From last lecture:

**Ion Flow During an A.P.** (reference 2.17)
- Fact 3: K+ channels are a bit slower than the NA+ channels
- NA+ in -> Depolarize
- K+ out -> Hyperpolarize
- Description of movement:
  - **Threshold of excitation** -> NA+ in by **diffusion and electrostatic pressure**
    - Channels opened by membrane potential = voltage-dependent ion channels
  - Voltage-dependent potassium channels are less sensitive than sodium channels, need greater level of depolarization and open later than sodium channels
  - **Peak of action potential** ~ 1msec, sodium channels -> refractory, cannot open until membrane reaches resting potential, no more NA+ can come in
  - **Voltage-dependent potassium channels are open**, K+ move freely, inside is positively charged, K+ out by **diffusion and electrostatic pressure** -> membrane potential normalizes, potassium channels close
  - **Membrane potential normalizes**, another depolarization will open them
  - **Membrane overshoots** 70mV, gradually normalizes. Sodium-potassium transporters remove spare Na+ ions and retrieve spare K+ ions

**Conduction of a Depolarization**
- In dendrites: 'Passive propagation', there is an attenuation of a signal transmission
- If close to injection site, we see a bump in voltage
- If looking further away, the bump is smaller
- In a dendrite: the depolarizing stimulus (input) is attenuated along the branch
- Inputs far along the axon will likely have little overall effect

**Conduction of the Action Potential** (reference 2.19)
- In axons, 'active propagation' the signal is regenerated, no attenuation
- No matter where you are on the axon, you will find the same action potential
- **All-or-none conduction Law**: either you have an action potential or you don't (no half or extra potential)

**Saltatory Conduction in an Axon** (reference 2.21)
- If the stimulus is large enough, it will produce the sodium input and potassium output
- Decreases for few millimeters underneath myelin sheath then action potential regenerates at nodes of Ranvier
- 260 mph, travels very quickly
- "jumping" kind of conduction

**Rate Law**
- **The greater the stimulus, the greater the number of action potentials (per second)**
- Spontaneous action potential: not related to stimulus, they occur before or after
- **Elicited Action potentials**: occur due to stimulus
- During stimulus there is a certain amount of action potentials per second that occur
- If bigger stimulus, there will be a greater number of action potentials, but not larger action potentials
The Synapses:

The Synapses
- Neurons are 'simple' computing devices
- Brain functions (including cognitive functions) rely on the activity of networks of interacting neurons
  - **Interactions** = synapses

Synaptic Morphology
- Pre/post synaptic sites
- Types of synapses
- Synaptic vesicles
- Neurotransmitter

Axonal Transport
- "stuff" moves along the axon microtubules (axoplasmic transport)
- Microtubules add rigidity to axon
- Questions: What stuff? Where does it go?
  - From soma to terminal boutons

A Synapse: The parts (reference 2.23)
- Synaptic vesicles are filled with neurotransmitter molecules
- Terminal bouton does not touch dendrite, there is a gap called the synaptic cleft (very tiny)
- Darker line of membrane - postsynaptic density
- Electron micrograph (blows up to rate of 1 mil times)

3 Kinds of Synapse Locations (reference 2.22)
- **Axo-Dendritic**: if an axon makes synapse to either a smooth dendrite or a dendritic spine
- **Axo-Somatic**: make synapse on the cell body itself
- **Axo-Axonic**: synapse made on a synapse, (axon on another axon which makes a synapse on itself)
- Action potential runs along the presynaptic axon -> Arrives at: smooth dendrite, spine, or soma -> an action potential is/is not generated by the postsynaptic neuron
- This is how you go from one neuron to another
- Synaptic Physiology: the synapse is the place where 2 neurons 'talk' to each other. How does a synapse work?

Neurotransmitter Release (reference 2.24)
- 1st: Presynaptic action potential, anything else is ignored
- 2nd: Arrives at axon, and invades terminal bouton and the vesicles will fuse with membrane
- 3rd: Whatever is inside will be released out the synaptic cleft - neurotransmitters will be released
- Could be any number of vesicles
- Action potential of A triggers vesicle fusion at synapse
- Neurotransmitter molecules are released into synaptic cleft
- They are 'received' by the postsynaptic membrane in B by 2 kinds of neurotransmitter-dependent ion channels (aka receptors)
- Some vesicles that were fused will be recycled and turn into vesicles again

Ionotropic Receptors (Reference 2.25)
Normally the receptor channels are closed and the opening is too small for ions to go through. As soon as the right kind of receptor binds to it, the channel opens up and allows ions to move through either in or out.

Receptor is selective for which neurotransmitters open them and which ions go through (sodium, potassium, chlorine).

Neurotransmitters do not go through receptors (think lock and key).

**Fast and local action**
- Reflexes, perception, information processing
- EX: Neurotransmitter activates sodium channel receptor and will depolarize cell

**Metabotropic Receptor (Reference 2.26)**
- Second Messengers: Molecules that link receptors to ion channels, triggered by G-proteins
- Transmitter binds -> Activates Receptor -> Sends signal to nearby ion channel -> Activates 'Second Messengers' -> Open ion channels and intracellular effects
- **Slow and diffuse action**
  - Mediate the influence of hormones and drugs, state-dependent information processing
- Not one-to-one and can activate many ion channels

**IPSPs and EPSPs (Reference 2.27)**
- Excitatory/Inhibitory Post-Synaptic Potential
- **Examples:**
  - Sodium rushes in -> depolarization = EPSP
  - Potassium channel, potassium leaves since more inside than outside -> hyperpolarization (more negative) = IPSP
  - Chlorine rushes in -> hyperpolarization = IPSP
  - Calcium rushes in (nearly 0 calcium inside) and activates enzyme -> depolarization = EPSP
- One given neuron releases the same neurotransmitter at all of its synapses
- Can say if neuron is excitatory or inhibitory so the synapses will be all either excitatory or inhibitory

**Regulation of Release: Re-uptake**
- Recycling of neurotransmitter molecules
- **Help with fast, efficient neurotransmission (high signal-to-noise because of the recycling)**
- Neurotransmitter sitting in the synaptic cleft not binding to postsynaptic membrane are "wasteful"
- On presynaptic membrane, there are special channels that will re-uptake these molecules so they can be reused and are returned to terminal bouton
- Noise is the floating neurotransmitters (not supposed to, since the action potential is over and we need to terminate the signal quickly)

**Regulation of Release: Auto-receptors, Enzymatic Deactivation**
- **Auto-receptors:**
  - On the presynaptic membrane (aka presynaptic receptors)
  - Regulate synthesis and release of neurotransmitter (no ion flow)
  - Mostly metabotropic
- **Enzymatic Deactivation**
  - Acetylcholine (ACh) vs Acetylcholine esterase (AChE)
  - Neurotransmitter ACh, the enzyme that deactivates it is AChE
- Regulation of Release: Axo-Axonic Synapses (Reference 2.30)
- Presynaptic inhibition/facilitation
- Axo-dendritic synapse from B→C
- Axo-axonic synapse from A→B
- AB synapse helps (or interferes with) the BC synapse
- AB synapse exerts a presynaptic facilitation (or inhibition) of the BC synapse
- Will not change nature of BC but will make it work slightly differently

**Non-synaptic Communication**
- Fun fact 1
  - Some neurotransmitters are released diffusely (leak out) neuromodulators
  - They have slow and diffuse actions (peptides) and influence many postsynaptic targets
  - Involved in attention, emotions, pain sensitivity
  - One neuron has the potential to interact or affect multiple neurons by using a neuromodulator
- Fun fact 2
  - Most hormones are produced by endocrine glands in the body (adrenal glands, stomach, liver)
  - Some neurons produce hormones rather than neurotransmitters
  - Some neurons have hormone receptors (target cells)
  - Communication between nervous system and body (sex hormones and aggression, stress)

**Synaptic Physiology:**
- Presynaptic AP -> Vesicle Fusion -> Neurotransmitter Release -> Receptor Opening -> Ion Flow -> Postsynaptic potentials
- Electrical, mechanical, and chemical
- Neural integration in space or time

**Spatial Summation**
- **Post synaptic potentials from different synapses sum up at the soma**
- If A & B are excitatory, if any synapse it will be depolarization
- If C & D are inhibitory, if any synapse it will be hyperpolarization
- A+B = small bumps together = big bump(inhibitory post synaptic potential), big depolarization
- C+D = hyperpolarization = big hyperpolarization
- A+C = Cancels out, no post synaptic potential
- **When located in different places = spatial summation**

**Temporal Summation**
- **Postsynaptic potentials from the same synapse (but different action potentials) sum up**
- Stimulate A twice slowly (two EPSPs) = two bumps on top of each other, fast
- Stimulate B twice slowly (two IPSPs) = two bumps underneath each other, fast
- A has a higher chance for an action potential = only happens if you have enough depolarization, must be upward and pushes closer to threshold
- B would prevent neuron from "talking"

**Spatio-Temporal Summation (Reference 2.29)**
**Preview: When synaptic transmission goes wrong**
- Not enough neurotransmitter binding: Acetylcholine and Myasthenia gravis treated by inhibition of enzymatic deactivation
- Not enough neurotransmitter binding: Depression and Selective Serotonin Reuptake Inhibitors
- Weakness of postsynaptic receptors: Dopamine and drug addiction
- Too much binding: Dopamine and schizophrenia
- Death of presynaptic neurons that produce a specific neurotransmitter: dopamine and Parkinson's disease
- Charge in number/sensitivity of postsynaptic receptors: glutamate and learning and memory