Episode 74: Jingle Bell Sweaters
Physicists: Dr. Nicole Prent, Dr. Jacqueline Townsend

Transcribed by Denny Henke

Ben: Never be afraid. There's nothing which is known which can't be understood. And there's nothing which is understood which can't be explained. For over fifty episodes now my team and I have brought you to the very frontier of knowledge in physics and astronomy. And still our mission goes on: to present you with your birthright, an understanding of the universe. I've traveled the world seeking out a certain type of genius, masters of not only their academic disciplines but also at explaining their research in understandable ways and I've bestowed upon these women and men the title of Titanium Physicist. You're listening to the Titanium Physicist Podcast and I'm Ben Tippett, and now allez physique!

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Ben: It's summertime right now and the campus is hosting a bunch of camps for elementary school kids. It was my pleasure to be invited to give a half dozen talks to these kids and I talked to them about black holes. In the middle of one of these talks I got to the topic of event horizons and mention the Schwarzschild radius. What's a Schwarzschild radius they ask? And I explain the clever and tragic story about how Schwarzschild was a soldier in World War I, as he was dying in a hospital bed he discovered the mathematical model for what we now call a black hole. "Okay, but", interrupted one of the children, "Why do scientists always have such weird names?" And I looked at it and I said, it's not weird. And he said, it's spelled weird. And I said but it only has two syllables. Schwarzschild, Schwarzs-child, like Einstein. You know, they do have weird names I told the children. They do have weird names. Their names sound weird to us because they have strange sounds in them and they have strange sounds in them because they aren't English. You see, I explained, I need you to understand that scientists come from all over the world. Not just England, North America or Europe but China, India, Chile, South Africa, everywhere. Science and mathematics belong to all humanity. Not because of some beneficence of western civilization, but because the people from every culture, speaking every language and of every gender have contributed to the development of science and mathematics. Science and mathematics have only succeeded because everyone has contributed. So, when

you hear the name of a notable scientist they are going to sound strange to you. They sound strange to everybody. Japanese people have to learn the names of European scientists. Chileans have to learn the names of African scientists, Americans have to learn the names of Asian scientists. It's not a bug, it's a feature. It's not a problem that scientists all have weird sounding names, it's an acknowledgement of how diverse the history of science is and how science and mathematics doesn't belong to any one nation or ethnicity. Excluding people from the history of science might make the names easier to remember or say but we can't do it without their contributions. So, we should honor them by learning to spell their names: Schwarzschild. S c h w a r z s c h i l d! Okay, maybe I laid it a little thick on those kids. But it's important to me that we appreciate that a part of human nature resents having to learn about new things. Or, it hates relearning a more sophisticated picture of things we already thought we understood pretty well. It makes us feel less knowledgeable and it makes us feel less relevant. But it's part of ourselves that we just have to push through. We owe it to ourselves to push through it. Speaking of more sophisticated understandings, MRI machines are great but there's an even newer technique with a new acronym that's even better called ESR microscopy. Now, don't get grouchy, I know that you're pretty attached to knowing about MRIs. You even know what their acronym stands for: magnetic resonance imaging. But ESR, electron spin resonance is even better and that's the topic of today's show. Speaking of feeling resentful at learning new names, I hate how, now that I don't have time to watch awesome movies twice a month, I no longer have any idea who the popular actors and actresses are. I mean, Channing Tatum? What kind of a name is that? What's wrong with just having George Clooney in every movie? You know, he's that guy from *ER*. Anyway, I digress. Our guest today is an expert on all movies, especially classic movies. She's the host of the *Thirty Twenty Ten* podcast where they talk about old popculture from integral multiples of decades ago. Specifically she's the person who knows all the actors in all the movies ever and can tell you what Jackie Gleason ate for lunch 53 years ago today, welcome to our show Diana Goodman.

Diana: Ah, thank you, it was a ham sandwich.

Ben: Oh, wow. So, Diana, for you today I have assembled two old favorite Titanium Physicists, I call them the biophysics team. Arise Dr. Nicole Prent!

Nicole: Woo woo wooo!

Ben: Dr. Nicole got her PhD from the illustrious University of Toronto in biophysics, specializing in non-linear microscopy. She's a professor of physics at Okanagan College in Vernon British Columbia. Now, arise Dr. Jacqueline Townsend.

Jacqueline: (Crazy sound)

Ben: Dr. Jacqueline got her PhD from the University of Pittsburgh in biophysics, she's currently the lead science faculty at Colorado State University's Global Campus. Alright Dianna, let's talk about magnetic imaging. Okay, so, like, have you ever been in an MRI machine or ever seen an MRI machine up close?

Diana: Ah, yes. No, I have had an MRI, yeah.

Ben: Okay, so what's it like?

Diana: Um, it's kind of like being locked in a coffin, I mean, I'm in this sort of tube thing. The wall of it is inches from my face. It's making really loud banging and clicking noises and every now and then some voice comes out of nowhere and says okay, hold your breath.

Ben: Cool.

Diana: Yeah, I'm really, really lucky that I do not have claustrophobia.

6:49

Ben: That's great. That's a fantastic experience for what we're going to be talking about today. Because the mechanism for ESR, electron spin microscopy, is really similar to the mechanism for MRI machines.

Diana: Okay.

Ben: So, it all comes down to magnets. Ah, when was the last time you played with magnets.

Diana: Ah, the last time I put something on the fridge I guess.

Ben: Okay, cool. Um, did you ever play, with, like, bar magnets?

Diana: Ah, yeah. Yeah.

Ben: Okay, so, that's kind of what we're talking about. So, the elementary particles, like electrons and neutrons and protons, they all have magnetic fields.

Diana: Okay.

Ben: They all generate magnetic fields. And it's because they have something called spin, that's why spin shows up in the electron spin microscopy. That's what it's talking about. It's talking about the little magnetic field that the electron generates. Ah, but protons and neutrons both generate them as well and essentially it's just like a tiny, tiny, tiny, tiny, tiny little bar magnet. Okay?

Diana: Okay.

Ben: So,the best example of a bar magnet is like a compass. A compass is just a magnet. Right?

Diana: Yeah.

Ben: It's just a magnet that's encased in fluid or somehow isolated from the rest of the world so that it can spin freely on its axis.

Diana: Yeah.

Ben: And so it reorients its direction. It's always pointing north because when you put a magnet inside of an external magnetic field it will reorient itself so that it is pointing in the direction of the external magnetic field.

Diana: Right. Assuming something else magnetic isn't nearby, right?

Ben: Yeah, yeah. That's right. So, an MRI machine, that coffin that they put you in, the big donut shaped tube, that's just a huge electromagnet. So, what that's doing is it's generating a really, really large magnetic field that points down through the middle of the tube. Which is why they tell you to take off all of your jewelry and your pocket magnets and your hammer, right, before you go into the

room. Because once you go into this room with the magnetic field all this stuff is just going to get pulled towards the magnet and probably break a window. Or a wrist. Or whatever.

Diana: Okay. Alright. So, that leads to the big obvious question of how does spinning magnets around me be able to see my insides?

Ben: Right. So, let's just imagine a really simple case. Let's just imagine that you have a really straightforward magnetic field. All a magnetic field lines are parallel. They are all oriented, oh, I don't know, North! Why not? So, you imagine you take a really big source of a magnetic field, they are called solenoids, ah, like the one they put you in, an MRI machine. And that generates a really strong, powerful, uniform magnetic field inside of it. If you took a compass and put it on a table inside of it, that compass would reorient itself in the direction of the magnetic field. Okay?

Diana: Okay.

Ben: But if you shook it, it wouldn't be oriented towards the magnetic field anymore. It would be, kind of tilted off, right?

Diana: Mmmmhmmm.

Ben: And then it would wiggle back and forth and shed energy because orienting itself in the direction of the magnetic field is the lowest energy state of the system, it's called.

Diana: Okay.

Ben: So, the system will loose energy and then the magnet will be reoriented in the direction of the magnetic field. So, this is, essentially, what's happening... okay, so, let's imagine that there's just a single electron with its magnetic field inside our MRI machine. Just floating in space. It's magnetic field is going to be oriented in the direction of the external magnetic field.

Diana: Hmmhmmmmm.

Ben: So, what the scientists do is they hit the electron. They don't hit it with a hammer or a gun, the way we would hit a compass. They shoot, ah, a little pulse of electromagnetic waves at it. So, these electromagnetic waves, they have their own magnetic field. And the magnetic field from the electromagnetic waves, perturb the direction that the electron is pointing. The electron will reorient itself after it's been kind of kicked by this electromagnetic field and then it will be pointing in another weird direction because now it has a little bit more energy. But, just like the compass needle, eventually its going to shed the energy and realign itself with the external magnetic field. Does that make sense?

Diana: Yes.

Ben: There's two interesting bits here. The first one is that the amount of time it takes for our electron to realign depends on the properties of the electron. The intrinsic properties of the spinning thing. So, if it's got a lot of mass, it's going to take a long time to reorient itself. If it's got a little mass it will reorient itself quite quickly.

Diana: Mmmhmmmm.

Ben: And the second thing, is, by looking at the magnetic field produced by this electron we can detect its orientation. And we can detect when, how much time it takes to reorientate itself with that external magnetic field. So, what happens is, we kick it with a radio wave, it goes off kilter and then it reorients itself and we can detect that reorientation and we can figure out how much time it took for the atom to reorient itself and from there we can deduce properties about this particle.

Diana: Huh.

11:49

Ben: Does that kinda make sense.

Diana: Okay. Alright, I'm following you, yeah.

Ben: So, our bodies are more complicated than that. Ah, you know, inside of us, there's all sorts of chemistry going on. I'm kind of afraid at that word. But you have to deal with it in biophysics.

Diana: Me too. I had to take chemistry twice, so...

Laughter

Ben: You're twice as afraid of it as I am, but.

Diana: I did not have a good teacher the first time.

Jacqueline: You know what Diana, if it makes you feel better, I had to take chemistry twice too because I also had a bad teacher the first time time and I ended up publishing papers in international chemistry journals so that experience gets a lot of people.

Diana: Oh, wow. That is, like, seriously inspiring to hear. Yeah, it didn't put you off just because they couldn't explain molealities well. I still don't know what that word means, by the way.

Jacqueline: Oh, a mole is just a way of saying a certain number. So, like a dozen is 12, a mole is a much larger number. It's 6 followed by 23 zeros, give or take.

Ben: It's a chemist's dozen. A baker's dozen is 13 and...

Jacqueline: Yeah, it's like a chemist's dozen. A chemist's dozen is a lot bigger.

Ben: Okay. So, in our body there's lots of chemistry. So, if you have a nucleus, if it is attached to other nucleuses, going from an atom to a molecule then the other nucleuses around them and how they are attached together will determine how much time it takes for that magnetic field from that nucleus to reorient itself with the external magnetic field. So, what we see in nuclear magnetic resonance imaging, is, we're looking at how much time it takes for all these atoms to realign themselves with the external magnetic field. And the amount of time it takes tells us about the local chemistry. And so, from, there we go, okay, that's a spleen, that's a, what other body parts, lung, that's a bone, right. Because all these different body parts, all these different, the local chemistry of an atom or

molecule, determines how much time it takes for these things to realign. And so, by looking at the realignment time we can deduce information about what's inside of our bodies.

Diana: Okay, so, let me ask, kind of a weird question. How do you know where they started from if you're measuring them moving back to normal?

Ben: Oh! Just like if you took a bunch of compasses and put them in a big external magnetic field. It would take them a little bit of time to shed the energy and realign themselves with the external magnetic field. You could take a body or whatever and put it inside this big magnet and all the magnets inside with you will realign with this external magnetic field. Eventually. And so you just have to wait for enough time to pass and then you can say, oh, everything is aligned now, now it's safe for me to hit it with a pulse, knock everything off kilter and then see how much time it takes for the parts to realign.

Diana: Oh, okay.

Jacqueline: But you're not measuring the position of where they are. You're measuring that energy that is shed in the process.

Diana: Oh, okay.

Jacqueline: Yeah, so, we're not like, looking at a compass needle but we can measure that energy that is shed by that system as it goes back to normal.

Diana: Okay. I see. Yeah. Yeah. So it sort of, once it's, the amount of energy being shed is zero that's back to where it was when it began.

Jacqueline: Mmmmmhmmmm.

Diana: Got it.

Nicole: Yeah, so one of the important things in imaging is of course having a target. So, when we're talking about MMR or ESR, how do we not, like, image everything. So, the key thing with this spin resonance is you need to have something that is unpaired. So, when you have a paired system you end up with no net magnetic field. So, if you go back to your compass needle, right, which is

your little bar magnet and you put another bar magnet on top, the opposite poles are going to line up so that this little needle now has no net magnetic field and it's not going to align to the external magnetic field that it's in. And if you perturb it, it's not going to oscillate. It's just going to relax to some other random position. And this goes for both, MMR with we're talking about the magnetic fields in the nucleus um, and then we'll learn from Jacqueline about with ESR how we're talking about the magnetic fields from the spin electrons.

Diana: Okay.

Nicole: So, yeah, so this paring makes the perturbation impossible. So we can get targeted. By targeting these certain nuclei or these electrons that are unpaired. That's what's special about them.

Diana: Okay. I think I'm following. Alright.

Ben: Let's reiterate. So, at the start, I was like, let's just imagine one all by itself. The magnetic fields produced by any two electrons is going to be about the same, well, it's going to be the same because electrons are pretty much identical, right.

Diana: Oh, the same, yeah.

Ben: So, if I have two bar magnets and I put them close to each other, what would they do?

Diana: They'll stick together if they've got opposite charges.

Ben: Right. They stick together but how do they stick together. do they stick together in a way where both of their norths are stuck together and both of their souths are stuck together?

16:55

Diana: No. It would be the opposite. Wouldn't it?

Ben: Exactly. So, the North sticks to the South and the South sticks to the North. And what you end up with is these two bar magnets are interacting with each other really strongly but then overall they kind of cancel each other out. So, once

you've stuck those two magnets together their magnetic fields are canceling out with each other and the system isn't really producing a magnetic field. And the system isn't really interacting with an external magnetic fields. So, if you have these two electrons and you make them cuddle up they are going to invert so that one is pointed down and one is pointed up. Or, so that their magnetic fields cuddle up and cancel out. And then after that you can't perturb them. They are kind of coupled off. They don't really care about that big external magnetic field so they won't necessarily realign themselves all the time with this external magnetic field.

Diana: Oh, okay.

Ben: So, if you have...

Diana: Right.

Ben: ... have one alone magnet, hey, all the story I've told you is perfect. If you have two, Nicole was saying that they won't really care if they are in a big magnetic field and they won't really care if you hit them with a radio wave. And the important thing here is that, every molecule has more than two electrons in it. Almost every nucleus has more than two nucleons in them. It's really common to see these magnetic objects cuddled up close together. And so, if they pair up you're not going to be able to use your magnetic perturbation trick to see what they are made out of, if they are cuddled up.

Diana: Okay. So, where does that apply to imaging?

Jacqueline: Kind of where we're going with this whole cuddling magnets and non-cuddling magnets is getting into a discussion of the differences between NMR which is the nuclear magnetic resonance which is used in MRI versus ESR which is the electron spin resonance which is what we're going to be elaborating on going forward in this discussion. So, with NMR we have the concept of isotopes which I know most people have heard of isotopes but don't necessarily have a full understanding of what they are. With isotopes it comes down to how many neutrons are in a nucleus and as far as the NMR techniques care, if there is an even number of protons and neutrons then it's not going to react. But if there is an odd number then we have the lone spin that will be detected. But because in a population of atoms you're going to have some isotopes so even if I normally have

an even number, some of my isotopes are going to be odd and viceversa. So, NMR is less selective because you're always going to have some odd and some even in your population. So, it's harder to get a perfectly clean signal. And when you're looking at bodies that can be useful because you want to be able to look at a bunch of different atoms in someone's body. Like if you're looking at something that's going on with their bones you can say, okay, I'm going to try and look at this whole population of atoms in a bone and depending on how you process the signal afterwards is how you get information from that and there's also contrast dyes that you can kind of hone in on that will help make that be a little more specific. Because with NMR you're getting a more generalized signal because you're looking at a lot of atoms which is good for certain purposes.

Diana: Okay, yeah, that's something I actually would love to know, even though I'm worried it's a little off topic. So, I once had a kidney infection and they did a CAT scan and they couldn't figure out what was going on. Then they did a CAT scan with contrast and all of the sudden it was really obvious what was going on. And I always wondered what exactly the contrast made it able for them to see that me screaming and going ow that my kidney's couldn't.

Jacqueline: Yeah, CAT scans get into x-rays which kinda work in a different way, so...

Diana: Yeah

Nicole: Yeah, they are absorbing.

Jacqueline: Yeah, contrast dyes work different than MRIs do. But basically in either case, um, when they put a contrast dye they are usually putting in some kind of really heavy atom. Like not radioactive but like boron or something that is really big solid atom with big solid signal. In either of those cases it helps them more clearly identify what they are looking for.

Diana: Oh, that makes sense.

Jacqueline: So, it's kind of like, if you have a bunch of tiny magnets in your body normally, they are putting a bunch of bigger magnets in your body.

Diana: Right.

Jacqueline: So they react more strongly.

Nichole: Yeah, and with your CAT scan it's more like density, like tissue density.

21:46

Diana: Hmm. Okay. Yeah, it was, always wondered how that worked. Didn't think to ask at the time because, like I said, I was in a lot of pain.

Jacqueline: It's not a fun time to have those discussions but then afterwards, sometimes it's like, oh, what were they doing?

Diana: Yeah. Well, it was like, they made me drink a milkshake and then I had to go do this again. Then I threw up the milkshake, ahhhhhh. Yeah, it was a bad time. Kidneys are jerks. What, I learned from the entire experience is that kidneys are jerks.

Jacqueline: Kidneys are jerks. Yeah, so, when we're talking about NMR, that's the Nuclear Magnetic Resonance and if you remember from your high school chemistry classes, the nucleus is the big thing in the middle of the atom with protons and neutrons in it. And the electrons are those really, really tiny things that aren't quite a particle and aren't quite a wave and they are kind of circling around in an orbit around the atom.

Diana: Yeah, that I held on to. I remember that part.

Jacqueline: Yeah, so, when we're doing NMR, we're looking at the big thing in the center of the atom and we're doing ESR, we're getting a signal from those little guys that are orbiting around. But again, so like, Nicole was explaining, about how if you have a pair of bar magnets, they kind of cancel each other out. The same thing works with electrons. And even though they all have a negative charge, they have this property called spin that behaves in a similar way. So if you have an electron with upspin and an electron with a downspin, it will kind of cancel each other out as far as its interaction with an external magnetic field goes. You know, some people might remember from high school chemistry, if you're doing the, let’s fill in the orbitals and they make you draw the little up arrow and the little down arrow.

Diana: Maybe... maybe.

Laughter.

Ben: In high school chemistry, when you are filling out the orbitals you fill out from the innermost to the outermost and each orbital, ah, that an electron can live in, ah takes two electrons, right?

Diana: Right. I remember that there's the different levels around the nucleus and it was, it was like two electrons in the first level and when that level is full it goes it to the next one.

Ben: That's right. It's always two because of, ah, Pauli exclusion principle, it's called. So, the Pauli exclusion says that there are these orbitals and you can't put too many electrons in one orbital but you're allowed two in each because one of them is spin up and the other is spin down. So, you can put two in each orbital but when there are two in each orbital their magnetic fields are going to cancel out.

Diana: Ahhh. Okay. Got it.

Jacqueline: And then sometimes, when you're filling out those orbitals, sometimes you have one leftover. Depending on what kind of atom you're working with. And that one leftover can interact with a magnetic field in the same way that a nucleus with an odd spin number can interact with a magnetic field. But, when we're detecting it we're detecting at a much smaller signal at a much higher frequency because we're going to really, really, really, the limits of what we can measure.

Diana: Right. So, you infer one tiny individual electron at the outside of an atom instead of the big, bulky, main part of the atom, right?

Jacqueline: Exactly. And the other interesting thing is that these are much rarer in biological systems than a nucleus that is going to interact with the magnetic field is. And that's because, of, getting into the chemistry word, covalent.

Nicole: Covalent bonds.

Jacqueline: Yeah.

Nicole: Yeah, like the free electrons are very reactive and essentially, in biology, they react themselves out of existence. Kind of think of it that way. Um, so, when you find one, it's really special, right. So, you can hone in on it, this is some of the stuff that Jacqueline does where you can add these special tags that might be reactive and the key thing is finding a stable reactive species. So, one that will actually let this free electron exist for a while, so you can probe it.

Diana: Hmmmm.

Ben: I think we need to emphasize the point you're making here.

Jacqueline: We need to back up the train.

Ben: There are obviously some atoms that have an odd number of electrons, right? And so they are going to have a lonely, unpaired electron that we should be able to detect with this. So, ESR, it shouldn't be hard to see atoms with free electrons. But, if we're talking about biological systems, everything's molecules, right. These molecules are attached together using something called a covalent bond. Some atoms, when they are making molecules, they attach together by sharing electrons.

Diana: Right.

Ben: So, what this means, essentially, is that when they are close enough together the electrons stop orbiting one atom alone and start, kind of, orbiting both.

Diana: Right

26:39

Ben: And in the process of doing this lots of these free electrons will pair out. And so in the molecules it's kind of rare, especially in biological systems, just full of body chemistry, it's really race to see solo electrons. Because if it's got a solo electron in will stick to something. Something else will want to share it's electron in a covalent bond. And so there's lots and lots of covalent bonds but anytime two atoms with odd number of electrons get in a covalent bond their electrons pair off and become invisible to ESR.

Diana: Okay, I think I'm getting this. So, the idea is, that, hypothetically, you know, finding the lone electron should be pretty easy but because we're dealing with a body, you know, it's not deep space, it's a body that are already complicated and full of goofy chemistry, there aren't a lot of them to find.

Nicole: Yes. Electrons basically govern the chemistry of the atom in the molecule, so, you put them all together and that's how you get your reactions. Well, free radicals um, generally something that people like to avoid. You've probably heard of anti-oxidants.

Diana: Mmmhhmmm.

Nicole: That's what people take those to sort of get rid of these reactive species. In general though, like, our body has lots of ah ways, to, combat them naturally, as well. Hence the reason why these lone electrons are extremely rare.

Diana: Oh, okay. So, is a free radical one of these atoms that has the lone electron.

Nicole: You got it.

Diana: That's why it's reactive with stuff, because it has just the one electron so it's looking for a buddy.

Nicole: Yeah.

Diana: Okay, cool.

Jacqueline: So, the cool thing is, is because these are rare, we can take advantage of that when we're studying biological systems in a way that we can't with NMR because nuclei that react with magnetic fields are common, but electrons that react with magnetic fields are rare and both of those properties can be taken advantage of in different ways. So, now I'm going to get into protein chemistry. So, we're getting lots of fun chemistry review in this physics podcast.

Diana: Noooooooo. So, I was a cinema major for a reason! So, nothing to do with chemistry.

Jacqueline: But you can do both like Heady Lamar.

Diana: That's true.

Jacqueline: She invented a new kind of radar which is actually what's used to tune the frequencies for ESR.

Diana: Really?

Jacqueline: So, there's a connection there.

Diana: Huh.

Jacqueline: Not her specific technique but a lot of the radar physics that was developed by people including Heady Lamar is used to tune the radio frequencies, admittedly at much higher frequency for techniques like ESR and NMR.

Diana: That is really neat. I knew that, yeah, the frequency hopping thing that is used in, like, wifi, but I didn't know that it was... huh.

Jacqueline: Yeah, Heady Lamar was really cool. So...

Diana: Yeah.

Jacqueline: So cinema and chemistry are not mutually exclusive necessarily. Okay, so I was going to explain about protein chemistry. Most of what's going on in your body involves proteins either acting as a structural element or doing stuff. So, there's your bones which are largely mineral but aside from your bones, um, and the lipids making up membranes that are kind of like holding all the sacks of cells together, a lot of what's going on in your body is either structural proteins. So, like your muscles doing stuff is proteins. Like most people are used to, like, oh, I should eat a lot of protein because it makes muscles. There's also what's called enzymes which are the molecules that do most of the life things that happen so. When you eat something it's broken apart by enzymes. When you're growing up and lots of stuff is getting built, it's enzymes that you're putting it together. So, these enzymes are making most of the life happen. Um, and so enzymes are proteins but not all proteins are enzymes. Does that make sense?

Diana: Yeah, got it.

Jacqueline: Okay. So, enzymes are proteins that do stuff and all proteins are made up of these things called amino acids which are, basically, kind of like Legos that build up proteins and they come in certain fixed shapes. Um, so, you know how Legos have the round bit that sticks out and then the other end that you stick the round bits into?

Diana: Mmmmhmmm.

Jacqueline: Amino acids kind of work in the same way, but in a line. You can't branch them out. You build them, basically, as a long sequence of different pieces. So, like, if you had a Lego that could only have one Lego stacked on top of it but you could have a bunch of different heights of Legos and shapes of Legos stacked on top of it really, really long, like a necklace. Here is the tricky part and this is actually, still one of the hardest problems in biology and medical science and biophysics that like, literally, hundreds of scientists are working on this problem, it's called the protein folding problem. Because once we have this long line of amino acids, it coils up on itself and folds into a very specific three dimensional shape that is dictated by those building blocks that were put in to it.

Diana: Mmmhmmmm.

32:02

Jacqueline: And we don't know all of the rules that dictate how that happens because there's so many different variables and ways that things could be folded up. It's like staring at a piece of paper and trying to figure out what origami you could fold it into. It is a really, really difficult problem.

Ben: It's kind of like looking at a string and thinking about, how, like, you could make a sweater out of it or you could make, like, two sweaters out of it.

Jacqueline: Yeah, it is.

Ben: ...together so there's only necks and arms, right. Like...

Jacqueline: Yeah, like, maybe it's going to be a slipper, maybe it's going to be ah, earmuffs, like, who knows. Like, who knows.

Nicole: Just a big ball of mess.

Jacqueline: Yeah, but the cool thing is, is they fold up into these very specific shapes and these shapes are what dictate what they are able to do. So, you know, you have your Legos and you build a little Lego boat, it's a little Lego boat and you have your proteins, like, I'm going to build this sequence of amino acids and it makes a very specific protein that might be an enzyme that has a very specific function. So you're probably thinking, okay, but how do we get from, like, little spinning electrons and what does this have to do with proteins folding up? Right?

Diana: Yeah.

Jacqueline: So, a cool trick that we can do is add a specific building block called a cysteine. We can make a tiny little mutation in that protein and put a cysteine in. And a cysteine has an atom on it called a sulfur that we can make a covalent bond with one of these electron spin labels. There's very certain molecules that can kind of keep that lone electron trapped in a stablized state. And so we can add those onto a protein or an enzyme. And so now we've labeled it and we can do ESR on it.

Diana: Hmmmm.

Jacqueline: So, why do we want to bother with all that? The even cooler thing is is now that we have this protein, with a label in a very specific spot and we know exactly where in the sequence that is, we can do ESR and get information about that molecule.

Diana: Okay.

Nicole: Yeah, because, remember the, you get information on it's environment based on its energy and the relaxation time.

Diana: Right. So, now you can actually see that even though in its sort of natural state it wouldn't have the free electron to make it visible to ESR.

Ben: Awwwww. Stupid analogy time. Okay, so, it's like, you got your yarn, it's just like a long protein chain. And you put jingle bells on your yarn and then you let it make itself into a sweater and you look at where they're jingling and depending, you know, what the bell in the armpits are not going to make much sound. The bell on the ends are going to make a ton of sound. And so, based on, looking at where the jingle bells are and how they sound, you can tell what shape the sweater is in. Or, rather, that it is a sweater at all.

Diana: Okay. That's an okay analogy. It's not that bad. I mean, I'm loving imagining this, like, ball of yarn knitting itself into a sweater while someone is hiding in the other room like, I can't wait to see what happens.

Jacqueline: I mean, that's kind of not far off. I'm kinda going to go back to the less jingly explanation now. Um, so, if we have the labels on the protein, we can get a lot of information about the shape of the protein. And then we can do other things to it. So, say, I want to design a medication that targets an enzyme. Like, say, oh, there's too much of this enzyme. I want to make something that binds to it. You can then say, okay, I'm going to do ESR on the molecule all by itself just kind of floating in a little tube and see what shape that is. And then add the drug to it and look at it again and see if the shape changed. Like, did it bind? If so, what shape did it bind? How did it change the shape? And that's really important information for things like drug design. Like. If you're trying to design a medication for something. It's also useful, for, like I said, this protein folding problem is this big, huge question. It's kind of like people talk about the hadron collider, is like this big, you know, in physics, like we're trying to finish out our atomic model. Like, the protein folding problem is the big question in biophysics. Is trying to figure out the rules that govern how proteins fold up because that is going to open up a big world of understanding of things like how do we design better drugs to help cure diseases better and stuff like that. Um, so, we can do things like, there's chemicals you can use to unfold a protein and then you can look at it and kind of watch it folding back up again.

36:52

And you may not get a 100% of the picture but you'll get part of the picture. That's, you know, it's a piece of a very big puzzle that's useful. Um, one of the other really important things that it's being used for, and this ties into, part of why, one of the many reasons the protein folding problem is so important, is that

there's an entire class of diseases called protein mis-folding disorders. That are diseases that are caused by a protein folding wrong and we don't know why the protein is folding wrong. And it causes a disease. And the one that almost everybody has probably heard of is Alzheimer's.

Diana: Ahw, so, a protein starts folding wrong and so it's no longer working correctly. Is that right?

Jacqueline: Yeah. So, it's no longer folding correctly, um, and when some proteins start folding incorrectly that tends to kind of trigger this kind of cascading event that makes other proteins fold wrong around it. And so you can get an accumulation. And so, when they talk about plaques, like, Alzheimer's plaques...

Diana: Aw, I see.

Jacqueline: Those are actually clumps of mis-folded proteins that are accumulating in your neurons.

Diana: Oohhh.

Jacqueline: And so, that's why studying this is so important. Yeah. So, we've gone all the way from your MRI machine through the nasty weeds off chemistry and we've come back out to, like this is how scientists are studying things like Alzheimer's.

Diana: Okay. I feel like I'm following along. Cool. Okay. So, I mean, that kind of answers the big overall question, is what can ESR be used for.

Jacqueline: So, Alzheimer's is a big one. You know, potentially looking at, you know, what sort of environmental conditions, maybe slow down this folding, speed-up the folding. You know, maybe help them fold correctly again. You know, looking at these conditions is actually really informative. Um, so, Alzheimer's is the big one right now. There's, you know, like I said, drug design, is key. The overall protein folding problem. There's also some other kind of less, my area of expertise, but there's applications in quantum computing. Yeah, so, because we're getting into the, ah, funky quantum world so it has applications for fuzzy circuits and quantum computing and things like measuring the amount of

radiation that someone's been exposed to. Um, so, like after the Fukushima incident, they can take a tiny chip of tooth enamel and use an ESR because the irradiation causes free radicals, in tooth enamel, that you can use to measure how much radiation someone's been exposed to.

Ben: Or, if you've been exposed to ionizing radiation, the more free radicals are in your body. And they look at tooth enamel because...

Jacqueline: They stay in your tooth enamel.

Ben: But that's bananas.

Nicole: There's also, I think, the link between the free radicals and cancer too.

Jacqueline: Right.

Nicole: You know, reacting with DNA and interfering with your natural end life for cells, your cell apoptosis.

Jacqueline: So, unlike NMR, we're not going to be sticking you in an ESR machine anytime soon because, as I mentioned, we're looking at much smaller signals. You know, you've had your NMR before, you're usually in that big loud thumping thing for awhile.

Diana: Yeah.

Jacqueline: I think I had one and I was in there for for like an hour. So, when we put a sample in the ESR machine because we're looking for much weaker samples, we have to run them for a lot longer. So, my samples are usually in there for about a week. So, we're not using this on people anytime soon because, you know, we're looking for such smaller things, we have to run the experiments a lot longer. Ah, we're still very early days so as Ben was saying, *five-ten-thirty*, you know, we're kind of at the very early days of ESR relative to NMR, but 30 years from now, you know, maybe we're using ESR to look at things like Alzheimer's progression or DNA damage for cancer risk or things like that. Who knows, it's very exciting, early technology.

Ben: Diana, in 30 years time, on your podcast, you can be like, well, you know that thing that everybody goes into, that fancy EMR machines, 30 years ago I was on that very popular podcast, right before that guy got really famous for that terrible incident.

Laughter.

Jacqueline: Diana, did you have any other questions?

41:37

Diana: No, I think that about covers it. I understand what it's for, how it works and kind of the scientific principles behind it. Um, I also understand, yeah, why it doesn't work very well on people even besides the amount of time because there aren't as many free electrons running around in your body. But, it sounds like you're heading in a direction to be able to, kind of, introduce them, or tag them, in a way. So, yeah, maybe one day there could be an ESR sort of scan for peeps.

Ben: Well that was fun. Thank you Nicole, thank you Jacqueline. You have pleased me. Your efforts have born fruit and that fruit is sweet, here is the proteiniest fruit I could look up. Nicole, you get a soy bean.

Nicole: Yum yum, chomp chomp.

Ben: Alright. And Jacqueline, you get a peanut.

Jacqueline: Crunch, crunch, crunch.

Diana: Wait, are peanuts fruit?

Laughter

Jacqueline: Technically they are legumes.

Ben: I'd like to thank my guest, Diana Goodman, host of *Thirty Twenty Ten*, thank you for coming on the show Diana!

Diana: Thank you for having me and thank you for taking the time to explain everything. I feel, I feel empowered with knowledge now. I'm going to go tell other people about it and probably get it all wrong.

Ben: Okay! Alright everybody, that was super fun and now it's announcement time. So, first, I'd like to ask you to give us a review on iTunes. Or, tell other people about us online. Why? Because lots of people love physics but nobody knows about our show, relatively. So, people find out about our show maybe they'll want to listen and then maybe they'll want to talk to you about physics and then everybody will be happy and physicsy.

On another note, we're still humbly soliciting your donations. Your donations go to paying our server fees and our project to transcribe all the episodes when they come out and fix up the website and buy people microphones and thank you very much!

You can send us one time donations through PayPal off of our website or you can go to our sweet Patreon site and give us a recurring $2 donation. This particular episode of the Titanium Physicists has been sponsored by a collection of generous people. I'd like to start by thanking the generosity of John Edelman for his donation. I'd also like to thank Janetco Fifenberg, Steve Smetherst, Magnus Cristisen, Bart Gladys, and Mr. Stewart Pollack. Our emperor Courtney Brook Davis, Mr. David Lindells, Mr. Carl Lockhart, our eternal friend B.S. and Randy Dazel. A Miss Tina Roudio, the enigmatic Ryan, a gentleman named Crux, and Gabe and Evan Weans, David D and Dan Vale, a Mr. Alex, WTL, Mr. Per Proden, Andrew Wattington, Mr Jordan Young and John Bleasy. A Brittany Crooks, James Crawford, Mr. Mark Simon, Two Songs Gang of One, Mr. Lawrence Lee, Sixton Linason, Mr. Simon, Keegan Ead, Adrian Shonig, Andreas from Knoxville, Cadby, Joe Campbell, Alexandra Zany is great, Weena Brett, Eric Duch, Atein Raymond, and a gentleman named Peter Fan, Gareth Easton, Joe Piston, David Johnson and Anthony Leon as well as Doug Bee, Julia, Nora Robertson, Ian and Stu. A Mr. Frank, Phillip from Austria and Noisy Mime. Mr. Shlowmo Delow, Melissa Burke, Yaseem Omarasazee, Spider Rogue, Insanity Orbitz, Robert Johnson, Madam Sandra Johnson, Mr. Jacob Wick, a Mr. Jon Keyes, a Mr. Victor C, Ryan Klaus, Peter Clipsham, Mr. Robert Haupen, Elizabeth Theresa, and Paul Carr. A Mr. Ryan Knewl, a Mr. Adam Kay, Thomas Shiray, a Mr. Jacob S, a gentleman named Brett Evans, a lady named Jill, a gentleman named Greg, thanks Steve, a Mr. James

Clausen, a Mr. Devon North, a gentleman named Scott, Ed Lowington, Kelly Weinersmith, Jocelyn Read, a Mr. S. Hatcher, Mr. Rob Arizato, and a Mr. Robert Stietka. That's it for Ti-Physicists this time.

Remember that if you like listening to scientists talking about science in their own words there are lots of other lovely shows on the Brachiolope Media Network. The intro song to our show is by Ted Leo and the Pharmacists and the end song is by John Vanderslice. Good day my friends and until next time, remember to keep science in your hearts.

47:23

Nicole: I always like to think of that Star Trek scanner, the all encompassing, just, beeeeep.

Diana: Oh, yeah, you just run it over

Nicole: That's when you get in into

Jacqueline: Dr. McCoy's scanner, yeah.

Ben: It occurred to me, oh, no, wait, that wouldn't work.

Jacqueline: Dr. McCoy's…

Ben: Okay, that thing, they always have…

Jacqueline: Well, I just think…

Ben: Yeah, what were you saying? Hello?

Jacqueline: I was just saying, like, Dr. McCoy's scanner's got to have, like x-ray. ESR, NMR, probably some stuff we haven't even thought of yet.

Ben: Well, it's like, the medical tri-corder's got like a thing that they are scanning you with, right?

Jacqueline: Everything

Ben: But, it's got to be reflecting off your bones and guts and you know, blood cells.

Nicole: Yeah, it's taking all the signals it's got to have…

Ben: But, like the intensity, that beam that it's hitting you with must be bananas. Right? Because it's not like it's passing through you and you're detecting ambient absorption. You're detecting back scatter off of it.

Nicole: True, but you're also thinking about modern technology too, right. As you go deeper you get more sensitive, maybe you could isolate the background noises, like, obviously there are some huge technological problems with this scanner. But yeah…

Diana: The fact that it's held in a shaky human hand is kind of the one that always bothered me. I'm x-raying, beep, oh, he's broke his legs but your hand was all over. And there doesn't seem to be like a display, really, like…

Ben: I love that, I love rewatching *Star Trek The Next Generation*…

Diana: How does he know what it said?

Ben: … because everybody glosses over what they're looking at on their little pads, they just look down, it's not like on camera and you're like oh, I wonder what they're seeing…