

**Human Physiology**  
**Dr. Sudip Mukherjee**  
**School of Biomedical Engineering**  
**IIT(BHU), Varanasi**  
**Week - 12**  
**Lecture - 01**

Hello everyone, welcome to another new class on Human Physiology. In the last few classes, we have been discussing topics such as our nervous system; we saw how the anatomy of our brains and spinal cords is structured and what the different functions of the various components and compartments are. We also discussed nerve injuries and how the process of repair happens. In this week, we will start with how neurotransmission works in our body, and then we will see the different processes that need to be done for neurotransmission. So, let us stick with it. So, what different concepts will be covered in this class? Mostly, we will start with the first phase of neurotransmission.

So, this is basically the first class on neurotransmission where we will discuss what resting membrane potential is, how resting membrane potential is attained, what graded potential is, how graded potential is attained, and what the different types of synaptic integration are. So, first we have to understand what neurotransmission is, right? So, neurotransmission is basically a kind of communication between the neurons. So, as we discussed in a few classes before, for example, if we are receiving some sensory type of responses or stimulations from the environment, those responses or stimulations generally go via nerves to our brain and spinal cord. where the like stimulation or responses get processed.

And once the process, the neuron eventually sends back the signal to our motor organs, like muscles. So, that, like the further reflex action and other types of actions, is generated. So, this communication that happens between neurons is eventually done by a process called neurotransmission. So, as you see, the nervous system basically relies on the communication between different neurons, and this communication happens in a combination of different types of chemical and electrical signals. So, in this class, we will discuss different types of fundamental concepts of neuronal communication; mostly, the focus will be on the resting membrane potential and graded potential, and in the next class, we will also discuss the action potential.

So, first we have to discuss what resting membrane potential is; it is very simple. Just consider that if a cell is at rest, what the potential would be called resting membrane potential. So, basically, the potential that is present or attained in a cell when the cell is at rest is called resting membrane potential. And in this case, the cell is not transmitting any signal, and basically, the resting membrane potential can be measured in millivolts, and it has been seen that across cells, more or less, the resting membrane potential value is about minus 70. So, you can see the value range is about minus 70 millivolts to minus 90 millivolts, but the majority of the textbooks you will see are mentioned as minus 70 millivolts.

So, what is the resting membrane potential value? So, it is minus 70 millivolts. As you can see, this negative charge inside this neuron is essential for excitability. So, we will discuss how this minus 70 millivolt occurred, but just remember that variations in resting membrane potential can occur in different types of neurons and even in different regions of the same neuron. So, there might be a variation of this resting membrane potential value; it may not be exactly the

same across different neurons, or even in the case of the same neuron, it might differ. So, let us see basically how we are getting to this minus 70 millivolt value for the resting membrane potential, right? So, what we said is that our resting membrane potential value is minus 70 millivolts, and we have to see how we are attaining this.

So, let us see if we consider this to be like a neuron, right? Let us consider that this is a neuron; this is a cell body, for example, right? And then this is the axon, right? It is an axon terminal. So, let us focus on any part of this membrane area, maybe near the cell body, and let us see what happens when we zoom out, okay? So, you see there are a few pumps and transporters mentioned that will go by one by one. So, what is happening first? Let us consider, to start with, that the potential is around 0 millivolt. So, to start with, let us consider this a hypothetical condition; this basically never occurs inside any cell, but let us consider that at a certain stage, hypothetically, the potential is around 0 millivolt. Now, what we know is that we have a lot of sodium-potassium ATPase pumps in the cell, right? So, what we have inside the cell is the sodium-potassium ATPase pump.

Right, and basically what they do is try to balance the sodium concentration inside the cells because, you know, normally what is diffusion? What is that? So, this is like if you consider this a cell; generally, sodium is low inside and sodium is high outside. In contrast, potassium is high inside and low outside. So, what happens basically through regular diffusion is that sodium tries to come inside, right? So, generally, normal diffusion happens, and sodium tries to come inside, while potassium tries to go outside by a simple, different type of diffusion mechanism. And now as a lot of sodium starts coming inside slowly, what will happen is that the sodium concentration inside the cell will increase, right? Because normal diffusion is happening and sodium is coming inside the cell, the sodium concentration is gradually becoming higher. And we all know that sodium attracts water.

So, basically, as the sodium concentration increases, more water will also enter the cell from outside, causing the cells to burst. So, that is why the cell needs an alternative machinery to remove this excess sodium out of the cell. And this we discussed during our ion transport class, and to maintain this ionic gradient or proper balance, we have this sodium-potassium ATPase pump that works as a primary active transport, where what happens is that 3 sodium ions go out and the cells only receive 2 potassium ions. Right. So, now in this way cells try to remove more sodium ions outside of the cell and only receive 2 potassium ions.

Now, you can tell right because it is removing 3 sodium ions; that means, let us see here for example, if 3 sodium ions are going out, that means how many charges are going out? 3 positive charges are going out, right? And then let us consider that 2 potassium ions are coming in; that means how many potassium, how many charge ions are coming in? 2 positive charges are coming in. So, 3 positive charges are going out and only 2 positive charges are coming in. That means the resultant inside of the cells will become a little bit negative, basically because more positive ions are going out and the cells are receiving only a few of the positive ions; that means the resultant charge will be negative, and how much this resultant charge actually generates is minus 5 millivolts. So, initially we had what we hypothetically considered to be 0 millivolts. Right, this is a hypothetical again; I am saying geometribles generally never attain.

So, one sodium-potassium ATPase pump works to balance the sodium and potassium ion concentration gradient in the cell; the cell attains a charge of about minus 5 millivolts. Hopefully, you understood correctly, and then let us see what happens. So, our cell has a lot of these potassium leaky channels, okay. What do we have? We have a lot of potassium leaky

channels on the cell membrane, and basically, we know that potassium concentration is high inside the cell and low outside the cell. So, what happens basically through diffusion? So, basically by diffusion, potassium ions go out of the cell, and there are a lot of leaky pore channels, a huge number of leaky pore channels present on the cell membrane.

So, a huge number of potassium ions basically go out, and as these positive ions go out, they leave behind negative ions like chloride, phosphate, etc. Basically, it creates an extreme negative charge or extreme negative polarity or voltage inside the cell. So, from minus 5 millivolts, once this step 2 is done, which is like a leaky potassium ion channel, the cell attains a potential of about minus 90 millivolts. Now, let us see how we will say this: what is the resting membrane potential? The resting membrane potential is minus 70 millivolts. So, eventually, how is the cell attaining minus 70 millivolts from minus 90 millivolts? So, let us see this is the third step here where cells also have different sodium leaky pore channels.

So, cells also have a lot of sodium leaky pore channels, and what we know is that sodium is generally high outside. And sodium is low inside, right? This is a natural ion concentration. So, the diffusion of sodium happens from outside to inside. But one thing you have to remember is that the potassium leaky pore ion channels are much higher in number compared to the sodium leaky pore ion channel. So, compared to the potassium that is going out, only a few sodium ions will eventually come inside, and as we know, sodium is positively charged.

So, what will happen if a few sodium ions come inside is that the potential will increase a little bit on the positive side, which means that from the minus 90 millivolts, which is actually attained due to a lot of potassium ions going out, the cells will attain a So, basically the three steps that contribute to the first step are the sodium-potassium pump or sodium-potassium ATPase pump. The main goal is to maintain the proper sodium and potassium ionic balance, and it basically occurs by an active transport-like mechanism using ATPase. So, in that case, because 3 sodium ions go out and only 2 potassium ions the cell accepts, the resultant is negative. So, the cell basically attains around minus 5 millivolts of charge. In the next step, as we said, the cells have a lot of leaky pores like potassium channels.

So, in the next step, cells have a lot of leaky pore potassium channels. A lot of leaky potassium channels, and we also said potassium is generally high inside and low outside. So, by simple diffusion, a lot of potassium ions will go out as the potassium ions leave the cell. Leaves like a lot of chloride ions and phosphate ions, which are highly negative. So, from minus 5 millivolts, in this step, the cell will become or attain a charge of minus 90 millivolts.

And then in step 3, as you can see, there are also leaky sodium ion channels, and sodium ions are generally high outside and low inside. So, basically, some sodium ions will come from outside to inside, and it would be lesser than potassium because we said that potassium leaky pore ion channels are much higher in number compared to the sodium leaky pore channel. So, only a few sodium ions will come inside; in that way, the charge, which was initially around minus 90 millivolts, will become minus 70 millivolts at rest, which is also called. So, basically, this potential is also called the resting membrane potential, right, or RMP? So, this is basically the way we got to this: whenever the cell is at rest, we attain a potential in the cell, which is the resting membrane potential, and the value of the resting membrane potential is about minus 70 millivolts. Hopefully, it is clear to you.

If you have further questions, please kindly discuss with us during our live session. Then let us see what the Nernst potential is. So, basically for any ion, whether it is sodium or potassium,

the Nernst potential is the potential at which the movement of the ion is in equilibrium. That means, if I consider it like a cell. For example, if the potassium ion is high inside the cell and low outside the cell, the diffusion mechanism will tell us that the potassium ion will move from inside to outside, right? But also, this is happening.

in their concentration gradient, right. So, this is happening through its concentration gradient, and that is why you call it diffusion. But as potassium ions go out, they leave a lot of anions, right? It leaves a lot of anions inside, and now what will happen is that these anions are negatively charged; some of the potassium ions can again get attracted through electrostatic attraction. So, basically, you see here two types of dynamic movement of ions happening all the time. One way is through the concentration gradient; ions are either coming out or going in, following the concentration gradient in terms of their diffusion process.

When these positive ions are going out, they leave behind certain anions, and these anions will further attract those potassium ions back to the cells via electrostatic attraction. So, there are like two types of movement happening simultaneously: in one direction, the potassium ion is going out, and on the other hand, the potassium ion is tending to come back. Whenever at a certain potential, this movement of the ion is in equilibrium. So, basically, the net equilibrium or the net movement of the ion will be 0, which means it will be in equilibrium; that particular potential is called the Nernst potential. And this is basically explained by this equation where the equilibrium potential, or Nernst potential, which is in millivolts,  $E$ , is equal to  $RT$  divided by  $ZF$ , where  $Z$  is the charge of that ion.

So, in the case of potassium, the charge would be plus 1, and as you know,  $R$  is the gas constant,  $T$  is the temperature, and  $F$  is the Faraday constant. And then it would be like  $\ln$ , which is the ionic concentration out divided by the ionic concentration in. So, this is the equation for the Nernst potential. This can be calculated for various ions, and it might also appear on the exam, where we can give you the concentration of the ions out and the concentration of the ions in. Standard values of  $R$ ,  $T$ , and  $F$  might be given to you, and in terms of the ion concentration or the ion balance of any certain ion, due to its valence, you can calculate what the Nernst potential of that particular ion would be.

So, this equation you can kind of read, and you can practice a few problems; it might be there in the exam. Then after we discussed the resting membrane potential, we had to discuss how the graded potential occurred. So, basically, what is a graded potential? Graded potentials are the small changes that happen in the membrane of the neuron. So, basically, what we initially said was that, for example, whenever the cells or various components of the cell or various areas of the cell are attaining a resting membrane potential, it is about minus 70 millivolts. But at minus 70 millivolts, the neuron or the cells are not performing any neurotransmission or signal transmission.

Now, to perform a signal transmission, a cell needs either a stimulatory or inhibitory kind of signal, right? So, basically, through our sensory input or through various types of other input, cells may receive some sort of inhibitory or stimulatory signal. So, either cell can receive stimulatory signals; basically, it will kind of stimulate the neuron, right? It will basically stimulate the neuron, or it can basically excite the neuron, or it will receive some inhibitory signal. So, basically, it can inhibit the neuron. And once the cell receives this quick succession of stimulation or inhibition, basically in the majority of cases, the stimulation and inhibition signals come via a neurotransmitter. We will discuss what type of neurotransmitter participates, but once the cells receive this type of localized change in the potential, then it basically attains

the graded potential and prepares the cell for the further neurotransmission process via action potential.

And in cases of resting membrane potential, what we said is that the majority of those channels were like voltage-gated channels, right? You remember that the majority of those channels were like leaky pore channels, and some were like those active transport channels. So, in cases of resting membrane potential, what we said was that the majority of those ion channels were either leaky pore-based diffusion channels or they were sodium-potassium active transport channels. But in cases of graded potential, we have mostly seen that the channels present here are the ligand-gated ion channels. So, in our ion transport class, you remember we discussed different types of diffusion-related channels, including leaky port channels, voltage-gated channels, ligand-gated channels, and mechanically gated channels. So, here in cases of graded potential, the channels are ligand-gated ion channels that facilitate basically facilitated diffusion.

So, basically, this kind of works in terms of favoring facilitated diffusion. And let us see now how the graded potentials are attained; basically, in cases of graded potential, as we said, there are two conditions it can arrive at: one is the stimulatory or excitatory condition, which is basically like a stimulation, or there can be an inhibitory kind of signal or an inhibitory kind of condition, which is basically an inhibitory type of signal. So, the excitatory or stimulatory response, or the potential, is called excitatory postsynaptic potential, or EPSP, and the inhibitory postsynaptic potential is called IPSP. So, why are we saying "post synaptic"? Because, again, we said, you remember that basically let us assume that these cells were initially at rest, right? So, these cells were initially at rest with a resting membrane potential of minus 70 millivolts. Now, this presynaptic, so this is a presynaptic neuron, this is a postsynaptic neuron.

So, this presynaptic neuron receives some signal. Like a stimulated signal via a neurotransmitter. Now, this presynaptic signal will release this neurotransmitter, which will again stimulate this postsynaptic neuron, and in this way, it will stimulate the next neuron, and the signal basically goes on. And how does this EPSP happen? You see that we have, as we said, kind of ligand-gated ion channels, right? And what do these ligand-gated ion channels do? This ligand-gated ion channel is activated whenever there is a stimulation of a neurotransmitter, for example, glutamate, or it can be something like acetylcholine. Different types of neurotransmitters actually stimulate when they bind to this ligand area, like the ligand binding area.

So, once this neurotransmitter binds with the ligand binding area, what happens initially is that you can basically consider here that there is a door or a kind of valve, and whenever this ligand binds with the area, this valve basically opens up. So, this valve, from a closed condition, basically opens up, allowing the movement of a lot of cations, for example, sodium and calcium, and you have to remember that sodium and calcium ions are high in number or reach a higher concentration outside of the cells compared to inside, where they are low in number. So, basically, diffusion is happening as the different types of cations, like sodium and calcium, come inside. It is bringing some positive charge. So, initially, the resting membrane potential, as you remember, was minus 70 millivolts, as some of the potassium, like some of the calcium and sodium ions, are bringing positive charge inside the cell.

The membrane potential of the cell changes from minus 70 to minus 55 millivolts, and this is called excitatory postsynaptic potential or EPSP. This minus 55 millivolt is also called the

threshold potential. So, this minus 55 millivolt is also called the threshold potential. Now, this happens in case of a stimulation. So, this side we mentioned in cases of stimulation.

Now, what will happen in cases of an inhibition signal or an inhibitory postsynaptic potential? Let us see, in that case, some neurotransmitters that are inhibitory neurotransmitters; for example, GABA. In the same way, they will bind to the ligand binding site, and once they bind, what will happen is that initially the gate was closed; once they bind, the gate will basically open, right? So, the gate will basically open the ligand-gated voltage channel; the ligand-gated channel gate will open, and as this ligand-gated channel opens, some chloride ions, which are negative in charge, will come inside. Basically, what will happen is that potassium ions, which are high in concentration, will

.. Inside the cell and low outside. So, potassium ions will go out and chloride ions will come in, and as you can see, because positive ions are going out or negative ions are coming in, basically that will attain a lot of negative charge. So, initially, the resting membrane potential was minus 70 millivolts. So, because of the lot of negative charge it generates, basically the potential will change from minus 70 to minus 90 millivolts. This is also called a hyperpolarizing kind of condition. Where the potential is basically becoming more negative from the initial resting condition to about minus 90 millivolts, and this potential is also called inhibitory postsynaptic potential.

So, two clear distinctions you see in cases of graded potential are where certain stimulation or inhibition based on neurotransmitters, when they bind with the ligand-gated ion channel, in cases of stimulatory, what happens, or in cases of excitatory postsynaptic potential, what happens, basically it opens up the gate. resulting in a lot of cations like sodium and calcium coming inside the cell, which attains a little bit of positive charge. So, from minus 70 millivolts of resting membrane potential, the charge becomes about minus 55 millivolts, which is also called threshold potential. In cases of inhibitory signals, for example, if GABA binds to the ligand-gated channel, it opens the gate, causing positive potassium ions to flow out of the cell or negative chloride ions to enter the cell. And all these kinds of results in attaining a negative charge inside the cell.

So, from an initial resting membrane potential of minus 70 millivolts, the cell membrane potential goes up to about minus 90 millivolts. It is clear to you. Then, lastly, let us cover this small topic, which is synaptic integration. So, basically, I will give you an example. So, basically, let us think that here the cells are at rest at minus 70 millivolts, and this is like minus 90 millivolts.

And so this is basically the resting membrane potential, and as we said here, we have minus 55 millivolts, which is also called the threshold. Threshold potential, which is also called a threshold potential. So, whenever a cell attains a threshold potential, it basically starts the neurotransmission process via action potential generation, and how it generates the action potential we will discuss in the next class in the second class of neurotransmission. But just remember the threshold potential; it is very important because whenever this action attains the threshold potential, then only does the action potential for the transmission of signals from the cell body to the action terminal generate. But how are we even coming to this minus 55 potential, right? Because initially, the cells are at rest, which is about minus 70 millivolt potential.

Now, you remember we have IPSP and EPSP, right? Let us assume the cells give some stimulatory signal, okay? So, cells are giving some stimulatory signals, but this can again fall down, right? Again, maybe the cells are giving the second stimulatory signal. So, one single stimulatory signal may not be enough for the cell potential to eventually reach the threshold potential, which is minus 55 millivolts. We need a lot of signals to be integrated together in order for the cell potential to become minus 70 to minus 55 millivolts, and this process is called synaptic integration. And this integration has two different types of procedures: one is temporal summation and the other is spatial summation. So, the first one is the temporal summation; in that case, a presynaptic stimulatory neuron, or the presynaptic neuron, is sending a stimulatory signal, maybe via acetylcholine, right? Acetylcholine or glutamate.

So, basically, they are sending different types of stimulatory neurotransmitters, and one presynaptic neuron is sending stimulation to one postsynaptic neuron. So, basically, let us consider this as the first signal; then, after that, it sends another repeated signal, and one by one, the signals get summed. Or the signals get integrated, and slowly, this reaches this threshold potential. And whenever it reaches the threshold potential, which is minus 55 millivolts, we can observe this process of neurotransmission, which is also called the action potential. I am saying this will be discussed in detail in our next class.

And the second procedure is spatial summation. In the case of spatial summation, multiple presynaptic neurons send quick, rapid stimulation or inhibitory signals, mainly stimulatory signals, to one postsynaptic neuron. So, together multiple presynaptic neurons can send the stimulation signal to the postsynaptic neuron in a much faster way because the signal strength will be greater, allowing for faster summation or integration to occur whenever the potential reaches from the resting membrane potential, which was about minus 70 millivolts. Threshold potential, which is minus 55 millivolts, what do we experience? We experience the signal transmission that is called action potential. So, this is the method of integration or summation of the signal, mainly for the stimulatory signal, which is either temporal summation or spatial summation.

So, hopefully you like the class. Do you know that the foundation of how you learn and remember lies in the remarkable ability of your brain's connections called synapses to constantly change their strength? This phenomenon is known as synaptic plasticity. So, activity questions: what would happen to the resting membrane potential if the sodium-potassium pump stopped working? Explain the resulting changes in ion concentrations and voltage. Try to solve this, and hopefully you are enjoying the human physiology class. If you have further questions, please discuss them with us in the live sessions.

You can also drop your questions by email. Thank you for attending today's class. Let us meet very soon for the next class on neuronal transmission. Thank you again.