

# BMD ENG 301 Quantitative Systems Physiology (Nervous System)

Lecture 11: Neurotransmitters

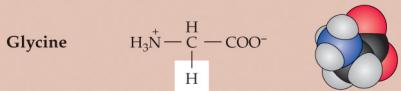
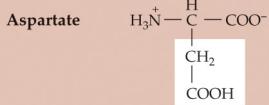
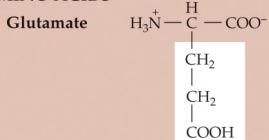
Professor Malcolm A. MacIver

# Examples of small-molecule and peptide neurotransmitters

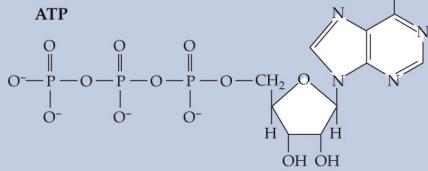
## SMALL-MOLECULE NEUROTRANSMITTERS



### AMINO ACIDS

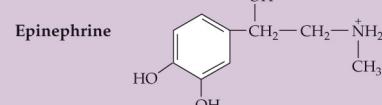
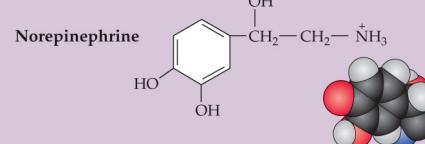
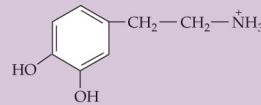


### PURINES

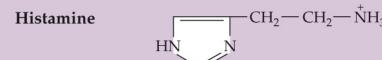


## BIOGENIC AMINES

### CATECHOLAMINES

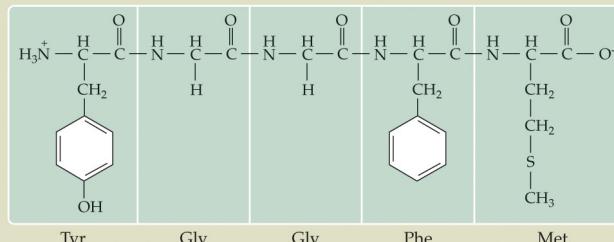
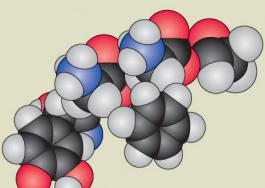


### IMIDAZOLEAMINE

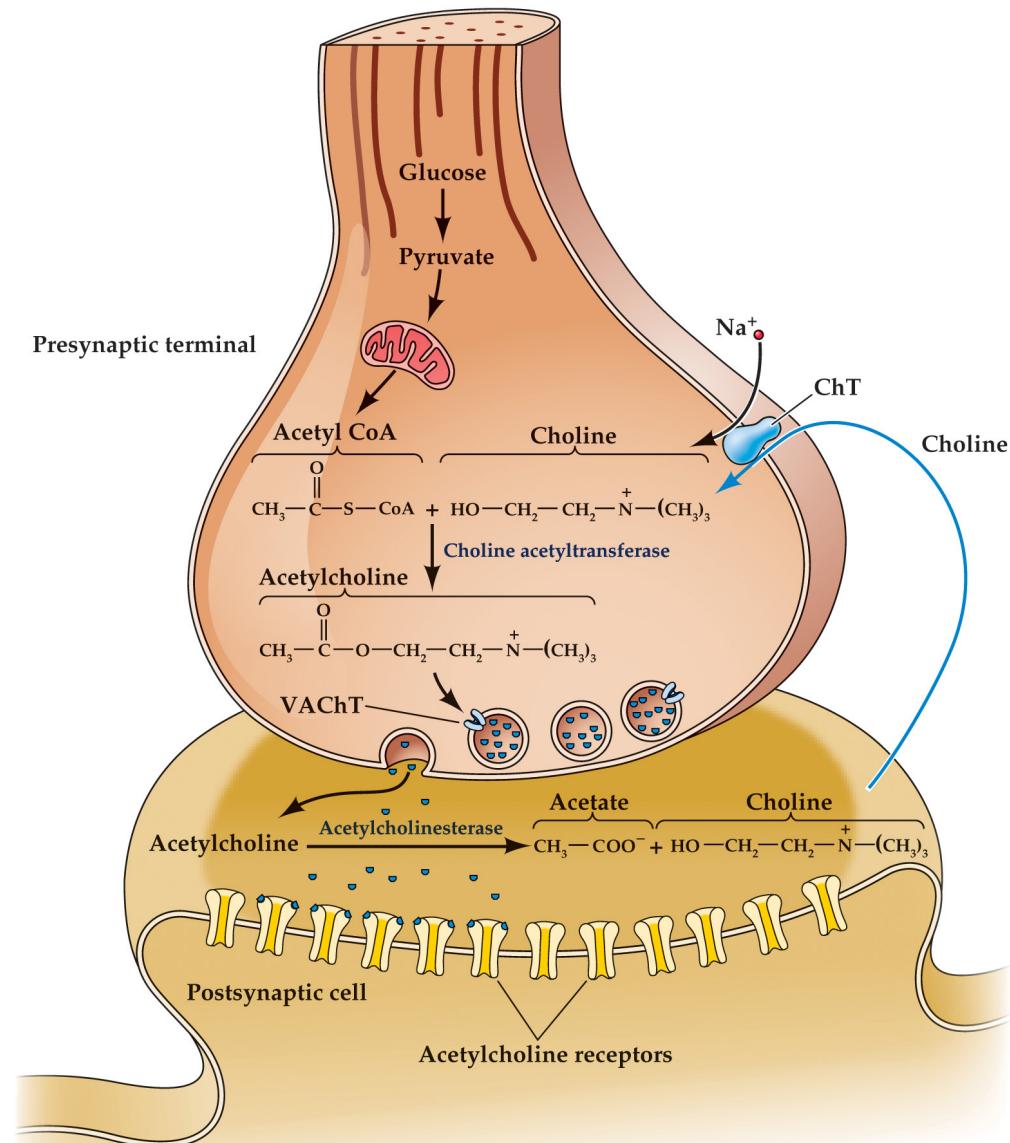


## PEPTIDE NEUROTRANSMITTERS (more than 100 peptides, usually 3–36 amino acids long)

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

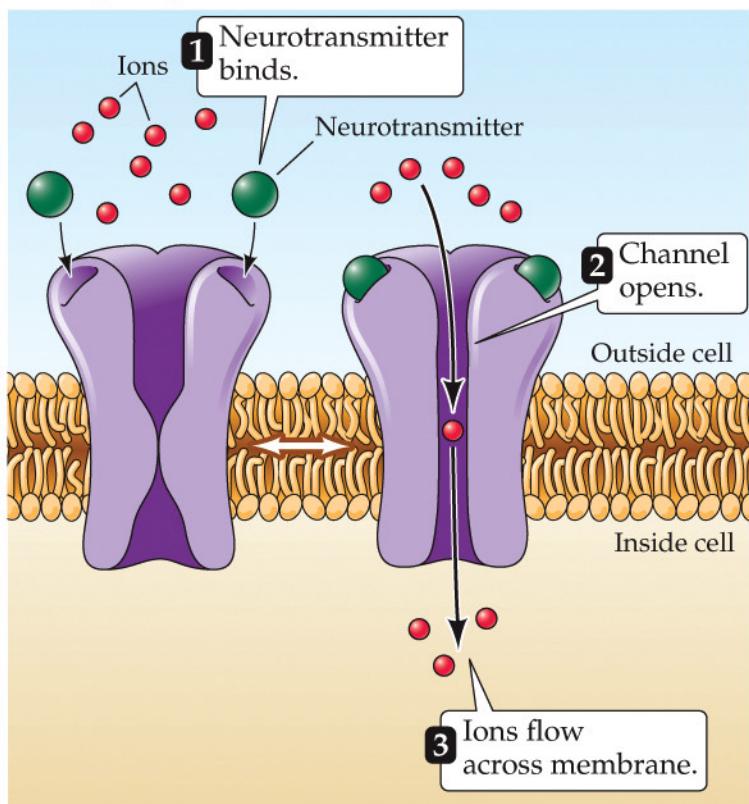


# Acetylcholine metabolism in cholinergic nerve terminals

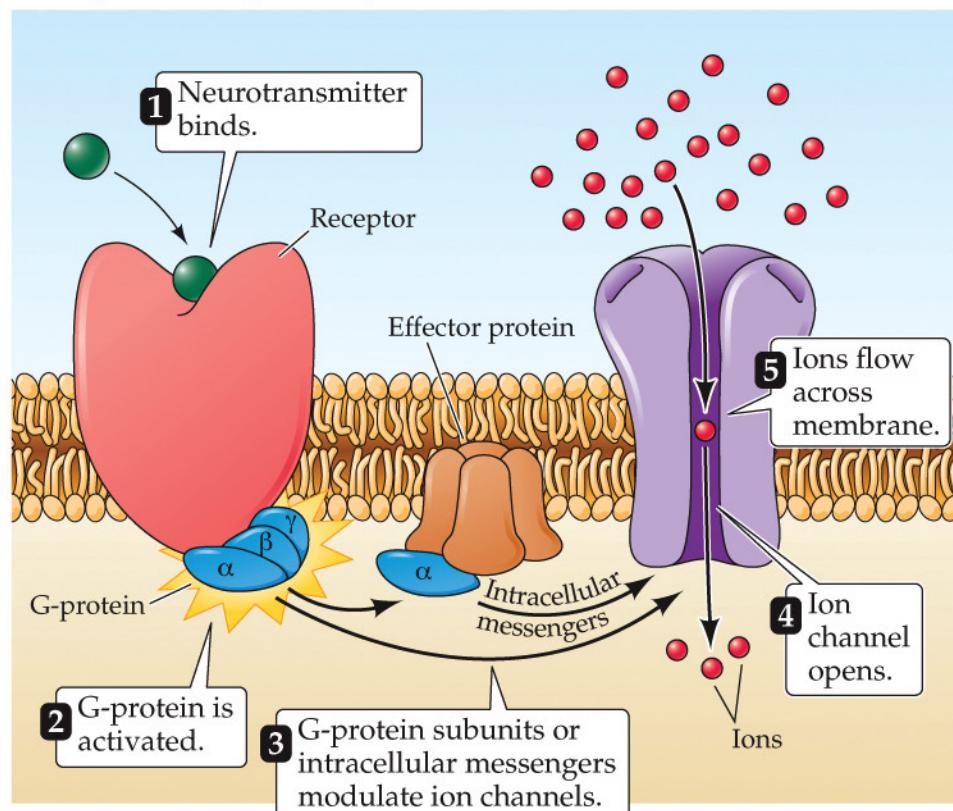


# Two different types of neurotransmitter receptors

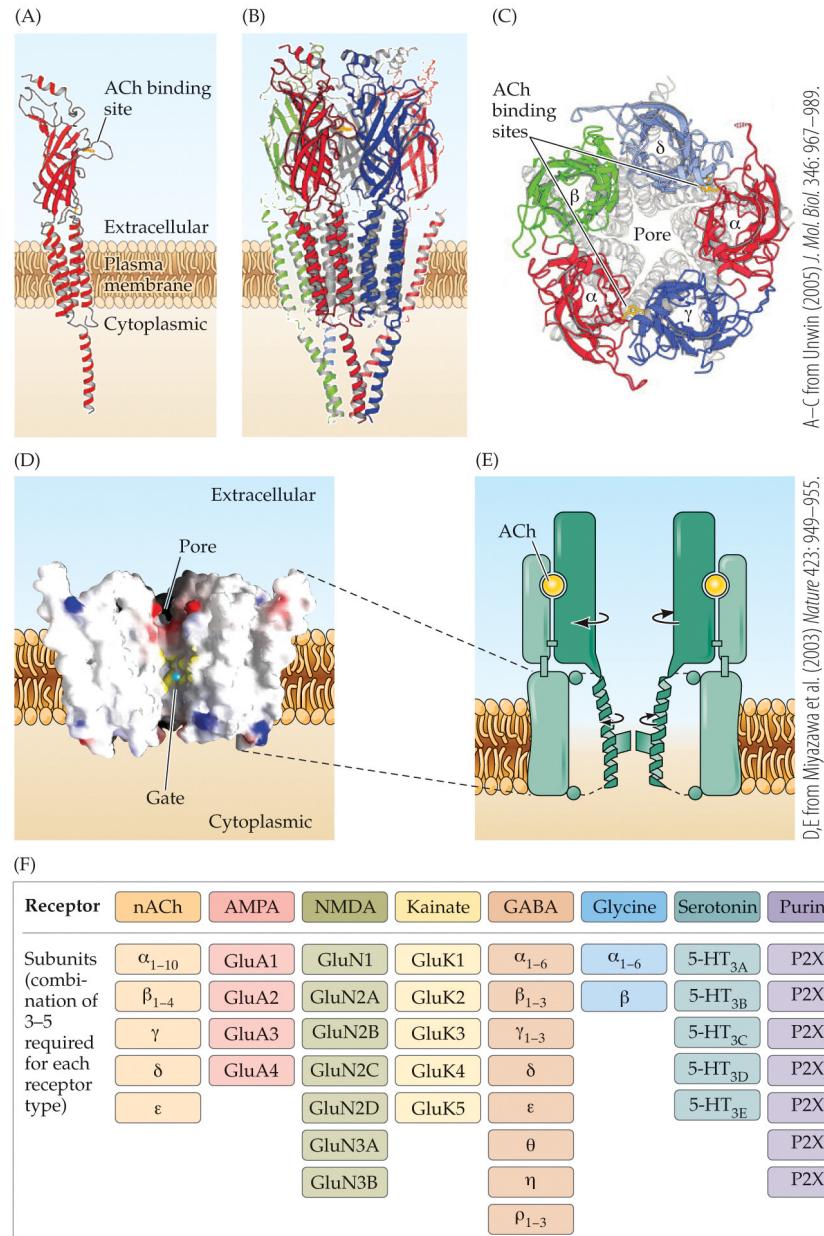
(A) Ligand-gated ion channels



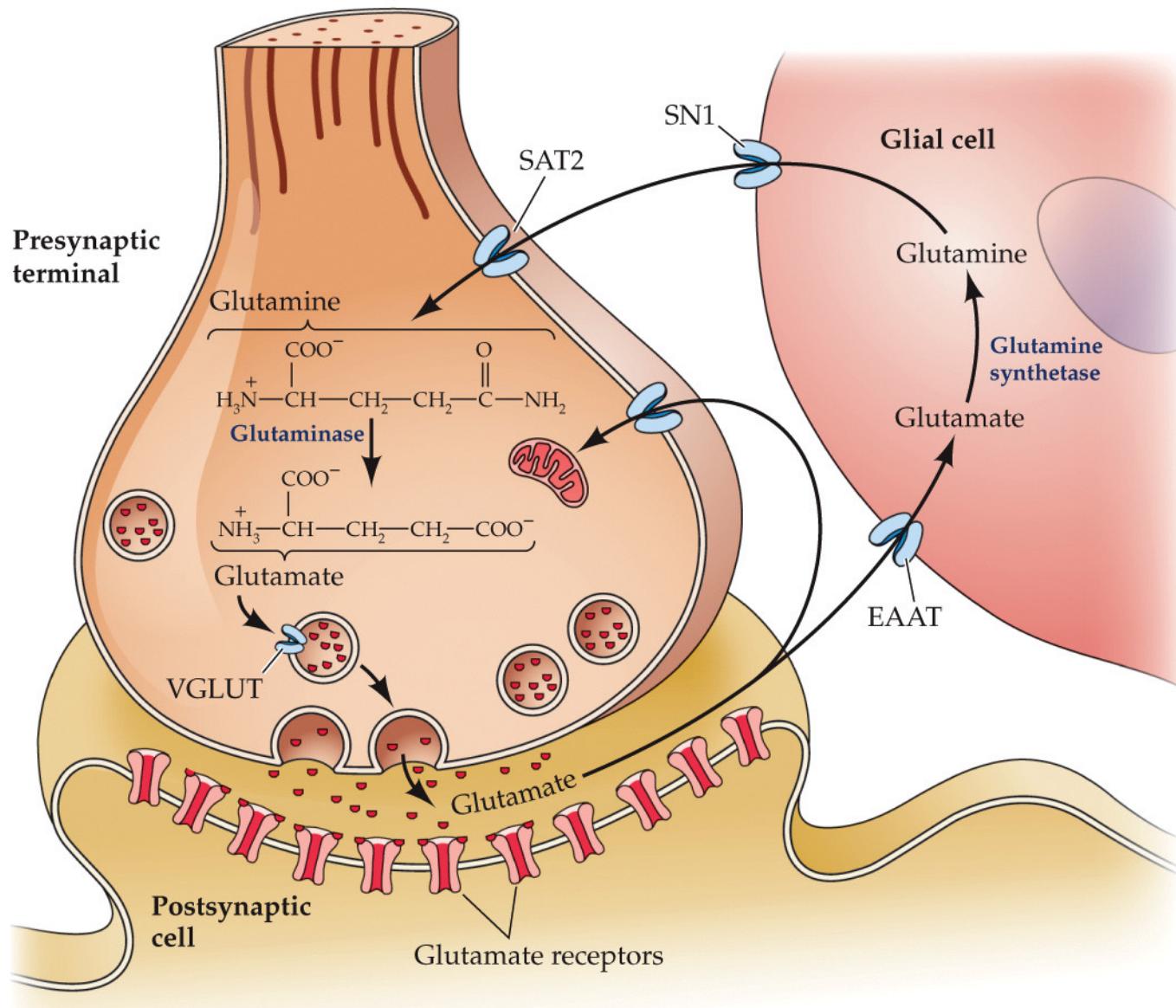
(B) G-protein-coupled receptors



# Structure of the nicotinic ACh receptor

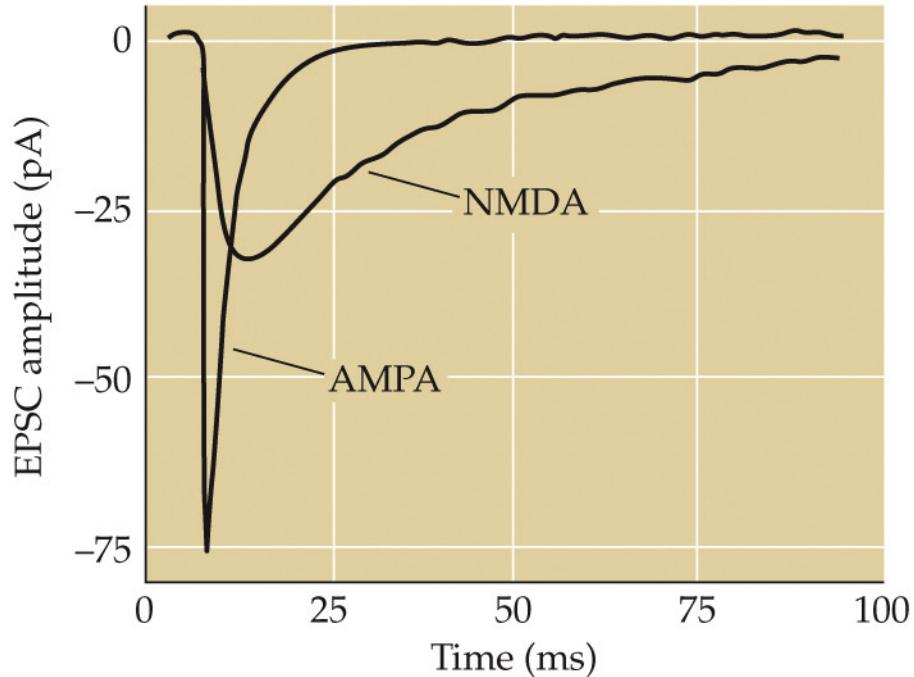


# Glutamate synthesis and cycling between neurons and glia

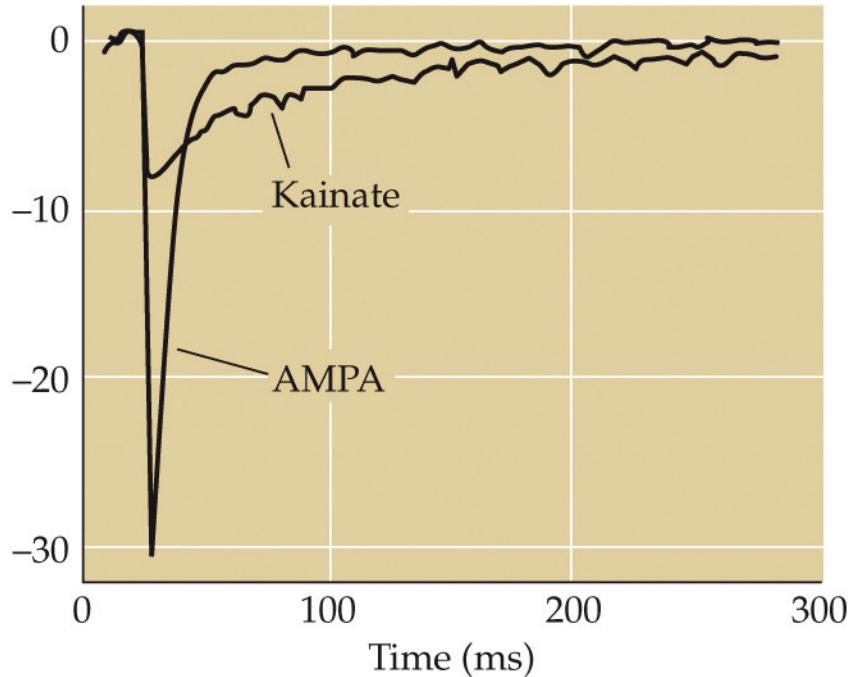


# Postsynaptic responses mediated by ionotropic glutamate receptors

(A)



(B)

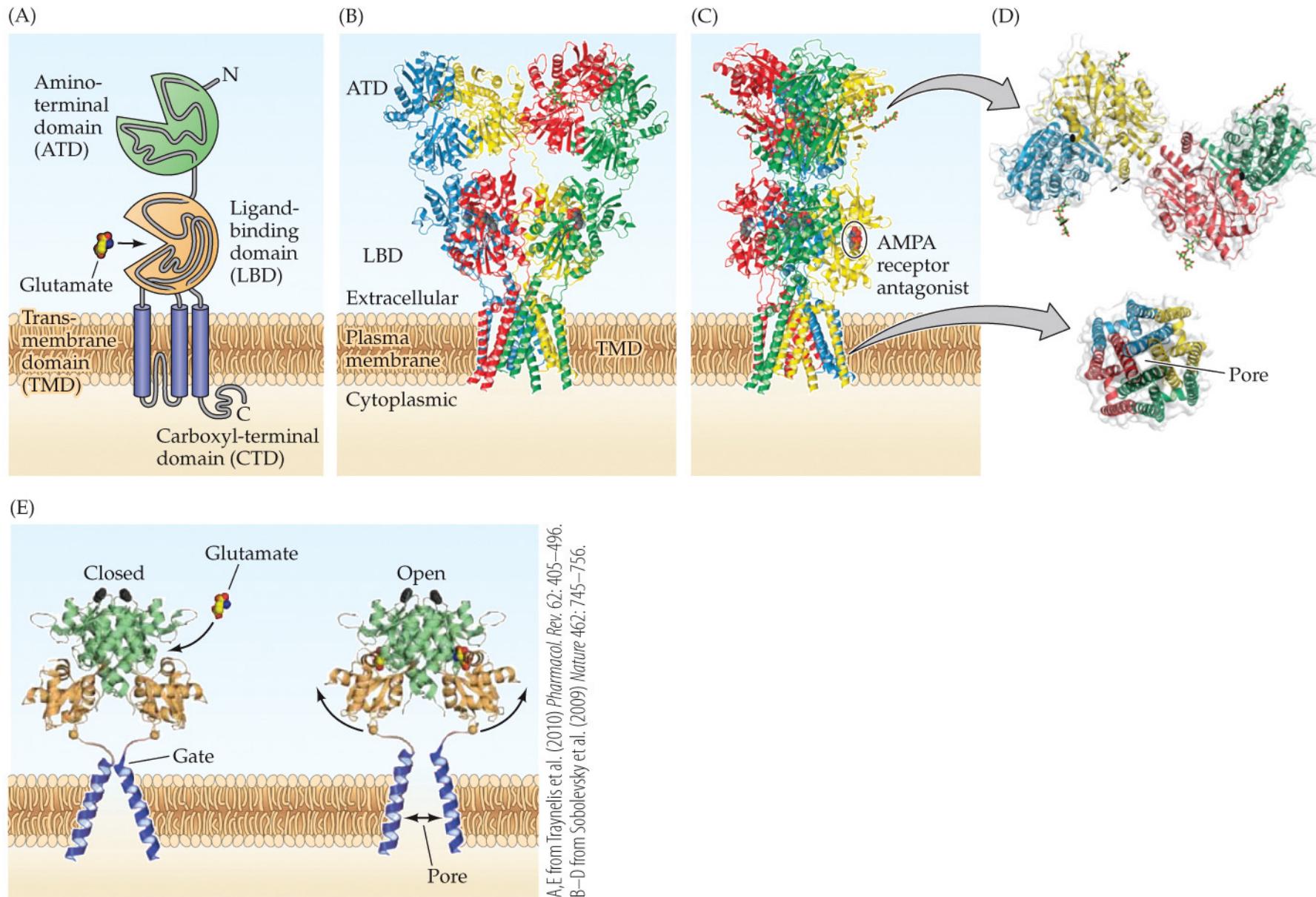


A after Watanabe et al. (2005) *J. Neurosci.* 25: 1024–1033. B from Mott et al. (2008) *J. Neurosci.* 28: 1659–1671.

**NEUROSCIENCE 6e, Figure 6.6**

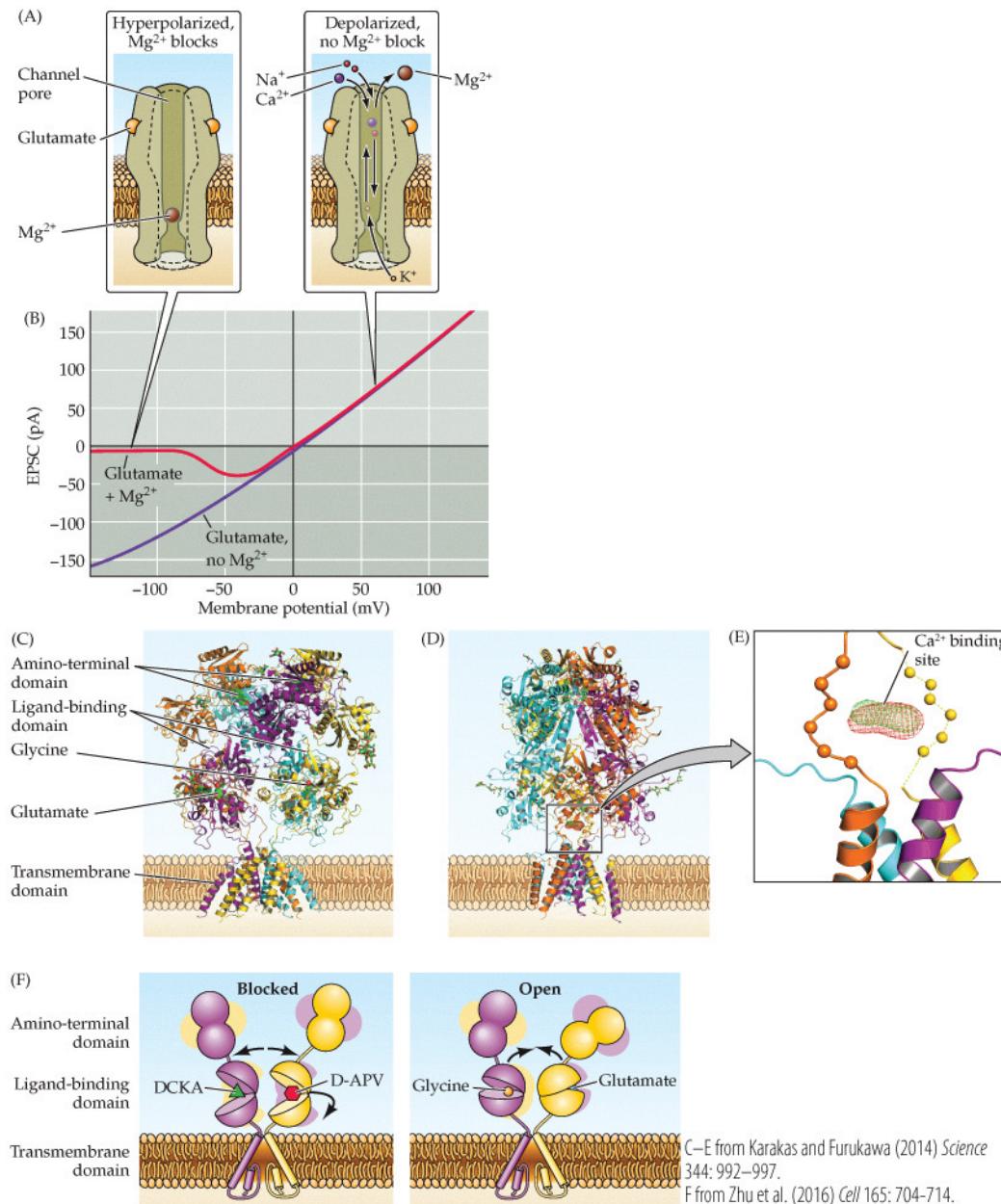
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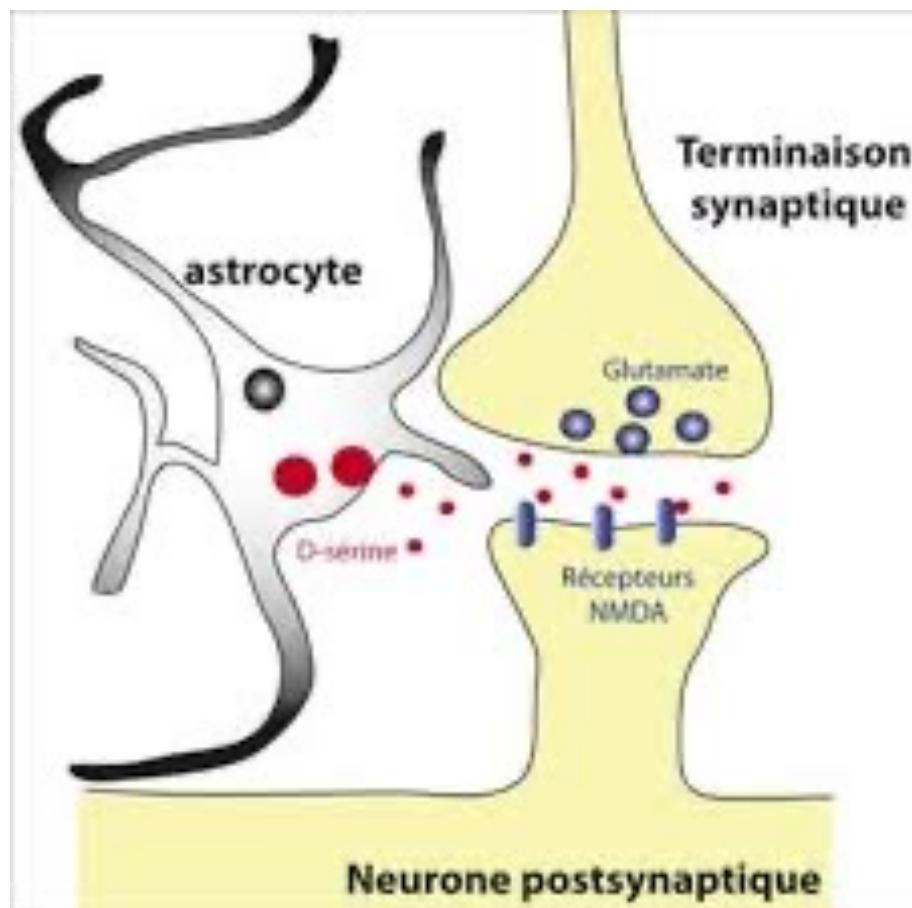
# Structure of the AMPA receptor



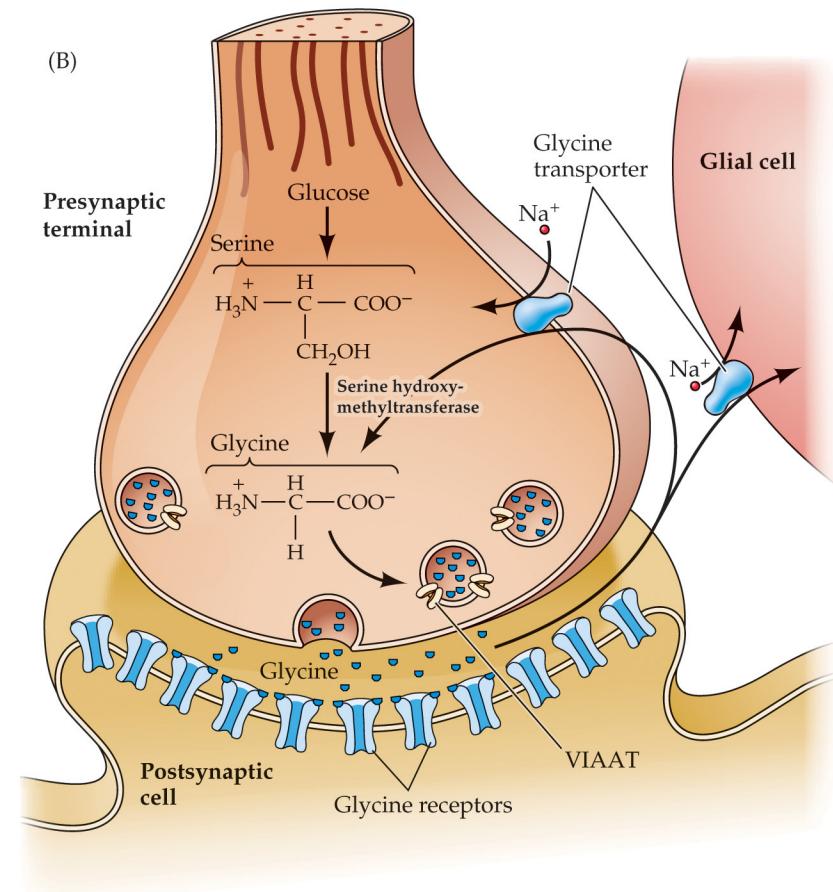
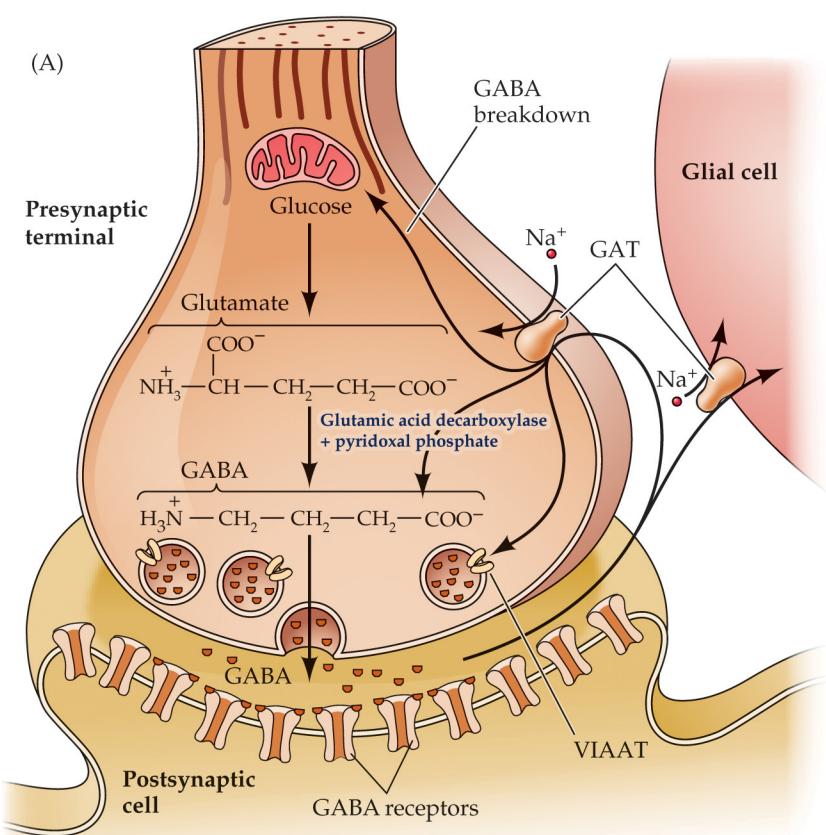
A-E from Tsien et al. (2010) *Pharmacol. Rev.* 62: 405–496.  
B-D from Sobolevsky et al. (2009) *Nature* 462: 745–756.

# Function and structure of the NMDA receptor





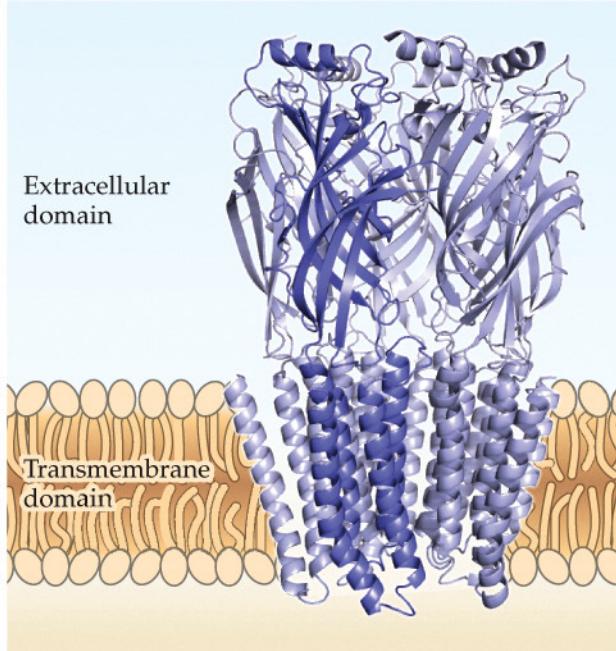
# Synthesis, release, and reuptake of the inhibitory neurotransmitters GABA and glycine



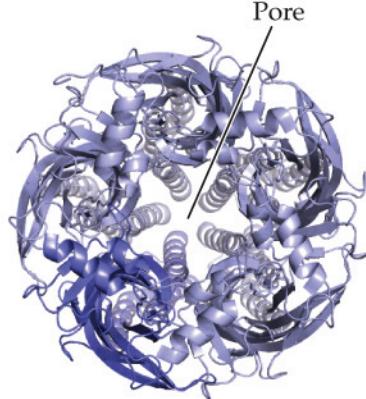
NEUROSCIENCE 6e, Figure 6.10  
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# Ionotropic GABA receptors

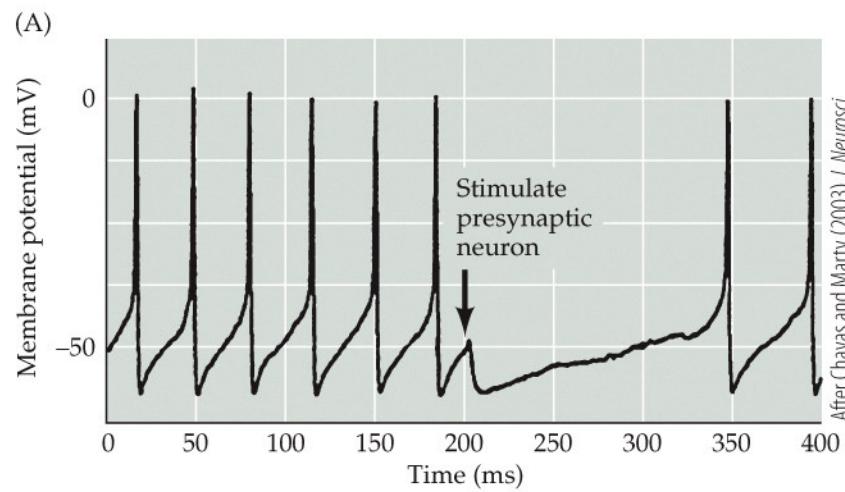
(B) Side view



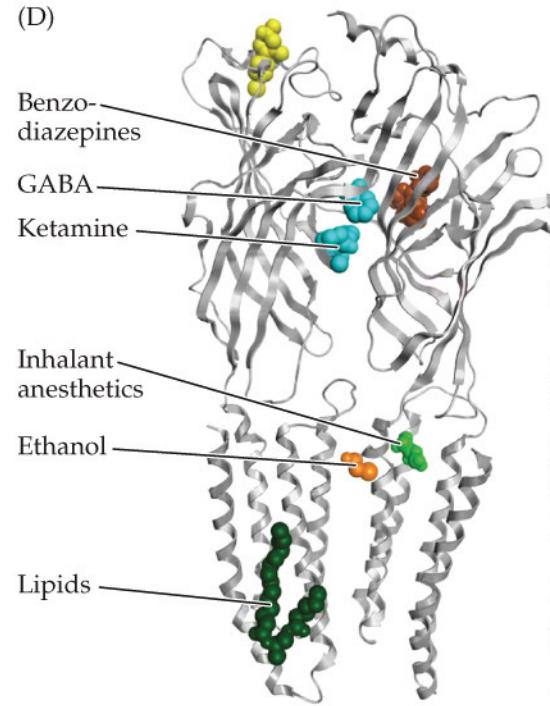
(C) Top view



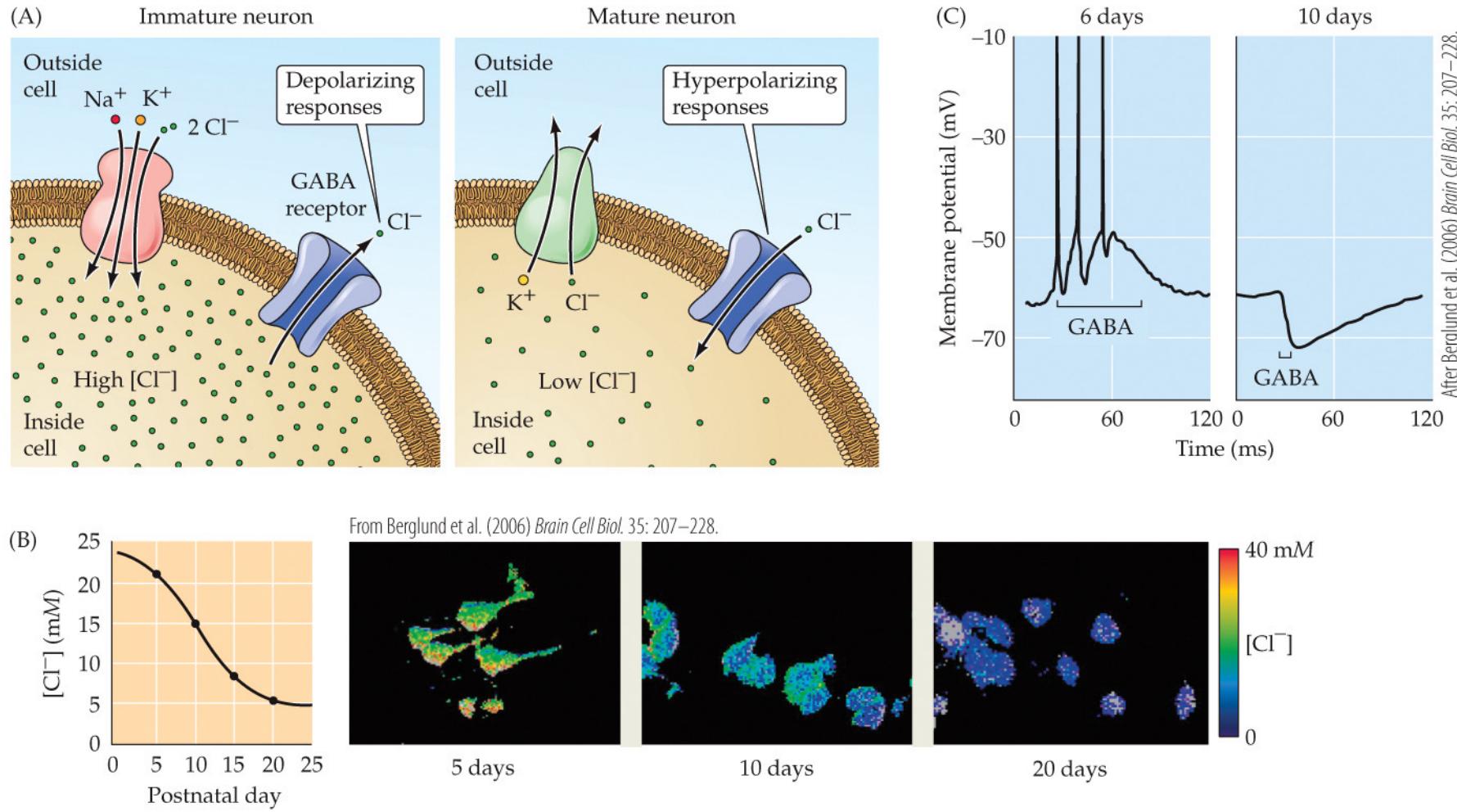
NEUROSCIENCE 6e, Figure 6.11  
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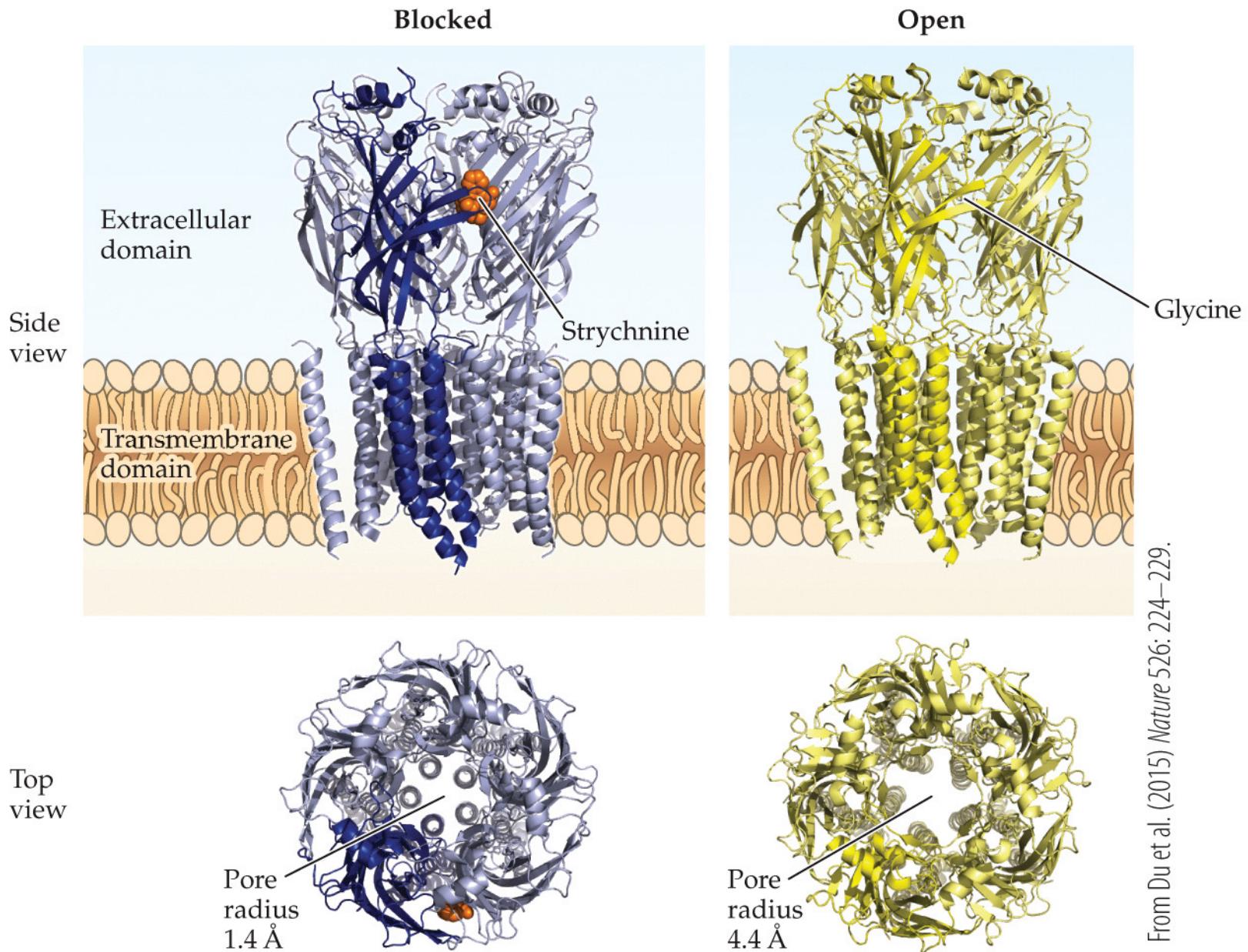
(D)



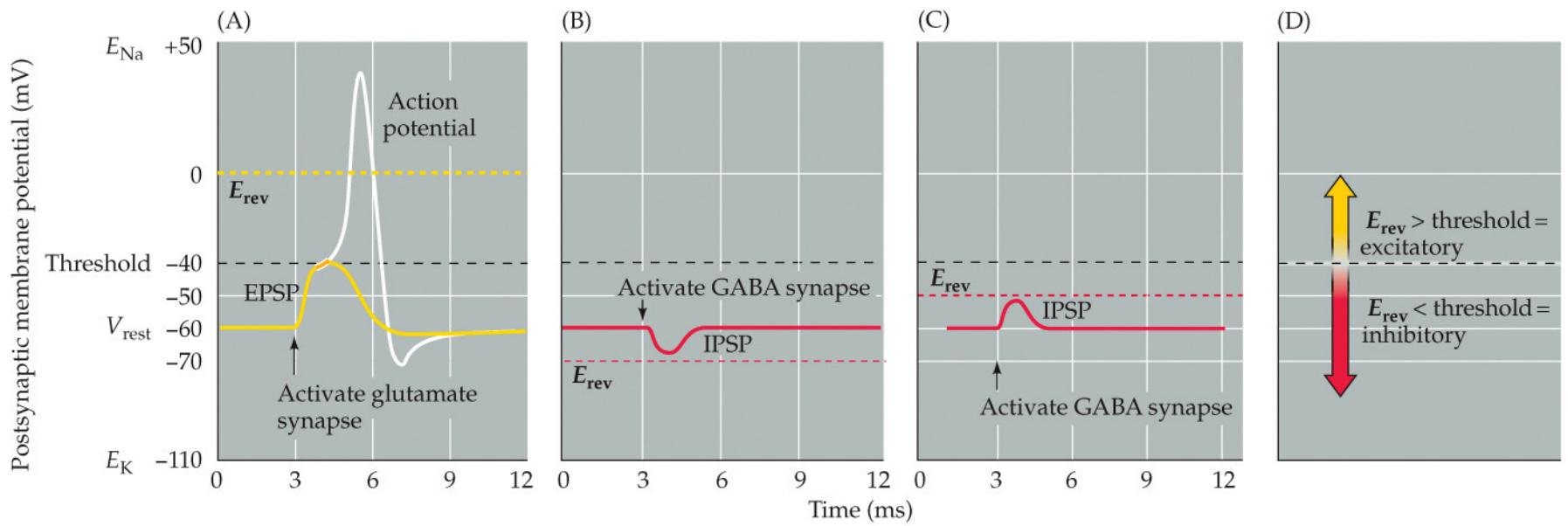
# Excitatory Actions of GABA in the Developing Brain



# Gating of glycine receptors



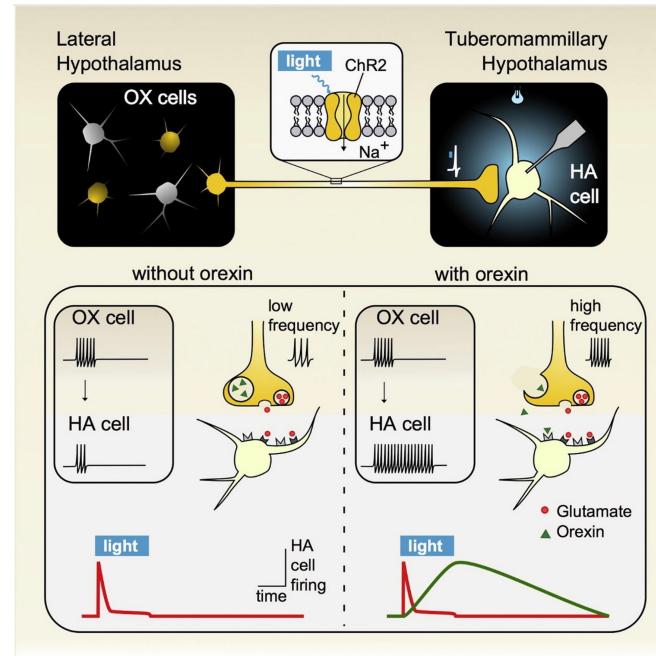
# Reversal potentials and threshold potentials determine postsynaptic excitation and inhibition



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

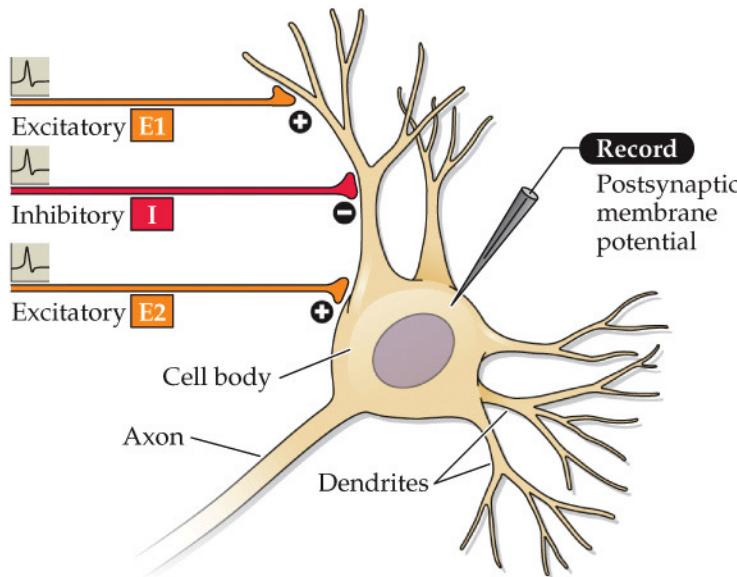
**TABLE 6.2 ■ Endogenous Opioid Peptides**

Name	Amino acid sequence <sup>a</sup>
<b>Endorphins</b>	
$\alpha$ -Endorphin	<i>Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-</i> Ser-Gln-Thr-Pro-Leu-Val-Thr
$\alpha$ -Neoendorphin	<i>Tyr-Gly-Gly-Phe-Leu-Arg-Lys-Tyr-Pro-</i> Lys
$\beta$ -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
$\gamma$ -Endorphin	<i>Tyr-Gly-Gly-Phe-Met-Thr-Ser-Glu-Lys-</i> Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu
<b>Enkephalins</b>	
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

<sup>a</sup>Note the initial homology, indicated by italics.

# Summation of postsynaptic potentials

(A)



(B)

