I. Action potentials and synapses
   A. Action potential (an impulse, depolarization wave)
      1. The way in which most neurons communicate with another neuron or an effector (a muscle or a gland).
      2. In order to generate an action potential a cell must have a resting membrane potential.
         a. The **resting membrane potential** is a difference in charge between the inside and the outside of the cell when the cell is at rest.
         b. A difference in charge is created by the presence of differing concentrations of positively and negatively charged ions inside and outside the cell and the movement of these ions through **ion channels**.
         c. Ion channels
            i. Functional proteins within the plasma membrane that allow ions to move through the membrane down their concentration gradient.
            ii. **Passive ion channels** are always open.
            iii. **Gated ion channels** are opened or closed in response to a stimulus (voltage change, mechanical stimulation, a chemical, light).
         d. A resting neuron has a greater concentration of Na^+ and Cl^- outside the cell.
         e. There is also a greater concentration of K^+ and large negatively charged proteins inside the cell.
         f. Passive ion channels allow potassium to leak out of the cell down its concentration gradient leaving behind the large negatively charged proteins that are too large to leave the cell.
            i. As the positive potassium leaves it would cause the inside of the cell to become more and more negative due to the large proteins.
         g. Passive ion channels allow positive sodium to leak into the cell at a much slower rate than potassium is leaking out.
            i. Since the positive charges are leaving at a faster rate than they are entering, a negative charge exists inside the cell and a positive charge outside the cell.
         h. As the inside of the cell becomes more negative the attraction of the negatives for the positive ions slows the flow of potassium out of the cell. At this point there is minimal ion movement and the resting potential is established.
         i. At the resting membrane potential there is a charge difference between the inside and outside of the cell at –70 millivolts.
         j. This charge difference is maintained by **sodium-potassium pumps** actively pumping sodium out of the cell and potassium into the cell before ion equilibrium can occur.
      3. An action potential is a rapid reversal of the membrane potential (from –70mV to +30mV).
         a. This reversal occurs due to a stimulus (chemical, mechanical, light, etc.) causing sodium channels to open and positively charged sodium to enter the cell. This depolarizes the cell (resting membrane potential becomes less negative) until a **threshold** (–55 mV) is reached.
         b. If this threshold is reached than an action potential arises.
      4. An action potential consists of 2 phases: depolarization and repolarization.
         a. Depolarization

i. If the threshold is reached (-55mV) this stimulates the opening of voltage gated sodium ion channels along the axon of the neuron. It specifically takes the voltage of –55mV to open them.
ii. This allows sodium ions to rush into the cell continuing the depolarization of the neuron to +30 mV at which time the sodium channels are closing.
iii. As the membrane potential passes through 0mV it also stimulates the opening of voltage gated potassium ion channels beginning the repolarization phase.

b. **Repolarization**
   i. Repolarization occurs when the membrane potential becomes more negative.
   ii. The voltage gated potassium channels are slow to open and completely open at about the same time the sodium channels are closing.
   iii. Once the potassium channels are open potassium rushes out of the cell repolarizing the neuron back towards –70mV.
   iv. Since the potassium channels are slow to close extra potassium may leak allowing the membrane potential to drop below –70mV (**hyperpolarization**).
   v. Once the cell has repolarized, sodium-potassium pumps will reestablish the original ion concentrations.

5. The action potential is **propogated** (spreads) along the length of the axon towards the terminal knobs due to the charge reversal stimulating the opening of adjacent voltage gated sodium ion channels. This initiates an action potential at the next point on the membrane. This spreading action potential is an **impulse**.
   a. On unmyelinated axons the plasma membrane running the entire length of the axon must depolarize to threshold and generate an action potential, therefore conduction is relatively slow.
      i. This is referred to as **continuous conduction**.
   b. On myelinated axons action potentials can only be generated at the exposed surface of the axon (**Nodes of Ranvier)** where the myelin is not covering it.
      i. This results in the impulse “jumping” from node to node.
      ii. This type of conduction is called **saltatory (discontinuous) conduction**.
6. Action potentials work on an **all-or-none principal**.
   a. A stimulus must be strong enough for the neuron to reach threshold. If threshold is not reached than the neuron will not generate an action potential.

B. Synapses
   1. The junction between the terminal knobs of a neuron and the cell it is communicating with (another neuron, muscle or a gland).
   2. The neuron before the space (sending the signal) is the **presynaptic neuron**.
   3. The neuron after the space (being stimulated) is the **postsynaptic neuron**.
   4. The actual space between the neurons is the **synaptic cleft**.
   5. Presynaptic neurons release **neurotransmitters** in order to stimulate the postsynaptic neuron.
   6. These neurotransmitters are stored in **synaptic vesicles** within the synaptic end bulbs of the presynaptic neuron.
   7. The release of a neurotransmitter into the synapse.
      a. When an action potential reaches the terminal knob voltage gated calcium ion channels open.

    b. Calcium ions flow into the terminal knob activating an enzyme that triggers exocytosis of the neurotransmitter into the synaptic cleft.

8. The neurotransmitter diffuses across the synaptic cleft and binds to **receptors** in the postsynaptic neuron's plasma membrane.
    a. Receptors are a molecule or cluster of molecules that can bind to a complementary neurotransmitter (hormones also bind to receptors).
    b. The receptor and neurotransmitters have matching structures so that a specific neurotransmitter can only use a matching receptor (**lock and key**).
9. The binding of the neurotransmitter to the receptor triggers a specific change in the target cell.
    a. At some cells it stimulates the opening of ion channels (allows sodium ions to enter the resting cell) in order to depolarize the cell stimulating an action potential.
    b. In contrast, it may also open channels hyperpolarizing the cell (allows more potassium out of resting cell) to inhibit the production of an action potential.
10. **Note**: only presynaptic neurons can release the neurotransmitter and it can only bind to receptors on the postsynaptic neuron ensuring a one-way-transmission of impulses.
11. Removal of a neurotransmitter
    a. Once the neurotransmitter binds to the receptor it is essential that the neurotransmitter be removed from the synapse to prevent continuous binding and stimulation.
    b. Some neurotransmitters are degraded by enzymes. For example, **acetylcholinesterase** degrades the neurotransmitter acetylcholine into acetate and choline. These molecules then reenter the terminal knob to be repackaged.
    c. Some neurotransmitters are actively pumped back into the terminal knob to be repackaged within synaptic vesicles (norepinephrine and serotonin).
12. Excitatory neurotransmitters
    a. Lower the membrane potential (cause depolarization) of a postsynaptic neuron.
    b. Acetylcholine
        i. The most common neurotransmitter.
        ii. Stimulatory to skeletal muscle.
        iii. Stimulatory or inhibitory to smooth muscle.
        iv. Inhibitory to cardiac muscle.
        v. Blocked by botulin toxin, curare and cobra venom.
    c. Glutamate
        i. The most common neurotransmitter in the brain.
13. Inhibitory neurotransmitters
    a. Increase the membrane potential (make it more negative, hyperpolarize) of a postsynaptic neuron making it more difficult to initiate an action potential.
    b. GABA
        i. The most common inhibitory neurotransmitter in the brain.
        ii. Enhanced by valium.
    c. Glycine
        i. The primary inhibitory neurotransmitter in the spinal cord.