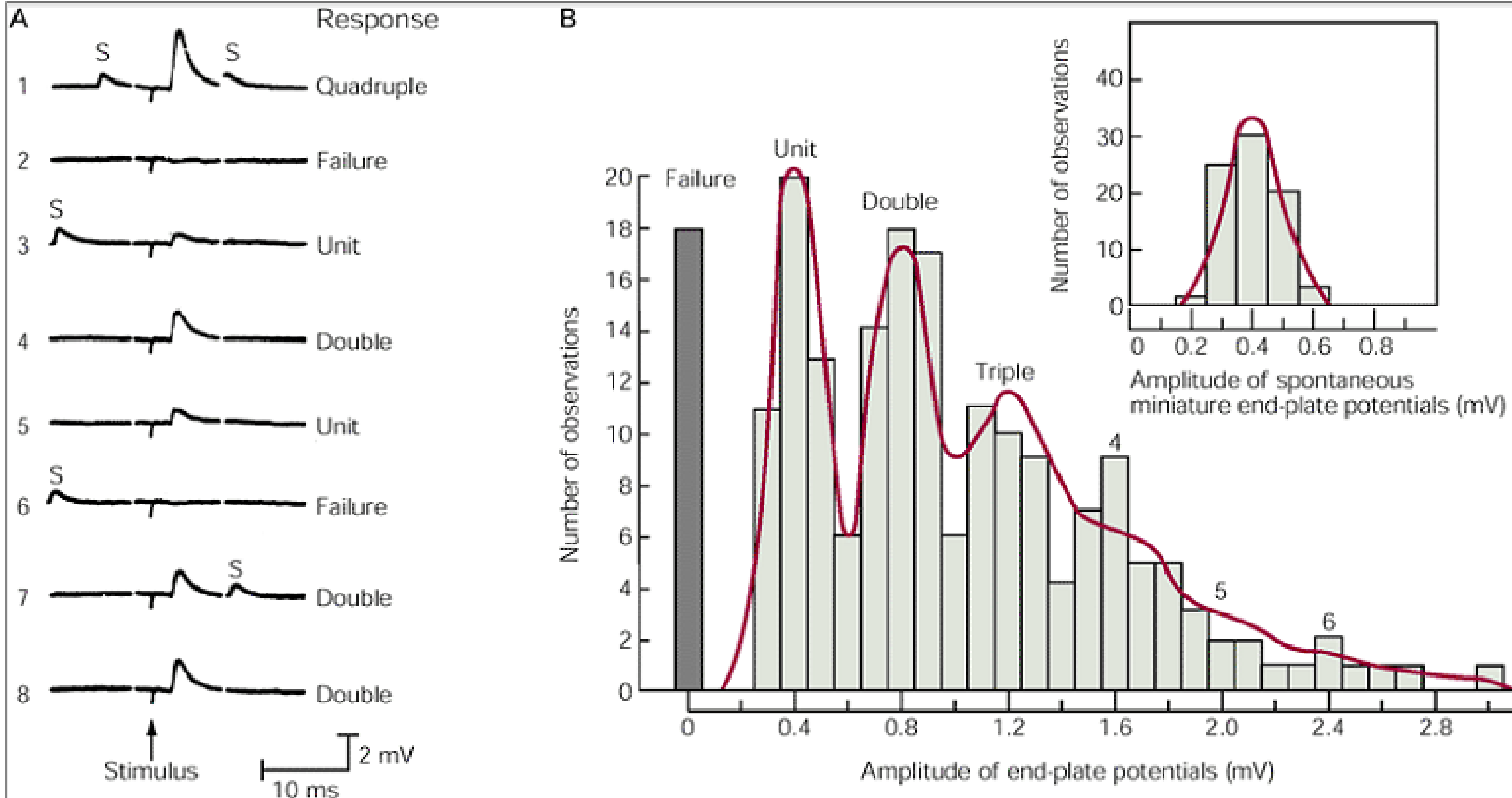
EPP通常触发动作电位



- EPP: 刺激产生, 数十毫伏
- MEPP: 没有神经刺激, 0.5毫伏
- EPP与MEPP非常相似
- MEPP: Ach少量自发随机释放所致

图 8-2 EPPs 和 MEPPs。一个肌细胞的膜电位记录。神经刺激诱发的 EPP 通常触发一次突触后动作电位。然而, 当 EPP 的幅度下降或动作电位被阻断时, EPP 的时程与 MEPPs 相似。

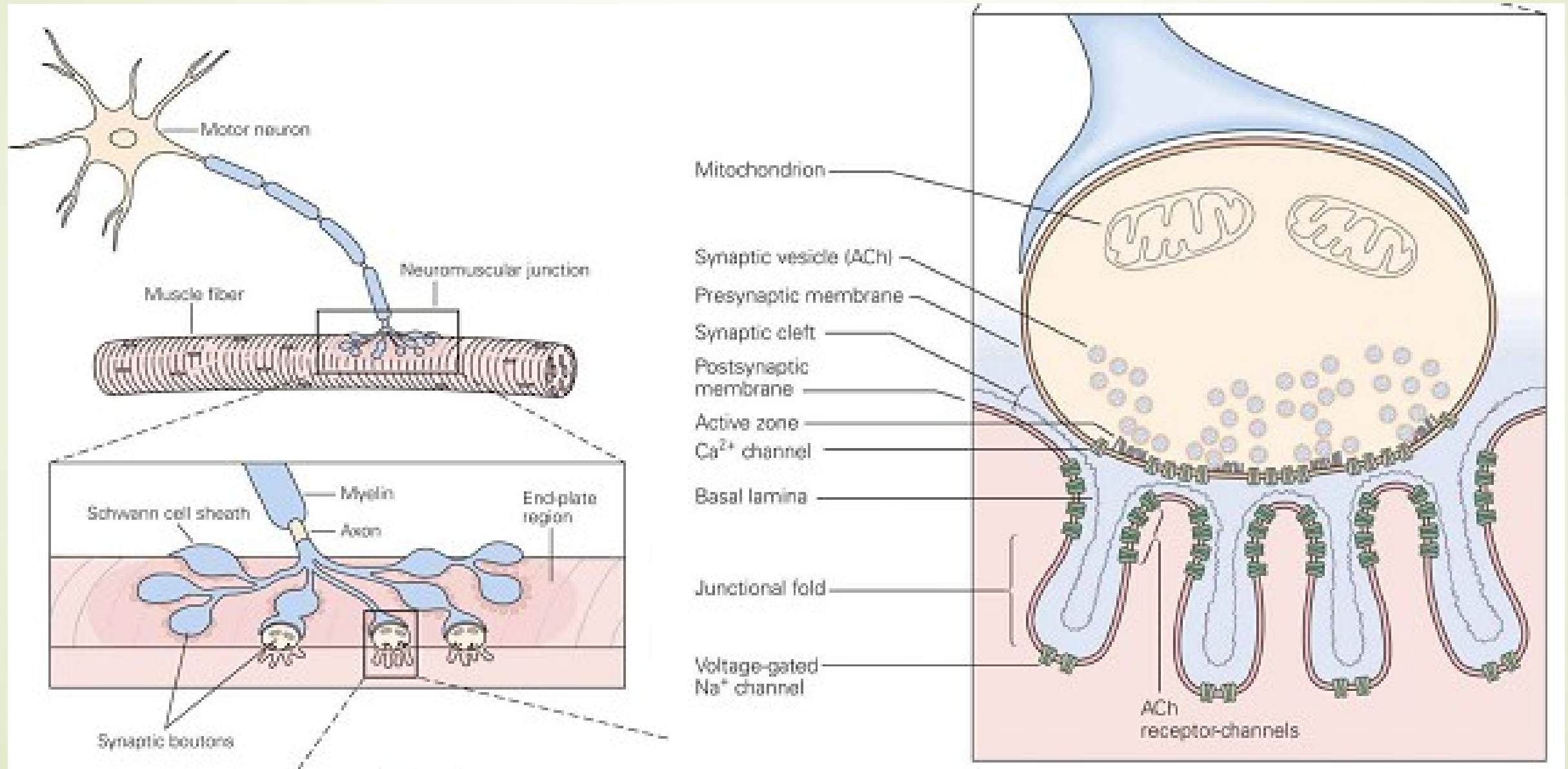
# 神经递质释放为量子式释放



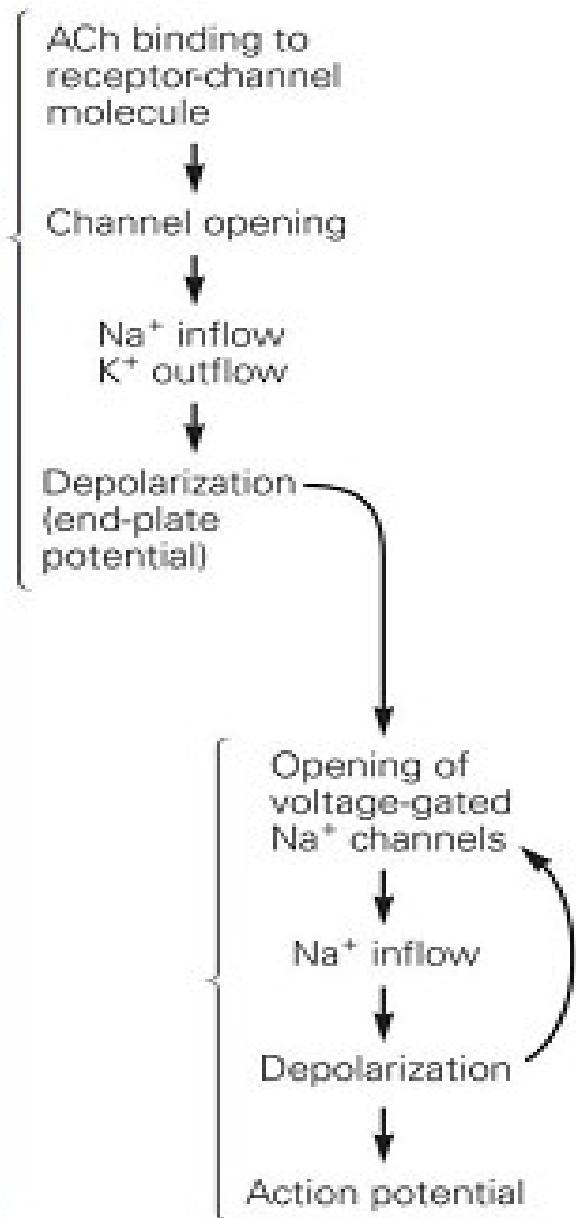
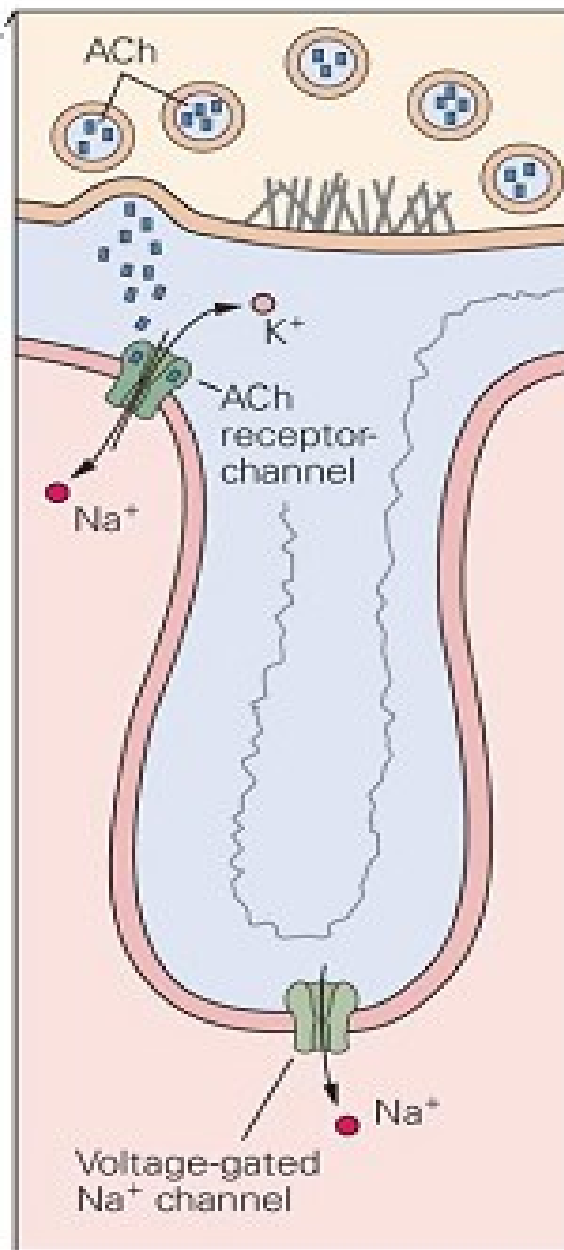
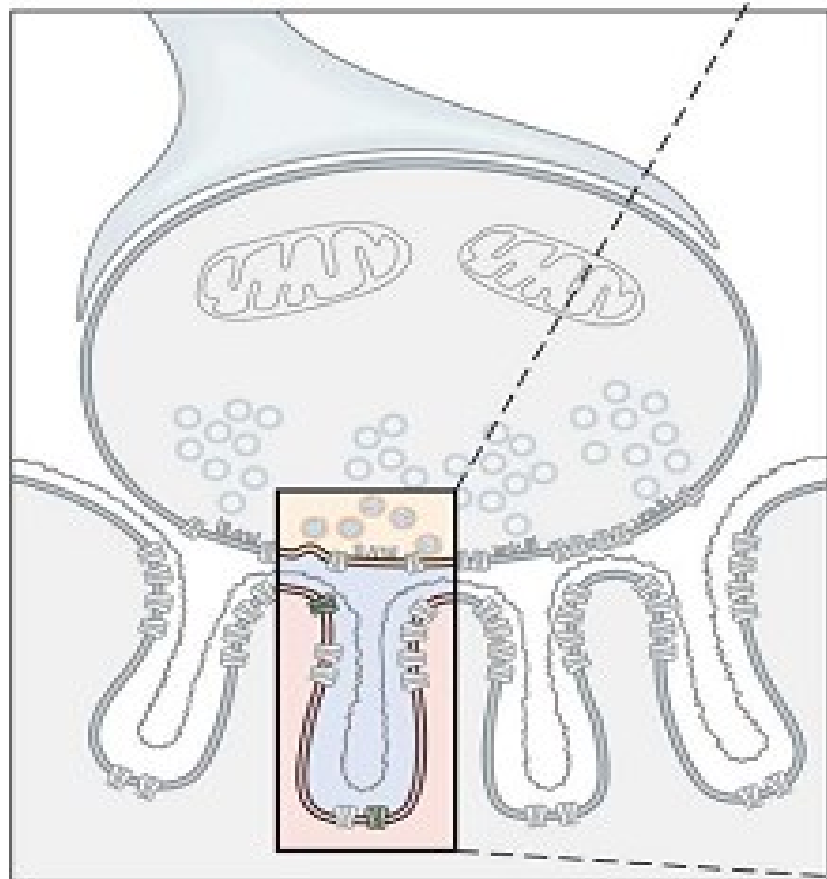
**Figure 14-6 Neurotransmitter is released in fixed increments, or quanta.** Each quantum of transmitter produces a unit postsynaptic potential of fixed amplitude. The amplitude of the postsynaptic potential evoked by nerve stimulation is equal to the unit amplitude multiplied by the number of quanta of transmitter released.

一个囊泡一个量子

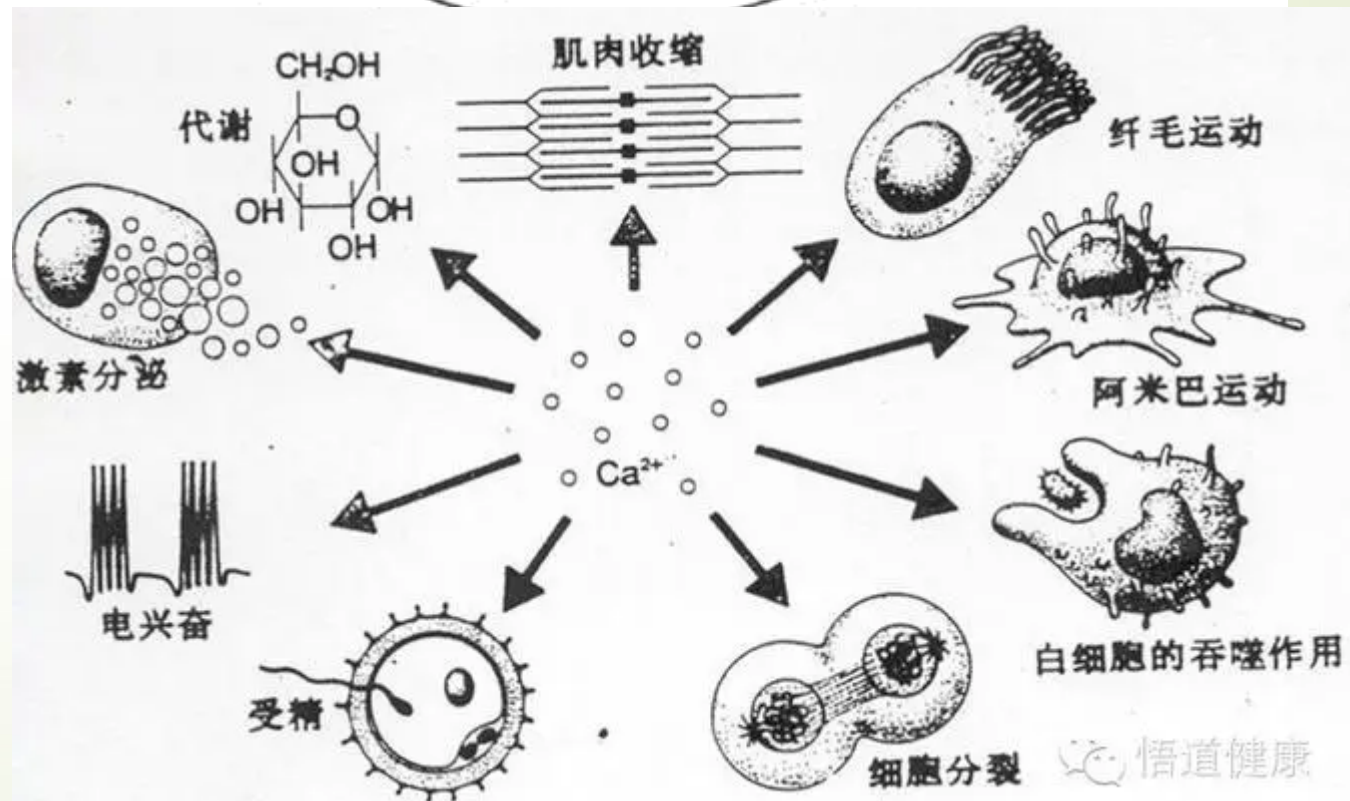
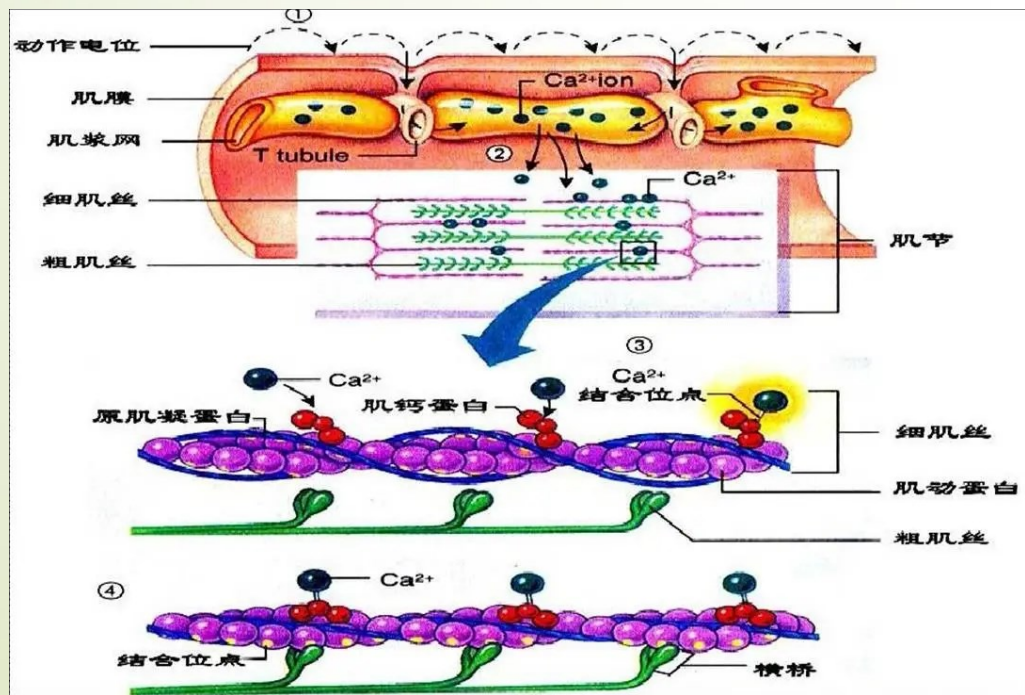
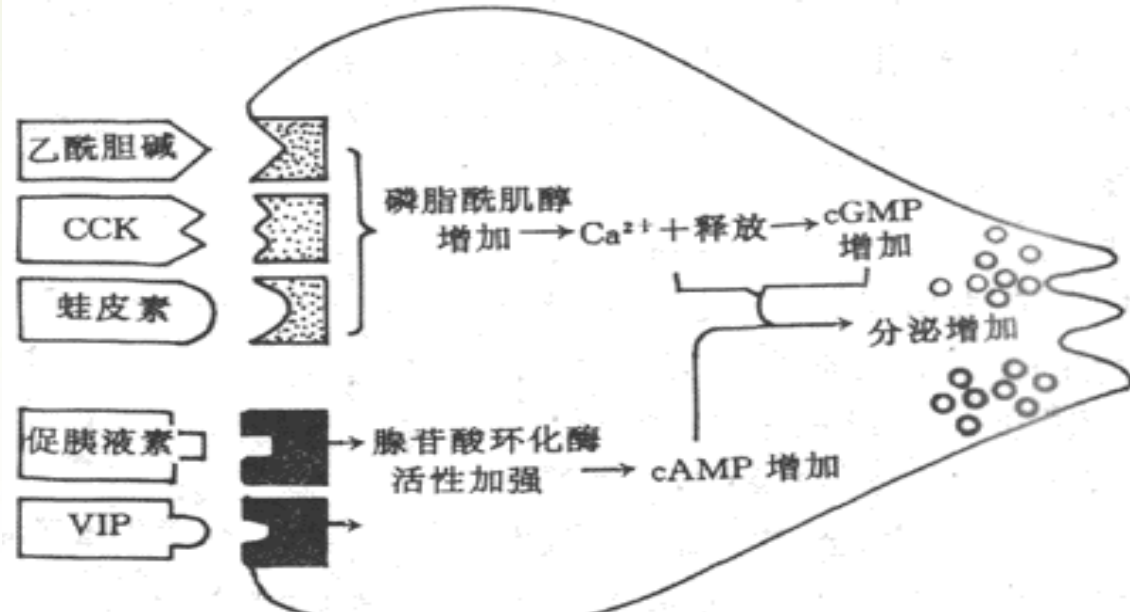
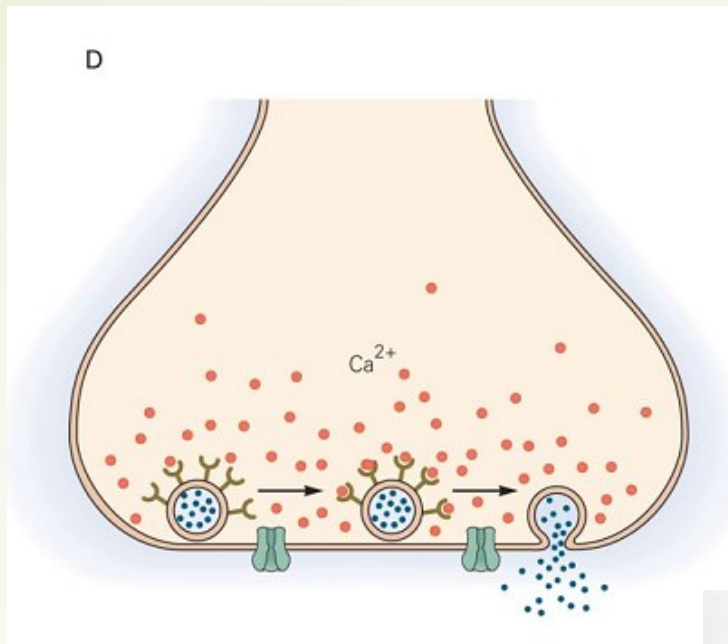
# 神经肌肉接头：研究化学突触传递的模型



# 神经肌肉接头信号传递过程

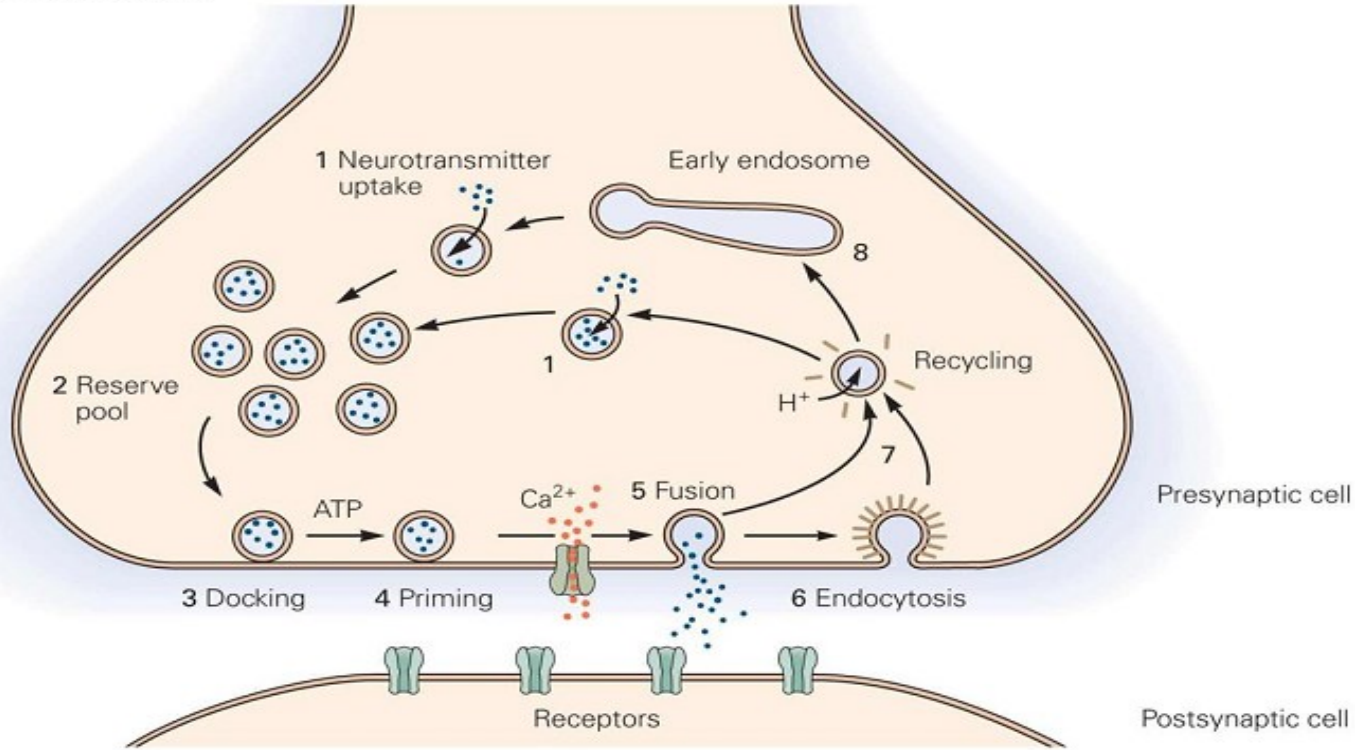


# 钙启动的生理功能

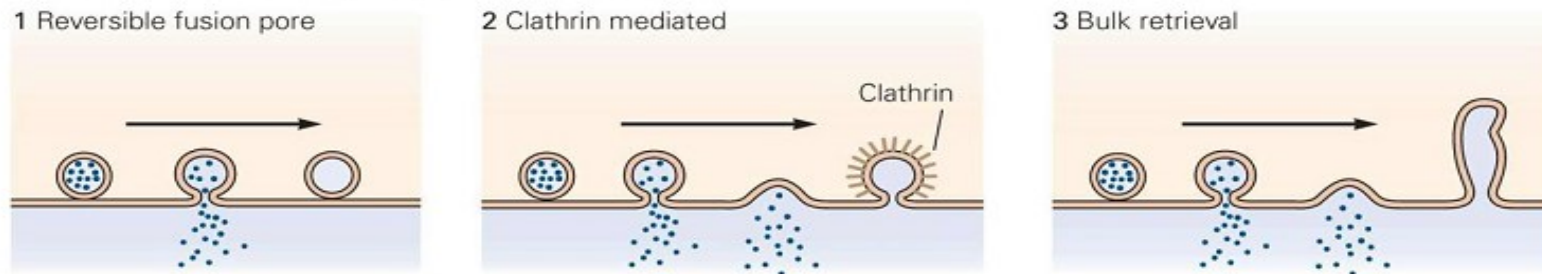


## 4、囊泡释放-回收循环机制

A Synaptic vesicle cycle



B Mechanisms for recycling synaptic vesicles



➤ 生成，停靠，启动  
(ATP)，融合/胞吐  
( $Ca^{2+}$ )，胞吞，再生

➤ 囊泡胞吐机制

➤ 囊泡入胞机制的三种假说：

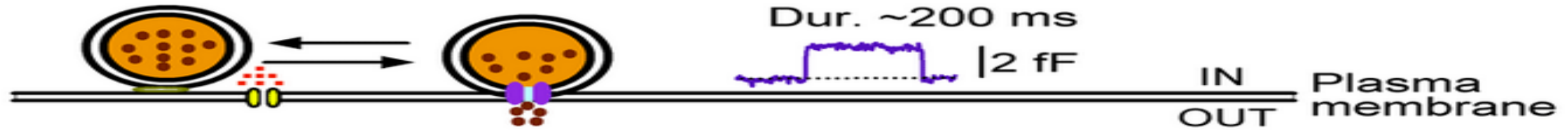
1. 可逆融合孔 (Kiss and Run)

2. 受体介导胞吞：网格蛋白 (clathrin) 依赖途径

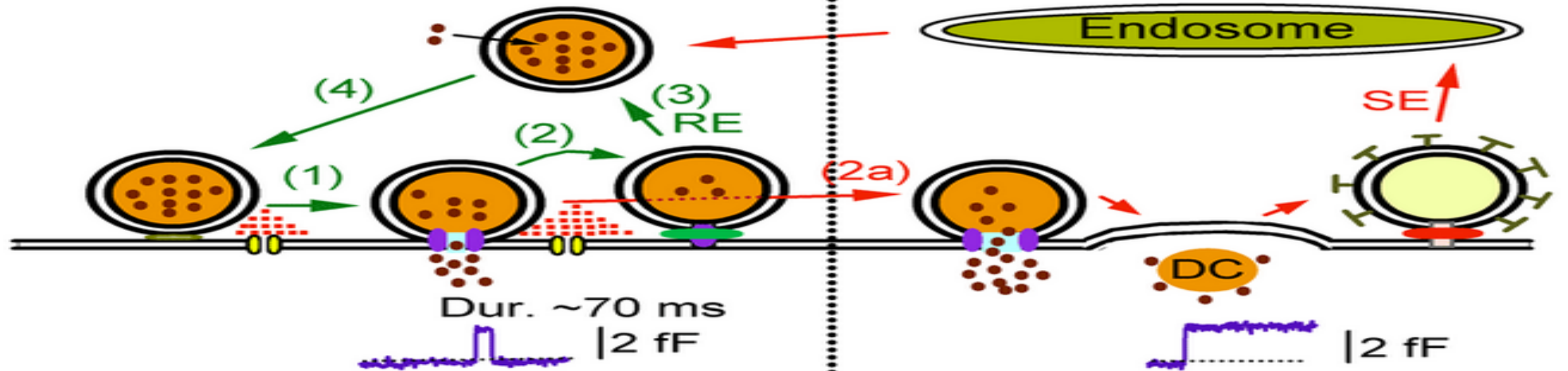
3. 批量内吞

# 胞吐的不同方式 (假说)

## 1. Kiss-and-stay (low stim.)

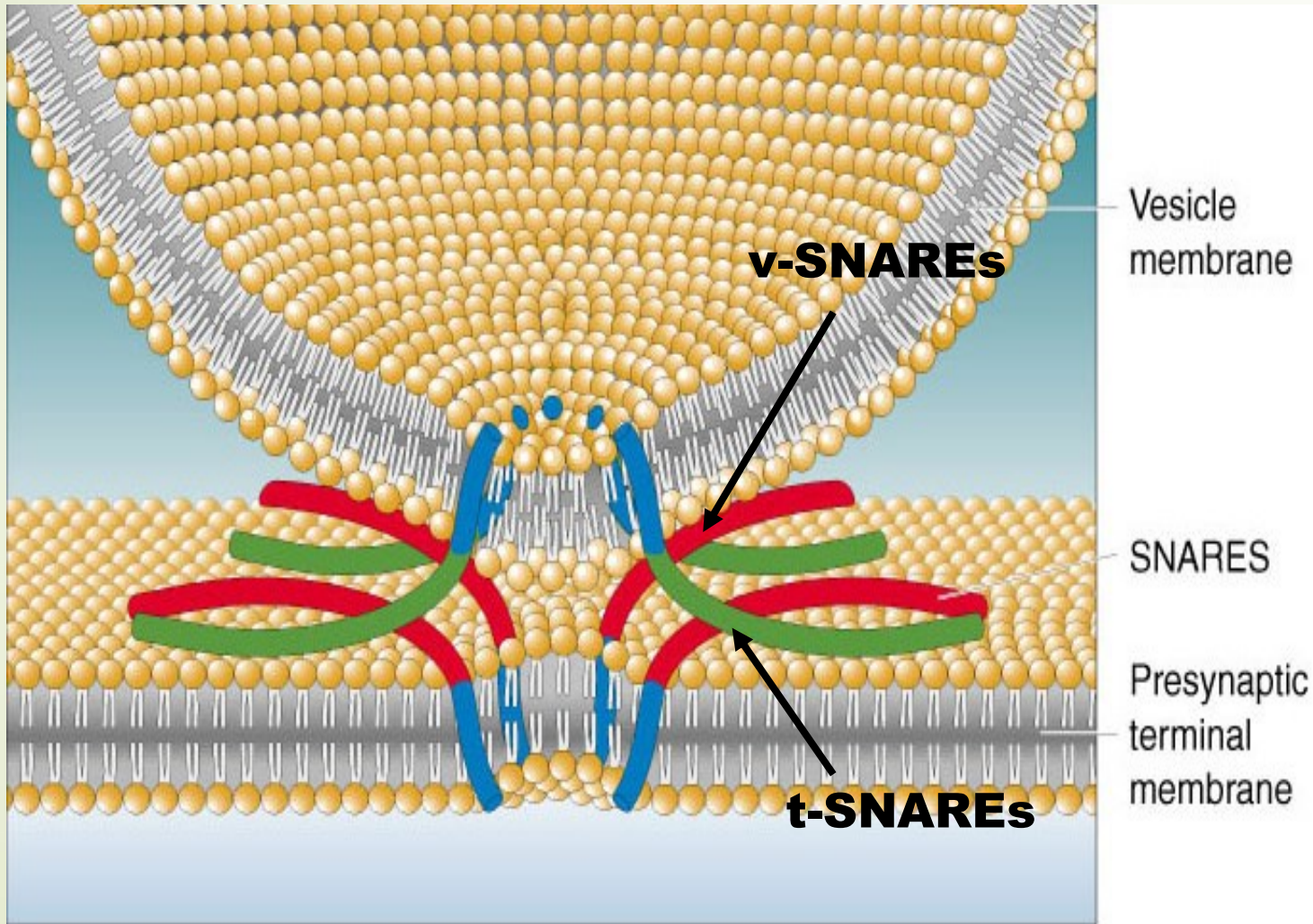


## 2. Kiss-and-run (moderate stim.) 3. Full fusion (sustained stim.)



- |           |                          |                               |
|-----------|--------------------------|-------------------------------|
| Dynamin-1 | Clathrin                 | Fusion pore (Aqueous channel) |
| Dynamin-2 | Ca <sup>2+</sup> channel | Ca <sup>2+</sup> ions         |
|           |                          | Catecholamines                |

# 囊泡融合：SNARE Proteins Drive Fusion

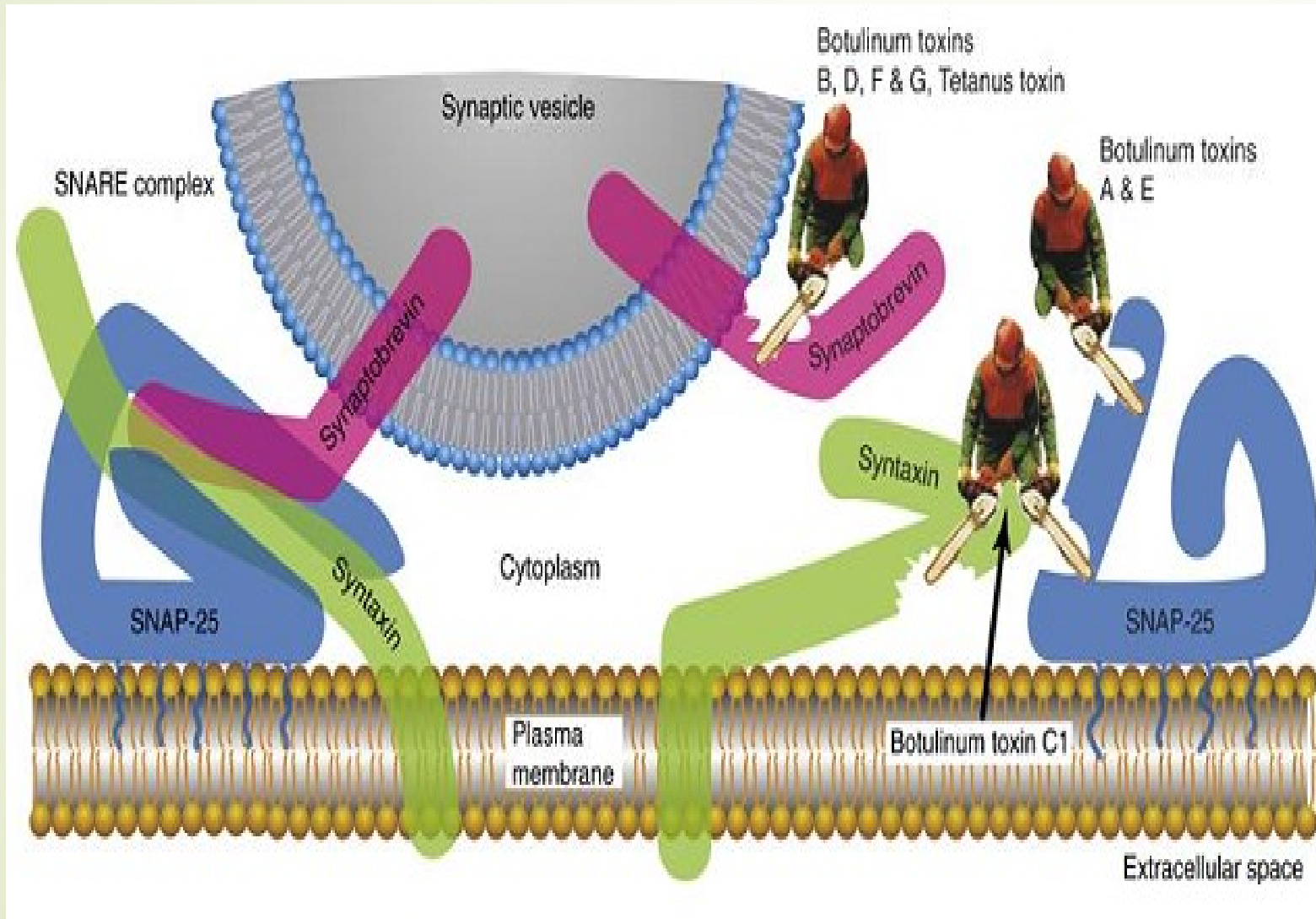


v-SNAREs bind with t-SNAREs to bring membranes together and induce fusion (exocytosis).

SNARE: soluble N-ethylmaleimide-sensitive factor attachment protein receptor proteins 可溶性N-乙基马来酰胺敏感因子附着蛋白受体

Figure A, Box5.3, Bear, 2001

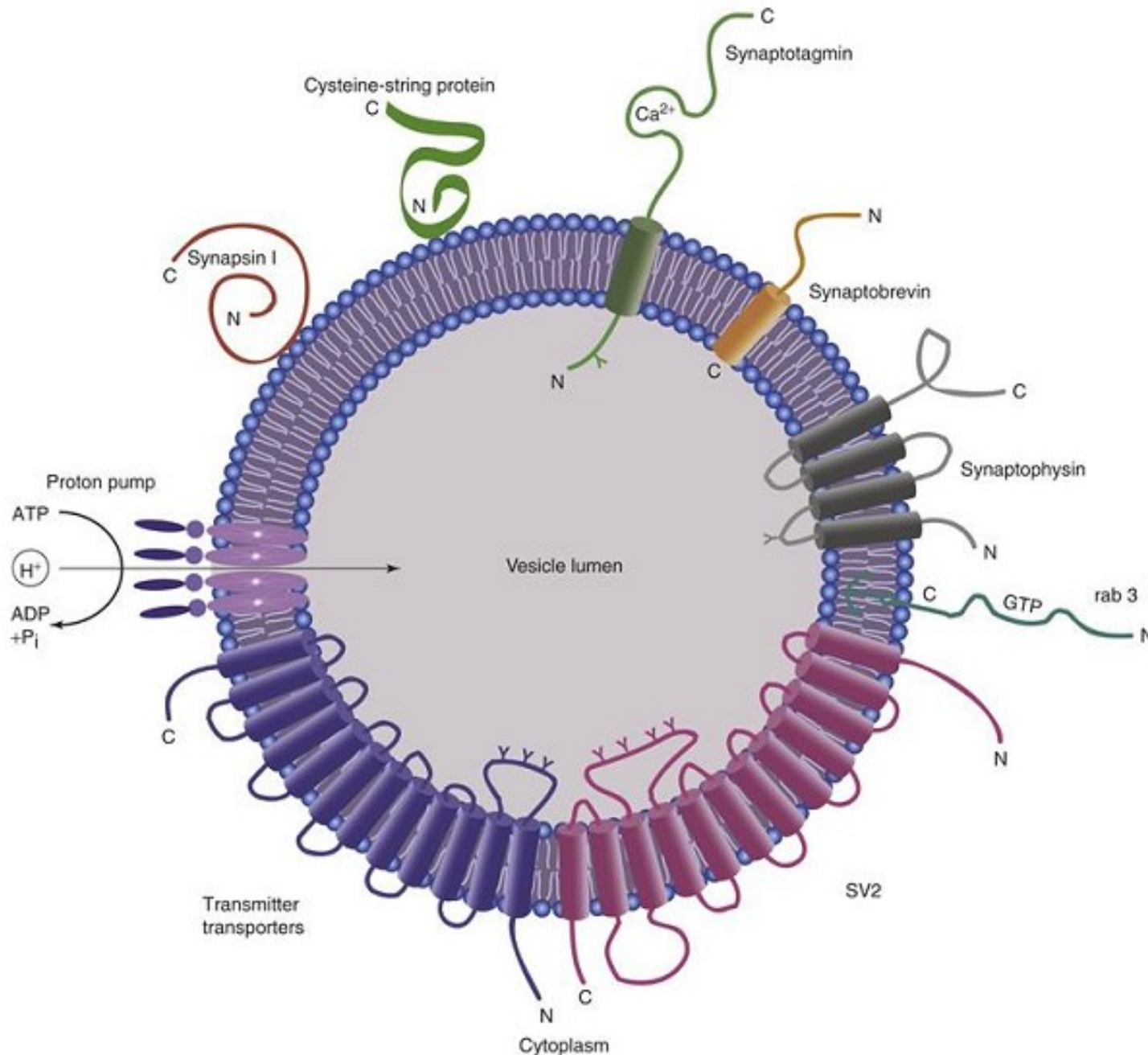
# 不同类型的SNARES



## 三种不同的SNAERS:

- 突触囊泡膜：小突触泡蛋白（synaptobrevin）
- 突触前膜：突触融合蛋白（syntaxin）和SNAP-25
- 神经毒素：botulinum toxin (BTX,肉毒素)；Tetanus toxin（破伤风毒素）

# 突触小泡膜表面蛋白



➤ 质子泵

➤ 转运体

➤ Synaptotagmin (突触结合蛋白, 钙激发, 启动SNARE形成)

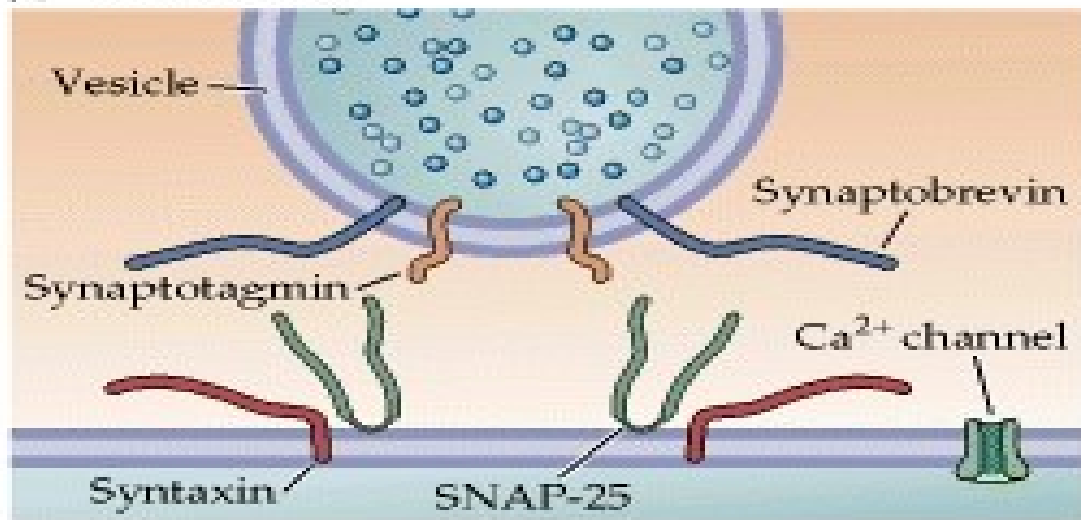
➤ Synaptobrevin (VAMP, 小突触泡蛋白, 组成SNARE)

Protein	Function
Syntaxin	SNARE protein present on plasma membrane (and on synaptic vesicles to a lesser extent); forms core complex with SNAP-25 and VAMP/synaptobrevin; essential for late step in fusion
SNAP-25	SNARE protein present on plasma membrane (and on synaptic vesicles to a lesser extent); forms core complex with syntaxin and VAMP/synaptobrevin; essential for late step in fusion
Nsec-I/munc-18	Syntaxin-binding protein required for all membrane traffic to the cell surface
Complexin	Syntaxin-binding protein; may stabilize an intermediate in core complex formation
Snapin	Binds SNAP-25; associated with synaptic vesicles; unknown function
NSF	ATPase that disassembles SNARE complex; likely to disrupt complexes after exocytosis
a-SNAP	Cofactor for NSF in SNARE complex disassembly

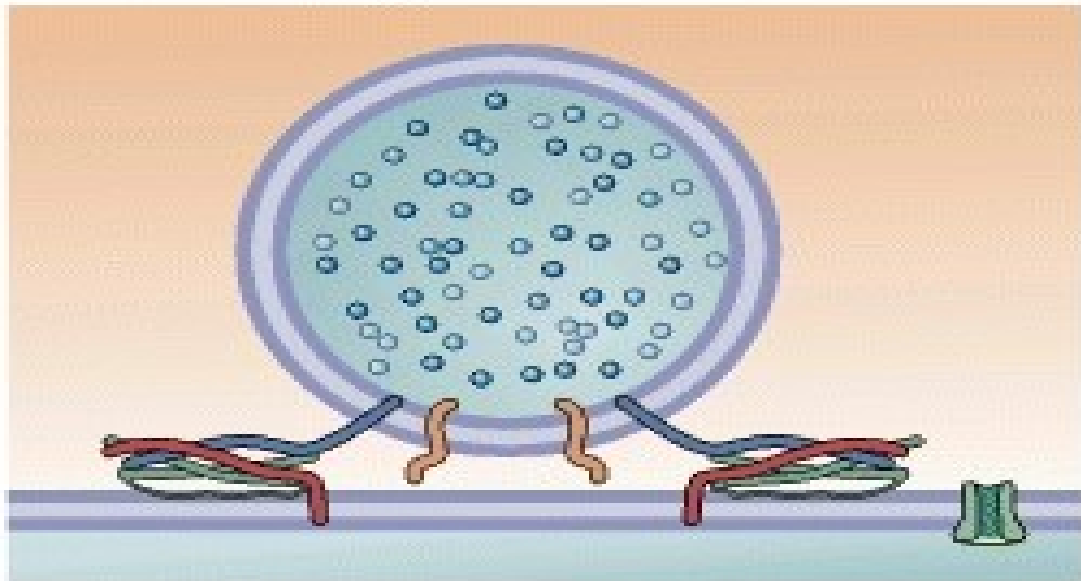
unc-13/munc-13	Active zone protein; vesicle priming for release; modulation of transmission by diacyl glycerol and Protein Kinase C
Rabphilin	C2 domain protein; Ca <sup>2+</sup> -binding protein; binds rab3 and associates with synaptic vesicle; modulation of transmission (?)
DOC2	Ca <sup>2+</sup> -binding C2 domain protein; binds munc-18 and SNAREs; regulates spontaneous fusions and asynchronous release
RIM1 and related proteins	Active zone proteins; bind rab3; modulation of transmission
Piccolo	Likely scaffolding protein at active zones
Bassoon	Likely scaffolding protein at active zone
Exocyst (sec6/8 complex)	Marks plasma membrane sites of vesicle fusion; not needed for synaptic vesicle fusion

# 突触前膜 与SNARE 形成相关 的蛋白

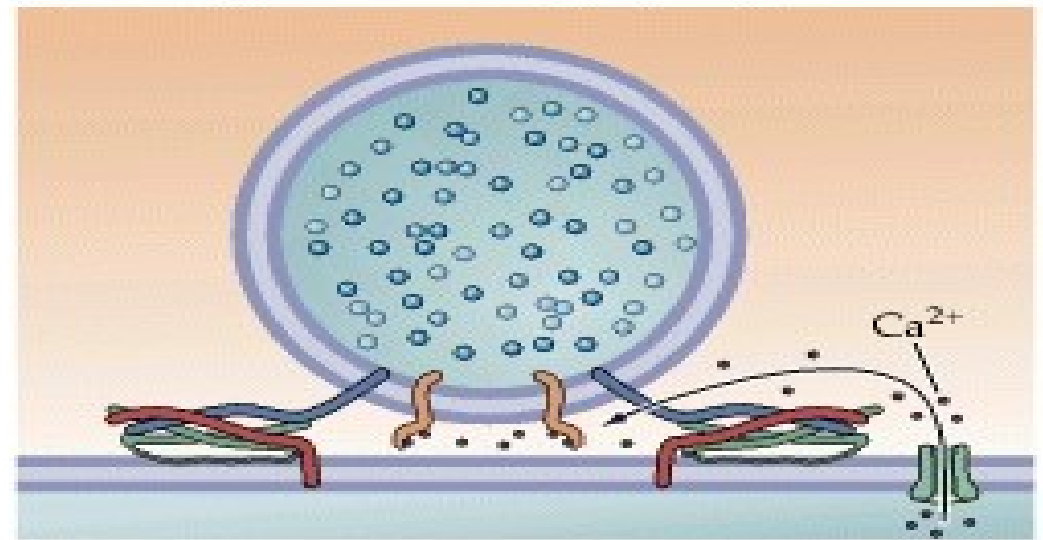
(1) Vesicle docks



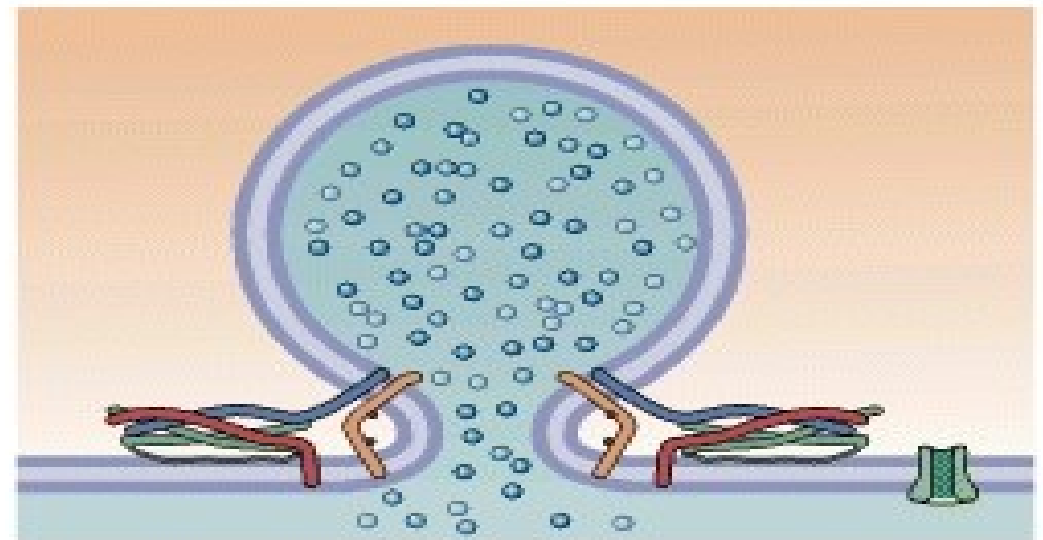
(2) SNARE complexes form to pull membranes together



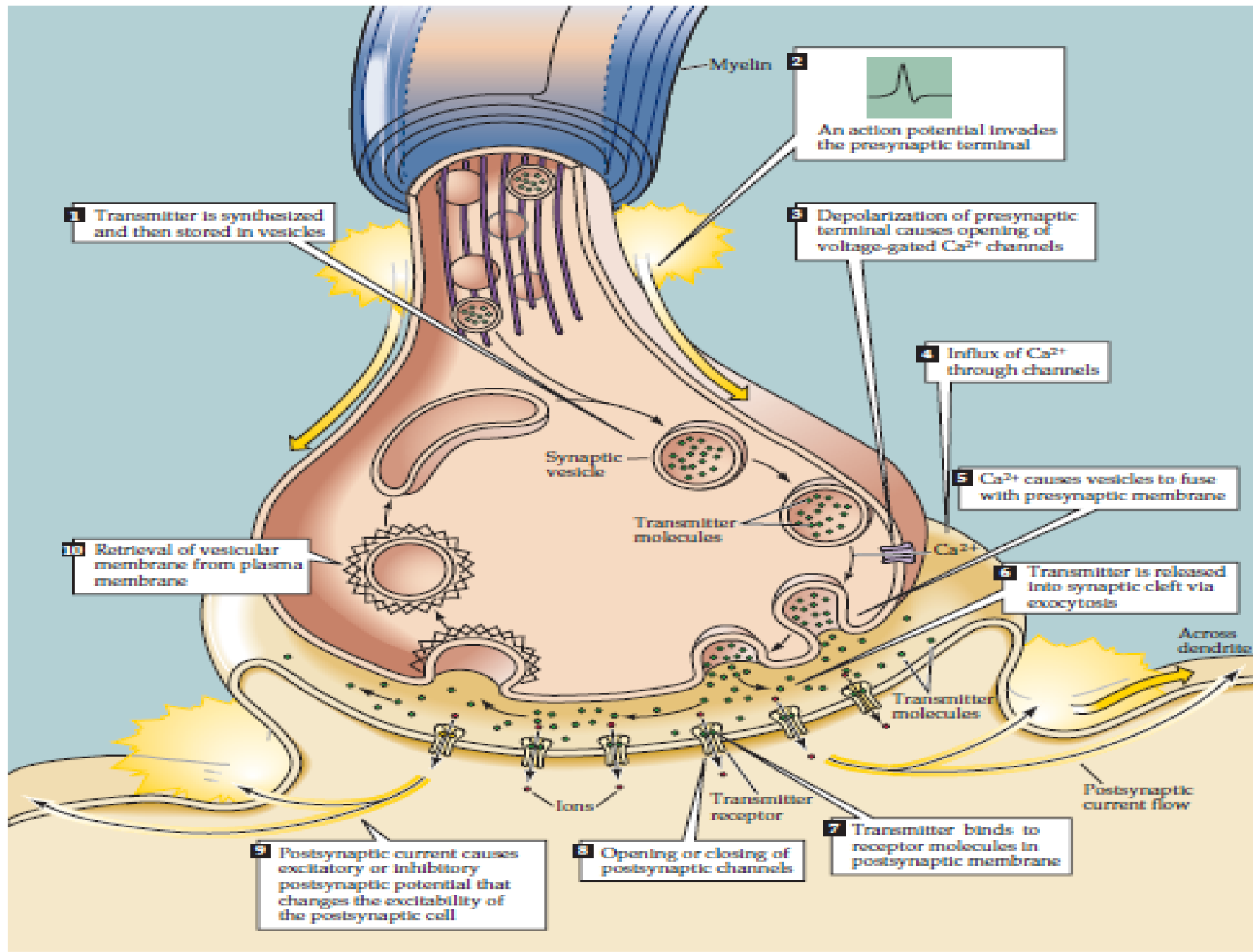
(3) Entering  $\text{Ca}^{2+}$  binds to synaptotagmin



(4)  $\text{Ca}^{2+}$ -bound synaptotagmin catalyzes membrane fusion



Synaptotagmin (突触结合蛋白) :  $\text{Ca}^{2+}$ 感受器



➤ 递质释放依赖于钙

➤ 递质释放是量子化的

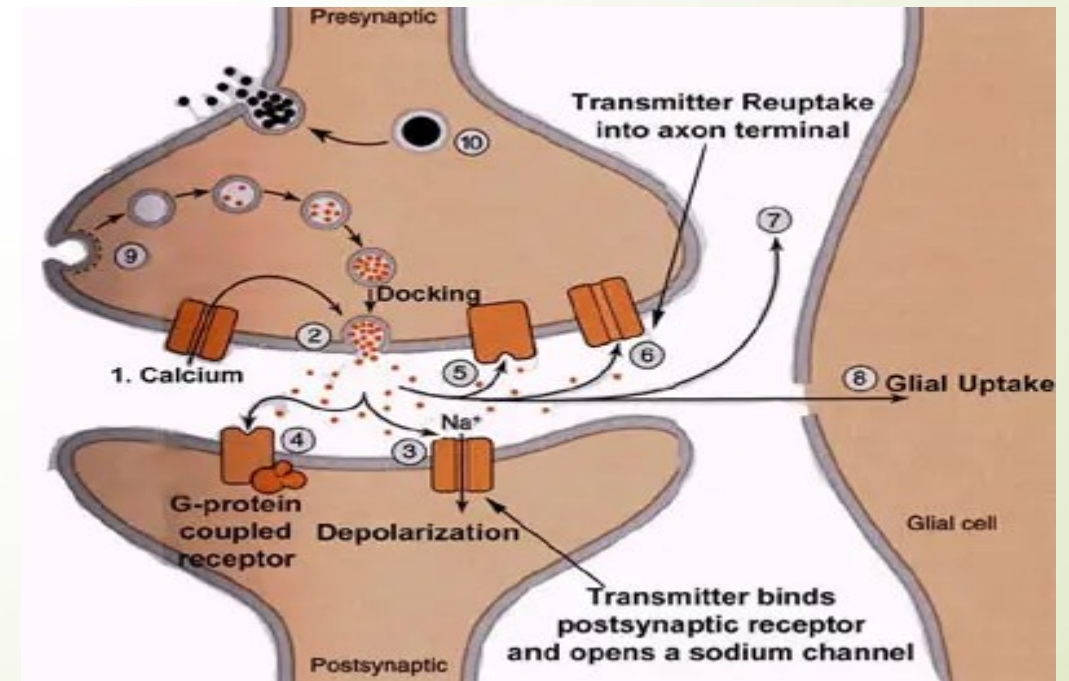
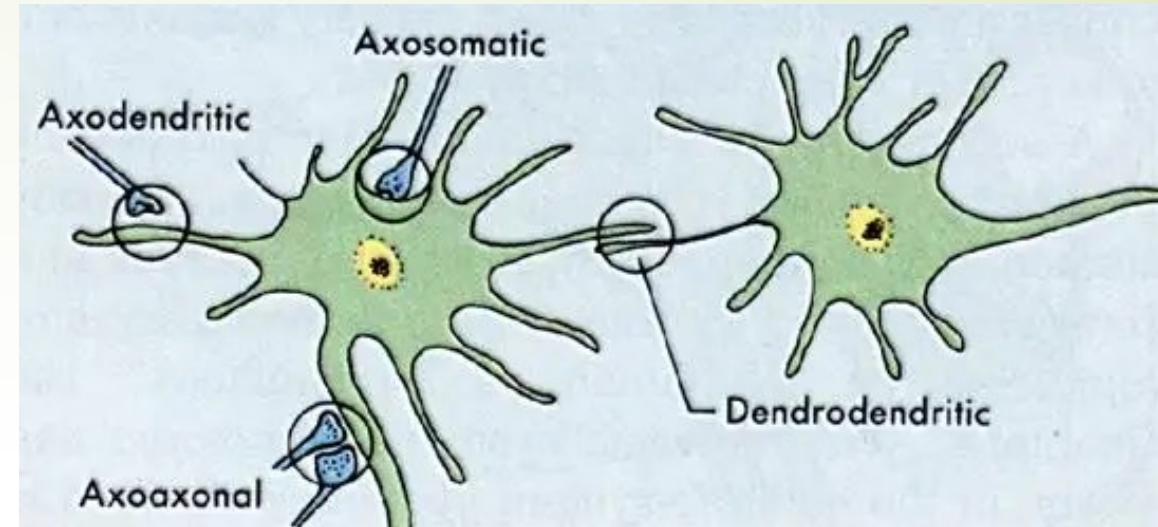
➤ 突触递质释放具有可塑性

## 5、化学突触传递的特性

● **One-way Conduction:** Excitatory transmitter is only found in the axon terminals. The presynaptic neuron can cause an action potential in the postsynaptic neuron.

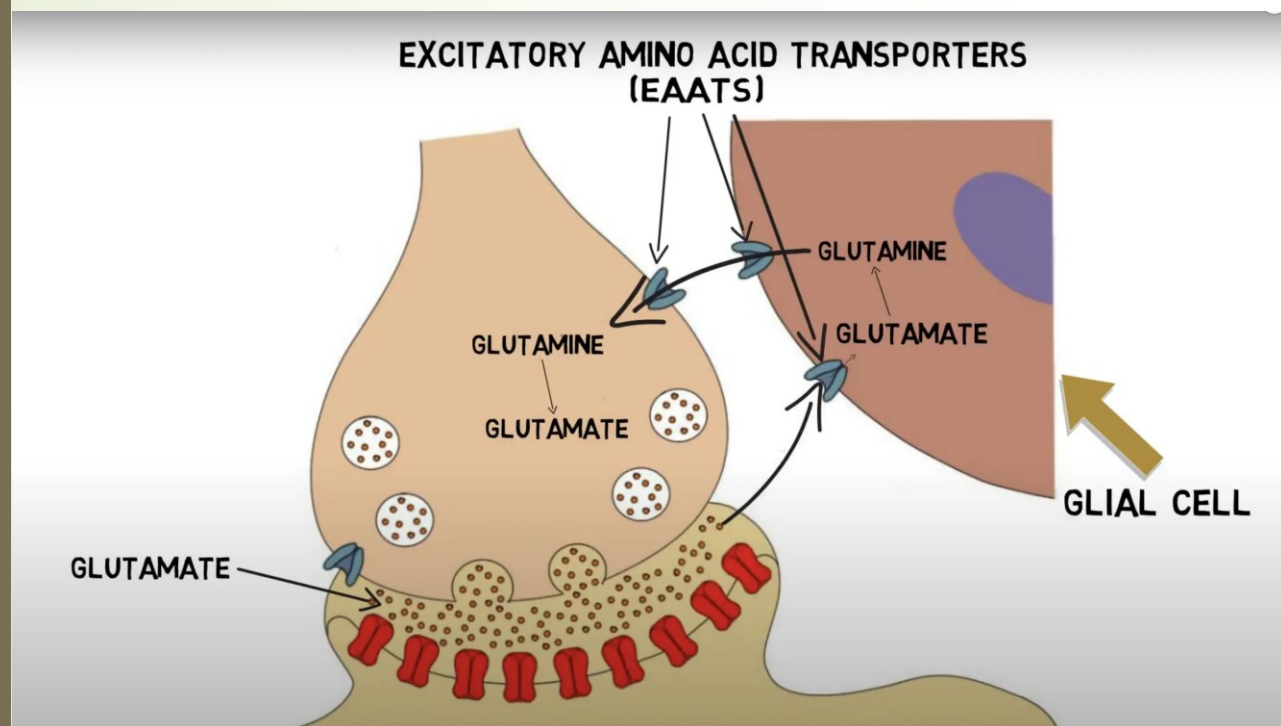
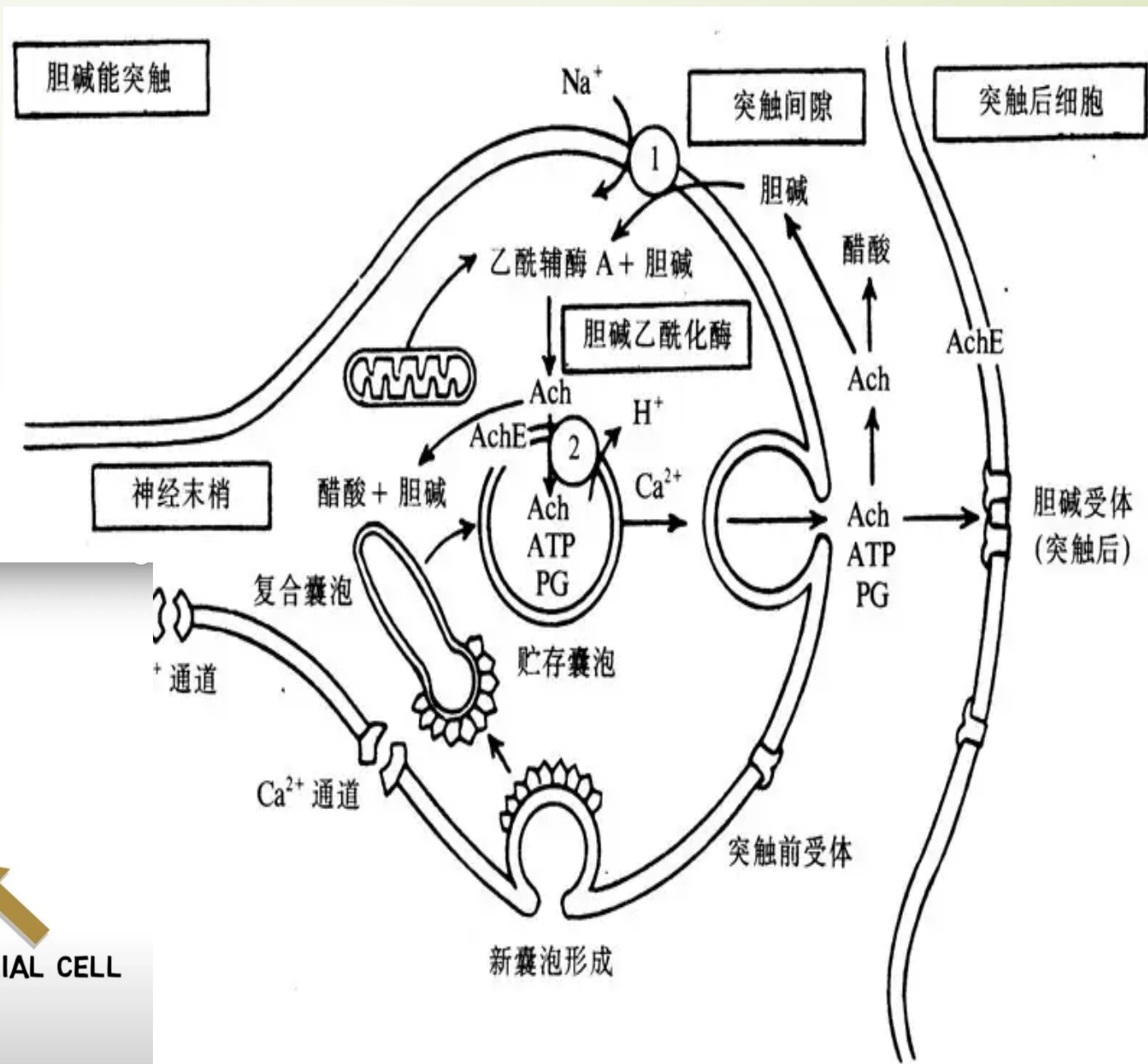
● **Synaptic Delay:** Time to release transmitter, move across cleft, and bind to receptors.

● **Synaptic Fatigue:** Depletion of transmitter from presynaptic terminals.



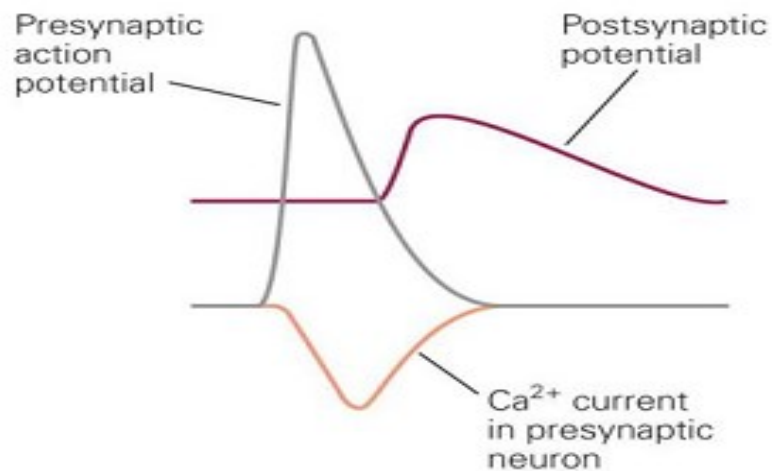
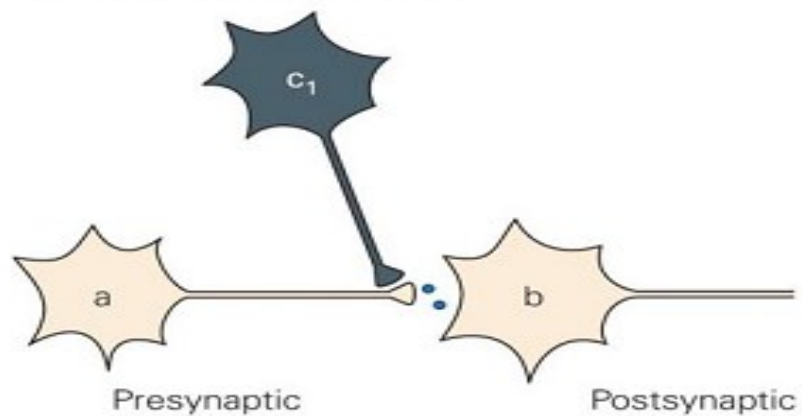
## 6、突触传递的调制

- 突触前机制：改变神经递质的释放
- 突触后机制：影响突触后电位
- 影响突触间隙中的递质：胆碱酯酶；递质重摄取抑制剂等

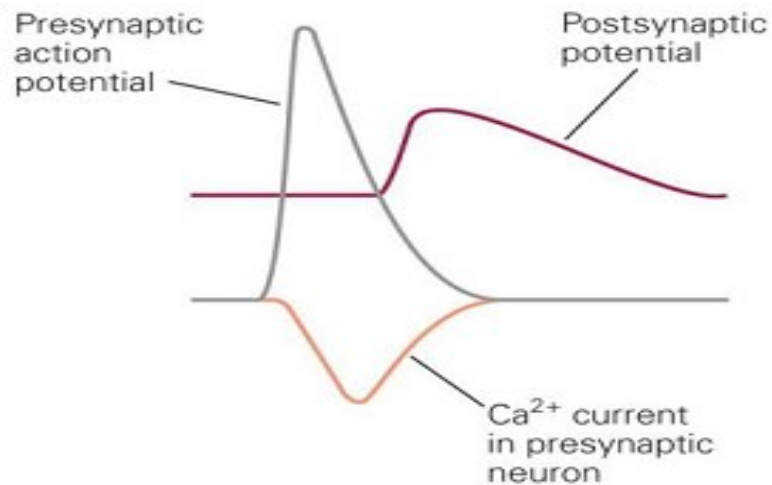
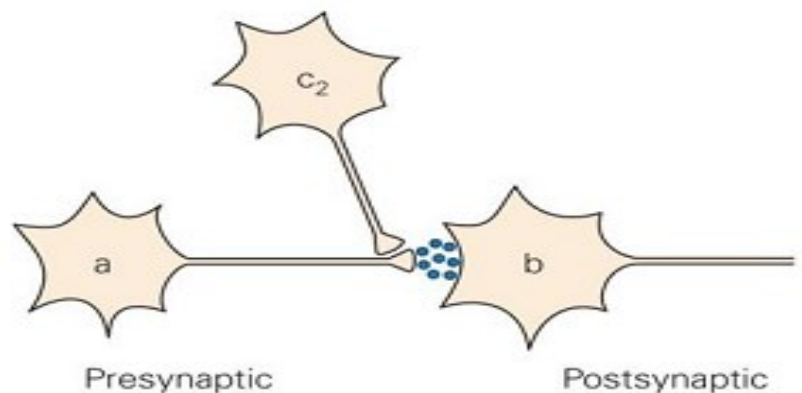


# 突触调制——突触前机制

A Presynaptic inhibition



B Presynaptic facilitation



# 突触调制——突触后机制

- ▶ 离子通道的磷酸化与去磷酸化：开关，电导改变
- ▶ 膜上离子通道数目改变
- ▶ 基因表达的启动：更多的离子通道，新突触的形成

