# 7.016 Recitation 15 – Fall 2018

*(**Note:** The recitation summary should NOT be regarded as the substitute for lectures)*



## Summary of Lecture 22 (11/2):

**Neurons and action potentials:** Ions can move across membranes through pumps and channels. Integral membrane proteins like these cross the membrane via transmembrane domains. Pumps are ATPases that set up the concentration gradients of ions across cell membranes, such that $K^+$ is high inside cells and other ions (such as $Cl^-$, $Na^+$, and $Ca^{2+}$) are high outside cells. A membrane potential is only set up by ions that move freely across the membrane through open channels, creating one side of the membrane that is more positive relative to the other side. This movement of ions does not dissipate the concentration gradient because the number of ions that move to generate a membrane potential is very small compared to the number of ions that need to be pumped to create a concentration gradient. Most cell membranes only contain open $K^+$ channels and thus only $K^+$ flows freely across membranes through channels; $K^+$ is high inside, causing it to flow outside, giving the inside of cells a negative membrane potential.

Ions can move across the membrane through open ion channels. Two forces act to dictate this movement – the concentration gradient and the electrical gradient. Ions move down their concentration gradient through channels, and ions move towards the side of the membrane that harbors the opposite charge.

Neurons are the cells of your nervous system that make connections with each other to transmit impulse/ signals. Each neuron has a cell body (where the nucleus lies), dendrites (multiple small projections that receive signals from other cells or from the environment), an axon (one large projection that sends signals to other cells) and an axon hillock (where all the changes resulting from the signals of the pre-synaptic neurons are summated and a decision whether or not to trigger the action potential is made). The place where the dendrites of one neuron communicate with the axon of another neuron is called a synapse.

Action potentials are the characteristic changes in membrane potential that propagate down the length of axons, unidirectionally at each point on the membrane from the hillock to the terminus. An action potential begins when a threshold membrane potential is reached and voltage-gated $Na^+$ channels are induced to open. Once $Na^+$ rushes in, the inside of the cell becomes positive, and this triggers the voltage-gated $K^+$ channels to open. Thus $K^+$ rushes out, restoring the membrane potential back to normal (roughly –70mV). Action potentials do not vary by amplitude; the maximal membrane potential is always +50mV. Instead, action potentials vary in frequency. The axons of motor neurons are coated in a myelin sheath that allows action potentials to travel down axons faster by allowing them to jump from node to node between patches of insulation.

**Neuron synapses:** A neuron receives signals at its dendrites and sends signals down its axon. A synapse occurs wherever the axon terminus of one neuron meets the dendrite of another neuron (or a muscle cell). At a synapse, the electrical signal of an action potential is converted to the chemical signal of a neurotransmitter, and then this is converted back into an electrical signal in the post-synaptic cell. This occurs because, when an action potential reaches the axon terminus of a pre-synaptic cell, voltage-gated $Ca^{2+}$ channels open, and intracellular calcium induces the exocytosis of neurotransmitters into the synaptic cleft. The exocytosed neurotransmitters then bind to receptors in the dendrites of the post-synaptic cell. These ligand-gated ion channels are then opened, leading to changes in membrane potential that are summed at the axon hillock. If the sum of all these changes is greater than threshold, the post-synaptic neuron will fire an action potential, first at the hillock and then at each subsequent location down the axon to the axon terminus.

Neuromuscular junctions are synapses where a nerve cell contacts a muscle cell. The neurotransmitter that is released from the neurons at neuromuscular junctions is Ach (acetylcholine). The release of enough Ach will trigger the muscle cell to contract. Ach is cleared from the synapse by an enzyme that cleaves Ach called Ach esterase.

Nerve-nerve synapses use many different neurotransmitters. Some neurotransmitters are excitatory; their receptors allow the flow of ions that causes the inside of the post-synaptic cell to become more positive, making the cell closer to the threshold needed to fire an action potential. Other neurotransmitters are inhibitory; their receptors allow the flow of ions that causes the inside of the post- synaptic cell to become more negative, making the cell farther from the threshold needed to fire an action potential.

There can be many, many inputs to a postsynaptic cell, and the summation of all of these inputs occurs across the cell body. If the excitatory inputs are sufficient to depolarize the membrane at the axon hillock, the voltage-gated $Na^+$ channels at the axon hillock will open and an action potential will be generated.

Synapses are dynamic, and changes at the synapse can alter the communication between neurons. This regulation can be due to alterations of the receptor such as a change in the concentration or number of a receptors, a change in the type of receptor, or a change in the affinity of a receptor for the neurotransmitter. Synaptic regulation can also occur due to alterations of the neurotransmitter (NT) such as a change in the amount of NT made, and change in the degradation of NT, or a change in the re-uptake of NT. If a pot- synaptic neuron receives repeated signals from a pre- synaptic neuron, it can cause a change in the number and types of receptors on the post- synaptic neuron and depending on the neurotransmitter it receives it can result in a long- term potentiation (increased responsiveness) or long- term depression (decreased responsiveness).

**Neuronal connections:** There are approximately $10^{10}$ neurons in the human brain each of which makes approximately $10^5$ synapses. Furthermore, there are approximately 500 different kinds of neurons based on different locations, the neurotransmitters they secrete and neurotransmitter receptors they have. Taken together these can form a very complex circuitry, mapping of which is an extremely challenging task! Numerous techniques can now be employed to map the neuronal circuits.

**Optogenetics:** In this technique, the idea is, you can control neuronal activity by light. This technique makes use of the light gated channels that are found in many microorganisms. You express the gene encoding these channels as a transgene in a specific neuron. These channels are ionotropic that are activated by light of a specific wavelength and allows the diffusion of ions and may be used to understand neuronal circuitry. This can be used to understand the function of a particular class of neuron in a specific location at a given time. The following link and the lecture slide further describe this technique and its importance.

http://video.mit.edu/watch/optogenetics-controlling-the-brain-with-light-7659/

**Questions**

**1.** Under resting conditions which ion(s) has a higher concentration inside the neuron? Which channels/ pumps maintain the resting membrane potential?

**2.** During depolarization phase, which ion(s) has a higher concentration inside the neuron? List the channels/ pumps that maintain the resting membrane potential.

**3.** What are nodes of Ranvier in neuron and how are they related to the conduction of action potentials?

**4.** Which cell types have a resting potential and which can generate action potentials?

**5.** Dopamine is one of major neurotransmitters in the mammalian brain that regulates mood, cognition and locomotion. Dopamine acts on two types of receptors: the D1 receptor is an inhibitory ligand-gated channel, while the D2 receptor activates the G proteins, and is excitatory. The released neurotransmitter is taken back into the presynaptic cell for re-use.

**a)** On what part of the neuron are the dopamine receptors localized?

**b)** The D1 receptor is inhibitory and transports $K^+$ ions. Would $K^+$ be moved into or out of the postsynaptic cell? **Explain** the mechanism underlying this inhibitory effect.

**c)** The D2 receptor is excitatory, and its ion targets are believed to include $Ca^{2+}$. Would $Ca^{2+}$ be moved into or out of the postsynaptic cell? **Explain** the mechanism underlying this excitatory effect.

**6.** At any one synapse, you can find multiple neurotransmitters and multiple receptors. If several different excitatory and inhibitory neurotransmitters and receptors are being used at a single synapse, explain how a postsynaptic neuron "decides" whether to fire an action potential or not.

**7.** Draw an action potential. Label the resting membrane potential, depolarization phase, repolarization phase on your drawing and list the channel/ pump responsible for establishing each phase.

**The Key**

**1.** Under resting conditions which ion(s) has a higher concentration inside the neuron? Which channels/ pumps maintain the resting membrane potential?

*Open channels (open $Na^+$, open $K^+$, open $Cl^-$) which allows specific ions to diffuse down their concentration gradient and $Na^+K^+$ ATPase pump that pumps 3 $Na^+$ ions out for every 2$K^+$ ions getting into the cell.*

**2.** During depolarization phase, which ion(s) has a higher concentration inside the neuron? List the channels/ pumps that maintain the resting membrane potential.

*$Na^+$ ions (due to voltage gated $Na^+$ channels, but can also include $Ca^{2+}$ due to ligand gated $Ca^{2+}$ channels.*

**3.** What are nodes of Ranvier in neuron and how are they related to the conduction of action potentials?

*These are non-insulated regions on the axons between the myelin sheath where you see the action potential*

**4.** Which cell types have resting potential and which can generate action potential?

*All cell types have resting membrane potential but neurons and muscle cells can generate action potential.*

**5.** Dopamine is one of major neurotransmitters in the mammalian brain that regulates mood, cognition and locomotion. Dopamine acts on two types of receptors: the D1 receptor is an inhibitory ligand-gated channel, while the D2 receptor activates the G proteins, and is excitatory. The released neurotransmitter is taken back into the presynaptic cell for re-use.

**a)** On what part of the neuron are the dopamine receptors localized?

*The dopamine receptors are located on post-synaptic membrane.*

**b)** The D1 receptor is inhibitory and transports $K^+$ ions. Would $K^+$ be moved into or out of the postsynaptic cell? **Explain** the mechanism underlying this inhibitory effect.

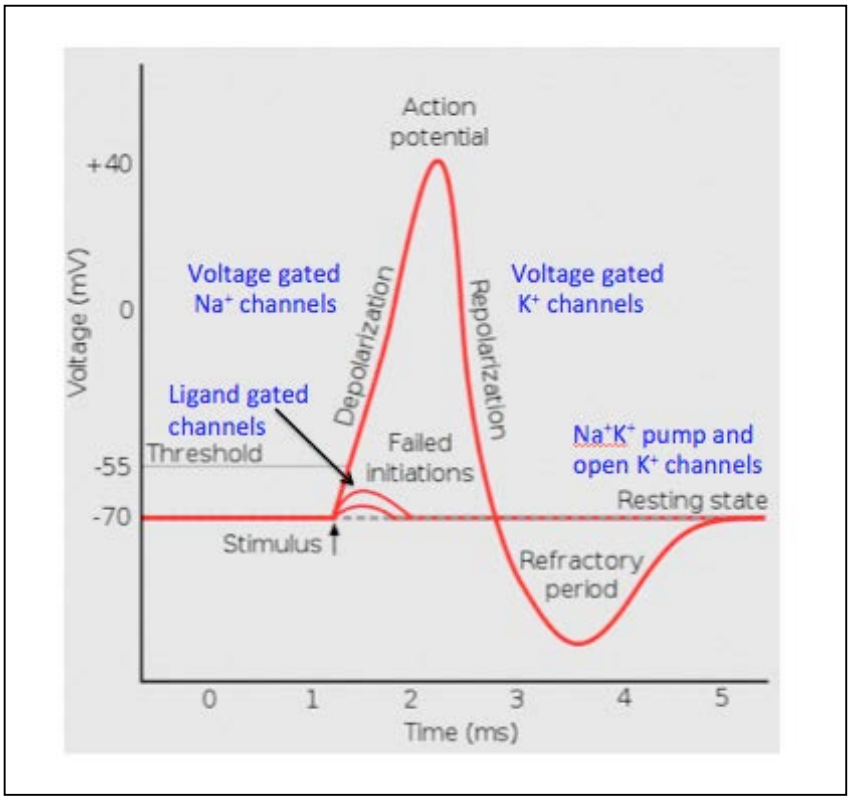
*At resting membrane potential the concentration of $K^+$ is higher inside the cell compared to outside. The binding of dopamine to its D1 receptor will therefore move $K^+$ ions out of the cell. As a result the membrane potential will be more negative relative to that at the resting state i.e. it is hyperpolarized, and further from threshold potential. Thus the chances of the post-synaptic neuron to fire an action potential will be reduced.*

**c)** The D2 receptor is excitatory, and its ion targets are believed to include $Ca^{2+}$. Would $Ca^{2+}$ be moved into or out of the postsynaptic cell? **Explain** the mechanism underlying this excitatory effect.

*The D2 receptors will promote the movement of $Ca^{2+}$ ions into the cell, since $Ca^{2+}$ concentration is higher outside the cell than inside. Thus, the inside of the cell becomes more positive relative to the unstimulated state; and the membrane potential will become closer to threshold potential and an action potential.*

**6.** At any one synapse, you can find multiple neurotransmitters and multiple receptors. If several different excitatory and inhibitory neurotransmitters and receptors are being used at a single synapse, explain how a postsynaptic neuron "decides" whether to fire an action potential or not.
*The decision whether to fire an action potential or not is made at the axon hillock of the post-synaptic neuron that summates all the changes, which take place when the cell body of this neuron synapses with the axon terminus of multiple pre-synaptic neurons.*

**7.** Draw an action potential. Label the resting membrane potential, depolarization phase, repolarization phase on your drawing and list the channel/ pump responsible for establishing each phase.



# 7.016 Introductory Biology
Fall 2018