Mathematical Aspects of Biomedical Electronic System Design
Lecture 07
Biological Tissues as disordered systems

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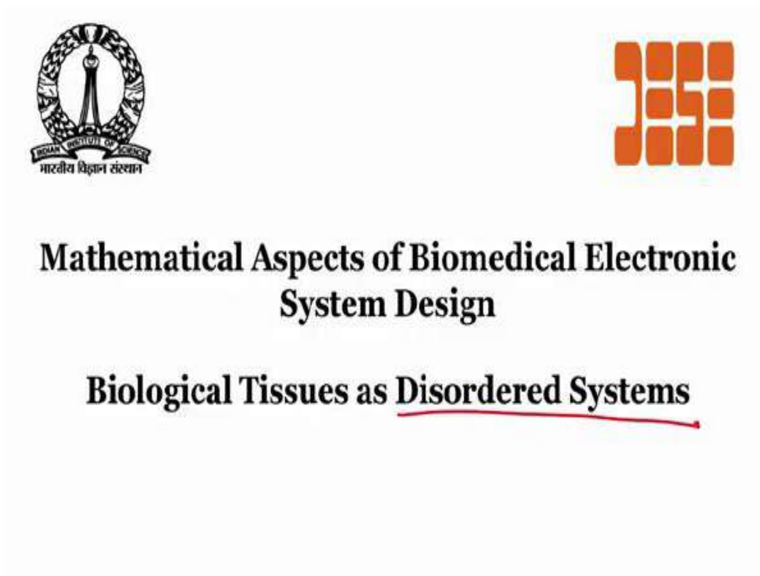

Hello everyone, welcome to the course mathematical aspects of biomedical electronic system design, this is a TA session, which will be focused on biological tissues as disordered systems and to share the TA for this course. This particular topic is considered to be an advanced topic in the field of biological systems, especially, when it comes to the application in biomedical device design and analysis of physical properties of tissues. So, let us begin with the first word that we see in this particular phrase which is not very common, which is disordered system. So, what does a disordered system mean?

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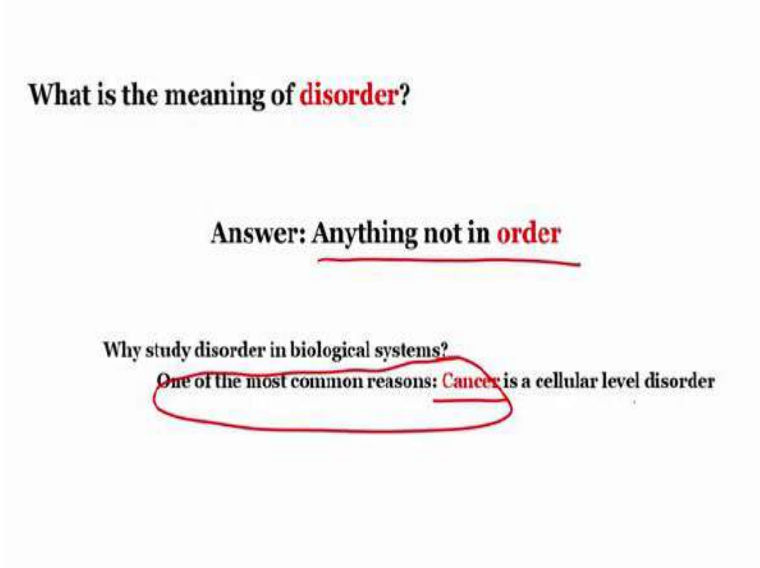

What is the meaning of disorder? Any layman would answer that, anything not in order then, why the question that arises here is why should we study disorder in biological systems. So, one of the most common reasons could be that cancer a very, a very big challenge in terms of medicine, in terms of medicine and in terms of research and a very, a very serious disease, which is spread, which is spread all over the world. And it is increasing by the way is a cellular level disorder.

So, let us understand that, how the cellular level disorder progresses in biological system, many of you would not be very familiar with a cellular level disorder in ordering. So, what we have done is, we have divided this whole TA session into three parts by giving examples. So, we took examples which are relevant to designing biomedical systems, and it will help you an understanding eventually disorder in biological tissues.

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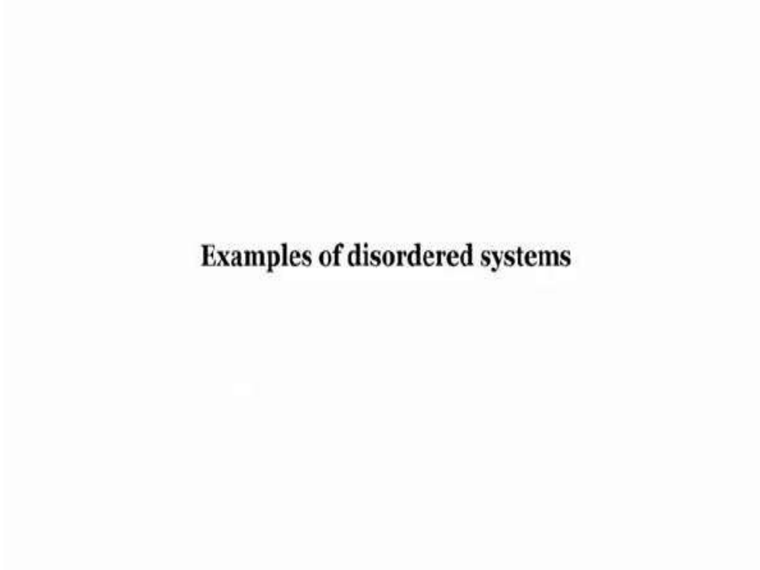

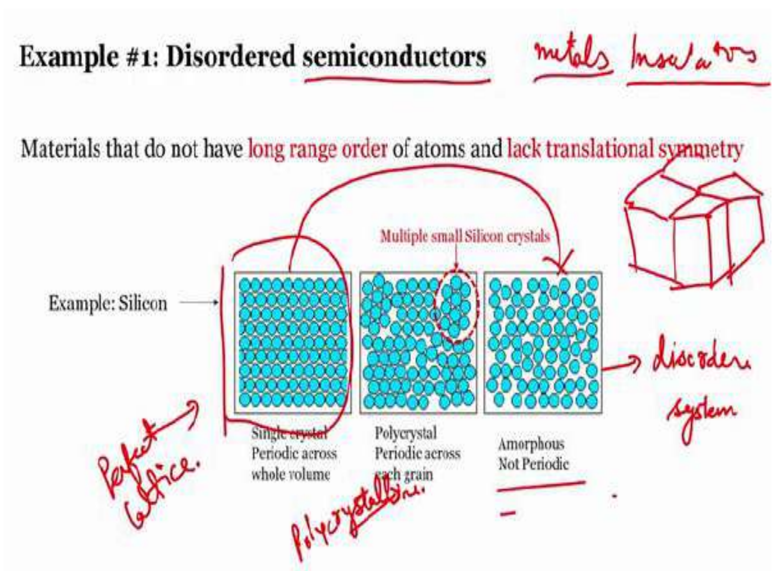

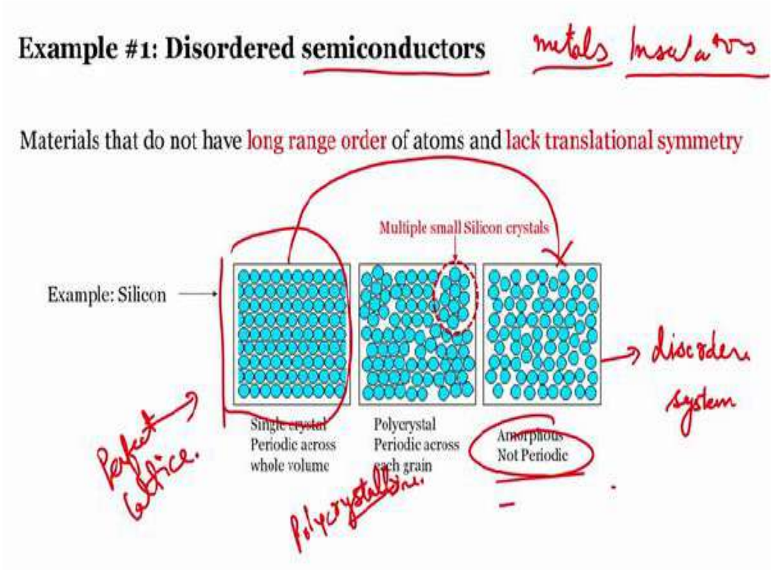

So, let us take one by one the examples, the first example is disordered semiconductors. So, most of you would have been aware of three types of materials namely metals, insulators and semiconductors, metals which seamlessly conduct electrons, insulators which do not conduct electrons, or charge carriers in semiconductors under certain conditions, certain voltages allow transport of charge carriers.

Now, within the semiconductors, there are different class, which can be defined depending upon the structure of the semiconductor. So, let us have a look at it. The first box that you see here, filled with blue balls, defines a very ordered structure, if you see all the rows and columns, it looks like a very ordered matrix is as if someone has put every single item one by one to make it perfect lattice and that is what it is called, this is something called as a perfect lattice. This is something you might have studied in your first semester of your undergraduate studies, as a part of modern physics.

Now, second class of material, you do not pay much attention to the complete order as you do in single crystal, but there is localized ordering, as you can see in patches, these atoms follow some kind of ordering locally, this kind of system is called poly crystalline. And the last one, which is of interest for us is amorphous and or not periodic. And this is a very classic example of a disordered system.

So, as now it would be very much clear to you, what exactly a disorder means, going from a complete order to a complete chaos, or an order to a disordered system, where there is no long range symmetry, there is no translation symmetry.

What does it mean by transition symmetry is? Let us say if you have a unit cell, a unit cell is the smallest component of any lattice. If you have a unit cell, let us say this is a unit, is a unit cell and you want to make the entire lattice with help of this unit cell you can do it by placing this unit cell at regular intervals, you can associate like this and then you can place another cell like this, you know and so on and so forth. In this way, you will have an entire system, or a solid created just out of unit cell, which is possible in an ordered system.

Contrary to that, in a disordered system or amorphous solid, this is not possible, because there is no such unit cell that exists because there is no order in the first place. So, let us see how does it affect the electronic structure of this, electronic structure of this system, when compared to the ordered system.

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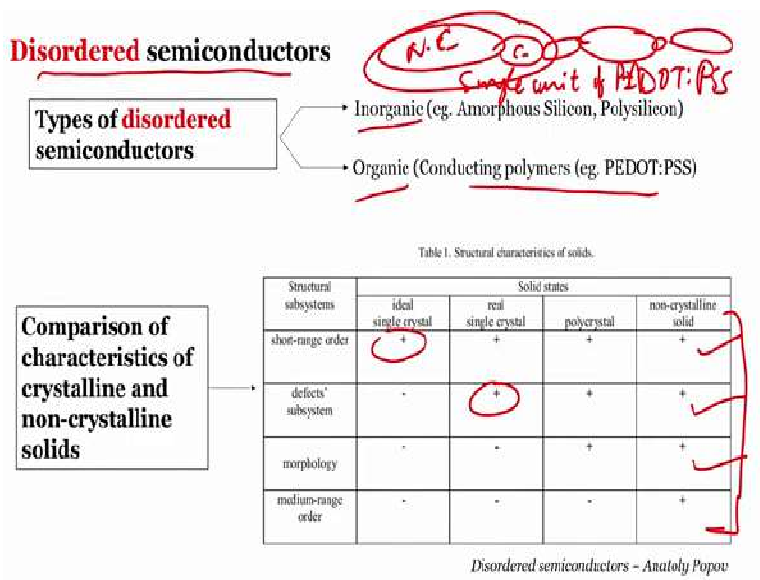

So, before we talk about the structure, let us see what are the examples of different types of disordered semiconductors and this is where I will try to emphasize why it is important for any biomedical system designer, to be aware of these kinds of semiconductors. So, disordered semiconductors can be classified into two depending upon the intrinsic constituent materials that are present there one is inorganic, like amorphous silicon, polysilicon, amorphous means completely disordered, poly means somewhere in the middle which we have seen in the previous slide.

Now, there are also some organic systems which are made out of polymers, polymers, we see in our daily life like, rubber band, plastic tumblers and all, but these, but those polymers are completely insulators, this is a different class of polymers. For example, let us take an example of PEDOT, PSS, where there is a non-conducting island, associated with the conducting island, this is a single chain of, this is a single unit of PEDOT PSS.

So, this is non conducting, this is conducting, in this way distinct polymerizes, there are several such conducting, non conducting chains, conducting non conducting chains, that form an entire unit of PEDOT PSS, which is eventually electric conducting.

But again since, since this particular polymer does not have any long range order, which means it is only locally ordered, if you see the entire structure, which is out of the scope of this course, you will find that one cannot deduce that okay this particular unit will repeat itself, it may repeat itself at spatially different, spatially different locations, there would not be any ordering spatially in the entire structure of PEDOT PSS to be able to call it as a crystalline structure.

So, what so how does it so how does it translate two different kinds of properties as far as disordered and an ideal single crystal is concerned. So, this is a small table that talks about different properties such as, short range order, defects of system, morphology, medium range order.

So, if we talk about an ideal crystal, the only common thing between all this is, short range order, ideal crystal will have short range ordering as well as long range ordering, which is not something surprising as a unit cell, which I discussed some time back, can repeat itself for a very small spatial arrangement, as well as for the entire length of the solid length and breadth of the solid.

Whereas, if we talk about a real single crystal, now what is the difference between ideal and real, due to the laws of thermodynamics, entropy can never be 0 and therefore, there will be some, or the other kind of disorder. And that is why real crystal will have some kind of defects and that is what is pointed out here.

In polycrystalline, there will be some ordering, but that will be localized ordering, there will be patches, where unit cells combined together to form order ordered areas, but globally, if we talk about the entire solid in a polycrystalline material, it will be disordered.

And then finally, our, our interest, which is in disordered cell semiconductor, or amorphous solid, it will have all these properties state, which is it will have short range ordering, it will be, it will be having a very high density of defects, and its morphology will be very different to us to give you an example, if you take us a clean and cleaved single crystal silicon wafer and if you take a polycrystalline silicon wafer, you can make it out just by the look of it, the, the axes which will be, which will be cleaved will give a different shining and that shining comes due to proper ordering of unit cells, which is absent in amorphous solids. So, let us see how does it translate to electronic band structure.

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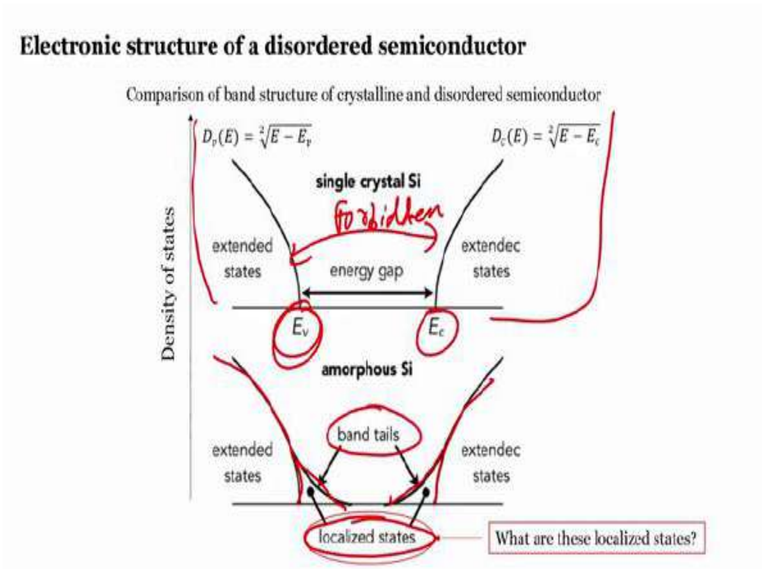

So, this is a very familiar diagram, most of you would be aware of this, that how in a single crystalline silicon, intrinsic silicon, I am not I have not doped anything in this, how the x, how the conduction band sorry conduction band and valence band are starkly defined and there is nothing in between, this is something called is Forbidden Zone. What does it mean? It means there cannot be any state available for the charge to or get occupied.

Now, this is something we know, let us see what is something we may not know, let us have a look at the density of states versus band diagram for amorphous silicon. In this case, even though the bands here like the case of single crystal are clearly defined, but emanating from either side are band tails, as you can see here, and these band tails have something called as localized states, localized state is a quantum mechanical phenomenon, localization is a quantum mechanical phenomena.

So, we would not go into much detail, but I will just give you a brief introduction that, what are these localized states and how do they create such a big difference as far as electronic transport is concerned between a single crystal and amorphous silicon.

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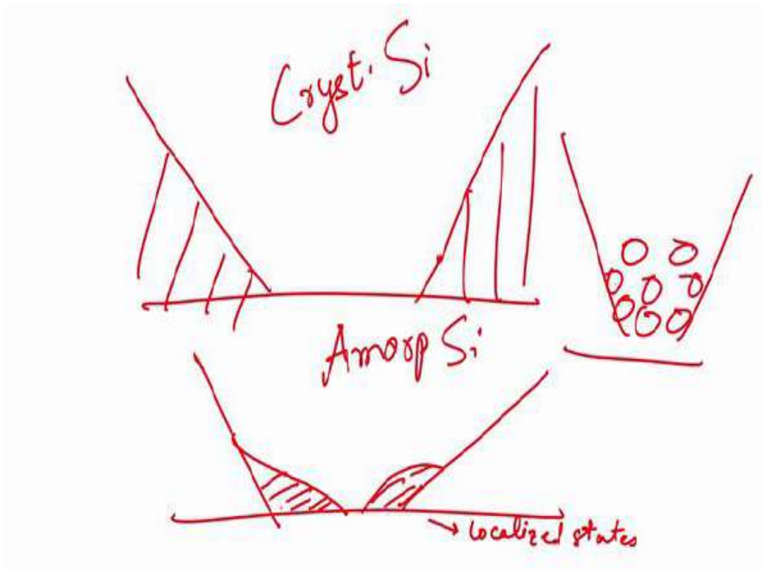

So, let us have a look at it, in a single crystal as we saw in the previous case, only these states are the allowed states, this is crystalline silicon whereas, in case of amorphous silicon, there are some tailings states, which also form the part of density of states configuration and have some allowed states and they are called localized states, in the sense that they are spread, which is in quantum mechanical terms called wave function is very localized, which means they are not continuous states, or in simpler terms you can think of them like puddles.

So, let us say, this is the forbidden state and these are puddles, these are puddles of states available for charges to occupy and this is something which makes them different from single crystal.

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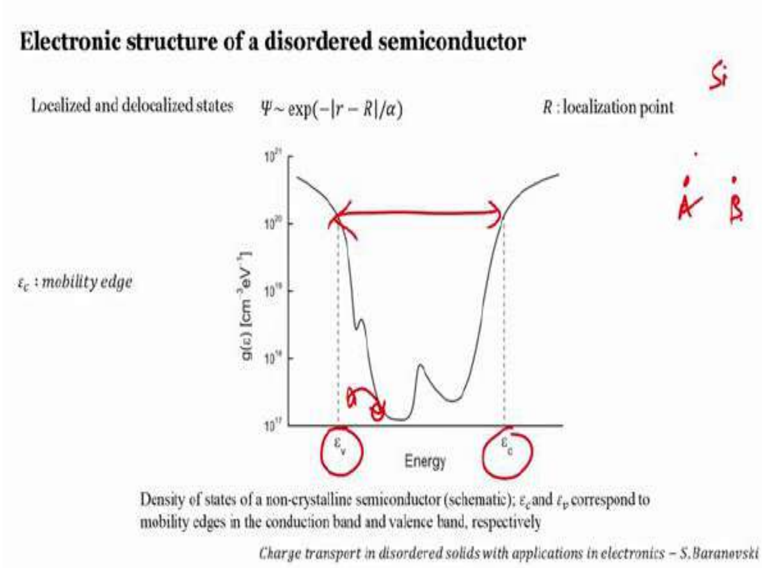

And this is how a density of state would look like for an amorphous silicon, in this particular example, so we can see that, there are conduction band and valence band defined, but also are defined in between these localized states, from this point to this point as marked between this arrow.

Now, what do they mean? They mean that, if there is something called as mobility edge, mobility as you would all know, it defines how, how fast an electron can move from point A to point B in a semiconductor under a given potential. In single crystal silicon, the mobilities are very high whereas, in compared to amorphous silicon, the mobilities are orders of magnitude lower, because of this puddles, which do not found continuous states. That is why going from one puddle to another puddle, some or the energy is lost, and that is why it results in reduction in the overall mobility of the semiconductor.

So, this is what is required from you to understand as far as this particular example is concerned, that disorder essentially means, there is a structural difference and how that structural difference translates to change in the electronic transport property.

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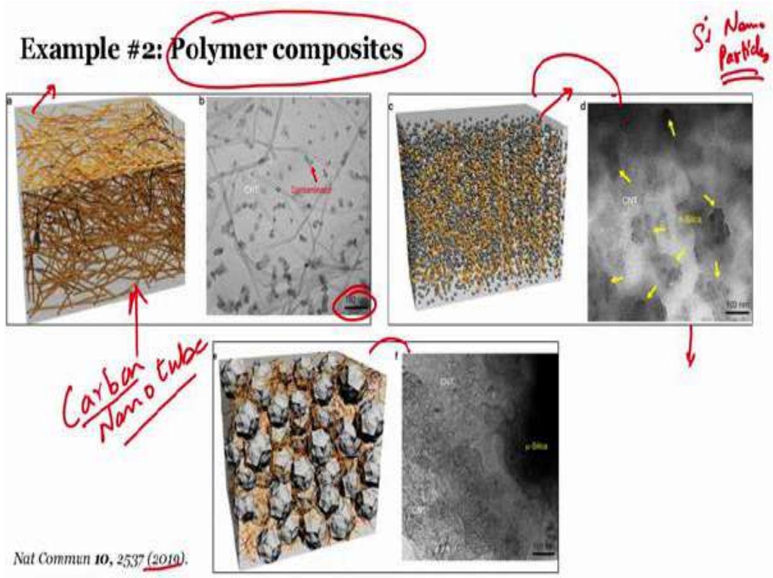

Now, let us go to another example of polymer composites. Now, many of you would question why I have, why have I chosen this example, the reason is many of the tissues, which are tested for biomedical and device design and biomedical systems applications such as breast cancer tissues, or, or some kind of heart tissues, they are nothing but composites.

As you would, as you would have referred to some other lectures in the same course, you would come to appreciate the fact that, these tissues are nothing but composites. They are composed of different structural elements, like nucleus, cytoplasm. And that is why knowing something, which has already been established and then going to the unknown to define is always easy.

So, that is why let us understand how a polymer composites, which is a very well established field works and how is that a disordered system and how electronic transport properties are studied in this particular field. So, that you when it comes to tissues, you will be able to appreciate this kind of understanding.

So, this is, this is an image, this is a collection of image taken from this particular work, you may refer to this work if you are more interested in this kind of field. So, so there is a schematic here and then there is a scanning electron microscopy image, which enables them to see at very high resolution like, we can see the scale bar is here is around 100 nanometer.

So, what they have done is, they have taken a polymer and they have mixed Carbon Nano tube, they have taken Carbon Nano tube and they have mixed together and then they have tried to see the electronic property of the entire system. In this particular figure along with Carbon Nano tube, they have also introduced something called as silica Nano particles. And then they have tried to understand the electronic transport property in this particular polymer composite.

In this last panel of the figure, which is E and F, they have increased the size of the nano particles of silica and then they have tried to understand it, how increasing the size affects the charge transport property. Now, what is the point of doing all these things? The point of doing all these things is the following, carbon nano tubes are essentially the conducting elements, polymer is non conducting, carbon nano tube is conducting, again silica is non conducting, and polymer is as again non conducting.

So, when you change the shape and size of a non conducting element in a polymer composite, how does it translate towards electronic transport behavior is something that is the highlight of this work, just to draw parallels and help you understand and appreciate what the similarity between polymer composites and tissues, carbon nano tubes can be thought of as collagen fibers, they do not exactly possess the same properties.

But in order to understand, or appreciate how they can be modeled as far as mathematical modeling is concerned, which is the focus of this particular course, it can be thought of that carbon nano tubes can be can be considered as collagen fiber in a tissue matrix, in an extracellular matrix of a tissue. And this is something you can delve upon, if you have any such thoughts, which might raise questions in your mind, which you are not able to understand you can always post it on the forum. So, leaving with you, leaving you with that thought, we will try to understand how transport can be understood in such composites.

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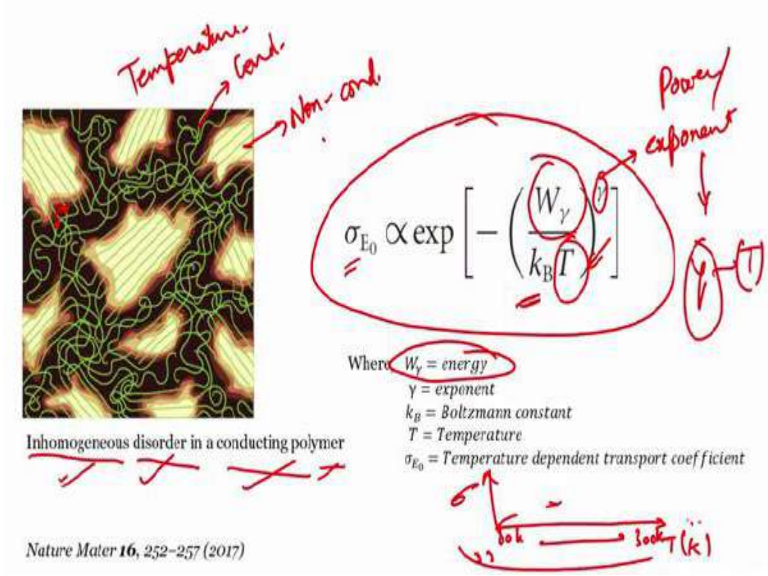

So, this is a 2D representation of the similar thing that you have seen in the previous slide. And so this is an inhomogeneous disorder conducting polymer. So, disorder you already know, conducting polymer is already discussed, inhomogeneous means, whatever mixing has been done between these conducting elements, and these yellow which are non conducting elements is not homogeneous.

There has been no proportion, which has been taken to ensure that, the spatial distribution of non conducting elements within the conducting elements, or vice versa will be uniform, or will follow certain set of order. It is just done at random to understand how the extent of randomness affects the transport behavior.

So, if we see at this equation, there are, there are, there is only, there are only two variables, this and this, because this is a constant, this is a output, and this is an exponent, which will be dependent on temperature. So, let us understand one by one each of them, before I begin with the description of this equation, it is important for me to state that, this kind of description can also is a very general description and can be applied to similar systems. Again, please pay attention to this, this can be applied to similar systems.

And as I had discussed in the previous slides, that polymer composites mimic biological tissues, this kind of transport equation is applicable to other biological tissues as well, because these are physical laws, they, they have been found universal across the systems. So, if you see this equation, the one of the most integrating components is this gamma, this gamma is called as an (exp), as you can see, it is exponent and in general in terminology also it is called an exponent, some people call it as power or exponent.

Now, what kind of exponent is this? So, this is this exponent defines, how that transport happens from one conducting island to another conducting island. How electron moves from here to here, under the influence of temperature. And that is why this entire fraction, which is of W gamma, over KB T is power to gamma, where gamma varies as a function of temperature. And that is why whenever these studies are performed, they are scanned for different ranges of temperature.

So, if you plot for conductivity versus temperature, which is the general plots for these studies, they generally go for lower temperature, by lower temperature, I mean, they will go for 80 Kelvin, or 77 Kelvin and from there they will go to room temperature. Some study, some studies also go for high temperature, but majority will go for lower temperature.

What is the reason? The reason is that, at lower temperature, the thermal vibrations which cause, which cause inadvertent transport from one conducting island to another are dominating the at intrinsic, or the natural transport phenomena. That is why in order to negate that, in order to negate the temperature dependent transport phenomena, they go to low temperature and then as a function of temperature, they try to see that how the transport phenomena evolves.

And that is how they calculate by fitting the equation, how this, how this exponent comes into the picture. With this exponent they would, they would also deduce the overall energy, which is required for an electron, or any charge particular or a hole in this case, to jump from one conducting island to another conducting island, and that is how the transport happens. So, this was all about conducting polymers, or polymer composites as to how they conduct charge.

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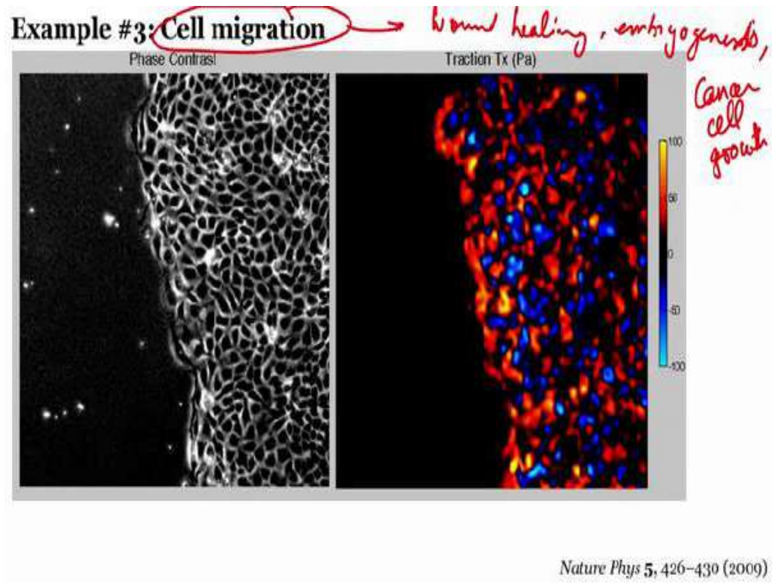

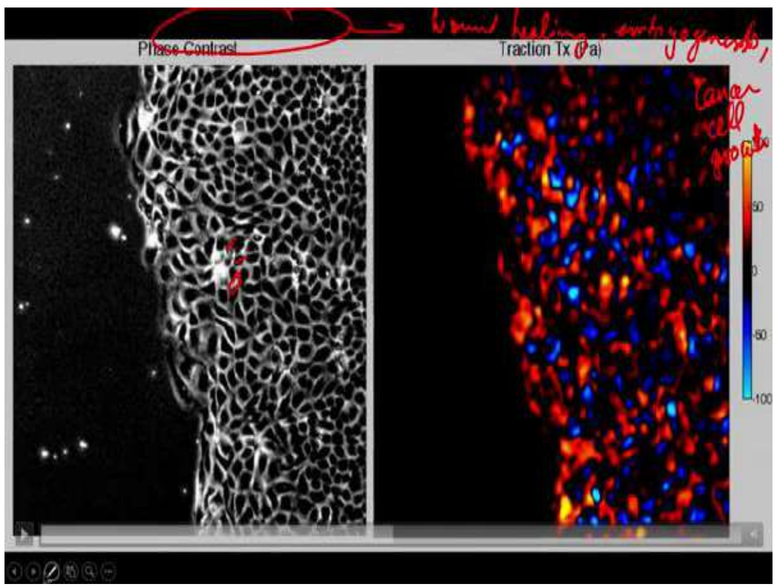

Let us go to a more unfamiliar realm, which is understanding transport in a physical sense, when only cells are concerned. There is no charge transport happening here, but there is a mass transport, which is spatial and time dependent mass transport, which is happening in biological system. So, that, that the topic chosen here, the example chosen here is cell migration, why cell migration is important?

So, whenever you see phenomenon like wound healing, or even embryogenesis which means, forum formation of an embryo and even cancer cell growth and proliferation, all these are nothing but example of cell migration. So, let us see in this particular video, how cells are migrating.

So, if you pay attention here, on the left hand side, you can see that this black part is a cell and these are the boundaries, whatever brighter sections that you see there. Now, how they are moving is very interesting, there is no such defined order in which they are moving. Furthermore, the cells are contracting and expanding at their will, there is nothing which is dictating, that which cell will contract at what time and which cell will grow in which direction at what time.

So, there are two uncertainties, one is spatial uncertainty and time uncertainty. So, when there are these kinds of uncertainty, what is the general approach we go for, as electrical engineers, or as engineers in general, we go for Fourier analysis. And that is what is done in this particular work.

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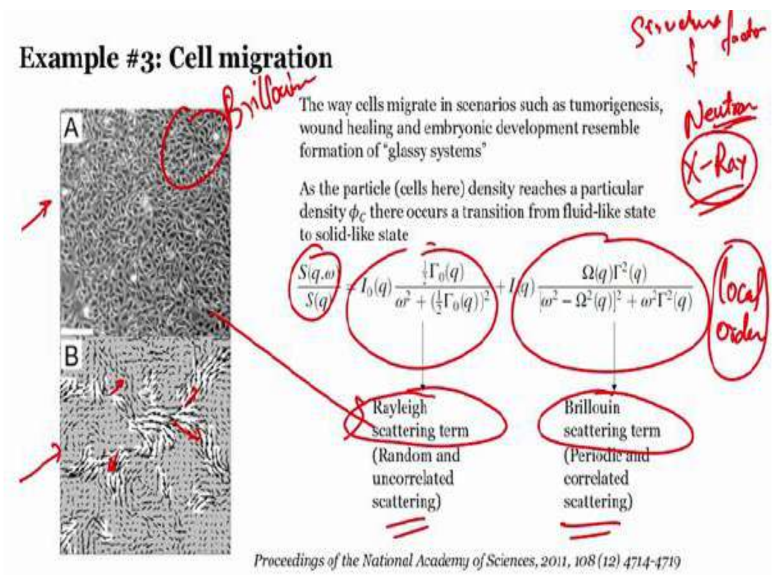

So, what they did was in a similar work, they analyzed the cell migration using a factor called as structure factor. So, structure factor, those of you who would have got modern physics course in undergraduate would be able to appreciate this, structure factor is nothing but Fourier transform of time and space dependent correlation between different particles. In this case those particles are cells.

So how these cells are correlating with each other, both in time and space domains? And why do we do all these things? We do all these things to understand, what is the associated disorder, what is the associated randomness in their growth, in their proliferation, or in their movement, this will give us an idea that how, how random is the process, how disordered is a system.

So, here are the two images, this is an actual image of the system figure A, and figure B is a kind of vector representation of the cell movement. So, figure B will give you more intuitive understanding of how cell migration is happening. Which is a still from figure, which is a still taken and shown in figure A, as we can see the directions, these arrows if you see here, this one, it is pointing in this direction, this arrow is pointing in this direction. For this, for that sake, this arrow is pointing in this direction.

So, what I am trying to say is, all these vectors are pointing in different directions, there is no correlation whatsoever between these vectors. And that is why, it forms a kind of disordered system. In order to characterize this disordered system, they generally go for structure factor analysis. So, that is what they have done here, the structure factor is analyzed. And there are two components associated with structure factor, or two kinds of scattering, which is associated with structure factor.

So, in general structure factor is analyzed by, by experiments like neutron scattering, or X ray diffraction, X ray diffraction is more common than neutron scattering, because of its complexity. So, you perform an X ray diffraction, and depending upon the spectrum, that you get, you try to see which of the terms are fitting in what kind of scattering phenomenon. In this case, they found that this kind of cell migration fits in two different scattering systems, first is the Rayleigh scattering, second is Brillouin scattering.

Now, Rayleigh scattering, you must be very familiar with whatever we see in the sky, the reason that sky is blue is because of the Rayleigh scattering, in the same Rayleigh scattering, which is random and uncorrelated scattering is found in this particular system. This system also has a component of Brillouin scattering, you do not have to think much about the details, which are given in the, which are given in the equation, this is just for qualitative understanding, to make you get off, to make you feel that how will disordered system will would look like, and what are the tools, that you can use to understand mathematically the extent of disorder in that system.

So, this Brillouin scattering term, consists of periodic and correlated scattering. So, the difference is there as we have mentioned in the previous slides, that there will be something called as local order and there will be case where there is complete disorder. So, this local order whatever is present in this particular system is captured by Brillouin scattering. And the complete disorder which is also called as chaotic is taken care of by Rayleigh system, is Rayleigh scattering term.

So, this, this entire, this entire discussion that we had on three different kinds of system by taking three different examples, three different varied example was just to give you a feel, as to how biological system and non biological system both of them, which are important to develop biomedical devices and understand biological tissues can be analyzed using different kinds of mathematical models, to understand what kind of physical processes are going there in one.

And second, what kind of structure dynamics are coming into the play, because you will, you will appreciate this further, when you go through other videos of this particular course. Wherein, they have discussed structures at cellular level, there are different components in a cell. And when these cells come together, and then they create disorder, how those components play a role in defining the physical properties of the tissue overall, is something which is still an open field and a lot of unanswered questions are there.

So, this topic, I believe, is something that is very, a very popular topic and has a lot of unanswered questions and a lot of opportunities are there for researchers to perform experiments, and these mathematical models will definitely help them understand, the insights, whatever is going on in these systems. Thank you.