When you think of the comic character the Hulk, you think BIG and that's what Dr. Biology does in this episode- he learns about a building-size instrument being used by a group of scientists. This monster instrument is called a synchrotron and is an important part of the XM2 microscope that is being built to look inside cells in a new way. Find out what biophysicist Gerry McDermott has to say about this powerful tool and also its link to the Hulk. Really there is a connection!

Transcript

Dr. Biology: This is "Ask-a-Biologist", a program about the living world, and I am Doctor Biology.

Hey! Check out those crazy sounds in the background. I'm standing on the catwalk above the Berkeley Lab's Synchrotron, also called the Advanced Light Source, or ALS.

In the previous show, we talked with Dr. Caroline Larabell and learned about her new microscope, the XM2, that uses X-rays to look inside cells. This microscope is the only one its kind in the world, and partly because it needs to be connected to a synchrotron to get the type of X-rays used to view inside the cells.

In fact, we talked about how this new microscope was able to do something similar for cells that we already do with our entire bodies, CAT scans. Which means computed axial tomography. In case you didn't know, CAT scan let doctors see our organs inside our body along with the other systems in 3D. And all this without cutting us open, which is a good deal as far as I'm concerned.

We also toured the National Center for X-ray Tomography, where the microscope is being built. It's one of several laboratories linked to the synchrotron. Today we get the added bonus of touring a synchrotron to learn how this giant, building-sized instrument works.

Our guest scientist and tour guide is Gerry McDermott, a biophysicist, who is part of the group building the XM2 microscope.

If you're the type that loves science fiction, you'll want to stay tuned because this has got to be one of the most amazing instruments built. It certainly looks like something out of a science fiction movie. From where I'm standing, I look around the entire building and there must be miles and miles of wires and tubes that look, well, a very colorful collection of different sizes of spaghetti.

Some of them are very giant; some of them are rather small. Some are red, some are blue, some are yellow, there's green. Every color you can imagine. All these wires and tubes then connect to dozens of instruments and mixed in with this scientific spaghetti is a very
common material we see in our own kitchens. Aluminum foil, now what's up with that?

Up next, our guest scientist will give us the inside story about how the synchrotron works and what seems to be a love of aluminum foil.

Before traveling here, I did some research and a little bit of reading on cyclotrons and synchrotrons and how they can make tiny things like atoms travel almost the speed of light. But just what the difference is between them and how they work was still a bit hazy. So, how about, Dr. McDermott, since we have you here, let's begin by talking about these different instruments.

**Dr. Gerry McDermott:** All of these different instruments and machines that you talked about are actually different stages in evolution, beginning with the cyclotron which was one of the very early instruments, maybe from the 1950's or thereabouts. The current instrument is called a synchrotron. That's the state of the art now. That's the most commonly used particle accelerator for doing biology.

**Dr. Biology:** And what are the particles we are accelerating?

**Dr. McDermott:** Usually they are electrons, tiny little subatomic particles. Kind of like back in the days, if you can remember, when televisions were big, old heavy things. The picture on a television was generated by electrons being fired at a phosphorous screen. We do something very, very similar.

We fire electrons from a thing called a gun, which is not really particularly more complex than a little filament of wire, like in an old incandescent light bulb. You have a piece of wire that's wrapped around in a coil, and you put some current and voltage across it and it spits off electrons.

Instead of hitting a screen, the electrons fly along a pipe that's been evacuated. This is called a linear accelerator. It's a big, long, straight pipe with nothing inside, nothing to interfere with the electrons path.

The electrons are accelerated using magnets. As the electron passes through the pipe, the magnets attract them and then repel them. So very quickly, the electrons begin to accelerate, they get faster and faster. Until eventually they get very close to the speed of light, which is 186,000 miles a second, which is really, really fast.

**Dr. Biology:** Wow, really fast. Let me get this, so we have the magnets and so they're basically either pulling the electrons or they're pushing them, right?

**Dr. McDermott:** Yeah. The electrons fired from the gun go along a tube; some magnets around the tube attract them. Then as the electrons pass through the magnet, they change and then it repels out the other side. So it's kind of like, in American football, they grab the ball at front and push it backwards through their legs to the rest of the team.

**Dr. Biology:** All right. I might have a silly question here. We know that all atoms have electrons. What I want to know is how do you separate the electrons from the rest of the
atom that you then use to accelerate around the synchrotron? Or do you leave them together? Is it the entire atom that's going around?

**Dr. McDermott:** When you heat a little filament, like a light bulb filament, electrons are spat off. The electrons are charged, they're negatively charged, so the magnetic field pulls them. Whereas the other particles don't have the same charge, they're much heavier, they're not charged, so you select the electrons only and the electrons are [sucking sound] sucked towards the magnet and the rest just kind of falls on the inside of the floor and nothing happens to it.

**Dr. Biology:** So the neutrons and the protons basically are too heavy, they don't go anywhere, and the electrons take off?

**Dr. McDermott:** Yeah, and on the filament you'll end up with a whole lot of atoms that are just one electron short. So you don't strip off all the electrons, you just strip off a few. The core of the atom is still clear. It's just some free electrons floating around and you accelerate them off and they get captured in the linear accelerator and then accelerated.

**Dr. Biology:** All right, so we've got these really fast electrons. We should talk a little bit that that's the linear one. But you actually have both a linear and something that's in a doughnut shape and we'll go on to that.

**Dr. McDermott:** The electrons, the linear accelerator, that's the long straight pipe, that just gets them very close to the speed of light. Then the electrons are bent using some big magnets into another circular pipe, or the pipe follows a circular trajectory. The electrons, once they're inside this pipe they are continually accelerated. And they go around and around and around, and every time they go around they get a little kick and they get a little bit faster. They go around, they get another kick, they get a little bit faster and they get closer and closer to the speed of light.

As you've probably seen from science fiction movies, nothing can go faster than the speed of light. If you do, then all kinds of horrible things happen, time goes backwards and it's just an all around disaster. So instead of going faster than the speed of light, the electrons begin to throw off some of this energy they get every time they get kicked.

The energy comes off in the form of heat and light and X-rays and ultraviolet light and infrared light, the whole electromagnetic spectrum. So electrons go round in a circle, get a little kick and as they go around for their next lap, they continually throw off light tangent to their circular path.

**Dr. Biology:** Now the magnets have some really interesting names.

**Dr. McDermott:** Yes, to keep the electrons going around and the keep kicking them with the energy, we have a whole series of different magnets. These are called insertion devises. We have bend magnets. We have super bend magnets. We have undulators and we have wigglers.

And the name, even this is very hardcore, high tech physics. The name describes exactly
what they do. So the bend magnets bend the electrons around a corner. The super bend bends them around a really tight corner. The undulators make electrons move up and down in a wiggling motions. And the wiggler does very big wiggles.

**Dr. Biology**: I love the names. I love them.

Early on some of these supercolliders were actually using atoms to smash them together and they broke apart into even smaller bits, which was rather unusual at the time. And they have these really cool names as well. My favorite are: strange and charm, which I think is amazing little sub-atomic units.

OK, so we've got this spectrum of light that's coming off of these electrons as they are accelerated. Let's talk about one other in particular, one that Dr. Larabell uses in her laboratory and they're using X-rays.

So, first of all, what's an X-ray?

**Dr. McDermott**: An X-ray is a form of light. It's a very high-energy form of light. Normal light, if you hold your hand up in front of a flashlight you block the light. X-rays are much, much higher energy and if the flashlight, instead of producing nice white, bright white light was producing X-rays, and you had Superman's eyes, you would be able to see right through your hand. Or if you put a piece of film behind your hand, using this X-ray flashlight, you would get an image of the film.

**Dr. Biology**: Yes, exactly if you've gone to the doctor, and you might have had a broken bone, and they did an X-ray, or if you go to the dentist they often do an X-ray. So a lot of us have actually seen what an X-ray film looks like but I don't know that we actually know how we can use the X-rays so it's kind of neat.

Now I've actually taken a flashlight and held it up against my hand and in some of the thinner areas you can actually see through it, it's cool. So we're just having a stronger form of light that can see through different materials. Let's go a little bit further; what are we doing with these X-rays at the synchrotron?

**Dr. McDermott**: Well in our case as a medical clinical diagnostic instrument called a CAT scanner. And if you are unfortunate enough to require a CAT diagnosis what happens is you lie down on a table and the table moves inside this huge donut shaped instrument. They are very commonly seen on medical drama programs. Inside the donut you have an X-ray generator, a small one, and an X-ray detector. Those move around inside the donut.

At the same time your table slides through. So you have lots and lots of X-rays taken of your body, your head, your abdomen, where ever happens to be requiring diagnosis. And when that happens the doctor can then generate a 3-dimensional picture of the piece of your body that they are interested in. That is called a CAT scan.

These are beautiful inventions, because our traditional X-ray is called a projection X-ray. You simply can see in two dimensions. So if you put your whole body in front of an
X-ray and you have film behind it, you get projection image. What that means is, it's a very flat two dimensional thing, so the ribs at the front of your body and the ribs at the back of your body all appear compressed on the film.

With a CAT scan you see in three dimensions. You can rotate around and you can see all of your internals organs, your heart, your liver, your lungs, your kidneys. And you can see it in beautiful detail.

What we are doing is, instead of your whole body going in the CAT scan we are trying to develop ways of just using a single cell or a single tiny piece of tissue and doing a CAT scan.

**Dr. Biology**: OK, now the CAT scan versus the X-rays. An X-ray is more or less a silhouette. So when you do this projection, you get the silhouette. And with the CAT scan, you really get to see the three dimensional structure.

So if you have ever done any gaming and you get to spin around a character and look at all the sides of it, that's what it allows you to do on the inside of the body, so we can actually look at the organs inside the body. That's really cool.

Now you've gone a step further because now we are just looking at a single cell and instead of looking at organs, we're looking at organelles. By the way, organelles literally means tiny organs.

So you have taken it really a big step into that teeny, tiny unit. What are we able to do inside the cells with this new microscope? By the way, if you haven't listened to the podcast on this cool new instrument that Dr. Larabell has, you have got to go listen to it. It's a fabulous instrument. It's huge. It doesn't look like any microscope you have ever seen.

OK, so let's talk a little bit about the inside of the cell and what we're seeing nowadays.

**Dr. McDermott**: Well, if you use a normal, or a regular light microscope, it is very hard to see any real detail inside the cell. There's a thing that light does, called refraction, where the light bends around the organelles and it becomes very confusing when you look at it.

When you use a light microscope you only see things in two dimensions. There are some ways to try and do three dimensions but the very nature of organelles and the way they interact with light, it makes up for some kind of murky You just can't make out exactly what's happening exactly what the shapes are. There always is a lot of doubt.

But in the same way that X-rays, going through your hand, give you so much more detail than simply a flashlight showing you some pieces of tissue that are thin enough to show you the blood and veins, a CAT Scan gives you beautiful, exquisite detail on the inside of the cell.
How all the organelles are organized, how big they are, how small they are, how they interconnect, how they interact as the cell divides and grows. How the cell looks inside, the architecture in a normal cell and then we can compare that to a cell from someone who has some particular type of disease.

**Dr. Biology:** Now as I look around at the synchrotron, from up here on the catwalk, I'm wondering about a few of the details. I mean, after all this is a really big instrument in a really big building. For example, just how much did this all cost?

**Dr. McDermott:** Oh, it was relatively cheap. A cool one hundred million dollars and that was back in 1987. So, I guess at today's dollar probably two or three hundred million dollars would be the correct amount.

**Dr. Biology:** Wow, and you also mentioned that it's constantly being updated. It's not as if it was built then and it's been in that state forever. As a matter of fact, you showed a really cool picture of the original control room and there were about, I don't know, four monitors. And now we just went in and looked and there are dozens of monitors, there's tons of information, there's all sorts of wonderful lights and flashing things. And there's always someone there watching it, right?

**Dr. McDermott:** Yeah. It's such a complex instrument and there are so many pieces that could go wrong. There's someone in the room 24 hours a day, seven days a week, including Thanksgiving and all the very nice holidays. Someone has to be in that room and watch all the monitors to make sure that nothing's gone wrong.

**Dr. Biology:** How big is the synchrotron? It looks big to me.

**Dr. McDermott:** In terms of size, it's about two-thirds the size of a football field. So it's pretty big, yeah.

**Dr. Biology:** It's pretty big. And there are others in the world that are even bigger, right?

**Dr. McDermott:** Yeah, yeah. There's a few. There's some in Japan and Europe, one in Japan and one in Europe. They're bigger. And the big daddy of them all is actually in Chicago at the moment in a place called The Advanced Photon Source. And it is huge. You have to cycle around it on a little three-wheeled bicycle.

**Dr. Biology:** Wow, to get around, that would be amazing.

OK. We talked about the light sources that we're getting out of the synchrotron. How bright is the synchrotron here?

**Dr. McDermott:** Oh, it's very, very bright. It's hard to describe and it would take me too long to count all the zeros, but if you know exponentials that the brightness of the sun is 10 to the 10 photons per second, and the ALS is about 10 to the 19, so it's nine orders of magnitude brighter than the sun, which is a one followed by nine zeros.

**Dr. Biology:** If it's a whole lot brighter than the sun, then it's really, really bright and we certainly aren't going to be looking at it with our eyes, are we?
Dr. McDermott: No. No, absolutely not. Although it's very bright, the sun is a huge, huge mass and there's a huge amount of energy coming from the sun. The light beam that comes out of the ALS is very, very small. It's about the thickness of maybe a human hair. It's focused in a very, very small area. But you still would not want to get it anywhere near your eyes or your body.

Dr. Biology: Now are most of the people that are using this facility for their light source, are they mainly using X-rays, are they using other forms of light?

Dr. McDermott: Oh, they use the whole spectrum of light. Facilities, synchrotrons like the Advanced Light Source produce energy across the entire range of the electromagnetic spectrum. So from ultraviolet, infrared light through visible light and out to hard X-rays.

Dr. Biology: Now this is another thing you could do on "Ask-a-Biologist", we have an article called, "Seeing Color". If you go there, there's a section in there that shows the light spectrum, both the visible and these other light spectrums that we don't think about a lot of times that are there, including microwaves are a light source. And it's a nice thing that if you want to get a visual, it's a great way to do it.

So is there anything unusual that has ever happened with the synchrotron here, it could be science or non-science, is there anything that comes to mind?

Dr. McDermott: I think the thing that most immediately springs to mind is the filming of the movie "The Incredible Hulk" maybe three, four years ago. Most of the science that's involved certainly in the first half hour or so of the movie was filmed at the Advanced Light Source. Watching the film was an incredibly interesting experience. Up to that point I always thought actors were grossly overpaid and underworked. And I got to see how difficult it is to make a movie and how much effort it takes to make a scene that lasts just a few seconds.

I also got to see some of the cool ways that they do computer animation, so yeah, that was a really interesting experience, watching that being filmed.

Dr. Biology: Did they get a film right where we're standing? Did they use this as a prop?

Dr. McDermott: Yeah. If you watch the movie, you'll see this scene that's sort of a little bit computer enhanced, but this is actually one of the scenes very close to where the Hulk undergoes his first transformations.

Dr. Biology: You know, when I walked in here, and I've been looking around the building, I said, "This is right out of a science fiction movie." And in this case, fact is better than fiction, right?

Dr. McDermott: Yeah. It's a combination of both.

Dr. Biology: Now speaking of science fiction and cool things in science and in fiction, what's that sound I'm hearing in the background?
Dr. McDermott: These are sounds that pumps make. These are incredibly fast rotating fans in a pump. It's kind of like if you imagine a jet plane engine, you know, when it's not operating you can see all the fan blades, and then as it begins to get faster and faster prior to takeoff you can see all the fan blades rotate really, really fast. This is what we have here is some pumps doing the very same thing, so they're compressing gasses.

Dr. Biology: Now the other thing I noticed, and I found amusing, is someone here selling or have stock in aluminum foil?

Dr. McDermott: [laughs] No. Everything's wrapped in aluminum foil and there's a very mundane reason for it. If you make a baked potato, the best way to make a baked potato in the microwave is to microwave it for a while and then wrap it in aluminum foil to keep the heat in and then let it cook on its own for a little while.

That's exactly what we're doing with all the instruments. We wrap them in heating tape, heat them up, and then wrap in aluminum foil and let them stay warm for a few days. And the reason we do that, we need everything to be under an extremely high vacuum, what we'd call a catastrophic vacuum leak. If the same thing happened in your car tire, the same level of leak, it would take more than 10,000 years for your car tire to deflate.

Everything has to be under extremely high vacuum and the only way you can do that is to heat all the molecules up so they're moving around really, really fast and then pump on it very, very hard with these fast moving turbo pumps. They're these pumps with a big fan that spins very, very fast.

So we heat them up, get the molecules moving really fast and then pump with a vacuum pump very, very hard and very, very strongly for maybe four or five days, or maybe even two weeks. And that sucks all of the air molecules and any hydrocarbon molecules that have come off your skin or any pollution. That just sucks everything out.

So the aluminum foil is just like the aluminum foil around a warmed baked potato, it's just to keep it very warm for two weeks.

Dr. Biology: We're standing on one of two rings. We have the linear part, the linear accelerator I can see, and there's an inner ring and an outer ring. What's going on there?

Dr. McDermott: Well, the inner ring is called the booster ring. It's smaller, as you said. The electrons come from the linear accelerator and they're held in this booster ring, where they're accelerated faster and faster. And once they get almost to the speed of light, then the electrons move into the larger ring, which is called the storage ring.

And in the larger ring, the electrons rotate around for eight hours. The same bunches of electrons spin around and around and around almost at the speed of light for eight hours. So they orbit, it's called orbit, they do that many, many, many millions of times and then at the end of eight hours we dump them. We run them in a piece of lead and then refill them with fresh electrons from the booster ring.
Dr. Biology: So right below us we have these electrons streaming underneath our feet at the speed of light.

Dr. McDermott: Very close to the speed of light. Yeah.

Dr. Biology: How cool is that? I mean it just amazes me. This is why we get into the science, just to be able to look at this and to think about what we can do with these.

You just never know where you are going to be when you get started. A physicist that gets into biology. A biologist that needs a big apparatus that's typically thought of for physics. So we have Dr. Larabell again, if we go to that show.

This is just one of the cool places. It must be great coming to work here.

Dr. McDermott: Oh, yes. It's one of the great things about being a scientist in a place like this. You come to work in the morning and you really don't know what you are going to do the rest of the day.

Dr. Biology: As I continue to look around the synchrotron, there is one disturbing thing. I see these flashing red lights. They are almost like the type you might see on top of an old police car. What are they telling us?

Dr. McDermott: They're telling us that the ring is energized, that means that it is actually operating just now. The accelerator, the synchrotron, when it is operating, nobody can go inside these concrete walls or concrete structures. Otherwise they would receive a potential lethal dose of X-rays.

So these lights warn us that the doors are all locked and that we shouldn't try to open them. Because it is a safety issue, if somebody even tries to open them, if they just turn the handle, the electricity that powers the synchrotron stops in less than a microsecond.

When the power is switched off the electrons immediately spin into the wall of the tube that holds them. No more X-rays are produced so it becomes safe immediately. So even if you walked over, you had the key, you turned the handle, before you got the key in the lock or even opened the door, the safety system would close the system down.

Dr. Biology: Let me ask you three questions. I do this with all my scientists.

The first question is: When did you first know that you wanted to be a scientist, or biologist or physicist? Was there a spark at one point that you can remember?

Dr. McDermott: I guess like most scientists, I'm guessing most scientists answer the same, that there has never been a time when you felt that it was a certain point. But I guess on of my earliest memories, my younger sister when she was born and my parents brought home from the maternity ward, I remember prodding her, as she was lying in her baby's crib, with a stick, to see what happened. I guess that science, when you see something you are always prodding it with a stick.
**Dr. Biology:** Ah, so you are an empirical scientist even at a young age. Empirical meaning, let's try it, see what happens. For science we think of it as experimentation and observation of the results.

OK, on to my next question: What if I took away your science career and you had to pick something else, what would you be?

**Dr. McDermott:** Oh, I would probably be a teacher. You may ask why don't I do that now. It's just too hard work. It's really, really hard. Really difficult, really tiring. So, yes, I probably would teach science.

**Dr. Biology:** All right. And the last question is: What advise do you have for up and coming physicists or biologists or those that are going to combine the two, what would you recommend for them?

**Dr. McDermott:** I guess the best sage advice that I got and it turned out to be very good, really good. My graduate school adviser he always told me just to do what you really enjoy and if you don't enjoy it, don't do it.

**Dr. Biology:** I have to agree. Not only enjoy but be excited about it. Science is fun and that's something that we often miss when we are going to class. We're in it not to be nerds; we're in it because we get to do some exploring. Almost on a daily basis we might see things for the very first time. Or discover a new species.

You could even solve the genetic mystery that would provide the cure for a disease. That's what science is about. It's not memorization, it's not doing hard equations, it's exploring, it's a frontier that is limitless.

**Dr. McDermott:** Yes, that's true and one of the fantastic aspects of way to look at this is, in the same building you have physicists you have mathematicians, you have chemists, biologists, cell biologists. One of the really interesting things is when you try to explain your cell biology experiment to a physicist. Quite often they will ask you very simple, very naïve questions, maybe they didn't even do biology at high school.

It's quite often those very simple naïve questions are the ones that turn out to be the most productive. Those are the questions where immediately when you ask it you think, oh, good grief, that's terrible. Then when you think about it constantly for days, then you realize that it's actually something really, really important.

**Dr. Biology:** Very fundamental. Actually we have people and I will say very brilliant people and they have ages ranging from, say, three years old on up to well even the adults I can count in. But I would have to say the young ones that send us questions that do exactly that. It sounds like, oh, that sounds so simple and then all of a sudden you think about it a little bit more and you think, well, that's not simple. It really does reveal a very keen awareness and very good observations.

I think that's one of the things scientists are good at. They are good at observing things and then trying to figure out what is going on.
Dr. McDermott: Yes, that's very true. Quite often you expect the most difficult questions to be asked by professors with thirty years experience and multiple Ph.D.s. It's actually very seldom the case. The most difficult question I ever get asked are actually by children and young students, you know. An eight-year-old kid will ask me a question and I cannot answer, no matter how hard I try.

That's one of the fantastic things about science that the more you actually learn, the more you realize how little you actually know.

Dr. Biology: How true that is.

I want to thank you for joining us here on "Ask-A-Biologist". It's been wonderful learning about the synchrotron.

Dr. McDermott: Sure it was a pleasure.

Dr. Biology: You've been listening to "Ask-A-Biologist". My guest has been Dr. Gerry McDermott, biophysicist and part of the team of scientists building the new XM2, X-ray Tomography Microscope, which is part of the National Center for X-ray Tomography.

They're located at the Berkeley Lab Synchrotron, which is in Berkeley, California.

The "Ask-A-Biologist" podcast is produced on the campus of Arizona State University. And even though our program is not broadcast live, you can still send us your question, using our companion website, the address is Ask-A-Biologist.ASU.EDU or you can Google the words "Ask-A-Biologist".

I'm Dr. Biology. Standing where one of the scenes from the movie "The Hulk" was filmed. You know what, I think I'm going to go out and rent the movie just so I can see what it looks like myself.