

INTRODUCTION

A. Definitions

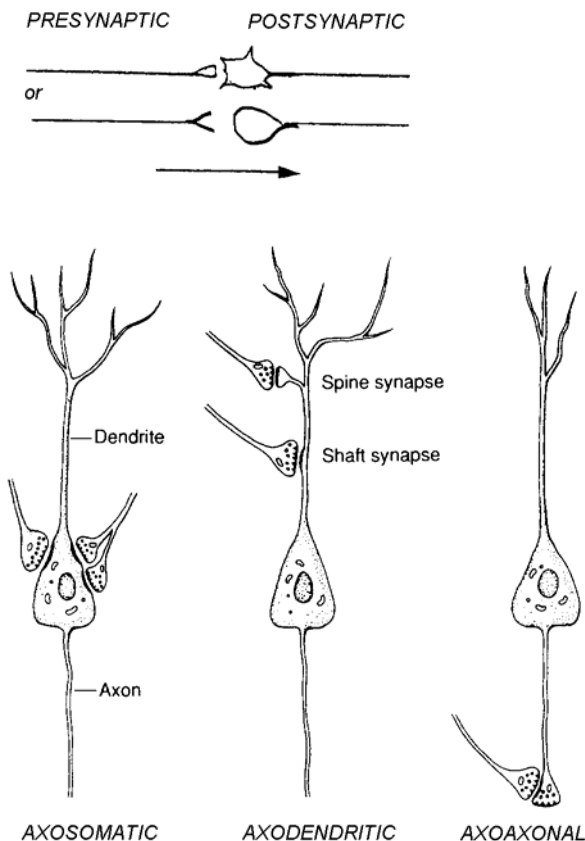
1. **Synapse:** junction between two excitable cells through which one cell influences the excitability of the other cell
2. **Presynaptic:** refers to the cell which influences the activity of the other cell
3. **Postsynaptic:** refers to the cell whose activity is influenced

B. Types

1. Chemically mediated synapses: presynaptic neuron releases a chemical or *neurotransmitter* that influences the excitability of the postsynaptic cell
2. Electrical synapses: electrical current flow due to presynaptic action potentials passes directly to the postsynaptic neuron through gap junctions (cytoplasmic continuity), and so influences the postsynaptic neuron excitability

Note: chemically mediated synapses are by far the most common and important type in the mammalian nervous system, and will be the focus of the following material

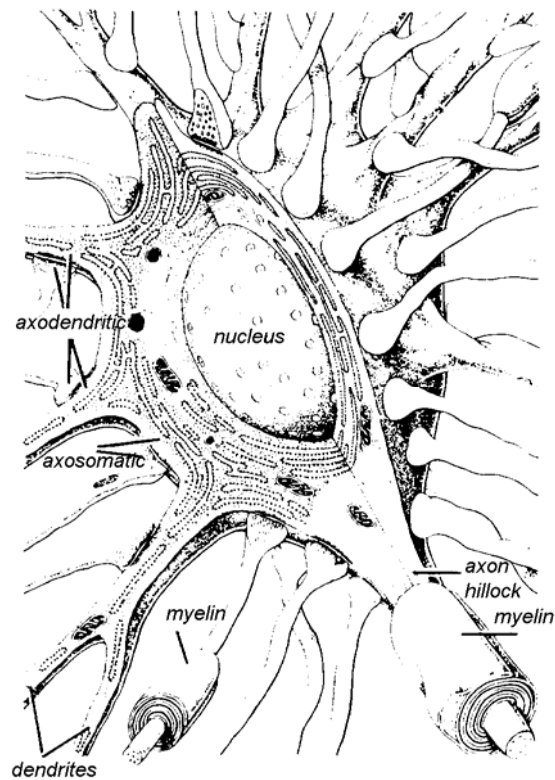
Note: a synapse is often schematically represented as



INTRODUCTION (continued)

C. Morphology

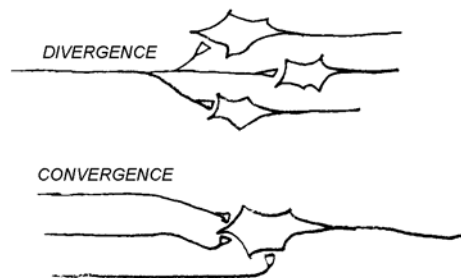
1. Site of synapse
 - a. axosomatic : presynaptic axon to postsynaptic soma
 - b. axodendritic: presynaptic axon to postsynaptic dendrite
 - c. axoaxonal: presynaptic axon to postsynaptic axon
2. *Presynaptic ending*: enlargement, sometimes termed the *synaptic bouton*; contains neurotransmitter-containing vesicles
3. *Synaptic cleft*: narrow space between presynaptic and postsynaptic cells
4. *Axon hillock or Initial Segment*: start of the axon where it leaves the soma



INTRODUCTION (continued)

D. Anatomical Organization

1. *Divergence*: each presynaptic axon generally has a number of branches that synapse with a number of postsynaptic cells
2. *Convergence*: each postsynaptic neuron generally has synapses from a number of presynaptic axons



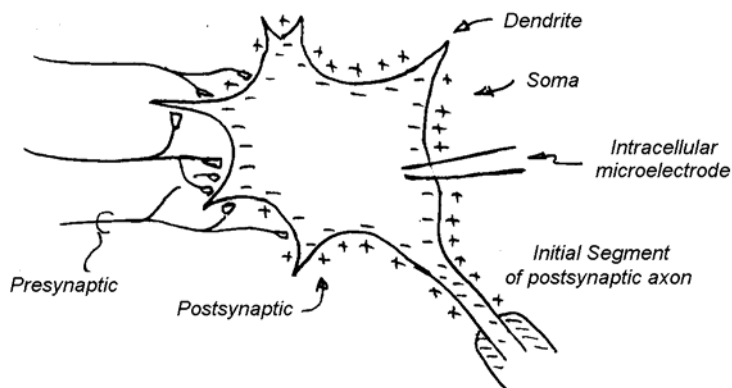
Note: Usually both are exhibited in nuclei and ganglions; that is, most presynaptic cells innervate a number of postsynaptic cells and most postsynaptic cells are innervated by a number of presynaptic cells.

E. General Properties

1. One-way conduction: a synapse transmits information from presynaptic to postsynaptic cell only, thus establishing a direction for nervous system information transfer
2. Synaptic delay: small delay (about 0.5 ms) between the time an AP arrives at the presynaptic terminal and the time the postsynaptic cell's activity is altered
3. Spatial summation: summation of the effects of several presynaptic cells on the postsynaptic cell
4. Temporal summation: summation of the effects of several closely spaced action potentials on the postsynaptic neuron
5. Some synapses are excitatory (increase the excitability of the postsynaptic cell); some are inhibitory (decrease the excitability of the postsynaptic cell)
6. Synaptic transmission is not generally one-to-one (contrast with the neuromuscular junction)

MECHANISMS OF SYNAPTIC TRANSMISSION (Chemical Synapses)

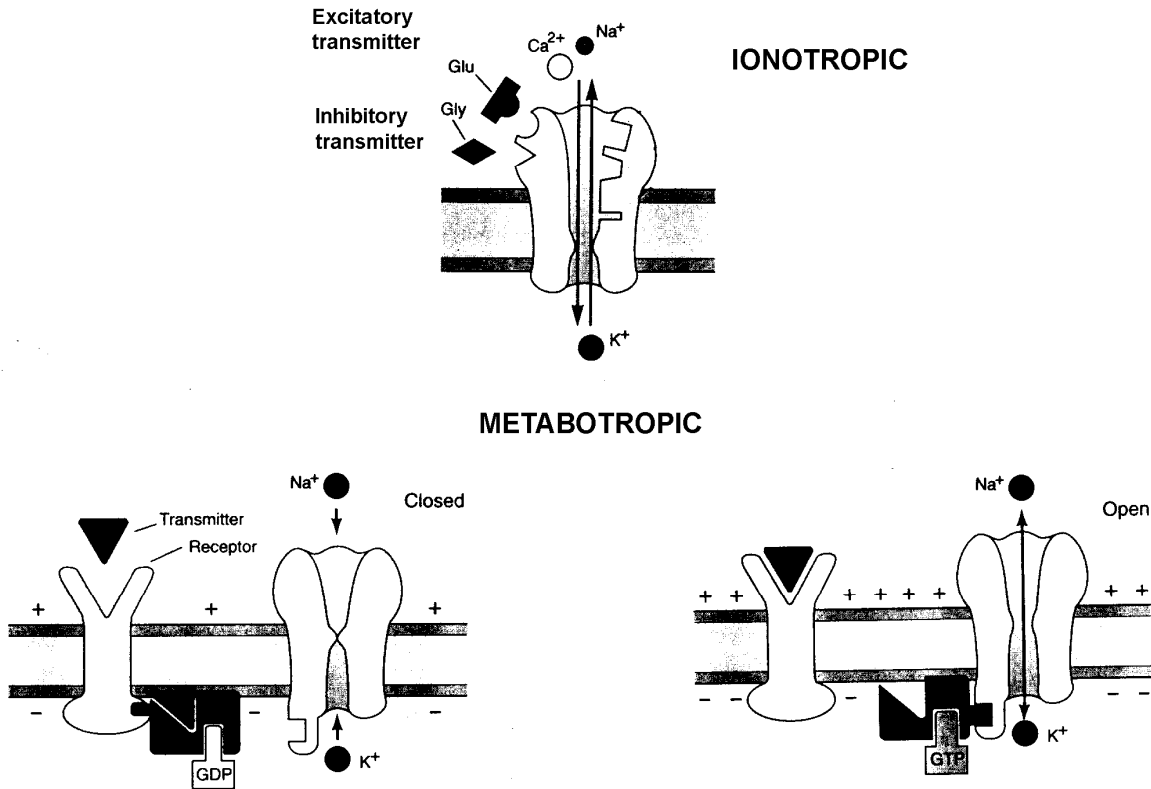
A. Schematic



B. Resting Postsynaptic Soma Membrane Potential \approx -60 to -70 mv, mainly due to a coupled Na^+ - K^+ -ATPase active transport pump (Na^+ pumped out of cell & K^+ pumped in), followed by back diffusion of K^+

C. General Sequence (similar to neuromuscular transmission)

1. AP propagates down the presynaptic axon to the presynaptic ending (and eventually dies out)
2. presynaptic ending depolarization causes ending Ca^{++} permeability to rise briefly by opening voltage dependent Ca^{++} channels
3. brief influx of Ca^{++} triggers release of stored neurotransmitter(s) from the presynaptic ending by vesicle fusion with the presynaptic cell membrane; there may be only one transmitter released or there may be more than one; meanwhile, the Ca^{++} is pumped out of the presynaptic ending by an active transport Ca pump in the ending membrane
4. transmitter(s) diffuses across the synaptic cleft to the postsynaptic membrane
5. transmitter binds to receptors on the postsynaptic cell, where it leads to excitation or inhibition of the postsynaptic cell. The mode of action of the neurotransmitter may be either
 - a. ionotropic synapse: neurotransmitter binds direct to a channel receptor, changing the channel permeability
 - b. metabotropic synapse: neurotransmitter binds to a receptor on the postsynaptic neuron, which initiates a sequence of intracellular biochemical reaction eventually increasing or decreasing the concentration of an intracellular substance ("second messenger") that changes the permeability of an adjacent channel



D. Excitatory Synapse

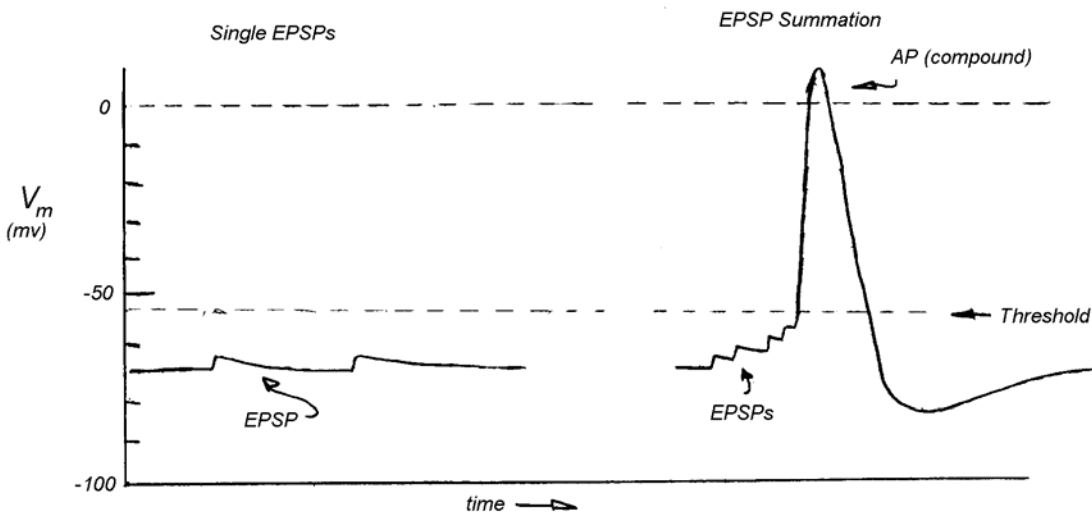
1. the binding of the transmitter(s) to postsynaptic cell receptors causes a small depolarization of the underlying postsynaptic membrane
 - a. depolarization due to opening of channels that increase permeability to both Na^+ and K^+ & sometimes Ca^{++} and/or Cl^- (nonspecific channel)
 - b. because Na^+ is so far out of electrochemical balance, the predominant ionic movement is usually Na^+ influx
2. depolarization spreads rapidly throughout the postsynaptic soma and the axon initial segment (axon hillock)

Note: the soma depolarization is termed an EPSP (**Excitatory PostSynaptic Potential**)

3. EPSP dies away over next several msec, as transmitter diffuses away from the receptor, and is
 - a. transported back into the presynaptic terminal and stored in vesicles (main mechanism at most synapses)
 - b. chemically inactivated
 - c. removed by the circulation

4. Characteristics of the EPSP
 - a. graded; not all-or-none; not regenerative
 - b. size depends on numerous factors, including
 - 1) number of presynaptic terminals activated
 - 2) quantity of transmitter released from each presynaptic terminal
 - 3) chemical environment (e.g. $\text{Ca}^{++}\uparrow \Rightarrow \text{EPSP}\uparrow$)
 - c. propagated passively (with decrement); thus limited essentially to soma and initial axon segment
 - d. single EPSP usually is small & insufficient to depolarize the postsynaptic membrane to threshold
 - e. EPSPs can sum
 - 1) spatially: EPSPs from different presynaptic terminals can add
 - 2) temporally: successive EPSPs from the same presynaptic terminal can add if they occur close together
5. Postsynaptic cell action potential

- a. due to summation of EPSPs to reach threshold
- b. excitation is initiated at the site with the lowest threshold, usually the axon initial segment (axon hillock) because it has the greatest density of voltage-gated Na channels
- c. once initiated, the AP is propagated (all-or-none) down the axon



6. Explains
 - a. unidirectional transmission
 - b. synaptic delay (due to the time required for the sequence noted above)
 - c. spatial summation (due to the ability of EPSPs to sum)
 - d. temporal summation (due to the ability of EPSPs to sum)
 - e. not one-to-one (requires a number of EPSPs to reach threshold)

MECHANISMS OF SYNAPTIC TRANSMISSION (continued)

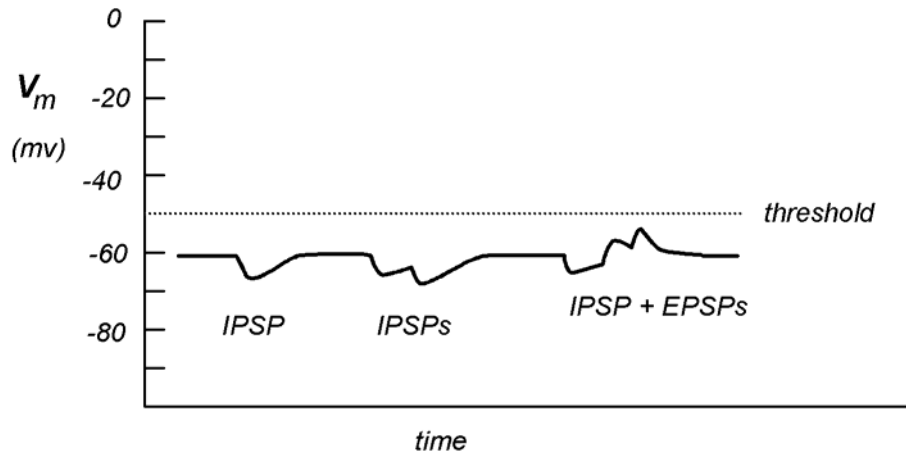
E. Inhibitory Synapse: **Postsynaptic Inhibition**

Same steps as for the excitatory synapse, except

1. binding of transmitter(s) to the postsynaptic membrane causes membrane to become less excitable
 - a. mechanism: increase in K^+ or Cl^- or both
 - b. result: membrane hyperpolarization and/or more difficult to depolarize membrane
 - c. thus, requires more/larger EPSPs to reach threshold
2. hyperpolarization spreads rapidly throughout the soma and axon initial segment

Note: soma hyperpolarize ion is termed and IPSP (Inhibitory PostSynaptic Potential)

3. IPSP dies away over next several msec



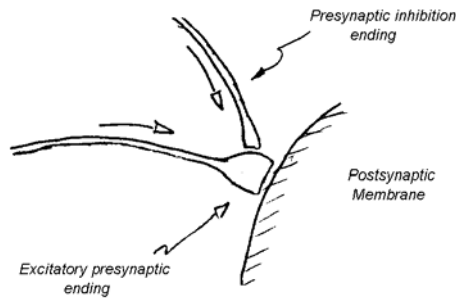
4. Characteristics of IPSP: similar to EPSP, except inhibitory
 - a. size depends on numerous factors, including
 - 1) number of presynaptic terminals activated
 - 2) quantity of transmitter released from each presynaptic terminal
 - 3) chemical environment (e.g. tetanus toxin and strychnine block inhibitory neurotransmitter action)
 - b. IPSPs can sum spatially and temporally with EPSPs and other IPSPs

F. Alternative Mechanisms

1. EPSPs can be generated also by transmitters that reduce postsynaptic membrane K^+ permeability
2. IPSPs can be generated also by transmitters that reduce postsynaptic membrane Na^+ permeability

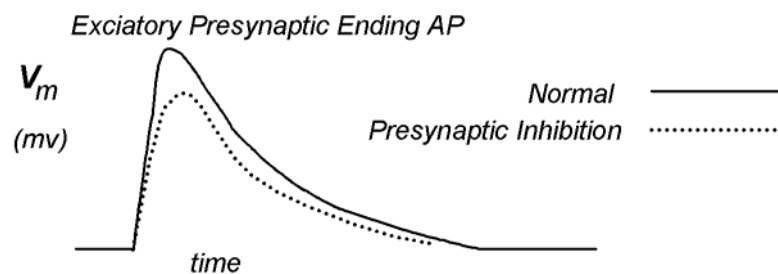
F. Inhibitory Synapse: **Presynaptic Inhibition**

1. Basis: reduction of the amount of transmitter released by an excitatory presynaptic ending
2. Mechanism: Inhibitory ending on the excitatory presynaptic ending



3. Sequence

- a. AP arrives at axon terminal of ending responsible for presynaptic inhibition
- b. release of neurotransmitter which
 - 1) interferes with depolarization-induced Ca^{++} influx at the excitatory ending; or
 - 2) decreases the amplitude of the excitatory ending AP by increasing K^+ and/or Cl^- permeability



- c. in either case, the amount of excitatory transmitter released by the excitatory presynaptic ending is reduced, which causes the resulting EPSP to be smaller

SYNAPTIC TRANSMITTERS

A. Wide variety of types, including

1. acetylcholine
2. amines (e.g., epinephrine, norepinephrine, dopamine, serotonin, histamine)
3. amino acids (e.g., glycine, glutamine)
4. purines (e.g., ATP)
5. peptides (e.g., substance P)

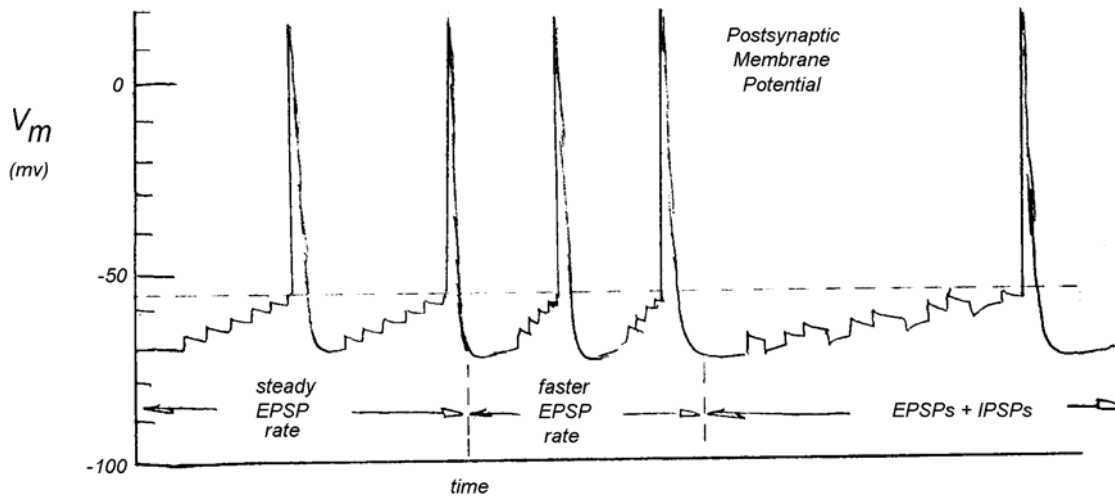
B. Each synapse is characterized by the neurotransmitters that are effective at that synapse

SYNAPTIC TRANSMITTERS (continued)

- C. A given neurotransmitter can be either excitatory or inhibitory, depending upon the receptor to which it binds on the postsynaptic cell

SUMMARY: POSTSYNAPTIC NEURON INTEGRATION

- A. Based on summation of influences from all active synapses on cell soma and initial segment
- B. Postsynaptic discharge frequency depends on $\sum EPSPs - \sum IPSPs$



SUMMARY: NEURAL CODING

- A. Coded as AP frequency for rapid information transmission
- B. Coded as membrane potential amplitude for integration
- C. Pattern

Amplitude \Rightarrow Frequency \Rightarrow Amplitude \Rightarrow Frequency, etc.

- D. Example: Simple spinal reflex

