ABBY NOYCE: So, talking about the nervous system. The nervous system is divided into the central nervous system, which is the brain and spinal cord. And then the peripheral nervous system, which is pretty much everything else.

Peripheral nervous system is sensory receptors in the neurons that bring sensory information back to the central nervous system. It's motor neurons that send the movement commands out to your muscles. It's things like neurons that control digestion, and neurons that control how different glands behave. That's the peripheral nervous system.

And that's not what we're going to focus on in this class, because we're interested in the processing that's happening in the central nervous system-- in the spinal cord, and in particular, in the brain. And the nervous system is made up of two main types of cells.

Neurons are nerve cells, they're kind of the stars of the nervous system. They're the ones who do this kind of information processing, they have inputs and outputs-- and we'll look in a minute at the structure of a neuron, how that works.

And then there's a second set of cells called glia. And we're going to run over the glia first, because they're simpler. There's a couple of different kinds of glia. The word glia comes from glue in Greek or Latin-- I'm guessing Latin, but I don't know. One of those kind of classic languages.

AUDIENCE: It looks like Latin.

ABBY NOYCE: Yeah, OK. And they got this name because the traditional view of this is that glia don't really do anything. They hang out, they're around neurons, they cushion them, they protect them, they're the support system. But the neurons are really the stars of the show. And more recently it's been shown that glia actually do a lot of really important things.

So there's four types of glia. There's astrocytes, which do a ton of important stuff in the brain. Astrocytes are star shaped cells, thus the name.

So astrocytes actually form syntaptic connections with neurons. So they actually can release a neurotransmitter, they can pick up neurotransmitters. They modulate-- have you guys heard of

the blood-brain barrier?

So for the most part your capillaries, your finest blood vessels, have kind of loose walls that nutrients and other stuff can go from your bloodstream into the cellular tissue. But in the brain, that's not true.

The capillaries in the brain are joined by tight junctions. There's no space between them for things to creep through. There's actually very few things that you can ingest that will go from your bloodstream into your brain where all these delicate neurons are kicking around.

And it's because of these astrocytes that they have little feet-- think if they're like a star-shaped cell, so all these little feet stick out. And line up right along the edge of the capillaries in your brain.

And make them form these tight connections, these tight junctions. So that you don't get all of the random stuff you're eating on any given day messing up your nervous system.

So astrocytes, they manage the blood-brain barrier. They change the amount of blood flow that's happening in your brain. So you guys probably know that one way that neuroscientists measure brain activity is by looking at how much blood flow is in the brain.

And it's turning out that actually astrocytes, these support system cells, are what's controlling how much blood flow goes to different parts of your brain. So we've got astrocytes, these guys are pretty cool. There's lots of people doing cool research on these guys right now.

And then there's two types of cells. One of them is Schwann cells. And one of them is oligodendroglia. And these both are cells that wrap around neurons with that tissue called myelin. And we'll talk about a myelin more in a little bit.

But basically, a neuron that is myelinated is faster than a neuron that's unmyelinated. So these guys, Schwann cells in the peripheral nervous system and oligodendroglia in the central nervous system, are helping to speed up axonal transmission.

And finally there's a set of glia called microglia that do immune reactions in the brain and in the nervous system. So glia, there's a lot of glia. There's more glia than neurons by mass in the central nervous system. But they're, for the most part, the support team.

AUDIENCE: What's the last one?

ABBY NOYCE: Microglia.

AUDIENCE: What do they do?

ABBY NOYCE: Microglia, they do inflammation. So if you get an injury of some kind and it's inflamed, there's more-- there's a signal that's sent out that brings your body's healing response to the area. Microglia do that in the central nervous system. They're also a big part of the immune response within the nervous system.

So we've got four types of glia. And again, so the traditional view is that these guys are the supporting role. There's more information coming out showing that they're much more heavily involved in the sorts of elaborate processing that people think of as the nervous systems, what the nervous system does, than was originally thought.

So besides glia-- I love sliding boards-- we'll put our glia up top. Then we have the rock stars of the nervous system. We get our neurons. So sketchy neuron diagram.

OK. So we have a neuron. Neurons are fun to draw. So the main parts of a neuron that you should know about are, neurons have a kind of central cell body area. Here's our nucleus, it's how you know it's the cell body.

And cell body has all of your kind of classic cellular structures. You've got your nucleus, you've got your Golgi apparatus, your ribosomes, lysosomes, all of this stuff, mitochondria. Mitochondria are kind of all over the place in a neuron, but they are there in the cell body.

Another word for cell body is the soma, and you'll see that as well. So it's this kind of central-- it does all the stuff that keeps the cell alive.

And then, so on this particular neuron, this is a neuron-- information on this neuron-- that's not mine. Information on this neuron is going this way. So around, on this side of the neuron, we've got our input, information input zone, with all of these little spines.

These are the dendrites. They're all over the place. And the dendrites take in information from other neurons. Or if you're out by a sensory receptor, then they might take information from a sensory receptor, from the photo receptors in your eyes, or the touch receptors in your skin.

Dendrites take information in, information goes this way. All of the information that comes in, you might have a neuron coming in here, and a neuron coming in here, all sending in different

signals.

And that information is integrated at the base of the axon here. This long tail is the axon. Information is integrated here.

And so there's either an excitatory input or an inhibitory input coming in. The neuron adds all of these things up. And if it reaches a certain threshold amount, then it sends a nerve impulse-- shazam-- down the axon. And it fires.

It releases neurotransmitter, a chemical-- there's a bunch of different chemicals that can be neurotransmitter-- out through these axon terminals. Where, hopefully, it's received by another neuron. It's the next one in the chain.

So vo-ahm. Neurons send information. So the thing about neurons is that they use two different types of communication. They use an electrical signal within the cell. So when there's information coming in, and it's doing this integration and transmitting it along the axon, that's an electrical change.

Then when it's communicating with other neurons at a synapse, at a gap between two neurons like this, it's using a chemical signaler. Questions?

AUDIENCE: Can you say that again?

ABBY NOYCE: Yes. So the nervous system uses two different types of signaling within a cell. So when it's taking input from other neurons and kind of trying to add it all up, at this integration zone, at the axon hillock here, it's using electrical signaling.

Within the cell, it passes an electrical signal called the action potential down the axon. And once that electrical signal reaches the axon terminals, the very tips, we change modes. And it causes the neuron to release a chemical, a neurotransmitter, into the synapse. Synapse.

So the synapse is that gap between one certain nerve cell and the next one. So the axon terminals of this nerve cell will scooch right onto the dendrites, usually, of the next one. And send more information along the chain.

So let's talk about what actually happens at a synapse in a little bit more detail. We'll do that one first. And then we'll go back and we'll do the electrical stuff. So here's our axon.

Here's our axon coming in to an axon terminal. I'll just draw one, although reality, an axon will

have tons and tons and tons of axon terminals. An axon can have hundreds of these. And here is-- scroll up again. Let's say a dendrite of the next cell.

So here's our synapse. So what's going to happen is the nerve impulse, the action potential, is going to come down the axon of the previous cell. And that's which kind of signaling, electrical or chemical?

AUDIENCE: Electrical.

ABBY NOYCE: Electrical, it's coming within the cell. When it gets here, it's going to trigger the cell-- back up a second. So cells have a membrane, right? High school biology, we're all good with this, a lipid bilayer.

And so one of the things about membranes is that different kinds of ions can only go through a membrane if there's a channel for them there. So we're going to talk a bunch today about different kinds of channels in membranes and what makes them open and close.

So this electrical potential comes along and it opens up a bunch of calcium channels, right here at the axon terminal. So we get our calcium.

AUDIENCE: Calcium ions?

ABBY NOYCE: Calcium ions, yes. Ca2+. And these calcium ions are going to go, fa-shoom, into the axon terminals. The electrical signal coming down the axon triggers this influx of calcium. Calcium is used all over the place in the nervous system as a signal of these different kinds.

In this case, calcium is going to come in and it's going to cause the release of neurotransmitters. So neurotransmitter is actually usually produced in the cell body, where all the complicated cellular mechanisms for building things are.

And it's going to be packaged up into little vesicles, into little packages. And so at any given point in time at the axon terminal, there's going to be a bunch of these little vesicles full of neurotransmitter hanging out.

And when the calcium comes in, it's going to cause one of these to actually scooch over to the membrane and bind with it. So that the neurotransmitter is released into the synapse.

AUDIENCE: So the calcium binds to membrane of the vesicle or the actual neuron?

ABBY NOYCE: The calcium binds to a receptor that's on the vesicle membrane, which then tells the vesicle to scooch over next to the membrane and kind of merge with it and release the neurotransmitter. And that's about all the detail I can give you on that. My bio-chem is not where I would like it to be. It's one of the things I want to take this year, a little bit better.

OK, so you get neurotransmitter released. And then what? Well, it's got to be noticed by the second cell. That this cell over here has to have a way of knowing that there is neurotransmitter in the synapse. So it's going to have receptor proteins.

These are our neurotransmitter receptors. They're hanging out.

AUDIENCE: Can we zoom in again?

ABBY NOYCE: Can we zoom in again? Let's see. Here's our synapse. And we've had a vesicle do its little merging trick. So the neurotransmitter's been released.

And what happens is-- and I can't draw this in a whole lot more detail. The way this works is think of receptor protein as being like a lock and a key, is the analogy that everybody uses.

So when a particular molecule comes along, and in this case, it's this particular neurotransmitter, it's scooches right into a slot in the receptor protein that's just the right shape for it. And it causes something to happen.

And depending on what kind of neurotransmitter and what kind of receptor we're looking at, you'll see different changes. So the neurotransmitter is released into the synapse. It binds to the receptor.

Maybe it'll open a channel. That's a pretty typical response. Maybe, sometimes, it causes something else to be released from the receptor and into the cell and cause another string of chemical reactions.

But the thing that's important is that in some way or another, this neurotransmitter that's released changes the probability of the next cell firing. It makes it more likely to fire or less likely to fire.

So once it's so-- backing up from the beginning, electrical signal and action potential comes down the axon, triggers calcium, calcium ions to flow in to the axon terminal. The calcium causes these vesicles to bind with the membrane and release the neurotransmitter.

The neurotransmitters is now floating around in the synapse. And it binds to a receptor on the postsynaptic cell. So people talk about at a synapse, you've got a presynaptic cell, the one who releases the neurotransmitter. And a postsynaptic cell, the one who has the receptors.

And they cause some change to happen. Some change in the probability that the postsynaptic cell will in turn fire.

AUDIENCE: It always has to do with the probability?

ABBY NOYCE: It's not going to be 100% sure, because--

AUDIENCE: No, I mean, like it always has to do with whether or not the next one's?

ABBY NOYCE: Yeah, it's going to change whether the next one fires. I mean, the exception to this is going to be like the sort of synapse that you see where our motor nerve comes down and hits a muscle, it's going to change. It's going to make the muscle contract, for example.

So that's not quite a synapse, but very much like one. Again, it's a neurotransmitter that's released that affects the next thing. So yeah, whether or not they fire is basically how neurons process information.

So each one gets all of this input and then decides whether or not it's going to send an action potential on down to the next neurons in its chain. So once it binds with the receptor, it's important that it not stay there forever.

Neurons fire pretty quickly. The maximum rate of firing for a neuron is about 1,200 impulses a second. So it's important that this receptor does its thing. And then, fa-shoom, gets the transmitter out of there. To clear it out, let it kind of reset a little bit.

And there's two main ways that that neurotransmitter is cleared out of the synapse. There are enzymes that break down neurotransmitters.

AUDIENCE: On the outside?

ABBY NOYCE: In the synapse, yep. So you might have an enzyme, this is a hungry enzyme. [ROARS SOFTLY] It's going to break down the neurotransmitter.

The other thing that can happen is, you can actually have the original cell can have its own receptors for the neurotransmitter that actually [SUCKS] act like vacuum cleaners and slurp it

back up, out of the synapses. This is called reuptake.

So the neurotransmitter is reuptaken by the presynaptic cell, who then can just repackage it back into a vesicle and be ready to use it again the next time a neurotransmitter comes along.

So there's a lot of recycling of neurotransmitter as well.

AUDIENCE: Wait, so what's it called?

ABBY NOYCE: That process is called the reuptake.

AUDIENCE: Do all the neurotransmitters always get recycled?

ABBY NOYCE: More or less, not all of them. So for any given neurotransmitter, you're going to usually see either an enzyme that breaks it down. And usually that will break it down all the way, it'll break it down to some precursor that is then brought back into the cell. And it's remanufactured from that precursor.

But if it's reuptaken, then yeah, it will just get repackaged and used again.

Oh hey, terminology, I forgot that. So there's two main types of receptors, like I said. One of the most common types of receptors are ionotropic receptors. And an ionotropic receptor opens an ion channel when the neurotransmitter binds to it.

So one of the most common of these is-- let me see if I can get this right-- glutamate, which is a really common excitatory neurotransmitter. It has an ionotropic receptor that lets in calcium ions. So it lets calcium ions in.

Again, you're getting an ion inflow through an ionotropic receptor. And then the receptors that caused these longer-term slower changes by releasing, usually, a protein that does-- then causes other cellular changes-- are called metabotropic receptors.

And they're slower, but they tend to cause longer lasting changes in the cell. They might make it more sensitive to this neurotransmitter, or less sensitive, cause it to put out more receptors so it is more-- again, increasing the sensitivity.

AUDIENCE: And then some would do both?

ABBY NOYCE: Some neurotransmitters will have both types of receptors, but at any given synapse, you're only going to see one or the other.

So like acetylcholine has both an ionotropic receptor type and a metabotropic receptor type, but you're not going to see that at the same synapse. You'll see some over here and some over there, usually, because they do different kinds of things.

People feeling pretty OK about this? Cool. All right.

So that makes something a neurotransmitter? If you are a brain scientist, or if you were a brain scientist 50 years ago, more like, and you were looking at a substance that was existing in the brain. And you wanted to prove that it was a neurotransmitter. What sort of criteria might you look for?

How would you know it's a neurotransmitter and not just something that is kicking around loose in the brain? Doing something else, maybe. Modulating something else.

AUDIENCE: Because it came out of the cell?

ABBY NOYCE: Good. So it's released by the presynaptic cell.

AUDIENCE: It does something when it gets up to-- when it binds to the receptor on the next neuron.

ABBY NOYCE: Yeah. So exactly. So when you stick it-- so if you take the substance and you put it on this neuron, then it changes how that neuron behaves.

AUDIENCE: Can I just read the other two here?

ABBY NOYCE: Sure. You've got [INAUDIBLE]

AUDIENCE: Number three, after it has transmitted its signal to this neuron, it must be deactivated rapidly.

ABBY NOYCE: Yeah, OK.

AUDIENCE: And number four, it must have the same effect on the postsynaptic neuron. When applied experimentally, the signal is once secreted by presynaptic neuron.

ABBY NOYCE: Good. OK, so another of thing to look at is whether the presynaptic neuron has the mechanism for synthesizing this molecule. Does it have the enzymes that it needs to do that?

OK, so we've talked about what's happening at the synapse. Let's talk about how these chemicals, these neurotransmitters, actually are causing changes on these postsynaptic

neurons.

So getting back to this whole lipid bilayer membrane idea. Neurons have a bilayer. Remember, these are the cell membranes that you all probably saw in bio at some point.

They look like head, two tails, head two tails, head two tails, two tails, head. All the lipids lined up against each other. Yes, hydrophilic heads and hydrophobic tails.

So and it's those hydrophobic tails--

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: Ah, we were wondering. Come on in, Ms. [? Nagitt. ?]

AUDIENCE: Sorry.

ABBY NOYCE: No worries.

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: No worries. So it's those hydrophobic tails that are the reason that ions, that charged particles, can't get through the membrane. Those hydrophobic tails don't want to interact with anything that's got a charge on it like that.

So some ions in a neuron-- in a neuron there's some channels-- remember, we talked about ions can go through a membrane if there is a channel for them.

So, for example, most of the time potassium, good old K+, potassium ions, there are potassium channels that are always open. Potassium can kind of go in and out of the neurons whenever it wants to.

And potassium is a big player here. So potassium floats free. And then on the inside of the neuron, are a bunch of proteins, different kinds of proteins doing different things, that are negatively charged. Protein and ions.

And outside, there tends to be a lot of sodium. And sodium is positively charged. And then potassium, free range, potassium can go wherever it wants.

So there end up being two competing forces on the potassium. The potassium is positively charged, the inside of the cell is negatively charged, potassium wants to scooch itself inside.

So if we're looking just at a cell membrane here-- here's our membrane-- in, out. Here's our sodiums, sodiums, lots of sodiums. Proteins inside.

So there is an electrostatic force pushing the potassium into the cell, because the inside of the cell is negative and the outside of the cell is positive. So potassium, because it's positively charged, is getting pulled in by that negative charge on the inside of the cell.

So we have an electrostatic gradient pulling potassium in. Because, again, there's open potassium channels. Potassium can pretty much drift freely across the membrane as much as it wants.

But as potassium starts to come into the cell, there starts to be-- eventually, there's going to be more potassium inside the cell than outside. And at that point, you start to see osmotic pressure.

There's also a force on the potassium to diffuse evenly throughout the intracellular and the extracellular spaces. So potassium starts coming in. But eventually, there's a diffusion gradient.

So not all of the potassium ends up inside. Some amount of it has to stay outside. And what the neuron ends up with is this point where the electrostatic pull pulling the potassium in, and the diffusion pole pushing the potassium out are balanced at a certain ratio of charge and potassiums inside.

AUDIENCE: Polarity?

ABBY NOYCE: Yeah, at a certain concentration, you could say that.

AUDIENCE: But this is just over the certain section of the axon?

ABBY NOYCE: This is when the neuron is at rest, when it's not actively sending off an action potential. This is going to be true across the entire cell.

So at rest, the potential, the difference in charge across the membrane, is about-- it depends on who you ask. We'll say minus 70 millivolts. So it's more negative inside than outside.

And that's the point at which the potassium inside and outside are balanced across both these forces. It ranges usually between about minus 50 millivolts and minus 80 millivolts.

There's differences for different kinds of neurons. There's differences for different species. Minus 70 is a good middle-of-the-road number.

So this potential, this is called the resting potential. And again that potential word just refers to the difference in charge between the inside of the cell and the outside of the cell. We good?

So remember, we talked about these ionotropic tropic receptor types. They open up ion channels. They're going to let other ions in or out of the cell. Usually, not a potassium channel. Letting more or less potassium in isn't going to make a big difference.

But you might see ionotropic receptors that open sodium channels, that open chlorine, which is a negatively charged ion, channels that open calcium channels.

And any of these ions coming in, being able to cross this membrane is going to change the potential. So if, for example, this neurotransmitter was a channel that let in sodium, then we're going to get some positive ions coming in. It might go from being minus 70 millivolts to, say, minus 60 millivolts.

And that would be localized. That would be like right here, where the receptor is. And so one of the big ways in which receptors change the probability of the postsynaptic cell, the next cell firing, is by letting in these different ions that are changing the potential across the cell.

And if this cell keeps firing lots and lots of times, more sodium is going to come in. More sodium's going to come in, maybe we're going to have sodium come in at this receptor. And it might change it more. It might make it minus 50 millivolts.

And again, that's localized. So the difference is going to get weaker as it goes away from the synapse. So it might get all the way down to minus 50 millivolts right at the synapse, a little bit further it might still be minus 60 millivolts. Further away it might still be minus 70 millivolts.

But if we've got lots of synapses all doing this at once-- we'll have another one come in-- and they're all sending in more sodium into this cell, then this cell is going to depolarize all over the membrane. It's going to become-- that potential difference is going to get smaller.

And at this all-important integration zone, the axon hillock, there's a threshold. If the axon hillock gets to this threshold value of about minus 50 millivolts, then, shazam, the neuron sends off an action potential that goes flying down the axon and causes it to release neurotransmitter down at the axon terminals.

AUDIENCE: And would these synapses all be from the same cell, or can they be from other?

ABBY NOYCE: They could be from a whole bunch of different neurons. So these are clearly pretty simplified sketches. Like, a neuron like this, like if it's a pyramidal neuron in the cortex, could have inputs from hundreds different cells or more.

The number of synapses in your brain is staggeringly huge. And I don't have it on hand today.

AUDIENCE: Would they mix together?

ABBY NOYCE: Yeah, so you'd get input from different cells. Usually, you'll see either cells that are all in the same region talking directly to each other, or cells bringing in input from far away and kind of integrating it. So you'll see cells doing both of those things, but usually not quite mixed together.

AUDIENCE: Does the neurotransmitter have to come from all different-- from all of the dendrites, or could an action--

ABBY NOYCE: So it depends on a couple of--

AUDIENCE: --terminal in the right place?

ABBY NOYCE: It depends on a couple of things. It depends on-- if just this one cell was firing, but it kept firing, and kept firing, and kept firing, kept firing, and so that sodium gets to keep coming in, and coming in, and coming in, then you'll get summation over time, sort of.

And that could be enough to get this area to that threshold value. Or you could also see this one fires a little bit, and that one fires a little bit, and that one fires a little bit. And you get spatial summation, where you're adding up inputs from different parts of the cell, that bring it to the same thing.

But, for example, what happens if maybe at this synapse, these receptors let in chlorine ions. What's going to happen?

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: It gets more polarized, right. It gets hyperpolarized. It might go to minus 80 millivolts. So if you've got an inhibitory synapse, like this, it's making this cell less likely to fire. By making it hyperpolarized, by making it harder for an excitatory input to bring it all the way down to that

threshold value.

So this is how neurons integrate lots of information. They have inhibitory synapses that make them less likely to fire. And excitatory synapses that make them more likely to fire. Two different kinds of input coming in.

And they add them up, and if, at any given point in time, the membrane potential at the axon hillock here-- this is the axon hillock. And it's this just kind of little bump, right where the axon starts going off from the cell.

If it gets to minus 50 millivolts right there, then it triggers a chain of stuff that is the action potential.

AUDIENCE: Is it always [INAUDIBLE] 50?

ABBY NOYCE: It's pretty close. Again, there's a little bit of variation among the cells, and among species. It's usually about 20 to 25 millivolts less than the resting potential that's usually-- so you'll see a range in the resting potential and you'll see a correlating range in the threshold.

AUDIENCE: So what [INAUDIBLE] the different types of synapses [INAUDIBLE].

ABBY NOYCE: So there's excitatory synapses that makes the cell more likely to fire by depolarizing it. So they're going to usually let in a positive ion that brings the potential of the cells closer to zero, closer to being even.

And there's inhibitory synapses that make the cell less likely to fire. And usually they'll do that by bringing in a negatively charged ion that hyperpolarizes the membrane, makes it get even more extreme difference between the inside and the outside. So it makes it harder for it to reach that threshold value at the axon hillock.

AUDIENCE: Couldn't they [INAUDIBLE] tell the cell to release positive [INAUDIBLE] already?

ABBY NOYCE: Hmm?

AUDIENCE: Tell the cell to release positives, and that would also bring it down.

ABBY NOYCE: I'm sorry, I don't--

AUDIENCE: If the cell body releases positive ions instead of taking them in, that would also?

ABBY NOYCE: Yeah, so you might--

AUDIENCE: That would be similar to if it took in a negative.

ABBY NOYCE: Yeah, I don't know if that-- I do not know that that happens, which is not to say it doesn't, but it's not something that I know about. Because the two positive ions that are kind of at the center of how neurons work are sodium, which is-- the force is going to be pushing sodium in.

And potassium, which doesn't really-- which is already balanced. So these aren't like active transport channels. They aren't using energy to pull these things in. They're just taking advantage of the gradient forces that want to push the ions into the cell already.

So all the sodium's outside, the sodium wants to go in. The chlorine is all like-- the chlorine's all outside and wants to go in.

The sodium has got both an electrical and a diffusion gradient pushing in the same direction. And when you have an action potential, then it takes advantage of that. But before we talk about that, let's take five minutes to get up, walk around, stretch.

So we have an action potential, an electrical signal coming down the axon terminal. And then what happens?

AUDIENCE: A calcium ion [INAUDIBLE].

ABBY NOYCE: Right. Voltage-gated calcium channels open up. Calcium goes where?

[INTERPOSING VOICES]

ABBY NOYCE: In, binds to the vesicles, good. What do the vesicles do, someone else? Someone else?

AUDIENCE: Binds to the presynaptic membrane.

ABBY NOYCE: Yeah , they merge with the membrane. And what do they do?

AUDIENCE: The let go of the neurotransmitter.

ABBY NOYCE: Yeah, they open up, they release the neurotransmitter into the synapse. And then what happens?

AUDIENCE: [INAUDIBLE]

ABBY NOYCE: Sure.

AUDIENCE: The neurotransmitter binds to the receptor proteins of that postsynaptic neuron?

ABBY NOYCE: Right. Usually on the dendrites of the postsynaptic neuron. But you'll also see synapses right on the cell body. You'll even see synapses onto like the axon terminals of other cells, that actually affect just how much neurotransmitter gets released and things like that.

But the prototypical synapse is from the axon of one neuron to the dendrites of the next. So they'll bind to the receptors here. And what happens when a neurotransmitter binds to a receptor?

AUDIENCE: It either causes ion channels to open, or--

[RINGTONE MUSIC]

AUDIENCE: Oh my god.

AUDIENCE: I'm sorry.

AUDIENCE: --it causes more or less receptor proteins to appear on the membrane.

ABBY NOYCE: Yeah, so it either causes ion channels to open or it triggers a cascade of biochemical effects that cause long-term changes, one of which can be creating more membrane proteins.

So that depends on if it's an ionotropic or a metabotropic receptor. And if it lets in ions, what happens? What happens if it lets in positive ions, like sodium?

What happens to the postsynaptic cell when those positive ions come in?

AUDIENCE: The action potential depolarizes.

ABBY NOYCE: The membrane potential, yeah. So it goes from its resting potential, it gets less polarized. And so is that excitatory or inhibitory?

AUDIENCE: Excitatory?

ABBY NOYCE: Yes, good. And if it's a negative ion, like chlorine, coming in? Then it's inhibitory, right. It's going to hyperpolarize the membrane, make the difference between outside and inside bigger.

And make the neuron less likely to fire, because, of course, the neuron wants-- in order to fire,

the membrane potential, right in here, has got to reach that threshold level of minus 50 millivolts. Cool. OK.

So what happens-- if it reaches this minus 50 millivolt channel-- we are going to do a zoomed in on one of these boards. When it reaches this minus 50-- need more layers-- all right.

When it reaches this minus 50 millivolt level-- so here's our axon. [EXHALES] All along the length of our axon are voltage-gated sodium channels. So they are channel proteins, like we've been talking about.

The ion that they let through is sodium. And these guys open or close depending on what the potential, the voltage, across the membrane is. And this is why that minus 50 millivolt threshold is important.

Because once the potential reaches minus 50 millivolts, this sodium channel-- and, of course, there's like a bajillion of these, right, there's tons of them-- opens, which way is sodium going to go, in or out?

AUDIENCE: In.

ABBY NOYCE: In, right. Sodium comes in. And because there's tons of these all along, lots and lots and lots of sodium comes in.

So if you were measuring the potential across the membrane right here, with like an electrode on the inside, and an electrode on the outside, and measuring the difference between them, what you'd see is-- here's zero. Here's our resting potential, minus 70.

You see the neuron just hanging out. And as input start coming, in it might go up to that all-important minus 50 threshold level. And then as the sodium comes flooding in, the potential is going to depolarize.

It's going to go way past the zero line. It's actually going to go all the way up to about-- way up. It's going to go all the way up to about positive 50 or 60 millivolts, in the other direction from it, because so much sodium just comes pouring in right at once.

So it's this extreme depolarization. It actually flips the potential across the membrane.

All right, and then these sodium channels are on a timer. They open very briefly, a few milliseconds, they close. But in the meantime, the cell is now full of sodium.

And in the meantime, when we get this extreme depolarization, when it goes all the way to the interior of the cell being positive relative to the exterior, that triggers-- and they'd be right in here, but I'm going to draw them on the other side for space-- we're going to have another set of voltage triggered channels.

These ones are for potassium. Good, old potassium. And so remember that potassium was at its equilibrium point when the neuron's at rest. It's balancing the electrostatic gradient pulling it in and the diffusion gradient pushing it out.

But now with the interior of the cell is more positive than the exterior, the electrostatic gradient is pushing potassium out. The diffusion gradient is pushing potassium out. There's already more of them inside than outside.

And so this flood of potassium-- gates open, potassium goes pouring out of the cell. And so this actually ends up bringing the spike back down. It dips a little bit down below the resting potential, because potassium is just going out so fast, with such extremeness.

AUDIENCE: So it's like-- could it compare to simple harmonic motion, where if you displace a pendulum, it's not just going to stop at the bounds. It's going to move back the other direction.

ABBY NOYCE: Yeah, sure. I don't know if that's a good par-- I don't know if the underlying principles are similar enough for that to be a good parallel, but you can think of it that way.

AUDIENCE: What I mean is like, you can't expect it to stop at the bounds, it's just going to go a bit further than it needs to.

ABBY NOYCE: Just a bit. Yeah. So it actually undershoots here. And again, just like these guys are on a timer, potassium channels are on a timer. So they're going to close.

And then we're back to just our resting set. So remember, there's some potassium channels that are open all the time. Potassium can do some amount of moving back and forth.

But this is like complete potassium permeability when this happens, so the potassium can move much faster than it can when the neuron's at its resting state. Yes?

AUDIENCE: Won't it eventually mess up the gradient in terms of confusion, because there's more sodium inside?

ABBY NOYCE: So, yes. So the final thing that happens is that there's a sodium-potassium pump along the membrane that takes-- sodium-potassium pump is going to take-- let's see. Three sodiums and two potassiums and swap them.

And this is not taking advantage of the diffusion gradient. This actually takes energy. This is one of the ways that your neurons maintain that resting potential in its correct balance, is this sodium-potassium pump.

Some people say that like more than half of the energy your brain uses is just that constant sodium out, potassium in, sodium out, potassium in, pump that's running all the time.

So these guys reset the neuron back to its resting potential. Now the thing that happens is-- so we've talked about this happening right here, at the axon hillock.

But this axon goes and goes and goes and goes and goes. And all along it-- we'll run it behind our graph there-- all along it are these voltage-gated sodium channels.

So these sodium channels needed it to be depolarized past that minus 50 millivolts state. And then they bring in sodium. And the sodium is going to diffuse a little bit. And that means that the next receptor in the chain, this next piece, is going to be depolarized past that minus 50 millivolt threshold.

So this one is going to open. And sodium goes in and it's going to diffuse a little bit. And then this one's going to open. And sodium is going to go in. And so this is how the signal gets propagated all the way down the length of the axon.

Each set of voltage-gated sodium channels lets in sodium, which depolarizes the next chunk of the axon.

AUDIENCE: So it's the same threshold for all--

ABBY NOYCE: All of these, yep. So the first place where you start seeing them is at the axon hillock there. That's where you first see these voltage-gated channels. And then all down the axon, they just keep staying there.

All the way out to the axon terminals, where, remember, we have a voltage-gated calcium channel. So when this change in potential hits the terminals, it's that voltage across the membrane change that triggers calcium to come in to do the release of neurotransmitter at the

synapse.

Questions? Want to walk through it one more time? Yeah, OK.

So at the axon hillock, we start to see these voltage-gated-- so they're triggered by the potential across the membrane-- sodium channels. They let positively charged sodium ions in.

And they're triggered when you get to that minus 50 millivolts threshold potential. These guys start to open. And as they open, sodium comes pouring in. Tons and tons and tons of sodium gets shoved in to the inside of the axon.

There's a diffusion gradient pushing the sodium in. The sodium is all outside, it wants to spread out evenly. So it's being pushed into the axon by that.

There's also an electrostatic gradient pushing it in. Because at minus 50 millivolts, the inside is more negative than the outside. The positively charged ions are drawn to that negative charge.

So sodium floods in. Then these guys close. They're only open for a little while and they close up again.

But all of that sodium coming in depolarizes the neuron-- not just that mine is 50 millivolts that we were talking about before-- way up, so that the inside is at like plus 50.

The inside is more positive than the outside because of all these positively charged sodium ions that came, shoom, coming in.

Then once it gets way up so that the inside is more positive than the outside, we have another set of voltage-gated channels. And like I said, you're these are going to be interspersed with these guys. I just drew them down here to give us some talking space, thinking space.

And these are potassium channels. So even at rest, the membrane is kind of permeable to potassium. There are some potassium channels open. But it's going to diffuse slowly across the membrane.

But when these guys open up, when these voltage-gated channels open up-- again, there's tons of them-- potassium now has both a diffusion gradient, there's more potassium inside than outside. And an electrostatic gradient because now the inside's positive, pushing these positive potassium ions out.

So the potassium pours out through these channels. And the potassium, so much potassium comes out of the cell that it not only goes back down to minus 70 millivolts, it actually goes a little bit below that. It undershoots before coming back up to the resting potential.

So after the sodium and potassium have done their thing, we have a sodium-potassium pump that uses energy, that actually pushes sodium out of the cell and potassium in. It's kind of cleaning up after this extreme membrane potential thing that just happened.

So these guys are using ATP, using energy, to push this stuff back into its proper resting alignment. And then this has propagated all the way down the length of the neuron because all of these sodium channels that are making it go are voltage-gated.

So each time the sodium comes in, it diffuses a little bit, it depolarizes the next section of the membrane, and that opens the next set of sodium gates, which lets in more sodium, which depolarizes the next section of membrane. And it goes, shazam.

So when people talk about a neuron firing, usually what they're really talking about is a transmission of that-- or a nerve impulse-- they're talking about this action potential that travels down the neuron's axon to the axon terminals.

Who thinks they get it? Raise your hand, if you think you get it. Raise your hand if you think you get it well enough to explain it to somebody else. All right, cool. Reasonably good. Anyone want to look over--

AUDIENCE: How does it restore at the end? When the potential [INAUDIBLE]

AUDIENCE: Is it because of the pump?

ABBY NOYCE: Yeah, the sodium-potassium pump throws guys out, and these guys in, it goes back to it's resting. And so the sodium is all getting pushed out, and remember, the potassium still has some amount of freedom of movement.

So this clears all the potassium out and then clears all the--

AUDIENCE: Oh, is it the sodium [INAUDIBLE] and the potassium coming in.

ABBY NOYCE: Sodium goes out, potassium comes in. So as the sodium gets cleared out, the potassium can float around and get itself back to its original resting potential. Really, the important thing this

pump is doing is getting all that sodium back out of your cells.

So one of the important things-- back to glia for a minute. One of the really important thing that astrocytes do is they monitor the levels of potassium floating around in the extracellular fluid, outside between the cells.

Because if you think about it, when a neuron fires, this potassium all comes pouring out of the neuron and into the extracellular fluid, into the space between them. And that could mess up the other neurons around it, because the resting potential is based on the balance of potassium.

So if all of a sudden, we dump a lot more potassium into the extracellular fluid, then the balance between the diffusion gradient and the electrostatic gradient is going to change. The potential of those neurons is going to change. And it could all get messed up.

So astrocytes actually soak up some of that potassium and release it back.

AUDIENCE: Wouldn't that pump actually depolarize the cell, because you're letting more positive ions out than in?

ABBY NOYCE: Yes, but because potassium can diffuse slowly, but freely, then its electrostatic gradient pulls in some more potassium to balance it.

Like we talked about. So there's a diffusion gradient on potassium, pushing it out of the cell at rest. And an electrostatic gradient that pulls it in. So this would have those off-balance for a while, so that you'd have the electrostatic gradient pulling in more potassium than is being pushed out by the diffusion. Yeah?

AUDIENCE: Would people being under the influence of drugs, would that affect the way that's being done?

ABBY NOYCE: Yeah. So most drugs that affect the way your brain works actually work at the synapse. They'll either act like a neurotransmitter at a synapse or they'll block a synapse so that its neurotransmitter can't-- train of thought.

AUDIENCE: Bind to the receptor?

ABBY NOYCE: Yeah, so its neurotransmitter can't bind properly. They'll get in that spot, they'll stick well enough to fit in that spot in the receptor. But they won't have some key property necessary to actually activate it.

AUDIENCE: Would affects would that have? Would it just wait until the drug wore off?

ABBY NOYCE: Depends. So there's actually-- ever gotten like Novocaine at the dentist or something? Novocaine works. It's only localized, but it works by actually blocking those voltage-gated sodium channels.

So the pain nerves in that area can't send signals because they have no way of propagating an action potential. So your pain receptors are jumping up and down going, oh my god, somebody is cutting holes in your mouth. But this signal cannot get to your brain because these gates are blocked by the Novocaine.

So the sodium can't come in, the action potential can't happen, the information from your pain receptors just doesn't get there.

AUDIENCE: That's cool.

ABBY NOYCE: Yeah. It's cool. Best class I took in college with psychopharmacology. Talks about all different classes of drugs and what they do, different neurons. Not just illegal drugs, like psych drugs, like antidepressants or anti-anxiety drugs. All sorts of cool stuff.

Another one that interferes with these, with the sodium gates, is the toxin that gets into shellfish that are exposed to red tide. So red tide is an algae that blooms periodically.

And then shellfish are filter feeders, so they eat the algae. And there's a toxin in it and it's not just localized, like Novocaine, it gets all your neurons. So like the neurons that go to your muscles that tell you to breathe. Yeah, not good. This one will kill you and that is how it does it.

OK so the other thing I wanted to talk about, really quickly, is we talked about Schwann cells and oligodendroglia or oligodendrocytes, some people will call them.

And what these guys do is they myelinate axons. They produce this fatty substance called myelin inside their cells. And they wrap themselves around an axon.

So an axon that is myelinated-- so this is going to be like the white matter in your brain. Or the long-distance nerves that go out through most of your peripheral nervous system, that is myelinated.

And it's going to have this stuff coating it. And it leaves these little gaps. But it's actually going

to be able to do one all the way around. It's actually going to be wrapped all the way around the axon.

So this is myelin. People usually refer to it as a myelin sheath that coats the axon. So again, Schwann cells are doing this in the peripheral nervous system, like your motor and sensory nerves, where some of them, the faster ones.

And oligodendroglia are doing it in the central nervous system in your brain and spinal cord. And what happens with this stuff is, if we look at how we were just showing how transmission works, with all of these channels along the ends, on a myelinated neuron, conduction is faster.

Because what happens is you get a channel here, or a bunch of channels here, letting in sodium. And then instead of having to open channels all the way along here, it's just diffused, and you get a change in potential.

So the conduction actually hops between the bits of sheath.

AUDIENCE: So it would take longer if you had to wait for all the ions to diffuse all the way down to the end.

ABBY NOYCE: It's faster. And I think this is a hole in my physics understanding of what's going on.

AUDIENCE: [INAUDIBLE] localized, so that you can have [INAUDIBLE] more dramatic changes in potential?

ABBY NOYCE: Yeah, maybe because you've only got a few spots where you can see that change happening, it's all concentrated. I don't know. I feel like it's faster. It's a lot faster.

It's called saltatory conduction, which is from the Latin word for to dance, which is kind of cool. Because it's like this little potential change skipping down the axon, boink-boink-boink.

So yeah, it's faster because it hops between each of these places. And the physics of why that happens have never quite made sense to me. And I was looking at it again today, and just being like, OK, I don't get it, but I believe you.

So if anyone manages to read it and figure it out, please let me know.

AUDIENCE: I think it's similar with, say, we had a chain of [INAUDIBLE]. So it's going from this side to the other. And then, say, had a race. Have a chain of students versus just one kid.

The one kid has to run to touch this wall, and then run across the room to get to that wall. The

other kids just to have to slap each others' hands as soon as they get the previous.

ABBY NOYCE: Yeah.

AUDIENCE: That's a good analogy.

ABBY NOYCE: Sure. So anyway, it's faster because it only has to do it these individual sections, it doesn't have to do it along the whole stretch of the axon.

AUDIENCE: Also, if you had the axon completely covered with the--

ABBY NOYCE: With the myelin.

AUDIENCE: No, with the channels.

ABBY NOYCE: Ah, OK.

AUDIENCE: That would like-- that would mean that you wouldn't have just sections, but as soon as there was a certain potential, it'd start immediately taking in the sodium. And that would actually-- the effect would diffuse down the axon, as it goes further and further. It's like diminishing returns.

ABBY NOYCE: Yeah, I don't know. Maybe I'll look at it again tonight.

So saltatory conduction in myelinated neurons, myelinated neurons are faster than unmyelinated neurons.

Have you ever noticed that you stub your toe, and you get two different kinds of pain. You go, oh my gosh, ow, that hurts. And it's really fast and then it goes away very quickly.

And then there's this second like, ooh, ow, that really hurt. Like there's these two very different characteristics of pain that you get for any kind of sharp injury like that.

So the first kind of pain comes from one kind of pain receptor. And it's on these very fast myelinated nerves. So it comes to your brain first. We don't need a demonstration.

And the second kind is on these slower nerves. So it doesn't get to your brain as quickly, but it doesn't adapt. The first kind is like, it tends to adapt.

So your pain receptors-- it's like, OK, OK, we know we know it hurt, and it goes away. It just

stops listening to the pain receptors.

The second kind says, nope, I'm going to keep telling the brain about it, keep telling the brain about it. So it doesn't get there as fast, but it lingers a lot longer.

And so that's a difference between a myelinated and an unmyelinated nerve carrying the same message. All right, anyone have questions? Cool.

AUDIENCE: So is it the myelinated that lingers, or is it the?

ABBY NOYCE: No, the myelinated is fast. And those are usually-- and those are, in this case, in that pain transmitter case, in particular, those are the nerves that adapt to the continued input and start ignoring it pretty quickly.

And then these other neurons are slower, but they're more persistent. They're just like nope, keep telling brain. Keep telling brain. Yup, it still hurts. Yep, it still hurts. Hi, your toe still hurts. You guys know what I'm talking about, right? OK.