Nanobiophotonics: Touching Our Daily Life
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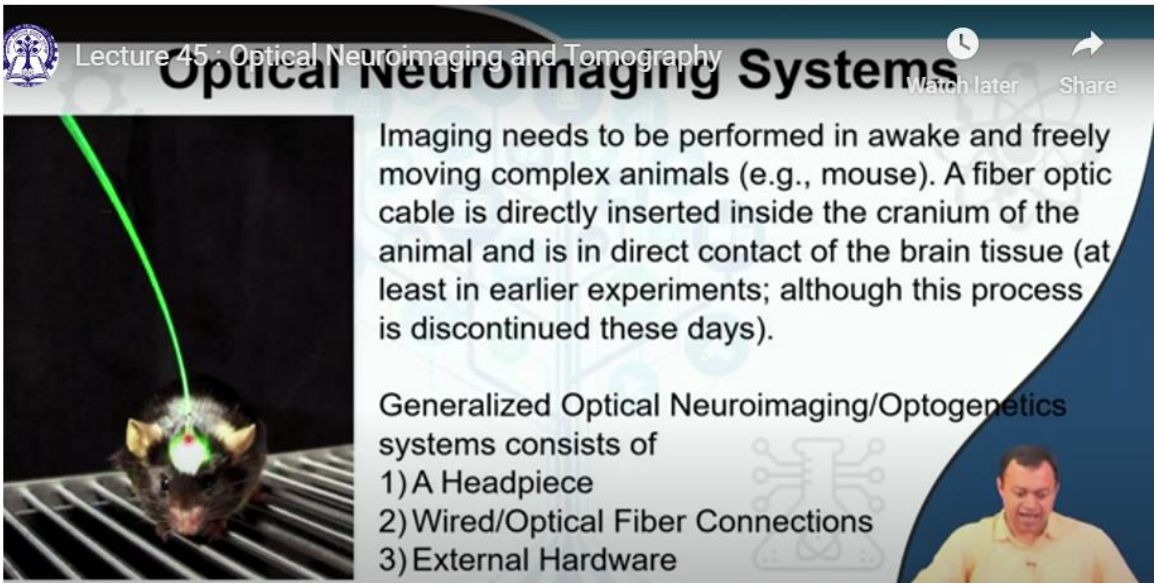
Lecture No. 45
Optical Neuroimaging and Tomography

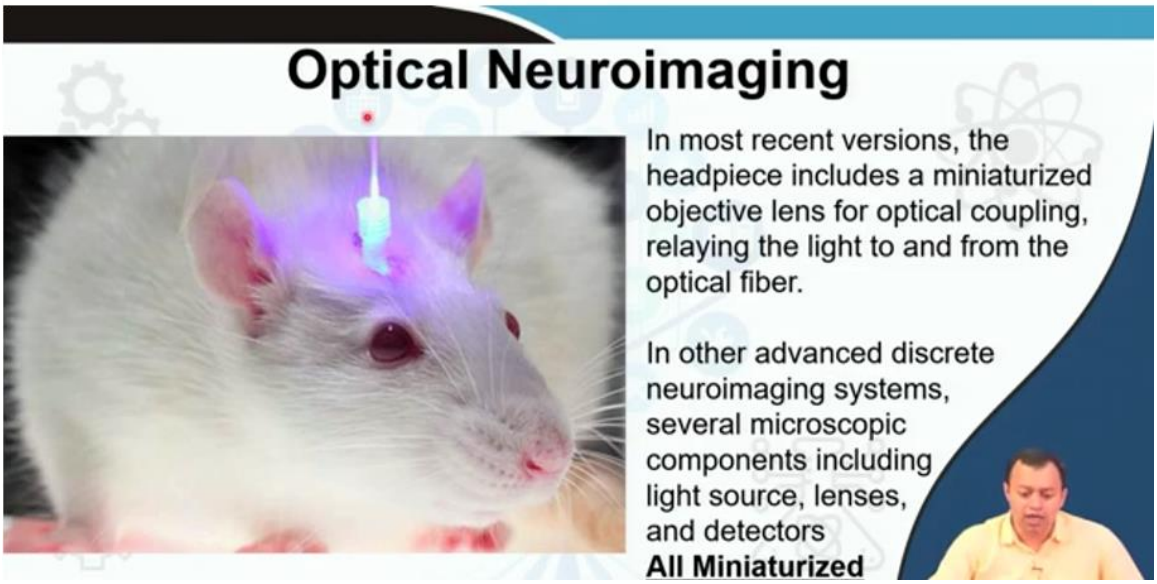
Welcome back specifically to those of you who are still continuing after the onslaught of you on biology. So, today we are going to finish the topic of the principles of optogenetic technology and today we are going to discuss optical neuroimaging and tomography.



So, what exactly is an optical neuroimaging system? right this is an optical neuroimaging system this is an optical fiber containing a laser light and that has been inserted into the cranium of the mouse there is a small hole well not so small in this particular case hole has been done inside the cranium inside the head of the mouse and that is then connected with a optical fiber the optical fiber contains a laser of a specific wavelength and that is made to illuminate certain areas of the brain. those brains can contain certain antibody or photoreceptor cells that you have artificially created opsine based cells, opsine based genes GFP or anything like that and that has resulted in a particular behavior that you can modulate. by shining light so imaging needs to be performed in wake and awake and freely moving complex animals eg mouse there is no point dissecting taking out the brain and trying to understand it if it is not connected with a live freely moving complex animal. A fiber optic cable is directly inserted inside the cranium of the animal and is in direct contact of the brain tissue at least in earlier experiments.

Although this process is discontinued these days because obviously ethical conditions, what happens when your experiment is finished? You take out the What happens to the hole? This hole is inside the skull. The brain is exposed. If the brain is exposed, very soon it will get infected and problem will happen. So, generalized optical neuroimaging or optogenetic system consists of a headpiece, a wired optical fiber connection and an external hardware which is then connected which is trying to analyze the light that has been sent.

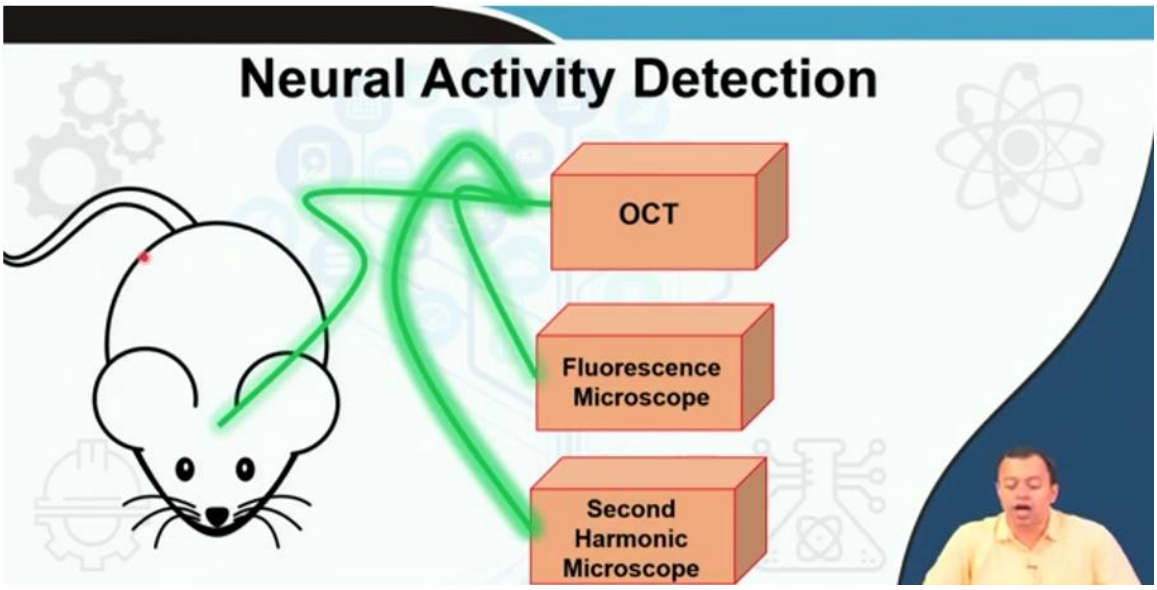
We need to understand or illuminate different part of the of the brain and thereby trying to modulate the behavior, the cognitive functions of the mouse and thereby try to fully map the brain neuron by neuron and understand the various diseases various injuries various anomalies that takes place your memory is better than my memory i am able to drive better you are able to drive less better how how these traits how these general traits keeps on happening right so you can cook far better than me though I have the same materials how exactly all of these are happening which part of the brain is allowing you to do any of these right.



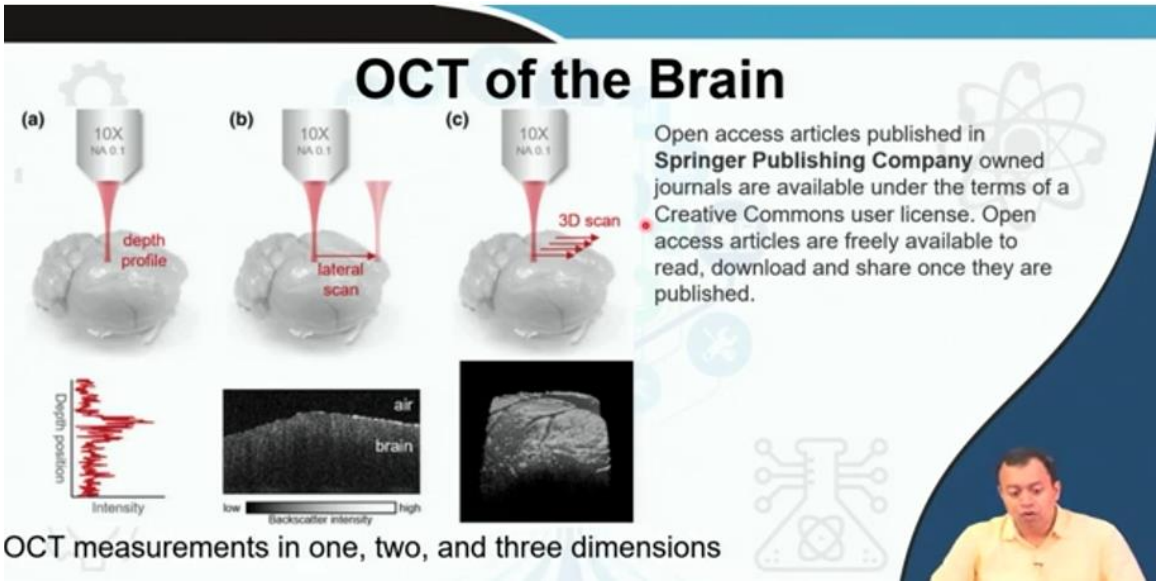
So, in most recent version the head piece including a miniaturized objective lens for optical coupling replying the light to and from the optical fiber. See you have made a small hole and you have inserted this entire LED based system along with modulator this contains transmitter and receiver. So, the light is being sent and certain cases the reflected light is being taken back connected with some sort of a some sort of a. hardware based system, a computer that analyze the transmitted and reflected data and perform some sort of a function.

You can switch on and off the laser, you can modulate this laser that has been connected inside the brain of a live animal and try to map the behavior with respect to light being

fired at different parts of the brain. different frequencies of the light are being absorbed by different parts of the brain if the mouse is already containing the obscene genes. Remember the obscene gene that we discussed in I think lecture number 40 and 41. So, the other advanced discrete neuroimaging systems, several microscopic components including light sources, lenses and detectors all miniaturized are put in this small area. You need to see where you are focusing your light on, your light is also focused. So, maybe there is some sort of a lens that is carrying all this information and that is getting back and we need to understand this.

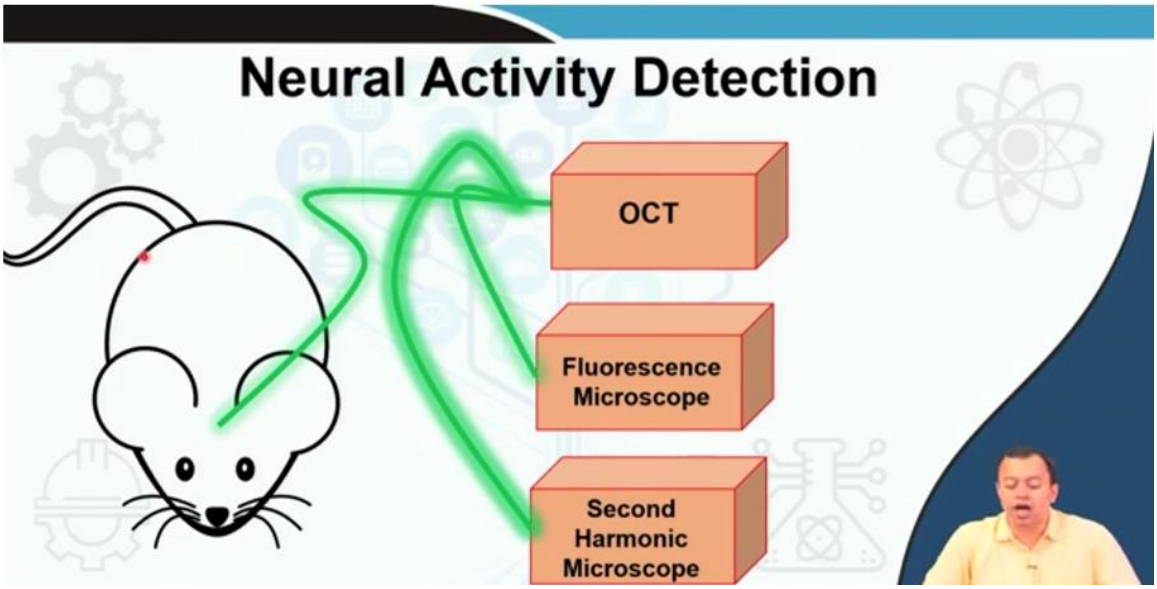


So, the neural activity detection, once you have connected it with an optical fiber, once you have connected it with an optical fiber such as this, such as this, this optical fiber can very well then be connected to several different hardware. You can connect it to an optical coherence tomography machine, coherence tomography I think we discussed OCT, you connect with a fluorescence microscope. You also connect with the second harmonic microscope the one which works on non-linearity and try to understand the signal that is coming out by exposing the mouse brain. Optical coherence tomography these days or micro CT is very very popular these days where you do understand a tomography a mapping of the surface of the brain is done by sending A fluorescence microscope on the other hand, if you have been able to tag, if you have been able to level the brain with either nanoparticles or some kind of fluorescence leveling mechanism, you can utilize them and you can map different areas of the brains.
when a particular function is being performed, it is eating, there is a predatory behavior, it is eating, it is sleeping, it is afraid, it is running around the mouse that is. And of course, the second harmonic microscope where you have tried to see collagen fibers etcetera which absorbs a particular set of photons or particular set of two photons. in this non-linearity and they can very well be utilized.



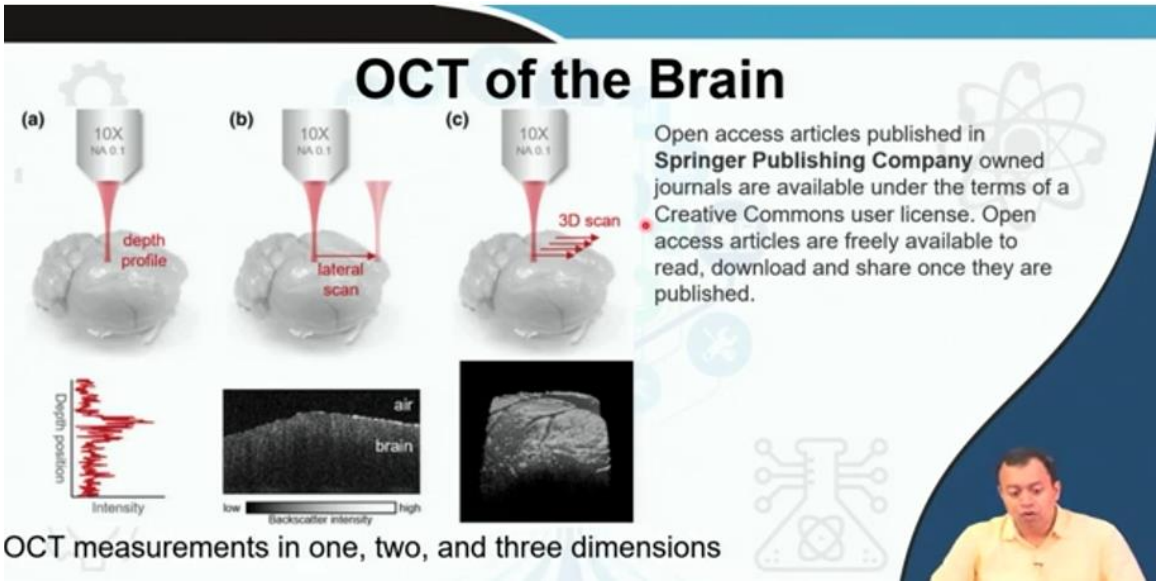
So, it is very common these days to do OCT micro OCT of brain optical coherence tomography where the depth profile where a particular light is being sent and it is get reflected back it is connected with another part of the light you have probably seen I am just repeating itself two branches of optical fiber cable goes on one is connected with a tissue. eye or brain and another connected with some sort of a movable mirror.

The light reflected back from both of these both of these fibers are made to interfere among each other. If the path traveled by both lights is same the interference will be coherent otherwise it will be incoherent by changing the mirror of the other branch. from one end to another end, you can try to map or try to make the interference coherent. and from that the movement of the mirror you can understand the overall depth profile of the of the tissue that you are trying to focus trying to understand and in this particular case the brain of a mouse is being done there are several aspects you can you know make the laser go up and down thereby trying to understand the depth profile you can make the laser move in x y direction this is z this is depth in the x y direction that is lateral scan. and of course, you can have depth and movement depth and movement thereby providing a 3D scanning resulting in some kind of a 3D mapping of the entire brain.



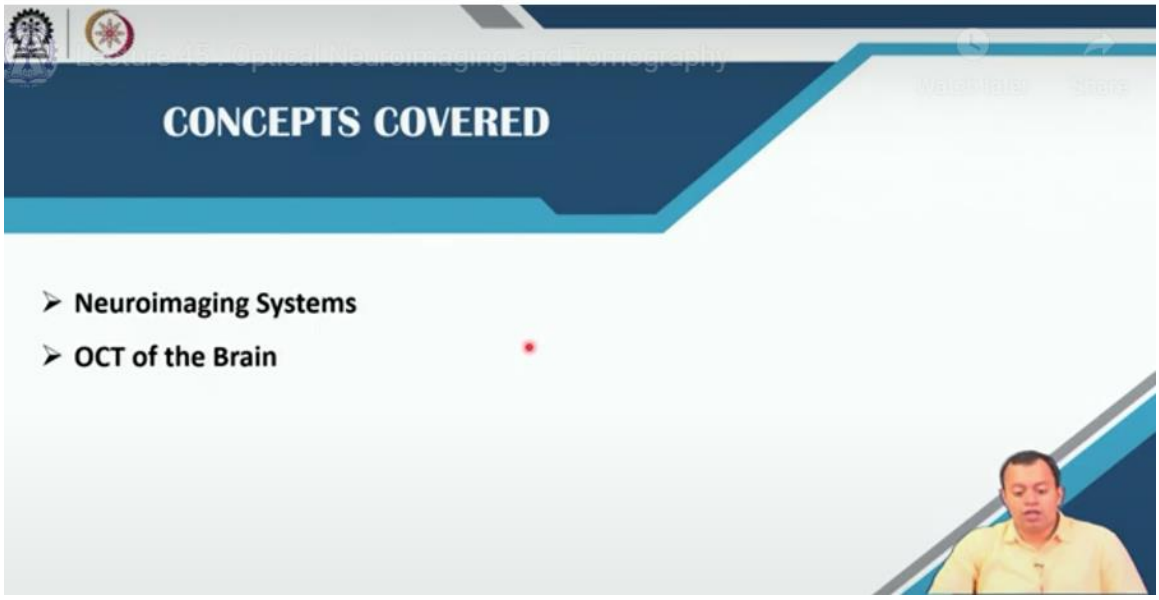
This when connected simultaneously with the fluorescence microscope with different areas being tagged think about it. So, the entire brain you have mapped. different areas of the brain are then connected with labeled with different fluorophores, fluorochromes, nanoparticles, quantum dots. you have then sent another set of light which is absorbed by this fluorophore. The electron goes from lower level to upper level then comes back to a lower level emitting another electron that is being measured that is being captured by the optical fiber again and that is being placed into fluorescence microscope.

and you are able to see which particular part of the brain is firing, which particular part of the brain is having a higher electrical potential resulting in what sort of behavior in the mouse. At the end of the day you have to do that at a live mouse, at a live complex freely moving animal, otherwise the entire process finally gets defeated. Simultaneously, you can also while you have mapped the brain, you can send set of light two photons per say two photon microscopies, which will be absorbed in certain areas, which will not be absorbed. When you are comparing it with the overall 3D map of the brain, you can see certain areas are illuminated, certain areas showing black, those black areas are the one where the two photons are absorbed. you send initially these 2 photon areas. Overlap one on top of another and the two photon areas where there is there are black eye the two photons have been absorbed particular characteristic of a specific protein or a specific molecule which shows second harmonic generation i e two photons are absorbed and emitting one single photon the additional photon some photon is coming up. So, that some photon is then again returned back and is imaged. So, those areas the shades of areas those can immediately be mapped and you overlay whatever you are getting here and you overlap it with this whatever information you are getting whatever image you are getting and you overlap both of them on top of optical of the three-dimensional brain, three-dimensional brain tissue, the three-dimensional brain image that you have found



and thereby you are able to completely map the three things together there and corroborate it with a specific behavior of the brain. mouse resulting in its resulting in analysis of its basically mapping the brain. If you have been able to connect it with some kind of an electrical impulse by putting a chip and then firing it deliberately.

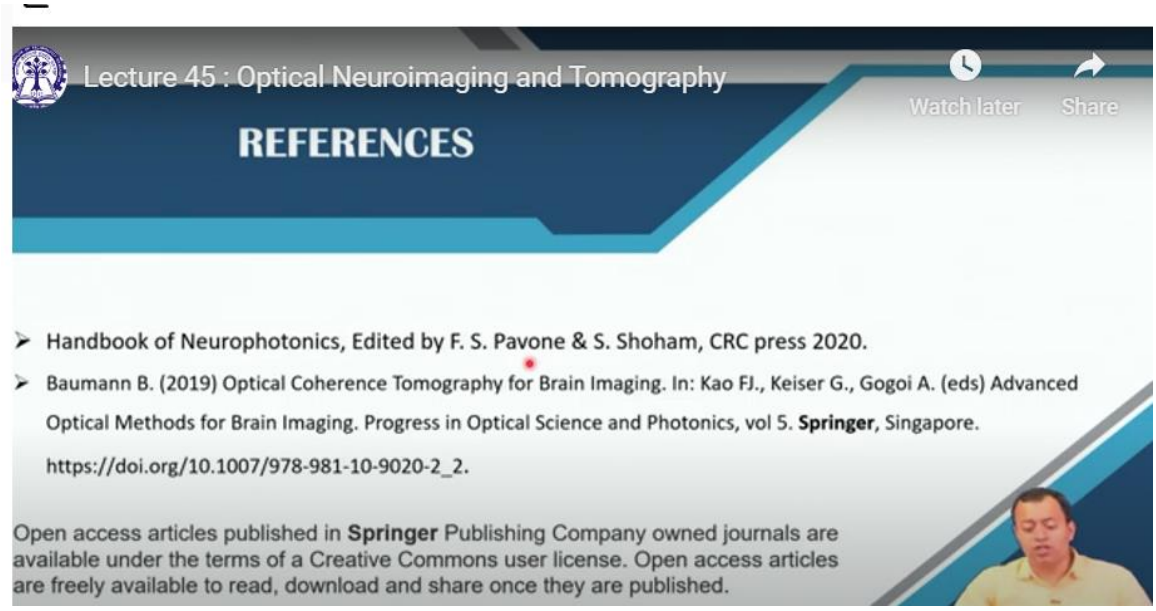
You are able to map the electrical potential along with the optical connections along with three-dimensional map of the brain and that results in the so-called neuroimaging or neurophotonics that is exactly the topic of our next chapter.



So, these are the concepts that I covered. I think I have given you sufficient information in this particular module for those of you who are completely new to neuroscience. I tried to

keep the neurobiology part bare minimum as I said. There could be certain mistakes, please verify the information, please verify the slides that I am providing you.

Now, that you have enough information about which part of brain works, what is neuron, what is soma, what is myelin sheath, what are all these glial cells, what are neurotransmitters, chemical and electrical synapses, how this occurs. In the next module, we will try to mostly focus on the imaging part and the next module we will try to see how you can repair, how you can cure any problem and what are the latest topics that are being discussed. held in this area of optogenetics and neurophotonics.



So, these are the topics, these are the references. I strongly suggest you go and read this book, I think available in the internet as well, Handbook of Neurophotonics.

And of course, several of these papers are currently very hot topic in neurophotonics and optogenetics. So, thank you very much.