

Nanobiophotonics: Touching Our Daily Life
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Lecture No. 03
Why do this?

Hello, and welcome back. We will continue our discussion on the topic of Nano Biophotonics. And, this is module 1. So, we will keep on in this entire module making a case for why nanobiophotonics is interesting and what nanobiophotonics can do specifically for you right. So, the first two chapters were mostly introduction, what nanobiophotonics is where can we utilize it. In today's module specifically, I would like to argue why nanobiophotonics is a necessity.

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Few techniques of Photonics used in Medical Diagnostics

1. Spectroscopy
 - Absorption, Emission, Scattering
2. Light Microscopy
 - Fluorescence, Raman, LSCM
3. Multimodal Approaches
 - PET Imaging
4. Chip Based Analysis
 - Biochip for POC diagnostics (Lab-on-Chip)
5. Optical Manipulation and other Enabling Technologies
 - Optical Tweezers, PDT, Optofluidics, ML, AI, IoT.

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What is the point? Why do any of this anyways? So, see photonics or nano biophotonics per say allows us with several different technological tools that is obviously, because thanks to physics that we can apply on a regular basis to understand medicine to understand human health. You obviously, know about spectroscopy Raman spectroscopy infrared spectroscopy we will be learning a little bit about that. These are purely chemistry physical chemistry parts. I told you that photonics has this tendency or nanobiophotonics have this tendency to incorporate technologies from several other domains. So, spectroscopy chemistry physics they incorporated it and using the techniques of spectroscopy nowadays it is possible to detect diseases I myself am personally involved in doing such research and

in the future courses in the future topics for this particular course I will be sharing some of them.

You obviously, have light microscopy, microscopy perhaps you know have you know gone leaps and bounds and nowadays we are able to even image individual atoms. So, physics or photonic technologies per say or electronics engineering or engineering in general have had allowed us with several path breaking technologies several technological breakthroughs that has made us go directly into the health care directly onto the medicine background. Apparently very few of them were initially used in medicine like spectroscopy was purely a chemistry phenomenon Raman spectroscopy was utilized from a physics point of view, but nowadays you see that they can very well be incorporated in biology. we have chip-based analysis this is purely nanotechnology-based topic we can utilize light to light with a mechanical force light can be utilized to exert some sort of a mechanical force and thereby pluck nano particles nano objects and we can utilize optical tweezers and all of this. So, several different branches that already exist machine learning artificial intelligence internet of things that exist apparently separate from one another could be incorporated in nanobiophotonics in order to try and solve health care issues. So, my argument is that there are existing technologies already you do not necessarily need to develop new technologies in order to understand or in order to sustain or in order to utilize nanobiophotonics.

There are already existing technologies in different domains chemistry physics engineering etcetera just bring them together incorporate them together and previously like things were used to detect a chemical material trying to see the atomic configuration of that of that unknown object instead of doing that let us now utilize it focus it along with on a medical domain and thereby you can try and see a disease from a completely different perspective using already existing technologies such as these. So, this is just an example do not go too much detail on to that we will be discussing several of them individually they are part of individual chapters. The argument that I want to make here is that there are technologies that exist that could simply be incorporated in nanobiophotonics and they can they can work pretty well. There will be seamless and smooth matching and you utilize those already existing technology that you know that you are already an expert on, but apply it to something different apply it to something completely different such as health care.

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Important Field of Application in Medicine

Medical Discipline	Application/Example
Cardiology	Intracoronary Diagnostics, Microcirculation, Varicose vein treatment
Dentistry	Dental Diagnosis: Caries, Stress/Cracks, Pulp Vitality Dental Laser Surgery: Endodontic Therapy, Prosthetics
Dermatology	Skin Diagnosis: Melanoma, Injuries, Acne
Oncology	Tissue based cancer diagnostics, Tumor detection, Analysis of Biopsies
Ophthalmology	Retinal Angiography, Early detection of Alzheimer's disease

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There are several applications in of photonics or photonics based technology or nanobiophotonics in medicine we can work in cardiology where varicose vein treatment we can diagnose those intra coronary problems micro circulation etcetera dentistry is very ripe for application of laser or photonic technologies dental diagnostics prosthetics I myself I am utilizing spectroscopic mechanisms to detect oral cancer dermatology skin diagnosis oncology tissue based cancer diagnostics I am involved in this ophthalmology all of these things can be utilized using photonic technologies that you have previously been trying somewhere else, but now they could very well be brought in to look into a disease from a very fundamental from a very nano scale point of view. So, the question comes like why do this we already have you know biopsy techniques and endoscopy and what not in order to detect diseases. Pathology is an entirely separate field in which you utilize pathological techniques staining and staining a particular patch of tissue and looking it under the microscope to go into far you know complicated details extraction of proteins from that particular tissue and look into it. So, already these techniques exist whenever you are trying to detect cancer in a tissue or in a blood or somewhere else there exist gold standard established techniques. Why bringing new technology from a completely separate field like chemistry or physics why do Raman spectroscopy or why do laser scanning microscopy to detect diseases.

Well the argument here goes that a) these are very fast whatever time it takes for a person to stain a particular tissue put it under the microscope and then utilize the knowledge in order to understand it far faster diagnostic is possible I am not saying I am not saying it is always done or it already established, but it is possible using micro spectroscopy technique for technique applicable in photonics to to diagnose the same cancer to diagnose the same

disease at a much faster rate without human intervention. The potential is there the potential is there. Mark my words I am not saying that one is bad one is good I am saying that this has the potential to do something nanobiophotonics has the potential to perform something that already existing diagnostic techniques presently lack. I am not saying that nanobiophotonics is the only one which shows potential there are other advantages of other techniques. There are 1001 techniques, but since this is the course of nanobiophotonics it is my duty to argue towards it right just like lawyers just like lawyers. So, I will be putting my client's case forward and my client is nanobiophotonics. So, nanobiophotonics can deal with disease detection at a much faster rate because it is light secondly, it is non invasive you do not have to extract something it is possible possible not necessarily it is done on a regular basis it is possible that you can simply send a bunch of light with different wavelength different frequencies different energy focus it into certain part of the human body collect the light reflected out of it understand the light that has been absorbed in that particular area of the human body and thereby understand the chemical composition of that specific area and what has previously changed or how much chemical composition has changed with respect to a healthy or with respect to a reference tissue or a reference area of the same kind right. This is possible without you know doing some kind of punch biopsy where a portion of the tissue is taken out and you know stained and then put in under a microscope etcetera. So, there are potential and we believe you me we need this significantly we need this significantly because although my country has made tremendous leaps in health care still we have one of the highest maternal mortality ratios.

The image is a screenshot of a YouTube video player. The video title is "Lecture 03 : Why do this?". The main content of the slide is titled "Societal Relevance" and contains the following text: "Maternal Mortality Ratio of India has declined by 8 points from 130/ 100,000 live births in 2014-16 to 122/ 100,000 live births in 2015-17 (6.2 per cent decline) This translates to 2000 additional mothers saved annually in 2017 as compared to 2015. Total annual deaths declined from 32,000 maternal deaths in 2015 to 30,000 deaths in 2017. This translated to every 20 minutes a mother dying due to pregnancy or childbirth related cause." Below this, it states: "Maternal mortality is considered a key health indicator and the direct causes of maternal deaths are well known and largely preventable and treatable." The UNICEF logo is visible at the bottom of the slide. The video player interface shows a progress bar at 12:13 / 33:30, a play button, a volume icon, and a "YouTube" logo.

That is death of mother and or child or sometimes together during childbirth and that is simply unacceptable look at this shocking figures yes we have made tremendous progress

and UNICEF says that the total annual deaths have declined, but still we have 30,000 deaths almost 3 lakh deaths in 2017 alone of mothers trying to give childbirth trying to trying to give birth to babies 3 lakh 4 lakh deaths during birth simply because of unhygienic conditions or simply because you have some sort of very easily treatable infection is simply unacceptable. As a society we have to make this to something similar to first world countries like less than a hundred deaths every year due to childbirth. These figures are shocking and remember maternal mortality death of a mother during childbirth what should have been perhaps the happiest moment of a person's life is converted into a tragedy and this is a tremendous key health indicator with direct causes of maternal death as well as and most of them are largely preventable and treatable. That is the point they are largely preventable and treatable why we are not doing it because well the answer is even more shocking currently in India there is no regular screening of UTI, UTI stands for urinary tract infection infection in the urinary tract region specifically for women specifically for pregnant women women who are able to give birth and facility for diagnosis of UTI is not available at peripheral government health centers. Most maternal death occur because of UTI, UTI infection is because based on there are several other aspects, but most common is an infection by this bacteria E. coli. Now E. coli is one of the most common bacteria those of you who are from a microbiology background or medical background or even biotechnology background you will be starting if you have not already started with bacterial culture with E.

coli. E. coli is the most common bacteria that is utilized by you know undergraduate students in practicing their laboratories you can create it you can kill it you can you know manipulate it. So, anybody who is suffering from E. coli based

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Societal Relevance

Urinary Tract Infection among Pregnant Women at a Secondary Level Hospital in Northern India

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Abstract

Background: Urinary tract infection (UTI) during pregnancy is frequently associated with complications. Currently, in India, there is no regular screening for UTI, and facility for diagnosis of UTI is not available at peripheral government health centers. **Objective:** To estimate the proportion of pregnant women with UTI among antenatal clinic attendees in rural Haryana. **Methods:** Eligible participants were pregnant women attending antenatal clinic of secondary care center of rural Haryana from March to May 2015. Consecutive sampling was done to select pregnant women. Interview schedule was administered to the selected women, and midstream urine sample was collected. Urine sample was plated on MacConkey agar, and colony count was done using standard methods. **Results:** A total of 123 pregnant women were included in the study. The proportion of women with symptoms of UTI on the basis of history was 33.3% (95% confidence interval [CI]-30.7, 35.9), and UTI by colony count was 3.3% (95% CI - 2.4, 4.5). The presence of UTI was found to be significantly associated with the presence of any symptoms of UTI on multivariate analysis (odds ratio [OR]-7.35 [1.95, 27.77]). **Conclusions:** The burden of UTI among pregnant women attending antenatal clinic of a sub-district hospital was considerable, more so among the women that presented with symptoms suggestive of UTI. The study suggested that considering the burden of UTI and its complications, diagnosis of UTI at a resource-constrained setting like a secondary care hospital can be done after screening women for symptoms suggestive of UTI.

Key words: India, pregnant women, rural, urinary tract infection

INTRODUCTION

Urinary tract infections (UTIs) are bacterial infections with a prevalence of approximately 150 million cases annually. The economic burden is more than 6 billion U.S. dollars. About 50% of women and 12% of men experience at least one symptomatic UTI during their lifetime, and as many as 30% of 100,000 live births in India annually. This translates to 2000 Total annual deaths in 2017. This translated to 1000 deaths related cause. Direct causes of maternal

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excellent culture medium for bacteria in areas of urinary stasis.¹⁰ These changes along with already short urethra and difficulty with hygiene due to the distended pregnant belly increase the frequency of UTI in pregnant women. UTI may present in pregnancy either as asymptomatic bacteriuria or as symptomatic infection. The prevalence of

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disease or infection could get immediate antibiotics very cheaply available and can get treated absolutely no problem UTI is not like blood cancer or Alzheimer or Parkinson's it is simply a normal disease an infection that has happened in that has happened in the urinary tract and that could simply be treated with over the counter antibiotics. Antibiotics that you can get from any pharmacist any medicine shop, but how do they know? Currently in India there are no regular screening of UTI and facility for diagnosis of UTI is not available at peripheral government health centers. We simply do not have this much diagnostics capacities they are not available at health centers or Anandwadi places or you know village hospitals. So, if you are not getting diagnosed by it you have mild discomfort you bear it. when the child is about to take birth this infection you know exaggerates it manifest further and you know several different like septicemia or several other kind of complication can come and this has resulted in this huge amount of maternal mortality rate.

These are UTI's are bacterial infection with a global annual incidence of approximately 150 million cases, but all of them are treatable all of them are treatable what do we need what are we lacking? We are lacking simple cost effective tools that can rapidly detect that can detect a UTI that has happened to a person either at the privacy of their own home if I can I can detect pregnancy using those pregnancy detection tool kit at the privacy of my own home why cannot I detect urinary tract infection it is exactly the same procedure it is exactly the same procedure either those kinds of techniques are required those equipment those tools are required which are cost effective which can be done either at the privacy of your own home or can be put in this either rural areas or peripheral health centers and to be done by minimally trained people. You do not require a highly sophisticated pathologist or doctor to do this. When you are detecting pregnancy at your home using that home pregnancy detection tool you are not utilizing any specific you know talented individual expert a specialist simply it is two blue lines means pregnant no blue line means not pregnant why cannot we do that with UTI? we need to do that with UTI so that you know yes at 10 rupees 15 rupees 20 rupees medicine is required which is less than dollar one US. I have had contracted this disease I need to go to the medicine shop get some antibiotics and then retest and maybe if I am clear I am good or visit the doctor anyways. We need to develop technologies we need to develop technologies that are smaller that are cheaper that utilizes light making it far cheaper that do not require any expert any specialist to tell me that I am suffering from a particular infection. Let us start with UTI nanobiophotonics have the capacity have the potential to provide these kinds of home diagnostics or diagnostic tools that require no specialized intervention.

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Disease Burden of India

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YLLs = years of life lost

Tuberculosis (325,000 deaths)

YLLs per 100,000 (percentage of all YLLs)	Percentage
>1300	(2%)
800-1300	(22%)
<800	(76%)

Respiratory infections (342,000 deaths)

YLLs per 100,000 (percentage of all YLLs)	Percentage
>1800	(4%)
1,300-1,800	(26%)
<1,300	(70%)

Diarrhoea (19,000 deaths)

YLLs per 100,000 (percentage of all YLLs)	Percentage
>2400	(2%)
1600-2400	(37%)
<1600	(61%)

National Burden Estimates of healthy life lost in India, 2017: an analysis using direct mortality data and indirect disability data

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The Lancet Global Health

18:54 / 33:30 Issue 12 Pages e1675-e1684 (December 2019)

DOI: 10.1016/S2214-109X(19)30451-6

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Quite similarly this is another shocking picture that I want to discuss remember YLL stands for years of life lost a person who have contracted diseases such as tuberculosis or respiratory infection of diarrhoea several of them are dying in my country these are the shocking statistics and because of that how much productive year of that person years of life lost how much productive year of the person is simply frankly speaking lost this person if had alive would have contributed towards the economy building the economy of the country economy of the society. And the shocking thing is these diseases tuberculosis respiratory infection and diarrhoea are diseases from the previous century which we have already won over. Diarrhoea TB respiratory infection have been detected analyzed understood and you know almost eliminated from a substantial portion of the earth very few people you will hear have died out of diarrhoea in Europe northern America or Australia New Zealand, even how many people do you think have had died of diarrhoea in our Asian countries such as Russia, China, Korea, Japan and look where we stand with these states particularly where the years of life lost in is in significant amount.

If any one of you are interested I will ask you to go through this paper ah published in the Lancet Global Health 2017 and this give shocking statistics that people in my country are dying out of diseases that are completely preventable cheap medicines are available subsidies are there. You can simply visit any chemist shop any run of the mill doctor anybody will prescribe you this and you can live at the end of the day lives will not be lost, but the shocking statistics shows that because of lack of diagnostic lack of understanding these many numbers of life are getting lost for something completely preventable. We as individual human beings we have scientists' doctors academics have to come together. We need to produce technologies not just proof of concept methods, but actual cheap

technologies that can immediately diagnose immediately diagnose what sort of disease that has happened. The point that I want to make here is that technology such as this already exist we do not have to invent anything new home pregnancy detection kit already exist it is simply detecting those pregnancy hormone present in the urine if it can detect hormone why cannot it detect another chemical that probably is being secreted by a bacteria. At the end of the day home pregnancy detection kit is detecting a particular chemical a hormone the pregnancy hormone present in urine. So, why cannot we see that it is detecting bacteria or presence of some other chemical compound associated with a bacteria or other pathogens. Technology already exist we just need to bring 2 and 2 together and create 4 and this is incumbent it is incumbent on us as a society as academics as doctors as scientists as engineers as people from physics chemistry mathematics background to bring together.

So, that by 2027 we see a significant improvement on to this the point of me taking this course is perhaps some of you will actually be interested to create this healthcare technologies that will actually go into the market and save some human lives. And believe you me there is several amounts of communication gap. Biology and physics or biology and engineering per say or biology and mathematics per say have not been the best of friends. Rutherford Henry Rutherford once said that in science there is only physics everything else is stamp collection. So, I do not know whether you will disagree or agree with that the fact of matter remains that irrespective of whether I am collecting stamp or doing quantum mechanics I need to talk with the other fellow I need to discuss it with the other person to see the world from that person's point of view. There exist a communication gap between engineers and doctors there exist a communication gap between physics mathematics with respect to chemistry and biology there exist a gap between medical personnel pathologist radiologist as compared with people who are into lasers or spectroscopy.

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The Communication Gap

- Which Disease to Focus?
- Nano Bio Photonics Research too Technology Driven.
- Lack of Knowledge on Unmet Medical Needs.
- Missing Knowledge of Technical Potential.
- The great chasm between Physicians and Physicists!

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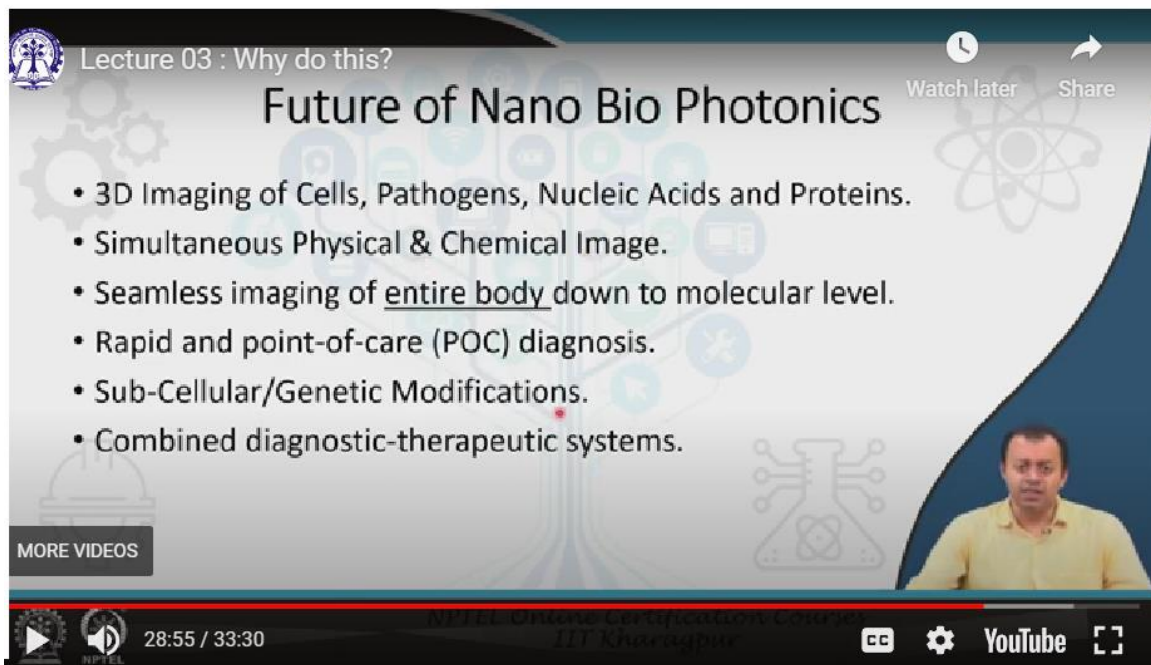
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We need to understand which disease to focus I think I give you a hint of some of these diseases in my previous slide. And some of the research that goes on in photonics domain in general nanophotonic nanobiophotonics in particular is too much technology driven as in its proof of concept it is like also ran like I also once ran in the marathon I did not continue after like say 5 or 10 minutes I did not continue I went home, but it is working like that that you can detect a particular disease using biopsy I can also detect using this particular technique, but your technique is standard so keep on using your technique. Too much technology driven as if it is simply a proof a proof of concept also it could be utilized that does not cut it that simply does not cut it we have to detect we have to put something that is better the keyword here is better more advantageous faster cheaper more accurate than the previous one. Instead of simply saying that you can do it using this technique I can also use it this technique simply will not cut. We need to talk with doctors we need to talk with healthcare professionals we need to talk with actual people in the ground and understand that what sort of medical needs they are looking for in the past 2 or 3 years there had been a huge focus on the coronavirus pandemic granted it was one of the most significant pandemic of this particular century and may it stay like that I nothing bigger than this comes in the near foreseeable future, but there exists several other diseases some of which I told you in the previous slides that are killing on a regular basis so called a silent killer.

So, called a silent killer every day mothers of my country are dying simply for something preventable a pandemic granted is completely new we need time to understand it develop a vaccine, but whatever required to understand tuberculosis or diarrhea has already been known it is in 18th or 19th century we have already figured that out we just need to do it faster cheaper at a large scale nanobiophotonics have the capacity to do that and this chasm

this this I would not use the term chasm I will use the term canyon a gap exists between physicians and physicists doctors and engineers no good believe you me no good comes out of you know staying in silos staying in ghettos staying in your separate you know comfort zones I am an engineer you are a doctor your world is different my world is different unless we breach this gap unless we talk with one another physicians and physicists we can never expect our science to progress do you think those scientist Newton Einstein etcetera simply stayed in one direction or one area and thereby they progressed. So, as students of different background it is incumbent upon you to breach the gap and talk with somebody from a different area from a different expertise not necessarily of science, but of arts commerce etcetera because remember whatever affects anyone directly affects everyone indirectly.



The image is a screenshot of a YouTube video player. The video title is "Lecture 03 : Why do this? Future of Nano Bio Photonics". The main content is a list of bullet points:

- 3D Imaging of Cells, Pathogens, Nucleic Acids and Proteins.
- Simultaneous Physical & Chemical Image.
- Seamless imaging of entire body down to molecular level.
- Rapid and point-of-care (POC) diagnosis.
- Sub-Cellular/Genetic Modifications.
- Combined diagnostic-therapeutic systems.

The video player interface includes a "Watch later" button, a "Share" button, a "MORE VIDEOS" button, and a progress bar showing 28:55 / 33:30. The YouTube logo and other icons are visible at the bottom.

So, what are the future of nanobiophotonics we will see several of them in our coming topics we will have 3D imaging of cells pathogens we will need to have simultaneous chemical and physical images we need to detect a disease have manifested in a person from a nanoscale level to the entire body. So, all of those things in order to do that we have nanobiophotonic technologies it has the potential to go through all of this and significant amount of research is been going on where a seamless imaging of the entire body starting from the top level to the molecular level can be done using nanobiophotonic technologies.

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Scientific Journals and Conferences

Journals	Conferences	Funding Bodies
Nature, Nature Photonics, Nature Nanotechnology	CLEO, OSA	India: SERB-IRHPA, DST-Nanomission, DBT-NanoBio, DHR-Grant in Aid
Optics Express, Biomedical Optics Express	SPIE	United Kingdom: EPSRC, BBSRC, MRC, SUPA.
Science, PNAS	IEEE Photonics Conference	European Union: Horizon 2020, ERC, FET, Marie Skłodowska-Curie Actions
Nanophotonics, Journal of Biophotonics		USA: NSF, NIH, DoD

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There are several scientific journals some of them are world famous nature photonics proceeding of the ah national academy of science of America science they regularly feature topics or research breakthroughs on nanobiophotonics.

So, if you are further interested please follow these journals several of them are available with a subscription, but several of them are available free of cost open access you can access it or if you are into a university library most universities have subscription for that. So, just go on to it. It does not matter whether you are fully understanding many of the topics there, but your knowledge will slowly increase start with something follow these journals the Nobel prize perhaps you know come from several of these journals from articles published in several of these journals. There are several conferences that keeps on happening ah S P I E's, Clio optical society of America IEEE institute of electronics and electrical engineers photonics conferences several of those proceedings are live streamed several of these where scientists come and discuss their research ah they are recorded and they are available free of cost in social media you can just simply google do an internet search on nanobiophotonics lectures, photonics lectures, lectures on disease detection using light and beautiful beautiful lectures will come up one or two of them might be mine own not so beautiful. And obviously, there are several funding bodies grant bodies that give you money so that if you have an idea per say of how to utilize nanobiophotonic technologies for disease detection understanding disease or cure of a disease they exist in India we have science and education research board, department of science and technology, department of biotechnology, department of health research obviously, Indian council of medical research those are the Indian bodies then internationally you have United Kingdom's EPSRC engineering and physical science

research something I forgot European Union obviously, have Horizon 2020 I think this is Horizon beyond 2020 has gone, but I had applied for Horizon 2020 unsuccessfully in the United States there is national science foundation, national institute of health, department of defense. So, these are the government or private bodies or semi government bodies that fund you that give you money to carry forward your research.

So, if you are a scientist if you are a student look out for the grants that are provided by them Marie Curie reaction regularly fund students for their I think PhD or post-doctoral research you can get a funding from here to go to I think Europe and do your research there and you will be funded by these organization. NSF NIH also regularly fund students to perform research especially in area of medical diagnostics apart from other topics of course. So, I think I have tried to make an argument now hopefully you will accept some of my arguments and based on that let us continue our studies on nanobiophotonics. Thank you very much.