Mathematical Aspects of Biomedical Electronic System Design
Professor
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Lecture - 23
Tissue Electrode Interface

Welcome to the course Mathematical Aspects of Biomedical Electronic System Design. Today, we are going to cover the topic Tissue Electrode Interface, in different tier sessions across. Then, you might have been taught about how a particular tissue or a basic unit rather cell can be modeled in terms of electrical parameters, such as resistors, capacitor; and how it can help us in understanding its physical property by modeling it in terms of such elements, such as resistors or capacitors.

Now, once you have understood how tissues or cells can be modeled in terms of electrical equivalent parameters. The next step, the next logical step rather would be to make use of the existing electrode technology using micro fabrication methods. And then try to study what exactly is being measured when you put an electrode on top of a tissue. What are the properties that you can measure? Can you delineate between for example, a normal tissue from a cancer tissue? So, these are some interesting examples that we are going to study in, in coming few 30 minutes.

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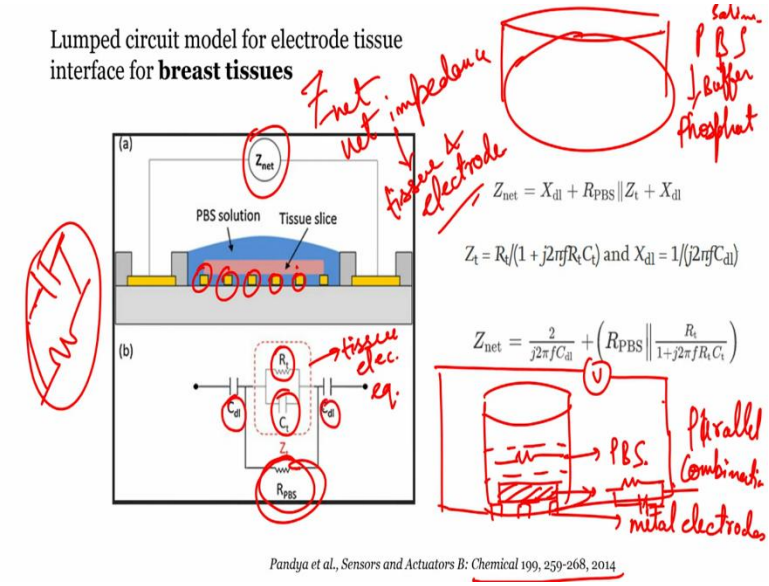

So, I have taken one example from, from a journal article. In this particular work what they did was they created, they created an electrode interface; and let say this is a well. This is filled with

PBS; PBS is Phosphate, B is Buffer, and S is Saline, Phosphate, Buffer, Saline. It is a buffer solution used to maintain the pH value constant, and it is found to be compatible across most of the biological tissues, which are used for such experiments.

So, the medium, the medium in which this tissue slice was placed was phosphate buffer solution and then there were electrodes below this. As you can see here these are the electrodes, these are gold electrodes. And then this this was the tissue slice, and this is the PBS solution. Now, you have been taught, how to model a tissue slice, like it will have a conductive component constituted by extracellular or intracellular matrix.

And how like a lipid layer can be modeled in terms of capacitor and the extracellular membrane by a resistor; and the combination of both of them by resistor and a capacitor. Similar thing we will take forward from there like how this particular combination along with tissue can be used to develop or come up with an expression. With an expression for the net impedance Z_{net} here is net impedance of tissue and electrode; so, let us see. So, let us begin with tissue.

So, tissue will contain a resistive element in extracellular matrix and by lipid bilayer membrane of that offers capacitive behaviour. Apart from that the PBS in which this entire tissue is placed will provide another resistance. Now, if you can see here this PBS surrounds the tissue like you can imagine it to be a well. This is a well, in which this is PBS filled well; and somewhere here the tissue slice is kept, the shaded region that you see here is the tissue slice.

And below the tissue slice, there are metal electrodes; metal electrodes which are connected to a power supply and a measuring unit. Now, what we can see from here is the resistance offered by the PBS, if you can, if this is the resistor, I can draw it here; and the resistor capacitor combination which I will draw here. If you see this together you can easily make it out that these two are in parallel combination. And that is why if you can see here this particular part is tissue electrical equivalent, and this is the PBS; that is considered to be in parallel with the tissue.

Now, the second interesting thing is the C_{dl}. Now let us understand what does this C_{dl} means. And why there are two C_{dl} elements which are capacitive. What do they mean, what is their significance, and how it can affect the measurements, especially bio impedance measurement? So, all these, so all these measurements which involve measuring impedivity, resistivity; it is called bio impedance measurement. So, what is this C_{dl}?

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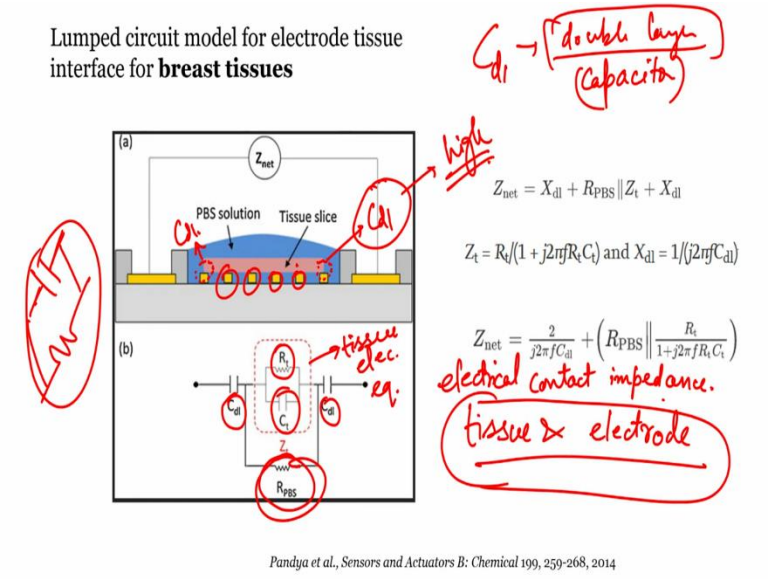

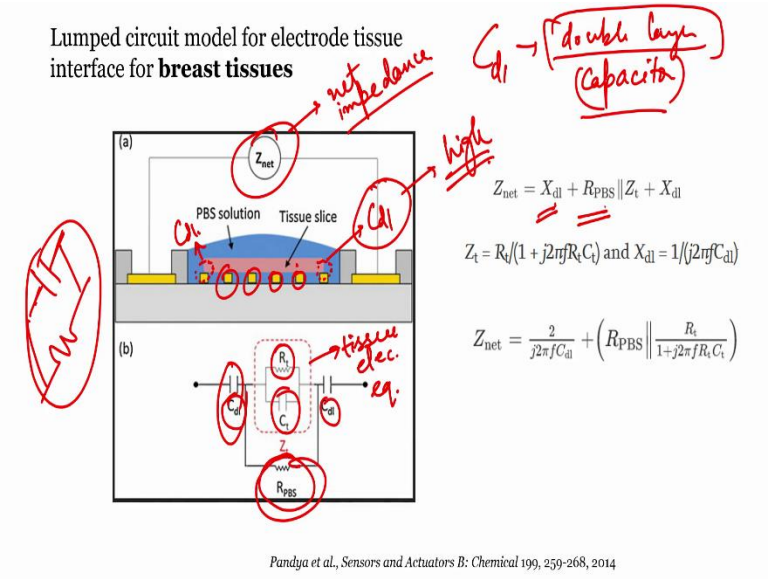

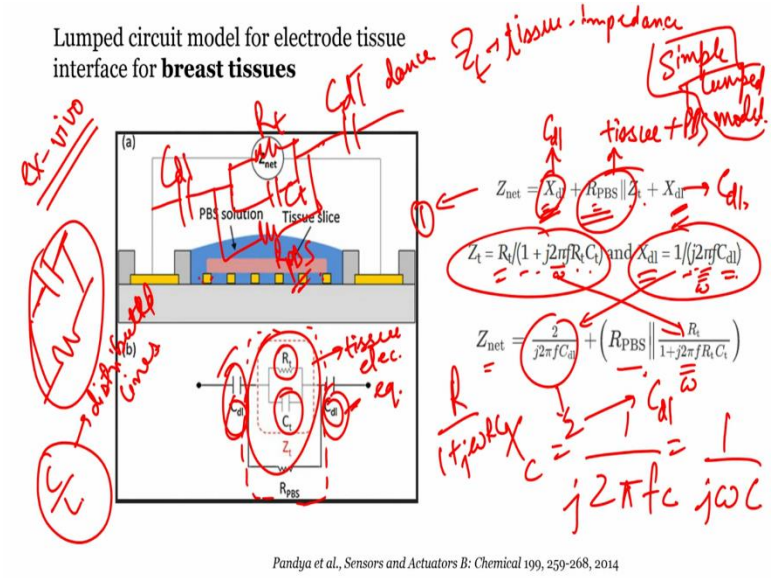

Pandya et al., Sensors and Actuators B: Chemical 199, 259-268, 2014

C_{dl} is double layer capacitor or a double layer capacitor. Now, what is this double layer? dl stands for double layer. So, this double layer is constituted by the electrode and the tissue; so, if you can see here this part and this interface if you see, this part and this interface if you see, this entire thing is called double layer; I will draw the same here. These two are double layers. Now, what is their significance?

This provides the information that how much is the impedance between the tissue, the contact impedance, and electrode; and this can affect the measurement to a great extent. Let us say you do not have a proper contact; when I say contact, I mean electrical contact. When you do not have electrical contact between tissue and the electrode; what would it mean? It would mean that this value will be very high. Because there will be lot of parasitic elements and which will mostly be capacitor; that will lead to very high overall impedance.

Now, that overall impedance we will come to in the next few minutes. But, for now, for your understanding, this concept just is to signify the importance of C_{dl}, which is double layer or capacitor, which is formed between tissue and the electrode interface. Now, let us look at the overall circuit and how the expression develops. So, as we can see here the Z_{net} as which is the net impedance, which I had mentioned earlier.

So, Z_{net} will be given by reactance of the double layer; so, this is the reactance of the double layer. Since, it is a capacitor, it will just have a reactance; and then you will have in addition this entire thing this entire thing will be in series with this double layer. So, that is why this is your caused

by C_{dl}, this is your tissue plus PBS; and this is again C_{dl}. So, now you are able to imagine it again, the elements; let us have a look at it again. X_{dl} corresponds to reactance offered by this capacitor which is doubled layer, which is between electrode and tissue.

This expression which is resistance offered by PBS Phosphate Buffer Saline solution, which is in parallel with the Z_t; Z_t is tissue impedance, tissue impedance, and Z_t is given by a parallel combination of R_t and C_t. And then again there will be another X_{dl}, because tissue is contacted by the electrode on two sides; this is one side, this is another side. So, it can, if I were to draw the resistor-capacitor combination here, it would look something like this.

Just for your better understanding you will have a resistor and a capacitor parallel combination; here will be a resistor and then there will be a capacitor. This will be C_{dl}, C_{dl}, this will be R_t, this will be C_t; and this will be RPBS. So, till this point it is clear? So, now what you will do? You will substitute the values individually for each of these components.

Let us begin with the first one X_{dl}. X_{dl} will be given by what is the expression for any capacitor? $\frac{1}{2\pi f_c}$; or $\frac{1}{j\omega C}$. In a similar way we can write here $X_{dl} = \frac{1}{j2\pi f}$, which is ω; and C_{dl} which is the double layer capacitor, which again I am emphasizing the fact again that it is formed due to the electrode tissue interface.

Now, Z_t. Z_t is impedance, overall impedance, overall impedance of the tissue. This is overall impedance of the tissue by itself; it is not in contact with the electrode. This is, that is why I am just trying to make things clear in terms of electrode tissue interface impedance and tissue impedance alone. There are two things; one is electrode tissue impedance which is C_{dl} here. And there is tissue impedance which can be given by R_t; since these two are in parallel.

So, once you have a parallel R_c combination what will be? It will be $\frac{R}{1+j\omega RC}$; this is what it is written here. R 1, $\frac{R}{1+j2\pi f}$, $2\pi f$ is ω, Rc and j, this expression is clear, this expression is clear. Now, let us substitute these two expressions in let us call it this equation-1. So, when we substitute this in equation-1 what do we get? We get $Z_{net} = \frac{1}{2\pi f C_{dl}}$, plus this will be the parallel combination between R_{PBS} + Z_t. This is by 2 C_{dl}; one on this part and one on this side.

And then there will be this central element which is a parallel combination of resistance offered by PBS and Z_t. What you get finally is R_{PBS} in parallel with $\frac{R_t}{1+j2\pi f R_t C_t}$; this is again $\omega R_t C_t$. This is the expression that we have put here; and this is the expression which we have put here.

So, this was one of the examples just to demonstrate how you can measure, or how you can come up with an expression. This is the simplest model; this is a simple lumped model. What do I mean by that? We are not taking any distributed element; distributed element means capacitance per length, per unit length. Why we are not going for this?

Because the length, the length of the overall experiment, experimental setup does not warrant us to go for this kind of distributed element, which is generally used in transmission lines. Transmission line mostly electrical engineers or electronics engineers would know; others do not need to bother about it. For others this is a lumped model, lumped circuit element model, lumped equivalent circuit model.

So, we have seen a type of tissue which is a breast tissue here. So, this breast tissue was exercised after let say a procedure of biopsy; and then it was stored in formalin and then it was brought to a lab and then it was measured. These types of experiments are called ex-vivo, where in you are bringing in the tissue somewhere in the lab setup; and then you are measuring it with your experimental setup.

Now, let us see if you want to measure in vivo, which means you have your device which is portable; and it can be taken to any place, in any hospital setup. And then you want to measure the impedance or potentials. Now, many of one of, now many of you would wonder how we can measure potential from tissues. We supply potential and then we can measure the impedance; till now that has been our general understanding.

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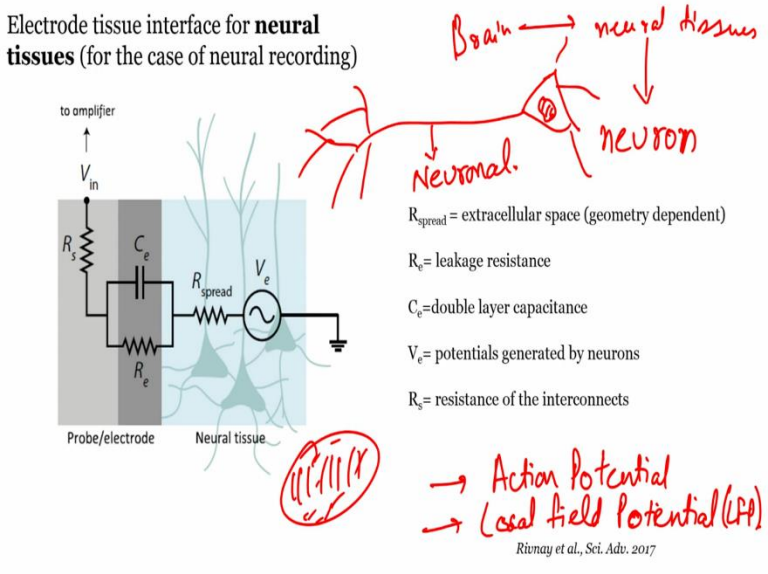

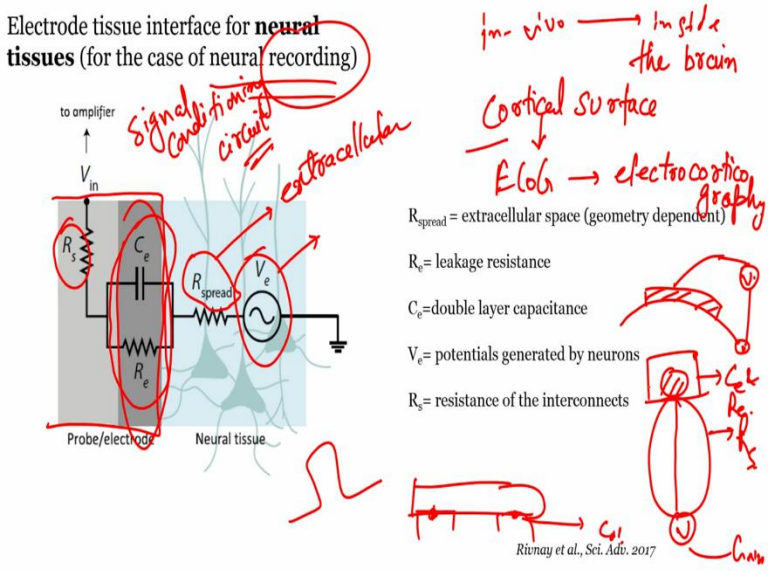

In the next slide we will see how we can measure potential from a tissue. So, what kind of tissues generates potential that is the first question one should ask? So, the kind of tissues that generate potentials forms the most important part of out body which is brain. And the tissues which are associated with brain are neural tissues; and the simplest unit of neural tissue is neuron.

So, this example when you can see, this is an example of neuron. So, neuronal tissues generate potentials, I will not go into the details of the biology over there; that will be another session in itself. So, neuronal tissues generate potentials and a single, a single neuronal potential is called as action potential; it is called as action potential.

And when many such neurons, imagine there are, there are millions and millions of neurons in our brain. So, let us say when there are bunch of neurons when they generate potentials across a large spatial domain. So, let us say this these are, this is a particular part of a brain and these are, these lines are nothing but neurons. So, each neuron is generating some potential; collective potential of such neurons is Local Field Potential or LFP.

Those who are interested can read further about these two terms. But we will restrict our discussion only with reference to the context which is electrode tissue, electrode tissue interface, and electrode tissue impedance. So, let us see how electrode tissue interface exists for a neuronal tissue.

How is this neuronal tissue different than the breast tissue that we had discussed? It is different in two ways; this part of the discussion is different in two ways. One, here we are talking about in-vivo. In-vivo means we are taking the device or the sensor, and we are placing inside the body; in this case inside the brain.

So, we, so the standard operating procedure would be to perform a surgery, and then, and then create an opening; and then expose the cortical surface. And the signals that you will record from a cortical surface, electrical signals that you will record also called neural recording from a cortical surface is called ECoG or electro corticography.

So, let us see what all different elements are there. As far as the recording of neural signals is concerned, so this is the probe that you have implanted on the cortical surface. And the signal which is being recorded will be sent to a signal conditioning circuit; so, let us see each element individually; let us begin with the neural tissue.

As I had mentioned each neuron generates some potential which is called action potential; and collective firing of neurons generates local field potentials. So, this can be considered as potential generated by neurons; this is neuronal potential. Then there will be something called as R spread; so, this is associated with extracellular space.

So, in some other TA classes, you definitely would have been taught about intracellular and extracellular; and extracellular is generally associated with resistive contribution in terms of electrical equivalent. So, this is extracellular space in cortical surface. Now, this is where it comes

the interesting part. This again is the interface between electrode and neuronal tissue; this C_e again will be double layer capacitance.

Remember the double layer capacitance that we had talked about for the breast tissue. So, in case of breast tissue too in the previous slide we had talked about electrodes; and on top of that there was a slice of tissue. And this part the impedance offered by this was C_{dl}, in a similar way this is the name is changed; the concept remains the same. This is C_e or double layer capacitance, R_e is the leakage resistance. So, like you have leakage capacitor at the contact, similar way you have leakage resistor.

And finally, you will have R_s, R_s is nothing but interconnect resistance. So, just to give you an idea what exactly would this system would look like? So, imagine this to be the cortical surface and this to be the electrode, so, the shaded region in the electrode. And then this is connected, let us say this is a ground point and both of them are connected to a voltmeter; this is a very simplistic view.

The electronics associated with neural potentials recording is very complex; because of several reasons which is out of the scope of this particular TA session. So, this electrode let us say it consists of recording sites and then interconnects which are then connected to this, which are connected to this recording system.

So, this shaded area is the part where this these things come; and this part which is the interconnect is R_s. So, this when in, so this electrode, this recording electrode when it comes in contact with the tissue, I am drawing the tissue for simplicity in the form of a square; this will form the C_e and R_e component, electrical equivalent C_e and R_e. And R_s will be the interconnect of this, of this electrode, neural recording electrode.

So, this was just to give you an idea that how electrode tissue interface can not only mean you are supplying the potential and then measuring the impedance; but it can be the other way you are measuring potentials. And there are several applications for measuring neuronal potentials; it can be used to understand several neurological disorders, such as epilepsy, stroke.

In a similar way this kind of this kind of interface can also be drawn for neural stimulation. Wherein, here you are recording, there you are stimulating; there you are stimulating current

pulses. In that case also you can work out for, you can work out for electrical equivalence, when a particular electrode comes in contact with a neuronal tissue.

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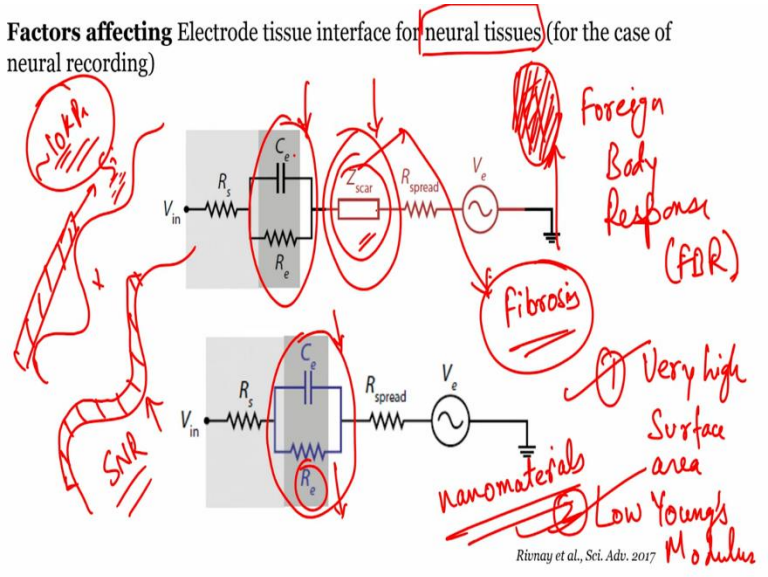

Now, one more important aspect which we thought of bringing out in this TA session was that what are the factors that affect electrode tissue interface, and how those effects can be modeled? So, these are some real time or practical issues which can help one in designing electrodes, and also modeling the electrode tissue interface for understanding the potentials which are recorded; especially in this case for neural tissues.

So, we are seeing a case there are two equivalent circuits drawn here. In one case you can see Z scar, apart from that all the other things were common as the previous case; in which we had seen an electrode in contact with neuronal tissue for neural recording. So, what does this Z scar mean? Whenever you insert any foreign object, the first response of our body is foreign body response; it is termed as Foreign Body Response or FBR.

Now, this FBR can also be in terms of neural tissue considered as neuroinflammatory response; which means if any foreign object is being inserted, in this case electrode it causes inflammation or adverse effect to the tissue. It can cause breakage of the tissue, or it can cause blockage of the blood flow inside the brain. When such things happen, body has automated response, wherein it will develop a protective coating around the electrode. And that will that is something called as fibrosis; I am not going into the detail.

And that fibrosis will prevent any kind of signal being recorded accurately. It will offer an impedance and this Z scar is the impedance offered by this particular phenomenon. In a similar way, this Z scar can also have, it can also occur if you are having; if you are, if there is a presence of blood in between the electrode and the tissue. So, there is Z scar can also be due to blood as well.

Now, then the question arises is there any way to improve or improve this improve the overall electrode tissue interface. And what does it mean? Reducing this quantity and eliminating this quantity. This quantity we cannot eliminate, because by default electrode tissue are two different materials; there will be some double layer capacitance, and some resistance, leakage resistance associated with that. But this Z scar is something that can be totally avoided.

The one way to avoid that Z scar is to use electrodes which have very high surface area, and have very high surface area; and second low young's modulus. So, if an electrode is a very high surface area, what is the advantage it offers? It offers the advantage of making better contact with the neuronal tissue.

Because if you consider human brain, it is having gyrus and silica; which means if you have seen human brain anywhere either phantom or in pictures, it will have some kind of shape something like this undulations like this. Now, if your electrode is sitting like this, let say this is your electrode shaded region. Imagine the kind of electrode tissue interface that it will have for this case, when compared to the case where electrode is conformable to the tissue.

So, what will be the difference? The signal to noise ratio will be very high, in this case when compared to this case. Also, if you have a very stiff material acting as an electrode, it can cause; because bodies, body tissues have young's modulus around 10 kilo Pascal's, this is a very general value. For different kinds of tissues these value can be even smaller or little higher. But these materials say for example, silicon will have, will have, will have young's modulus; at least three to four orders of magnitude higher than this particular value.

So, what will it cause? It will cause scars; it will cause rupturing of neural tissues; which will result in processes like fibrosis or neural, neuroinflammation anti-inflammation processes. So, what we were discussing is, if you have a very stiff material; when I say stiff, it is mechanically stiff, something like silicon.

And if you place it on cortical tissues and if you insert it, first of all if you insert and then place it on the cortical tissue; it can lead to adverse response from the, I would rather say preventive response from the body which is called neuroinflammatory response or foreign body response; which can result in fibrosis, which can lead to coverage of the tissue with fibers; which are generated as a result of fibrosis.

Contrary to that if you have a material which is mechanically soft, and has young's modulus compared to that of comparable to that of neural tissues around 10 kilo Pascal's; then, there will be two advantages. First, it will have low young's modulus and also the contact; that it is making with the neural tissues will be better, or improved when compared to such stiff materials; which will result in reduced value of double layer as well as leakage resistor.

This can also be added with materials which have known, which are known to have very high surface to volume ratio; which is something like nonmaterials. Let say you have carbon nanotubes or graphene; these materials have very high surface to volume ratio. So, if these materials when combined with the mechanical softness of substrates like polymers, can result in both of these parameters, being satisfied resulting in overall reduction in the impedance offered by tissue electrode interface; which in turn results in improved quality of the recorded signal.

Now, this brings us to the end of this session. What are the takeaways? Takeaways is takeaways are as follows. One, in order to model any kinds of tissue electrode interface; you need to know what kind of resistors and capacitors are there. We took a case example of breast tissue, wherein there were two double layer which are capacitors on either side offered by tissue electrode interface.

And the tissue impedance itself and the medium the; now, remember medium may or may not be there. You may or may not have PBS, so you do not have to follow it point to point. In fact, this is just a direction in which you can think about. In a second case, we took the example where you are not record, you are not measuring impedance by supplying voltage. But you are recording potentials which is the case for neural recording.

And we saw what all elements are there in case of neural recording, wherein an electrode makes a contact with the neural tissues. Then we saw what are the factors in which electrode tissue interface specifically we took the case for neural tissues, can get affected. And what are the methods that

can be used to develop devices, which can mitigate the tissues raised by conventional materials; or biological responses when conventional materials are inserted in cortical in a brain and placed on a cortical surface.

I hope this lecture helps you in improving your understanding on electrode tissue interface. Thank you so much for listening, if you have any doubts, please feel free to put up the questions on the forum. Thank you.