

Lecture 3 Review

This review is intended as a brief summary of the lecture. I hope it will help you to focus your studies. It is not intended to provide you with an exhaustive review of the material that was covered. It is also not intended to provide a review of everything you will need to know for the exam. If a topic that was covered in lecture is not mentioned on this review, you should not take that to mean that you do not need to know that material.

Axons (the **pre-synaptic cell**) form connections with their target cell (**post-synaptic cell**) called a **synapse**. There are two types of synapses: **electrical** synapses and **chemical** synapses. The structure of these two types of synapses was reviewed during an earlier lecture and you should know the structural details of these synapses. Chemical synapses are the most common type of synapse. At chemical synapses, a chemical signal called a **neurotransmitter** is released from the axon terminal into the **synaptic cleft** and activates receptors on the **post-synaptic membrane**. The release of neurotransmitter from the axon terminal is triggered by the arrival of the action potential. The depolarization of the axon terminal by the action potential triggers the opening of **voltage-sensitive Ca^{++} channels**. The opening of these channels allows Ca^{++} into the axon terminal down its electrochemical gradient ($[\text{Ca}^{++}]_i = 0.0002\text{mM}$, $[\text{Ca}^{++}]_o = 2\text{mM}$, $E_{\text{Ca}^{++}} = +123\text{mV}$). By mechanisms that are not entirely understood, the increased concentration of Ca^{++} promotes the binding of synaptic vesicles to the pre-synaptic membrane of the axon terminal and the release of neurotransmitter by **exocytosis**. This process involves a family of proteins called **SNARE proteins** that are found in both the cell membrane and the membrane of the synaptic vesicle. These SNARE proteins bind to one another when Ca^{++} concentrations rapidly increase following the opening of the voltage sensitive Ca^{++} channels. Normally, only a few synaptic vesicles release their neurotransmitter in response to a single action potential. The amount of neurotransmitter released in a given period of time depends on the frequency of action potentials arriving at the terminal. The higher the frequency of action potentials, the more neurotransmitter released.

When the neurotransmitter is released it diffuses across the synaptic cleft and binds to membrane-bound receptors on the post-synaptic membrane. The binding of neurotransmitter to receptors on the post-synaptic membrane initiates a response in the post-synaptic cell. Most neurotransmitters have receptor subtypes that mediate different responses in the target cell. Table 6.1 from the book list some of the receptor subtypes. The effect of a neurotransmitter on its target cell is determined by the receptor subtype expressed on the target cell membrane, rather than the neurotransmitter. There are two types of post-synaptic responses: **fast synaptic responses** and **slow synaptic responses**.

In **fast synaptic responses** the receptor is generally part of an ion channel in the post-synaptic membrane. These ion channels consist of membrane spanning protein subunits that together form a pore through the membrane. The activation of these ion channels will allow ions to move across the membrane leading to a change in membrane potential. These ion channels are called **chemically-gated channels**, because they are activated in response to a chemical signal, the neurotransmitter, rather than a change in membrane potential, as are the voltage-sensitive channels. The change in membrane potential that results from the movement of ions through the channels is called a **post-**

synaptic potential (PSP). If the ion channel opens to allow Na^+ ions to enter the post-synaptic cell, this will create a wave of depolarization in the post-synaptic cell. This wave of depolarization is called an **excitatory post-synaptic potential (EPSP)**, because it brings the membrane potential of the cell closer to the threshold for initiating an action potential. If the receptor is linked to an ion channel that allows Cl^- ions to enter the post-synaptic cell, then the cell membrane will hyperpolarize. This type of post-synaptic potential is called an **inhibitory post-synaptic potential (IPSP)** because it moves the membrane potential away from the threshold for initiating an action potential. The amplitude of the PSP is determined by the number of ion channels that open, the more channels that open the greater the amplitude of the PSP. The number of channels that open is determined by the amount of neurotransmitter released from the axon terminal, which depends on the frequency of action potentials arriving at the axon terminal.

Most neurons are contacted by thousands of axons. If the PSPs from two or more of these axons occur together, then the PSPs will sum together. This is called **summation**. There are two types of summation: **spatial summation** and **temporal summation**. You should know the differences between these types of summation. You should also understand how PSPs sum together ($\text{EPSP} + \text{EPSP} = \text{larger PSP}$, $\text{EPSP} - \text{IPSP} = \text{smaller PSP}$).

Once a PSP is initiated it spreads through the cytoplasm of the post-synaptic cell. For the most part, the spread of the PSP is passive; i.e. it is not conducted. Some longer dendrites have voltage-sensitive Na^+/K^+ channels that help the PSP along, however, this is not typical. As it spreads away from the initiation site the PSP will lose amplitude due to resistance to current flow in the cytoplasm and to the leak of current across the membrane. If the PSP is large enough to reach threshold when it arrives at the axon hillock, then it will initiate an action potential. If the PSP is below threshold, then no action potential will be initiated. The axon hillock is capable of initiating multiple action potentials in response to a single EPSP. In general, the greater the amplitude of the EPSP, the higher the frequency of action potentials initiated by the axon hillock. To summarize how information is passed from neuron to neuron: The frequency of action potentials initiated by the post-synaptic cells is determined by the amplitude of the PSP, which is determined by the number of ion channels that open, which depends on the amount of neurotransmitter released by the pre-synaptic axon terminal, and the amount of neurotransmitter released by the pre-synaptic terminal depends on the frequency of action potentials in the pre-synaptic cell. This is fundamentally how information is coded and relayed within the nervous system.

In the **slow synaptic response**, the post-synaptic membrane receptor consists of a single membrane spanning protein that is linked to a membrane-bound G-protein rather than an ion channel. There are a variety of G-proteins, and each has its own neurotransmitter receptor. When the receptor binds its neurotransmitter the G-protein is activated. The G-proteins carry out their action on the post-synaptic cell in one of two ways. Some G-proteins act by closing or opening ion channels, which alter resting membrane potential. These G-protein-gated ion channels usually stay open longer than neurotransmitter-gated channels. As a result the change in membrane potential due to G-protein gated channels lasts longer than a PSP. Other G-proteins activate membrane-bound enzymes that catalyze the synthesis of **second messenger systems**. These second messenger systems cause changes in protein synthesis in the post-synaptic cell resulting

in changes in cell metabolism. Receptors that initiate metabolic changes in the post-synaptic cell are referred to as **metabotropic receptors** to distinguish them from receptors that cause changes in membrane potential by closing or opening ion channels, which are called **ionotropic receptors**.

I finished up the material that will be covered on the first exam by discussing neurotransmitters. There are **four main families of neurotransmitters** used by the nervous system: **acetylcholine, peptides, amino acids, and amines**. You should know the types of neurotransmitters included in each of these groups as discussed in lecture. In addition to these four groups, more recently a group of chemical signals called unconventional neurotransmitters have been defined. The **unconventional neurotransmitters** include gases, such as nitric oxide (NO) and carbon monoxide (CO), and purines such as ATP. Little is known about the actions of these unconventional neurotransmitters, and whether they should be considered neurotransmitters or neuromodulators is still being debated. For example, NO and CO are not contained in synaptic vesicles and their release is not calcium dependent. Also, these gases are released from post-synaptic cells and act on presynaptic cells by diffusing across the presynaptic cell's membrane and stimulating cyclic GMP formation and thereby altering the presynaptic cell's metabolism. According to **Dale's Principle**, a neuron uses only one type of neurotransmitter. This principle is violated by most neurons that use peptide neurotransmitters, these neurons usually also release amino acid or amine neurotransmitters along with the peptide neurotransmitter. Nevertheless, neurons that use a particular neurotransmitter have certain characteristics, which were reviewed in lecture. You should know these characteristics for the exam.