Advanced Neural Science for Engineers
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Lecture 35
Neural Implants: Fabrication and Characterization

Welcome students. Let us continue our discussion in Advanced Neural Science for Engineers course on Fabrication of Neural Implants Part II.

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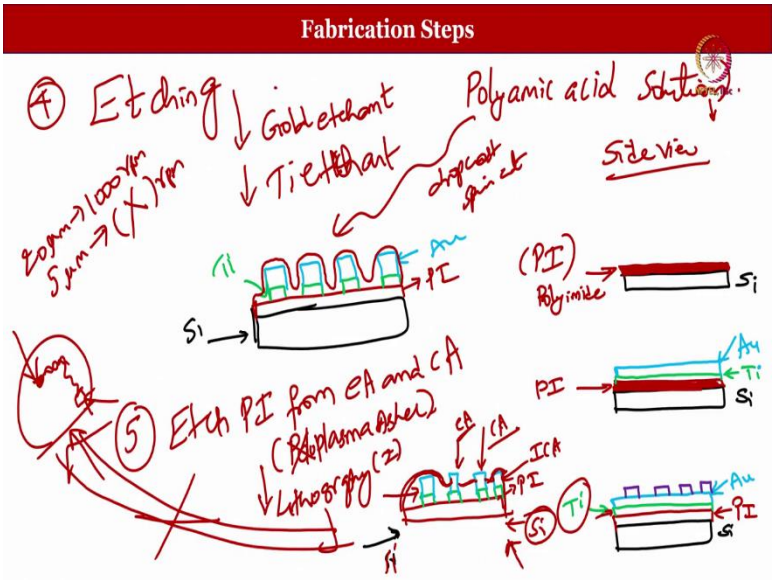

So we have discussed this part in the previous lecture, and we have seen series also and of course, I did not get into the details because it is already been taught to you. You are aware of it. I do not want to bore, but the thing is this how it works.

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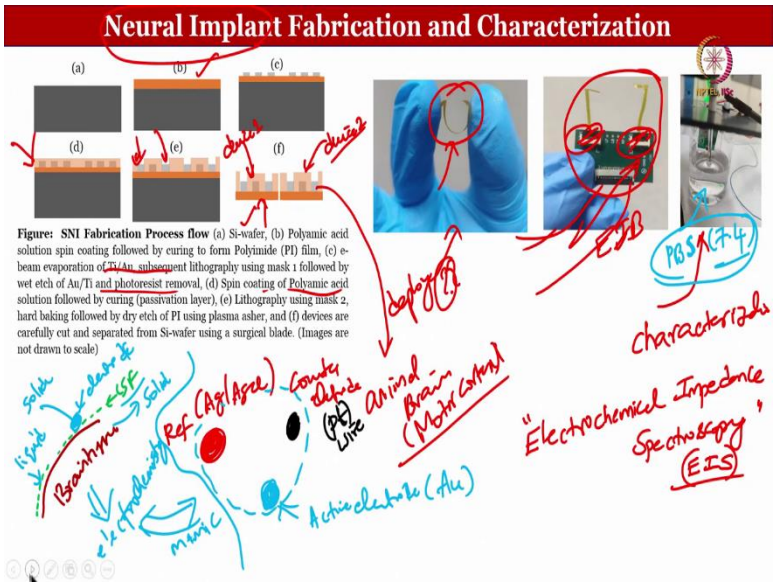

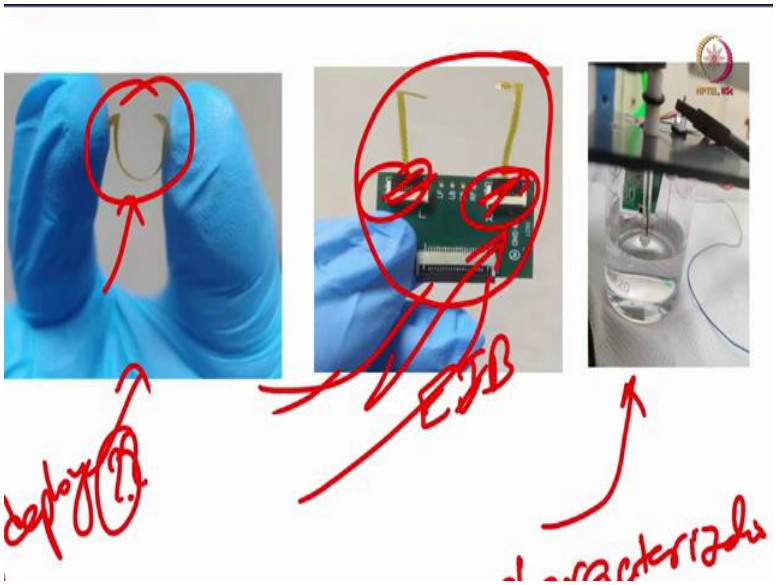

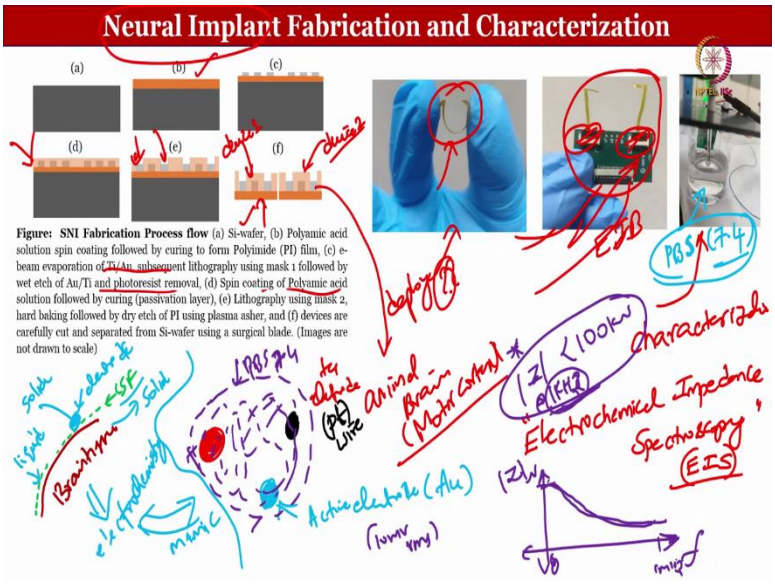

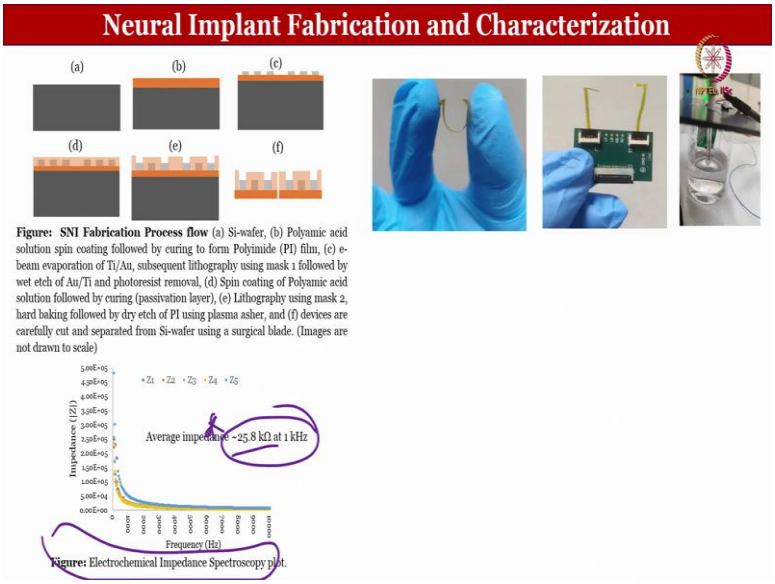

So if I summarize all these things, if you look at this and these are the device. If you look at this, this is the device, and I am holding that device in my two fingers and then see how flexible is that device is going to be. You know, because once it is taken out of this silicon we can cut it from the device, from the silicon and then how it looks like, already I shown you how it looks like on this.

With the help of FPC connector, we have connected it to, what is this called? Electrode interface board. And this will have some cable, which goes to electronic systems. And before we go into the characterization, let us see just overview of how does it look like. So first, we

have considered a silicon wafer, then polyamic acid solution coating, followed by the curing and all those things. Then you have something called as deposition.

You can see titanium and gold deposition after the photoresist is removal. Then again, spin coating of the polyamic acid. Why? Because to form a passivation layer. After that again, some areas need to be exposed, that exposed using a plasma asher. And devices are cut carefully. Let us say this is device 1. This is device 2. What is this device here, is what the neural implant. That is a neural implant I am talking about. Neural implant 1, neural implant 2.

So it is not like only one neural implant you will get it. You can get some 8 to 10 neural implants if it is a 3 inch silicon wafer. If the size of the silicon wafer is more, then you will get more neural implants, more area is required. So at a time you will get a bulk of implants. It is not like just a single implant that will come. Then you are going to deploy these implants on the animal brain. Where is it? Interest is in motor cortex.

But how do you know whether this works or not? How do you check? You might have done everything extraordinary, but made some mistake or in the process something would have gone bad or something, how to characterize it? So depending on which nature that you are looking at, let us say if we are looking at recording. And if you are just looking at recording the signals from the brain, you need to perform some kind of characterization.

If you are looking at stimulation, then you need to do something else, which is little about different. Now, you look at this setup, this is called characterization setup. This technique is called Electrochemical Impedance Spectroscopy. This is EIS, also called as acronym. So what happens is, if you look at this, if I just zoom in a bit. You see wherever the hand is pointing out, this is a reference electrode Ag AgCl electrode.

And there is a counter electrode here, and behind our sensor is there. So I cannot take it in 3D angle, so I just took it in this angle. And you can have three connectors going outward. So this is also called a three electrode system. In this three electrode system, what we will have is, you have a reference electrode, in this case, Ag AgCl electrode. And you have counter electrode. And this is counter electrode.

Let us say this counter electrode, I am writing X, do not think that the X is means it does not exist. I will just put this color here. This color here. This is generally a platinum wire. Now, what you do is, what is this blue color stuff? This is our electrode, active electrode, in our case, gold. Now, people were wondering why suddenly this guy came in? What is this actually? The solution is nothing but a PBS. Which is, the pH is around 7.4. Phosphate buffered saline with the 7.4 pH.

Why suddenly this guy came? What is it to do with the characterization? People might be wondering. Now, I told you already, briefly in the first lecture. In the initial lecture, I think one or two lectures before we saw this is a brain tissue, brain, and there is a CSF, this is a fluid, right? CSF. And you have the electrode that is coming from the device. This is electrode that is touching it.

Means essentially, you are not touching the brain tissue directly. You are in touch with the CSF, which is a liquid or viscous. So if you imagine this that is where the concept of electrochemistry comes into picture. It is not just a, let us say this is solid. I know electrode is a solid, and brain tissue is also kind of, let us say worst, because I am an engineer, I can worsely say about some biology. If a doctor says there, it is okay, fine.

So solid, and in between there is a liquid interface. Are you getting it, this is a liquid interface. That is where this concept of electrochemistry comes into picture. So what we are trying to do, is we are trying to mimic, we are just trying to mimic. We are not exactly saying, this is true because brain environment is different and the environment that we are taking is different. But what is environment that we are creating is PBS 7.4.

This is acceptable range of the PBS, it is 7.4 pH, which people can use it to characterize the device. So in between there is a line. Just a minute, let me remove this. Right now, you know already reference electrode, counter electrode. This is three electrode system, and we have two electrode system also, but we will not get into the details. But for now to understand, why PBS 7.4 is clear, right? So let me take this another color. This color.

Now this is all immersed in the PBS 7.4. This is PBS 7.4. And what we do is, in electrode impedance spectroscopy, you apply a voltage between reference and active electrode. And then, let us say 10 millivolts RMS, you apply. AC signal, right? And you measure what is the

impedance seen by the active electrode. So you have impedance, magnitude in ohms, and then you have frequency, then you get some plots.

So you know the voltage, and then this electrochemical impedance spectroscopy set up. This is also called as electrochemical workstation. It can sense the current, and then voltage by current will give you impedance. So the impedance with the magnitude and phase angle will also be, there will be plotted. So at 0 DC it is more, and as the frequency increases, then it is going to go fall. So one has to characterize this.

And generally I am saying, if the impedance at 1 kilohertz, let us say is less than a 100 kilo ohm. Let us say for example. Then this is fairly acceptable range of the electrode for the recording. Why 1 kilohertz? Because the action potentials in the brain are in the range of kilohertz. So generally we can characterize, there has become like a nomenclature to characterize the device, our electrode at 1 kilohertz. So you can take multiple other frequency also because you are increasing the frequency from 0 to let us say 1 megahertz or whatever it is.

Similarly, we also have something called as cyclic voltammetry. We are not going to discuss in detail, but I am just going to present you what are the techniques that are available and why they use it. The techniques and all is not part of this course, there is no scope for this, so we will just quickly move on. Let me erase the ink. So after characterization, if you see this is the electrochemical impedance spectroscopy plot, and you can see how the plot looks like.

And when we compute the average impedance of the 5 electrodes is around 25.8 kilo ohms for the specifications that we have considered. And then this is fairly good for the recording.

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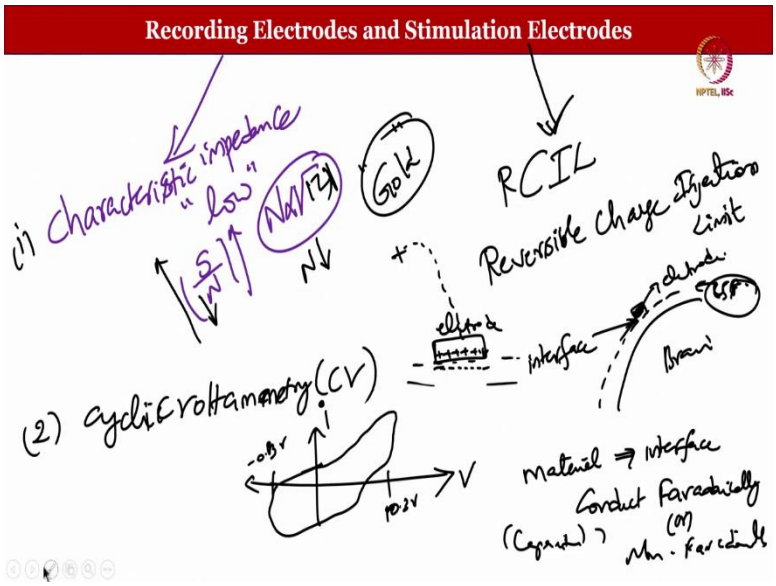

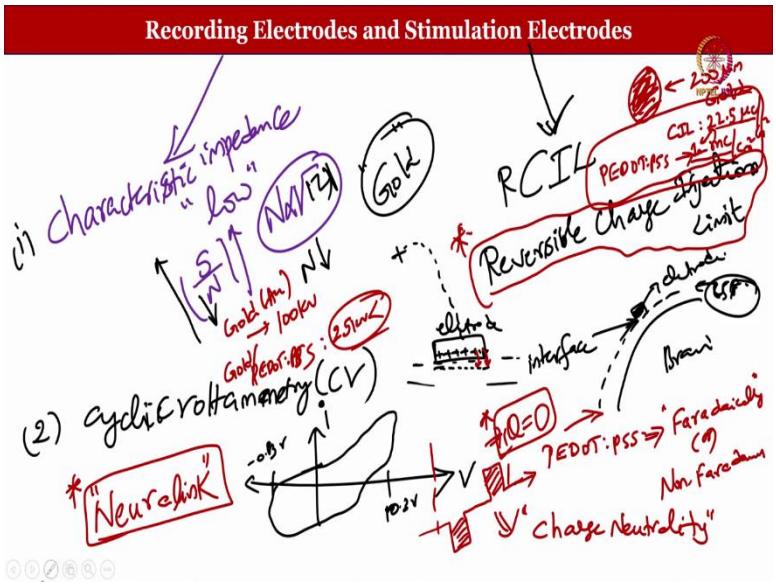

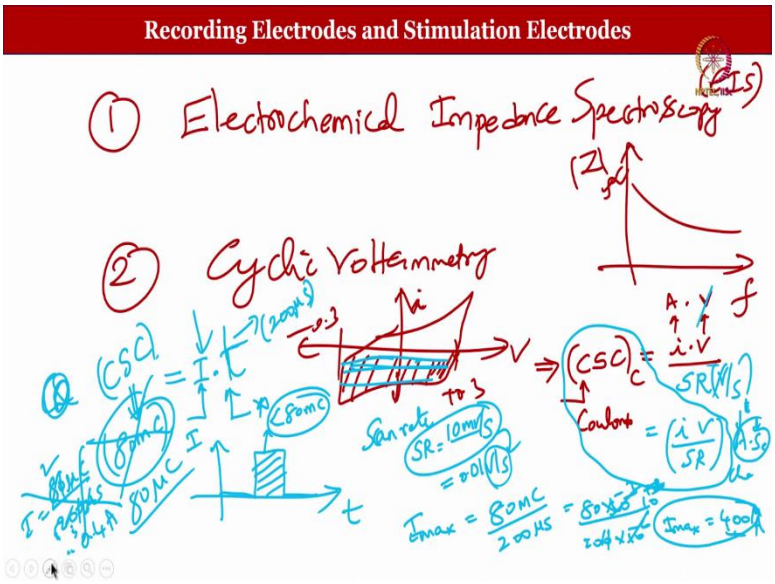

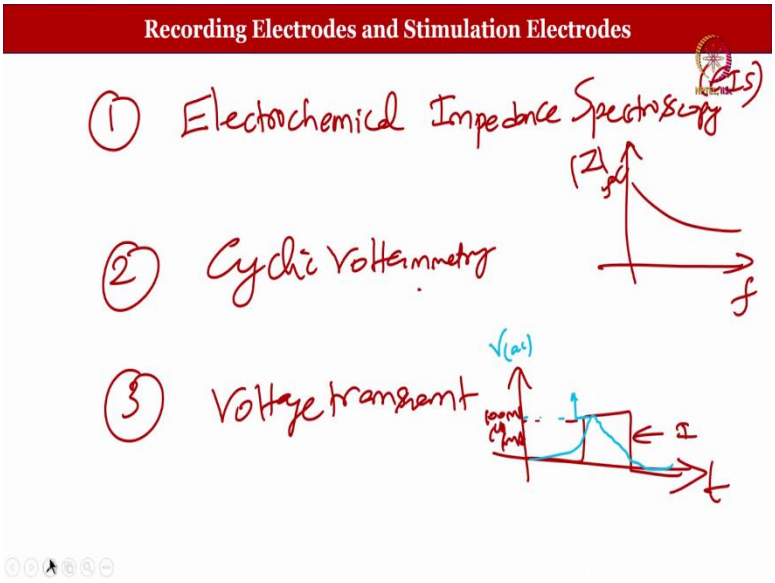

So for the recording electrode, what is important is the characteristic impedance should be fairly low. It should be low. Why? Because signal-to-noise ratio will be high, because noise proportional to delta or something, something like this R, right? If the resistance or impedance, let us say magnitude of Z. So just to give you magnitude Z. What happens is, when the magnitude of Z is low, then the noise will be low.

When the noise is low, signal-to-noise ratio for the same signal is going to be high, and you fairly want signal-to-noise ratio to be very high. And same story the other way. This is first technique, which is EIS, and the second technique is going to be cyclic voltammetry, CV. This

is not that capacitance voltage characteristics of a transistor or something. This is CV, where what we do is, you have current on the y-axis, voltage on x-axis.

And with some scan rate, you vary the voltage. Let us say there is water window limit, let us say, whatever is the limit, let us say, minus 0.3 volt to let us say plus 0.3 volt. I am not saying this is the water window limit. There is some water window limit, so you vary the voltage from minus 0.3 to 0.3, and then just, the plot could look like this. Something like that, okay? I am told you I am very weird in drawing this. I am not getting to details of this. So you can refer it online, good study material for this.

Now, from this what is the inference we can get is, we can understand, whether the conduction is happening Faradaically or non-Faradaically, all those things we can try to estimate from there. Also, then there is something called a stimulation electrode. Of course, we want characteristic impedance to be low. And then for the stimulation electrode what was important is charge injection limit, reversible charge injection limit. What is this? Reversible Charge Injection Limit

What is that is, for example, now this is what we already discussed. So when there is a brain, there is a brain, and on top of that, there is a CSF. Now, on top of that your electrode is coming, some sitting here. So eventually there is an interface here. There is interface between electrode and the CSF. Now, depending on the material, the interface conduct Faradaically or non-Faradaically.

So when you say non-Faradaically then it is capacitive, capacitive conduction. That means that, I just give you glimpse of it, capacitive means just a rearrange of the charge takes place. Now, if you look at the interface, there is electrode here. There is electrode. If you apply some voltage, that means you are essentially, applying some charge. Then there is a charge accumulation takes place here, rearrangement accordingly.

The ions that are present in the CSF, other ions that are present in CSF could be Na plus or K plus or whatever it is, the ions that are present, or chlorine, Cl minus, all those things. So if the interface is non-Faradaic or capacitive, then the charge rearrangement will take place. There is no transport of charge will take place on the interface. There is no transport takes place. No physical movement of the charge takes place. And gold is best example for that.

But how much charge you can inject is limited, if it is only non-Faradaic. Suppose if the same gold, so let me erase some of the stuff. Now you understood interface and all those things. Let us say the same gold is coated with PEDOT:PSS then it will conduct both the ways. So PEDOT:PSS, what is PDOT stands for? Polyethylenedioxythiophene polystyrene sulfonate. And then this interface conducts both, Faradaically or non-Faradaically.

Non-Faradaically is nothing but a capacitively and Faradaic. Faradaically means there is a transport of charge takes place from here to here. And the idea here is when you are working on the brain stimulation, when you inject the charge, you are disturbing the charge neutrality of the tissue, which will be damaging to the tissue. You should never disturb this charge neutrality. So what you do is, when you stimulate, let us say you supplied negative charge.

Then in the next phase you have to supply positive charge and retrieve that. So when you gave a negative charge in this cycle, then you have to supply positive charge and then retrieve it. I mean, just change the polarity, and then retrieve it. So this is called as a charge neutrality. So at the end of the stimulation, your total charge that you injected onto the brain is 0. So that the environment will not get disturbed.

So now for example, I will take 400 micron, or 200 micron dia, 200 micron dia gold. This will have a charge injection limit. Let us say it is around 22.5 micro coulomb per centimeter square. If I take the same thing, coat it with the PEDOT:PSS. It will raise to milli coulomb per centimeter square, 1 milli coulomb per centimeter square. You see the difference is 40 times. Now, how does that affect? See it is 22.5 micro coulomb per centimeter square. This is 1 milli coulomb per centimeter square.

For same area, you can now inject more charge for PEDOT:PSS. So suppose if the application demands more charge, the more charge mean more current, then you cannot use gold for the application. You can use gold coated with PEDOT:PSS. You are understanding this? So this is also one of the critical aspect. That is why when you are choosing these neural applications, first of all, we need to think which material I can use such that I can reach my end objective.

Let us say in this application, we want recording as well as stimulation, and also I want to tell you one more thing, PEDOT:PSS coating with the gold has shown to have very much lower

impedance, compared to gold. So that is also what we need to think about it. So using PEDOT:PSS can give a better recording as well as stimulation.

So just to give you some numbers, let us say some case you get a 100 kilo ohm, this is for gold, then gold coated with PEDOT:PSS it is not just a PEDOT:PSS, you have a gold coated with the PEDOT:PSS may give you around 25 kilo ohm or even less than that. I am just giving you rough estimate of that. So how to coat the PEDOT:PSS, again, different methods are there. You can do spin coating of PEDOT:PSS solution or you take EDOT and then PSS and then do electropolymerization and then get it right.

Generally electropolymerization is preferred for the neural applications because the PEDOT:PSS film that is electro deposited using electropolymerization is more stable when compared to spin coating. So that way, and when you talk about charge injection limit, here you already saw, right? If it is gold, then it is around 22.5 or something or less than 22.5 micro coulomb per centimeter square.

If it is PEDOT:PSS it is around 1 milli coulomb per centimeter square. This is just, I gave you some numbers. There are a lot of terms and conditions for that followed by that. I am just giving you so that you can understand the essence of this.

So PEDOT:PSS we know, so generally that is why, I know you might have seen recent demonstration of the Neuralink team on monkeys. They used PEDOT:PSS probes to record the signals from the motor cortex region of a macaque monkey. So this is all about like, recording and stimulation.

Now what happens is once we are ready with the recording as, so how to understand character, I mean, we are talking about characterization, right? So I went into this irreversible charge injection limit and all those things.

So how to compute it? So I just erase everything on this. So first step is that, what is the first characterization technique that we discussed? Electrochemical impedance spectroscopy. Magnitude of Z, this is in ohms with respect to frequency. The plot will look like this. This is also called as EIS characterization.

Second thing is cyclic voltammetry, i versus v famous looks like this. From this you can compute something called as charge storage capacity, CSC. The cathodic phase, I am not getting into details of cathodic phase and all those things. Very important, just to understand that. Now, how to get the charge storage capacity? This is nothing, but what are the units of charge, you know coulomb. What we can do is, you can compute the area under the graph of one phase, cathodic phase.

So what generally you will get is i into v, if you compute the area. Now, what are the units of current is ampere, what is the unit of voltage is, I mean, volts. Ampere into volt is not a charge, so what we do is something called as, when we are doing the cyclic voltammetry, I told you there is a lower limit. There is a higher limit. Let us say minus 0.3 to plus 0.3, there is something called as scan rate.

There is something called as scan rate means, there is something called as, you increase this voltage at 10 millivolt per second. This will become a scan rate, SR. That is nothing but 0.01 volt per second, so 10 millivolt is nothing, 0.01 something or whatever it is the number. The unit is volts per second. Now what you do CSC, how they compute is? Integrate the area under the graph of one phase and then divided by the scan rate.

You can get lot of material on this when you go to electrochemistry characterization and all that, I am not discussing much about it, but I also want to give the emphasis of how it is helpful. The units of scan rate is volts per second. Now you see now I v by SR, and this is ampere into second. This is current i, I mean, this current into time, right seconds. Which will be a charge. Now you got the charge.

Now once you got the charge Q, I mean charge storage capacity. Then this charge, I can just model it as current into time. Means, let us say I have 80 milli coulomb in hand, I can modulate the current that I want to stimulate and the time that I want to stimulate. So let us say I can have I versus t. If I take I versus t. So the area under this graph should not be less than 80 milli coulomb. Do not go beyond that, because you end up displacing more. Now, you know time generally we stimulate for 200 microsecond, then based on it you can calculate what is the current that you can give maximum.

Now once you get the Imax, let us say for example, according to this, what is the value? 80 milli coulomb divided by 200 microsecond. This is 80 into 10 power minus 3, divided by 200 into 10 power minus 6. So this is 10 power plus 3, 10 power plus 3 and 200. And this is around Imax, is around 400 amps. I gave some imaginary number, but in real time, this is not the case. This is not 80 milli coulomb, it will be somewhere very less.

It is in the order of micro coulomb or something, so obviously it will become micro ampere current. So this could be 80 micro coulomb or something like that. So if it is 80 micro coulomb, what is I? 80 micro coulomb divided by 200 microsecond, and this and this gets canceled. This is 0.4 ampere, is around 400, whatever is the number. Do not worry about the number. I just want to give the flow of this. How does it look like?

Now there is one more technique through which you have to check whether this much current is possible or not, and that is something called as Voltage Transients or Chronopotentiometry. Where you take the same EIS setup and then apply the voltage to one of the electrode. What are the current that you are looking at? Let us say according to this calculations, you got some 1 milli ampere current or 10 milli ampere current, or 100 milli ampere current, whatever is the current.

Now that 100 milli ampere you have to apply and then see what is the voltage that is observed. And it should not cross the water window limit. If it cross the water window limit, then it is going to disperse the ions that represent in the CSF. What are that water that is present, CSF, H plus, and OH minus. So that is also one more important criteria as a name you do voltage transients analysis.

Now you apply the current that you are looking at, whatever is the current, 100 milli ampere or 1 milli ampere whatever, I am just giving a rough crude estimates. So then you measure the voltage seen across that particular active electrode. And something like that. This peak should not go beyond the water window limit. There is a water window limit, I think minus 0.8 to plus 0.5 subjected to corrections. So it should not go beyond that.

So once you complete that, then your electrode is ready. Your electrode is ready for the stimulation or recording.

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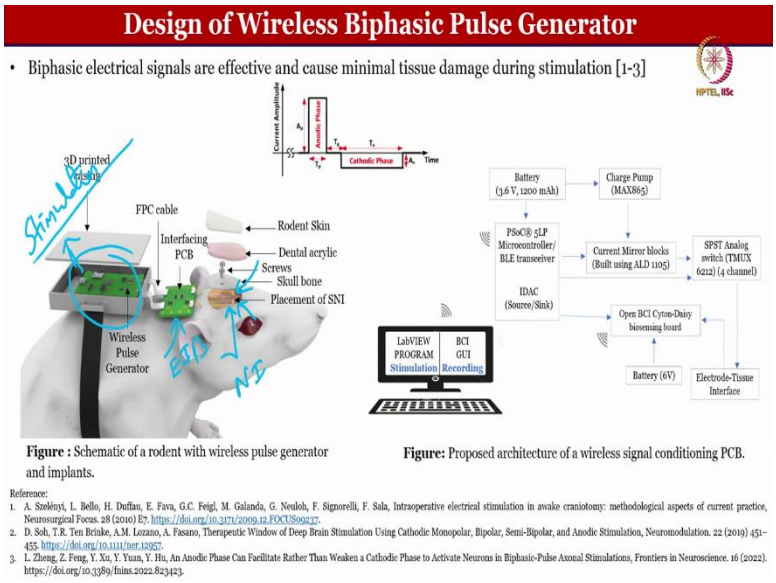

Figure : Schematic of a rodent with wireless pulse generator and implants.

Figure: Proposed architecture of a wireless signal conditioning PCB.

Reference:
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So then, already we talked about biphasic and all those things. Now you look at this, these are neural implants. Neural implant. One is on the right side, one is on the left side. Then it is connected to interfacing PCB, electrode interface board. Then this is connected to electronic systems. This is electronic system for stimulation. Now, what are the different blocks that are present in this stimulation and all those things, we will see in the next lecture.

Thank you. See you soon.