Mathematical Aspects of Biomedical Electronic System Design
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Lecture 18
Optical Properties of Tissues and Mathematical modeling

So, welcome back for this session on continuation with the biomedical optics. So, before we move forward let us understand what are different constituents of the tissue which is present within this biological organization.

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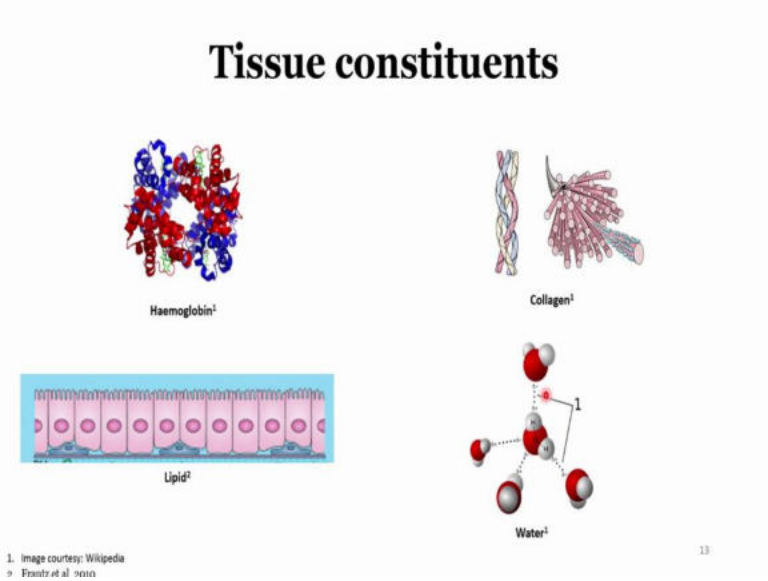

So, what you see over here is, what do we have over here? We have hemoglobin within these tissues. Hemoglobin also has, so what is the purpose of hemoglobin? The purpose of hemoglobin is to transport the oxygen so it has the, the ferrous compound inside, or ferrous ion which actually gets attached to this oxygen and it transports the oxygen from one place to another.

Now, there are two states of hemoglobin. The one being the oxygenated hemoglobin and another is deoxygenated hemoglobin. So, in this case what you see is that there are two different ways to characterize the hemoglobin, that is oxygenated hemoglobin, that is also known as HbO, and deoxygenated hemoglobin that is known as HbR, or reduced hemoglobin.

Another (con) constituents is collagen which drastically affects the optical technique. The third one is the lipids. One of them is this lipid that you see on the, phospholipid that you see as a, which is part of the basal membrane. And then finally, is the, the next one is the water. So, in the case of water what you see is H_2O and the oxygen makes a particular angle with the hydrogen ions.

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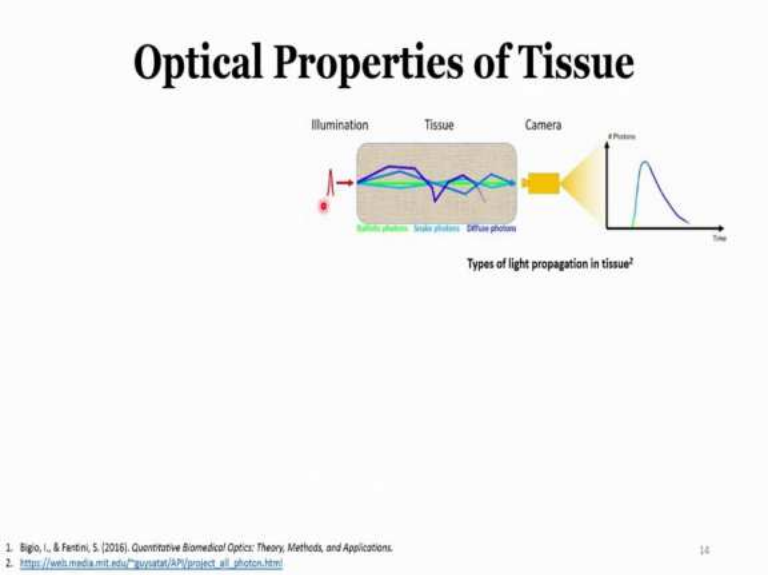

So, let us see what happens once we pass the illumination, that is, the light, through the tissue. So, what do we see we see that, so there is certain type of laser, or light that I am passing. So, I am passing a pulse of light. I am not passing the continuous light, but I am only passing the light for a very small duration of time.

And what you can see on the right is there are different types of photons, or not types of photon, the type of photon is only single, but the way that the photon interacts with the tissue is different. For example, what you see is the ballistic photons. So, this ballistic photon which is in green color is the one that reaches the first. So, here you can see that it reaches the first, that is the green color.

And the next is the sky-blue colored snake photons. So, the ballistic photon as you can see does not undergo or goes very minimal number of scattering events. Snake photons are the photons which undergo the scattering which is again not main, many, it is like less numbers still. The lowest being in the case of ballistic photons.

And then finally we have the diffused photons. The diffuse photons are the photons which scatter the highest. In the case of a turbid media such as tissue we will always see the cases of diffused photons when the tissue dimension is like more than 1 mm or 2 mm. So, in this, these cases when the dimension of the tissue increases, in this case, in such cases the diffusion nature is going to be more dominant. And in the next few classes we will also talk about the diffusion process, we will talk about the transport equations and how those can be used to characterize or reverse engineer the optical properties of the tissue such as scattering coefficient and absorption coefficient.

So, here you can see that the ballistic photons are the one which goes minimum scattering and arrives first, and then it is the snake photons over here which arrives after the ballistic photons and then the whole lot of other photons that you see over here are the diffused photons that arise after the snake photons.

And you also see a certain trend over here that it is not actually a Gaussian, but it has, this peak has a long tail. And this tail would also help you to understand the scattering coefficient of the tissue. So, we will get to know about this at a later stage once we try to learn the mathematical model, but this is what is actually happening in the hindsight of the light which is propagating through the tissue.

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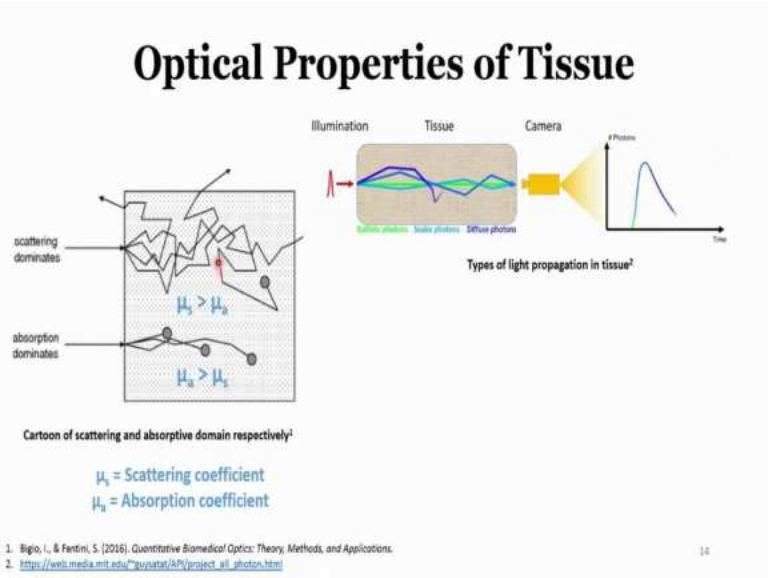

So, if we want to now characterize how much scattering is going to happen or how much absorption is going to happen, we introduce two variables, the first being scattering coefficient and the second is absorption coefficient. So, in the first case that you see in the top, we assume that this top part of the tissue is highly scattering. In such cases you have μ_s, that is μ_s is higher as compared to the absorption coefficient, that is μ_a.

So, in that case you can see that there is lot of scattering that is, scattering events that are going to occur, and this is the current state of the photon for, for example here. Some other photon you can also see that actually comes out of the tissue, which would not be actually getting detected by the detector which is placed on the right side. Very few photons you see that are actually being detected.

Some of the photons actually get reflected backwards. So, you can also have a detector on the back side to actually detect the, the backward reflected or backward scattered photons. In the bottom part what we assume is that μ_a, that is, absorption coefficient is higher as compared to the scattering coefficient. So, what we observe over here is that the photons are getting absorbed rather than getting scattered. So, here, it is still getting scattered as you can see over here. There are slight scattering events. And, but eventually they are getting absorbed within the tissue.

So, in such cases you have absorption coefficient is more than the scattering coefficient. But in most of the cases of the, of the breasts where there is a presence of tissue you will see the event or on the top, that is the top case that you see over here. The scattering coefficient is more than the absorption coefficient. For the, other contents where you have more fluid content of the stroma of the breast tissues, or extra cellular matrix you will see the bottom kind of events, bottom kind of case which is going to be more dominant, dominant.

So, this is the case where you see the macroscopic view of the interaction of light with the tissue. But what about microscopically? So, what if we draw the cell structure and then see how the cells are interacting with the light.

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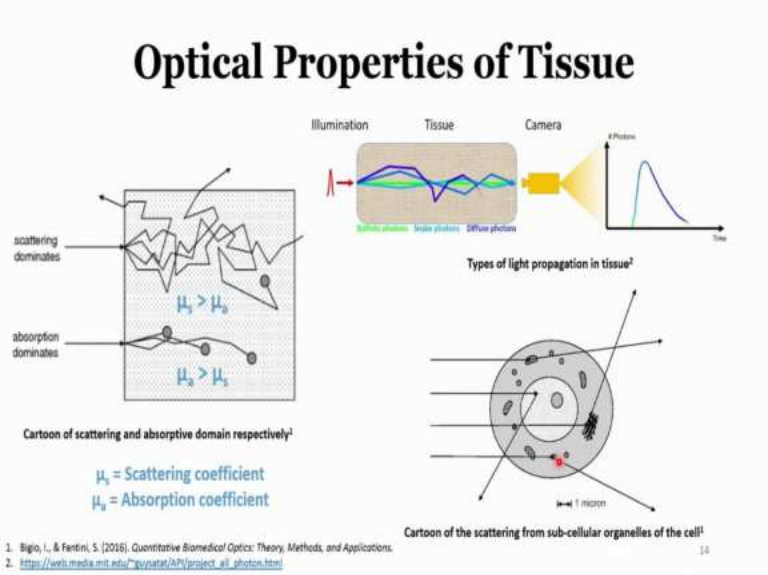

So, let us draw a cell tissue over here. So, not a tissue but only a cell over here. So, what you see over here, this is a single cell. It has many organelles on the right side. So, it has the golgi apparatus, it has nucleus, this is the nuclei, and the other components or organelles within these cells over here. You have mitochondria, and, and this is the light that I am going to pass through this cell. So, what do we see over here?

We see that some of the organelles are actually refracting the light. So, the light is passing through this and then it is getting refracted by a certain angle. We also see that the light is hitting the nucleus inside this cell and it is getting back scattered. Some of the photons which pass through the cells and its gets refracted to very high angle, very large angles. And then again there are some other photons which are getting refracted, again, with some other organelles of the cells. So, this is what happens in, microscopically once the light interacts with the tissue. So, this being just a cartoon, but eventually there are lot of number of cells which are present and this occurs in lot of instances.

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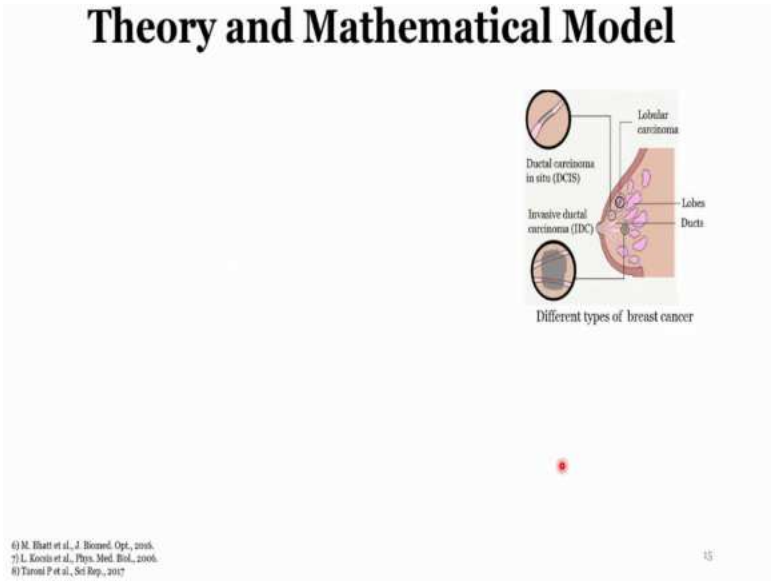

So, let us go forward and come up with how the theory and mathematical modeling happens for the light-tissue interaction.

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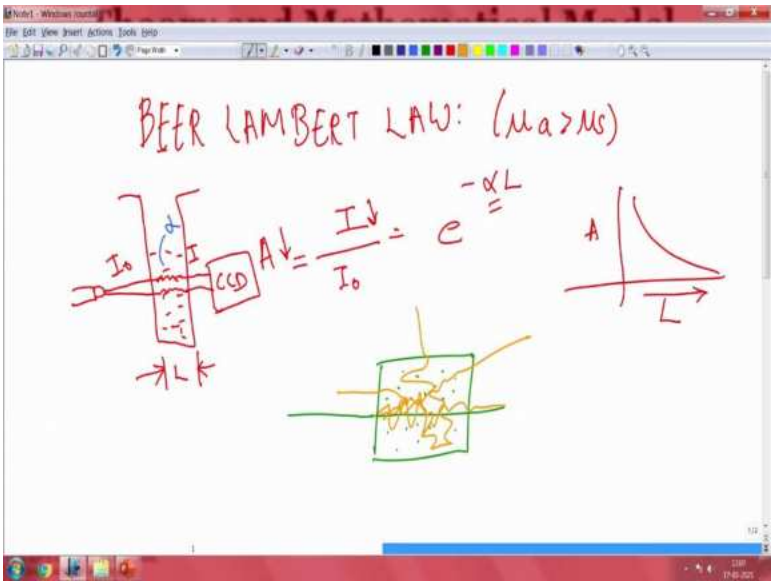

Now, coming to the first part is where people started to work with Beer Lambert law. So, you have the Beer Lambert law. So, what do we have over here? So, we have, and this is the case where your assumption is μ_a is more than μ_s so your absorption coefficient is for higher than the scattering coefficient. And you take a tube, for example, and you pour a liquid over here. And this is strictly for this kind of cases only, not in the case of turbid medium tissue.

And what we do is we have this LED, or the LASER. And we shine the LASER over here and it undergoes some scattering, and then it comes out from over here, and here we have the camera, could be a CCD, for example, a charge coupled devices over here. And what we see over here is the light intensity that is I_0, and the light which is getting detected by the detector. So, over here, this will not be I_0, it would be I.

So, now if I want to relate this I with I_0 naught, that is, initial and the final, so how do I relate it? So, its related by

$$\frac{I}{I_0} = e^{-\alpha L}.$$

And L is the thickness of your column, or the tube that you are pouring a particular liquid. And α over here is the property which is exhibited by the liquid.

So, as you can see over here if you plot it as the length of the tube actually increases, you will see an exponential decay of the optical density. So, it is also known as optical density, that is, a log of the ratio or you can also call it, it might not be the correct way to define the optical density, you can also call it as kind of a attenuation.

So, how much the light is getting attenuated, it is in a walk sense you can just tell it that it increases as the length gets increased, the attenuation is going to get reduced. In other words your A is getting reduced when the I, that is, the light which is traversing the liquid medium is getting reduced. So, this is the case when we have the Beer Lambert law, which is very simple case when we have the liquid present in the column.

But when we have the tissue, so for example, when we talk about the tissue, so light which passes the tissue is not going to just go like this because having a lot of components as you already see. So, even a single cell has many components, so it will not just go just straight out of a, of this tissue but it will undergo a lot of scattering over here. And some of it can go outside, some of them can actually go forward also, and some of can go backwards, some of them can go with a particular angle.

So, its going to be, the absorption is not going to be more dominant but the scattering is going to be more dominant. So, the Beer Lambert law might not be the best way to actually quantify the optical properties of the tissue. So, which law is going to be better? So, what people did is they

come up with a new set of laws for the optical propagation through the tissues, and that is known as the modified Beer Lambert Law.

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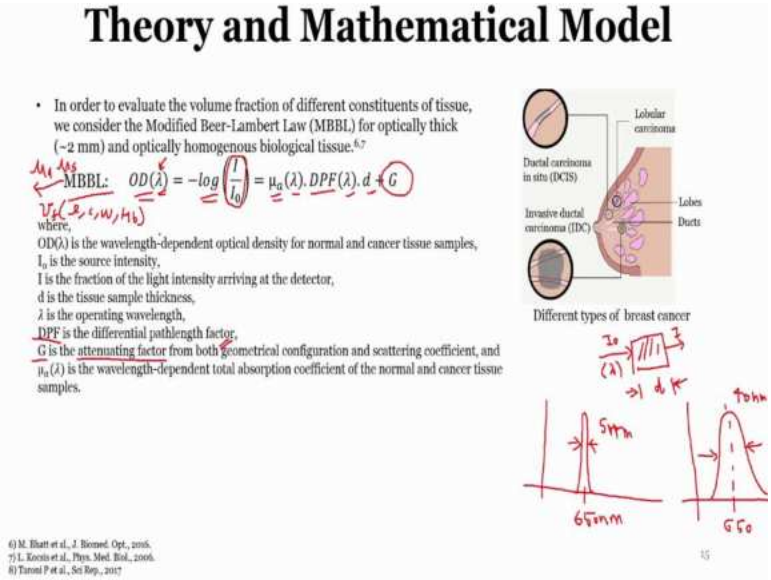

So, here you can see this, we talked about $\frac{I}{I_0}$ earlier. This is the attenuation. If you take the log of that attenuation, you get this optical density. And that is again a function of a particular wavelength. So, again you have this tissue, you pass this light over here. So, you have I_0 and you have I.

The light that you pass is also having a certain wavelength. So, if you see these LASERs, LASERs have very short bandwidth. So, for example, you have 650 nanometers wavelength. So, it has a very less bandwidth, maybe around 5 nanometers. But in the case of LEDs, and is what our lab is working on, on using very cheap LEDs, you have very high bandwidth.

Again, we still are working with 650 nanometers, for example. And, but it has a large bandwidth over here, which is around 40 nanometers, for example. So, we have the function which is of, which, function dependent optical density, which is optical density with the function of λ. And then we have, again, the absorption coefficient. So, this is again a function of wavelength.

And then we have, we have introduced a new term which is known as differential path length. So, here is the definition of differential path length. Again, which is a function of λ. And then this is the D, that is the thickness of the tissue. And this is D over here, and then finally we have the factor G.

So, this G is actually the attenuation factor. And that is from both the geometrical and the scattering coefficient. And we do not want this term, so we will try to remove this term out of the equation. And the way to do that would be, we are going to make lot of assumptions. The first assumption is that the geometrical configuration for all these measurements is going to be the same. And the scattering which is going to occur from them is also going to be the, similar. So, that is a kind of assumption that we do in this Beer Lambert law. So, we are going to use this Beer Lambert law, and finally we are going to quantify, we are going to finally quantify the optical properties of the tissue, μ_a, μ_s.

We also have other properties of the tissue. So, let me just, yeah, so we quantify μ_a, we quantify μ_s, and we also have quantified the volume fraction of the different constituents of the tissue, as we talk about. We talk about lipid, we talk about collagen, we talk about water, and then we also talk about hemoglobin. So, these are the different, different constituents that we can actually quantify, the volume fraction of those constituents. Looks good. So, we are going to use this modified Beer Lambert law instead of the Beer Lambert law.

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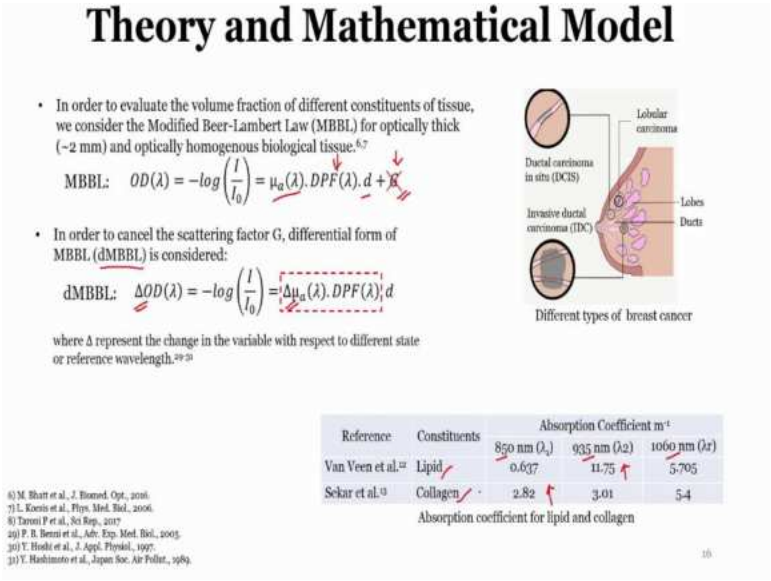

So, going to the next is how do we eliminate the G, that is the attenuation factor. So, this is the same equation, modified Beer Lambert law. Earlier we only had μ_a, μ, μ_a as a function of wavelength, and d. But now we also have introduced the DPF and the G. So, in order to actually do away with the G over here, what do we do is, we go to a differential modified Beer Lambert law, which is also known as dMBBL.

And with this we can actually do away with the G part, that is, we negate the G part. So, what do we add is this Δ term to negate the G part over here. So, now we do not have the μ_a but μ_a is the difference in the μ_a as a function of wavelength for two different states. The two different states could be like inhale and exhale, would be a simple example. So, it could be some other way.

For example, we were talking about analyzing the quenching of the hand tissues. So, quenching of the tissues could be one of the case. Or when we inhale and exhale. So, when we inhale, we have more oxygen present inside the lungs. And when we exhale, there would be less oxygen which is present within the lungs. So, this is also going to change the two different states of the properties. Looks good.

So, so we all, already have the absorption coefficients for different, different constituents such as a lipid and collagen for different, different wavelengths. For 850 you can see that liquid has 0.637 per meter of μ_a, that is, the absolute coefficient. For 935, again, we have the, the absorption coefficient for lipid and collagen. And for 16, sorry, 1060 we also have the absorption coefficient for lipid and collagen.

So, what we see is that at 850 nanometers you can see that the absorption coefficient of collagen is very, very high as compared to the lipid. In the case of 935 you can see that the absorption coefficient of the lipid is more as compared to the collagen. So, based on this we can actually quantify the constituents of the tissue, or the composition of the constituents of the tissue. For example how much is the constituents of the collagen, and how much is the constituents for the lipid.

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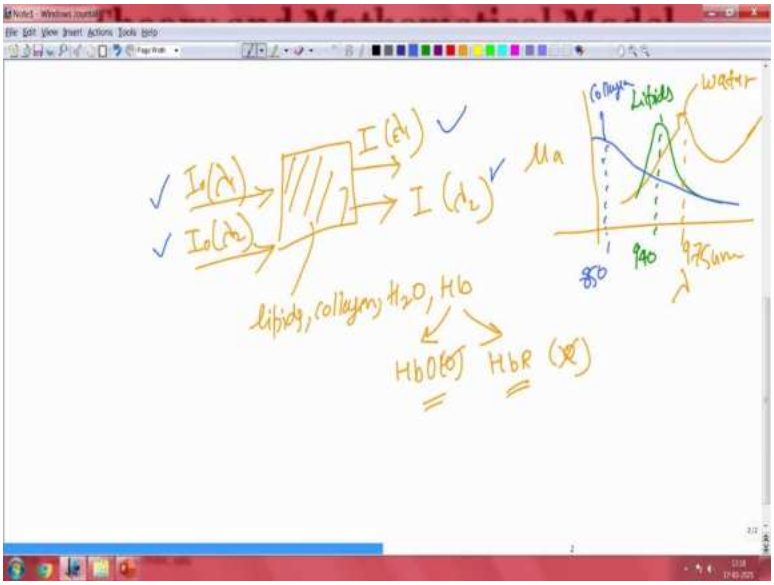

So, for example what we do is, again if I go to my screen over here, again, we have the same tissue. So, instead of passing through a single light λ_1, and detecting, so I will have $I_0(\lambda_1)$ and I detect it as I of, oh sorry, I need to make it $\lambda(\lambda_1)$. I detect it by detector with $I(\lambda_1)$, and I have one more light that I pass through this tissue. I have $I_0(\lambda_2)$ and I detect it $I(\lambda_2)$.

Now, what do we have is, for example, we say that this tissue has different constituents. So, for example, it has lipids, it has collagen, it has water and it has hemoglobin. As we discussed hemoglobin could be of two states. It could be oxygenated hemoglobin, or it could be reduced hemoglobin, which is also known as HbR. So, either it would be carrying the oxygen or it would be not carrying the oxygen. So, in this case oxygen is not there, but in this case the oxygen is present.

So, in both the ways it will actually behave differently. For example, if you now draw the wavelength as a function of absorption, or μ_a, what you observe is that for the water, for example, the, the peak will actually rise somewhere at 975 nanometers, and then it reduce and then it finally increases after that wavelength.

In the case of lipids what you see is that there is a peak of absorption specifically at 940 nanometers. So, in the case of water, it is around 975, in the case of lipids it is around 940. And then for the other constituents, which is collagen, you can see that collagen has very high absorption, and it is like similar to this in the case of collagen.

So, over here it is like very high in the case around visible range of light. And that may make sense also because it is kind of a fibrous content, and it actually absorbs a lot of light within this wavelength, maybe at 850 nanometers. We can just write it as 850 nanometers. And that is what we have used over here. So, the way the light actually gets absorbed at different, different wavelengths is different for different, different constituents. For hemoglobin again, its, it varies accordingly. For both hemoglobin, oxygenated and deoxygenated, it actually varies. So, what do we have over here? So, what we have is two different wavelengths, λ_1 and λ_2, and we detect λ_1 and λ_2 light from here.

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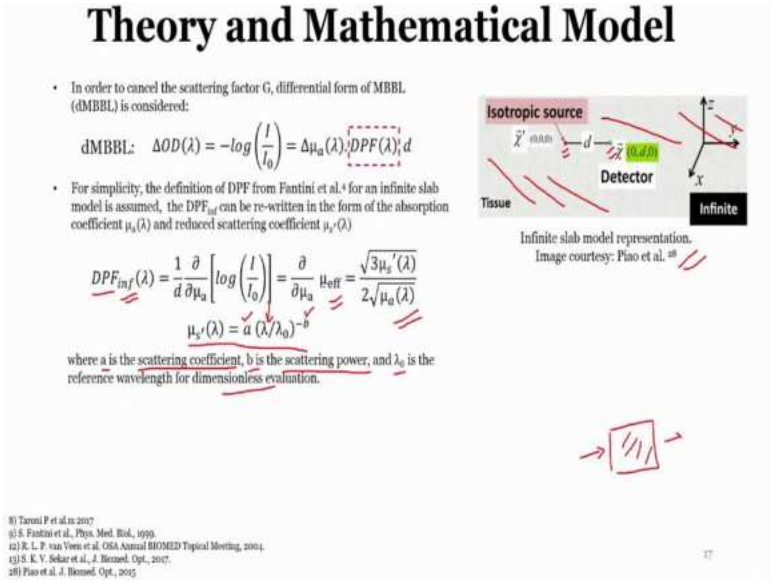

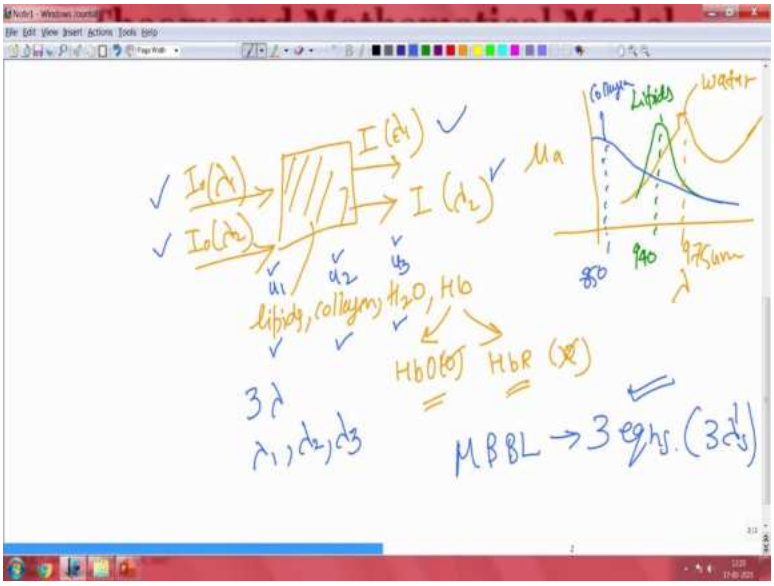

Now, let us go to the, our slide show. So, this is what we are doing right now. We are passing the light through the tissue at different, different wavelengths. The number of wavelengths will depend on the number of constituents that we want to evaluate. So, for example, coming back over here if I want to evaluate only lipid collagen and oxygen, these three constituents, I will need to have three different wavelengths. I need to have λ_1, I need to have λ_2, and then finally λ_3. And from the modified Beer Lambert law, I will get three equations.

So, I have three unknown. So, this is my unknown 1, unknown 2, unknown 3, and I have three equations because of three different wavelengths. So, I am able to now calculate the composition of lipid, collagen and oxygen, or sorry, this water. If I want to have four, I want to quantify four constituents, then, then I need to have four different optical wavelengths. In our case, in our lab we did it with two optical wavelengths, that is lipid and collagen only. So, we had operated at two wavelengths. Looks good.

So, let us move forward. Over here what do we observe is there are two different, two different parameters. The first one is μ_a, and second one is DPF. In the case of differential path length, I need to make this a more simpler implications. So, what I do is, instead of assuming the light to be passing through this tissue like this, and getting detected by like this, what I assume is a simple infinite slab model.

So, this is, on the right side, this is known as infinite slab model. So, which means that the source that you see over here is somewhere over here, and this is the detector, and both the source and detector are inside the, the tissue, completely within the tissue. I am not assuming it as a, the light is coming, which is present outside the tissue. I am assuming it to be inside the tissue. It is kind of a very simplistic, the most simplest assumption that you can use to proceed further.

With this approach what I can do is, is I am going to in, simplify the DPF for the infinite media over here. And I take this as the derivative of the log of the intensity, and then I can write it in the form of the effective μ, that is, the effective attenuation coefficient, and which, this would, that, that would be a derivative with respect to the μ_a. And finally, what I do is, I get this equation.

And where μ_s, is again related to the operating wavelength over here and this a and b are the property of the tissue, a being the scattering coefficient, and b being the scattering power. So, for different tissues, or different parts of the tissue, for example lipid, collagen, fat, adipose kind of tissues, fiberblast, so all of them have different, different (constitu) or different, different values of

a and b. And λ_0 over here is the reference wavelength. And then, and that is, to, just to make this as dimensionless. So, with this now we have simplified the DPF to a μ_a and μ_s, and we are going to quantify the μ_s over here with the equation of

$$\mu_{s'}(\lambda) = a\left(\frac{\lambda}{\lambda_0}\right)^{-b}.$$

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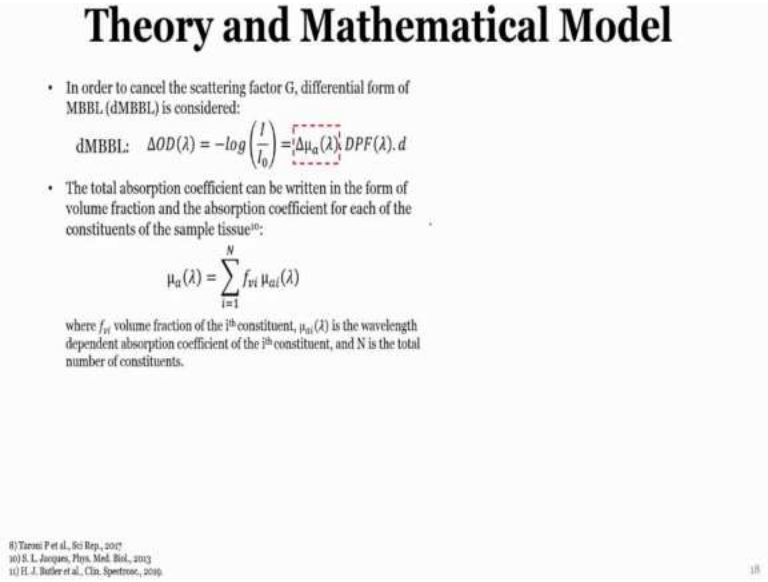

The next part is the μ_a. Now how do I simplify the μ_a, in the terms of tissue constituents? So, one of the way is to write the μ_a into small, small, small contribution from each of the constituents.

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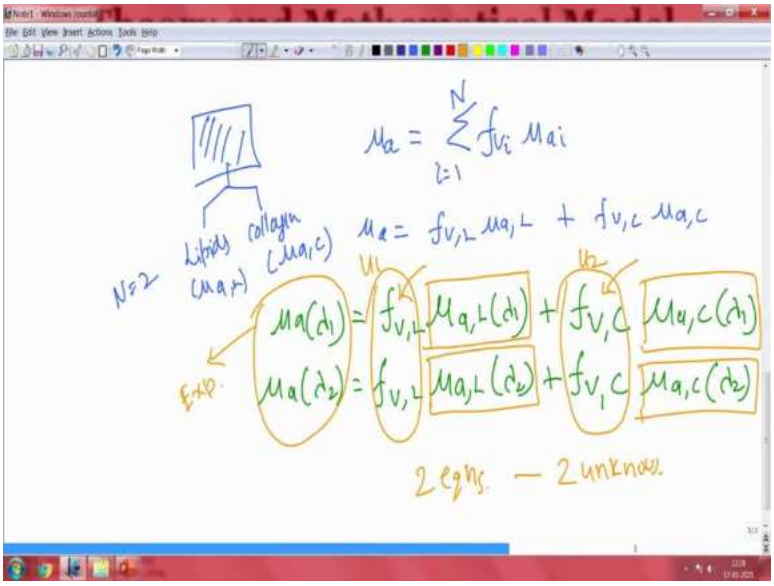

So, for example what I am going to do is, I am going to add one more page over here, and what I assume is the tissue over here, and this tissue, for example has only two constituents, for examples. So, I have lipids and collagen. So, what I assume is that the contribution from lipid would be $\mu_{a,L}$, and contribution of collagen would be $\mu_{a,C}$. So, what I can see that complete, total absorption, or total absorption coefficient would be

$$\mu_a = \sum_{i=1}^{2} f_{vi}\mu_{ai}$$

I assume only two constituents or actually it can be N. i going from 1 to 2, oh sorry, it could be N, i going from 1 to N. And N, I am assuming it to be 2 over here. So, I can elaborate my equation to

$$\mu_a = f_{v,L}\mu_{a,L} + f_{v,C}\mu_{a,C}.$$

So, this is my absorption coefficient for two different constituents.

Now, I can also make it a function dependent μ. So, for example, this I am going to write it that μ_a, μ_a is going to be for a certain wavelength, λ_1. And I can write it as the volume fraction of the lipid is not going to change based on the wavelength. But the absorption coefficient will actually change.

So, I can write it as, like this for a single wavelength. And for the second wavelength I can write it, for second wavelength I can write it as

$$\mu_a(\lambda_2) = f_{v,L}\mu_{a,L}(\lambda_2) + f_{v,C}\mu_{a,C}(\lambda_2).$$

The next question is what do we know from our knowledge, from our knowledge from our seniors or people who have already researched? What do we already know? We know the absorption of lipid at a particular wavelength λ_1, for example. Not for example, actually we know. For most of the wavelengths in the range that we want or the range that we are operating we know.

So, we know the absorption coefficient of lipid at a certain wavelength. We also know absorption coefficient for a second wavelength. We know the absorption coefficient for the collagen for the first wavelength, and similarly we know absolute coefficient for the second wavelength. What do we do not know? We do not know the volume fraction of lipid and volume fraction of the collagen. So, these are the two unknowns.

So, you have unknown 1, you have unknown 2, and you have two equations. So, what do we do is, this is what we are going to get from the experiments. And we want to put it inside this equation and we are going to say of two equations, we have two equations, we have two unknowns, so we can quantify the volume fraction for the liquid and collagen. So, this is, eventually this is what we are going to do in our next formulation.

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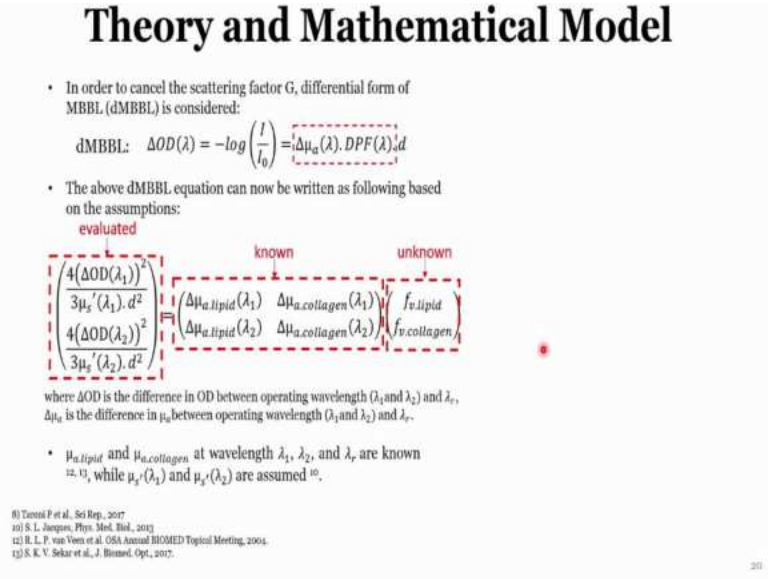

So, as we have discussed what do we observe is the effective, or the total absorption coefficient is a function of summation of the constituents, multiplication of the volume fraction and absorption

coefficient. If there are two constituents then you have two parts, if you have three constituents, you have three parts, and so on and so forth.

So, eventually you can write it like this. This is what we have written some time back for two different wavelengths. And now I, I need to expand both of them together. So, using the differential Beer Lambert law you can actually simplify this equation as this form over here. And mind it that this μ_a is not just μ_a but it is a $\Delta\mu_a$. And this $\Delta\mu_a$ means that it is the absorption coefficient at, the difference of absolute coefficient at two different wavelengths, or it could be a (absorb) difference of absorption coefficient for two different states at the same wavelength, as I am saying without quenching of fist and quenching of fist.

So, this could be two different states, for example, two different states could be breathing of the person, inhale and exhale. This could be two different states. So, this μ_a is not just a single value but it is a difference of two different states at that particular wavelength. So, here again, what do we know? We know this μ_a for the wavelength, for two different states, for lipid and collagen. We also evaluate this optical density. So, again, this is a difference of optical density of that particular wavelength. And this is what we evaluate with the, with our experiments. So, this is what we also know. The unknown is the volume fraction of the lipid and collagen.

So, from these two equations we can actually back calculate the volume fraction. So, this is what we have done and we, we come up with these values of volume fraction, and from this we can actually quantify whether it is diseased tissue or it is a normal tissue. For example, in the case of cancer or tumor, there is more collagen as compared to normal. In the case of normal tissue there is more lipid content as compared to cancer. So, once we quantify the volume fraction, we can actually get to know if whether it is, the part of the tissue is normal or cancer.

So, that is it for, for this session. The next session, we will get to know more about this technique. We will try to learn, or we try to see the actual images of the diffused optical imaging and we will see which part is normal, which, and how we can actually differentiate as cancer. We will talk about the different techniques such as continuous wave diffuse optical tomography, time domain diffuse optical imaging, and then frequency domain diffuse optical imaging. We will also talk about diffusion equation and how we can approximate the diffusion transport equation with simple P_1, P_n approximation to simplify the equations and quantify the bulk optical properties. Thank you.