

Introduction to Neurophysiology 3

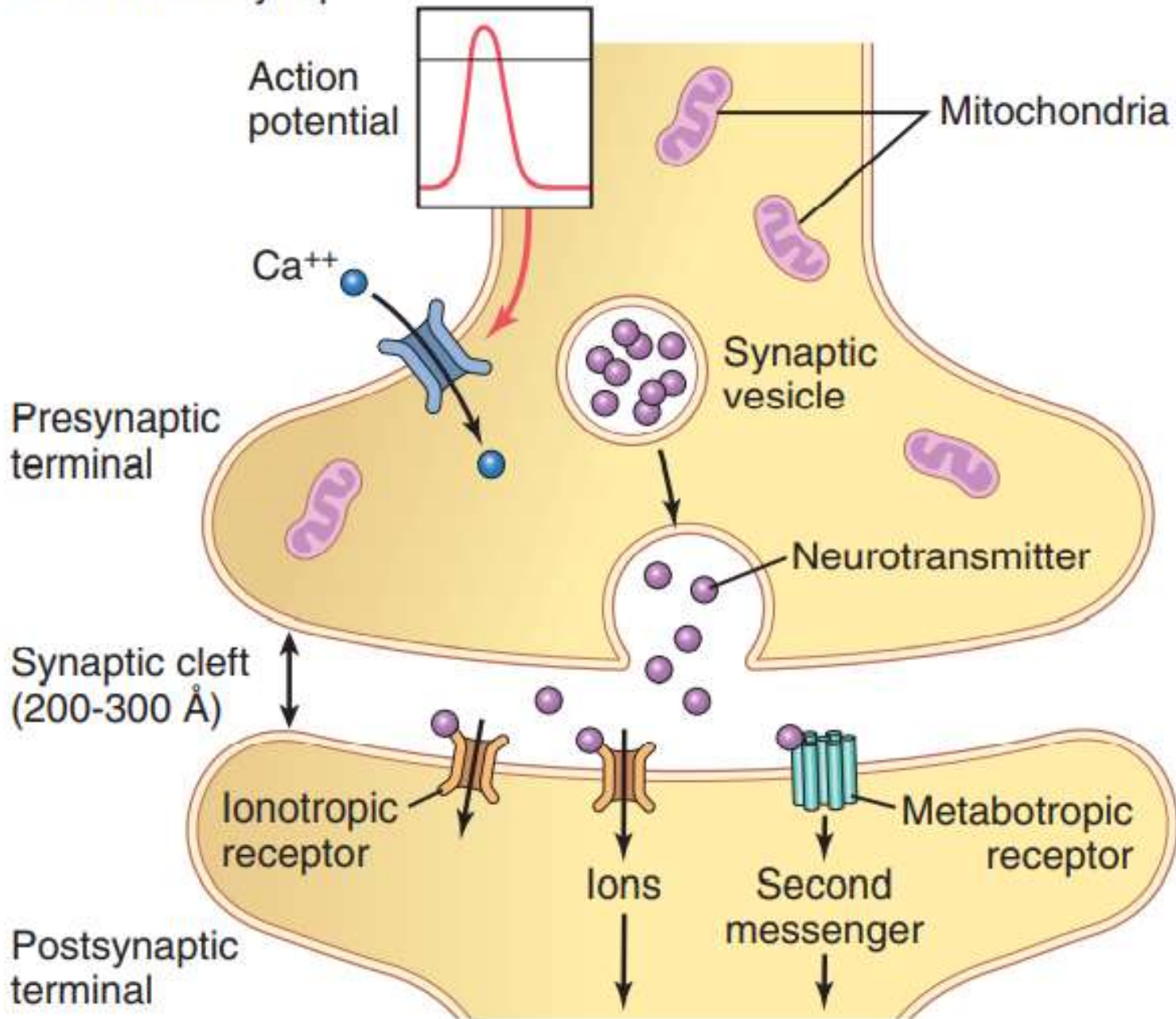
Neurotransmitters

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A Chemical synapse



Small-Molecule, Rapidly Acting Transmitters

Class I

Acetylcholine

Class II: The Amines

Norepinephrine

Epinephrine

Dopamine

Serotonin

Melatonin

Histamine

Class III: Amino Acids

Gamma-aminobutyric acid

Glycine

Glutamate

Aspartate

Class IV

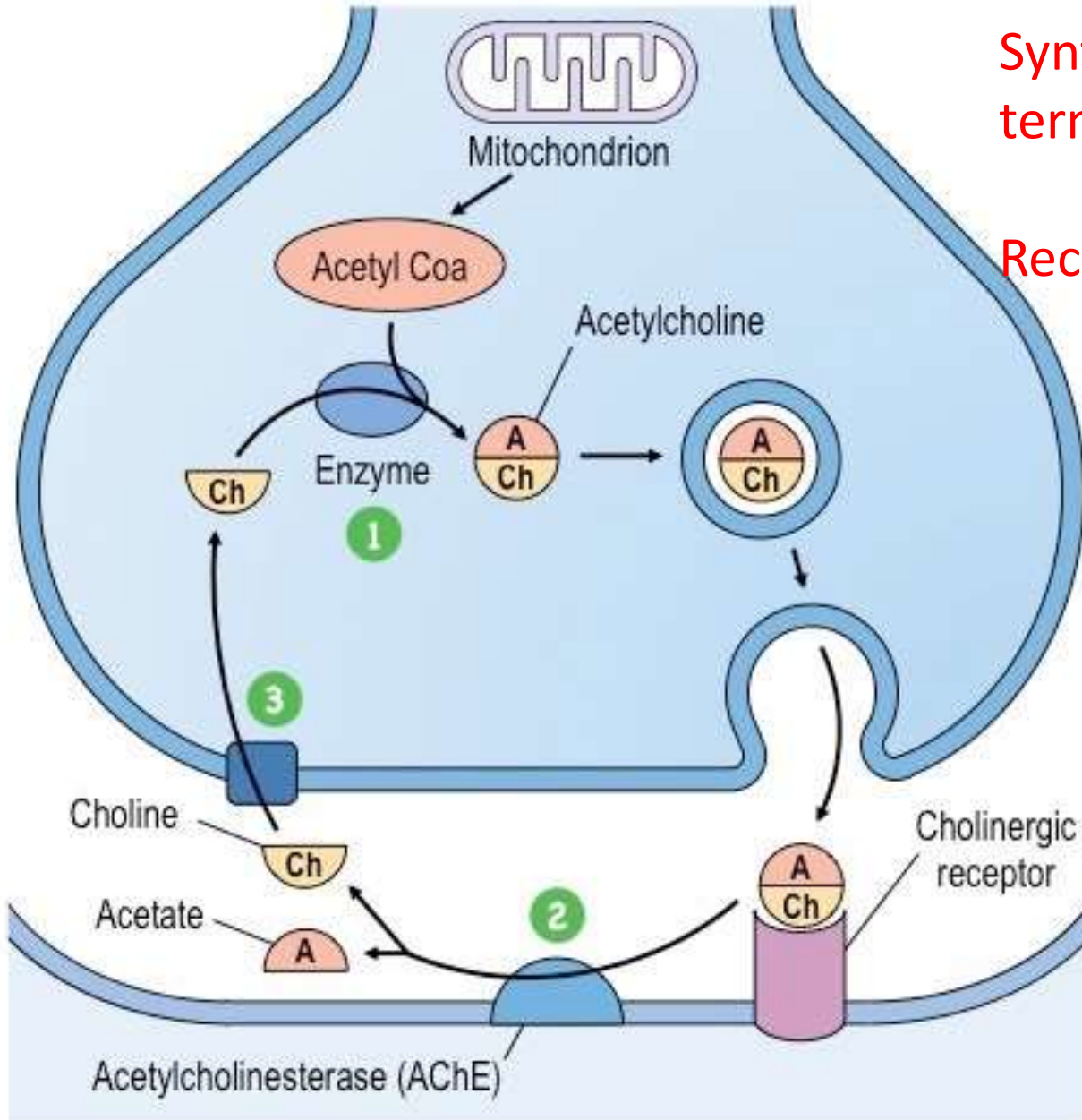
ATP

Arachidonic acid

Nitric oxide

Carbon monoxide





Synthesis in presynaptic terminal

Recycling

rapid

1 Acetylcholine (ACh) is made from choline and acetyl CoA

2 In the synapse, ACh is rapidly broken down by the enzyme **acetylcholinesterase (AChE)**

3 Choline is transported back into the axon terminal and used to make more ACh





Neuropeptides

Hypothalamic-Releasing Hormones

Thyrotropin-releasing hormone

Luteinizing hormone-releasing hormone

Somatostatin (growth hormone inhibitory factor)

Pituitary Peptides

Adrenocorticotrophic hormone

β -Endorphin

α -Melanocyte-stimulating hormone

Prolactin

Luteinizing hormone

Thyrotropin

Growth hormone

Vasopressin

Oxytocin

Peptides that Act on Gut and Brain

Leucine enkephalin

Methionine enkephalin

Substance P

Gastrin

Cholecystokinin

Vasoactive intestinal polypeptide

Nerve growth factor

Brain-derived neurotropic factor

Neurotensin

Insulin

Glucagon

From Other Tissues

Angiotensin II

Bradykinin

Carnosine

Sleep peptides

Calcitonin

Neuropeptides

- synthesized in the neuronal cell body.
- packages into vesicles.
- transported along the axon to the axon terminals.
- traveling at the slow rate.
- vesicles release their transmitter at the neuronal terminals in response to action potential.
- Usually, the vesicle is autolyzed not reused.

Neuropeptides

- smaller quantities of neuropeptides are usually released.
- neuropeptides are generally more potent than the small-molecule transmitters.
- They often cause more prolonged actions.
- Metabotropic receptors

Nitric oxide (NO)

- It is not preformed and stored in vesicles. Instead, it is synthesized almost instantly as needed.
- It diffuses out of the presynaptic terminals over a period of seconds rather than being released in vesicular packets.
- It diffuses into postsynaptic neurons nearby.
- In the postsynaptic neuron, it usually does not alter the membrane potential greatly but instead changes intracellular metabolic functions that modify neuronal excitability.

Acetylcholine

- Acetylcholine is secreted by neurons in many areas of the nervous system such as:
 - motor neurons that innervate the skeletal muscles (NMJ).
 - neurons of the autonomic nervous system.
 - Basal forebrain
- In most cases, acetylcholine has an excitatory effect.

Acetylcholine

- Receptors are nicotinic (ionotropic), muscarinic (metabotropic: GPCR).
- Myasthenia gravis.
- Alzheimer's disease.

Norepinephrine

- A Norepinephrine is secreted by the terminals of many neurons whose cell bodies are located in:
- the brain stem, specifically, locus ceruleus that plays a role in wakefulness and arousal.
- also secreted by most postganglionic neurons of the sympathetic nervous system.
- Depression
- ADHD

Dopamine

- A Dopamine is secreted by neurons in nigrostriatal, mesolimbic, mesocortical, and tuberoinfundibular pathways.
- Receptors D1-D5
- Parkinson's disease
- Psychotic disorders (motivation and reward)

Glycine

- A Glycine is secreted mainly at synapses in the spinal cord.
- It is almost always an inhibitory transmitter.

GABA

- A Gamma-aminobutyric acid (GABA).
- it is the main inhibitory neurotransmitter.
- R: GABA-A (Cl channel), GABA-B (GPCR)
- Epilepsy

Glutamate

- A Glutamate is the main excitatory neurotransmitter.
- R (ionotropic: AMPA, NMDA), metabotropic (mGluR)

Serotonin

- Secreted by raphe nucleus of the brain stem.
- Control mood, sleep, appetite, pain.
- Depression.
- R: 5-HT₁₋₇ (ionotropic and metabotropic)

Substance P

- Neuropeptide
- Sensory neurons, spinal cord, hypothalamus.
- Pain transmission (chronic pain), inflammation and stress.

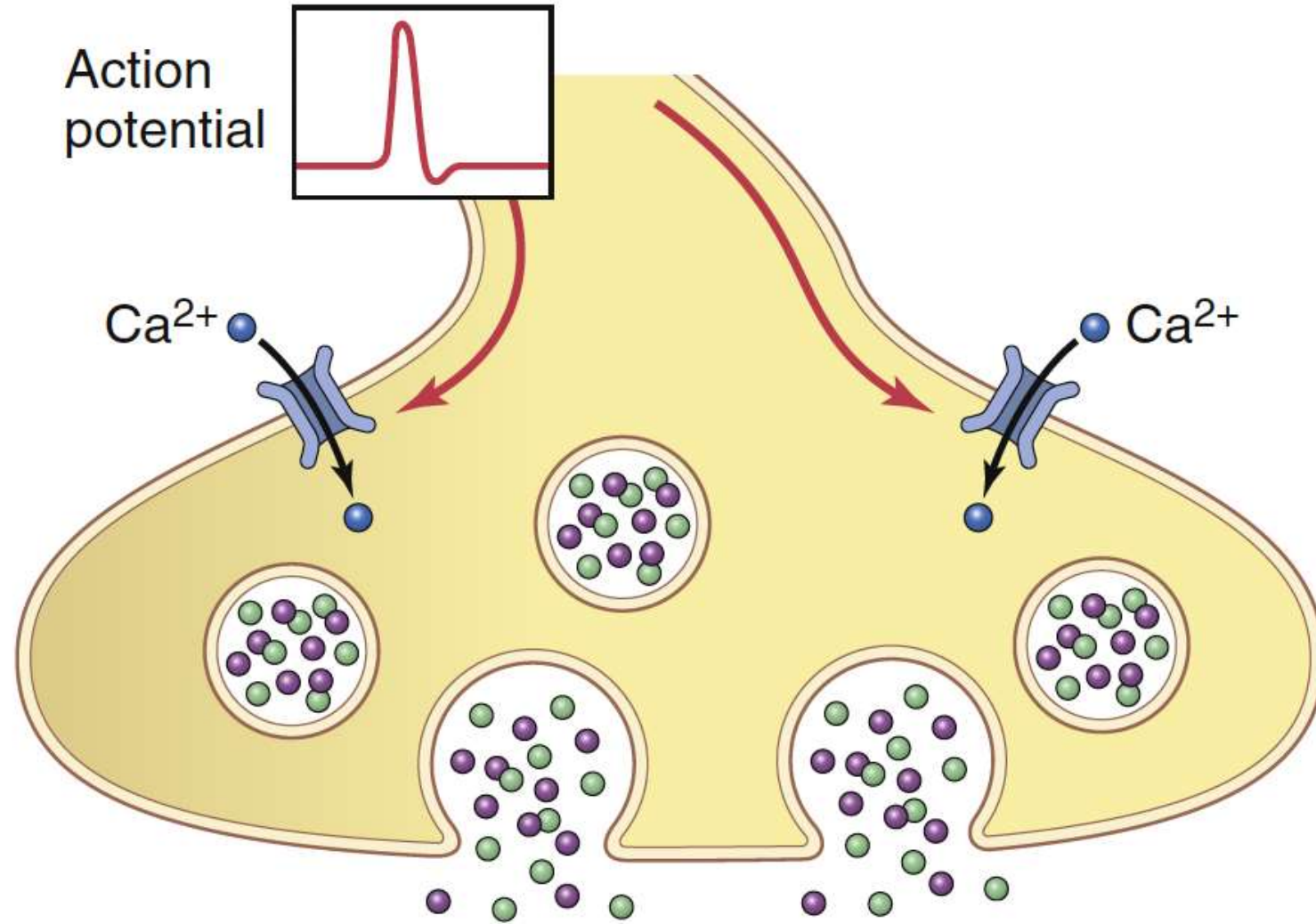
Oxytocin

- Neuropeptide
- Produced in hypothalamus and Released from posterior pituitary.
- Control contractions of uterus during labor
- Ejection of milk during lactation
- Social bonding and emotional behavior

Co-transmission

- Slowly acting neuropeptide transmitters and rapidly acting, small-molecule transmitters are often stored and released from the same neurons.
- In some cases, two or more of these transmitters are co-localized in the same synaptic vesicles and are co-released when an action potential reaches the presynaptic terminal.

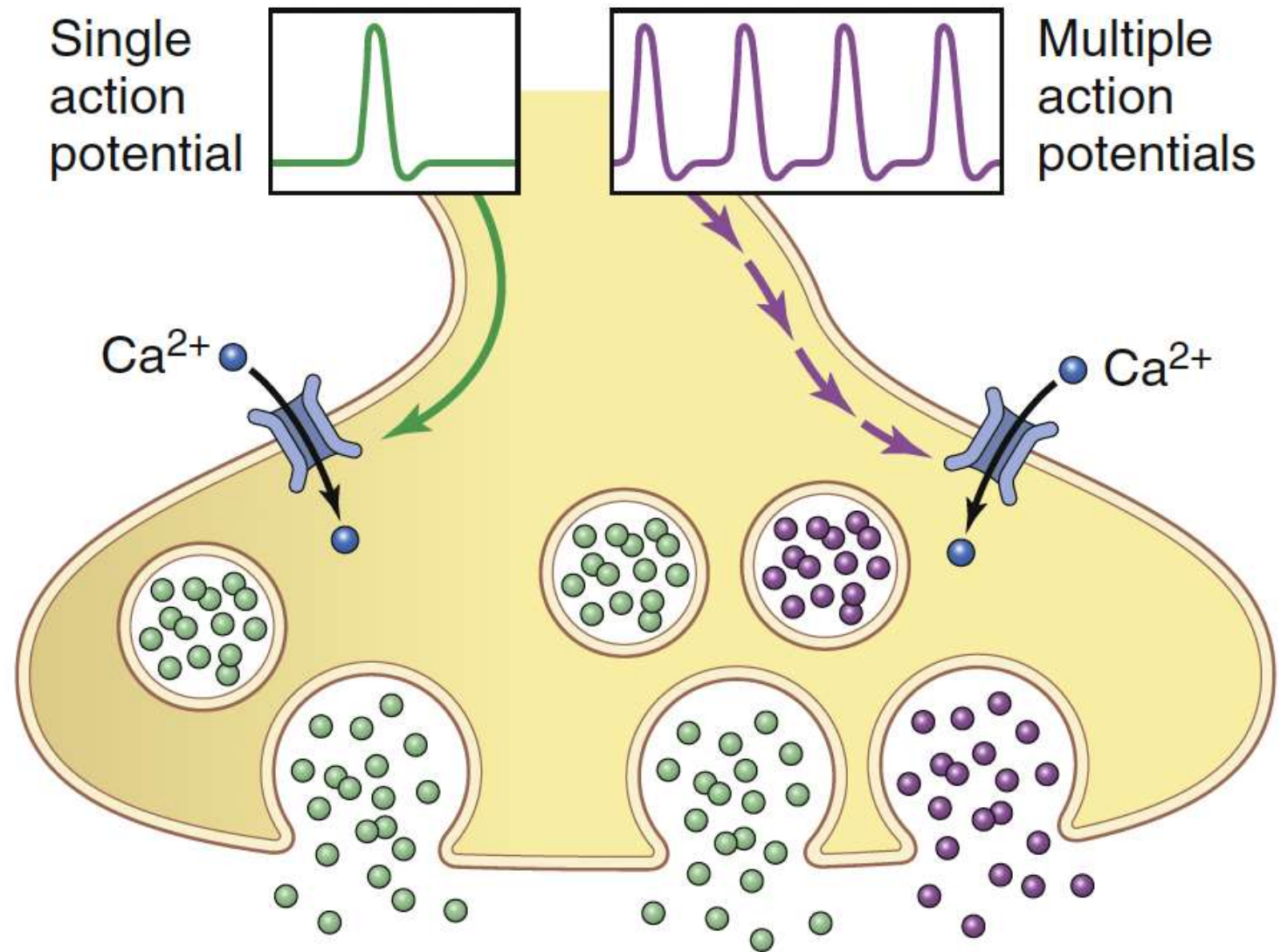
A Co-release



Co-transmission

- In other cases, these transmitters may be localized in different synaptic vesicles of the same neuron and contribute to co-transmission of signals to a postsynaptic neuron.
- Moreover, their release may be differentially regulated because of different calcium ion sensitivities

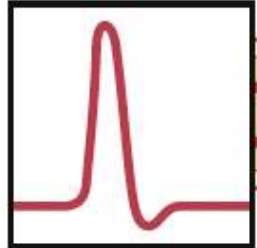
B Co-transmission; differential Ca^{2+} sensitivity



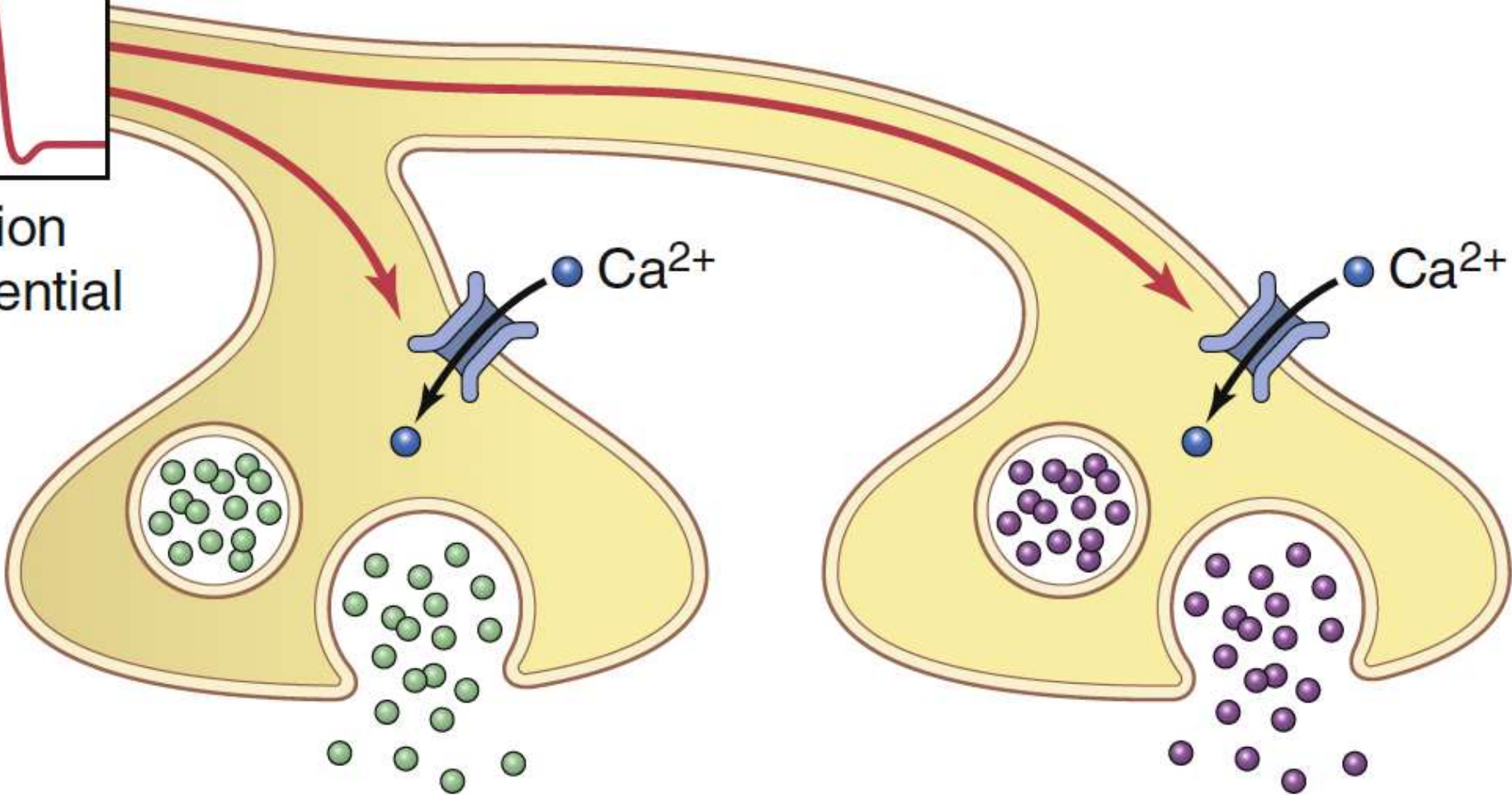
Co-transmission

- Or spatial segregation of the vesicles on different boutons

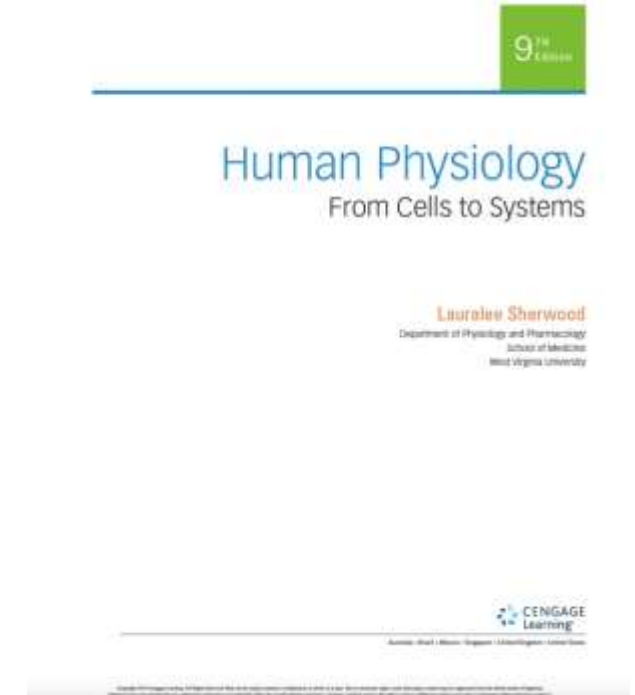
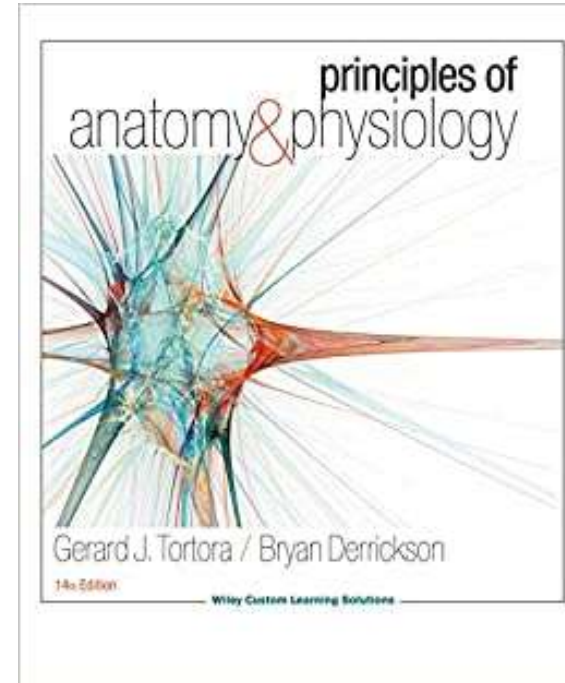
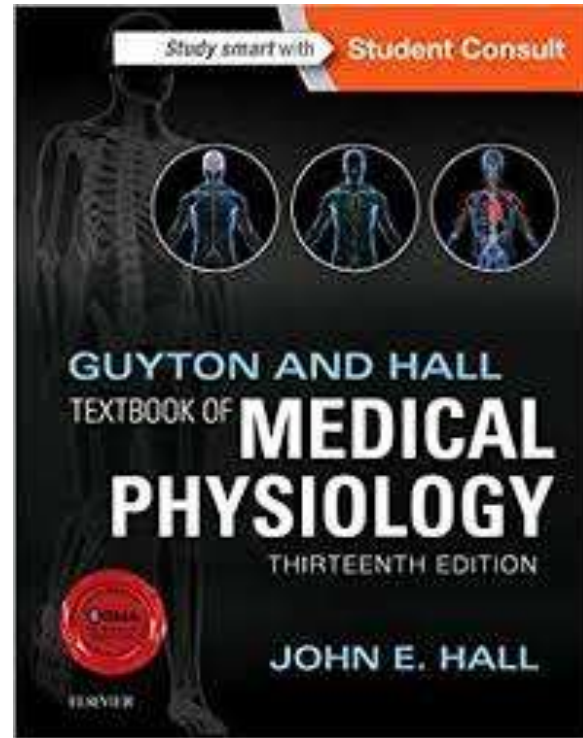
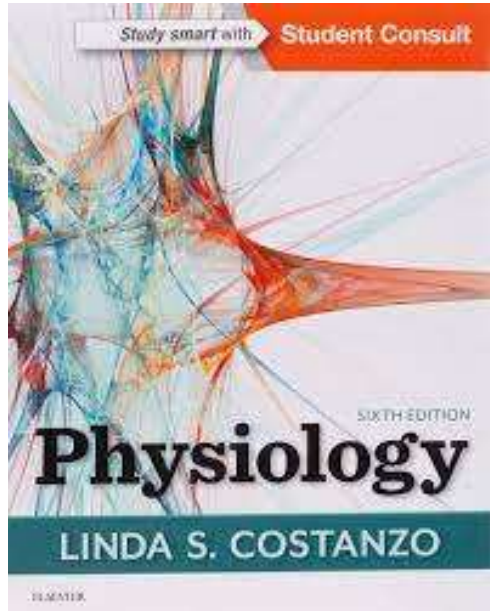
C Co-transmission; Spatial segregation



Action potential



References





Questions? Feedback?

Thank you

