

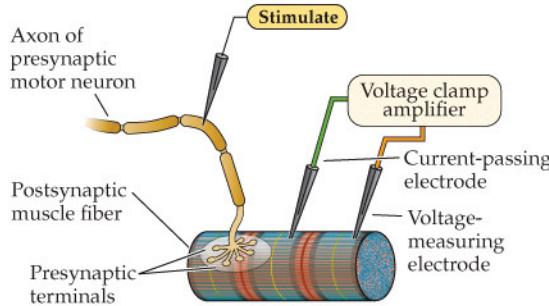
BMD ENG 301 Quantitative Systems Physiology (Nervous System)

Lecture 11: Neurotransmitters
2022_v3

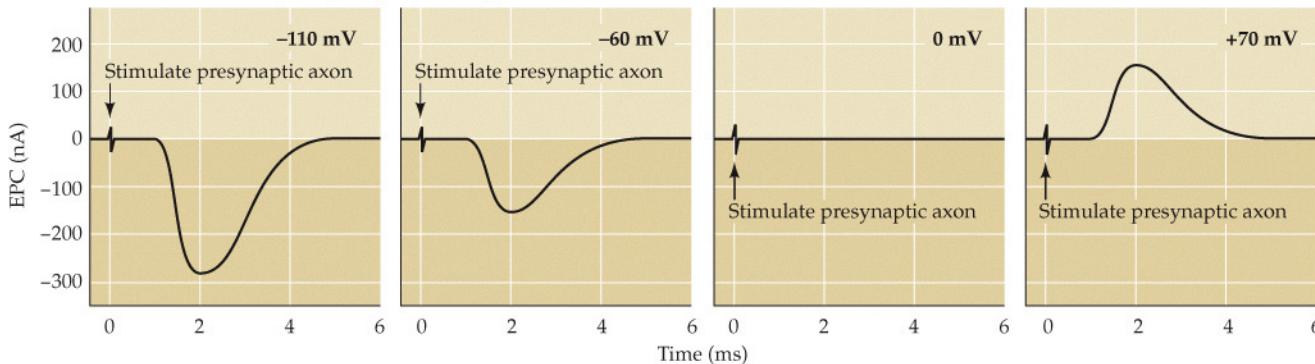
Professor Malcolm A. MacIver

Influence of the postsynaptic membrane potential on end plate currents

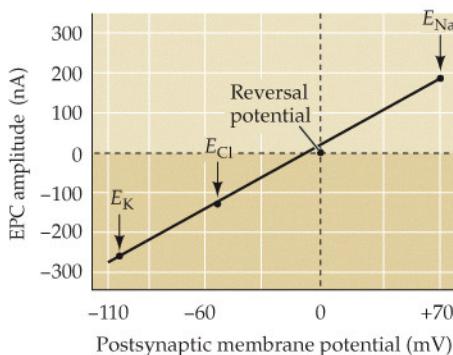
(A) Scheme for voltage clamping postsynaptic muscle fiber



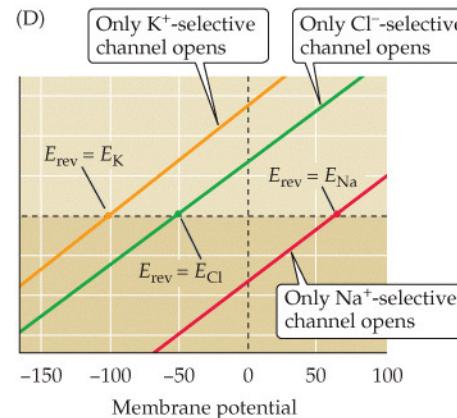
(B) Effect of membrane voltage on postsynaptic end plate currents (EPCs)



(C)



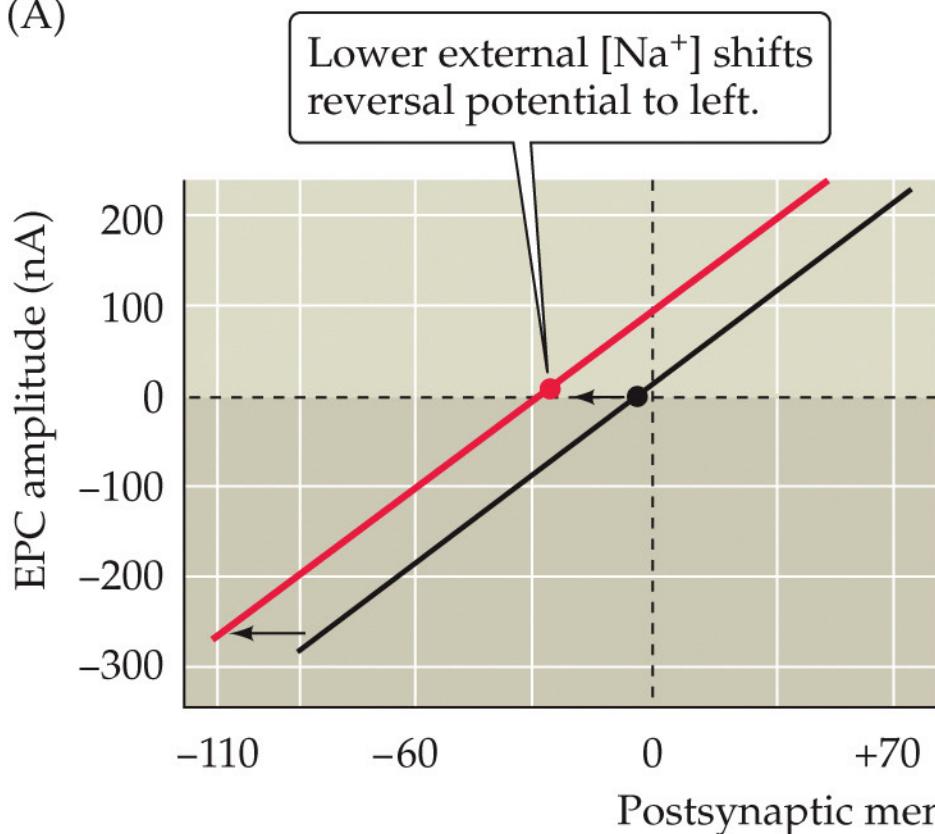
(D)



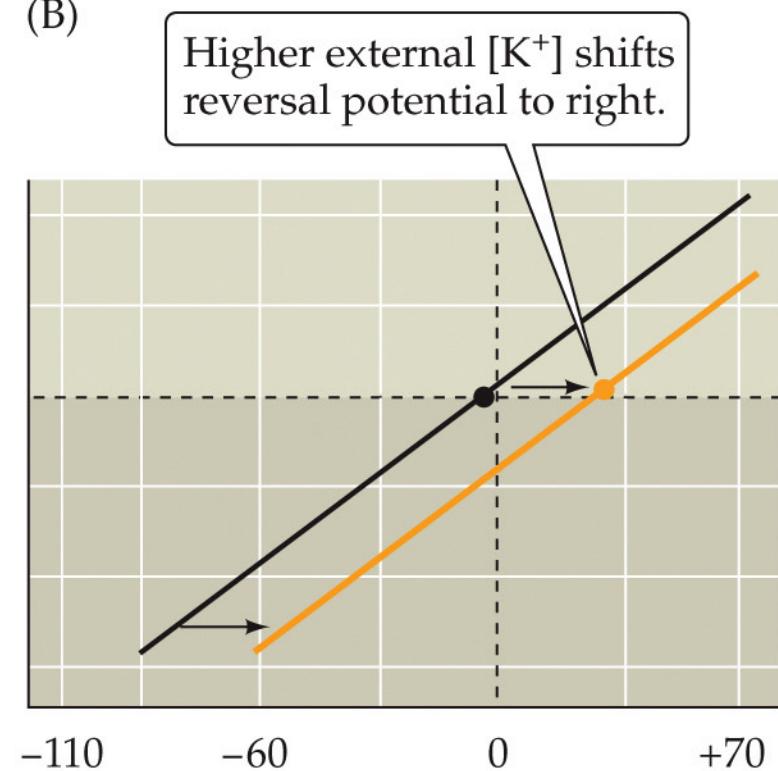
After Takeuchi and Takeuchi (1960). *J. Physiol.* 154: 52–67.

Reversal potential of the end plate current changes when ion gradients change

(A)



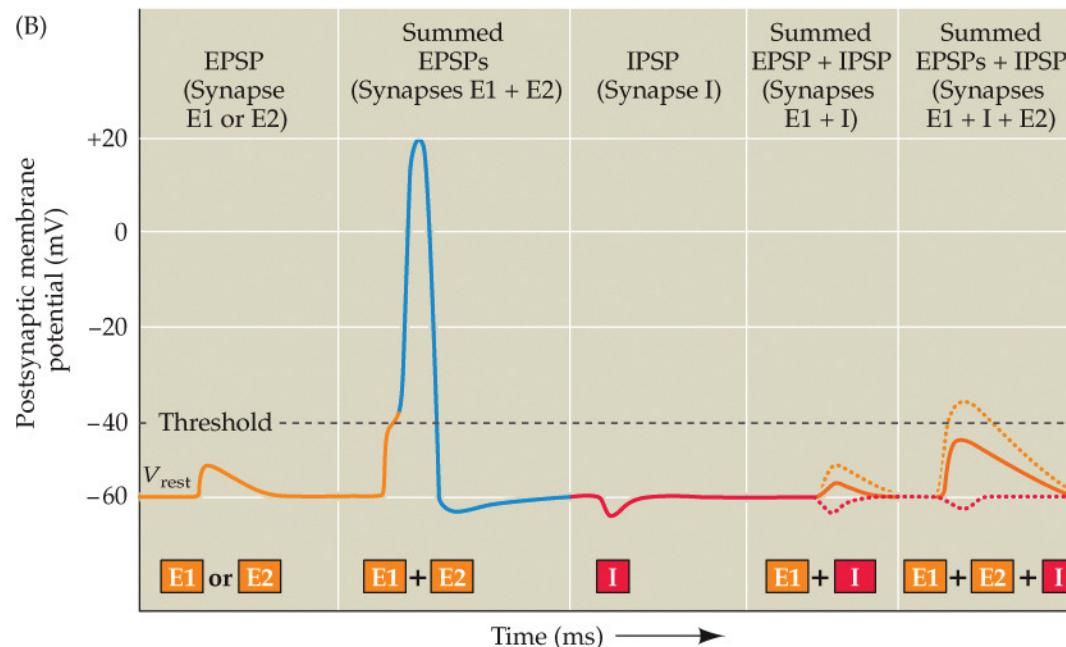
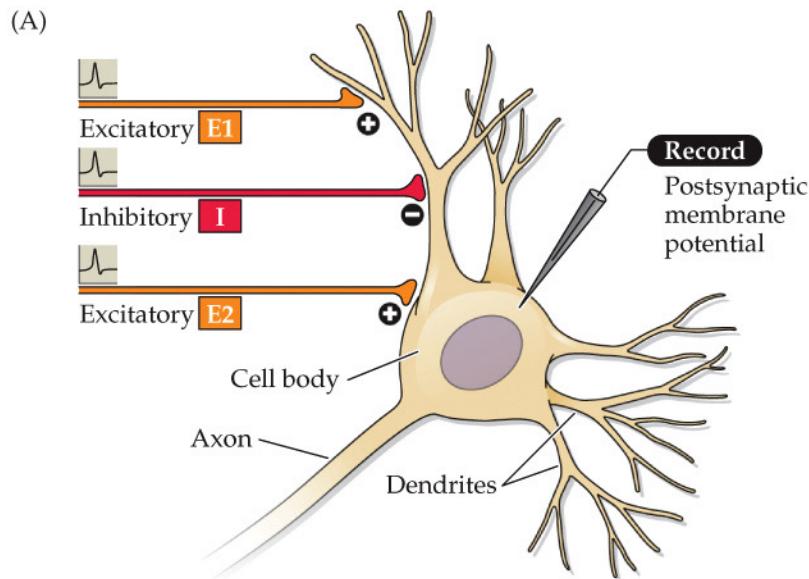
(B)



After Takeuchi and Takeuchi (1960) *J. Physiol.* 154: 52–67.

NEUROSCIENCE 6e, Figure 5.17
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Summation of postsynaptic potentials

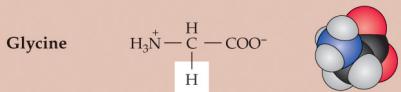
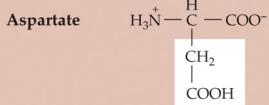
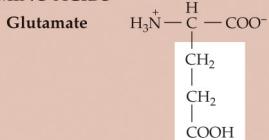


Examples of small-molecule and peptide neurotransmitters

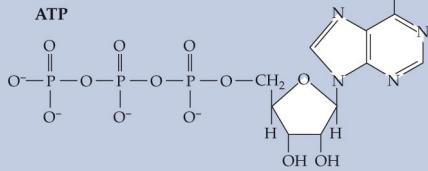
SMALL-MOLECULE NEUROTRANSMITTERS



AMINO ACIDS

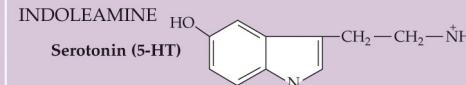
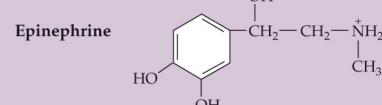
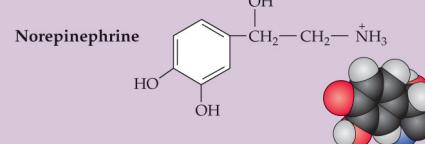
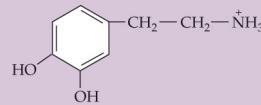


PURINES

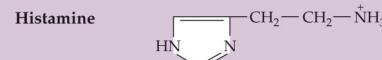


BIOGENIC AMINES

CATECHOLAMINES

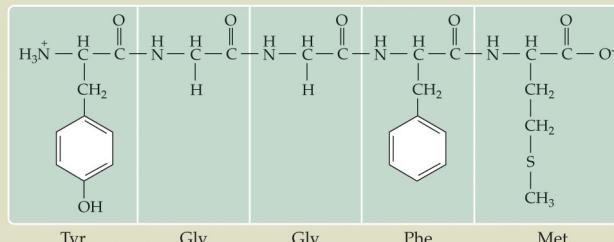
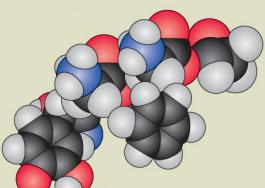


IMIDAZOLEAMINE



PEPTIDE NEUROTRANSMITTERS (more than 100 peptides, usually 3–36 amino acids long)

Example: Methionine enkephalin (Tyr–Gly–Gly–Phe–Met)



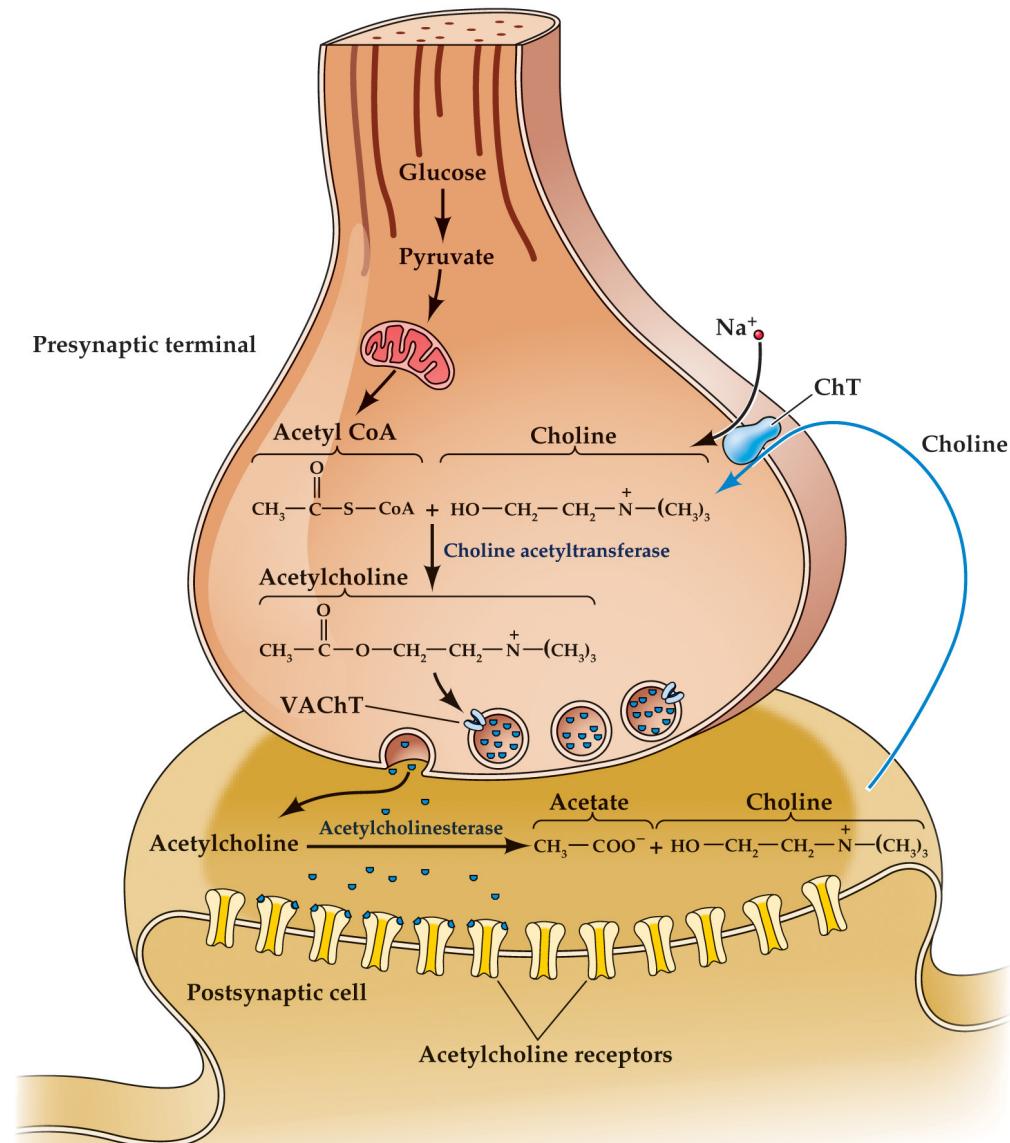
Functional Features of the Major Neurotransmitters

TABLE 6.1 ■ Functional Features of the Major Neurotransmitters

Neurotransmitter	Postsynaptic effect ^a	Precursor(s)	Rate-limiting step in synthesis	Removal mechanism	Type of vesicle
ACh	Excitatory	Choline + acetyl CoA	ChAT	AChE	Small, clear
Glutamate	Excitatory	Glutamine	Glutaminase	Transporters	Small, clear
GABA	Inhibitory	Glutamate	GAD	Transporters	Small, clear
Glycine	Inhibitory	Serine	Phosphoserine	Transporters	Small, clear
Catecholamines (epinephrine, norepinephrine, dopamine)	Excitatory	Tyrosine	Tyrosine hydroxylase	Transporters, MAO, COMT	Small, dense-core or large, irregular dense-core
Serotonin (5-HT)	Excitatory	Tryptophan	Tryptophan hydroxylase	Transporters, MAO	Large, dense-core
Histamine	Excitatory	Histidine	Histidine decarboxylase	Transporters	Large, dense-core
ATP	Excitatory	ADP	Mitochondrial oxidative phosphorylation; glycolysis	Hydrolysis to AMP and adenosine	Small, clear
Neuropeptides	Excitatory and inhibitory	Amino acids (protein synthesis)	Synthesis and transport	Proteases	Large, dense-core
Endocannabinoids	Inhibits inhibition	Membrane lipids	Enzymatic modification of lipids	Hydrolysis by FAAH	None
Nitric oxide	Excitatory and inhibitory	Arginine	Nitric oxide synthase	Spontaneous oxidation	None

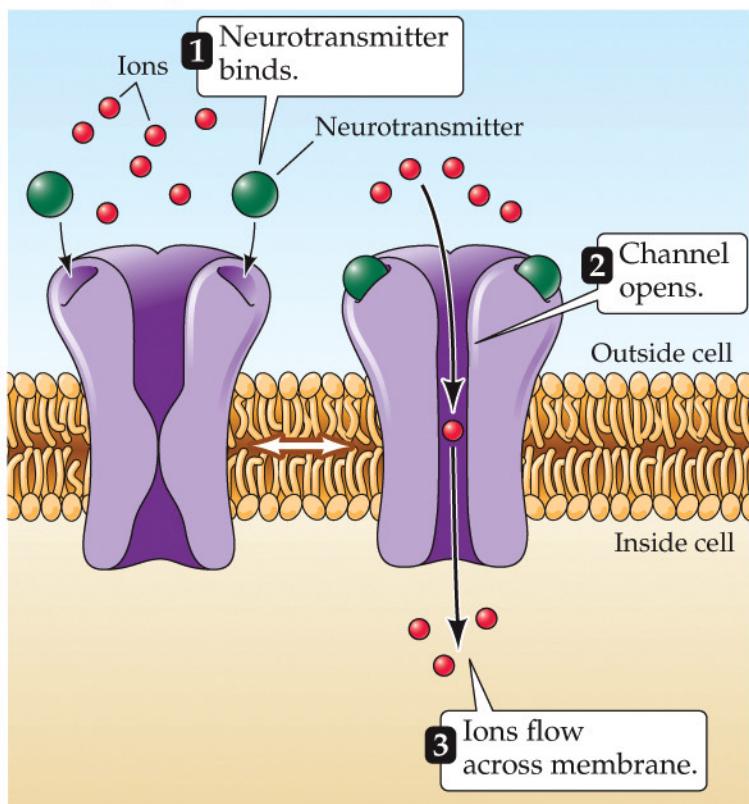
^aThe most common postsynaptic effect is indicated; the same transmitter can elicit postsynaptic excitation or inhibition, depending on the nature of the receptors and ion channels activated by transmitter.

Acetylcholine metabolism in cholinergic nerve terminals

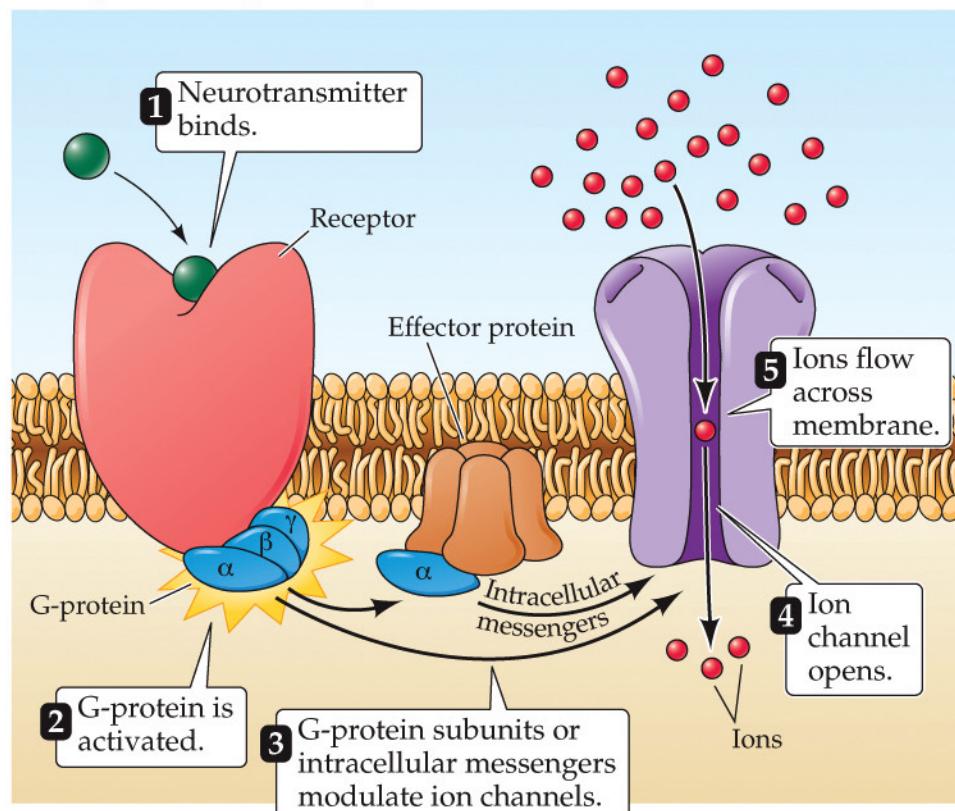


Two different types of neurotransmitter receptors

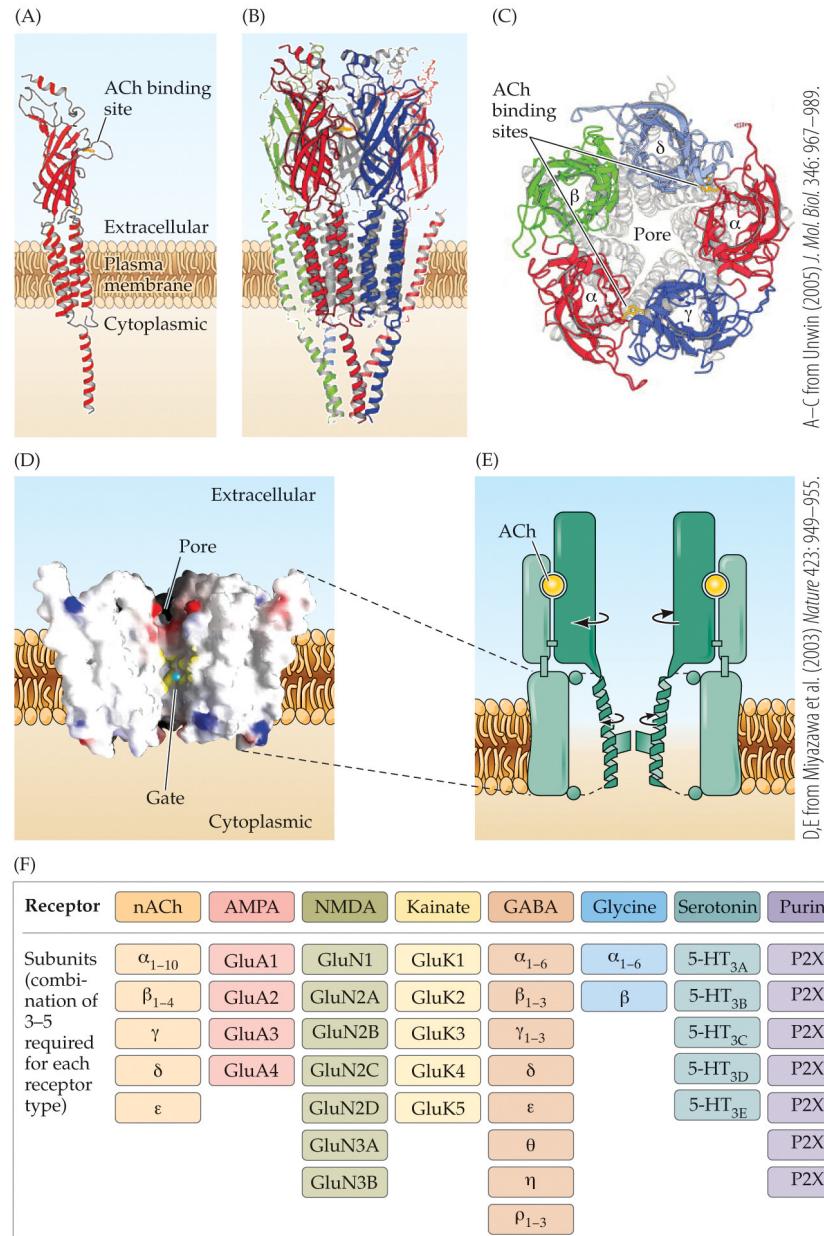
(A) Ligand-gated ion channels



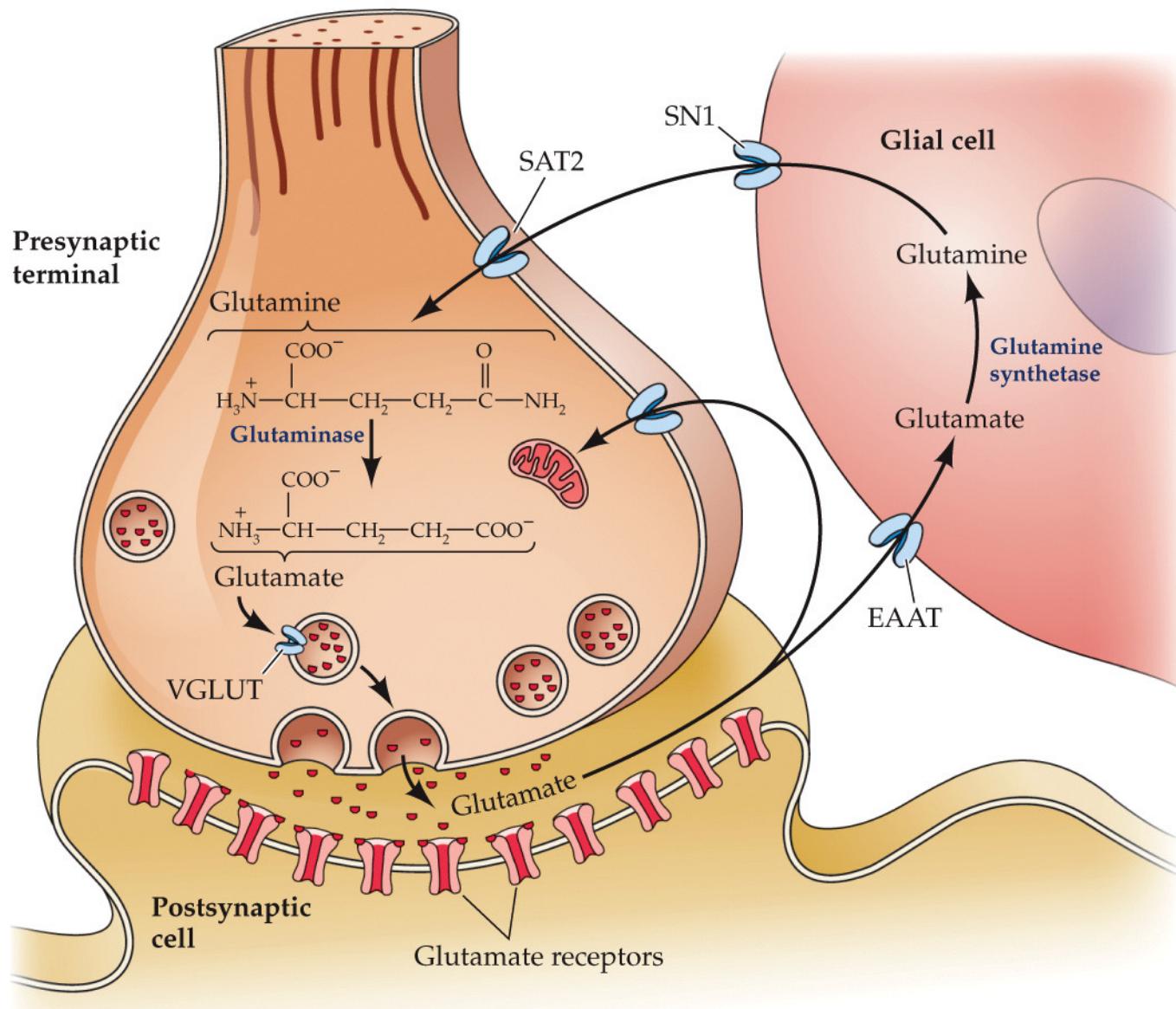
(B) G-protein-coupled receptors



Structure of the nicotinic ACh receptor

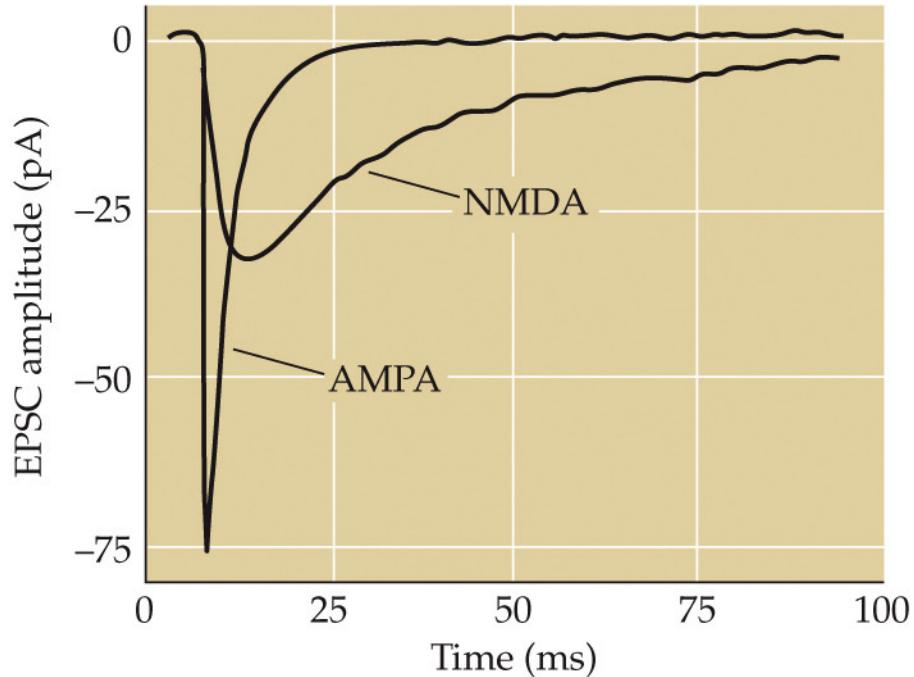


Glutamate synthesis and cycling between neurons and glia

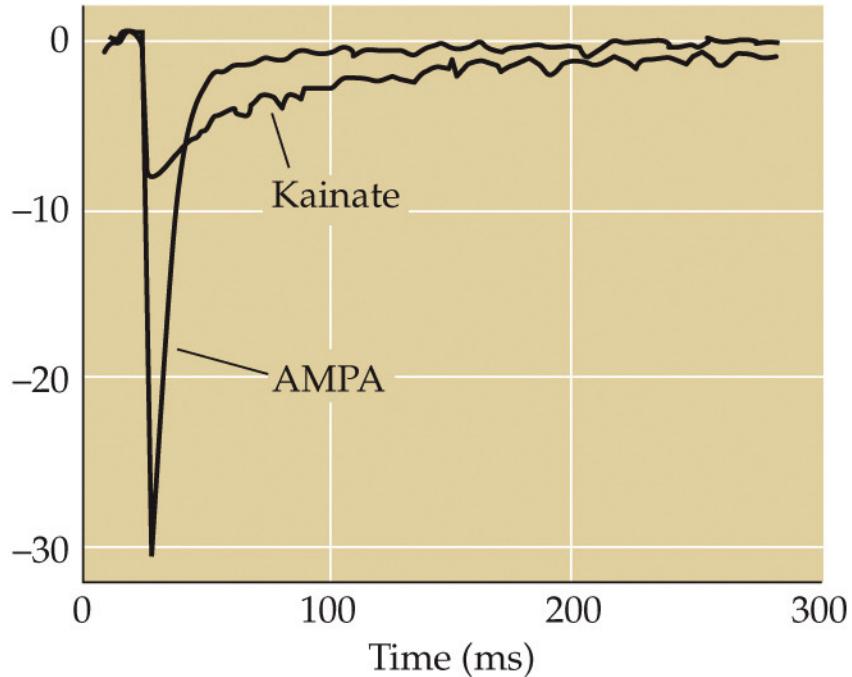


Postsynaptic responses mediated by ionotropic glutamate receptors

(A)



(B)

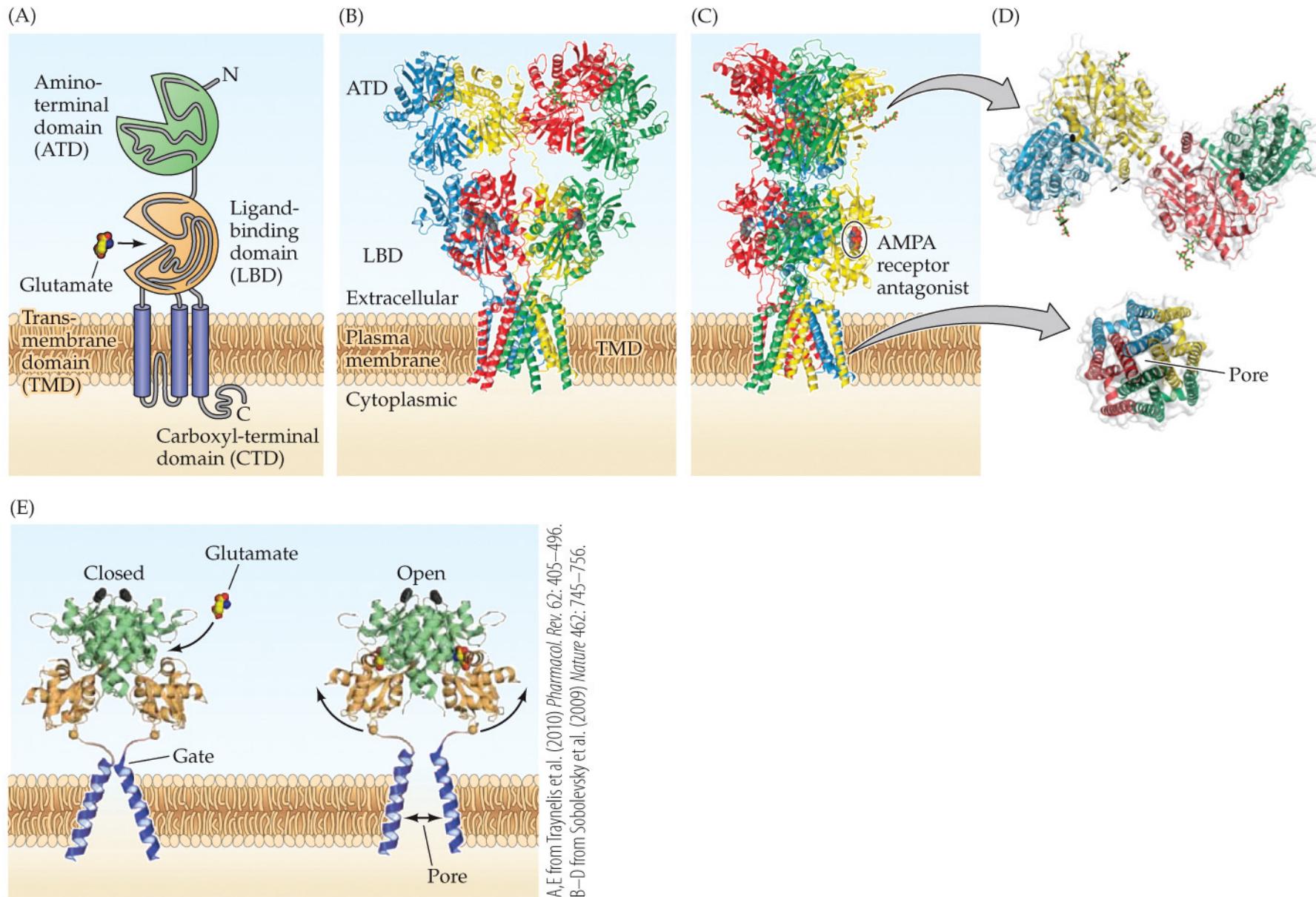


A after Watanabe et al. (2005) *J. Neurosci.* 25: 1024–1033. B from Mott et al. (2008) *J. Neurosci.* 28: 1659–1671.

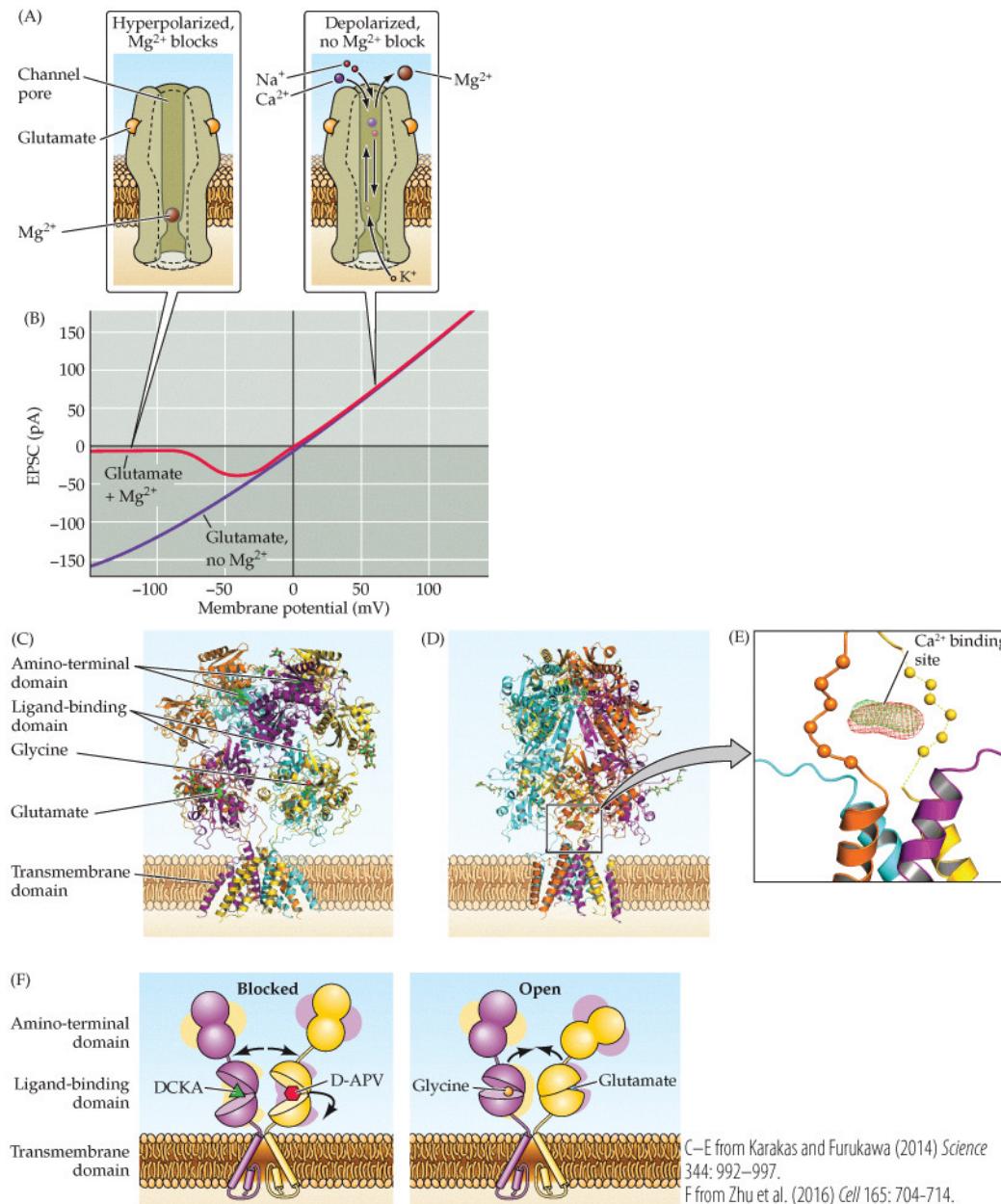
NEUROSCIENCE 6e, Figure 6.6

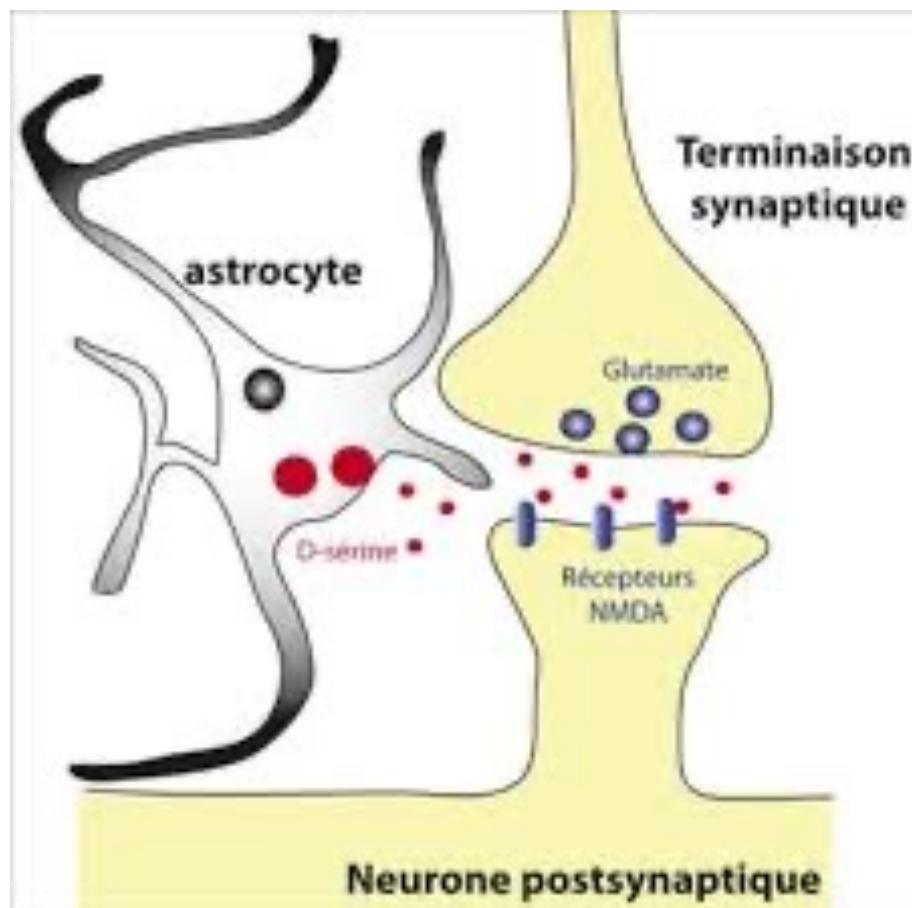
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Structure of the AMPA receptor

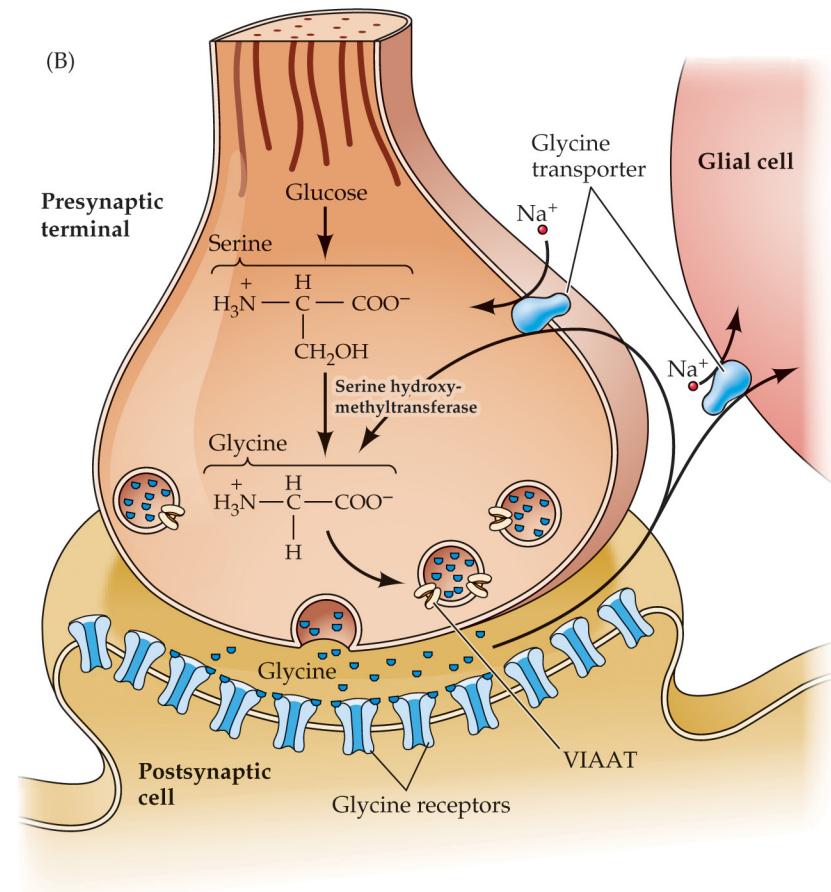
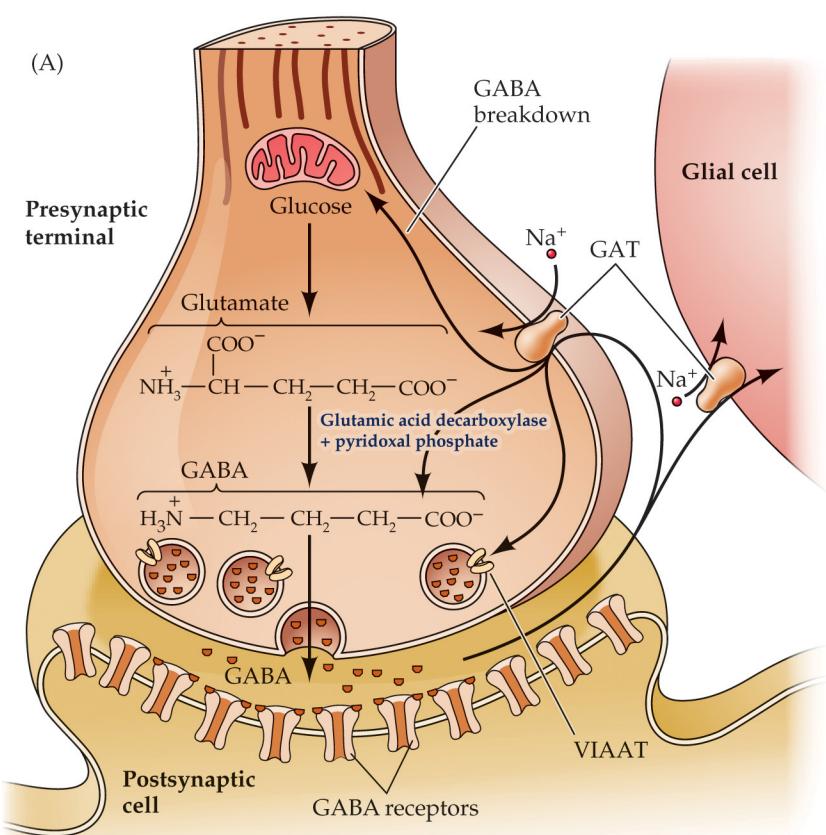


Function and structure of the NMDA receptor



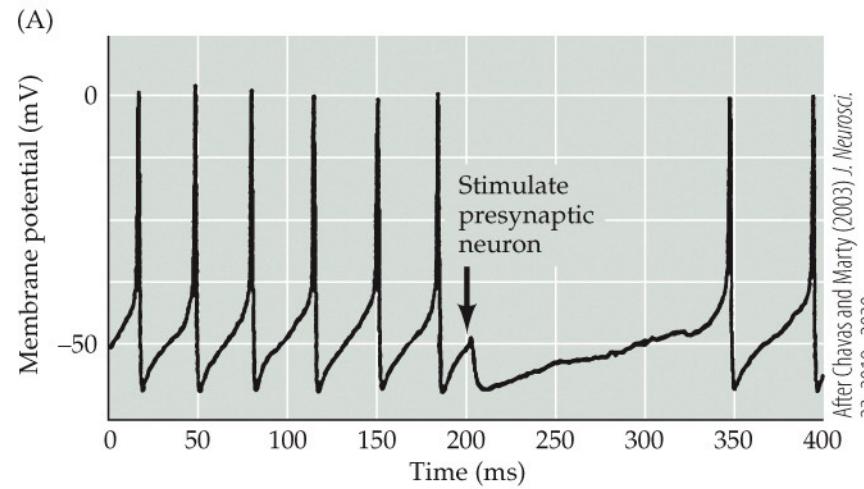


Synthesis, release, and reuptake of the inhibitory neurotransmitters GABA and glycine

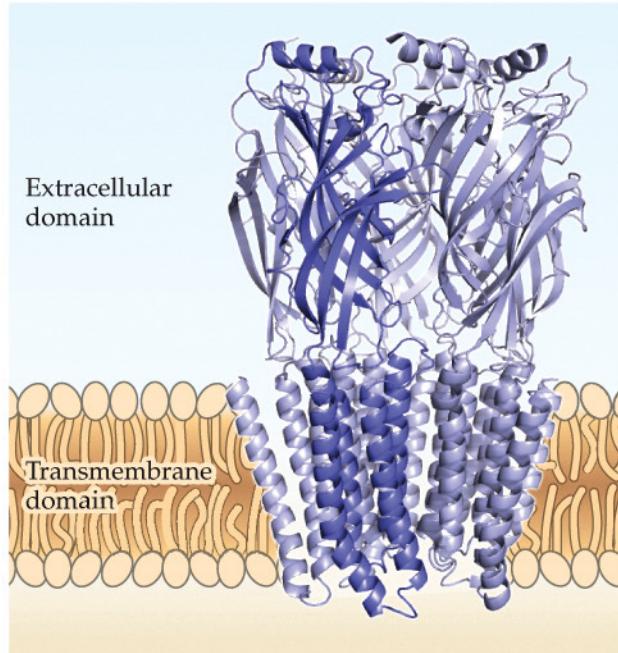


NEUROSCIENCE 6e, Figure 6.10
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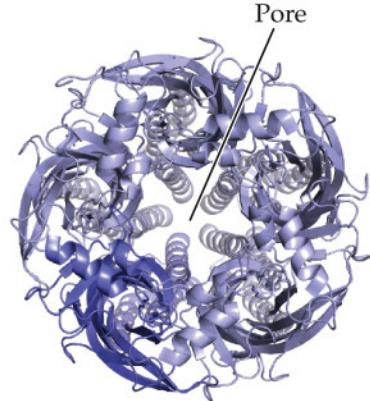
Ionotropic GABA receptors



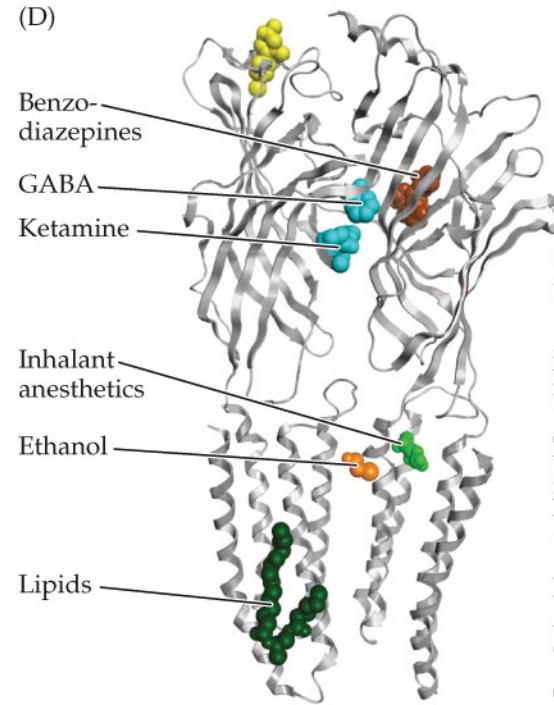
(B) Side view



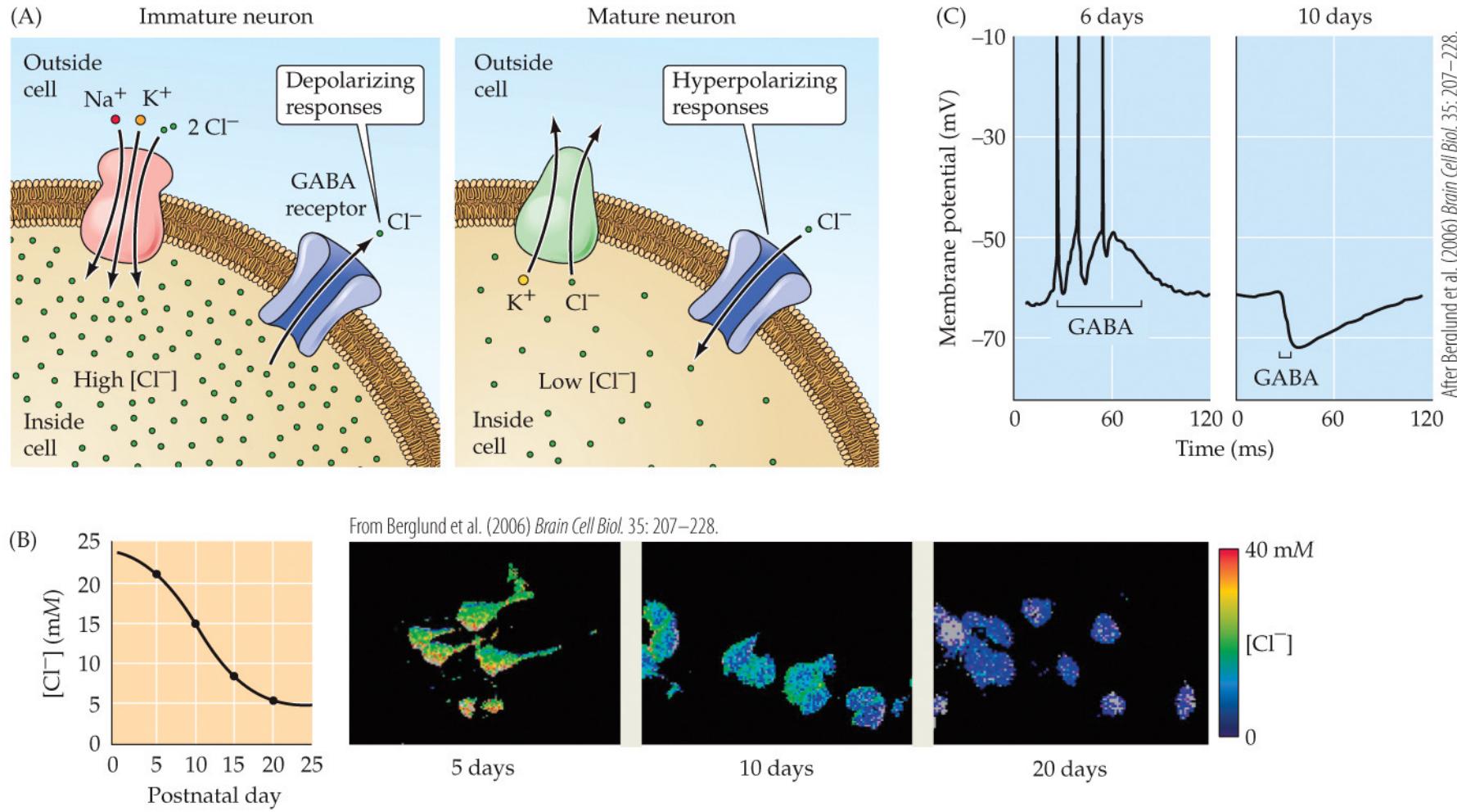
(C) Top view



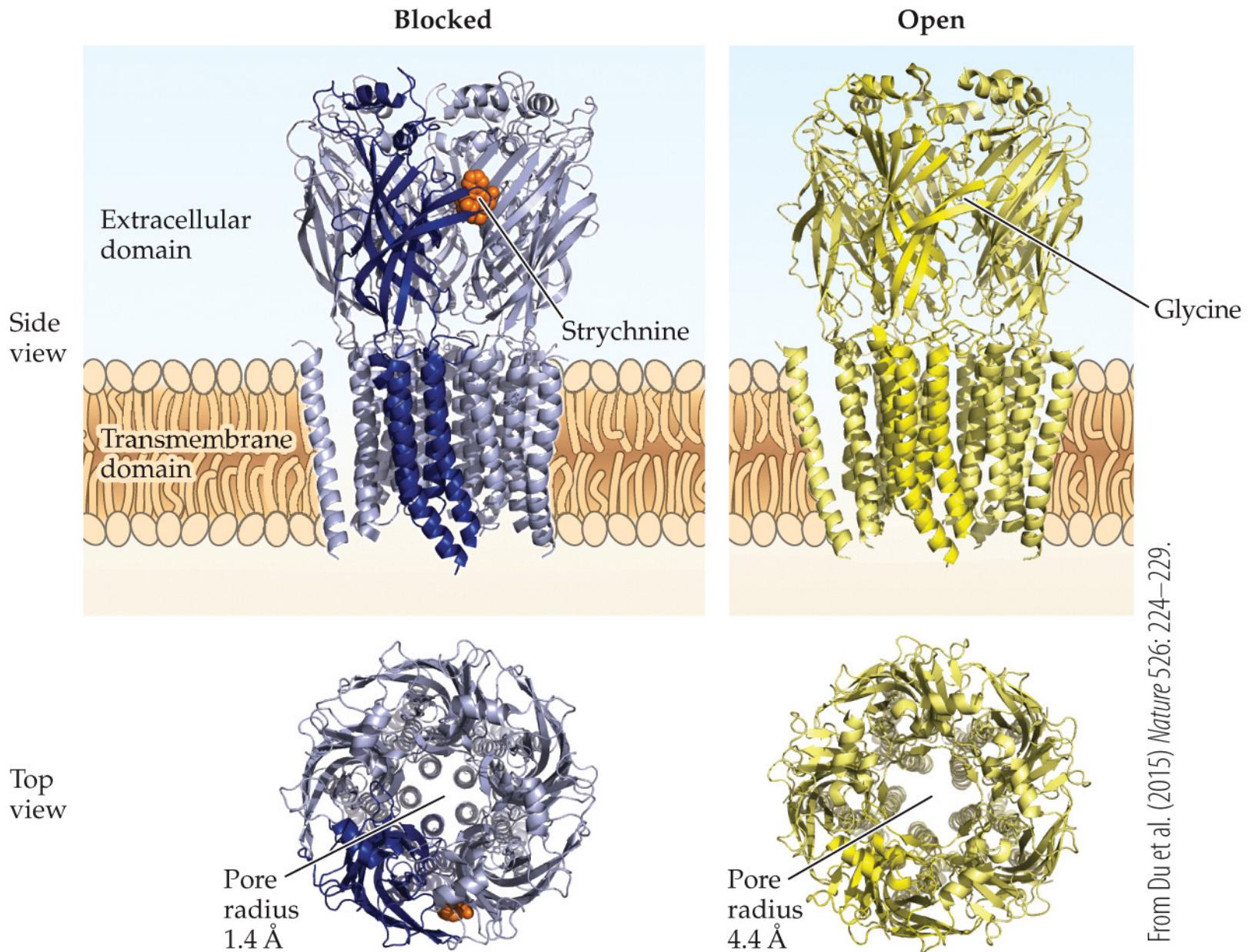
(D)



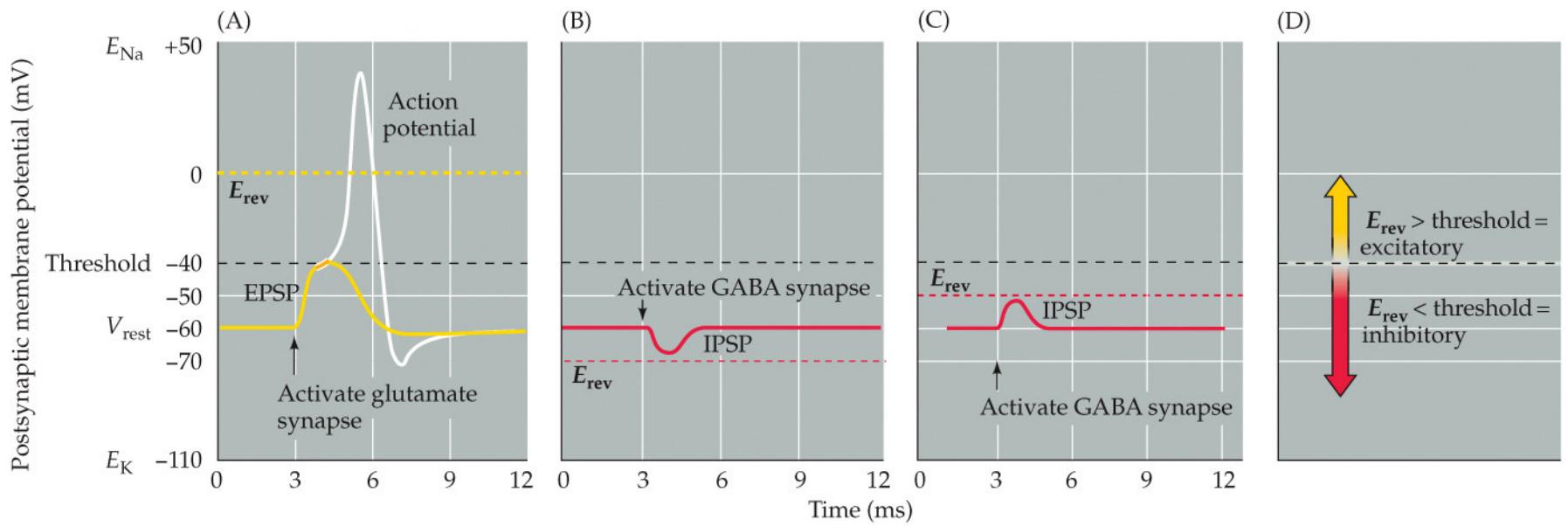
Excitatory Actions of GABA in the Developing Brain



Gating of glycine receptors



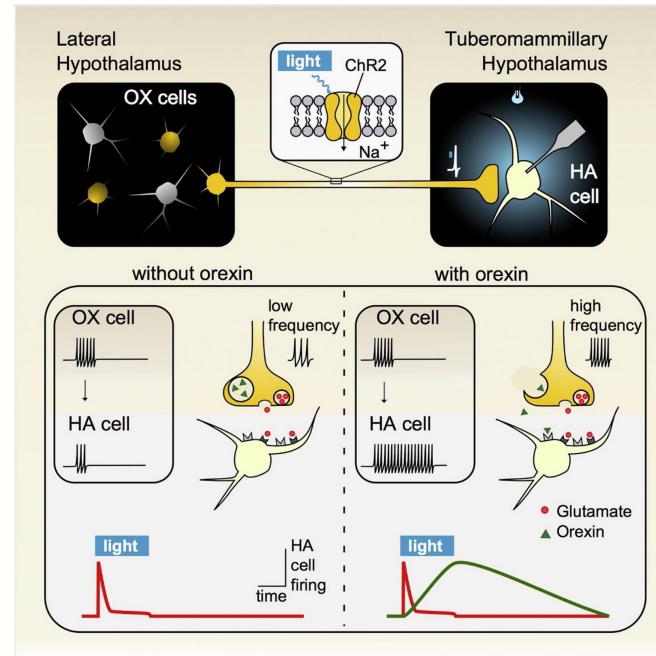
Reversal potentials and threshold potentials determine postsynaptic excitation and inhibition



NEUROSCIENCE 6e, Figure 5.19
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Chap 5, p.89:

Formal criteria have been established to definitively identify a substance as a neurotransmitter. These criteria have led to the identification of more than 100 different neurotransmitters, which can be classified into two broad categories: small-molecule neurotransmitters, such as ACh, and neuropeptides (see Chapter 6). Having more than one transmitter diversifies the physiological repertoire of synapses. Multiple neurotransmitters can produce different types of responses on individual postsynaptic cells. For example, a neuron can be excited by one type of neurotransmitter and inhibited by another type of neurotransmitter. The speed of postsynaptic responses produced by different transmitters also differs, allowing control of electrical signaling over different timescales. In general, small-molecule neurotransmitters mediate rapid synaptic actions, whereas neuropeptides tend to modulate slower, ongoing neuronal functions. In some cases, neurons synthesize and release two or more different neurotransmitters; in this case, the molecules are called **co-transmitters**. Co-transmitters can be differentially released according to the pattern of synaptic activity, so that the signaling properties of such synapses change dynamically according to the rate of activity.



From: General Principles of Neuronal Co-transmission: Insights From Multiple Model Systems
By Erik Svensson et al. 2019

Amino acid sequences of neuropeptides

(A) Brain-gut peptides



(B) Opioid peptides



Amino acid properties

- Hydrophobic
- Polar, uncharged
- Acidic
- Basic

(C) Pituitary peptides



(D) Hypothalamic-releasing peptides



(E) Miscellaneous peptides



Endogenous Opioid Peptides

TABLE 6.2 ■ Endogenous Opioid Peptides

Name	Amino acid sequence ^a
Endorphins	
α -Endorphin	<i>Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-</i> Ser-Gln-Thr-Pro-Leu-Val-Thr
α -Neoendorphin	<i>Tyr-Gly-Gly-Phe-Leu-Arg-Lys-Tyr-Pro-</i> Lys
β -Endorphin	<i>Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-</i> Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu- Phe-Lys-Asn-Ala-Ile-Val-Lys-Asn- Ala-His-Lys-Gly-Gln
γ -Endorphin	<i>Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-</i> Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu
Enkephalins	
Leu-enkephalin	<i>Tyr-Gly-Gly-Phe-Leu</i>
Met-enkephalin	<i>Tyr-Gly-Gly-Phe-Met</i>
Dynorphins	
Dynorphin A	<i>Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-</i> Pro-Lys-Leu-Lys-Trp-Asp-Asn-Gln
Dynorphin B	<i>Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Gln-</i> Phe-Lys-Val-Val-Thr

^aNote the initial homology, indicated by italics.