PROFESSOR: Last time, we were talking about endogenous activity as one of the determinants of pattern movement. We know very little about that, except a little bit from invertebrates. Except we do know about circadian rhythms, which is a more general regulator of movement.

And I've just summarized here the three major types of concepts that help us explain patterning in movement. But then there's a couple of things I've added here. Plasticity in these mechanisms-- we're learning about plasticity in synapses which will affect the first two here, but endogenous, CNS activity, especially when single cells generate it, they have these pacemaker proteins that are engaged in this constant cycle where they're changing membrane potential. There's just about nothing known about plasticity, and yet it would be critical if that were a mechanism for timing. And we know what a problem timing is in neuroscience. So I think that's a big deficiency in the field.

And I also point out here, my other plus here is neuromodulators that can alter the overall state of the brain can alter how these patterns are produced. And that concept is being used in studies of invertebrates. Again, my example here is Eve Marder at Brandeis, who studied invertebrates for many years, and the patterning of how they control pattern movements.

All right. The very last topic, which won't take us very long, is control of the overall state of the brain. I think the chapter is clear enough. You can read it, but I'll just review some major points. What controls it and how many states are possible. Nobody else tries to deal with how many states are possible, so I try it a little bit in this quote.

So we want to know the anatomy of these changes in overall state of the brain. And we mean drastic changes in state, like going to sleep or becoming aroused from sleep or from drowsiness, becoming hyper-attentive, become dominated by some particular feeling or other. Even if it's something simple like a feeling of hunger, it can really change the state of your brain.

And a lot of the states that we know, humans go through and animal probably do too, we don't know a lot about. We know some of the [? coralis, ?] because we can record electrical activity. That's what the electroencephalograph does. But it doesn't allow us to specify anywhere near the number of states that should be possible when we go through the anatomy.

So there's two very different types of mechanisms that could control a change in brain state. One of them you don't hear much about. And that's, if you look at the top here, the second one, chemical secretions into the cerebral spinal fluid, which can affect a lot of the brain.

The study I usually cite for this is a study that's often forgotten about. But if you have a sleeping rabbit and a wide awake rabbit and you have a cannula in the cerebrospinal fluid, if you take a little bit of the fluid out of the sleeping rabbit and inject that into the cerebral spinal fluid of the awake rabbit-- and of course you do the controls-- but anyway, the awake rabbit will go to sleep. Not studied very much, but I think the cerebral spinal fluid is a medium of conduction in the brain. It probably affects things other than the overall state, but at least we know that it is possible.

What we do know more about is the widely projecting axonal systems. You know, if we deal with very primitive animals like amphioxus is just one example. Many invertebrates, in fact, if you look at their dendrites and their axons, it looks like they're all very widely spread, or at least many of them. Brains like ours become more compartmentalized, more specific, more specialized. But to achieve integration and changes in state, we have specialized systems with widely branching axons. All right.

In this question, I ask you to describe four axonal systems. They're very widely projecting. What are those four that we usually think of? So cholinergic is the first. And we mentioned that when we were talking about brain stem. Remember, I showed those very widely branching axons of the hindbrain. Those are almost always cholinergic.

What's a word that tells you-- monoaminergic. And what are the monoamines?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Those are the two catecholamines-- dopamine and norepinephrine. Those are both monoamines. But catecholamines are a subset of monoamines. And what's the other monoamine? Serotonin, 5-hydroxytryptamine.

All right. And then, in more recent years, mainly due to discoveries at Harvard, like Cliff Saper, we know about other really widely branching systems. Now, when I was a student, we knew nothing about it.

All right. So this is that example we had earlier of the widely branching catecholamine using neuron of the reticular formation, the hindbrain. You can see how widespread its distribution is. There are a number of them like this.

Obviously, when they become active, they're affecting the state of the brain stem. And if you're affecting the thalamus here, these midline nuclei, their projecting tubes have axons that project to the specific nuclei that go to various cortical regions. So they're affecting the state of most of the central nervous system.

This is a cartoon of the catecholamine systems. The neuron and the brain stem is like this one. But there's a group of neurons at the base of the brain-- nucleus basalis of Meynert. And there are neurons outside of nucleus basalis that project like this too.

They don't include the acetylcholine containing axons in the striatum. Those are interneurons. They use acetylcholine. So all acetylcholine cells are not like this. But these are very widely projected. We usually hear about nucleus basalis in discussions of Alzheimer's disease because they tend to degenerate. And they project to the entire endbrain throughout the limbic system, throughout the neocortex. Here you see them going to the hippocampus.

All right. So this is from a medical school book where you see them in the human brain. That's a little bit of optic chiasm that sort of fell off in histology, so it should be up here. But this is where nucleus basalis is. This is anterior [INAUDIBLE], so you're in front of the thalamus. You're in that basal forebrain region, which we'll be talking more about in the second half of class.

This is all corpus striatum in here, where you find those acetylcholine interneurons. But the ones in the basal nucleus here, you can see, they just indicate their very widespread projections to the human hemisphere. And that's true of many other mammals as well.

So here are the monoamine systems, serotonin, norepinephrine and dopamine, the catecholamines. The first two, serotonin and norepinephrine we know play major roles in the control of sleep and waking, and more generally in arousal states. The serotonin axons, which are very widely projecting, begin in these midline nuclei, the nuclei of the raphe in the brain stem-- midbrain and hindbrain. You already find those kinds of axons in amphioxus, so they're throughout all of the chordate kingdom.

And we know they're important in humans at least in mood stabilization. We give re-uptake inhibitors like Prozac that affect human mood control and prevent the wide swings in mood. They also occasionally cause people to commit suicide. But if I'm giving an announcement on TV, I've got to say that. This can cause death, this can cause this, that-- I would never take any of those when I hear those commercials.

And then the catecholamines, like norepinephrine, we know it's also very important in arousal states. And we know it does play specific roles in switching from one state, sleep, to another. And dopamine has more specific effects. It has somewhat more limited distribution-- not as limited as we used to think. But we know it's very important in reward and reinforcement types of learning.

So this is a typical medical school illustration of these widely projecting axons. It basically shows you in sort of a cartoon form, where the cells are. These are right on the monoamine in the brain stem. So this is that huge pons. You can see, these are mostly in the hindbrain.

And it shows them-- I think this is a later one from Lennart Heimer's books. You can see, it projects down to the spinal cord, projects to the cerebellum, projects to the thalamus, projects everywhere-- very widely projecting, and that's really all you can get out of these.

But there is a little more specific knowledge about the serotonin axons if you look at the raphe nuclei here in the caudal midbrain. You'll see that there's a dorsal and a more ventral raphe nucleus. And they give rise to somewhat different axons. They look different. This is called a thin varicose axon system. And here's a very different kind of axon system. They called it basket axons. They've got thicker branches and different, larger endings.

And if you look at a place like hippocampus or striatum, you see those two structures get only one of those two types. See, the basket axons are going into the dentate gyrus. The striatum is getting the thin varicose axons. But they're both going into the neocortex. And we don't know nearly enough about separate functions of those two types of axon for the serotonin system.

And now here's a picture of the norepinephrine. These are amazing cells that you find in this area here called the locus coeruleus, named because of the blue pigment there. In rats, there's literally just a few hundred cells, and it projects everywhere. And they're very thin axons.

And the cells aren't all that big, and yet they project more widely than any type of cell in the brain. There is a group in the lateral tegmentum of the hindbrain that also projects, but less widely. It's these locus coeruleus cells that project to the entire forebrain.

And it's interesting, because if you give a toxin for the norepinephrine axons, just by giving this early in life, you can destroy all these axons going into the endbrain. And when you do that, you don't kill the cells. Instead, they compensate by increasing their projection at the brain stem. So the whole brain stem gets super-dense norepinephrine innervation. It's a kind of pruning effect of the sort that we've seen in the [INAUDIBLE] system.

All right. And this shows the noradrenaline system in the rat. And the one I put in the book is this one. It's exactly that figure, except I took out a lot, for the simple reason that some of these are just mistakes. They're drawn anatomically incorrect.

I have the advantage of being a neuroanatomist, and I notice these things when I read these summary figures that people mess up a bit. But what I am showing here is that even in the brain stem, even though the norepinephrine may be a little less in the spinal cord, cerebellum, and midbrain, it's still there. It's densest in the endbrain.

All right. And then here's the dopamine system. Here's an earlier figure, and here's a later figure. This earlier figure is what you see in most medical books. It shows that in the neocortex, it's prefrontal. And then it also goes into limbic structures.

So you see it going into hippocampus septum, amygdala, and they show it originating in these two structures we've talked about in the midbrain. We've mainly so far talked about the ventral tegmental area. And we defined the limbic midbrain areas. It's the area that's closely connected to the forebrain limbic system structures.

But then more recent as these techniques have become more sensitive, they discovered, well, there is a lighter projection that goes all the way back, including into the hippocampus, including into the visual areas of the cortex, that does use dopamine. And there's even some going into the midbrain.

There's been a little debate about that. I show it coming here from-- this is my figure, which was a modification of a summary figure by people that had studied the system earlier and had this kind of pattern. It could be these other groups here give rise to the midbrain, dopamine, and we still don't know a lot about the functions of that in all these structures. Notice that there are dopamine cells in the olfactory bulb as well.

All right. Well, it turns out, those four systems are not the only systems, as I mentioned. We already knew that in the thalamus, the older parts of the thalamus, there are cell groups with very widespread projection. There's one located right on the midline that was studied here at MIT in Nauta's lab by Miles Herkenham, who's worked for many years at NIH.

He found that this little cell group projects to the entire neocortex, but just way up in layer one. So it's only getting to the dendrites of the neurons all over the neocortex. That's this one. But since then, and I mentioned Cliff Saper at Harvard, discovered a number of cell groups that also project very widely. Not quite as widely, perhaps, as the norepinephrine, serotonin. One of them uses melanin concentrating hormone.

Another uses the peptides hypocretin and orexin. They were well known because defects in the gene for those substances that are used as neurotransmitters in the system leads to forms of narcolepsy. And some of those connections are still not fully understood.

There's another system that uses corticotropin releasing hormone, a hormone that's found, for example, a lot in the amygdala. And it was initially known just from anorexia states, but now we know it is more widespread.

This is one picture from those studies. In this particular picture, they show on the right in blue the distribution of norepinephrine. Remember, I used blue for norepinephrine in that rat picture before. And here you see it distributed all over the neocortex, all over the limbic cortex down here, and in the hippocampus, throughout the thalamus and hypothalamus.

But in red, on the left, they show these orexin hypocretin cells. And their axons are distributed very widely. They're most concentrated in the hypothalamus and parts of the amygdala. But then, in a more scattered way, you find them throughout most of the rest of the hemisphere. So it's another widely branching system.

So that leads me, then, to that final topic, well, how many brain states are possible? So what I did for this is just make some simplifying assumptions. I say, let's just take four of these systems of the brain stem, and let's say that they just have three possible states-- no activity, low activity, high activity. And then we add to that four of these diencephalic state-changing systems and make the same assumption, they have three possible states.

So that gives you eight systems. Now, if we assume they can operate independently, and there are actually some interconnections between them. But if we assume they can operate largely independently, then the number of possible states would be three to the eighth, 6,561 states.

And if you just assume that it could have four possible states, it goes up to 65,536 states. So that's what I mean when we say that-- and these are very easy assumptions to make, because studies of the activities of interneurons indicate that they might have many more possible states than the few I'm assuming here.

Just remember these states are largely independent of sensory motor cognitive activity. They certainly interact with the emotional activities, motivational states, but they appear to operate pretty independent of those as well.

All right. This is just a little about the evolution where amphioxus is missing norepinephrine. It has dopamine and serotonin. Hagfish and lamprey, still very primitive vertebrates, have all of those systems. They may not have all of the others I mentioned.

All right. We've already said what we need to say about those things. So I'll go on to what you guys are most interested in here. This is what I did. Now, first of all, you had that homework three, where I gave you the worksheets and I told you to do this stuff. Any of that's fair game for the exam. If you did it, you're already prepared there.

And then I selected questions on the book chapters. So for chapters one and two, I only took seven. Chapters three and four, just again, a small group of questions. In fact, that goes beyond three and four. That's five to seven. So three and four, again, there's only five questions.

So I'm reducing the number of questions a lot. And I've divided it according to the book chapters. These aren't classes, because they don't always match completely. So I used book chapters here to get these questions. So it still comes out to quite a few questions. There are 74 questions.

And then I listed some names. Are there any names here you cannot remember? Remember Fritsch and Hitzig were? That might be a more difficult one. Those are the guys that mapped the motor cortex for the first time. They did it in dogs and humans during the Franco-Prussian War.

They found this one area with the lowest thresholds, the smallest currents they could still elicit movement. And they defined that as the motor cortex. I left Betz out, the guy that discovered the giant cells there. You should certainly remember who Ramon y Cajal was and that he used the Golgi stain. He was a very comprehensive neuroanatomist. He studied the entire central nervous system and some of the peripheral nervous system as well. His brother, Pedro Ramon, was more of a comparative anatomist. Whereas Ramon y Cajal studied mammals.

Sherrington-- what did Sherrington do? He was a physiologist. He worked out the properties of synapses before we could see synapses with the electron microscope. He knew about inhibitory and excitatory synapses. He knew about thresholds. He understood how neurons work.

In fact, his article on the spinal cord, he studied mainly spinal animals, spinal [? calves ?] largely-- that is, an animal with a spinal cord transected, and he artificially respirated them for a lot of his studies. He wrote the article in *Encyclopedia Britannica* on the spinal cord, and I believe a modified version of it is still used in the *Encyclopedia Britannica*, that's how good it was. Even though this guy worked-- he was working at the previous turn of the century, early 1900s.

And Otto Loewi, discoverer of chemical transformation. He studied the heart, remember? His famous experiments on the accelerator and decelerator nerves of the heart.

Hans Spemann, he's credited with the discovery of induction of the nervous system by a specific tissue that turns out to be the notochord. And now we even know the molecule. You remember the molecule? Sonic the Hedgehog. I don't think I put that here. I don't think I did.

But Rexed may be the most difficult one. That was the guy who gave the layers to the spinal cord. He changed the way we talk about the anatomy of the spinal cord, the way we use his numbers all the time. Ross Harrison, first used tissue culture. He was one of the first guys to see living growth cones. We First saw those in tissue culture.

Karl Lashley is actually better known as the pioneer in physiological psychology, or brain and behavior studies, that are experimental in nature. There were of course many clinical neurologists before Lashley. But he took the methods of experimental psychology, controlled experiments, and applied it to studies of brain and behavior.

And he was the one who wrote about-- I mention him twice, actually three times in the class. If you want to find it, most of you can probably search that text, right, and find his name. But the last time he was mentioned, it was because he wrote that famous paper, "The Problem of Serial Order in Behavior," proving that rapid learned movements of humans had to be centrally programmed. So when we over-learn something, we basically are programming our brain that can produce a movement without needing any feedback or anything.

He also studied the optic tract projections using a stain for degenerating myelin. Remember what that was? Nauta used silver stains-- much more sensitive. It was Markey, the Markey method. Anyway, Lashley used that and did a pretty accurate job. He didn't discover the projection of the hypothalamus, and other very tiny projections of the optic tract. But he knew the main ones, just from that experimental study.

You remember who Nauta was-- discovered the silver stains used for the staining degeneration. And then two more-- Levi-Montalcini and Hans Kuypers. Levi-Montalcini discovered what? She did it with Viktor Hamburger. They discovered nerve growth factor. The first of a family of molecules we call the neurotrophins, the most well-known growth factors in the nervous systems.

There are other families as well that are not neurotrophins that have been discovered since, but when you just say nerve growth factor, you always mean that first one that Levi-Montalcini and Viktor Hamburger described. If you just remember her name, that's fine. She died just recently, at age over 100. And then Hans Kuypers who, with his student Lawrence, are well known for their studies of descending pathways, both their anatomy and their function in primates and monkeys.

OK. Now, this is the last thing I did. These are just definitions that you should go down through this list and see if you remember all these different words. Most of them you probably will know. You should be able to find all of those.

So that's it. Are there any parts of the class now that you particularly want to go over? I can go over any of these. We've already gone over the answers to all these questions in the class, so you can find them by searching your class notes. Remember, one was the general introduction, a little bit about glia and method.

I asked the major difference between the tract tracing methods of Markey and Nauta, Nauta being more sensitive it didn't depend on getting myelinated axons. He did the un-myelinated ones also. And it was much more sensitive, but not as sensitive as some of the more recent methods.

What are those more recent methods? Methods that use axonal transport in various ways, where you use the transport mechanism of the axon to inject something that's still in transport. It could be a fluorescent molecule. A lot of them used are fluorescent molecules.

They're very easy to use. You don't have to use any histochemical technique. You just inject them. They're transported on the axon. And then you just need a good method of fixing and cutting the brain, and then looking with a good fluorescent, a very sensitive fluorescent microscope and look for the fluorescence. Do any of you remember what diffusion tensor imaging is?

AUDIENCE: [INAUDIBLE].

PROFESSOR: It uses magnetic resonance imaging, and the computer's programmed to pay attention to diffusion of water molecules. That's right. And water molecules, when it comes to these big bundles of axons in the brain, tends to move down the axon, not across. And they use that to follow bundles of axons.

And unfortunately, the cognitive psychologists now think they're studying connections in the brain. They think we don't need animal work anymore. We can study connections in the human brain. I hope you realize how silly that is, because it's not even as sensitive as the Markey technique, where it doesn't get connections at all. But it does give you the position of the big bundles of axons in the human brain, or any brain that you use diffusion tensor imaging to study.

And that's important, because now we can specifically relate those major pathways in human to the studies done in monkey and other animals, especially the primates, because humans are of course one of the primates. So that's what diffusion tensor imaging is. I asked for its advantages and its limitations. Its advantage is you don't have to kill the animal-- big advantage. And you can trace major bundles of axons.

Disadvantages-- resolution, you cannot get down to the single cell level at all, and you cannot trace axons all the way to connections. But when you see them coming-- and you don't even know which direction they're going, major limitation. But if you see axons coming in and out of a gyrus in the brain, you can be pretty sure they're either starting there or ending there, because they wouldn't go up into the gyrus and then go out again. It wouldn't make a lot of sense for them to evolve that way.

All right. Some of these are just definitions, like primary sensory neurons and motor neurons, immediate network neurons. So you remember the midbrain structure that's greatly enlarged in predatory [INAUDIBLE] fish? They're depending a lot on vision for their hunting, and they don't depend a lot on learning. So it's the optic tectum. Unlearned, visually triggered fixed action patters, used in tectum more than any other structure. So they orient towards prey animals, and those neurons are specifically triggered by the types of movement that prey animals make.

The frog, another animal-- it's a predator, it collects insects and worms. He's got a tectum similarly programmed to respond to worms and bugs. If it's a bug moving around like that, the tectal neurons are buzzing away just like the-- but the frog just sits there and fixates. But if that bug stops and he's within range, then the frog attacks with the flick of his tongue and grabs the insect, all controlled from the tectum.

What was the major cause of the first three major expansions of the forebrain in evolution? That's number one-- started as an olfactory structure, see it growing out there at the very front of the brain. And the early cortex was all olfactory. In most primitive animals, the olfactory bulb connects to everything in the forebrain.

OK. Then, what was a later reason that it expanded more? Sorry?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Other senses invaded the forebrain. How did they do that? Mainly projections from places like the midbrain tectum, which was very large already. Any large structure projects all over the place, and it projected right into the [? tweenbrain, ?] and the [? tweenbrain ?] connects to the endbrain structures, both striatum and cortical.

And by invading the striatum, it took advantage of the kinds of learning that the striatum had already developed for factory guided behavior. That's the speculation. It is very likely to be true. We know that habits in mammals still depend on those pathways through the striatum, except that the inputs to the striatum in advanced mammals becomes more from the cortex. It doesn't come from the thalamus. But still, even we have those connections from the older parts of the thalamus, right into the striatum.

All right. And then, the third expansion. I can't hear you.

AUDIENCE: [INAUDIBLE].

PROFESSOR: Exactly, with mammals. The neocortex evolved out of the dorsal cortex, which was initially-- if you look at the dorsal cortex in reptiles, for example, it's a parahippocampal area. And the parahippocampal areas do, in those animals, get some other sensory inputs. But the big change was new layers, new types of migration into the hemisphere. That led to neocortex, which as we know, have a lot of advantages for functioning. It expanded a lot.

So those were the three major expansions. It didn't lead to the gigantic nature of the human brain. Well, it did eventually, but there were later expansions that occurred as well. There was a late expansion of the association areas, for example, that led to things like language and other things that we do with our cortex.

Remember the name cynodont? You remember. The mammal-like reptiles, right. And I used early cynodonts because the late cynodonts are much more like mammalian brains. So I wanted something that was more like an amphibian brain, and the early cynodonts were like that. But the evolution of those animals is what led to mammals.

So what expanded when neocortex expands? Animals with really big neocortex, they have other big things too. Cerebellum is one. What projects to the neocortex? The thalamus. So the thalamus gets big too. If cerebellum gets big, what else gets big? The pons-- gets input from the neocortex and projects to the cerebellar cortex.

OK. So you could say any of those things. Cerebellum, pons, thalamus, they all get bigger as the neocortex gets bigger. And if you said something like cerebral peduncle in the midbrain, that would actually be true too. They're the axons coming from neocortex going down to the brain stem, the hindbrain and the spinal cord.

So you know why the face is not part of the dermatome maps? Because the dermatomes are areas of the body surface innervated by what?

AUDIENCE: [INAUDIBLE].

PROFESSOR: Yes. And by what going into the spinal cord. Spinal nerves, the dorsal root of the spinal nerve. So for every pair of dorsal root, you have a dermatome, one on either side, actually. But it doesn't include the face, because that is innervated by trigeminal nerve, fifth cranial nerve, exactly.

And remember that peculiarity when we're talking about dorsal column nuclei. I showed the section through the dorsal column nuclei, and I said, the whole body surface is represented there. Nucleus gracilis, the lowest part of the body. Nucleus cuneatus, the upper part of the body, but not the face.

So how is the face representative? Descending nucleus of the trigeminal nerve. The brain stem trigeminal complex, secondary sensory cells of the trigeminal system, has a descending nucleus that goes all the way into the upper part of the spinal cord, and that's where the face is represented. And if we have pain in the face, it's that part in the upper part of the spinal cord that's being activated.

So what's the oldest descending somatosensory pathway? Spinoreticular. In medical school, you'll learn it's the spinothalamic, because they ignore-- not all medical school. Some of them talk about spinoreticular also.

Remember the raccoon and the coatimundi? There's a figure there. What is the raccoon good at? Manual dexterity. He can get in your garbage cans. The coatimundi can't do that. So what is different about the somatosensory cortex? The representation of the digits of his forelimbs, much bigger in the raccoon-- so big that there's a separate gyrus for every digit. The coatimundi's just got a much smaller little area there, because the surface area of cortex corresponds basically to dexterity. The same is true in the motor system, their motor acuity. You can talk about motor acuity as well as sensory acuity.

I ask you actually to know those four basic cellular events that Wolpert talks about, because they're all important in manning developmental processes. Remember what they were? Adhesion, contraction, growth, movement. They interact, of course. And you can apply them to the growth cone and explain how axons grow. Except you also have to know about membrane addition.

Remember the two types of cell division, symmetric and asymmetric. Symmetric, they both stay in stem cells. In asymmetric, one of them migrates away. The other one keeps dividing. Lateral horn, you talk about dorsal horn, ventral horn, the spinal cord. There's that little bump on the side.

Where's the little bump? Thoracic and upper lumbar. Thoracicolumbar or thoracolumbar system, it's the sympathetic nervous system. They're the preganglionic motor neurons of the sympathetic nervous system. Why are they called motor neurons? Because the axons leave the cord. Well, where's the ganglionic motor neuron? It comes from the sympathetic ganglia, which are all along the side of the cord, all the way from the neck, all the way down to the small of your back.

Plus, a few ganglia that sit out in front, the pre-vertebral, like the celiac ganglia, more commonly or popularly known as the solar plexus, because it's a popular place for a boxer to hit another guy, in the solar plexus, so he doubles over and loses control of his guts. Sorry, but I've got to use some graphic language here to get you to remember that.

But OK. If you have trouble and cannot find answers to some of these things, use the forum. Because if you don't, I won't answer, because I want everybody to get the same information. But you should be able to find answers to all of these, either in your notes for the class or right in the book. So I hope that's helpful to you, help you getting ready for this. Now you don't have all this uncertainty, I don't know what's going to be on this exam. You do know what's going to be on the exam-- this stuff.

AUDIENCE: [INAUDIBLE].

PROFESSOR: I won't tell you how it's going to be written. I might change-- for example, just with these definitions or some of these answers, I could put matching questions. But if you know these, you'll certainly be able to answer those.

All right. That's the fairest way I know to get you guys ready. And I wish you all well. We're not going to meet on Friday, because I know you are in a hurry to get out of here. But I will want you to read the chapters on the chemical senses, taste and olfaction. I think it's pretty straightforward in the book. I will answer any questions you have if you have any about them, so that way we can get started with the visual system when you come back.