Good morning. Thank you. So, I want to continue today on the theme of neurobiology. Last time we spoke about the action potential mechanism. Today I'd like to go from action potential to the synapse. But let me briefly remind us what we say. So, I'm going to give section zero a recap here.

The relevant things that we said last time was there's a membrane potential which at rest is about minus 70 millivolts as the membrane potential, and that's what we work with. That membrane potential is set up by concentration gradients. More calcium, more potassium on the inside. More sodium on the outside. More calcium on the outside. And I'm also going to mention chloride, there's more chloride on the outside at 116 millimolar, four millimolar on the outside.

These concentration gradients are set up by various different pumps.

They're there all the time. Then we have this resting channel.

So, here we have transporters.

We have a resting potassium channel. It means that it's open all the time. It's not activated by anything.

That allows potassium to leave. Potassium leaves until it builds up this membrane potential about minus 70. At that point it is electrically unfavorable for more positive charges to go out into the more positive environment. Notwithstanding the greater internal concentration. And we reach an equilibrium potential of minus 70. We then have some voltage-gated channels.

And the voltage-gated channels come in two flavors here.

We have the voltage-gated sodium channel. The voltage-gated sodium channel opens itself up around minus 70. Oh, sorry, around minus 50. So, if you can get up to minus 50 it opens up. Then your sodium rushes in. It shifts the membrane potential from minus 50 to zero to plus 50.

The channel shuts. Somewhere around plus 30 or so opens the potassium channel, the voltage graded potassium channel, and allows the potassium to rush out and restore the resting potential.

The effect of this is that, if this is zero here, we have a resting potential. If we climb up a little bit above it we shoot up and then we come back down. And then a millisecond or so later another action potential could go down that same neuron.

And, last of all, if we look along the length of an axon, an action potential here causes charges to migrate over which launches an action potential here which causes charges to migrate over which etc., etc. propagates an action potential down the length. It's a beautiful system.

And then the very last thing was that by insulating this we were able to make the conduction velocity go faster by effectively making the effective length be shorter there being a whole bunch of electrically insulated regions. So, that's it. It's a beautiful piece of engineering. How do we know any of this is true?

As an interesting side point, I might just mention that when this was worked out, this was worked out by two folks called Hodgkin and Huxley.

Hodgkin and Huxley won a Nobel prize for this beautiful work on this squid giant axon which is the fastest axon that there is.

And here we're not talking about the giant squid somebody raised last time. It's an ordinary squid. It has one big fat axon. It's sufficiently big that you can just like stick a wire in the middle of it and all that. It's a very big axon.

It's a very, very high diameter axon.

And they were able to measure these things electrically.

And on the basis of the electrical measurements they made in different kinds of solutions, they were able to infer the existence of sodium channels and potassium channels.

But this all happened mid 20th century. And they certainly couldn't see any. They couldn't clone them.

They couldn't see anything. And so the notion that there were individual molecular channels that swung open, did all this stuff was an indirect inference, maybe kind of a little bit like Mendel's inference of a gene or Sturtevant's inference of genetic maps. But more recently people have come along with an extraordinary technology, also these people won a Nobel prize for this because it was way cool, which is called the Patch Clamp. The patch clamp is the following ridiculously simple technology. Suppose I were to make a glass pipette.

So, this is a cross-section of a glass pipette.

So, it goes around like that. And I could bring it up really tight up against the membrane. And suppose I did it in such a way that I could get a really great seal and I just have a teeny patch of membrane. Suppose that teeny patch of membrane had just one channel in it. And now, so this is a pipette, suppose I were to rip off that patch of membrane from the cell, poor cell, and have a glass pipette with a little patch of membrane on its end with a single isolated ion channel. Now, if I measured the current through this channel by putting it in an appropriate solution, maybe I ripped off a resting potassium channel, OK? If I put this in a potassium solution and I apply a current, I apply a voltage difference, I should be able to see a current. And you can actually measure a current. Even more cool, if I do this and I've ripped off a voltage-gated sodium channel, then it turns out that I ought to be able to

study its properties by changing the voltage on it and measuring the current as a function of the voltage.

And, well, it turns out that if I do this I'm able to measure in resting or in these voltage-gated channels current flows conductivities, actually, what I'm really measuring is the conductivity of the channel like this, I can see the channel opening and closing and opening and closing quantily. I can measure quantily the conductivity. That's not quantum mechanics. It's just quanta measurements of the conductivity. What would happen if I had two channels that had been ripped off? Now I'd see it go like this.

Well, maybe another one opens. Oops, now one closes. Now the other one closes. And quite remarkably you can get this. So, you can study single molecule, single molecular channels.

You want to know how this channel opens and at what voltage it opens?

Just dial in the voltage and see if it's open. Do you want to know how long it stays open? Just turn it on and see how long it stays open. It's really cool. You want to see if any other chemicals could affect it, any ions, any other intracellular or extra cellular chemicals? You can do it.

So, the ability to study isolated single channels came along with patch clamping. And what it allows is a tremendous study of the biophysics of individual channels.

And, whereas, before people had to look at the total conductivity of an entire axon. Now they're able, and from that infer the behavior of single channels, now what they can do is study the behavior of single channels and synthetically build up a picture of the total conductivity of an axon from its individual components and see if the components we've identified are sufficient to explain the behavior that we see. Anyway, that's patch clamping.

Lots of fun. So, now, what I want to turn now to is signaling at the synapse.

So, we have our cell body here. It's got its dendrites on it.

Here's our axon. We've managed to get an action potential started on it and it moves all the way down.

Now we get here to one of the synaptic terminals.

The electrical signal makes it all the way to the synaptic terminal, but how does it affect the post-synaptic cell?

Well, let's get a close-up of that.

Here we go. Here's the synaptic terminal. We've got our action potential coming. Action potential coming.

And then it gets here. Action potential's arrived.

I would like to release chemicals into the synaptic cleft, the space between the pre and the post-synaptic cell.

I'd like to spill out chemicals that are neurotransmitters.

So, the pre-synaptic cell conveniently has vesicles, little membrane-bound vesicles with prepackaged neurotransmitters.

OK? These prepackaged neurotransmitters have been conveniently synthesized by the cell and they're just sitting there waiting to be released in response to an action potential.

When the action potential comes, it causes these synaptic vesicles to fuse -- -- with the membrane. And in fusing the insides become continuous with the outsides, here's a little fusion picture here, and the neurotransmitters leak out. OK?

How does it do that, though, mechanistically?

How in the world does an action potential cause these vesicles to fuse with the membrane? Well, somehow it's got to read out electrical activity into some kind of a chemical activity intracellularly. Here's what it does.

When the electrical signal comes down, remember originally the membrane potential is negative, but when an action potential comes by what does it do to the membrane potential? It reverses it.

It makes it positive inside briefly. OK? So, this is the sign of an action potential, an AP coming down.

In this membrane we have us another voltage-sensitive channel.

This voltage sensitive channel is a voltage sensitive calcium channel.

OK? Who would like to design a voltage-sensitive calcium channel?

What should it do? What would you like to have its opening and closing properties be? When does it open?

At a positive charge. So, when you get to a positive membrane potential it swings open. And then what does it do?

Lets calcium move. Which way does calcium want to go?

In because it's more out. So, what's going to happen is in response to the action potential calcium will rush in.

Now, calcium, you will recall, was in vanishingly small traces inside, 0.1 micromolar we said. And influx of calcium is a very serious matter and it is sensed by variety of proteins.

In particular, there is, floating around in the cell, a protein here called a calcium-dependent protein kinase.

The calcium-dependent protein kinase is a protein that is capable of putting a phosphate group.

Its kinase puts a phosphate group on other proteins.

So, the calcium-dependent protein kinase over here will go along and catalyze the addition of a phosphate group to other proteins.

So, it will enzymaticly catalyze this. But it only does so in the presence of calcium. So, when there's calcium in the cell, the calcium-dependent kinase is activated and it runs around and sticks phosphate groups on specific target proteins.

You know where one of those target proteins lives? In the vesicles.

The vesicles happen to be a target for this. So, the vesicles have a protein on them. And in one of these extraordinary coincidences in molecular biology, the protein on the synaptic vesicle happens to be called, coincidently, synapsin.

OK? It's not actually entirely a coincidence that it's called synapsin. It was named synapsin because it was found on the synaptic vesicles, obviously. And so what happens is when the action potential comes down it causes the calcium channel to open in response to positive voltage. Calcium comes in, actives at the kinase. The kinase phosphorilates synapsin.

And now the phosphorilated form of synapsin likes to bind to something in the membrane. That's it. How many of you still know what a Rube Goldberg machine is? Good. OK. This is one of these just great, well, others of you should look it up on the Web because they're just great cartoons, the Rube Goldberg cartoons about the machine where the rooster crows startling the cat which tugs the thing with causes this to flop which causes the eggs to go in the pan which causes the thing to cook which causes whatever.

And I always think about these in terms of great molecular Rube Goldberg machines. So, this is the Rube Goldberg machine that gets this synaptic vesicle to fuse there.

OK? Good. Every bit of neurobiology has a molecular mechanism to be explained like this. So, now let's go onto the next bit. How does this signal gets sensed at the next cell? What are we up to?

Number three. So, let's look at a specific junction.

Instead of looking at the junction between two nerve cells, let me start with the junction between a nerve cell and a

muscle cell, the neuromuscular junction. OK? So, I've now replaced my post-synaptic neuron by a muscle fiber here. This is a muscle fiber. So, when it spritzes out the stuff the neurons that innervate muscle fibers, actually, I'm going to expand that a bit, the neurons that innervate muscle fibers, here's the muscle, and I'll put it at some distance here, muscle, spray out a particular transmitter in response to the calcium influx. And that transmitter is called acetylcholine, henceforth ACH.

Acetylcholine is spritzed out into the synaptic cleft and comes out.

And what do you think acetylcholine is going to do?

I've got to send the chemical signal to the next cell.

I've got to somehow send that signal to the surface.

It's going to bind to something on the next cell.

You know the deal, right? So, it's going to have to bind to a protein on this cell. And, remarkably, what it binds to is called an acetylcholine receptor. OK? Very reasonable stuff. An acetylcholine receptor. The acetylcholine receptor happens to be an ion channel, but it's not a voltage-gated ion channel. It's not an ion channel that opens in response to the voltage. It's an ion channel that opens in response to acetylcholine.

It's what we'd call a ligand-gated ion channel because it's gated by a ligand, acetylcholine. So, this guy here is a ligand-gated ion channel which, when acetylcholine binds to it, swings open. And what it does is it allows in sodium.

Bingo. Now, when sodium comes in what happens? Action potential.

But what a second. This is a muscle.

All membranes have the machinery to have an action potential? Nah, liver cells are pretty passive.

You do this to a liver cell it kind of sits there.

But muscle cells do have an action potential mechanism.

They do respond here like a neuron, an action potential. And so what happens when I open up some sodium channels to the resting potential of my muscle? What was the resting potential of my muscle? About minus 70. What happens when I open up these ligand-gated sodium channels? Sodium rushes in. What does it do to my membrane potential? It makes it more positive.

What does that do? It triggers an action potential spreading throughout the muscle. And because the muscle has an action potential -- -- all you have to do is manage to get this going in a little patch of the muscle and it spreads throughout the muscle fiber.

One neuromuscular synapse will be sufficient to activate the muscle, in principle, because you have this action potential mechanism.

And then when the action potential fires in the muscle it actually causes other channels to open, including some calcium channels.

The calcium channels cause calcium to come in. The calcium causes your muscle to contract because of sliding of actins and myosins and things like that. That's how it works.

That's this Rube Goldberg machine. All right. So, let's get ready.

Let's fire. Let's send a neuromuscular signal down.

Contract. Now here's the problem. I've got all this acetylcholine sitting around in my synapse activating the ligand-gated sodium channel causing sodium to come in, but I would like to relax my muscle, please. What are we going to do about this?

I could trigger another channel, and maybe it could be a delayed acetylcholine activated yeah, dah, dah, dah, dah, dah, dah, that's possible. I could have it close itself. These are all perfectly reasonable possibilities, and we're going to refer them to the engineering committee.

What else? You could get rid of the acetylcholine some other way.

It turns out the latter is the solution here.

We would like to have some enzyme that chews up the acetylcholine.

How about acetylcholinesterase? So, let's put acetylcholinesterase, ACHE, acetylcholinesterase in the synaptic cleft.

Then when I spritz acetylcholine it gets to the other side, but very rapidly the acetylcholinesterase is degrading it.

And so it has a very short time of persistence in the synaptic cleft. OK? That works. So, that's how I run a neuromuscular junction. OK?

So, acetylcholinesterase is very important. Now, again, as with many of the things I've talked about, we really

know these things are true when we're able to inhibit them in different ways. So, I want to take a moment and talk about drugs and toxins. Because they help us to probe these different processes. Anybody ever have fugu?

Does anybody know what fugu is? What's fugu? It's a blowfish.

Right. It's a puffer fish eaten in sushi, and it's an extraordinary delicacy. And why is that? Right. Because it's one of the only sushis where you really have to worry about improper preparation, not just giving you food poisoning or a stomachache or something like that, but it's lethal prepared incorrectly. The reason it's lethal incorrectly prepared is because the blowfish has a specific poison called tetrodotoxin. So, if you eat sushi, so, in fact, chefs in Japan require a license to prepare fugu for customers. Every once, every couple of years some famous actor or personality prepares his or her own fugu and dies from it and it's in the papers. Seriously. This has happened to people. They're able to do this. Anyway, tetrodotoxin, tetrodotoxin is from puffer fish, fugu. Why does this stuff kill you?

It turns out that what tetrodotoxin does, this wonderful poison from this sushi, is that it irreversibly binds, irreversible binding and inhibition of voltage-gated sodium channels.

Why would this be an inadvisable thing to have?

Suppose you irreversibly bound to and inhibited your sodium channels, your voltage-gated sodium channels, what would you be unable to accomplish? An action potential.

This is ill-advised to be unable to accomplish an action potential.

You can imagine that what it leads to then is a paralysis and a very serious one, and if it's irreversible this is not a good thing. There are other things. Has anyone ever fired poison darts in South American jungles? [LAUGHTER] Well, if you have, you would have tipped them with qurare. Qurare is used to make poison darts. What qurare does is it reversibly binds, still not good, but it's a reversible binder to the acetylcholine receptor and it prevents it, it blocks the binding of acetylcholine.

Your acetylcholine receptors, therefore, cannot respond to your acetylcholine. What will that do?

A flaccid paralysis because you're unable to move your muscles.

So, if you were trying to shoot prey in the forest and you send the poison dart that has qurare, it will cause the animal to then flop over. Yes? Snakes. Ooh, what kind of snakes? Venomous steak snakes, yeah. [LAUGHTER] Like bungarus snakes, the really poisonous ones.

So, it turns out, great question, that they make something called alpha-bungerotoxin. Venomous snakes, next

thing on my list, exactly. The only improvement they make here is that this is an irreversible binder to the acetylcholine receptors. Very impressive stuff. Different stuff. We'll come back to jellyfish. But, basically, everything you know out there that's noxious is being noxious in some way that affects molecular biology. Not all of it affects the nervous system. Those of you who like to collect mushrooms may wish to avoid amanitas mushrooms. They make amanitas.

Amanitan is an irreversible binder that affects polymerase, RNA polymerase. Not a good thing to lose either. So, all parts of this course have interesting poisons that will affect it but we'll focus on the poisons effecting neurobiology today.

And then there's a human made thing. Do you remember the, well, those of who have heard of World War I, nerve gas or, in particular, who remember the attack in the Tokyo subways with sarin, a particular kind of nerve gas. Do you know what that stuff does?

It is a potent inhibitor of the enzyme acetylcholinesterase.

What would happen if I inhibited your acetylcholinesterase?

The muscles tense up and I'm unable to relieve them because, just like I was doing there, because my acetylcholine is not broken down in the synapse. So, this is a nice menu of interesting poisons and fun facts to know and tell and good things to avoid. There are more drugs and things that we can come back to.

So, now let's talk about, let's move onto other synapses.

Let's take a look at nerve-nerve synapses.

So, we looked at a nerve muscle synapse. What were the properties of this nerve muscle synapse?

Well, it had the property that a single neuron innervates a single muscle fiber. All right? This was a one-to-one single fiber, sorry, single neuron, single fiber.

When we get to nerve-nerve synapses, they're more complex. Multiple different nerve terminals may synapse upon the same neuron, as I indicated last time. There might be a thousand different nerve terminals synapsing on the dendrites of a postsynaptic cell, but let's look at one of them for a moment. Then we'll come back to how a thousand can work together. So, here's one.

And here's my dendrite that I'm synapsing on here.

The nerve terminal releases into, sorry, into the synaptic cleft some neurotransmitter. It turns out there's a wide

variety of neurotransmitters that get released while the neuromuscular junction involves acetylcholine. One example that might be involved here is something called glutamate. What's glutamate?

It's an amino acid. Glutamic acid. It's the ion of glutamic acid. That actually is a neurotransmitter.

Ever have monosodium glutamate. Does anybody get a headache from monosodium glutamate? I do. That's because it's a neurotransmitter. It messes with brain chemistry.

So, glutamate. Glutamate is released.

And what is does is there is a channel on the post-synaptic cell that binds glutamate. And it, too, is a ligand-gated ion channel. And it could be, for example, a sodium channel.

Other neurotransmitters might use other channels.

What happens if I spritz some glutamate on a dendrite of a cell that has a glutamate-activated sodium channel?

What will happen in that dendrite? Sodium will rush in causing the membrane potential to become depolarized and then positive and then causing an action potential? No. It turns out that that last bit doesn't happen because the dendrites don't have the action potential machine. The action potential machinery is interestingly confined to the axon. It's not found on the dendrites.

So, when we spritz with glutamate, what will happen is if this is a glutamate-bearing synaptic terminal the membrane potential here will become locally positive. But it is not an explosive regenerative action potential because there are no voltage-gated sodium channels that are going to open in response to that local depolarization. So, it became a little positive over in this corner of the neuron. Now, if it gets a little positive over in this corner of the neuron, you know, it's going to draw some negative charges from over here, right, to offset that local positivity. But if it's just a local little patch of positive then it draws a little bit of negative charge. But is that going to be enough to depolarize over here? No. So what do you want to do?

Have more. Suppose I have two glutaminergic synapses and they fire, it might be. Probably not.

Maybe they have to fire at the same time. Maybe if I have a hundred out of a thousand. Imagine that I have a hundred different glutaminergic synapses that fired simultaneously then what will happen? I'll get positive charges at all of them.

And maybe that's enough to draw some negative charge away from the axon and start an action potential going, or maybe not. Maybe you need two hundred. What if they don't fire at exactly the same moment?

Well, the minute one fires it makes it locally positive, but then it starts restoring itself so that if they're separated in time they're not as effective as if they happen simultaneously.

So, we have an extraordinary complex analog integration circuit here. The analogy integration circuit depends on the temporal arrival of these signals.

And what else does it depend on? The number of the signals. So, let's get this down. We're going to integrate the signals here.

It'll depend on their timing, the number, and the geometry, because it turns out that doing it at different places in the, now, I drew my dendritic tree, the dendrites as all these little hairy spikes coming off the cell body, but the dendrites are vastly more complex than that. Some cells have elaborate dendritic trees. The dendritic tree, the dendrites of some neurons, here's the cell body, can go off in all sorts of wonderfully complex patterns. And it may be more effective to hit synapses close to the cell body or synapses on different parts of the tree. And so that the entire shape of that dendritic tree can have an effect, and where you're hitting it has an effect. So, whereas the action potential is a very simple thing, which you might say just replace it by a wire for our computer modeling studies, goodness, nobody has actually succeeded in building a perfect model of the integration properties of an dendritic arbor for a single neuron.

They can get guess and approximations.

So, there's an amazing integration that's going on here.

But it turns out that it's more complex than that because, you see, I said that we had these, say, glutamate neurotransmitters here that were causing positive charges to rush in.

It turns out there are other neurotransmitters that activate other channels in the membrane. And, for example, there are some neurotransmitters that activate, like glycine, another amino acid activates ligand-gated chloride channels.

So, glutamate, one amino acid activates sodium channels. Sodium rushes in. Glycine activates chloride channels.

What will chloride do? It can come in.

What will it do when it comes in? Negative. Oh, my goodness. So, when glycine is spritz on the post-synaptic cell chloride comes in and the cell becomes locally more negative. These are called inhibitory synapses.

By contrast those that admit positive ions excitatory synapses.

Neurons can have both inhibitory and excitatory synapses on their dendrites. So, the postsynaptic cell will be receiving positive signals, positive ions coming in from excitatory synapse and negative signals, inhibitory signals with negative ions coming in.

The integration of charge in the dendritic arbor is an integration problem of the timing, number, geometry and sign, positive or negative, of these activation signals.

That's what's going on. And what happens is the neuron integrates these signals, positive and negative. So, we'll make this one a glycine neuron, negative, negative, negative.

All that integration takes place right over here in the region of the cell called the axon hillock, which is the first place that the action potential mechanism is found. And, of course, that integration is nothing more and nothing less than figuring out whether the membrane potential gets above minus 50. If it gets above minus 50 it fires.

OK? Yes?

Does the nucleus participate in the, in what way would the nucleus participate?

It's an interesting question. I mean the nucleus does, in a sense.

The geometry of that cell body there has some effect on the electrical properties and all that, but if you think about the timescales. How often do neurons fire? At a frequency often of about a millisecond. So, that means everything I've just old you, this complex integration problem is occurring within a millisecond. The processes in the nucleus that I think about typically of transcription and translation and all that are operating several orders of magnitude more slowly than that. You know, they'll operate, even in the best of circumstances, at seconds, and often at more than that, minutes before you could get transcription and translation and stuff like that going. So, the nucleus, I think, for the most part, better get its act together by producing stuff and getting it out to the periphery, but probably through the expression of the genome can't do much in a relevant millisecond or so.

But I wouldn't be shocked if some neurobiologist knows better than I do that nucleoli do something. I mean there are many cleaver things that are going on. I'm sure a cell has wasted anything, but with respect to the operations we've talked about probably not.

OK? But I'm always reluctant to say something never happens in any possible way. All right. So, now how does all this get stuck together? Well, not only do we have this complex integration within the dendritic arbor but, of course, the neurons are stuck together into circuits themselves.

If we had more time I would draw the circuit that you use to integrate complex functions in calculus, but not having

much time I'm going to just go for a much simpler circuit here.

I'm just going to go back to nerves and muscles. And here we go.

Suppose I tap right here below your knee. What happens?

There's a reflex. Let's at least get that going, OK? What happens is when I tap there above your patella, here's your kneecap here, there's a sensory neuron.

The sensory neuron brings out a signal and it goes into the spinal column here. This is a reflex.

It doesn't need to go up to your brain. You don't need to think a lot about it. And it goes into the spinal column here into the dorsal root ganglia. This is a cross-section.

The, sorry, sensory neuron comes in here. And what it does is that sensory neuron makes a synapse, and actually another synapse, and it makes a synapse on a motor neuron. The motor neuron comes back and synapses on that very muscle. It is the simplest possible circuit.

I sense, I send one sensory signal up into the spinal cord, there's an excitatory positive synapse onto a motor neuron, this motor neuron fires and contracts my muscle so I go back.

At the same time, this guy makes another synapse, a positive excitatory synapse on a little cell that is an interneuron, that's an intermediate neuron. That intermediate neuron makes a synapse on a second motor neuron, but this is an inhibitory synapse.

That motor neuron sends its process out and is affecting the opposite muscle. So now what happens?

Let's get this straight. I hit over here.

And the signal goes back to my spinal cord. The sensory neuron causes one motor neuron, directly by firing on it, to contract. It causes an interneuron to fire that inhibits the opposite motor neuron. What happens if you inhibit the opposite motor neuron? You relax the contraction, or you at least don't contract the opposite muscle.

So, what happens is you send a positive signal to the muscle on one side and you inhibit the signal to the muscle on the other side.

It's a very simple circuit. It's got one sensory neuron.

Two motor neurons. One interneuron. It's got two positive excitatory synapses. It's got one negative inhibitory synapse.

That's about it. Presumably, everything else that goes on in daily life is basically the same thing. This is probably what eating lunch is like, falling in love is like and things like that, although the details remain to be worked out for exactly how that stuff works. There is a large collection of, I give you the simple examples because obviously we don't know a lot of the complex examples. There is a lot more to this.

If had time in the course we could go into what's known about more circuits. I joke. We know about the circuits that help you see vision, that allow you to pick up signals in your retina, transmit them back and reconstruct things with positive and negative signals that allow you to see a straight line, for example, and recognize a straight line.

And there are patterns of cells that send positive signals and negative signals, and when you integrate them you can get a signal if and only if there's a straight line at this angle in your visual field.

And people know about that kind of stuff, but some of the more complex stuff we don't know about. There are lots and lots of neurotransmitters, glutamate, glycine, histamine, serotonin. ATP can be a neurotransmitter.

Adenosine can be a neurotransmitter. There are peptide neurotransmitters.

Endorphins, oxytocins and even gases. Nitrous oxide is a neurotransmitter.

And then some of the drugs you may know work by affecting these neurotransmitters. Prozac and the general class of selective serotonin reuptake inhibitors. Prozac effects a specific process with a neurotransmitter.

There's a neurotransmitter serotonin. After it's fired out, instead of acetylcholesterase being in the synapse destroying it or some other enzyme destroying it, it's taken back up by the cells.

If you could inhibit the process by which you take up your serotonin again, the serotonin would last longer in your synapse and you would be happier, give or take, roughly speaking to the extent that more serotonin is a good thing. And that's what Prozac does.

Actually, it's one of the things Prozac does. There's good evidence now that Prozac does other things, too, including causing neuronal cell growth, but that's a whole other story.

There are things like cocaine. Cocaine is a bad thing because it inhibits certain sodium transporters and other things.

And if you go through all of the different psychoactive drugs they're affecting different parts of these processes. So, for Friday I've invited a colleague who is a real neurobiologist, I'm not a card-carrying neurobiologist, to talk about some of the more far out things of learning and memory.

Andy Chess who's a good friend and a colleague is going to talk about learning and memory. And then have a good time with him, and I'll see you subsequently.