Nanobiophotonics: Touching Our Daily Life
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Lecture No. 46
Functional Near-Infrared Spectroscopy (fNIRS) of the Brain

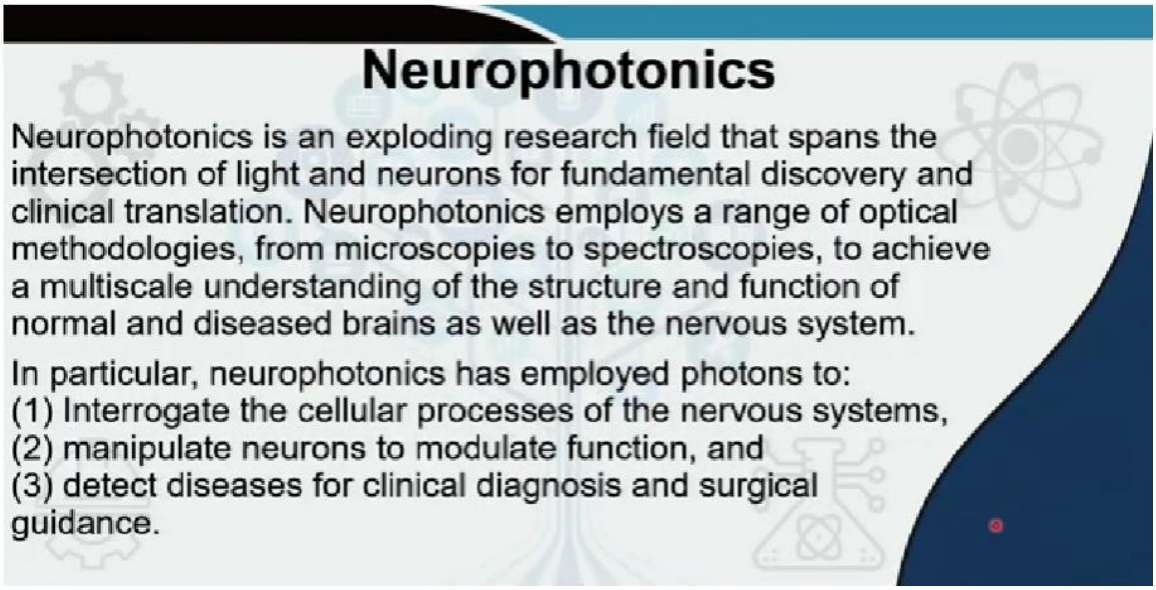
Hello and welcome. We are going to start the next module, module number 10 today, which is the introduction to Neurophotonics. So, as I said in introduction to Octogenetics that is previous module, module number 9, Neurophotonics and Octogenetics are complementary topics. They are very often these terms Neurophotonics and Octogenetics used interchangeably and many of the areas between Neurophotonics and Octogenetics overlap. So, it is very difficult at this present moment to differentiate that this is specifically Neurophotonics and this is specifically Octogenetics. You will find several topics that I am going to teach in this particular module matching that of any popular Octogenetics book.

Quite similarly, the topics that we will be discussing in Octogenetics, the next chapter as well as the previous chapter, chapter 9 and chapter 11, you will find in some very good Neurophotonics book as well. So, my advice at this present moment to you is do not worry about the nomenclature or the semantics. Neurophotonics or Octogenetics both more or less tries to describe the same thing that is interaction of light with the nervous system. Now both light is a big word, what kind of wavelengths you are using, what is it a pulse, is it continuous, it is laser light, this is a broadband light, what intensity, is it a fluorescence or is it just normal reflection, normal topography and at the same time as we have seen in the previous lectures, nervous system is also quite huge.

It is not just limited to brain and the spinal cord, but nerves are present almost every other part of our body and they are connected with the central nervous system, they are connected with the peripheral nervous system. If we are looking for interaction of light with neurons, which exact part of neurons because neurons can be very big at least their axons as we have seen can be very big, we are looking at the axons, we are looking at the dendrites, we are looking at the synaptic cleft. So, there are all these different divisions and these divisions, these separate areas are all joined together, all joined together in this entire field of Neurophotonics or Octogenetics. So, it is quite ok and quite natural for us to you know overlap and go between one to another. So, just because the name of the topic is Neurophotonics does not mean that it will not fall under the optogenetics field.

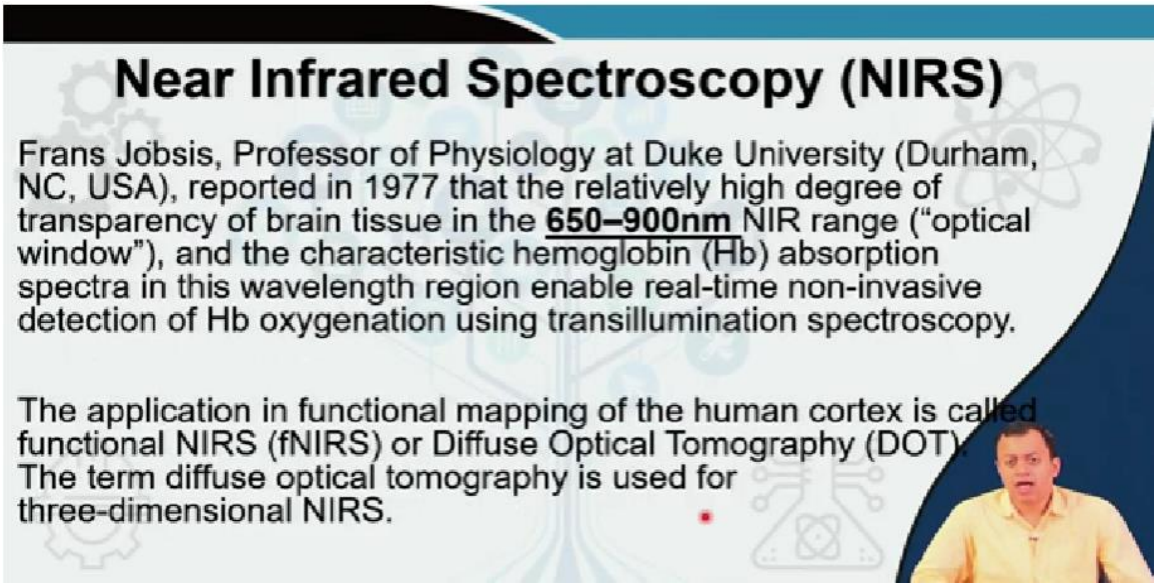
Opposite is also true, if anything starts with optogenetics does not prevent you from labeling it as some part of Neurophotonics and working on to it. Both optogenetics and

Neurophotonics deals with interaction of light with the nervous system that is the enough definition. So, today we will start the topic of Neurophotonics and I thought that I will try to start with our comfort zone spectroscopy. Here we are going to discuss about the functional near infrared spectroscopy of the brain. Now, let us see what are the actual or the academic definition of Neurophotonics is.



So, Neurophotonics is an exploding research field that spans the intersection of light and neurons nerve cells. By this time, you should know what neurons are, otherwise go back to previous lecture, this would not make much of a sense if you do not understand what neurons are. So, Nanophotonics is an exploding research field that spans the interaction of light and neurons for fundamental discovery and clinical translation. So, this is the point not only we want to understand how the neurons work, how the message is passed through, how the neural circuitry works, how the interaction happens between muscles and neurons, how the message is passed, but we also want it for clinical application i.e. we also want to understand if we could modify or modulate or try to give some kind of a therapeutic intervention for a person suffering from a neural diseases, neural diseases like motor neuron disease, Alzheimer disease, Parkinson's disease, epilepsy so on and so forth. Can we understand how neurons work and if a neuron is not working try to make it work that is overall the aim of Neurophotonics. Neurophotonics employs a range of optical methodologies from microscopes to spectroscopies to achieve a multi scale understanding of the structure and function of normal and diseased brain as well as the nervous system. Again, brain is merely a part of the nervous system perhaps the most important part, but other parts are also necessary and just a brain just by itself will not be able to achieve any function whatsoever unless it is connected with both the central nervous system as well as the peripheral nervous system. So, we use multi scale methodologies spectroscope, microscope, lasers what not and we try to understand the structure and function of diseased brain as well as other parts of the nervous system.

In particular Neurophotonics has employed photons to interrogate the cellular processes of the nervous system basically try to understand what neurons look like, how they work, how they send the information, the electrical pulses, the resting potential, the message, the electrical pulse all of those things how they are passed through. Manipulate here comes the control part since it is in technology not just merely science not only we are I mean we are not just satisfied with understanding what the neurons are, but how they function. And most importantly if we can control the functions. It is not enough for us to manipulate or understand well it is not enough for us to simply see or understand the functioning of neurons, but we want to manipulate, control and modulate their functions. At the same time obviously, that is the idea of Bio-Nanophotonics detect diseases for clinical diagnosis and surgical guidance.



So single most important aspect of Neurophotonics something that has recently started is Near Infrared Spectroscopy NIRS many of the times it is called Functional Near Infrared Spectroscopy FNIRS. So, what exactly is NIRS or FNIRS? So in 1977 Professor Jobsis of Duke University figured out that between 650 to 900 nanometer 650 to 900 nanometer range is an optical window it is particularly a frequency where the brain tissue is transparent i.e. if a light falling a wavelength of light falling between 650 to 900 nanometer that is around orangish or reddish to you know near infrared range red and near infrared very very near infrared this light is simply transmitted by the brain tissue without much of absorption or reflection. So, the reddish light or 900 nanometer infrared light is simply passed through passed through by the brain tissue without any absorption of this particular wavelength.

However, this particular wavelength of light 650 to 900 nanometer is absorbed by hemoglobin present in blood. So, understand this brain tissue is not absorbing this light blood is absorbing this light. So characteristic hemoglobin absorption spectra in this

wavelength regions enable real time non-invasive detection of hemoglobin oxygenation using trans illumination spectroscopy. What does that mean? That mean that near your cranium near your brain just below the brain there is some amount of blood and then you have the brain tissue. Now understand this there is something called in blood brain barrier.

There is a semi permeable membrane of endothelium cells. What are endothelium cells? Endotheliums are the cells that make the inner lines of veins or arteries. So, there is a semi permeable filter made of this endothelium cells between brain and rest of the blood vessels. Blood do not directly go into the brain. Your brain basically does not have blood vessels.

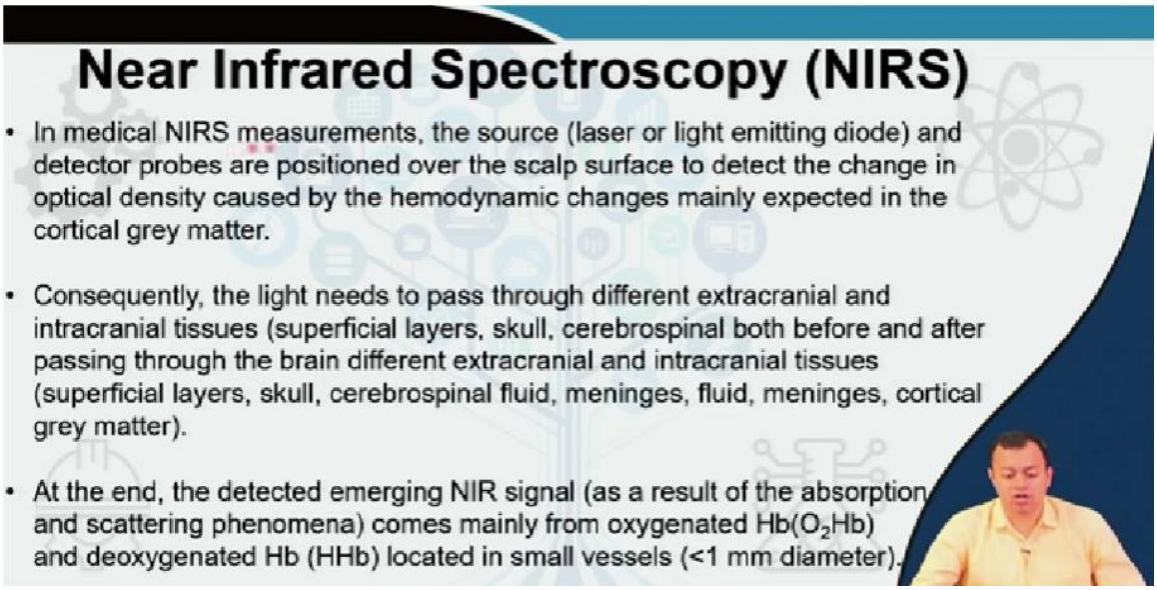
There is a filter a membrane that prevents blood from crossing over onto the brain and thereby since brain is this important your body has evolved itself to have some sort of a barrier between blood and brain. This is the blood brain barrier. This is a filter so that any infection that has happened in blood any virus any bacteria that has that has come into your blood do not immediately pass through this blood brain barrier and attack can attack the brain. So, your brain is always protected. Your brain is always protected.

There are cerebrospinal fluid that can go through etc blood but blood is to be prevented directly from going into the brain. There are certain viruses even bacterias that knows how to penetrate through this filter and those diseases are particularly difficult and very very dangerous and sometimes fatal. One prime example is meningitis. Meningitis bacteria or meningitis virus, meningitis can be caused by both bacteria different types of bacteria as well as viruses as well as fungus which can penetrate through this blood brain barrier and attack the brain and thereby causes huge amount of distress. Now you have your skull your cranium then some blood vessels and after that the brain tissue starts after that the brain tissue starts blood and the brain tissue have obviously gap both internally and outside.

There are no blood vessels there are no blood vessels inside the brain. There is however brain are getting oxygen from one hint cerebrospinal fluid but there are other examples as well. So, if you are sending some amount of light you know inside the brain you have seen previously with the mouse etc. A particular wavelength of light is simply passing through is passing through the brain tissue but it is actually being absorbed by hemoglobin. Now hemoglobin can give you information about the presence or absence of oxygen in that particular blood that is near the brain.

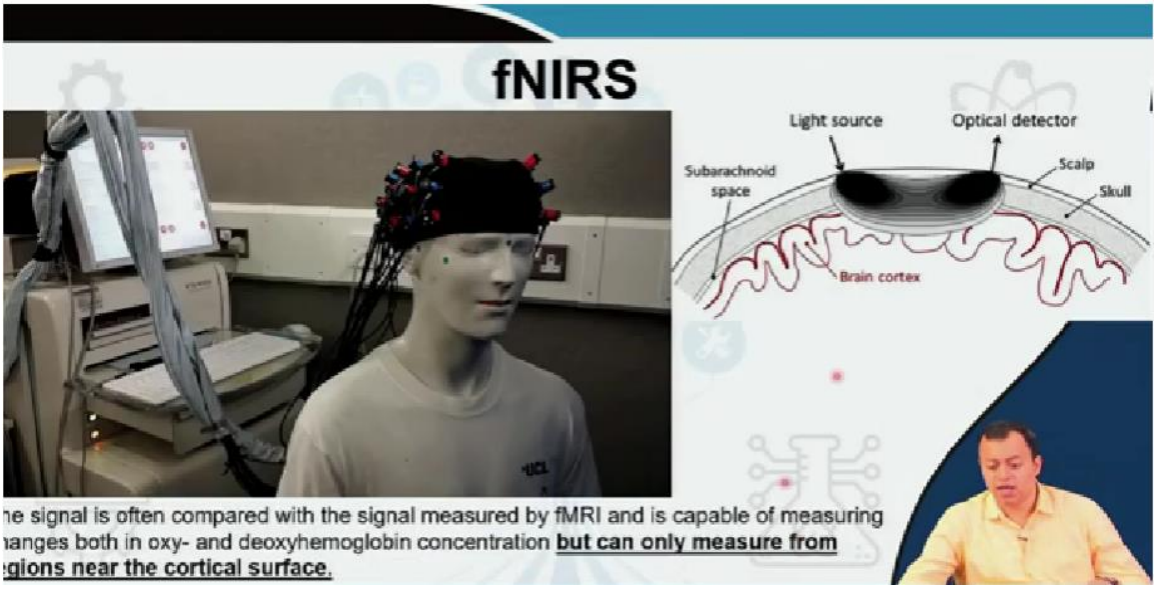
So functional near infrared spectroscopy utilizes this particular phenomenon. So, the application of functional mapping of the human cortex or diffused using diffused optical tomography to find out the diffusion of blood or the presence of oxygenated blood or deoxygenated blood near the cerebral cortex or near the brain. It is not penetrating the brain blood does not goes inside but near about in the periphery in the boundary in the

boundary there should be some amount of blood which has some amount of oxygen some amount of non-oxygen and if we can predict if you can see if you can understand it and from that we can predict the internal functions of the brain that is the overall idea. So, in medical NERS measurement near infrared spectroscopy measurement the source laser or light emitting diode and the detector probes are positioned over the scalp. This is scalp surface to detect the change in optical density caused by the hemodynamic.



It is blood blood changes mainly expected in the cortical gray matter. Gray matter is the tissue brain tissue that is you know connected on top of which there are some amount of blood on top not inside. Consequently, the light needs to pass through different extracranial and intracranial tissues superficial layers, skull, cerebrospinal both before and after passing through the brain different extracranial and intracranial tissues layers etc. At the end the detected emerging NIR signal as a result of absorption and scattering phenomena comes mainly from oxygenated and deoxygenated located in small vessels 1-millimeter diameter very very close to the actual brain tissue. So, you try to find out the amount of oxygen oxygenated blood as well as deoxygenated blood close to the surface of the brain.

The brain itself again does not have blood vessels there are oxygenated blood near the brain as well as deoxygenated blood near the brain. So, on top on the periphery of the brain how the blood is present what are the oxygen conditions etc. you try to see using near infrared spectroscopy using the wavelength 650 to 900 nanometer that is not absorbed by brain but is absorbed by the hemoglobin present in blood. So, this is very very simple you see this is the brain cortex this is the brain cortex and these are the places these are the places where the blood is present this entire part is brain this entire



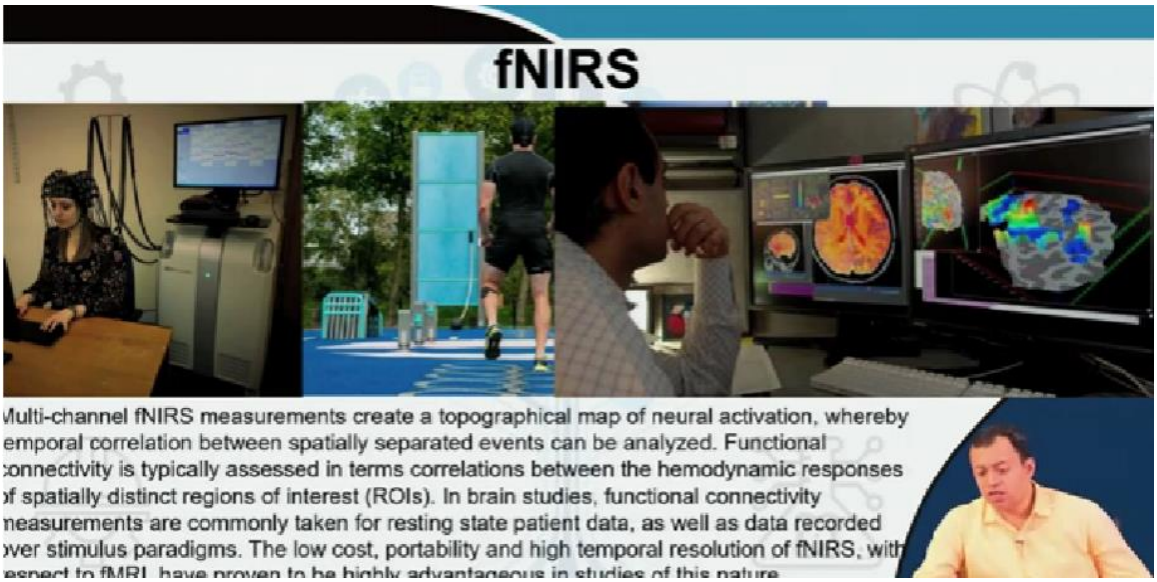
part is brain which is not absorbing this the 600 to 900 650 to 900 nanometer wavelength of light and this is your skull this is your this is this is your skull it has tissue it has cranium it has some sort of fluids etc. So you put these kinds of LEDs on top of the skull on top of the skull this is the light source it sends 600 to 900 nanometer 650 to 900 nanometer wavelength of light it penetrates through the skulls through the cranium through the bone goes into these you know extracellular fluids etc.

near the brain near the brain cortex this part is not absorbed and whatever is scattered whatever is absorbed by the blood vessels the presence of blood oxygenated blood is then reflected absorbed and you are getting it through an optical detector here the blue is the input red is the output blue is the input red is the output and you are trying to measure the amount of oxygen present in the blood that is just above your brain tissue that is just above your brain tissue. So, this this this thickness layer is your skull this is your skull contains bone contains scalp hair of course it has its own intracellular extracellular fluids cranium all of those things there is some I cannot pronounce this some amount of inter inter space between the brain cortex and the blood vessels. So, the signal is often compared with the signal is a measured by magnetic resonance imaging and is capable of measuring changes both in oxy and deoxy hemoglobin concentration but it can only measure from regions near the cortical surface nothing below. So just just periphery what is the condition of blood just below my skull just below my skull and above my brain this boundary skull brain the small small tiny boundary which has some amount of blood vessels it tries to find out the presence of oxygen how much oxygen is present in those in in in in that inter intermediate layer interfacial layer between skull cranium better term cranium and blood this small gap that has blood it has it has it tries to figure out here there are no blood vessels here there are no blood vessels. So, problem is simply it can only measure from regions near the cortical surface it can only measure in the region that is at the periphery at the

outside of your brain it does not go inside the brain well what could be done but this is thereby pretty safe pretty safe pretty safe right.

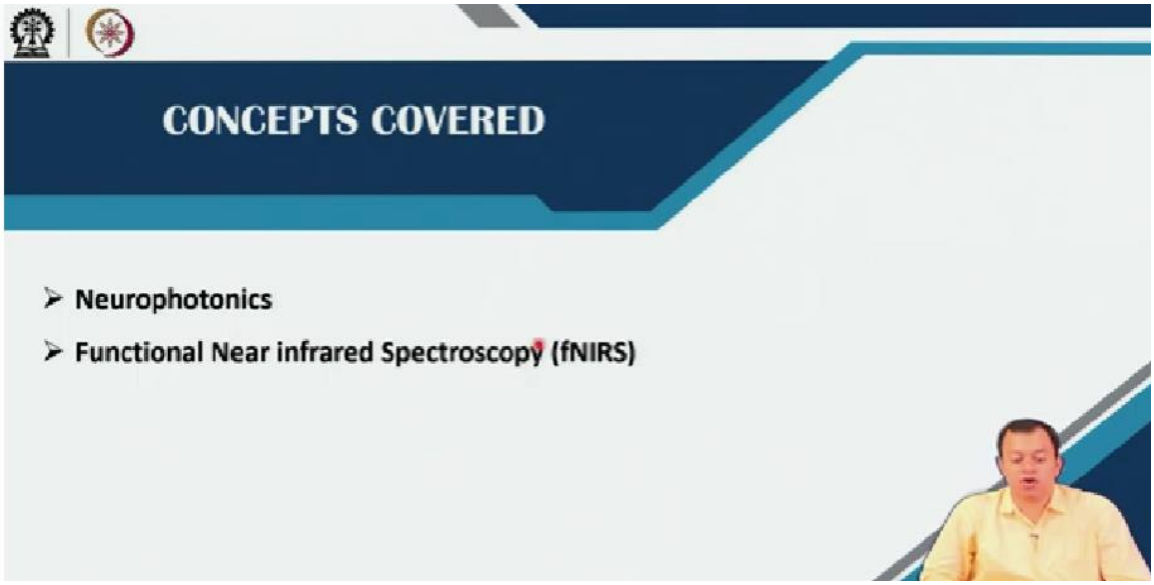
Multi-channel function on NIRS measurement creates a topographical map of neural activation whereby temporal correlation between specially separated events can be analyzed. So you can be asked to do you know regular functions normal everyday typing or even jogging and even simply sitting and thereby the blood activity the oxygenation and deoxygenation of the blood near your neuron and as your neurons are firing if they by in turn requiring more oxygen less oxygen what are the interaction of them or at least what are the interaction of those neurons particularly at the topmost level of your brain with respect to the blood vessels what kind of you know interaction they have with respect to blood can be simply mapped can be simply covered while I mean not affecting the person not affecting the person directly at all right. Functional connectivity is typically assessed in terms of correlation between hemodynamic responses blood responses oxygenation deoxygenation or at specially distinct regions of interest you want to see what happens to the blood vessels between mother and the child at a specific region near the brain when they are happy they are cuddling they are together or when they are running doing some kind of physical activity or when they are doing some sort of a mental activity like this person is been given to solve some mathematical questions or some visual cues are being given and from that aptitude you know you have done this aptitude test you have to figure out between some options how your brain works how neuron fires from a point of view of the blood vessels nearby. You are trying to map the function of the brain as viewed from the oxygenation or deoxygenation blood that hemodynamic response. So, it is an indirect way it is an indirect way and under no circumstances you will be able to know what is happening inside the brain you are trying to figure it out what is happening at the periphery from this, but still this gives plethora of good information you should not be thinking that this is not proper or not complete.

Most importantly it gives something that other techniques failed and that is a live human being doing day to day work and mapping the brain activity as such using light without hampering the person's health in any way without hampering the person's health how much do you think it would be risky to you know map the activities of a child and compare and correlate with that of mother's brain activity how it has to be incredibly safe otherwise these would not have been allowed. In brain studies functional connectivity measurement are commonly taken from resting state patient data either animals or fishes zebra fishes etcetera or if it is human being then the person has to be sedated or during MRI scan the person has to be you know completely lying down a resting state patient, but here you are able to provide different types of external stimulus mental stimulus physical stimulus it has to person has to jump between different hoops and thereby measure the different brain functions as a function of the blood oxygenation blood deoxygenation hemodynamic response. The low cost portability and high temporal resolution of fNRIS with respect to f functional MRI have proven to be highly advantageous in studies of the nature understand the fundamental advantage in IRS measure you do not have to sedate the patient you do not have to open up the brain you do not have to risk destroying the person's brain there is very very little risk there has to be some amount even 0.01 percent of risk associated with any experiment, but as you can see it is it is it is pretty pretty less and thereby you go and measure the oxygen

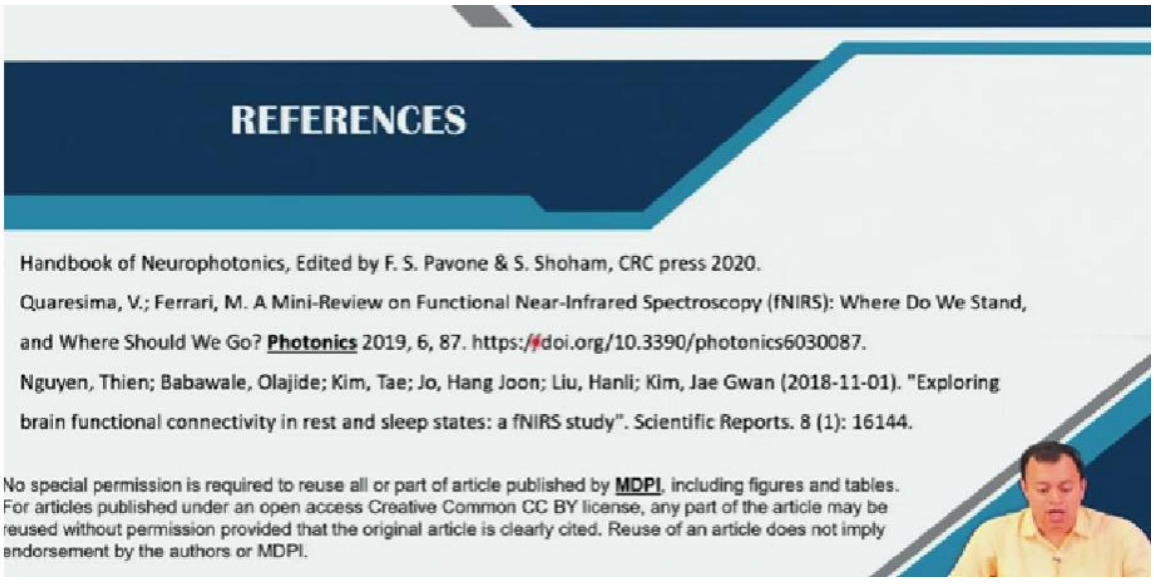


saturation you all have understood pulse oxygenator the oximeter that you put in your finger to find out the amount of blood in amount of oxygen in your blood from which you are calculating whether a person is perhaps suffering from covid or not it is something similar bad analogy, but still you are unable to understand the entire activity of the brain inside it, but you are trying to see the oxygen level outside the brain and try to see which areas are firing getting more oxygen getting less oxygen as you are performing some kind of a mental tasks versus you are performing some kind of a physical task right. It gives

you very high temporal resolution and most importantly you do not have to give any drug any you do not have to sedate any anesthesia to the person you can instead of using putting it on rats or mice or zebra fish or drosophila fruit fly you use it on actual living breathing human beings and try to map their brain and try to correlate this data with the type of external stimulus external information external work that they are doing.



So these are the concepts covered in the first topic of our neuro photonics we discussed about FNIRS and if you are more interested please go through these particular references



that I have gone through this review that I found very very interesting functional NIRS where do we stand by Ferrari and Carasima and I will see you in the next class. Thank you very much.