Biophotonics
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Lecture No. 55
Bionanophotonics Applications

Welcome back. We are at the end of our module number 11. And in the previous few classes, I have tried to give you all the concepts that you think would be necessary, that I think would be necessary for you to understand how several of these integrated chips, lasers and whatnot are being made. Today, let us try to see how these techniques, lithography as well as fabrication techniques, thin film deposition techniques could be utilized in several bionanophotonics application.

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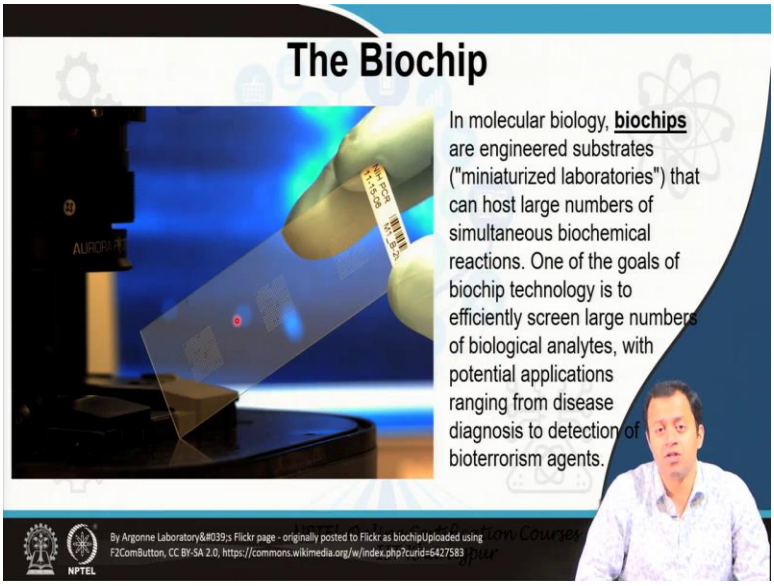

So, the first one that I want to bring to your attention is the biochip. You must have heard of these biochips. Biochips are miniaturized laboratories that can host a large number of simultaneous biochemical reaction. So, these are areas per se. These are areas containing different types of, say, for example, areas that has a different optical response upon attachment to a specific analyte. Meaning, these areas represents thousands of different say, optical resonators or biosensors. Optical biosensing, we have discussed.

Maybe one of, each one of these dots is one such array, the metamaterial that you saw is quite similar to that and each one of them have their individual property, individual sensing capability.

Thereby, a large number of simultaneous biochemical reaction needs, can be done. Make no mistake. Each of these dots could be different from one another. Each of these dots in itself can contain millions of other arrays, which could be similar or different. You are able to see this with your own eye because they are few millimeters or maximum 800, 900 or even 300 micrometers. That is, the I think the limit of human eye.

But 300 micrometers by now you have seen atomic scale or molecular scale differences. You have seen split ring resonators, which are 1 micrometer or below size. So, you can make a calculation of how many of this 1 micrometer scale metamaterial could come inside one such a dot which is 300 micrometers by 300 micrometers. So, all of them could be different, all of them are basically miniaturized laboratories that can host a large number of simultaneous biochemical reaction.

Remember, nanotechnology has enabled us to go smaller and smaller. We can have simultaneously large number of optical biosensors, a different plethora, a variety of optical biosensors at the same chip with some area as buffer, as some area which we have not been used. This is the overall product of such nanofabrication that we saw previously.

One of the important goals is to screen a large number of diseases. We can screen large number of diseases or detection of several different biochemical agents, because we have a variety, a number of optical biosensors all over here. One of them will be able to target a very specific reagent, a very specific analyte that we are trying to see. And if it happens using some kind of an optical source, say for example, one of them will fluoresce upon getting contacted, upon getting immobilized, upon getting attached by a specific analyte, we will be able to detect that fluorescence, and thereby, we will be able to detect that the presence or absence of that analyte from the person's body or body fluid.

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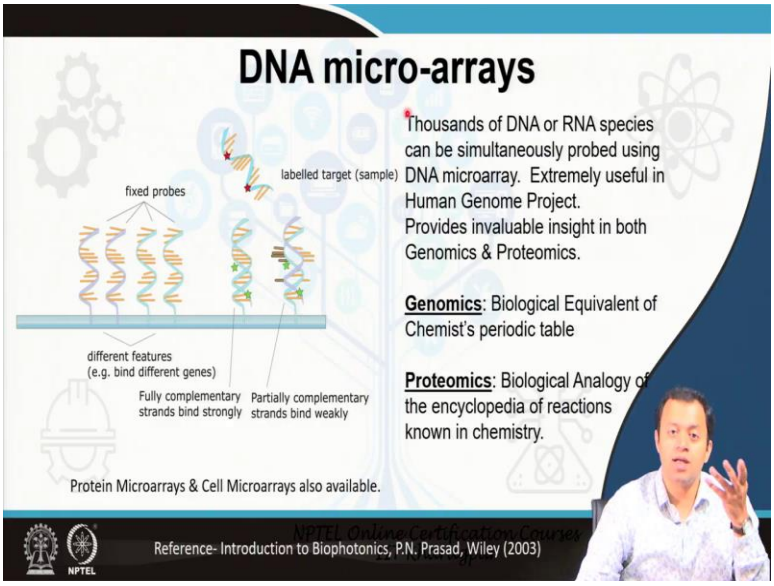

A DNA microarray technique utilizes one such thing. So, different substrate, all those different substrates that you saw, all those different dots that you saw, these different dots, they can contain millions of these fixed probes, a single strand of DNA. I think I would have discussed this before. And you can extract large amount of DNA from a person's blood which you can then label and then made it fall into all those different fixed probes that are already fixed. If they are complimentary, one of them will be, because you have done n number of these probes all over those places.

Remember, these probes are 5 nanometer or less. How many, 5 nanometer can then again fall into 1 metamaterial, 1 split ring resonator of 1 micron by 1-micron size calculate it. If they are matching, they will complementary attach. If they are partially matching or not matching, they will be weakened. Then you can simply wash them off. And since they are labeled, you can look through it under the microscope and thereby see that this area is fluorescing.

Remember, the output, remember the external target is labeled. Previously they were not fluorescing. Only upon attachment this will fluoresce. These are not attached, weakly attached and will be removed. This is basically the idea of DNA microarray, where a large number of, simultaneously large number, thousands of DNAs or RNAs can be simultaneously probed using DNA microarray.

So, suppose I have extracted some blood from a patient and then I have tried to do DNA extraction of, from that blood. I do not think I have to tell the medical or life science students how to do a DNA extraction. So, let me just repeat a very simple protocol for the electronics engineers or the physics. Life science students cut me some slack if I am making any mistakes. So, this is what I have done myself. And by no way this is the ultimate or this is the purest or this is the best DNA extraction technique.

What I did is those blood that I have taken out, I have subjected it to some kind of a phenol chloroform or thiol-based solution. Put it into a centrifuge. The centrifuge at a very high centrifugal force the G force 4000 RPM probably, has rotated it. Basically, a gradient reaction has formed. They broken it up using that phenol chloroform and that thiol mixture. And depending on the molecular weight, it has homogenized. Basically, the blood and the solution and everything has homogenized when you have rotated it, centrifuged it as a very high speed for a specific period of time.

Depending on the weight, I have RNA, single strand on top then I have DNA gradient at the middle, and finally, the debris which contained proteins, which has been extracted out from the blood that I have extracted from a person. So, you add this mixture. Put it in some kind of a centrifuge. You know what centrifuge is. You have seen centrifuge the machine that rotates at a particular G force, centrifugal force, and it divides your test tube in which you have put that solution and that blood together into three different layers according to the molecular weight. RNA first lightest, then DNA double stranded and finally, the remaining part is protein and other debris.

So, that DNA have been extracted. I have precipitated it in alcohol. And then some amount of purification, some amount of washing. I got this which I labeled. You know by this time how labeling can be done. And then I have put it on top of this DNA microarray. And by that I can have thousands of DNA or RNA, several of the matching, several of them not matching into a particular kit. And they are extremely useful in the human genome project. I have not worked on human genome project. I was just trying to see the DNA of a mouse.

But this has been extremely useful in human genome project, where one, at a time several thousand DNAs and RNAs can simultaneously be probed and it provides valuable insight into genomics and proteomics. For those of you from non-life science background what are genomics

and proteomics, I found it from this analogy to be very useful for me who is from a non-biological background. Genomics gives you the equivalent of a chemist's periodic table. Remember the periodic table where you have all those elements hydrogen, helium, lithium, boron, etc. and so on and so forth. Genomics gives you all those sequences ATCG this sequence, particular chromosome, particular DNA, particular etcetera, etcetera.

Proteomics, on the other hand, is the biological analogy of the encyclopedia of the chemical reactions. So, you have a finite number of elements hydrogen, helium, carbon nitrogen etc., etc. How do they combine together and what kind of chemical reaction they form to form, to produce what kind of a compound? Say, for example, 2 hydrogen atoms combined with 1 oxygen atom and they combine and they form water. This water then mixes with, I do not know, sodium or carbon dioxide and then forms a third compound. So, that entire process, the encyclopedia of the reactions this is proteomics.

So, genomics gives you the sequence. Proteomics gives you the protein or the output of such sequence. So, this sequence can express a specific protein, can express, can result in certain protein. And this protein may cause sickle cell anemia in your body, may cause early blindness, may gives your skin color a particular hue or make the color of your hair brownish or blondish or black. We can now have all of them arranged or probed or understood in a fraction of couple of minutes using your DNA microarray techniques.

And since you can have DNA microarray, you can also have protein microarray and cell microarray, where a large number of these things will be made to bind using antibody, antigen reaction or these kinds of aptamer sensing or these kinds of things at a time.

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And then they developed this gene chip. So, the matches, if you are thinking that why this match stick is put, this is just to show you the size, the overall size of a gene chip. So, this is the overall gene chip for human and this is the gene chip for mouse. Thousands of genes which are fragments of DNA that could generate proteins can simultaneously monitored to study the effect of certain treatment, diseases, developmental stages or gene expression. For example, microarray-based gene expression profiling can be used to identify genes who mutates upon response to pathogen or any other kind of reaction.

So, you have a reference of the person at a normal condition. Now, then you have put some sort of another DNA expression on it to see if the person's DNA or genes have changed upon response to a specific pathogen, a specific virus or after smoking or after consuming alcohol for a long period of time something has triggered which has resulted in some sort of a mutation, which might give rise to some sort of a disease. And see how small they are as compared to a match stick. You can carry these in your pocket. I had to purify my DNA. I have to extract my DNA from blood.

But as the way the technology is going, perhaps we will not even require to purify anything, simply blood, you take it, you put it into some sort of a chip and without having any extraction of DNA or cell or protein through it, it can do its own measurement. It can do its own sensing and be able to detect it.

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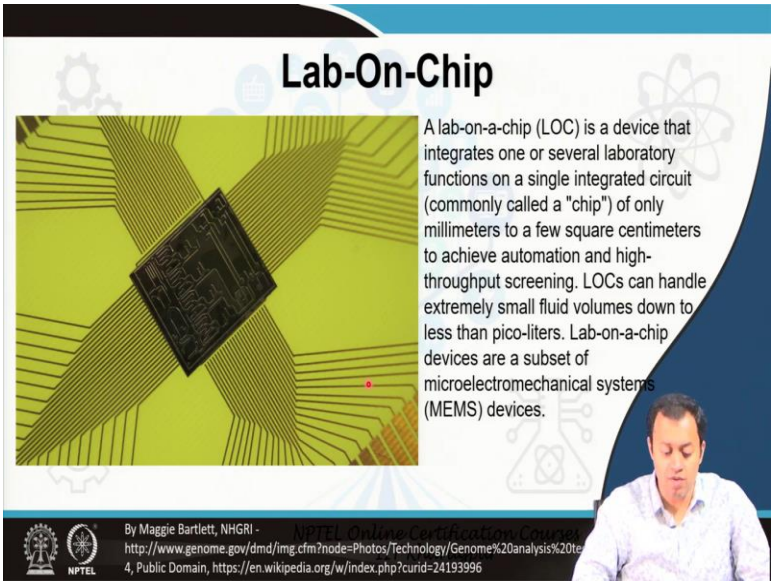

How, if you feel it is science fiction, I will tell you, no that is science. We now have lab-on-chip. Does this not look like a microchip or processor, but this is actually a lab-on-chip which utilizes microfluidics as well as extremely small volume of liquid. It can bring in some picolitre of liquid it can bring in. These are the chip which has different areas that are defined for different types of sensor and it uses not only just photonic sensor, it also uses this microelectromechanical system, MEMS device.

Some of you probably know microelectromechanical system. This is basically miniaturized motors, a device, a microelectromechanical considered a motor. Now imagine a 1 million times smaller molecular motor, so you have somewhat rough idea of a microelectromechanical system. Though the definition is slightly complicated than that, but you get the point. It is a mechanical device. It is an electromechanical device at a microscale or a nanoscale.

We have MEMS and NEMS, nanoelectromechanical system. I think there is a separate course. If you want to know, there is a separate course in NPTEL on MEMS and NEMS and these are coming up very, very strongly, So, MEMS could be a part of this lab-on-chip. So, soon we will have this lab-on-chip coming up where it can be put in your own phone or it could be put somewhere you can purchase from a supermarket or a pharmacy.

Put some drop of your blood or saliva or any other body fluid and not only it gives you yes, no diagnostic of pregnancy non-pregnancy, diabetic non-diabetic, sugar level this sugar level not

that, virus present not present, it gives you an entire history, the entire medical information that you probably need, the entire information, copying or understanding or calculating or analyzing every single gene of your body.

And then you can connect it with some sort of an IoT device, Internet of Things device which can take the information into the cloud, which will then analyze, which will then churn and give you information in your mobile phone with a text message or send an email which has the exact detail of your entire medical history and the diseases that you might be susceptible to in future. So, this lab-on-chip is something that is coming up extremely strongly and this is something that is going to save countless amount of human lives.

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So, that brings me to the end of module number 11, nano biophotonics, application of nanotechnology in biophotonics. There is only one chapter remaining. Please feel free to drop me an email regarding what you think the course have been, where it should be improved, what I can do or what I have not done, should be done, what other topics that you should, you would have wanted me to discuss, but remember, I have a very, very specific fixed time and I have to add as many topics as possible, which I could explain it to you. There is no point trying to teach you something which I myself would, do not understand or I not understand fully or I myself, my own concepts are weak, there is no point of me telling you that.

So, probably you have understood that I have not gone that deep into biology. That is not my background. But I think I have been able to give you sufficient amount of biological information that is enough for biophotonics. If you want to go further detail, then I would ask you to go for a specialized biological course, not an interdisciplinary course, but a biology course. Or if you want a specific quantum physics, quantum mechanics or nanophotonic course, go for a photonics course then. This was my chapter number 11. The last chapter is remaining that is optogenetics and neurophotonics.

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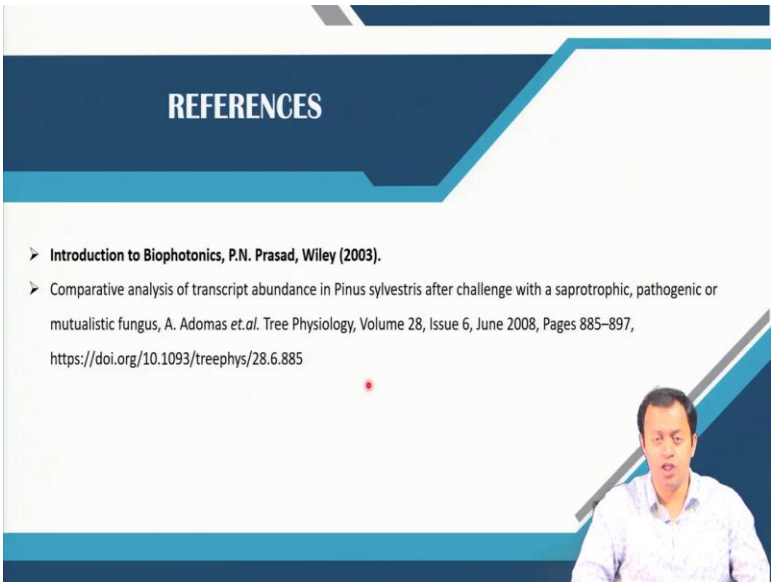

I hope to see few of you in the last class as well.

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Thank you. Thank you very much.