Synapses

A. Types of Synapses
   1. Electrical Synapses
      - gap junctions → direct electrical connection between cells
      - uncommon in the nervous system
   2. Chemical Synapses
      - most common type in the nervous system
      - release a chemical neurotransmitter which binds to a receptor
        presynaptic cell (neuron)
        - axon terminal (synaptic end bulb)
        - synaptic vesicles - contain neurotransmitter
        - synaptic cleft
        postsynaptic cell (neuron or muscle fiber)
        - receptor proteins

B. Synaptic Transmission
   neuromuscular junction: synapse between a motor neuron and a skeletal muscle cell
   acetylcholine (ACh) is the neurotransmitter
   - ACh binds to receptors on the postsynaptic membrane
   - ACh receptor is a chemically-gated (ligand-gated) ion channel
   - opening of chemically-gated channels results in a graded postsynaptic potential (PSP)

   Synaptic Transmission at the Neuromuscular Junction

   1. Action potential arrives at the presynaptic axon terminal.
   2. Voltage-gated calcium (Ca^{2+}) channels open in the presynaptic membrane, allowing Ca^{2+} ions to flow into the presynaptic cell.
   3. Synaptic vesicles migrate to the presynaptic membrane, releasing acetylcholine (ACh) into the synaptic cleft.
   4. ACh molecules diffuse across the synaptic cleft and bind to postsynaptic ACh receptors.
   5. ACh binding to receptors opens chemically-gated ion channels in the postsynaptic membrane. These channels are permeable to Na^+ and K^+ ions.
   6. Na^+ ions flow into the postsynaptic cell, causing a graded depolarization of the postsynaptic membrane (an EPSP).
   7. ACh is rapidly broken down by acetylcholinesterase; ion channels close and membrane returns to resting state.

Postsynaptic potential - graded potential in the postsynaptic cell membrane that results from binding of neurotransmitter to receptors (synaptic transmission).

1. **Excitatory postsynaptic potential** (EPSP)
   - depolarizes the postsynaptic membrane toward the threshold for an AP
   - can result from opening of Na^+ channels or closing of K^+ channels
   → increases the likelihood of an AP forming in the postsynaptic cell

2. **Inhibitory postsynaptic potential** (IPSP)
   - hyperpolarizes the postsynaptic membrane or holds it near the resting level
   - can result from opening of K^+ channels or Cl^- channels
   → decreases the likelihood of an AP forming in the postsynaptic cell
C. Neural Integration

1. Synaptic Inputs
   - neurons have multiple inputs from other neurons
   - EPSPs and IPSPs formed at the dendrites and cell body spread toward the trigger zone
   - APs are triggered at the axon hillock only when the membrane reaches threshold

2. Neural Networks - connection pathways between groups of neurons
   a. divergent pathways
   b. convergent pathways

3. Summation
   - summation of many EPSPs and IPSPs determines if APs are formed in the postsynaptic cell
   a. spatial summation - EPSPs from different synapses can add together or
      IPSPs can cancel out EPSPs
   b. temporal summation - EPSPs can add together if they occur close together in time

D. Receptor Types and Mechanisms of Action

1. Cholinergic Receptors - bind to acetylcholine (ACh)
   a. Nicotinic cholinergic receptor (e.g., neuromuscular junction, autonomic ganglia)
      - ion channel-receptor
      binding of ACh directly opens chemically-gated channels, allowing Na+ to flow in
      - fast response, direct
      - always excitatory
   b. Muscarinic cholinergic receptor (e.g., parasympathetic target cells: heart, GI tract, etc.)
      - G protein coupled receptor (GPCR)
      binding of ACh to receptor activates a G protein, activated by binding of GTP
      activated G protein subunit interacts with a K+ ion channel, causing it to open or close
      - slower response, indirect
      - can be excitatory or inhibitory

2. Adrenergic Receptors - bind to norepinephrine (NE) and epinephrine (Epi)
   a. alpha (α) adrenergic receptors
   b. beta (β) adrenergic receptors

E. Classes of Neurotransmitters

1. acetylcholine
2. amines
   - norepinephrine
   - dopamine
   - serotonin
3. amino acids
   - glutamate - excitatory in CNS
   - gamma-aminobutyric acid (GABA) - inhibitory in CNS
   - glycine - inhibitory in CNS
4. neuropeptides
   - e.g., endogenous opioids
5. gases
   - nitric oxide (NO)

F. Synaptic Pharmacology (examples)

1. nicotinic cholinergic synapses
   - botulinum toxin - blocks ACh release ("Botox")
   - curare - blocks ACh receptor
   - nerve gas - inhibits ACh-esterase
2. muscarinic cholinergic synapses
   - atropine - blocks muscarinic ACh receptors
3. monoamine synapses
   - MAO inhibitors - block breakdown of NE, dopamine, & serotonin (non-selective)
   - SSRIs - selective serotonin reuptake inhibitors → ↑ concentration of serotonin at synapses
      clinical application: antidepressant drugs