Ask a Biologist vol 023 Topic: Nanobiology Guest: Stuart Lindsay

Tiny Matter -

It turns out that scale matters when it comes to tiny objects in the nano world. How tiny are we talking about? The nano world has objects billions of times smaller than what we normally see with our eyes. Physicist and nanobiologist Stuart Lindsay talks about nanotechnology and what might be possible in the future using these tiny objects.

Transcript

Dr. Biology: This is Ask-a-Biologist, a program about the living world, and I'm Dr. Biology. In today's show, we get a chance to learn about some very tiny things and how they behave differently. What we'll be talking about are part of what we call the nano-world.

In fact, it's very likely you've heard the word "nano" before. There's nanotechnology, nanoengineering, and of course nanobiology. All these words use the prefix "nano," but just what does it mean? Well, it means "extremely small," and to be more precise, "nano" describes things that are a billion times smaller than a meter. Now, if you're not a person that uses the metric system, a meter is about 39 inches long.

Now, if you're like me, it's not easy to understand just how really small one-billionth is, mainly because we can't see them; they're too small. So let's try this out. Get a piece of paper, a ruler, and a pencil. Once you have all these items, draw a line one inch long. For those that use the metric system, you can draw a line 2.5 centimeters long, which is about the same as an inch. And for those that don't have these items, don't worry about it; I just want you to imagine such a line.

Remember, it's only one inch long and about one-36th of an inch wide, depending on the width of the tip of the pencil you're using. Next, we're going to magnify the line 100,000 times to see just how big it will get. Doing a little math, we see our magnified line now measures 8,333 feet long, which is more than a mile and a half, and it's 231 feet wide.

Now, this helped me get the idea of scale, but I still needed some help understanding how big this magnified line is. So I took the dimensions of my favorite car--it's a bright yellow 1974 Volkswagen Beetle--and I calculated about how many I could fit on the magnified line. It turns out I could place about 625 of my favorite cars, end-to-end lengthwise--this is on the magnified line--and about 46 of them side-by-side across the width.

If we fill the rest of the space on the line with cars, we could put a total of 28,750 cars. And that, I have to say, is a lot of yellow Volkswagen Beetles.

And this, well, it's only if you magnified our line 100,000 times. But what would happen if we magnified the line a billion times? By the way, a billion is written as a one with nine zeros, which is four more zeros than our line activity we just did.

If we pretend our line magnified a billion times is a giant piece of carpet, how much area do you think we could cover? Do you think we'd be able to use it to cover all the ground in your city? Maybe the entire state of Texas? Would there be enough carpet for us to do all the continents on the Earth? Remember, there are seven continents. Or could there be enough to cover the entire earth, all across the land and oceans? What do you think?

Well, after searching Wikipedia to find out the area of different land masses, and using a little more math to calculate the size of our line, it turns out our magnified line, that, remember, began only as one inch long and one-36th of an inch wide, now magnified a billion times would be enough to carpet all of South America and have a little bit left over. Now we begin to get an idea of scale. And I hope this gives you a pretty good idea of how large something becomes when it's magnified a billion times.

In today's show, our guest scientist will help us get an even better idea of what the world looks like and how it behaves when we look at things that are a billion times smaller.

Dr. Stuart Lindsay is the director of the Center for Single Molecule Biophysics at the Biodesign Institute at Arizona State University. He's also a professor in the physics and chemistry departments at ASU. Professor Lindsay has been investigating the nano-world and, in particular, the nanobiology world, for more than 20 years.

Today, we get to learn what is found in this tiny world and how things this small don't always behave the same as objects that are part of the world we can see. I'm also hoping that we get a chance to talk to him about a very interesting hobby he has. Welcome to the show, Dr. Lindsay.

Dr. Stuart Lindsay: You're welcome, Dr. Biology.

Dr. Biology: So we just went through an activity to get an idea of how large something becomes when it's magnified a billion times. How about we go the other direction and first talk about tiny things that exist in the nano-world? Can you describe some of the things we might see if, say, we could shrink down to the size of a nano-object?

Dr. Lindsay: Well, the world would look very different to you if you were a little nano-person looking around you. Things wouldn't look solid the way they do to us in the big world. In the tiny world, you'd see that you can't shrink forever, because you get down to the size of the atoms and the molecules, the very tiny components of which everything is made.

The second thing is, these atoms and molecules, your neighbors in the nano-world, would look incredibly different from the objects in the big world. In fact, they'd have fuzzy edges, and you wouldn't even be certain if they were there at all or not. And that's because the nano-world is ruled by a very strange set of laws called quantum mechanics. So things behave differently in the nano-world.

The second thing you'd see is that these atoms and molecules are rattling around, colliding with each other. It's actually a very violent world down on the nano-scale, and we just don't see it in the big world. It's very different.

Dr. Biology: Well, you're a professor in the department of physics and chemistry at ASU, and many folks may not think about it, but physics and biology and chemistry, man, they're a great combination. And you certainly have been involved with all of them for quite some time. In fact, you're one of the pioneers using a cool instrument called an atomic force microscope, and you use it to see into the nanobiology world. Can you talk just a bit about the atomic force microscope?

Dr. Lindsay: Sure. The atomic force microscope is an amazing little instrument--I think you'd be shocked, if you saw one, at how tiny and simple it is--that uses a probe dragged over a surface to feel at the atomic scale. And what is so staggering about this instrument is it operates very simply. It's easy to make. It's cheap to make. But it gives you a set of eyes that can see on this nano-scale, so you don't have to imagine anymore; you can see atoms.

The instrument itself was so easy to use and opened so many scientists' eyes to what happens at the nano-scale that it was really the invention of the AFM that brought the word "nano" into the popular consciousness.

Dr. Biology: I can remember, actually, when I first heard about an atomic force microscope. I come from a background where I'm using light microscopes and electron microscopes. And an electron microscope can be huge; it can take up a whole room. So I'm thinking of an atomic force microscope, without seeing any descriptions in any of the journals.

And the first time I went to see one, I was so struck, because I walk in, it's smaller than a coffee can, and it's hanging from a set of bungee cords. And it looks so simple, but it has such a very powerful capability about it. Well, the AFM is just one tool you can use to explore the nano-world. What are some of the other instruments? Because, quite frankly, again, we can't see it, so we have to have these special eyes to get down into that billion times smaller world.

Dr. Lindsay: Well, you mentioned another one, the electron microscope, and that complements the atomic force microscope. The atomic force microscope will feel over a surface, touching atoms. The electron microscope actually passes beams of electrons through nano-objects, and so you look at the depth of the object.

Other tools, one can put optical dyes that will re-radiate light onto nano-objects. And even although the light microscope can't see on the nano-scale, it can see the little colored flag that you've attached to your nano-object, so you can follow the motion of single molecules, for example.

Dr. Biology: OK. Besides being very small... we talked about this really violent world, if we were able to get that small, the nano-objects are also very interesting and maybe even more interesting because of the way they work. They're so small that the usual principles don't apply. Can you talk about some of the ways nano-objects behave differently?

Dr. Lindsay: Sure. So, if I stuck a hunk of sodium on the desk it would just sit there. But if I put sodium in water, and it dissolves into atoms, it undergoes a very violent reaction, but it does that because of the way that it's jostled by the water molecules. So atoms are the things that take part in chemical reactions, so... a bulk lump of anything is quite stable, it's not going to go anywhere, but you take sodium and put it in water so that it can dissolve to its constituent atoms, and you get a really violent explosion. So chemical processes are actually driven by these violent collisions that occur on the nano-scale.

Dr. Biology: Let me get this straight. If you go down small enough, things that appear stable at a large scale actually are explosive.

Dr. Lindsay: That's true for some materials, absolutely.

Dr. Biology: And sodium, we're just talking about simple table salt?

Dr. Lindsay: So, table salt itself can undergo reactions in solution: once again, a crystal of table salt looks nice, perfectly stable stuff that's going to sit there on your dinner plate, but actually when you put it into water and it dissolves into its constituent atoms--they're actually called ions because they carry charges--it becomes pretty reactive stuff. And as a matter of fact, if you drive cars in the cold parts of the United States where the put salt on the road, you know it's reactive, because your car falls to pieces as the salt makes it rust.

Dr. Biology: Ah yes, yes I do recall, growing up in Colorado actually and the mountain roads there with the salt. Well on a previous show, we got to talk about when good cells go bad, and it was, in particular talking about cancer cells, and we got to talk a little bit about genes and genomes with Dr. Michael Barrens. Dr. Barrens explained that the genome is the entire set of genes, the instruction book that tells how an organism is going to be built and how it's going to work. What we didn't talk about was how long it took to sequence the human genome the first time, and there was a project called The Human Genome Project. So, how much did it cost to do the Human Genome Project and how long did it take to do it?

Dr. Lindsay: Well we can go back to your favorite word Dr. Biology - billions. It cost billions of dollars and so... the kids listening to this program, I think now understand that that's an awful lot of dollars, and it took more than ten years.

Dr. Biology: OK. So now why did I bring that up? I brought it up because I'm reading about your research, and one of the things that's interesting is that your research is actually looking towards a future where an entire genome can be sequenced in a few hours. How will nanotechnology help reduce the time it takes to sequence a genome?

Dr. Lindsay: Well the way genomes are sequenced right now is that they're chopped up into very small manageable fragments, and so each fragment can be chemically analyzed, and then an enormous computer puts together a vast amount of work and finally figures out the sequence of the genome. If you could take the strand of DNA, which is what it encodes the genome inside a cell, and stretch it out--and by the way if you could do this and remember that it's nano dimensions--it's got so many component pieces that if you did this, you'd have a six foot string of DNA, taken out of a single cell. Amazing right?

Now imagine if you could pass this six foot string through a tiny little reading head that instead of chopping the DNA up, walked along the DNA and said, "This is this letter of the code, this is the next letter of the code, this is the next one..." and so on. And there are ways that this could be done, and we've made pretty good progress actually on some of the way that you can read bits of the code, and we're now working on trying to put together the little reading head that would do this.

Dr. Biology: At the nano-scale. Well, if you're able to do this, about how much do you think it's going to cost, instead of billions of dollars?

Dr. Lindsay: Well, the National Institutes of Health has a thousand dollar genome program. It's going to take a while [laughs] till it gets to that level. So it's called the thousand dollar genome program, and we'd like to think that costs would come down to that, or even less if it becomes widely available. And there's really no reason why it shouldn't be possible to sequence an entire genome, certainly in time scales of many hours.

Dr. Biology: Wow! We go from taking over 10 years to sequence the human genome to several hours, and from billions of dollars down to thousands of dollars, or a thousand dollars. This is exciting stuff! But do you see that, besides the plus side of sequencing a genome rapidly and at a relatively low cost, there's also a negative side? Could we talk just a bit about both the pluses and minuses of this brave new world of individualized gene sequencing?

Dr. Lindsay: OK. Well, let's start with the pluses. The pluses are that we're given generic medicines and treatments by our doctors. They figure everybody who presents a certain set of symptoms is going to get cured by the same course of treatment. And you know and I know that that just isn't true. So if you can read the genome of every individual, you can tailor medical treatment to a way that matches the way their body's actually put together. So that's the great benefit.

Some people would argue that if insurance companies got a hold of this information, it would make our life difficult. And as someone working in this field of biomedical research, let me say the single most frustrating thing, to me, is that the United States, spending more than any other country in the world on health care, is ranked 27th in outcomes. Our political system for administering health care absolutely stinks. And speaking not as a scientist, but as an American, we should be ashamed of that and fix it.

Dr. Biology: OK. Well, that's a good point, and one that I'm sure everybody would like to maybe chime in on at our website.

We've talked about the benefit and drawbacks of improving the time and cost to sequence an individual genome. The benefit, you talked a little bit about. I'd like to go into a little more detail. For example, I like the idea of custom medicines. And in particular, we think of, say, cancer, as a singular type of disease, when in fact there are many forms of cancer. And even if the different forms of cancer, whether it be breast or skin or lung cancer, they all behave differently in each person. So this individualized medicine sounds like it could be really cool.

So, is there something in the nanotechnology world of the near future that might help us treat cancer that we should be made aware of?

Dr. Lindsay: You're right. Cancer's a very individual disease. And if you had your own chart of the dangers that confront you because of your genome, Dr. Biologist's own genome, you could take evasive action. And it may just be as simple as avoiding certain foods, or knowing that you've got to avoid bright sunlight or what have you. This is something you could be told as a kid. And I'm sure that a large fraction of the people who get sick with cancer could just avoid it altogether.

If you were one of the unfortunate folks who got it, then a treatment could be chosen that's tailored to your particular type of cancer. Because I think, as we learn more about individual genomes, our understanding that cancer is already a complex disease, well, it'll look simple by comparison with what we're going to learn about. And we're probably going to learn that there's almost one type of cancer per person.

Dr. Biology: That brings up an interesting point. Nanotechnology, nanoengineering, nanobiology--we're really just at the beginning, aren't we?

Dr. Lindsay: Yes.

Dr. Biology: What do you see will be the future for nanobiology? And I'll say 25 years out and, say, 50 years out. And if you can go as far as 100, please do.

Dr. Lindsay: OK, well I think there are two things that I am sure are going to happen. If you build things on the nano-scale: Instruments, machines and actually computers are a good example. They work as well as they do because they have nano-components in them. You can process huge amounts of information.

So, biology goes from being a generic description of how a frog is put together to a molecular description of all the various types of frogs that genomes make. So, you go from having textbooks worth of information to having billions of textbooks worth of information and nanotechnology will build the instruments and the information storage systems and the data analysis processes that will turn biology into a manageable subject. That's one thing.

The second thing is that as we understand nano-processes and nano-machines, as we get to sort of be bodies with this atomic world I was talking about at the very beginning. And we look more closely at these processes that occur on that leg scale, we will start to understand how biological machines work.

In other words, what makes a muscle contract, what makes a cell swim, we will understand that at the molecular level. So, we will have an insight into the processes of life and understand them in a way that right we understand cars or radios because they will become simple to us when we have the tools to look at them properly.

Dr. Biology: Am I going to have a computer that will basically be the size of my fingernails?

Dr. Lindsay: We are pretty much there already, right. So, I think computing is an area in which nanotechnology has gone about as far as it can go. It is a very interesting limit in the process, which is you simply cannot handle information very much more densely without boiling up your computer chips.

So, computers of course they will get smaller and more and more powerful, but if the nano-tools that go with it, if the chemical analytical tools, the tools to let you look inside cells. In fact the tools that let you follow the life of things at the nano-scale, the very tools to let you do what I talked about at the beginning of this program, which is to shrink yourself down and become a nano-observer at the nano-world. Those tools will be made available.

Dr. Biology: Oh now, that is cool, that is what I am looking for. If you want to be a nanobiologist, do you start out in physics or do you start out in biology or can you start out anywhere you want as far as the sciences?

Dr. Lindsay: Well, I am kind of prejudiced because I started our in physics, but it is very interesting. I mean I think physics is a great thing to learn if you want to learn other stuff, but it is a very bad idea to stop at learning physics. Because trust me, the world is a lot more interesting than balls rolling down inclined planes [laughs], but physics gives you a great set of tools.

By the same token, I know a lot of biologists who are really great at physics and math. And one of the wonderful things about how we teach people today is there is much more of an integrated approach. You no longer are a physicist, a chemist, a biologist, but you get a chance to take classes in everything. And this is great because this means each individual with those individual genomes can go do what interests them most. The key though is spending time learning science.

Dr. Biology: Right and I will have to say that, of course, being on the biology side, I am prejudiced. But I am only prejudiced in the sense I think biology pulls all those disciplines together. You are right, we do use physics at times, we use chemistry at times, we use math often and it is just a really nice discipline to pull those components together.

Dr. Lindsay: Absolutely.

Dr. Biology: Well, one of the things I would like to do on this show is ask three questions. All my scientists that come on here, I always want to know these, so the first one is: When did you first know you wanted to be a scientist and I will say slash biologist, but we will say physicist in this case too?

Dr. Lindsay: When I was a little boy and actually sort of sadly I thought atomic bombs are really cool things, right. I mean little boys like big explosions. I don't think that way now, but I remember being absolutely fascinated with the nuclear weapons program and the idea of radiation, radioactivity and so on. And so I think when I was about six or seven, I remember writing to my father that I wanted to be a nuclear physicist.

Dr. Biology: Wow, since you were seven and nuclear physicist? OK. If you weren't a physicist and you weren't working in nanobiology, I am going to take the scientist basically away from you, what would you be?

Dr. Lindsay: So, I can't be a scientist?

Dr. Biology: Right.

Dr. Lindsay: I would probably be a construction worker, is that OK?

Dr. Biology: Absolutely. Big buildings or homes or what do you want to build?

Dr. Lindsay: Oh just anything, I love building stuff.

Dr. Biology: You love building stuff? That is very cool. Well, on a side note, you have a very interesting hobby, it is called spelunking and that is a very cool name for exploring caves. How did you ever get started exploring caves?

Dr. Lindsay: Oh, by accident. You know, when I was a young teenager, I had the bad habit of smoking. And when you do that at the school, you have to find a place to go hide to do it, right. And so, I with some buddies happened to find a cave entrance and this was just thrilling. A little hole under a rock and you go into the little hole and suddenly you are in this big room with a vast shaft that disappears into the bowels of the earth, I mean how exciting can it get.

Dr. Biology: So, how long have you been doing this then?

Dr. Lindsay: Oh I think since I was about 12.

Dr. Biology: Wow!

Dr. Lindsay: OK, which is a very large number of years, you are going to be kind to not my bosses how many.

Dr. Biology: I am not going to, you are right. Actually, we had a guest on here and I think one of the things I said about being a scientist, one of the key components is never lose the child in you. So, I always say that my scientists are very young...

Dr. Lindsay: They are childish.

[laughter]

Dr. Biology: Well, you know, if you are not easily amused, if you don't really like seeing things that will not necessarily blow up, but you want to see things happen even on the nano-scale, maybe science isn't for you, but for those that are really intrigued by simple things, I think it is really the way to go. One more question, what advice do you have for young scientists?

Dr. Lindsay: Well, pretty much what you just said, don't lose the magic. Because I think when you start learning about science, there is just a wonder about these amazing things that the brilliant men and women who have been scientists before us have discovered. I mean it is just the whole world of ideas, but then a wonderful thing happens to you if you stick with it for long enough, you know. You go do a piece of research and you go into it thinking one thing and mother nature picks you up and slaps you around the face and says, you know, you doofus! I didn't work like that.

And I think to me a best and most exciting thing about science and it will come after some years of sticking with it is when you learn, you are basically dumb, but the rules of science generate new knowledge. And the first time you are in a lab and you find new knowledge is one of the biggest thrills in the universe.

So I'd say to kids who are getting interested in science now and reading the books, stick with it because a time is going to come when you can make discoveries for yourself. And in fact, you know, when you are little kid it is nice to think, yeah I know how the world operates, everything around me is secure and nice. It is actually a lot more exciting to know that you really don't know, but you can find out some of it.

Dr. Biology: That is excellent advice. And maybe there will be some of the future nanobiologists out there.

Dr. Lindsay: Maybe.

Dr. Biology: Well Dr. Lindsay, thank you for visiting with us today and letting us in on the tiny world of nanobiology. After talking with you, I can hardly wait to see what the future has to bring.

Dr. Lindsay: Thank you.

Dr. Biology: You have been listening to Ask-a-Biologist and my guest has been Professor Stuart Lindsay, the Director of the Center for Single Molecule Biophysics at the Biodesign Institute at Arizona State University. In case you might want to see all the mathematics used in the line activity, just visit the podcast section of Ask-a-Biologist and click on the "content" link for this episode.

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