Neurobiology

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Lecture 4.2: Electrical synapses (gap junctions)

Hi everyone, welcome back to neurobiology. In the last video we started talking about the contacts between neurons, the synapses. We saw that there was initially some controversy on whether the synapses are chemical in nature or electrical in nature. And it turned out that in fact there are both kinds of synapses that are present in the brain. So there are some chemical synapses in which the neurons are not connected to each other and the communication happens in the form of some chemicals that are released by the first neuron and those are received by the second neuron. And then there are electrical synapses in which the two neurons are directly connected to each other in the forms of some passages and these passages allow the movement of electrically charged ions directly from one neuron to the next, just as it happens within a neuron.

So these electrical synapses are also known as gap junctions and in this video we will take a more detailed look at these electrical synapses or gap junctions. As we have already seen a few times in this course, many important discoveries in neuroscience have been made in a variety of model organisms. The discovery of electrical synapses was made in this sea organism, the crayfish. And one of the reasons that people have been looking at crayfishes is that they have a reasonably complex motor neuron system, but these motor neurons are big in size and they are easy to record from.

So here is a schematic of the neurons between which the electrical synapses were found. One of these neurons is called the lateral giant fiber shown here and the other is a motor neuron called the giant motor fiber shown here. And these two neurons form a synapse here which is zoomed in. So this is the zoomed in image. So they form a synapse here.

The lateral giant fiber is the presynaptic neuron and the giant motor fiber is the postsynaptic neuron in the darker color here. And the way the electrical synapse was observed was using something like this. So you put two electrodes in the presynaptic neuron and two electrodes in the postsynaptic neuron. One of these electrodes is for stimulating the neuron by injecting current and the other electrode is for recording the response of the neuron, the membrane

potential of the neuron. So this electrode here is measuring the membrane potential of the presynaptic neuron that can be called the presynaptic potential.

And this electrode here is recording the membrane potential of the postsynaptic neuron. So that can be called the postsynaptic potential. Now what was found is that if you inject a small amount of current in the presynaptic neuron as shown here and you observe the membrane potential in that presynaptic neuron, so you see that there is a depolarization and if the depolarization is crossing the threshold of action potential, then an action potential is generated here. And on the y-axis, the change from the baseline is shown as opposed to the actual voltage. Now at the same time, you see that there is also an effect on the postsynaptic neuron and the peak here is reached at almost the same time as the peak here showing that there was very little delay between the activity in the presynaptic neuron and the postsynaptic neuron.

In the last video, we discussed that action potentials are important because they determine when a neuron communicates with a postsynaptic neuron. But that applies only to chemical synapses because action potentials control the release of the neurotransmitter. But that is not the case with the electrical synapses. So in electrical synapses, even if you have a graded potential, that is a small depolarization that is not large enough to generate an action potential, even that small depolarization can pass through to the postsynaptic neuron through an electrical synapse. So this we can show by doing a simple experiment on an electrical synapse.

So let's consider that these are two neurons that are connected by an electrical synapse here. Now you put two electrodes in the first neuron. So one is the stimulating electrode and one is the recording electrode. And in the postsynaptic neuron, you put another recording electrode. Now if we inject a small current pulse, a small depolarizing current pulse in the first neuron, in these two neurons, well of course the first neuron we will see that there is a change in the membrane potential.

It should show depolarization. And in the second neuron also, because this is an electrical synapse, we should see a small depolarization here as well. So this is what the actual traces would look like, a depolarization in the first neuron and a depolarization in the second neuron. And a somewhat smaller depolarization in the second neuron. The size is smaller here because of course this neuron is farther away from the site of stimulation compared to this neuron.

And because this is passive conduction, so the amplitude would decay as you go farther away from the site of stimulation. So this is a major difference from electrical synapses. In a chemical synapse, if you cause a sub-threshold depolarization that does not generate an action potential, then we will not see any effect on the postsynaptic neuron because no neurotransmitter would be released. But in electrical synapses, we would see an effect on the postsynaptic neuron. What do you think would happen if we give a negative current pulse instead of a positive current pulse

here? So if the current was hyperpolarizing, then in the first neuron we would see a hyperpolarization.

So the membrane potential would go down. And in the second neuron also we should see a similar effect. So we should see a smaller hyperpolarization here in the second neuron. So electrical synapses would allow both depolarizing as well as hyperpolarizing currents to pass through. That is true for most electrical synapses, although there are some exceptions.

So there are some channels that have rectification, that is they allow only either positive currents to pass through or negative currents to pass through. But in most cases, they would allow both the positive and negative currents to pass through. Let's take a look at an electrical synapse here. So this is the first neuron, the membrane of the first neuron, and this is the membrane of the second neuron. Normally these neurons may be separated by 20-30 nanometers, but at the point where they form the synapses, the two membranes come really really close, three to four nanometers apart.

And here we can see a lot of channels between these two neurons. So these are the channels that allow ions to pass through from one neuron to the other. If we look at it from top, this is what it looks like. So this is a real electron microscopy image of a gap junction, and we can see a lot of these pores in the membrane. These pores are basically formed by proteins.

If we look at the pores in more detail, this is what they look like. So you have half the pore or half the channel in the first membrane and half the channel in the second membrane. And each half channel or hemi-channel as it is called, is made up of multiple protein chains. So this is what a hemi-channel looks like. It has these six units.

Each of these units is called a connexion, and the whole hemi-channel with the six units can also be called a connexion. So these six connexions come together and in between they form a pore. And each connexion is made up of a protein chain that passes through the membrane four times. So it's a four transmembrane domain. Now one interesting puzzle is that how these channels align perfectly in the two membranes.

If they were not aligned together, then the electrical synapse would not function. And in fact, that might also be very damaging for the neuron, because now you would have opened up the cytoplasm of the neuron to the extracellular space. These pores have a 1.5 nanometer diameter, which is big enough for ions to pass through. And you don't want ions to be passing into the extracellular space through a large pore.

The way these two hemi-channels align together is because of interactions between the two units here. So if we look at a connexion in more detail, so you have the protein chain passing through

the membrane and then it forms an extracellular loop, then again passes through the membrane intracellular loop, through the membrane extracellular loop, through the membrane, and it comes in. So these intracellular parts of the connexion can be used for interactions with various molecules inside the cell. And these two extracellular loops can be used for interaction with the complementary partner. So these two loops per connexion means that there are 12 loops per connexion.

And these 12 loops in the two complementary connexions interact and these interactions are optimized when the channels perfectly align with each other. So that's how the two hemi-channels are able to align and the electrical synapses can function. What is the advantage of using electrical synapses? One advantage is that electrical synapses allow rapid and synchronous firing of the interconnected neurons. To make this point more clear, let's take a look at an example. This is a model organism, Aplysia.

It's also a sea organism. This is what it looks like. This organism has a very simple nervous system and it has a very interesting defense mechanism. So if some predator comes towards it and tries to hold it, then it suddenly releases a big burst of in the water. And this big cloud of ink confuses the predator and gives Aplysia a chance to escape. This ink is released by various ink glands that are present on its skin.

And these ink glands are controlled by motor neurons. Now for this defense to be effective, all this ink should be released in one go. So all the glands should be activated at the same time, which means that all the motor neurons should be activated at the same time. If the motor neurons were activated one after the other, then the ink would be released slowly and that might give time for the predator to catch it. So how does Aplysia ensure that all these motor neurons are activated together? It does it by using electrical synapses.

So here is the circuit underlying this phenomenon. It's a very simple circuit like reflex circuits in our brains. You have a sensory neuron that is connected to the tail. So if there is any stimulus that comes at the tail, then the sensory neuron is activated. And this sensory neuron is directly connected to these motor neurons that control the ink gland.

And these motor neurons are connected to each other by electrical synapses. So if any of the motor neuron gets activated, that activity would also be passed on to the other connected neurons. And all three neurons will be activated at the same time. We can verify this phenomenon by doing a simple experiment. So we artificially stimulate the tail and we make recordings from these three neurons at the same time.

Now this kind of experiment is possible in Aplysia because these neurons are accessible and relatively large. But in vertebrates such an experiment making recordings from three targeted

neurons at the same time would be very difficult. So here is the outcome of the experiment. Here are the three recordings from the three neurons. So this is the timing of the stimulus to the tail and we see that after some time there are action potentials in all the three neurons.

And these action potentials are very well synchronized. And once there is enough activity in the neurons, then a large amount of ink is released. So this simultaneous activity of motor neurons helps in releasing a lot of ink together and this synchronization is ensured by the presence of the electrical synapses. Thank you.