GERALD SCHNEIDER: We were talking about-- we were beginning to talk about models to explain habituation to novel stimuli, habituation of the orienting response. And we started with talking about central adaptation. I described what it was as the most parsimonious theory where synapses become somewhat depressed in their normal level of functioning with repeated stimulation, and then they recover over time.

The problem is this simple model, which is very much like sensory adaptation which happens in reception--

[BANG]

Well, the platform just collapsed. It's all right. It's all right. Why don't you just move it aside there and we-- Yeah, just don't put it back. [LAUGHS] Now, where was I? [LAUGHS]

AUDIENCE: [INAUDIBLE]

GERALD SCHNEIDER: The problem with it is it can't explain certain things, especially time-dependent effects. And that's what led Eugene Sokolov in Russia, in Moscow, to come up with a different kind of theory. So let's go through that theory, and then we'll go through some evidence for these theories.

Sokolov says that in our brain is a model of the world that represents the world out there, and it's always being compared with the perceived world. And he had distinct roles of the cortex, the reticular activating system, each having sensory inputs. So let's just see. He said in the cortex was this model, which is basically neural circuitry generating activity that is similar to the input. And it's compared with the input.

And he said, if there's a mismatch, the reticular activating system is activated, disrupts the model and changes it. So the sensory input can change the model. Well, it's not that dissimilar to [INAUDIBLE] model, who said that perception is a constant updating of that model. This is the way Sokolov drew his theory out. I've redrawn it from one of his publications.

He has a-- it's an information flow model with boxes. So here's the input. And he's got two outputs here, orienting movements and general arousal, the kind of arousal we were talking about earlier. So here's this neocortex box, and that's where there's a model of the world. Here's the reticular system. Each have sensory inputs.

Now, he says that here there's a comparison process going on. If the input here doesn't match the model, then there's a discharge. That activates the reticular system which produces the heavy area that just represents a general widespread effect on the cortex, basically to represent what we see in the EEG. When there's novel stimulus, you see a widespread activation, a system-wide change in the brain.

He also said that when there's a match, not only does this not discharge, but in fact there's inhibition of the input into the reticular system. Now, he was just postulating this on the basis of his behavioral data. So it's an information flow model, which he did try to relate to the brainstem reticular system and the neocortex.

Put it in a little different form the way I had in lecture four. Few of you struggled with this and may remember it. Here's our straight through processing model, which could be now in the cortex as well as in the spinal cord. The sensory analyzers. Comparator neurons, which are just interneurons in this pathway to the lower motor mechanisms which generate the response.

This should be a lot bigger because that's neocortex, the two major things going on in neocortex in very simple terms-- the imaging and the planning parts of the cortex. And here, this is constantly discharging to the comparator neurons. All neurons are comparators in a sense, comparing excitatory and inhibitory inputs.

So the mismatch then-- a mismatch allows the input to go through. Straight-through processing dominates the response. But if there's a match, if the model is predicting what's happening, then the planning mechanism is in total charge. This pathway is inhibited. This pathway activates the motor system. Only if there's a mismatch do you get the discharge. Here you inhibit that descending projection and reorganize the model.

Well, Horn dealt with this idea of comparison. He said, well, that's very simple. You can do that, and you don't need Horn-- you don't need the Sokolov model at all. Let's just look at the way neurons work. We can draw a very simple model here with two neurons, A and B. And we'll have a neuron here that will always fire according to the difference in activity between A and B.

So just look at what's happening here. A stimulates the neuron on the left. B stimulates the neuron on the right with excitatory input. Each neuron inhibits-- probably through an interneuron-- inhibits the other neuron. So if these neurons were passing-- which usually doesn't happen, but if there were a lot of spatial summation in those connections, it could happen-- the result would be that a difference in rate of firing between A and B would be what comes out.

Very simple comparator mechanism. He publish this in*Nature* magazine. It was a big deal for a little while when people were arguing about this. The problem with Horn's simple circuit is-- does it really maintain the straight-through processing model-- reflex type of model? Well, what could A and B correspond to?

Remember, Sokolov said that the problem is this reflex type model has difficulty in explaining-- central adaptation has difficulty in explaining temporal patterns, responding selectively to temporal patterns, habituating for temporal pattern. Well, a model like this, of Horn, says nothing about that. You still have to generate the model of the sensory-- of the temporal pattern. Doesn't solve that problem at all.

Sokolov's information flow model also-- he doesn't make any attempt to actually tell you how neurons do it. He just gives the different kind of information flow. But anyway, of course the telling feature here is to find out what kind of evidence is there? Which model represents more the way the brain works? My argument would be that both of them are true in different parts of the nervous system.

First of all, we can look in the visual system in the superficial layers of the spirit calculus that get input directly from the retina. And we will find units there that show very little adaptation for habituation to novelty. They just keep firing. No matter how many times you give a spot of light in the-- a little movement in the field, they'll keep responding.

So you do find neurons that correspond to the input side of these models. If you look in the deep layers of the colliculus of the rabbit-- and this work was actually done by Gabriel Horn-- you find that neurons will habituate, but they'll habituate independently to visual, auditory, and tactile stimulation.

The superficial layers get visual input, but the deeper layers get auditory and somatosensory input too. So in the deep layers, you get some neurons that respond independently to these three kinds of input. So here's my little cartoon of a neuron in the deep layers of the colliculus, and it's got three kinds of input.

So let's say we're stimulating a whisker. Somatosensory stimulation. This could be whisker stimulation. And we stimulate repeatedly. We've already mapped out the neurons' responses. We know where in the visual field it will respond to a little moving black spot, for example. We know that it will respond to a sound placed usually in a similar part of the field, around the animal's head. And we also find that it responds to the whisker that goes through that same area around the head.

So we stimulate the whisker repeatedly, and what happens is that the neuron fires less and less, shows habituation. So now the question is, well, now let's switch to the visual input or the auditory input. Has the neuron-- does the neuron respond less to those also? And the answer is no. It habituate only to one modality at a time, maintains its full responsiveness to the others. They will independently habituate.

So in other words, there's some kind of central adaptation going on before you get to that neuron. It could be right at that synapse, which is why I marked it there with red. And then over time, it recovers and the neuron has its full sensitivity again. That was based on unit recording from neurons in the deep layers of a rabbit colliculus.

There is direct evidence that the Horn type model certainly does happen, but the best evidence has come from Aplysia, the sea slug, the famous experiments by Eric Kandel and his group at Columbia, where they recorded from an identified neuron in the Aplysia, worked on the pathway for the gill withdrawal reflex, which is known to habituate. And they did all the behavioral work on this animal too. Then they did the recording, and then they did also molecular work on the neurons.

And they were able to localize physical changes happening right at the synapse on particular neurons, identified neurons in Aplysia. And it fit the Horn type model. I would consider that really the first demonstration-- discovery of an actual engram, the thing that Lashley was trying to find, the first time anybody really saw-- had direct evidence for a physical change happening that corresponds to a memory.

But it was for the simple kind of memory that we call habituation. Well, what about neocortical responses? Is there anything corresponding to the kinds of things that Sokolov talked about? Frank Morrell many years ago, before we had microelectrodes, was studying visual cortex with strobe light. He would give rhythmic flashes of light, like three-per-second flashes.

And he found that he could get a three-per-second following of that in the cortex. He found he could sensitize the cortex to this if he potentiated it using a drug or using lesions around it. But the point was he could get following in the cortex of the three-per-second rhythm. And then he did, as part of this work, a very simple thing. He would suddenly switch to, instead of bursts of three-per-second strobe lights, he would give a single strobe flash.

The cortex responded with three-per-second after repeated presentation of that stimulus. It didn't last very long. It would start responding at three-per-second, and then you would get an arousal response and it would wipe out that response altogether, basically like Sokolov would have predicted.

Sokolov himself did some physiology focusing on hippocampus of the rat, and he did find cells there that habituated. They also would discharge when a stimulus was suddenly omitted, so they would respond to the absence of a stimulus, indicating that they were tuned to novelty, not a specific stimulus.

I'm just noting there that all neurons are comparator units. He called them comparator units, but I think all neurons are like that. But at least he found something that responded in the way his model would predict. And there were other scattered descriptions in the literature, for example, in the work of Hubel and Wiesel at Harvard, were famous for their work on visual cortex unit responses.

But they would find-- they found units in the auditory cortex that would fire only, generally, when they were novel, but when the animal was paying attention. Attention isn't always easy to define, but as far as the behavioral evidence they had went, they found them. And they also found-- other people have found such things in the reticular formation.

I think the most direct evidence we have is still behavioral. There are recent studies going on that I'm involved in involving human imaging. And so I'm just going to describe to you quickly that. I've also mentioned before that this model we have certainly matches what we experience when we dream. We can generate an entire world. For those of you who have had hypnogogic imagery, you know how very realistic that image of the world can be.

The imaging studies that are most relevant here we call visual persistence phenomena. Let me just describe it to you. And while I'm starting to do that, I'm going to pass out some cards because I'm going to give you a little test-- survey, actually. It's not an exam. I just want to collect some information about you. Let me describe to you the kinds of things I see in my imaging abilities. So I'm one of the subjects of these experiments because I have this ability.

I'm looking at you here. Let's say I'm walking this way and I'm looking over there, and you're flowing past me. If I shut my eyes, I keep seeing you and you keep moving. You move in the predicted way. It's not a memory in the sense that it's what I just saw. It's what I'm about to see. If something's moving towards me and I close my eyes, the image I see of you with my eyes closed keeps getting bigger. It expands. It's a predicted image. It's also, of course, based on memory.

Now, in addition, I can pull up memory images, things I recently saw. I can look at you and close my eyes, and I remember particular ones of you. I could describe it in some detail. It's eidetic only for a very brief time. I'm not an eideticker in the usual sense. This is something that has not been studied very much.

And I want to find out if anybody in the class has something resembling this. So this is what I would like to do. Does everybody have the card? I have more here if you need them. First, watch me do it, and then you just try something similar. What I'm going to do, I'm going to take out my pen here, and I'm going to put a small letter on it, very distinct. I've put the letter A.

So do that. It doesn't have to be an A, but something that has a clear orientation. Don't put in O. Something with a clear up and down, at least different in the top and bottom. So that's why I use the A. Now, here's what I do. I hold it-- it works best if it's in a high contrast background. The chairs will do, or the blackboard would be good if I removed the screen.

Maybe I can give you a darker background there, the mountains of Southern China. Now, if you get-- what I want you to do is hold that someplace. Even the wall over there works well. And fixate it for a little while. Shut your eyes. Now, first of all, when you shut your eyes, can you still see the cart? Not just know that it's there, but actually see it? Don't have to tell me. I just want you to record.

Now, if you don't, try opening your eyes again and looking at it. Invigorate that image in your brain, and try it again. Now watch what I do. I'm going to do this. I'm going to look at that. I close my eyes. I see the cart. Now I'm going to rotate it 90 degrees. My eyes are still shut. What do you see when you do that?

Of course, if you don't see it at all, it's a little hard. [LAUGHS] And many of you won't see it. But if you do it a number of times, some of you might start seeing it. And then when you rotate it, do you see the card rotate? And what happens to the A? I'm not interested in-- I'm only interested in what you actually see and the phenomenon. So I want you to write on the back of the card what you actually see.

I can tell you what I see. I see the card rotate, but the A doesn't rotate. If I make the A really big, it will rotate, but the small A doesn't rotate. If I have a face on there, the little face of a person, same thing. I'll rotate it, but the face generally stays upright. Obviously, it's being handled differently in different parts of the brain, and I'm aware of the activity in different parts of the brain.

Why that is I can talk about in a minute. But what I want you to do is just write on the back of the card, "I saw nothing. You're crazy. Why are you putting us through this? I saw the blood vessels in my retina or I saw a vague looking rectangle that looked like a ghost, and I couldn't see the A." Or you might see the A, and then you describe what happens to it when you rotate the card.

There's dozens and dozens and dozens of experiments to do on this if you discover you have the phenomenon. Some people I find they think they don't have it, but when I encourage them enough and try various things with them, they start to see it. I actually think this is something we all have, but many of us are simply not aware of it.

I may have become aware of it because I have diabetes and I have to be aware of my internal states, my blood sugar levels. And I had to do that for many, many years without a tester. Now I have a tester. And I thought that was a really good theory until I found out that my daughter can do it too, and she doesn't have diabetes. So there may be a genetic component here. I don't know. My son also could do it when he was young, but he can't anymore. Now he says, "I see black. What are you talking about, Dad?" [LAUGHS]

But anyway, try that and write down on the back what you see. I will be very interested in knowing, and I will let the class know after I go through these. The phenomenon with the static images is what we originally called visual persistence, because people that have a positive after image. It's not retinal. It's very easy to show that it's not retinal. It's generated somewhere in the brain. And in fact, there's evidence that it's generated in many different areas because I can be aware of different kinds of images.

And I can talk a little more about this if you're interested, but right now I just want to know what you actually see, if anything. You want to help me collect them? Oh, could you put your name, if you don't mind? Because if you have it or something interesting, I will talk to you further about it. Otherwise, if you don't, I'll have to quote the card and find you. That'll be hard. So it'd be useful to me if I had your name also.

I can tell you we have surveyed classes before, and we've not been very successful at finding people that have these imaging abilities. I, by the way, grew up as a child thinking everyone could do this. It came as a great shock to me to discover that most people cannot.

We have also discovered that people that take a morphine-like-- a morphine drug for killing pain seems to have this ability sensitized, at least in the case-- we only have a few people so far, but it seems to enhance the awareness of these positive short-term visual memories, at least the memory part of it. I discovered-- I became convinced about the predictive nature of it when I went to a performance of the Boston Ballet, watched the dancers, very high-contrast with the spotlight on them with a dark background.

I could shut my eyes, and I would see the movements continue. If they were running across the stage, I could see them continue, and this could be repeated dozens of times. If I would open my eyes, I would find out that they weren't always where I thought they were because I couldn't predict perfectly what the dance would be. Thank you very much. I will let you know what turns out of that.

Well, we're going to leave that model there. In fact, there's little bits and pieces of evidence from now recording studies that do indicate other evidence for this kind of model. What we would like to do-- we only have three subjects in the Boston area and one out in Amherst now. But we'd like to find more people that have it, and we'd like to do some magneto encephalography.

That does not involve a magnet, just high amplification of magnetic waves from the brain. It's like EEG. But we have a good MEG machine at MIT, so I'll be working with [INAUDIBLE] And I may be doing also some work with Chris Moore, because if someone puts an object in my hand so I get the somatosensory image, I immediately see something. I see what I'm touching. That would be another test, but I wanted to limit the survey today to just the first part.

Visual system. We have time to get started with this. I'm going to tell you, first, about ablation studies. I will not get finished with this today, but I will take it up again after I return. We'll do a little bit of neuroanatomy, not too much. Review some simple phylogenetic comparisons. And then I'm going to talk today about residual vision after the primary visual cortex that receives the projections from the lateral geniculate body in the thalamus is ablated, completely wiped out. And then, later, I'll get to these other topics, but not today.

This is a [INAUDIBLE] diagram that shows the retina here, the representation of a retinal neuron, like retinal ganglion cell, with axons that project. This represents a group of axons. And it projects to multiple structures. Here I've outlined it. The main optic tract goes to the two geniculate bodies with branches that go into the geniculate bodies ending in little columns of termination. And then it goes to the pretactile area here in the superior colliculus.

Now, we call that the main object tract. In addition, there's little side branches we call the accessory optic tract that go to other structures. And before they get very far at all in the brain, there's a connection right at the base right above where many of the axons cross to the other side. That nucleus we already talked about, suprachiasmatic nucleus, often abbreviated SCM, but I abbreviated it SCH because CH is a common abbreviation for the chiasm. And I noted what the various structures are.

We're concerned with retina, lateral geniculate body initially. Later, we'll be talking about the superior colliculus. These are quantitatively the two largest structures that receive retinal projections. And then, the geniculate body projects to the visual cortex. Remember the diagrams we looked at once before. The midbrain. The projection to this structure at the roof of the midbrain.

If you do a cross-section, you cut like that through the middle of the midbrain in the rodent. You see the superficial layers of the colliculus standing out even with a simple cell or fiber stain. But if you do it experimentally, you can trace the retinal projections just to those superficial layers. The human has a corresponding structure at the roof of the midbrain, the superior colliculus, even though the colliculus is relatively much smaller in the human brain. In absolute terms, it's not. Other animals have a much larger superior colliculus. You see the superficial layer, how big they are. A much bigger representation of the retina than in the midbrain in animals like the tree shrew or the squirrel.

This is a textbook picture, and some of you have seen these. There's one like that in your textbook. Here, they've divided up the field. This is a visual field, color-coded for the area of binocular vision with the darker colors, and then the lighter colors here, the areas of the visual field you see only with the eye on that side if you're fixating the center right there.

And here, it's showing, if you're doing that, here's where it is in the retinas. So here it's going through the lens and being projected on the eyeball, the back of the eyeball. These are the eyeballs underneath the brain. And then it shows, color coded again, the axons from the two halves, right and left halves, of the retina, temporal and nasal haves, projecting in an organized fashion to the geniculate body, and some of them going on to the superior colliculus and the midbrain.

And then the geniculate body has an organized projection, the optic radiations we call that, the radiations going from the geniculate body, radiating through the internal capsule, and going up to the visual cortex at the very caudal end, the occipital area, of the neocortex. And here at the bottom they show-- if you were looking-- taking a medial view of the hemisphere where you would see that cortex. And they're just showing the topographic representation of the retinas there in the visual cortex.

So what they're doing then-- take our green pin here. This would be the optic radiations. Axons like that, going up to the visual cortex or area 17. You see they come out of the thalamus, through the internal capsule, which goes through the corpus striatum, and then up into the white matter of the cortex. And if they're coming from geniculate body, they're reaching-- almost all of them reach area 17.

And then other things happen. After that, there are some further projections. For example, cortex projects to other cortical regions. Those are called transcortical projections, of major importance in higher primates especially, basically the larger brain animals and the smarter animals. It's the one thing that's probably correlated with intelligence comparing across species the number of cortical-cortical connections in the brain.

So let's talk about the primary visual cortex. We knew a long time ago that people that have damage in the back of their head and it damages the cortex, the very caudal pole of the brain here, can experience a kind of blindness that they call cortical blindness. If they have damage to, let's say, just the right side of the striate cortex and not the left, they will have this blindness in the left half of the visual field. And it doesn't matter which eye they're looking with. They won't see things to the left of the fixation point.

They do have some residual vision. They have a sense of light and dark. They can tell differences in brightness. But according to all the early studies, they had no spatial vision. And it was studied formally by this man at University of Chicago, Heinrich Kluver in formal studies of the monkey using a visual discrimination testing apparatus.

And he would have them see two stimuli attached to strings, and they had to learn to pull one of them towards them in order to get their peanut or raisin. And he formalized this procedure and was able to get good visual discrimination performance in normal monkeys, but if they were missing striate cortex. He said that all spatial aspects of vision are abolished. They can't see even simple shapes and patterns. They can't tell if something's oriented vertically or horizontally, something as simple as that.

Rat studies were done by Karl Lashley, many of the early studies. He also claimed that the rats lost all patterned vision. They retained discrimination of light and dark. So basically, everything was in agreement. The human studies matched the monkey studies matched the rat studies, and people were quite happy with that. They weren't aware that there were some discrepancies.

I found them because I could read German, and when I was a graduate student here I found this study of rabbits, a study that was completely ignored. It was a study in the 1930s, rabbits with visual cortex ablation. Animals without the visual cortex, if you just show them food-- you're not making any noise. They're way out in a pen someplace. They would see the motion or see the food, and they would come running for it. And they would run accurately to the right place.

It was considered informal evidence. That was a time when there had been a reaction against any kind of clinical type data. You had to have formal, organized tests, quantitative measures, and so forth. So people stopped reading this kind of paper. I didn't. I found out that it's got to have some explanation what they're seeing. The rabbit obviously has spatial vision.

And maybe Kluver was wrong. I was a young graduate student, and I liked to think that maybe some people were just plane wrong. And I went ahead to prove that. And that led to-- could you wait a minute? We've got a little more time. So I then worked on a study of visual cortex ablation, and I also made superior colliculus ablation, using the hamster. And I was able to create a double dissociation.

Animals without the visual cortex indeed were like Lashley said. They couldn't do even something as simple as horizontal and vertical stripes. But they could turn and orient. They could localize things. Hamsters love sunflower seeds, and as soon as they see little motion of a sunflower seed, they will turn towards it. And within a week after a visual cortex lesion, these hamsters could do that. They recovered. That's spatial vision, to my mind.

I looked back in the literature and found only one cat study where they had made visual cortex ablation and had looked at various informal tests, and they also found some orienting. Was in fine print. Was ignored. I decided not to ignore it anymore, and I basically formalized a little bit that studied the tests of orienting.

And then I found that if I made colliculus lesions, I got an opposite type of thing. They couldn't orient at all they. Acted like they were totally blind when I showed them food. Tried to get them to find anything, they would wander around like they were blind. And yet in a formal testing situation, if they didn't have to orient to a door where the patterns were placed, they could actually tell the difference.

If I only required them to say yes or no to a pattern, they could do it. So the response I was using made a huge difference. And this is the way I interpret it. Here's the retina coming to the thalamus geniculate body, which goes to the cortex into the colliculus. And I said that these, through these intermediaries, go to different subsystems of motor control.

See, I came with physics training and an engineering background, and so I didn't think like a psychologist. And I had a big advantage there. I could see that, if you thought of just the connections and forgot about what this animal is conscious of, you could interpret it this way. Two different output control systems in the nervous system. And that led to a whole series of new studies on the monkey. And we'll start by talking about that when we come back. But Jordan, you wanted to-- where are you?