GERALD SCHNEIDER: And here in the front that asked me whether a bird's song would count as a fixed action pattern-- doesn't sound fixed. This is because they learn a lot. But you know that's true for every fixed action pattern, every instinctive behavior. There's always some learning involved. It's never fully formed.

Walking is a fixed action pattern in us. But in fact, we do learn things. And it develops a little bit over time. Some fixed action patterns have a lot of learning. And some, very little.

An action like sneezing would have almost none. But in fact, if I look at various people, even in the same family, sneezing, they'll all do it a little differently because they've learned. They've added some learning on top of it.

So we have a few things left from last time. I want to go over a few things. Examples of competition among axons during development, where axons will compete for terminal space-- they're either competing for growth factors or for occupancy of synaptic sites. But they're also contact interactions between adjacent axons.

I changed the heading slightly, but these are the same pictures you have on the printout for the last class. We're going to go through a series of simple examples. In every case, there's some competition among adjacent or overlapping populations of growing axons in the developing brain.

So for example, in the visual system, the two eyes project to the geniculate body, OK? The box there indicates the geniculate body. And then you see the two eyes. And axons from the two eyes just mix with each other. If you look with anatomical methods, you see that they're overlapping, OK?

But then there's a sorting out. They appear to compete in some way with each other. And those from the ipsilateral eye end up in one part of the geniculate from the contralateral eye in the other part of the geniculate, OK? So they sort out.

That also happens in the superior colliculus in abnormal situations where you create a colliculus with both eyes coming in to the superficial layers. Now, here's another example. Here, you have competition between, again, two overlapping populations.

In this case, as in the geniculate body, they sort out in somewhat different way. There's two types of axons. And although they're initially overlapping, in fact, I've drawn them as if they're all set, but they probably-- the terminal arbors would actually overlap. But then as they mature, one population ends up occupying the upper 2/3 of the layer. And another population ends up occupying the lower third.

There is a little bit of overlap between them still. But basically, they segregate into layers. So not so different from what happens in the geniculate body, except in this case, they're not axons from the two eyes.

Now they're from the same eye, but they're from different types of axon in the same eye. One is a larger axon, OK? Another one is a smaller, coming from smaller cells. And they end up terminating in these different layers.

There's other cases where two populations are in the same eye, where because they're coming from different cells, one axon type might grow bigger than the other and end up occupying more of the space than the smaller axon, OK? Many cases of that. Initially, they might be very similar, but they may end up occupying different amounts of space, though they might still overlap, OK?

Now, we know that these axons form topographic maps. Initially, we have one axon that might be terminating over a span of the collicular space. But then they segregate because each axon seems to compete best in one part of the tectum, depending on the chemical environment, OK?

So the chemical factors interact with these competitive interactions in sorting the axons into their proper places. OK, so just think of it in every case as a kind of competition between adjacent or overlapping populations of axons, OK? Very common in development.

Now let's talk about this intrinsic factor that, in a cell, when it's growing an axon, can vary in its ability to compete, OK? And we call this competitive growth vigor. The more growth vigor an axon has, the more it grows and the better it competes for terminal space.

But this can be modulated. It can be modulated by chemical factors-- for example, NGF in the case of tissue culture. You can see that the cells here had a lot more growth vigor than the cells here. Here, they're growing short, little, stubby axons and not going very far. Some of them are not growing much at all.

But if you add little growth factor, they grow much more vigorously. So it's possible, then, to modulate the growth vigor with these chemical factors.

There's also factors intrinsic to the cells. And in fact, something like NGF is synthesized by some neurons also. So sometimes, they make their own growth factor. And then how much they make will determine how they grow. They might respond separately to other growth factors in the environment.

OK, but now there's a couple of other things I want to consider briefly. One is later in development, activity can affect the growth vigor of the axon. So for example, axons representing the two eyes grow into the geniculi, segregate into different laminin. So you have different laminin, but all representing the same place in the visual field, so the corresponding areas of the two retinas.

OK, now all the cells in that column from representing the contralateral eye and the ipsilateral eye will project to the same region of the cortex, where we know there's another topographic map of the visual world. But now, and again, they grow in, and they overlap with each other early in development.

And then, just like in the geniculate body, they segregate. But now they segregate into adjacent slabs of tissue. We call them cortical columns. They're really like slabs. And if you look at it from the surface, they're like zebra stripes. Many of you have seen those pictures of representation of the two eyes in the visual cortex.

But what I want to bring out here is that if the activity of the two eyes is abnormally different-- so for some reason, perhaps the person is strabismus. And he starts suppressing vision in one eye. Or on one eye is patched because of an injury or something, OK?

The eye with the activity, with more activity, will end up occupying more space. And the eye with less activity will occupy less space. Children with strabismus will often suppress cortical vision in one eye, at least peripheral vision. And one eye loses acuity. And the other eye will actually have somewhat increased acuity.

So if you test the child with the two eyes, he comes in for an eye test when he starts school, they see very different acuity in the two eyes. It's because he's normally suppressing vision in one eye. I had that when I entered school.

So what do they do? They patch the good eye to increase activity. Now, if I had any strabismus, it wasn't noticeable. And I have coordinated-- the two eyes are coordinated.

But with that patching, over time, the acuity got better and better in the eye that it was so bad in. The other eye stayed about the same. And I ended up with about, instead of 20/20, I had 20/15 in the left side, better than normal, and 20/30 in the other eye.

So apparently, the columns representing the two eyes are still a little bit different. So that shows how activity-- and there's other examples of how activity can influence axonal growth. That tends to happen, of course, later in development, when the axons are more mature. But they're still growing, still competing, OK?

You can also vary competitive growth vigor with a lesion, OK? And I'm going to illustrate that by showing you what we call the pruning effect in axons.

Let's take the top one first. This just illustrates how we conceptualize it-- that early in development, the axon is just starting to grow terminals. It hasn't formed very many yet. Its growth vigor is very high.

It's growing in all the local directions from this terminal until finally, once it reaches a certain quantity of its terminal arbor, the growth vigor now is very low, OK? So it appears that these axons or cells are programmed to form a certain size of terminal arbor. And we have a number of experiments that indicate that.

So to test that, we can take an animal that's formed the terminal arbors. But now we'll create a lesion. We'll make a lesion in part of the brain that will kill some of the-- in the arbor, OK? Now, I've done this for conceptual purposes, but I am not going to go over all the experiments right now.

What that does is it increases the growth vigor in the remaining branches. So if it has a collateral branch here-- for example, this could be in the thalamus, and this could be in the tectum-- it will now increase its projections in those collaterals. They'll grow bigger than normal, as if in compensation for the loss of the arbors here.

And these will grow more also. So you'll end up with an arbor, a total arbor size about the same as it would have been normally, OK? But now it's growing them in a different pattern because of the damage.

So it's not that different from pruning a tree. If you have certain trees show pruning effects. Some do not. OK, a maple tree, for example. If you prune the top of it when it's young, you can create a better shade tree because the lower branches will sprout more. It'll become a wider tree and won't just grow a tall, slender maple tree. It'll be a broad maple tree in your front lawn.

That's a pruning effect. Many people that keep houseplants know this. Azaleas, for example, respond very vigorously to pruning. So these cells that not only look like trees, they also act in some ways like growing trees. OK.

Do people have the handout yet for today? You don't. Well, it'll be coming in a minute. I thought they would have it by about this time. They didn't realize where I had put it on the table upstairs, so they were looking for me instead of the handout. And I was off doing something else. Anyway, they will be in here momentarily.

We're going to start talking now about the motor system. And we'll do that all week. We're going to start talking about spinal reflexes, withdrawal reflexes, or the opposite of withdrawal, the magnet reflex, and the stretch reflex. We'll talk a little bit during the talk of these reflexes about intersegmental spinal organization.

Good timing. I've just started to talk about the motor system. We'll say a little bit about plasticity in the spinal cord. And then we're going to talk about higher systems of motor control because in the last--

On Friday, I would like to show you a film of a classic experiment about the role of descending pathways in primates. The experiments are on rhesus monkeys. And to understand that film, we have to review in a little more detail the descending pathways coming from the hindbrain, midbrain, and forebrain to the spinal cord.

And then if we have time, we'll talk a little bit about corpus striatum and cerebellum, some of the pathologies of striatal dysfunction, and the role of the striatum in implicit learning. If we don't get to that, we'll do it after the midterm. We'll just see how far we get this week.

A good place to start when you're talking about motor control is on the output side. We could be reflexologists and assume that we should start with the sensations triggering the responses. But I like to start with the motor system and then go backward into the CNS.

So we're going to look at muscle, where we find-- we magnify a little bit. We'll see these myelinated axons of the alpha motor neurons, the large motor neurons in the ventral horn of the spinal cord terminating on the muscle cells, multinucleate cells, long cells with contractile proteins, OK?

And then if we do a blow-up of the muscle endplate, we'll see that synaptic connections are made with the muscle at multiple points. And they trigger, basically, an action potential in the muscle. When that is triggered in the muscle, the muscle contracts, OK?

So it's similar to a neuron in some electrical properties, but its response is that of contraction, OK? It doesn't communicate. We don't have myoid conduction that I know of. Well, there might be a little in smooth muscle, but I'm not aware of it. Where muscles communicate with each other, almost all the triggering of contraction is through neuronal activity.

So if we start with the reflex model, remember, reflexology was the idea that all behavior can be explained in terms of S-to-R processing. Everything was a reflex, a simple reflex or a more complex reflex. Almost everything that Pavlov wrote about motor control was put it in those terms.

And both Pavlov and then later, Skinner and others, Thorndike preceding him, realized that S-R pathways could be plastic. You can get conditioning, learning. Pavlov talked about classical conditioning or Pavlovian conditioning.

Skinner talked about instrumental conditioning, like an animal solving a problem box. When he solves it randomly at first, he will then learn and repeat the moves that were rewarding. But they still stuck to the S-R model.

Now, we know and I've mentioned in the introductory lectures that the circuitry and individual cells are more complex. They have feedback. They have endogenous activity. They have modulation, whether by other pathways that makes S-R model a little bit difficult to stick to.

But if you're dealing an animal like a spinal animal, you've removed the brain, as it was done by Sherrington in his early studies around 1900, it works very well. And you can explain most of the behavior that you can get. And you'd say, well, what behavior can you get out of a spinal animal? Well, quite a bit, actually, OK? The spinal cord can do a lot by itself.

Why can't we see that in humans with spinal transection. Why don't we see more behavior? Why do they seem so incredibly paralyzed?

Remember spinal shock and diaschisis? When you have a huge number of excitatory connections removed, as in humans with a very large forebrain, it's very difficult to get normal spinal function. It's easier in animals with a smaller forebrain. But still, even with humans with spinal transection, they can learn to use spinal reflexes for a number of functions.

So we're going to now talk about two basic responses-- simple escape or avoidance responses and approach or grasping responses. We'll start with the withdrawal reflex. It's a cutaneous reflex. It's a flexion reflex, always involving at least two synapses.

And I want to ask here at the beginning, well, how do you know it's not monosynaptic? We'll go through some early studies that demonstrated that it involved more than one synapse. And these were studies that were done by physiological means with some knowledge of the anatomy. They had the knowledge of Cajal to do these.

But after we do that, then we'll talk about-- we'll mention similar responses in other modalities. I'll talk about the magnet reflex, which is the opposite, something you see more in babies than adults. We'll mention examples of higher influences on the spinal mechanisms and effects of novelty.

OK, so first of all, cutaneous reflex, called the withdrawal reflex. How do you trigger it? Well, a painful stimulus is the best way, OK? If we're operating on an animal and we want to be sure he's fully anesthetized, we test it by pinching, usually between the digits.

If you pinch yourself, you'll feel pain, but you probably won't withdraw because you're voluntarily reducing that. But if you do it to your friend, he's much more likely, if you suddenly pinch him, to pull back involuntarily. He thinks he's doing it on purpose. But in fact, it's an involuntary reaction.

You remember the picture from Descartes of a naked boy sticking his foot in the fire, triggering the withdrawal reflex because that's a reflex that spurred Descartes to start thinking in terms of nervous pathways, connections through the brain.

Let's first talk about the effects of the intensity of stimulation and how the effect spreads within the cord. Let's take a spinal cord and look at a top view like that. And take one dorsal root, OK?

And here would be the dorsal root ganglion. There would be many cell bodies there. We're going to let that represent a series of axons, OK? Sensory axons coming into the cord beginning, say, in the foot. OK, now that comes in. The axons actually spread up and down the cord.

And if we let-- it will show that termination. What I want to show here is that the termination is most dense right in the area of entry. And it becomes less and less dense when you get further from it, OK?

Now, the result of that is that with a stimulus that's not very intense, we might activate cells, bring them above threshold only in that region, OK? Because there's not enough spatial summation when we get further from the point of entry.

So what could happen, then, is that cells in this region could conduct action potentials and reach motor neurons, which then could go out and give the reflex, OK? Now, with more intense stimulation, what'll happen is it will spread over a wider region. You will reach threshold over a wider region because with more intense stimulation, now you have more temporal summation.

You'll activate cells over this entire region. So you get a spread of effect. But in every case, even with the low intensity stimulation, you are still activating this entire axonal tree.

So what about out here with the low intensities of stimulation? It's only the most intense stimulation that is going to activate that fringe of the distribution pattern of the axons. So the physiologists call that the subliminal fringe because the stimulation there was usually below the limen.

"Limen" means "threshold." So "subliminal" means "below the threshold." You've probably heard about studies of subliminal perception-- things you don't notice, but they're still getting into your nervous system. OK, but that was taken from this idea.

Why is that important? Why is the subliminal fringe important? Well, let's put in blue here descending pathways coming from the brain. OK? And have-- whoops. Supposed to be blue here.

And so here's the axons coming in. And let's say its main distribution is up here. Many terminations up here, OK? Now, the descending input might not be intense enough to trigger the cells there. And the sensory input coming from the stimulus here might also not be intense enough.

But the two together might be enough, OK? So you might activate this region of the cord, only with converging input coming from the brain and coming from the sensory input, coming into the cord. That's why the subliminal area is so important.

OK, now let's go to this question of how it was shown by the early physiologists that the reflex is not monosynaptic. And their experiments also gave the first measure of synaptic delay. Synaptic delay means the time it takes for activation on the presynaptic side to reach the postsynaptic side.

Why does it take time? Well, it doesn't take any time if the stimulus is electrical. But in almost all synapses in the CNS are chemical. And it takes time for molecules to diffuse across the synaptic cleft, bind to the receptor molecules there, and activate the cell, OK?

So let's go through the steps. They begin by recording from a ventral root. So look at this picture first. OK, and here's a recording device attached to the ventral root. And notice, this is the way the experiment was done.

I need my pointer. So they generally crushed the nerve here because they didn't want to activate anything in the periphery here. OK, so they're recording there. And the first place they stimulated is labeled two here, the little pipette here, going right into the region of motor neurons in the ventral horn, OK?

So that's described here. You record from the ventral root. You stimulate the motor neurons. And of course, you then record a volley of action potentials after a brief conduction delay. And I show that in the graph here, OK?

You stimulate, and after a brief delay, shown by the two lines there, you can record a volley of action potentials. Or if you had it connected to the muscles, you could record the muscle twitch. But we don't want the muscle twitch because we don't want to affect sensory inputs here at all. So that's why we crush the root, OK?

So that was the first experiment. Now, this is what Renshaw did. He pulled that electrode back until he was no longer stimulating motor neurons directly. He was stimulating interneurons, though, that contacted motor neurons. And he knew all this. He could guess that from the work of Cajal, OK?

But in his recordings, he could see that that initial volley suddenly went away when he pulled the electrode back a certain distance. OK, and then if he stimulated with the lower intensities, shown in the solid line there, he got a volley, but it was after a delay. The delay was 0.5 to 0.7 milliseconds.

And if he raised the intensity, it would become larger. If he raised it enough, he would start getting something like this initial one, followed by the later one, indicating to him that the current had spread with the higher intensities to directly stimulate motor neurons. But it was still stimulating interneurons, which required one synapse reach the motor neuron. So this was the first measure of synaptic delay, OK?

Lloyd then did a further experiment using the same paradigm. He moved his electrodes with the same setup here to the dorsal root. And if he stimulates with a intense enough stimulation, he's going to activate all the fibers. If he stimulates with a milder stimulation, he will activate only the large fibers, the largest fibers in the dorsal root, OK?

And again, the intensity was varied. And what he found was he got something similar to what Renshaw had gotten stimulating the interneural pool in the cord. He got a first volley. But then he also got later volleys.

And as he raised the intensity, he got additional-- he got greater amount of number of action potentials, more action potentials appearing in the ventral root. And they appeared to be harmonic spaced, similar at distances that indicated that it was simply one synapse, two synapses, three synapses, and so forth. OK?

He never got the artifact here because now his electrode was outside the spinal cord. So it wasn't spreading to motor neurons now. That's why he didn't get that artifact that Renshaw got here. Is that clear what's happening? OK.

So then the final experiment was to stimulate the cutaneous nerve. Now, if you go here, you can-- after the dorsal and ventral roots come together, you get into the peripheral nerve. And there are nerves out here that go only to the skin. Other nerves are mixed. They go to skin and muscle. And there's some go only to muscle. Just depends on where you are, OK?

So they found the cutaneous nerve, OK? Stimulated there with a sudden pulse of electricity. They corrected for the conduction time, OK?

And they found that with the cutaneous nerve, they never got this first volley. This one. There always seemed to be at least two or more synapses between the cutaneous nerve and the motor neurons, the activation of the motor neurons and the action potentials that actually appear in the ventral root, OK?

So that was how it was demonstrated that cutaneous reflexes are never monosynaptic. They always involve at least two synapses. And it was also the way they demonstrated the first evidence for a clear synaptic delay.

Now, when they trigger that reflex, the other things happen too. When you trigger at a flexion reflex-- let's say you trigger withdrawal of the arm-- not only do you activate flexor muscles, but you also relax extensor your muscles. That's called reciprocal inhibition.

OK, it's a pretty general principle. To avoid conflict, you get rid of the competing-- you reduce activity in the competing response systems. It happens in brain mechanisms too. It happens during fixed action patterns, OK?

Think of conflict in an animal. Now, if he gets stimuli that can trigger approach to food and escape from a predator, which would you want to inhibit the other response? Well, of course, the escape response should inhibit the feeding. And it generally does. The animal drops what he's doing and freezes or runs.

But it happens at this very low level in the spinal cord with reciprocal inhibition of extensors. I just point out here that it doesn't always work with higher systems. Should I watch TV, or should I study? Sometimes, you just experience the conflict. And as we grow older, we hope some of us may get better and better at resolving conflicts. But we never get rid of them.

Other things happen too. When we trigger this-- let's say we trigger withdrawal of the leg. There would be a tendency for the animal to fall over, lose his balance fairly easily. There's usually a crossed extension reflex.

So there will be fibers coming from interneurons that are triggered by the cutaneous activity, OK? We'll cross over to the other side. But instead of activating flexion, they'll activate extension, OK?

So often, if you see that happen, a person will go like that because he's extending the leg. And the initial movement is automatic. And then, of course, vestibular reflexes will come into play and tend to keep him on his feet, OK?

Now, if it's very intense, it won't just be his foot that withdraws or just his leg. He might get more general flexion of his body. In some cases, it's difficult to maintain balance. But generally, the crossed extension reflex will aid that maintaining of posture.

Let's just think briefly about other modalities. What happens with intense light? If light is very bright, you get something like a withdrawal-- from the stimulus, anyway-- because you get constriction of the pupils to protect the retina from too much light.

Contraction does other things too. It increases resolution, possible resolution of the image, even with poor focus on the retina. If the pupils are very small, you will still have an image that's in focus. That's the principle of the pinhole camera, OK? But the main thing here is that with intense light, the pupils will constrict to protect.

With intense sound, there's something very similar. There are actually little muscles in the inner ear that will tense up and reduce the oscillations of the middle ear bones and protect that system from damage.

Novel input does something very different. When input is very novel, we also respond. Now, just generally, to detect the novelty we need brain mechanisms of midbrain or forebrain. It tends to result in an increased sensitivity to stimuli. That happens in somatosensory, visual, auditory systems. Very different from the effects of intense activity that are threatening, potentially threatening.

Now, I mentioned that there's an opposite kind of reflex. You tend to see it in babies. If you take a baby, even a newborn, and stroke the back of its hand gently, often, it will extend the hand, even turn. And it's often followed by a grasp.

And of course, we think, what an intelligent, little child. He likes to grab my hand. But actually, it's a reflex, spinal reflex. Same is true of early smiling reflexes, OK?

And we normally don't see that in adults. But there are situations where we do see magnet reflexes. For example just take the second one here in brain-damaged patients. With large frontal lobe lesions, you can get enhancement of magnet and grasp reflexes.

So if you have a frontal lobe patient lying in a bed and the nurse walks by and she brushes his hand, he can turn out and grab her. And you think, what a fresh fellow. But actually, it could be a reflex. Could be a magnet reflex. And he might not actually know until after it's happened what's going on.

You can also get enhancement of the withdrawal reflexes with large parietal lobe lesions and other types of withdrawal reflexes. I've seen it in animals with large posterior neocortical lesions that damage parietal areas. So we call those automatisms. They can occur in spite of conscious efforts to control them.

What about normally? Well, we can certainly get enhancement of withdrawal reflexes. Let's look at this example. Say you've gone down into a dark basement. And you're looking for a tool there, and you can't find the light. And everything's fine until your apartment-mate yells down the stairs and says, oh, by the way, I saw rats down there today. What happens?

You touch almost anything, and you pull your hand back involuntarily because the threshold for the withdrawal reflexes has gone way down.

The other example I like is in broad daylight, and you're looking in tall grass, say, for a golf ball or a baseball. And you can't see, so you're groping with your hand. If somebody tells you, oh, there are snakes there, be careful, the same thing will happen. You'll enhance by descending activity to the cord. You'll enhance withdrawal reflexes. OK, so you will now trigger them with much less input.

So I mentioned the effects of stimulus novelty, how they increase sensitivity. Why would we want to be more sensitive? Partly because novelty can indicate problems, possible problems that something unknown will become more hesitant or show more fear and avoidance. That happens with increased novelty.

With milder novelty, we tend to show the opposite. We show curiosity, approach, and avoidance. And these are very general things that happen. You can study this in many different animals, but especially the mammals. I think all the mammals show a lot of curiosity.

When we deal with something like obtaining food or water, we have additional influences other than novelty. We have a special role of olfaction, which we know happened very early in evolution. And then with the other distance receptors, we got other effects important for approach and avoidance. In this case, mostly approach.

And limbic forebrain mechanisms became more and more important. And I'm just asking this for you to think about. What's the major additional influence of the limbic forebrain mechanisms? The limbic forebrain, we say, are the mechanisms that control our emotions and our motivations.

But we had that. Animals, even without much of a forebrain, certainly still approach food and water. They could still forage with midbrain and 'tweenbrain mechanisms. So what is the limbic forebrain adding?

One thing it does is it gives objects in the environment that are originally neutral-- it gives them what we call an effective tag. We tag things. We give them a property about how good they are or bad they are, OK? We do that to people too. And this is because of limbic system activity and limbic connections to the hypothalamus and other structures involved in foraging-- basically, modulation of the motivational effects of things.

In addition, it allows us, because of learning, to be rewarded by things that might not initially-- we might initially be rewarded by taste, primarily for taste of food. But then later, we learn certain foods taste good. Certain foods taste bad.

And we learn by their appearance. We don't have to taste them every time. OK, we learn to associate tastes with certain visual objects or even auditory or somatosensory, OK? That always involves the limbic forebrain.

OK. We don't have much more time. This is what we're going to do next time. We're going to talk about the muscle spindle organs, detection of muscle stretch, and go through these topics in talking about the monosynaptic reflexes of the spinal cord.