Synaptic transmission
1) Communication within the nervous system
2) A site of plasticity for learning and memory
3) A site of action for disease, psychoactive drugs

Ionic Mechanisms of Synaptic Excitation
Crayfish NMJ as a model for human brain synapses

Crayfish NMJ as a model for human brain synapses

Neuromuscular Innervation

Multi-terminal
Poly-neuronal
Inhibition
Often no APs

Uni-terminal
Uni-neuronal
Excitation Only

Mammals

Arthropods

See Synapse Tutorial on class web site for review
Crayfish NMJ preparation

**Figure A.2. Tail Segment.** D. Ventral view of a crayfish tail segment after dissection and staining with methylene blue. Note the ventral nerve cord (vnc), ganglia of the 3rd and 4th segments (g3, g4), nerves (n1, n2, n3), and the superficial flexor muscle (sf) with its attachment point (ma). Go **down** a layer to remove the labels. Go **up** a layer for Janus green stain.
Figure 8.A. Correlation of APs and PSPs. Action potentials in nerve 3 cause postsynaptic potentials in a fiber of the superficial flexor muscle. Note that there are at least four different size classes of APs and several sizes of PSPs.
Map Muscle Innervation Patterns
(Also better distinguish number of axons in nerve 3)

See G-PRIME for example of-
Muscle Innervation - Cross Correlation
EPSP trying to reach AP threshold

Synaptic integration

Spatial and temporal
Space constant important
Spatial summation

Time constant important
Temporal summation
Synaptic Inhibition

Two flavors:
   Algebraic Summation
   Shunting
How do they work?

Figure 8. D. Inhibition. The very large action potential is characteristic of the inhibitory motor neuron, and a small hyperpolarization follows it in the muscle fiber. It is unusual to see the inhibitory PSP because its reversal potential is so close to the resting potential.
Synaptic Inhibition

Stimulation of inhibitory nerve blocks AP production

GABA $\text{H}_3\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}^-$

Glycine $\text{H}_3\text{N}^+\text{C}^-\text{COO}^-$
Presynaptic inhibition reduces transmitter release
Types of Chemical Synaptic Transmission

A. Ionotropic
- Direct, fast

B. Metabotropic
- Indirect, ~slow
Action Potentials can arise from subthreshold depolarizations if they are not spontaneous

**Video 5.12. Postsynaptic firing.** This cell fires an action potential after receiving synaptic input from another cell. The postsynaptic potential can be seen as a bump preceding the action potential.
Stimulate presynaptic axon

![Diagram of a synapse with stimulation and recording](image.png)
Steps in ionotropic chemical synaptic transmission

1. Transmitter is synthesized and then stored in vesicles
2. An action potential invades the presynaptic terminal
3. Depolarization of presynaptic terminal causes opening of voltage-gated Ca\(^{2+}\) channels
4. Influx of Ca\(^{2+}\) through channels
5. Ca\(^{2+}\) causes vesicles to fuse with presynaptic membrane
6. Transmitter is released into synaptic cleft via exocytosis
7. Transmitter binds to receptor molecules in postsynaptic membrane
8. Postsynaptic current causes excitatory or inhibitory postsynaptic potential that changes the excitability of the postsynaptic cell
9. Opening or closing of postsynaptic channels
10. Retrieval of vesicular membrane from plasma membrane
Excitation: Conductance increase (resistance decrease): Channels in membrane open

Membrane potential goes towards $V_{\text{rev}}$ (Equil. Pot)
V_{rev} = E_{ion}

Results if EPSP were due to only Na\(^+\) or K\(^+\)
\[ I_{syn} = g_{ACh}(V_m - V_{rev}) \]

\[ (V_m - V_{rev}) = \text{Driving force} \]

Depolarizing because of large Na driving force

-60 mV
Conductance change due to multiple ions

\[ V_m = \frac{RT}{F} \ln \frac{P_K[K]_o + P_{Na}[Na]_o}{P_K[K]_i + P_{Na}[Na]_i}. \]

\[ (C) \]

Reversal potential

EPC amplitude (nA)

\[ \begin{array}{c|c|c}
0 & +70 & \\hline
200 & 0 & \\hline
-200 & -60 & \\hline
-300 & -110 & \end{array} \]

Postsynaptic membrane potential (mV)
Inhibition: Conductance increase (resistance decrease):

Membrane potential goes towards $V_{\text{rev}}$ (Equil. Pot)

Membrane potential goes towards $V_{\text{rev}}$ (Equil. Pot)
Most common fast transmitters

Proof of Neurotransmitter Identity??
  Presence
  Action
  Release
  Pharmacological Congruence
  Synthetic/packaging machinery

**SMALL-MOLECULE NEUROTRANSMITTERS**

- **Acetylcholine**
  \[(\text{CH}_3)_3\text{N}^+\text{CH}_2\text{CH}_2\text{O}^-\text{C}^-\text{CH}_3\]

- **AMINO ACIDS**
  - **Glutamate**
    \[\text{H}_3\text{N}^-\text{C}^+\text{COO}^-\]
  - **GABA**
    \[\text{H}_3\text{N}^+\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}^-\]

- **Glycine**

**INDOLEAMINE**

Serotonin (5-HT)

\[\text{HO}-\text{CH}_2\text{CH}_2\text{NH}_3^-\]

\[\text{N}\]
Freeze-fracture of NMJ
EM section of NMJ
Brain Synapse

Few vesicles at each synaptic site