Biophotonics
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Lecture 35
Biosensing with Optical Nano-Antennas

Welcome back, let us continue our discussion on optical biosensing with metamaterial-based sensors. So, we change the name a bit we started calling them nano antennas those split ring resonators, those split ring resonator is the actual term that Sir John Pendry used, but nowadays nano antennas are coming up.

In fact, nano antennas is also not that popular nowadays they are calling meta surfaces, meta surfaces are two dimensional forms of metamaterials usually made up of either dielectric or two-dimensional exotic material such as graphene or molybdenum diselenide or similar structure but at the end of the day for all and purpose they are metamaterials and they are split ring resonators.

So do not fall for different terminology they are one and the same, we try to add more catchiness onto it, so that it captures different people's imagination, split ring resonators as compared to optical nano antennas has a better ring and hence it was changed from trapped mode to dark mode to bound state continuum and I think it will further, further go change but overall their phenomena are either same or similar to one another. So, let us continue with our discussion.

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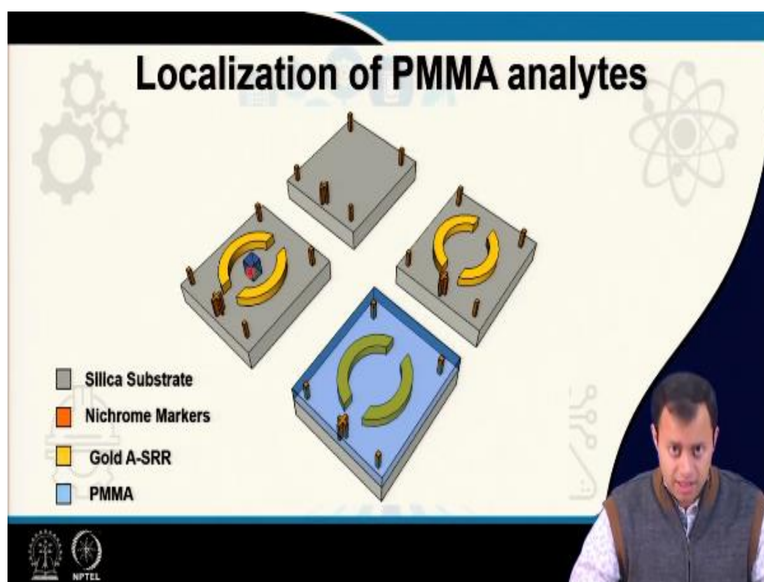

I told you that when you shine light on these kinds of structures there is an uneven distribution of electric field depending on the frequency. So, if the frequency falls on a particular that dark mode case most of the electric field, most of the optoelectric field will be concentrating here, if on the other hand this one is dominating, then this one will be resonating, this one will be not. On the other hand, if this one is dominating, then this one is resonating this one not. So, there is an electromagnetic hot spot, there are different areas where electromagnetic field is more, there are different areas where electromagnetic field is less.

So, the question comes that why do we need to cover the entire area with PMMA, why is analyte needs to be put in all over the surface? We can localize PMMA or we can localize analyte at very, very specific location where the electromagnetic field is maximum and thereby try to see, thereby try to see if my structure is strong enough, sensitive enough, selective enough to detect it. Well we did exactly that, this was the previous case that you saw in last class.

I now localized into this particular area, how do I do it again electron beam lithography is an entire nano fabrication course available in NPTEL just brush through electron beam lithography this is how ICs are made, well electron beam lithography is not used to make ICs, ICs are made using photolithography integrated circuits, by IC I mean integrated circuit, the processor in your mobile phone or your computer. We use the same technology here, similar technology here and I localized it, I myself personally localized it.

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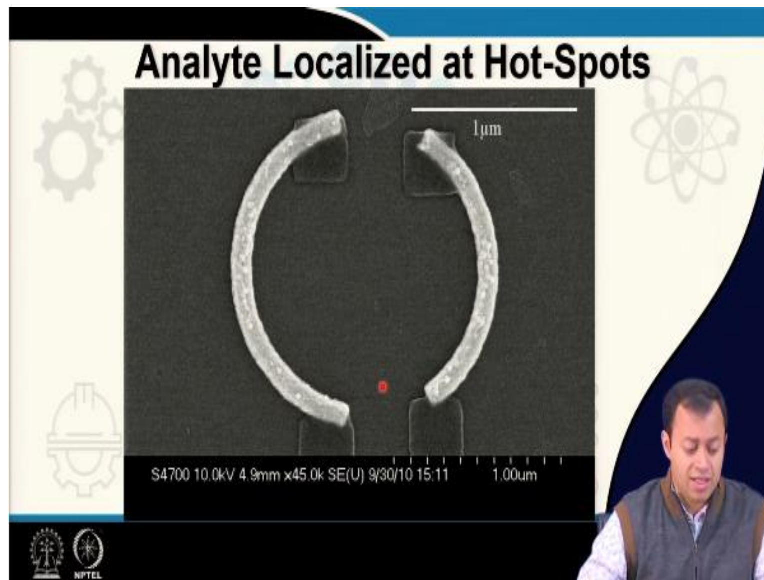

And this was the result, this is the result, see these are blocks of PMMA at specific location of my asymmetric split ring resonator and you know what are their size, coincidentally these sizes are 200 nanometers by 200 nanometers, thickness is 100 nanometers. So, 200 nanometer times 200 nanometer times 200 nanometer I have localized them. If I have localized PMMA and say the PMMA contains specific antibodies, that antibodies are again specific, specific to a particular antigen, I am obviously not saying the name of the antigen because that has come to your mind anyways and yes, that is correct.

If it is specific, specific to an antigen and it is capturing that antigen will I be able to see any red shift in my resonator's response? Remember resonators response depends on refractive index change, very, very susceptible, these hotspots are very, very susceptible to the resonance response of their surrounding material, the refractive index of their surrounding material. So, if I have this particular size, this is the exact size, this is the exact size of the virus that I had whose name should not be taken or that I have repeated so many times, this is the exact size of one single virus, how sensitive or how nicely can I detect it.

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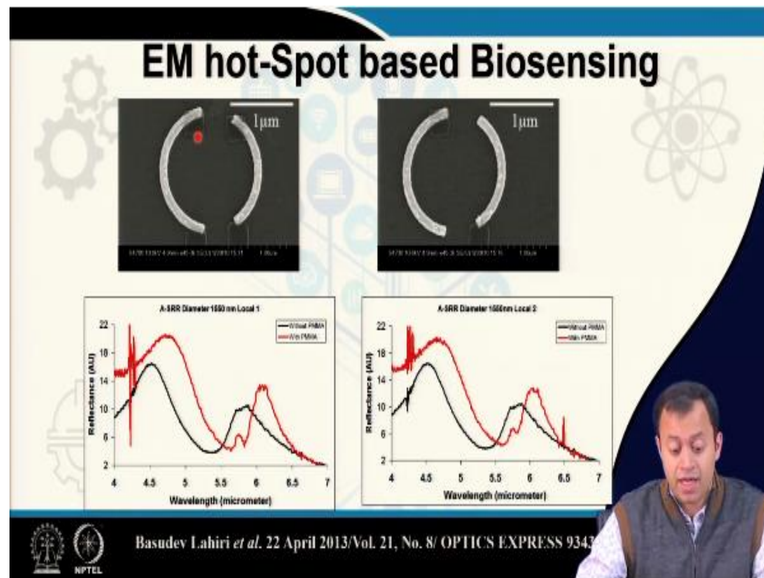

Well I will tell you, we started putting single molecule, single blocks here at specific locations and we still saw the red shift and we still saw the signature, although tremendously diminished, although tremendously diminished from the previous case because in the previous case the layer, the analyte layer was all over the surface, so it was exciting every single hotspot.

Here there are certain hot spot that are prominent in this area or in this area or I did not show you or in the middle part. So, it is a case of hit and miss, some areas are accepted some areas are not. So, thereby the sensitivity has reduced a bit but this is good enough and normal FTIR equipment which is well I would not say cheap but it is affordable for most hospitals and universities with structures such as this. How many more of these or how do you plan to utilize, sorry I am missing my point.

Can you actually detect couple of four or five viruses at a time? Remember viral load is important that gives us how much the infection has happened, so in the beginning stage the virus have not multiplied, so we need to detect how much virus is present in the patient's body and thereby medical students will probably correct me but depending on the viral load present in the patient the medication needs to be, the dosage of the medication needs to be customized, the dosage of the medication needs to be ascertained as well, if the viral infection is at different stage, at the final stage.

How many viruses are you able to detect, can it be directly proportional to the wavelength or to the red shift and the signature which should be unique to a molecular vibration and this molecular vibration has to be unique to a specific virus, can we not detect just a few viruses within couple of seconds? FTIR if any one of you have done gives this measurement in 36 second, RT-PCR that is the commonest method these days for detection of coronavirus from patient's blood, takes couple of hours and that that too determines gives you false negative and false positive.

This method relies on the molecular vibration. Now you may say, you may say that several viruses are very common to one another SAR COV1 and SAR COV2 are similar, yes, but the dissimilarity has to happen because of at least few molecules are different, if the entire molecular structure, entire genomic structure everything is 100 percent same then it is not a different virus it is the same virus.

There is some sort of mutation had happened, what does mutation means by that this time you know, some protein somewhere some amino acids some base pairs of DNA or RNA has changed and if base pairs are made up of different molecules, if proteins are made up of different molecules, anything is made up of different molecules and if the molecules have undergone change, even if structural change is there like coal and diamond both are molecules but the arrangement is different, then their vibration levels will be different, their vibration level will be different and I am detecting the vibration levels here and thereby pinpointing, a, what is present and how much of it is present.

What is present identifies a specific infection, a specific virus, a specific pathogen and the red shift determines the viral load. So, is problem solved, have I solved the problem, why has this not been used in detection of coronavirus, why have I not made this as a chip and sold in supermarket for you to utilize them at the privacy of your own home?

Imagine buying thousands of these kits from your local grocery store, putting some amount of oropharyngeal swab or blood or anything on to this, seeing if the color is changing if you can and then deciding whether you should self quarantine or not or you come to the hospital, a person, a pathologist take your blood take your oropharyngeal swab and perform this under FTIR, FTIR

determines IR frequency, this property in IR frequency which your eyes cannot see and within 36 seconds give you an answer yes or no.

Repeat it five different times to be absolutely certain, take 5 minutes, even then it is still less and within 5 minutes how many more patients can you screen at a time? Think about where we can utilize it, several questions came to me why biophotonics or where biophotonics and when I give you the introduction video that practical examples, detection of coronavirus, many people thought that is a vague example, yes, it could be utilized.

I am now giving you specific examples, I am now giving you specific examples where you will actually use and most importantly I have made this, so again coming to your point, if I can you can make it, you will make a better job than me. This thing is available, this technology is available, so all the doctors, all the pathologist do you want to have a try, do you want to have a go to it, can you give me some viruses, some pathogens, so we can have a dry run? Think about it. The laboratory is open we need to take a quantum leap, we can stay in our comfort zone of doing RT-PCR based sensing but maybe just maybe we have the technology available which is perhaps slightly better than RT-PCR, think about it.

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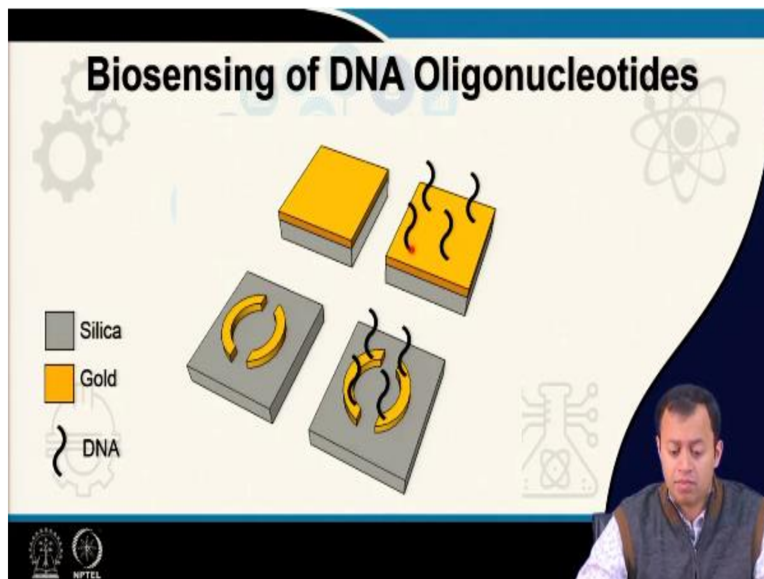

Obviously, if we have used PMMA as a probe material for sensing, PMMA as an analyte which is merely a proof of concept, what is preventing us from going from detecting DNAs, can we not

utilize it for DNA detection? Well we thought that, yes, we can utilize DNA detection where immobilization technologies will come up, remember we use thiol based immobilization, the thiol part, one part, it is a molecule which contains sulfur at one part which was connecting with the gold and the other part was connecting with the DNA, these are single standard DNA, hence I called oligonucleotides and we connected them with a gold thin film as well.

So, this is a resonating structure this is not a resonating structure, my resonators of these matches that of the resonance of the DNA molecules, DNA base pairs vibration this will have no resonance per se, this is simply scattering. So, what is the difference again between resonance and scattering? I do not know I forgot, maybe you can enlighten me and we perform the same function here chemical immobilization and put DNA here.

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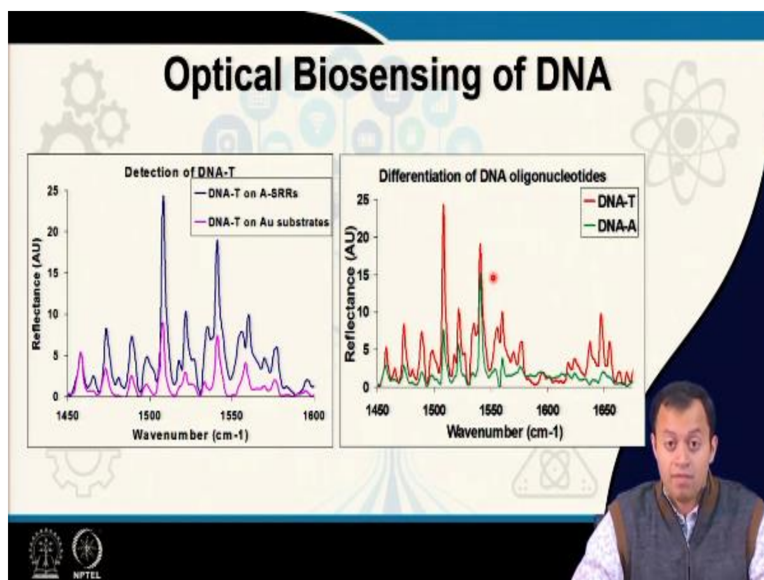

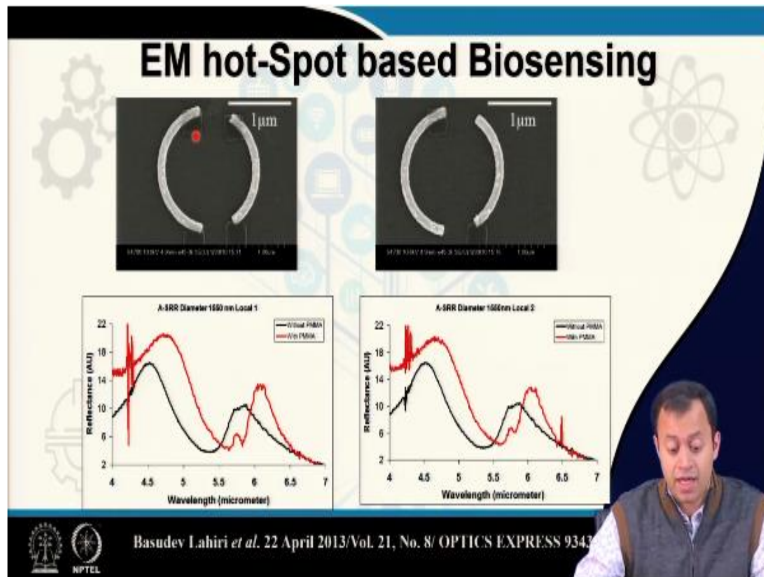

And the result was also quite nice, this is DNA T, T stands for thymine, thymine on asymmetric split ring resonators as compared to DNA thymine on gold substrates and you see how the A-SRRs have amplified. And this is not noise, this is basically this part the signature, we did the base pair, the baseline correction anyone who has used MATLAB and Excel know what I mean by baseline correction, we zoomed into this version and took out all the other noise we just took the curve away and there was fitting and everything.

And all of these peak represent a particular stretch, a particular vibration level, like you see in any other molecule these were thiamine and thiamine were vibrating at a specific level and just to prove to you that this is not noise, we saw somewhat of a diminished yet mirror type response with a simply gold substrate and then again to further prove it, we used two different sets of DNA oligonucleotides thiamine and A stands for again adenine, and you see the actual difference between two different types of base pairs, we were establishing single base pairs and thereby trying to see the initial signatures.

You remember first I have to make a database of known substances, then I will get an unknown DNA pair and then measure it and then compare it with either this or this and then say it has some amount of thiamine in some amount of A, so maybe this kind of materials could also be used as a sequencer. Biotechnology student please enlighten us what sequencer are, write it in the comment below what sequencer are for physics and electronics engineers.

Those of you who are curious just Google what sequence and sequencing machine is, what sequencer are but is this an equivalent of a sequencer, ultra fast rapid sequencer, can we utilize it, I am having the database here this is my work I am having the database here I need samples, I need to talk with hospitals, I need to talk with biologists, I need to talk with medical professionals and try to sequence.

Can I sequence the entire genome of a specific virus, a specific pathogen rapidly, can this be utilized as well? Well the jury is still out this is what I am working on, this is what my research is and I am counting on you to contact me to help me out to collaborate, to discuss science, so that whatever mistakes, since these are my work, I am bound to do some mistakes with my research team and thereby see how this can be improved, if we can save even one single life because of this technology why not.

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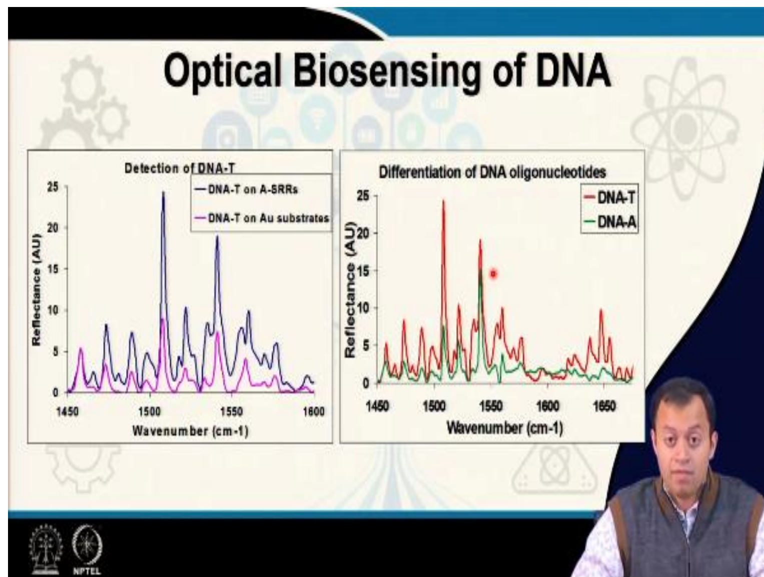
The Future

- Multichannel Plasmonic Microfluidic Biochemical Sensors

Gold A-SRRs
Microfluidic Channels

Different sized A-SRRs to detect different molecular resonances



So, what is the output, what is the future? Can we make some kind of a device such as this using microfluidics? Microfluidic I am not going to describe what microfluidic is, well the name itself suggests you have channels which carry very, very small quantity of liquid, any saliva, blood, nasopharyngeal swab, oropharyngeal swab that will bring in, there will be different sizes of split ring resonators, thereby resonating at different frequency thereby targeting different molecules, i.e., different pathogens.

You remember one of the primary problems of optical biosensing was we want to detect simultaneously different viruses, you might be infected by 10 different pathogens, 10 different viruses, each one of them are customized to detect or resonate or match the frequency of different viruses. If I can make such a structure there will be a microfluidic channel, microfluidic channel will slowly take the liquid which is any body fluid, blood or urine or oropharyngeal swab.

Or anything or non-body fluid as well it can happen which will contain the pathogen, different types of pathogen and depending on what kind of antibody you have set up they will get specified at specific location depending on what kind of antibody or thiol molecule you have set up, they will get attached to different locations and we will customize them we will it is a very catchy term these days being used I saw it in t-shirts as well ‘optimize’.

So, we optimize them to match specific frequencies, the specific vibrational frequency of specific molecules of specific pathogens and then a combination of IR as well as visible we have these chips, a biochip as a biochemical sensor and put and detect a plethora of different types of pathogens in our body, combine that with machine learning and IOT, so human intervention is not required, you get signal such as this, say this is the signature of T and this is the signature of A thiamine and adenine.

Your machine, your software is analyzing this is detecting this pattern recognizing this, at the end of the day, deep learning or machine learning is pattern recognition, it is recognizing this pattern the presence of this is or this shoulder is a determination of DNA T, human intervention is not required you simply put slides under some kind of a microscope, the microscope or FTIR microscope is connected with software, machine learning software it will go through this learning tool, learning algorithm and give you a yes, no diagnostics.

And that information that it will give it to you will be carried via internet via 4G or 5G connection. So, remotely so a patient is somewhere else in case of this pandemic, I somehow collected his sample, I call has collected his blood or nasopharyngeal swab, I got this information and this information is transmitted to her in real time. People can be monitored remotely, a particular area can be sealed, particular area can be quarantined instead of the entire city or entire block or the entire country.

Perhaps we have to look for multi-disciplinary solutions for interdisciplinary problems, this is exactly what I was telling you in the introduction video, these are just my work. Now needless to say there are plethora of different optical biosensors, photonic crystal-based sensor, Krichman configuration, plasmonic biosensors, then there are Raman's biosensor, microfluidic biosensors I could take an entire course and there exist an entire course on optical sensing which will come up in probably in the next semester. So, that you can utilize that you can learn for.

So, instead this is what I meant, instead of trying to see each one of them a bit I decided to give you a glimpse of what I can do, if you are interested then and if I have aroused some amount of curiosity in you then I am successful, if not well then in the next semester I will change this entirely and will teach you different types of sensors and describe each one of them at a time, you have to tell me since it is not that interactive as a normal classroom, I am not getting the

feedback directly but still whatever you decide I will take the criticism and I will try to improve or improvise or change or modify from next time onwards.

So, this is where I end this module, remember there is lot to unpack, lot to see and several questions I know you have, please feel free to ask this question in the forum or we are having a live session pretty soon you can ask me then, whichever you want I will try my level best to answer several of your question, you do understand there is a time constraint I always get criticized that my videos are too big instead of 30 minutes, 50 minutes is coming up so I try to reduce the content and when you try to reduce something has to be omitted, something has to be not told and that sometime causes problem. So, if there is something missing in the entire biosensing part please, please feel free to contact me I will try to answer to the best of my ability.

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So, these are the concepts cover.

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For the curious among you please download this, I am not selling it because it is free of cost so it does not matter. So, I shall see you in the next class with a new topic. Thank you, thank you very much.