# PHYSIOLOGY OF NERVOUS TISSUE

By

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$2^{nd}$ year/Lecture 3

# NEUROTRANSMITTERS AND RELATED MESSENGERS

- more than 100 neurotransmitters have been identified
- fall into four major categories according to chemical composition
  - acetylcholine
    - in a class by itself
    - formed from acetic acid and choline
  - amino acid neurotransmitters
    - include glycine, glutamate, aspartate, and $\gamma$-aminobutyric acid (GABA)
  - monoamines
    - synthesized from amino acids by removal of the –COOH group
    - retaining the $-NH_2$ (amino) group
    - major monoamines are:
      - epinephrine, norepinephrine, dopamine (catecholamines)
      - histamine and serotonin
  - neuropeptides

# CATEGORIES OF NEUROTRANSMITTERS



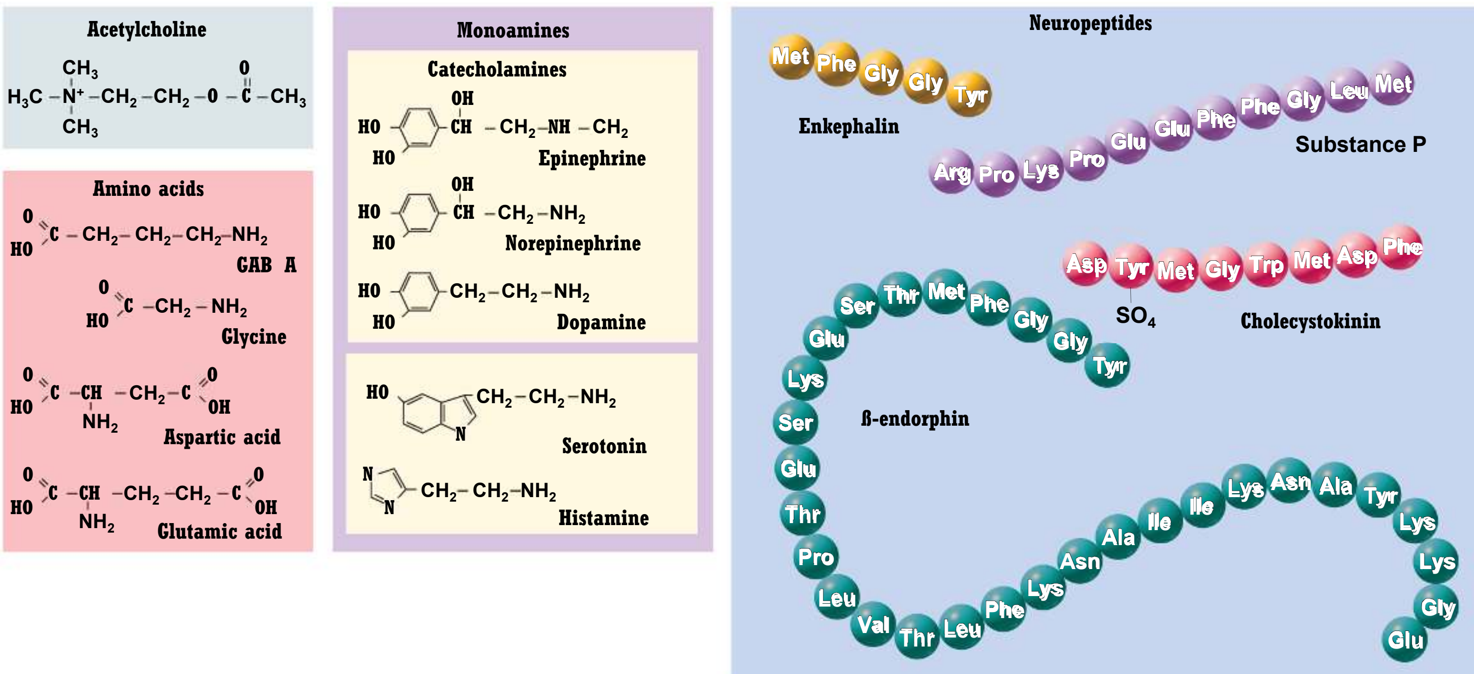


Figure 12.21

# NEUROPEPTIDES

- chains of 2 to 40 amino acids
  - beta-endorphin and substance P
- act at lower concentrations than other neurotransmitters
- longer lasting effects
- stored in axon terminal as larger secretory granules (called dense-core vesicles)
- some function as hormones or neuromodulators
- some also released from digestive tract
  - gut-brain peptides cause food cravings



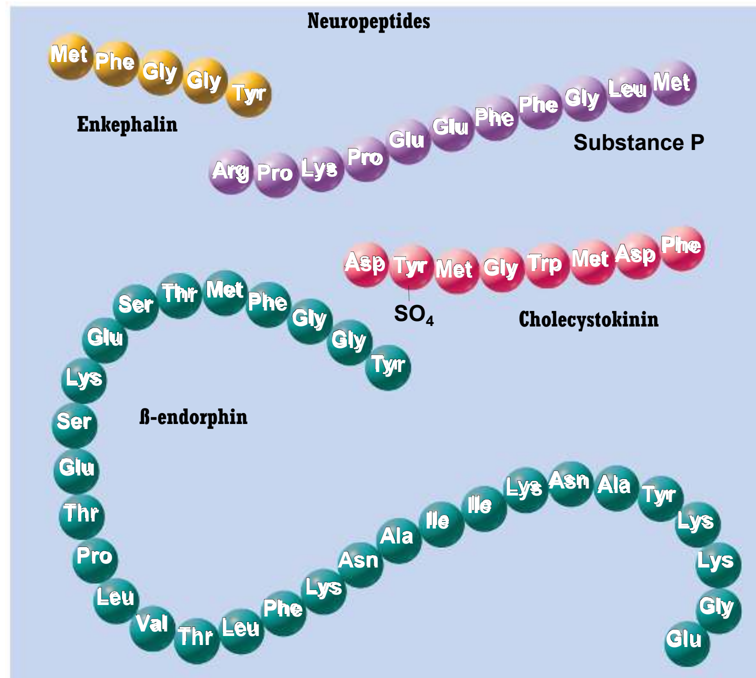


Figure 12.21

# FUNCTION OF NEUROTRANSMITTERS AT SYNAPSE

- they are synthesized by the presynaptic neuron
- they are released in response to stimulation
- they bind to specific receptors on the postsynaptic cell
- they alter the physiology of that cell

# EFFECTS OF NEUROTRANSMITTERS

- a given neurotransmitter does not have the same effect everywhere in the body

- multiple receptor types exist for a particular neurotransmitter
  - 14 receptor types for serotonin

- receptor governs the effect the neurotransmitter has on the target cell

# SYNAPTIC TRANSMISSION

- neurotransmitters are diverse in their action
  - some excitatory
  - some inhibitory
  - some the effect depends on what kind of receptor the postsynaptic cell has
  - some open ligand-regulated ion gates
  - some act through second-messenger systems
- three kinds of synapses with different modes of action
  - excitatory cholinergic synapse
  - inhibitory GABA-ergic synapse
  - excitatory adrenergic synapse
- synaptic delay – time from the arrival of a signal at the axon terminal of a presynaptic cell to the beginning of an action potential in the postsynaptic cell
  - 0.5 msec for all the complex sequence of events to occur

# EXCITATORY CHOLINERGIC SYNAPSE

- cholinergic synapse – employs acetylcholine (ACh) as its neurotransmitter
  - ACh excites some postsynaptic cells
    - skeletal muscle
  - inhibits others
- describing excitatory action
  - nerve signal approaching the synapse, opens the voltage-regulated calcium gates in synaptic knob
  - $Ca^{2+}$ enters the knob
  - triggers exocytosis of synaptic vesicles releasing ACh
  - empty vesicles drop back into the cytoplasm to be refilled with ACh
  - reserve pool of synaptic vesicles move to the active sites and release their ACh
  - ACh diffuses across the synaptic cleft
  - binds to ligand-regulated gates on the postsynaptic neuron
  - gates open
  - allowing $Na^+$ to enter cell and $K^+$ to leave
    - pass in opposite directions through same gate
  - as $Na^+$ enters the cell it spreads out along the inside of the plasma membrane and depolarizes it producing a local potential called the postsynaptic potential
  - if it is strong enough and persistent enough
  - it opens voltage-regulated ion gates in the trigger zone
  - causing the postsynaptic neuron to fire

# EXCITATORY CHOLINERGIC SYNAPSE



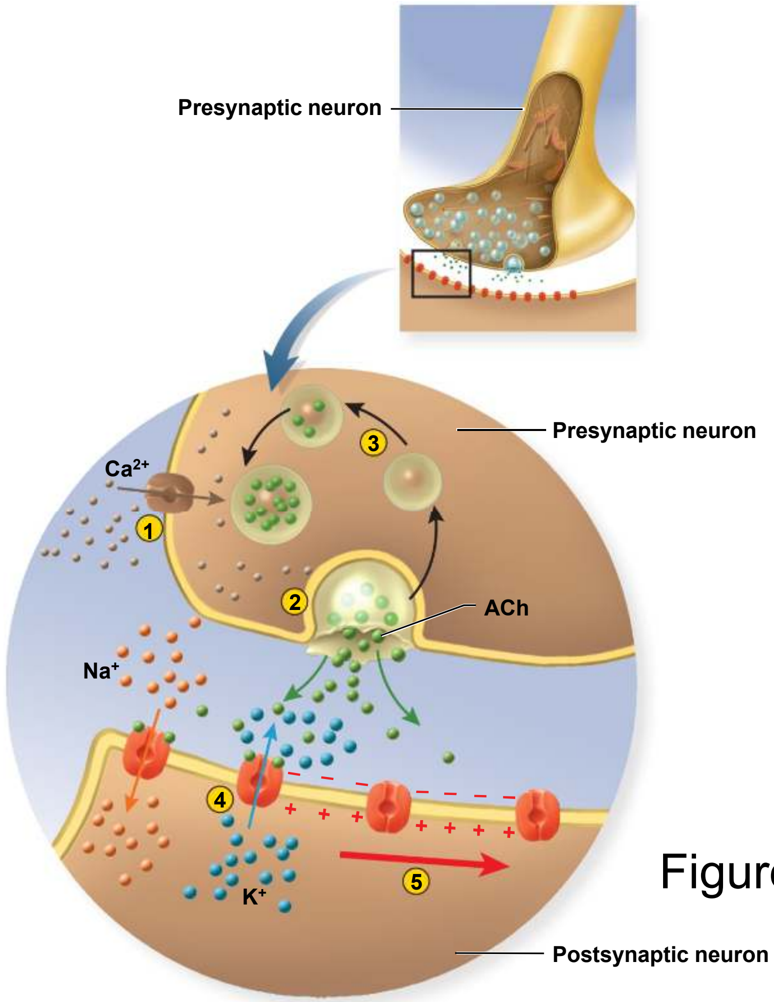


Figure 12.22

# INHIBITORY GABA-ERGIC SYNAPSE

- GABA-ergic synapse employs $\gamma$-aminobutyric acid as its neurotransmitter
- nerve signal triggers release of GABA into synaptic cleft
- GABA receptors are chloride channels
- $Cl^-$ enters cell and makes the inside more negative than the resting membrane potential
- postsynaptic neuron is inhibited, and less likely to fire

# EXCITATORY ADRENERGIC SYNAPSE

- adrenergic synapse employs the neurotransmitter norepinephrine (NE) also called noradrenaline
- NE and other monoamines, and neuropeptides acts through second messenger systems such as cyclic AMP (cAMP)
- receptor is not an ion gate, but a transmembrane protein associated with a G protein
  - unstimulated NE receptor is bound to a G protein
  - binding of NE to the receptor causes the G protein to dissociate from it
  - G protein binds to adenylate cyclase
    - activates this enzyme
  - induces the conversion of ATP to cyclic AMP
  - cyclic AMP can induce several alternative effects in the cell
    - causes the production of an internal chemical that binds to a ligand-regulated ion gate from inside of the membrane, opening the gate and depolarizing the cell
    - can activate preexisting cytoplasmic enzymes that lead do diverse metabolic changes
    - can induce genetic transcription, so that the cell produces new cytoplasmic enzymes that can lead to diverse metabolic effects
- slower to respond than cholinergic and GABA-ergic synapses
- has advantage of enzyme amplification – single molecule of NE can produce vast numbers of product molecules in the cell

# EXCITATORY ADRENERGIC SYNAPSE



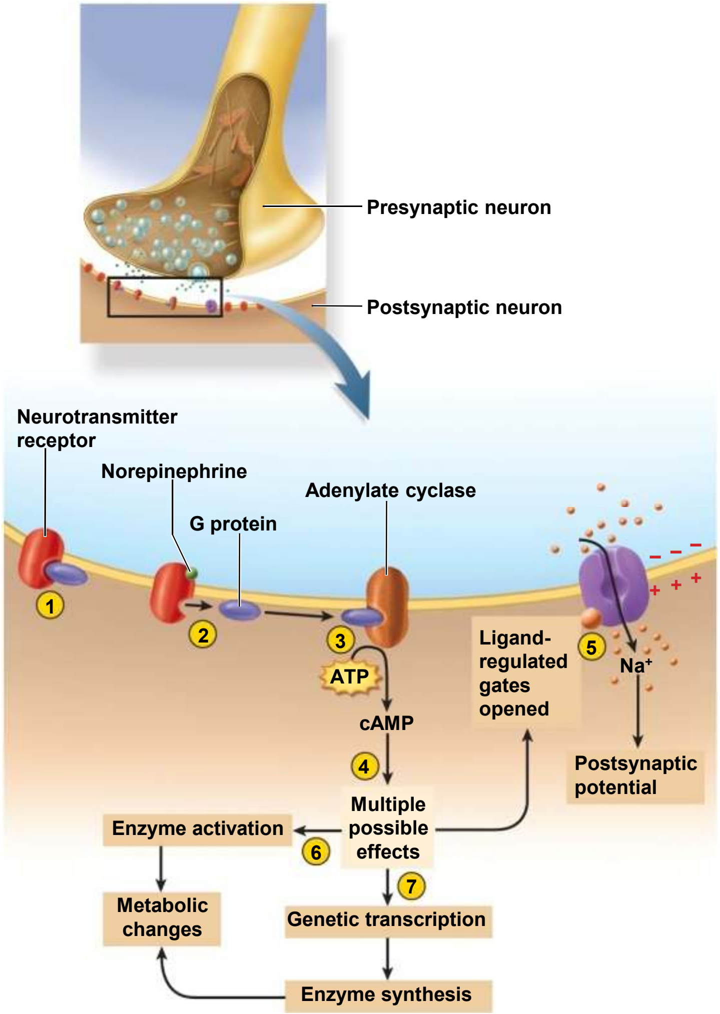


Figure 12.23

# CESSATION OF THE SIGNAL

- mechanisms to turn off stimulation to keep postsynaptic neuron from firing indefinitely
  - neurotransmitter molecule binds to its receptor for only 1 msec or so
    - then dissociates from it
  - if presynaptic cell continues to release neurotransmitter
    - one molecule is quickly replaced by another and the neuron is restimulated

- stop adding neurotransmitter and get rid of that which is already there
  - stop signals in the presynaptic nerve fiber
  - getting rid of neurotransmitter by:
    - diffusion
      - neurotransmitter escapes the synapse into the nearby ECF
      - astrocytes in CNS absorb it and return it to neurons
    - reuptake
      - synaptic knob reabsorbs amino acids and monoamines by endocytosis
      - break neurotransmitters down with monoamine oxidase (MAO) enzyme
      - some antidepressant drugs work by inhibiting MAO
    - degradation in the synaptic cleft
      - enzyme acetylcholinesterase (AChE) in synaptic cleft degrades ACh into acetate and choline
      - choline reabsorbed by synaptic knob

# NEUROMODULATORS

- neuromodulators – hormones, neuropeptides, and other messengers that modify synaptic transmission
  - may stimulate a neuron to install more receptors in the postsynaptic membrane adjusting its sensitivity to the neurotransmitter
  - may alter the rate of neurotransmitter synthesis, release, reuptake, or breakdown
- enkephalins – a neuromodulator family
  - small peptides that inhibit spinal interneurons from transmitting pain signals to the brain
- nitric oxide (NO) – simpler neuromodulator
  - a lightweight gas release by the postsynaptic neurons in some areas of the brain concerned with learning and memory
  - diffuses into the presynaptic neuron
  - stimulates it to release more neurotransmitter
  - one neuron's way of telling the other to 'give me more'
  - some chemical communication that goes backward across the synapse

# NEURAL INTEGRATION

- synaptic delay slows the transmission of nerve signals
- more synapses in a neural pathway, the longer it takes for information to get from its origin to its destination
  - synapses are not due to limitation of nerve fiber length
  - gap junctions allow some cells to communicate more rapidly than chemical synapses
- then why do we have synapses?
  - to process information, store it, and make decisions
  - chemical synapses are the decision making devises of the nervous system
  - the more synapses a neuron has, the greater its information-processing capabilities.
  - pyramidal cells in cerebral cortex have about 40,000 synaptic contacts with other neurons
  - cerebral cortex (main information-processing tissue of your brain) has an estimated 100 trillion ($10^{14}$) synapses
- neural integration – the ability of your neurons to process information, store and recall it, and make decisions

# POSTSYNAPTIC POTENTIALS - EPSP

- neural integration is based on the postsynaptic potentials produced by neurotransmitters

- typical neuron has a resting membrane potential of -70 mV and threshold of about -55 mV

- excitatory postsynaptic potentials (EPSP)
  - any voltage change in the direction of threshold that makes a neuron more likely to fire
    - usually results from $Na^+$ flowing into the cell cancelling some of the negative charge on the inside of the membrane
  - glutamate and aspartate are excitatory brain neurotransmitters that produce EPSPs

# POSTSYNAPTIC POTENTIALS - IPSP

- inhibitory postsynaptic potentials (IPSP)
  - any voltage change away from threshold that makes a neuron less likely to fire
    - neurotransmitter hyperpolarizes the postsynaptic cell and makes it more negative than the RMP making it less likely to fire
    - produced by neurotransmitters that open ligand-regulated chloride gates
      - causing inflow of Cl- making the cytosol more negative
  - glycine and GABA produce IPSPs  and are inhibitory
  - acetylcholine (ACh) and norepinephrine are excitatory to some cells and inhibitory to others
    - depending on the type of receptors on the target cell
    - ACh excites skeletal muscle, but inhibits cardiac muscle due to the different type of receptors

# POSTSYNAPTIC POTENTIALS



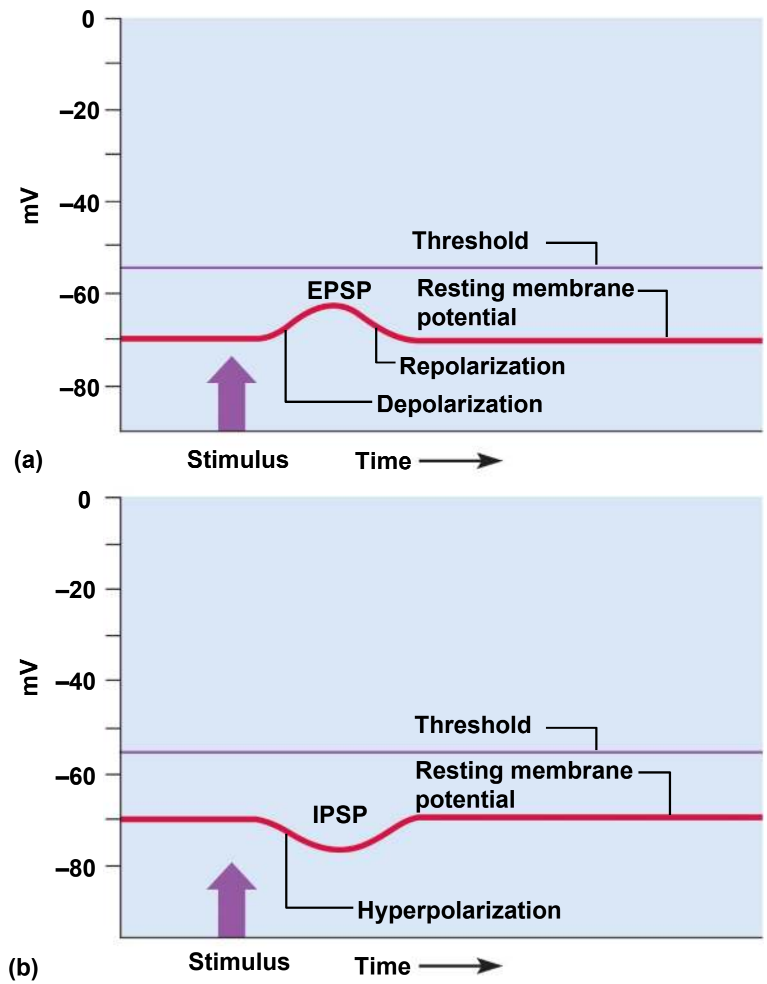


Figure 12.24

# SUMMATION, FACILITATION, AND INHIBITION

- one neuron can receive input from thousands of other neurons
- some incoming nerve fibers may produce EPSPs while others produce IPSPs
- neuron's response depends on whether the net input is excitatory or inhibitory
- summation – the process of adding up postsynaptic potentials and responding to their net effect
  - occurs in the trigger zone
- the balance between EPSPs and IPSPs enables the nervous system to make decisions
- temporal summation – occurs when a single synapse generates EPSPs so quickly that each is generated before the previous one fades
  - allows EPSPs to add up over time to a threshold voltage that triggers an action potential
- spatial summation – occurs when EPSPs from several different synapses add up to threshold at an axon hillock.
  - several synapses admit enough $Na^+$ to reach threshold
  - presynaptic neurons cooperate to induce the postsynaptic neuron to fire

# TEMPORAL AND SPATIAL SUMMATION



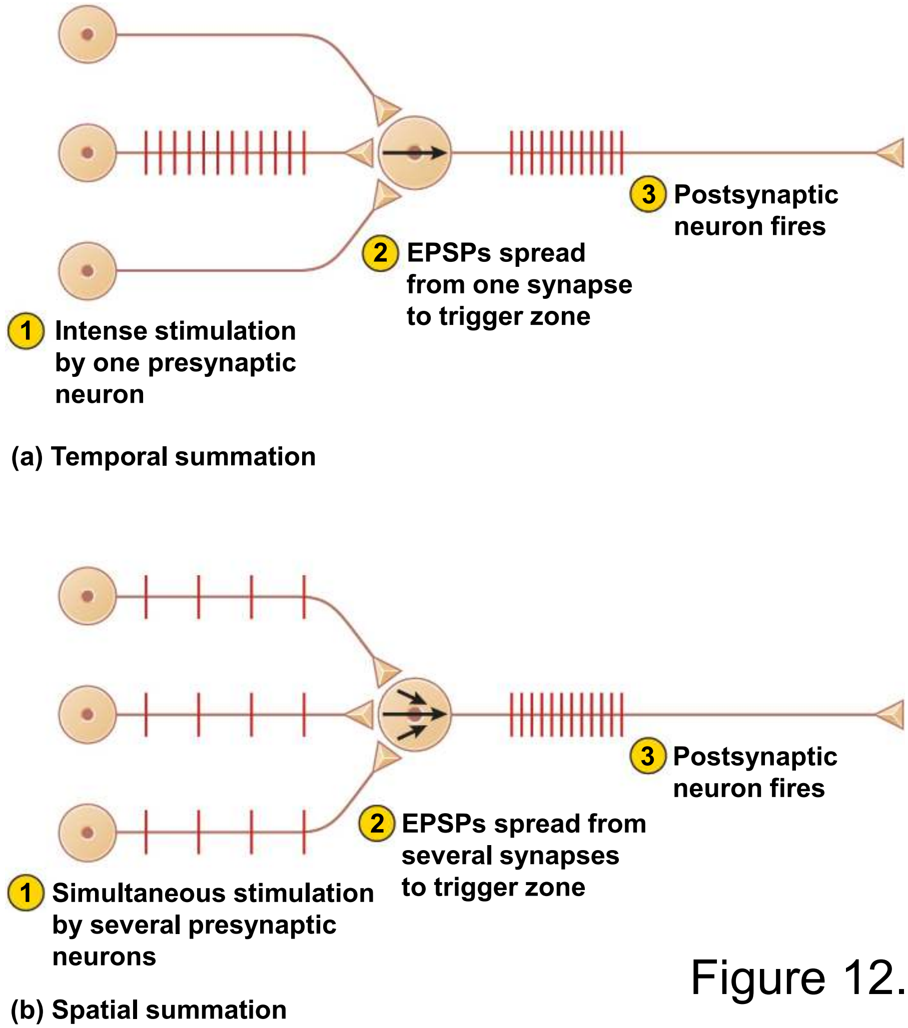


Figure 12.25

# SUMMATION OF EPSPS



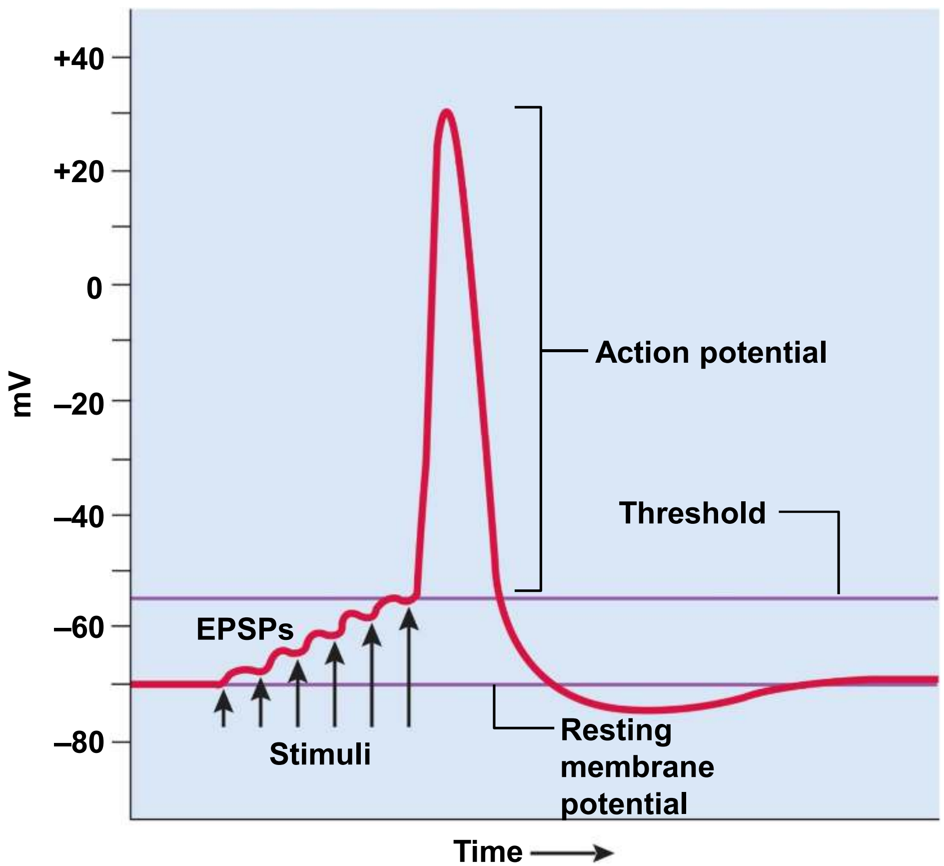


Figure 12.26

- does this represent spatial or temporal summation?

# SUMMATION, FACILITATION, AND INHIBITION

- neurons routinely work in groups to modify each other's action
- facilitation – a process in which one neuron enhances the effect of another one
  - combined effort of several neurons facilitates firing of postsynaptic neuron
- presynaptic inhibition – process in which one presynaptic neuron suppresses another one
  - the opposite of facilitation
  - reduces or halts unwanted synaptic transmission
  - neuron I releases inhibitory GABA
    - prevents voltage-gated calcium channels from opening in synaptic knob and presynaptic neuron releases less or no neurotransmitter



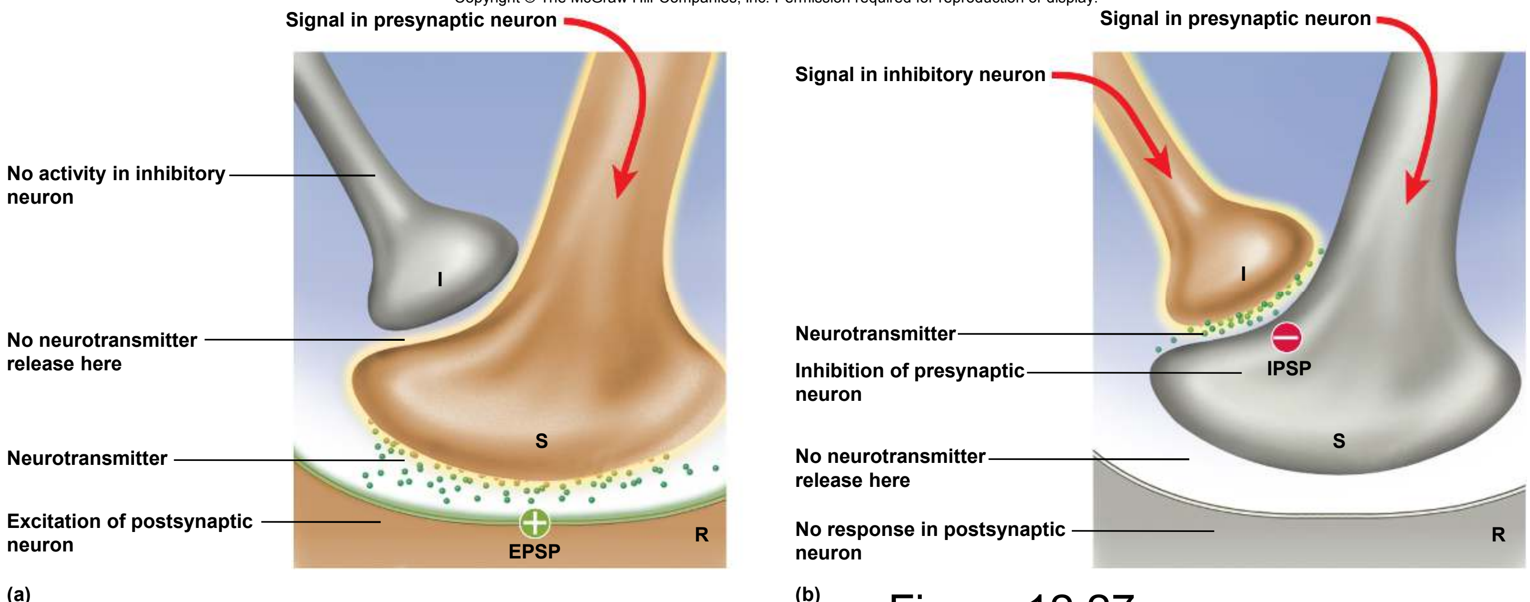


Figure 12.27

# NEURAL CODING

- neural coding – the way in which the nervous system converts information to a meaningful pattern of action potentials

- qualitative information depends upon which neurons fire
  - labeled line code – each nerve fiber to the brain leads from a receptor that specifically recognizes a particular stimulus type

- quantitative information – information about the intensity of a stimulus is encoded in two ways:
  - one depends on the fact that different neurons have different thresholds of excitation
    - stronger stimuli causes a more rapid firing rate
    - excitement of sensitive, low threshold fibers gives way to excitement of less sensitive, high-threshold fibers as intensity of stimuli increases
  - other way depends on the fact that the more strongly a neuron is stimulated, the more frequently it fires
    - CNS can judge stimulus strength from the firing frequency of afferent neurons

# NEURAL CODING



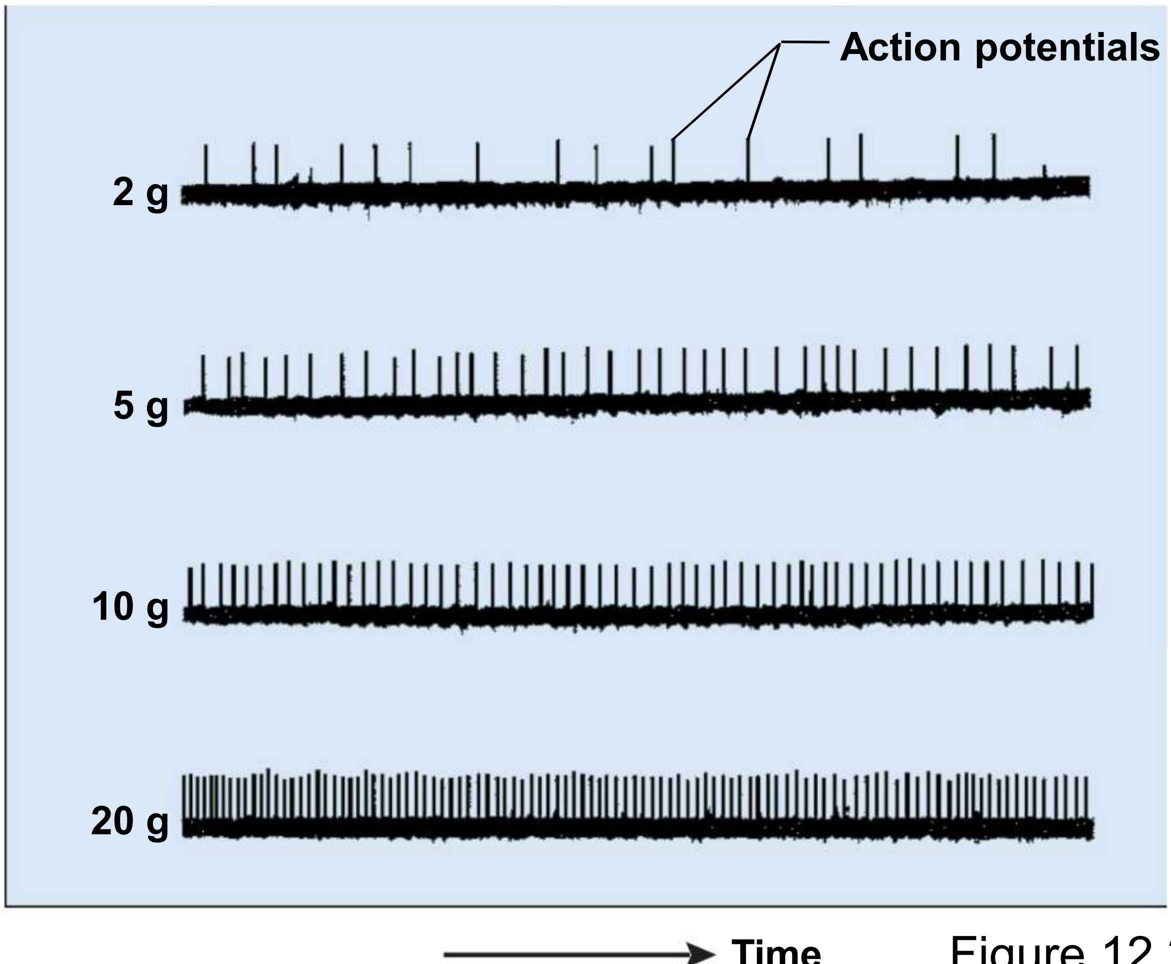


Figure 12.28

# NEURAL POOLS AND CIRCUITS

- neural pools – neurons function in large groups, each of which consists of millions of interneurons concerned with a particular body function
  - control rhythm of breathing
  - moving limbs rhythmically when walking

- information arrives at a neural pool through one or more input neurons
  - branch repeatedly and synapse with numerous interneurons in the pool
  - some input neurons form multiple synapses with a single postsynaptic cell
    - can produce EPSPs in all points of contact with that cell
    - through spatial summation, make it fire more easily than if they synapsed with it at only one point
  - within the discharge zone of an input neuron
    - that neuron acting alone can make the postsynaptic cells fire
  - in a broader facilitated zone, it synapses with still other neurons in the pool
    - fewer synapses on each of them
    - can only stimulate those neurons to fire only with the assistance of other input neurons



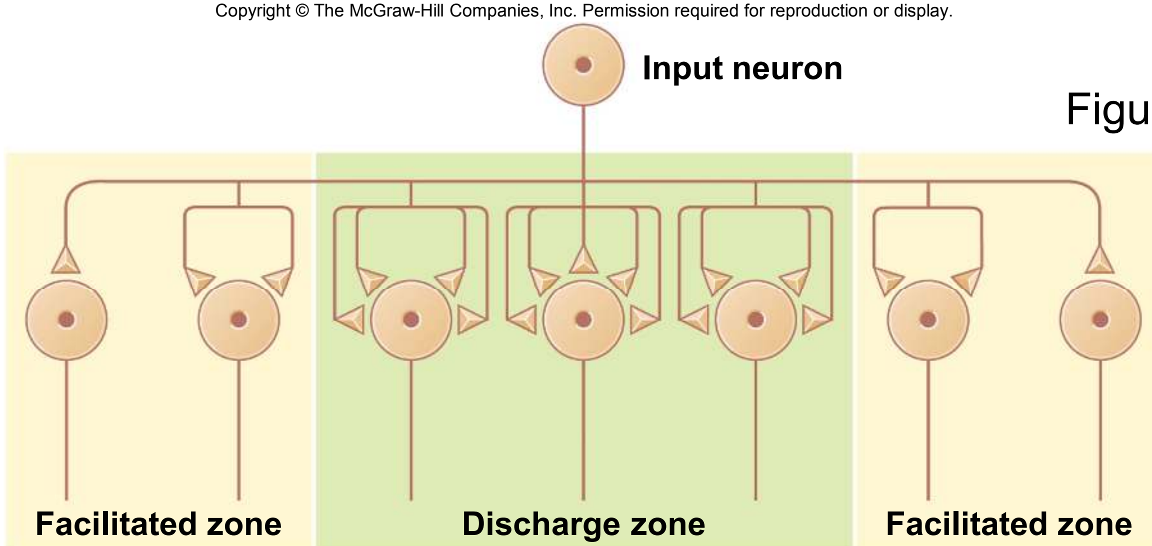


Figure 12.29

# KINDS OF NEURAL CIRCUITS

- diverging circuit
  - one nerve fiber branches and synapses with several postsynaptic cells
  - one neuron may produce output through hundreds of neurons
- converging circuit
  - input from many different nerve fibers can be funneled to one neuron or neural pool
  - opposite of diverging circuit
- reverberating circuits
  - neurons stimulate each other in linear sequence but one cell restimulates the first cell to start the process all over
  - diaphragm and intercostal muscles
- parallel after-discharge circuits
  - input neuron diverges to stimulate several chains of neurons
    - each chain has a different number of synapses
    - eventually they all reconverge on a single output neuron
    - after-discharge – continued firing after the stimulus stops

# NEURAL CIRCUITS



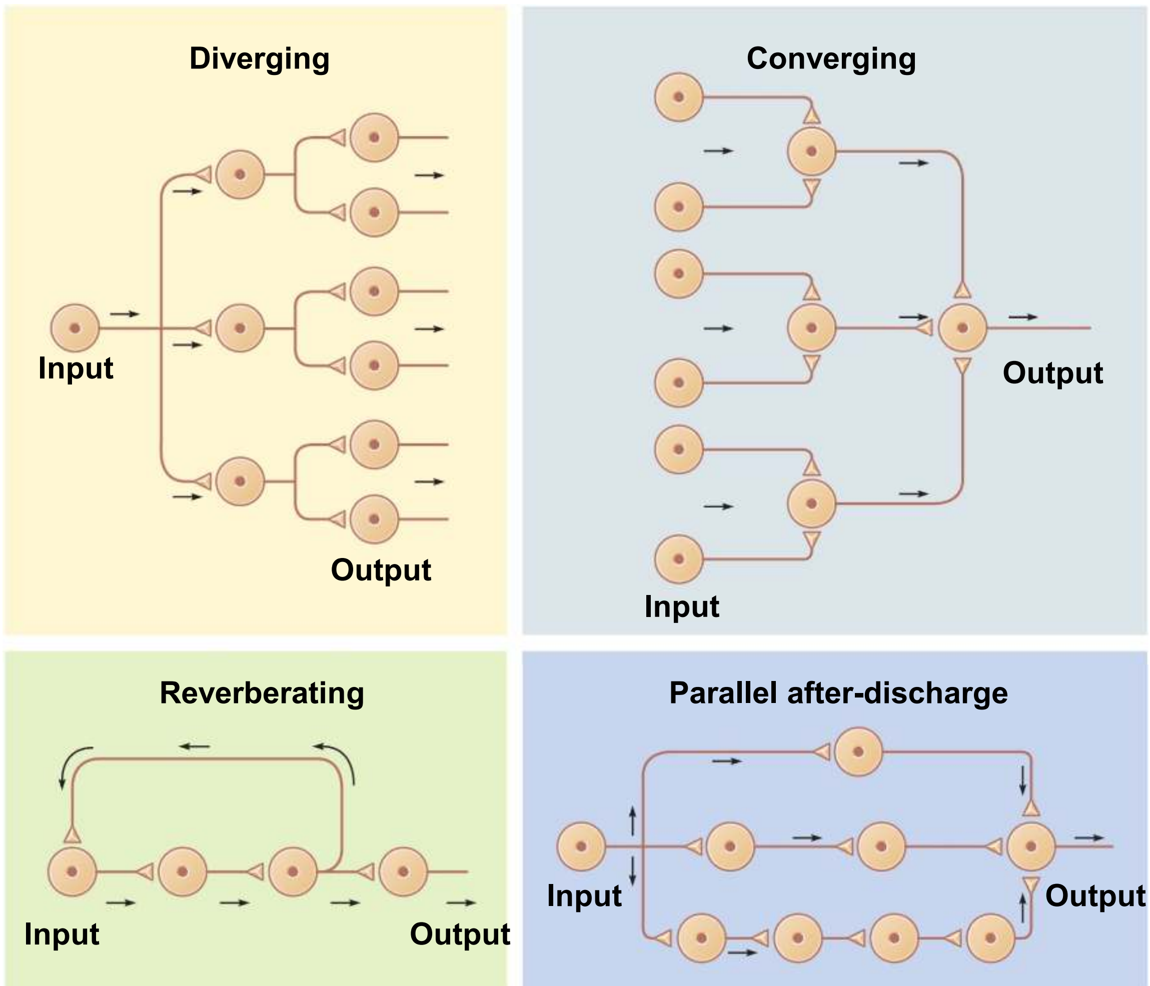


Figure 12.30