

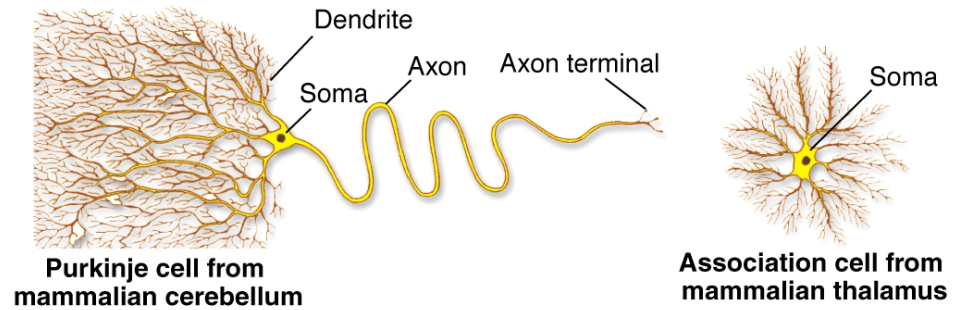
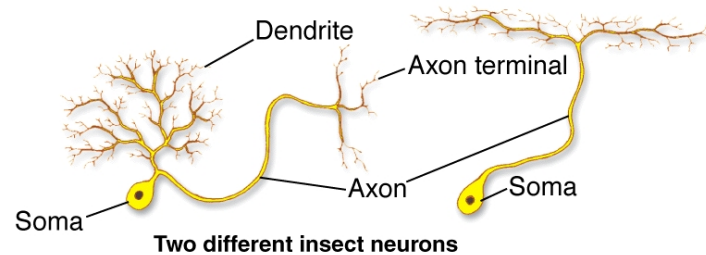
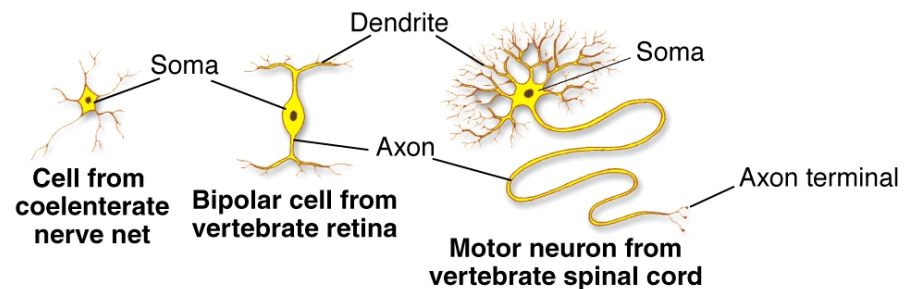
# Acetylcholinesterase

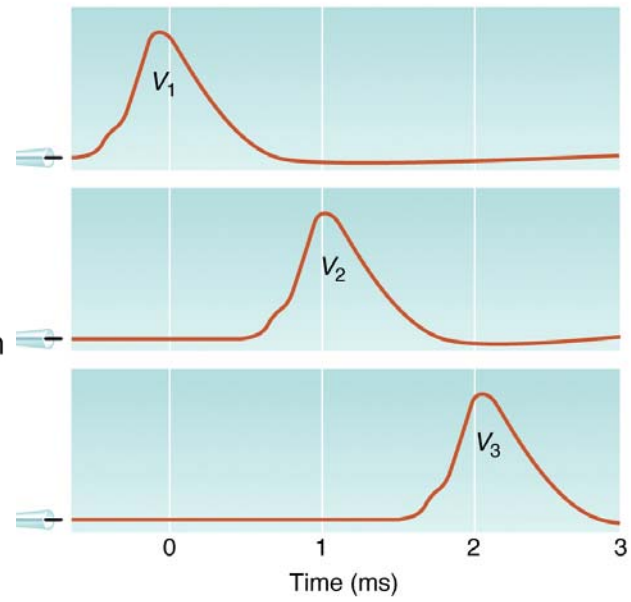
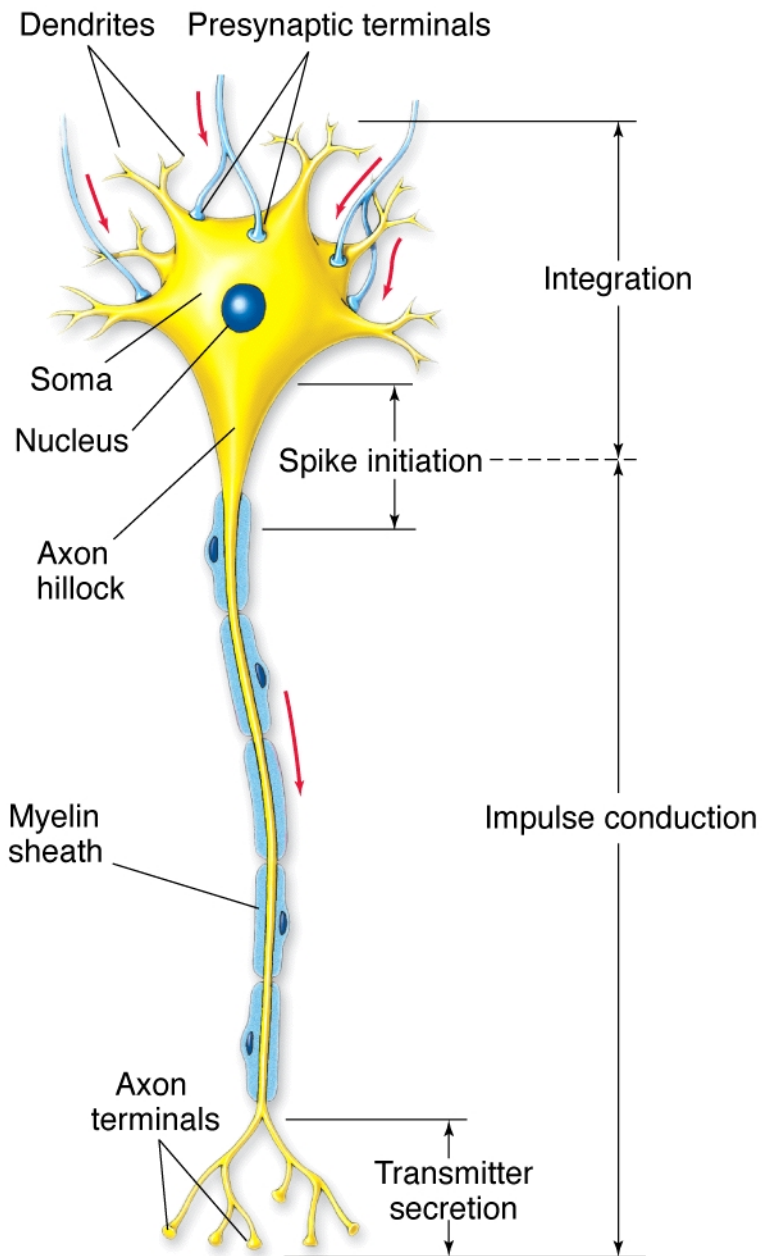
Starting with function. Consider  
1LFP (1<sup>st</sup> in PE, and then VAST)

In the latter, click on DUF28 for all the news.

# Nerves – a quick course

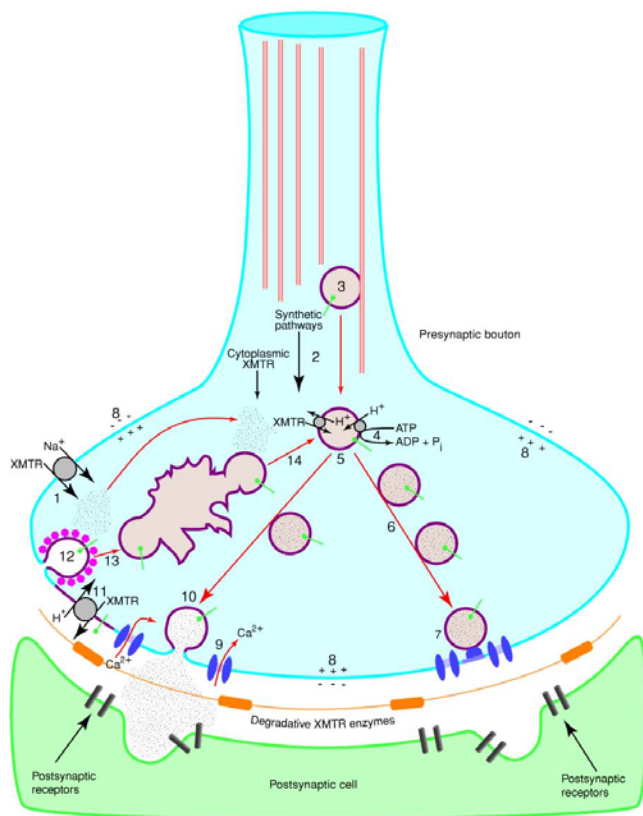
- Cell body like all others
- Dendrites (input)
- Axon (long distances)
- Axon terminals (synapses)



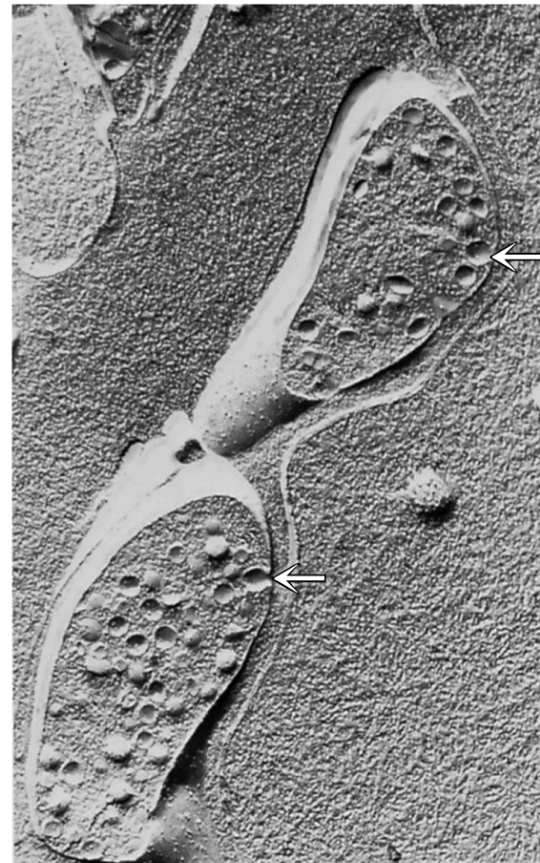


# Synapse

FIG 7.2



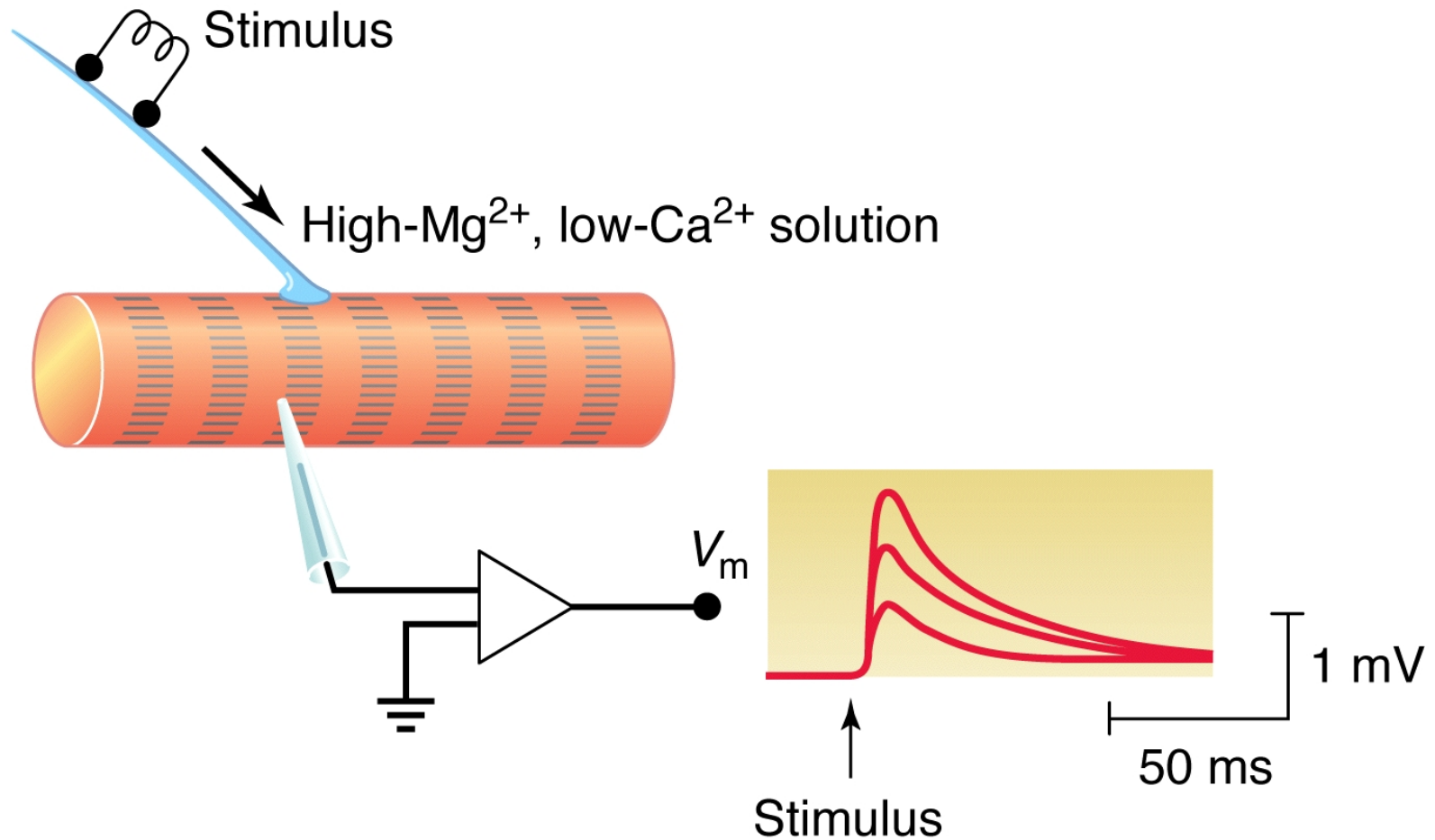
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0.2 μm

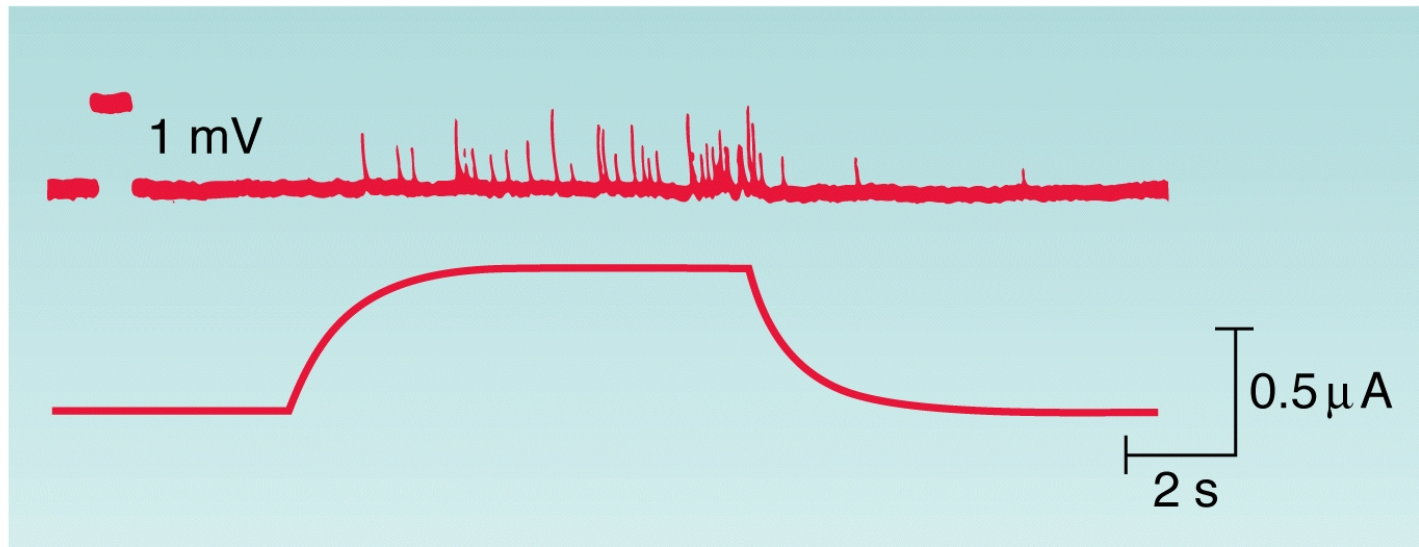
# Release of transmitter stimulates postsynaptic cell

(a)





(b)



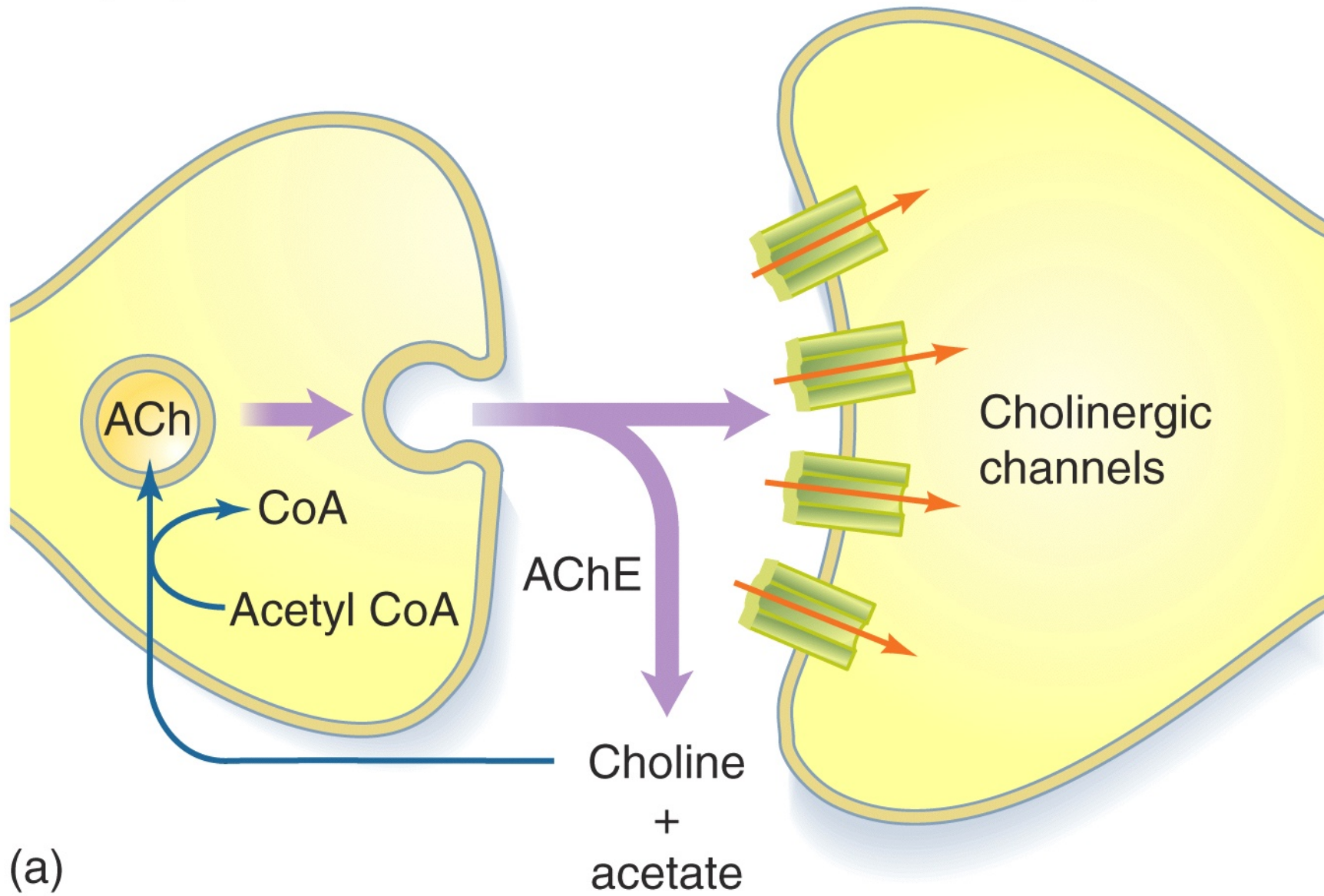
**Table 6-2** Typical small neurotransmitters, their structures, and functions

Neurotransmitter	Typical effects*	Structure
Acetylcholine (ACh)	Fast excitation; slow inhibition	$\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OCH}_2\text{CH}_2-\underset{\text{CH}_3}{\overset{\text{CH}_3}{\text{N}^+}}-\text{CH}_3$
Glycine (Gly)	Fast inhibition	$\begin{array}{c} \text{H} \\   \\ ^+\text{H}_3\text{N}-\text{C}-\text{H} \\   \\ \text{COO}^- \end{array}$
$\gamma$ -Aminobutyric acid (GABA)	Fast inhibition; slow inhibition	$^+\text{H}_3\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{COO}^-$
Glutamate (Glu)	Fast excitation; slow change in postsynaptic metabolism	$\begin{array}{c} \text{H} \\   \\ ^+\text{H}_3\text{N}-\text{C}-\text{CH}_2-\text{CH}_2-\text{COO}^- \\   \\ \text{COO}^- \end{array}$

\*Notice that the effect of a neurotransmitter depends on the properties of the postsynaptic cell. For most neurotransmitters, however, it is possible to identify their most probable effect.

Presynaptic terminal

Postsynaptic cell

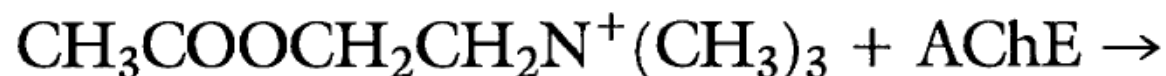






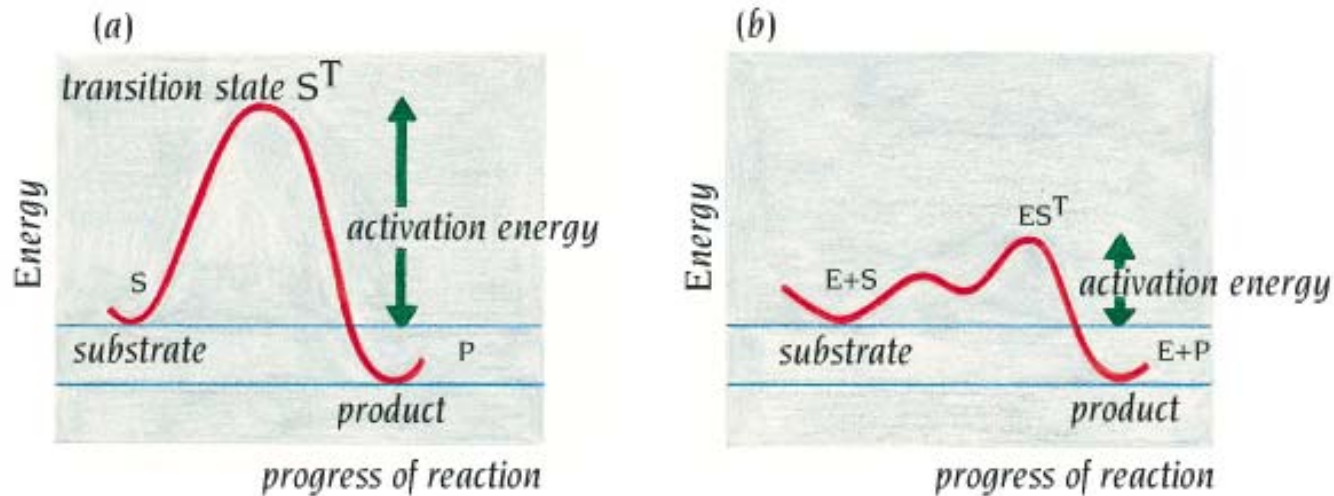
**Acetylcholine (ACh)**

# The reaction



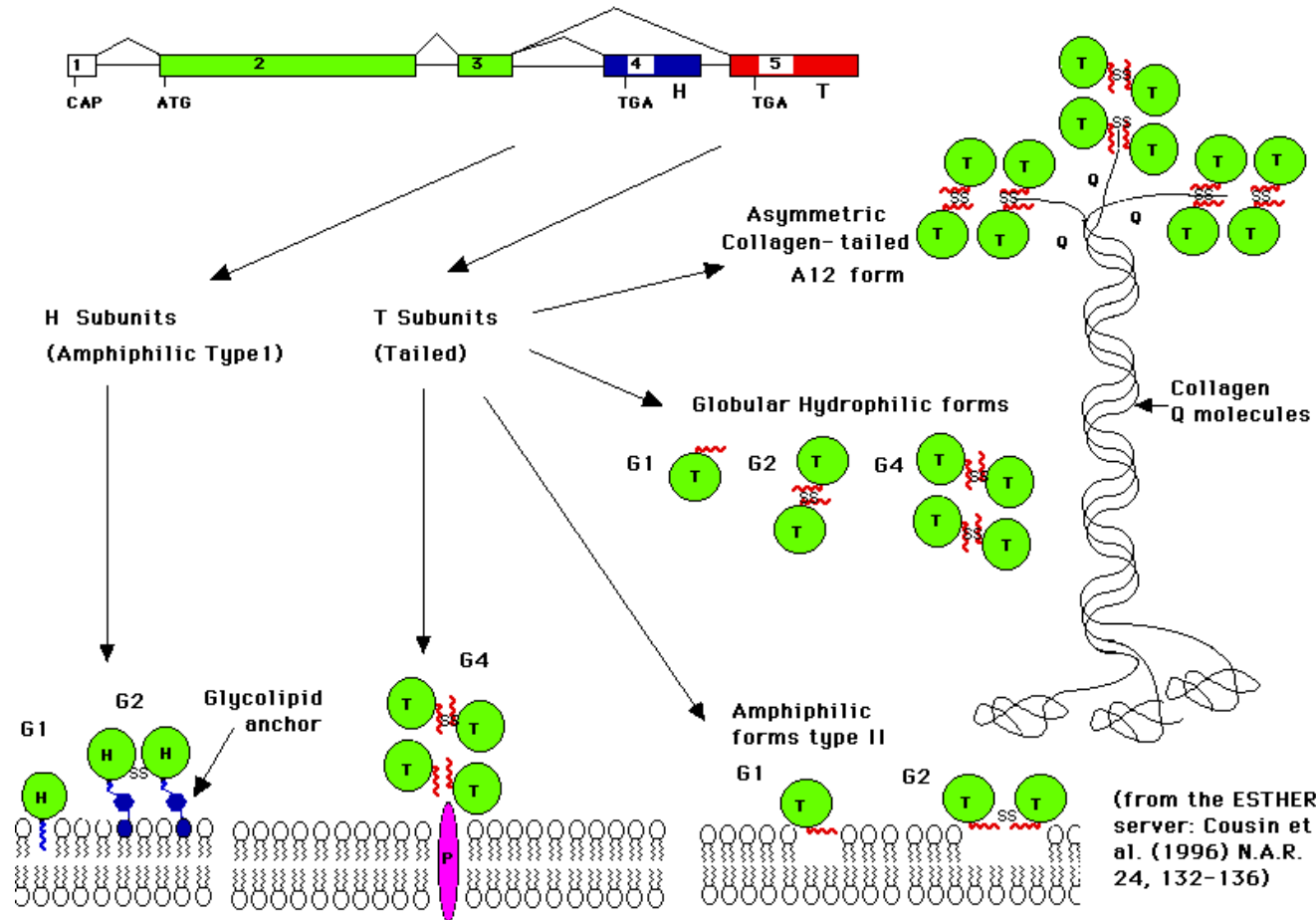
- Reaction occurs in steps
- Enzyme-substrate intermediate
- Ester hydrolysis (cf amide hydrolysis of a protease)

# How enzymes work



- Catalysis works by lowering the energy of the transition state
- Can lower the energy of the transition state by binding to it in preference to binding to either substrate or product
- Acetylcholinesterase does this well ( $k_{\text{cat}}/K_m > 10^8 \text{ M}^{-1}\text{sec}^{-1}$ ), which is at the diffusion limit for substrate encounter with enzyme
- Which brings MEPP (or synaptic potential) to a quick end

# Molecular forms



- Multiple products of a single gene
- Anchor AChase to the synaptic cleft (on presynaptic cell membrane, or on extracellular matrix)

# AChase inhibitors

- Famous nerve gasses
  - VX
  - Form covalent bond with AChase, killing it
  - Form bond at active site (serine)
- Alzheimer's treatments
  - Noncovalent inhibitors
  - Stimulate activity at weak cholinergic synapses

