Neural Science for Engineers
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Brain Stimulation
Lecture - 29
Introduction to Brain Stimulation

Welcome you to the course on Neural Science for Engineers, this is Sreenivas Bhaskara, TA of this course, and we are looking at Brain Stimulation. In the last lecture we have seen different aspects of brain stimulation and we have already covered extensively what is brain stimulation? How brain stimulation works and all.

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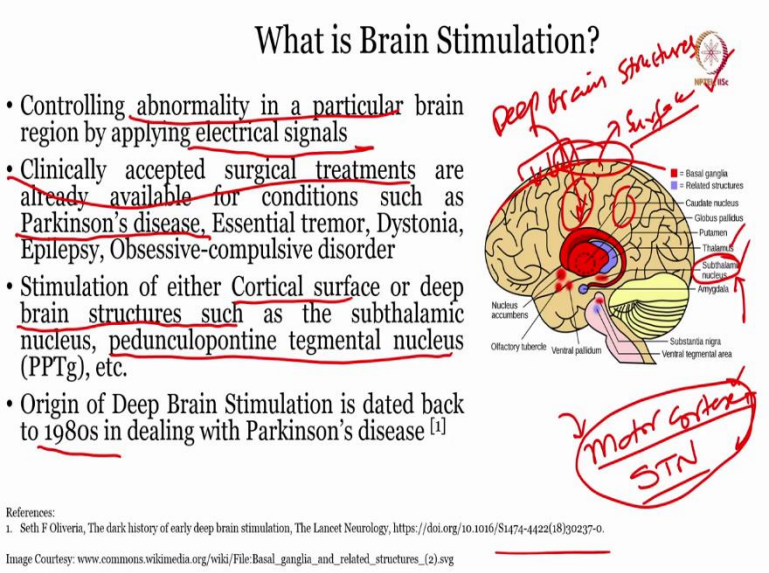

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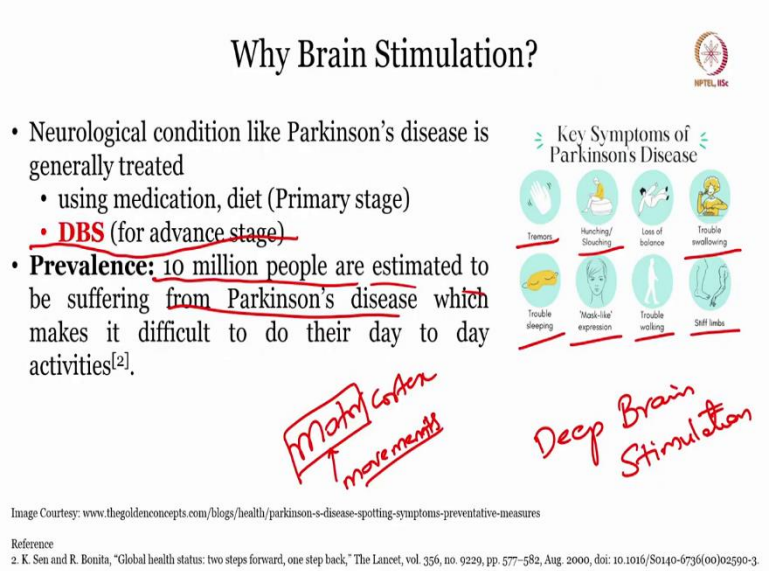

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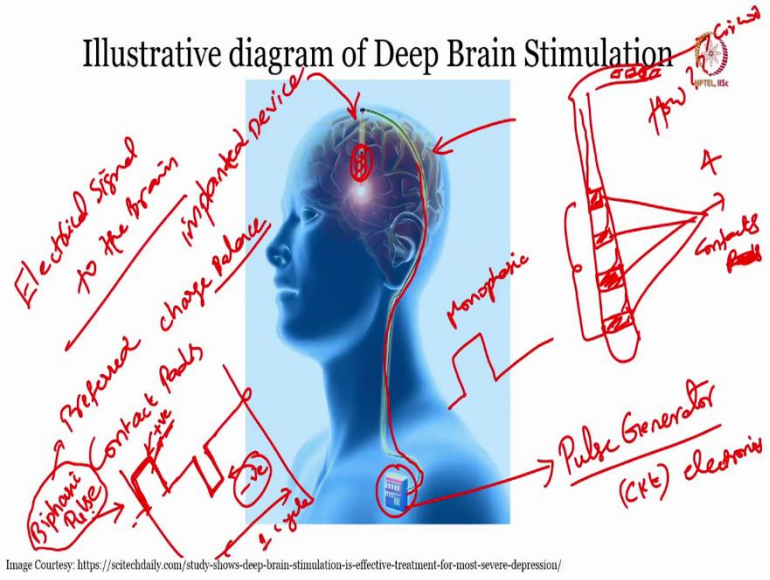

So, we have seen what brain stimulation is, why brain stimulation and generally we have seen in terms of circuit point of view how their deep brain stimulation takes place and we already know why deep brain, because you are in the deeper structures of the brain.

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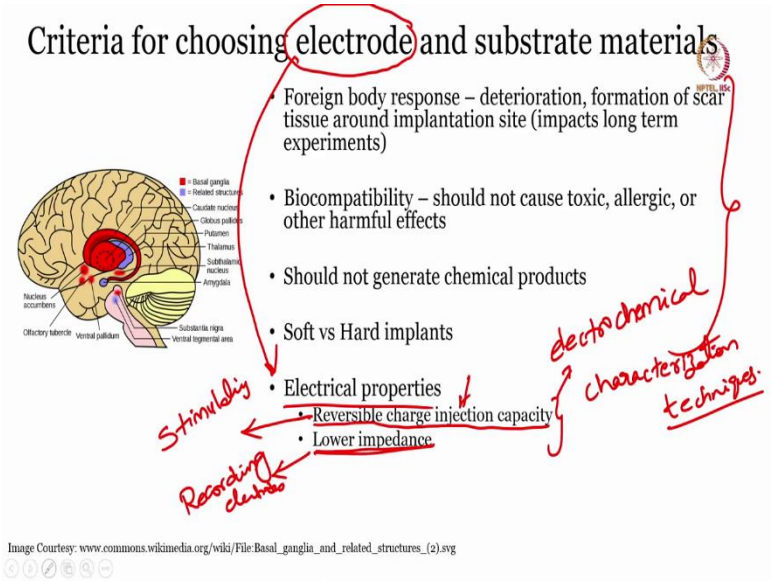

So, that is why it's called deep brain stimulation. We have seen these criteria last time but let us continue with the electrical properties. So, as you see here, there is something called reverse charge injection capacity and lower impedance. So, these two things are coming from electrochemical characterization techniques.

So, what does it mean? It has a lot to do, when it comes to reversible charge injection means you are injecting something, means for a stimulating electrode this is most important and lower impedance, this is very much important for recording electrode.

When you are recording signals like ECoG signals or local field potentials and all, recording type of electrodes this low lower impedance is very much important, very much important characteristic to consider. So, what are these? Just briefly I will explain because I do not want to get into the complex stuff of how the reactions takes place and all those things.

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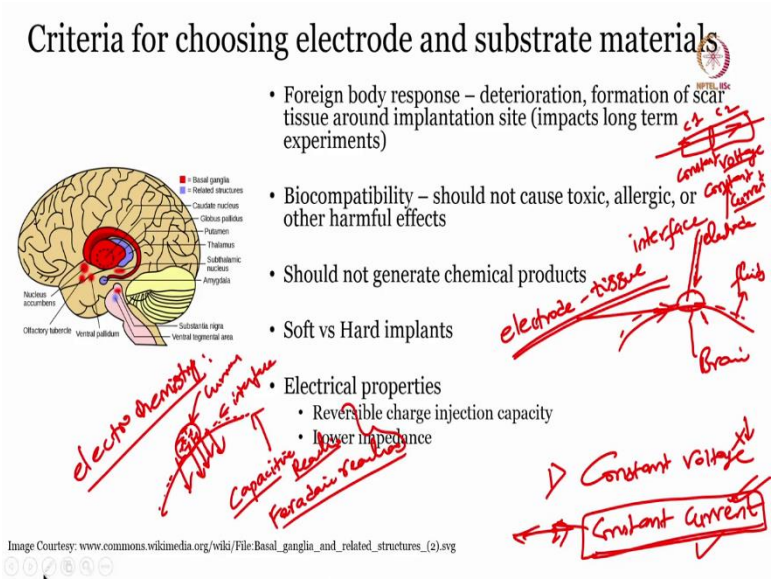

What we are trying to do is, there is a brain and across the brain there are fluids, on top of this I am putting an electrode.

And there is an electrode tissue interface. So, what happens is whatever the electrons or charges that are travelling when you are stimulating within the electrode, that has to be converted to the ionic chargers across the electrode tissue interface. It is not like one conductor to another conductor it is going like this.

This is conductor 1 and conductor 2, the flow will be same it is not like that ok. It is it is really complex chemistry that are involved. So, it comes under the part of electrochemistry. So, what we are trying to see? I am just giving a overview. Now, according to this what happens is, you cannot inject whatever we want.

Suppose when I say inject whenever you apply some potential to this or generally these electrodes, we can excite them using a voltage source, I mean constant voltage sources and we can also use constant current sources, anything we can use. So, let me write here clearly, I can use constant voltage to excite the electrode, or I can use constant current.

Now, we use most preferably constant current, because irrespective of whatever the impendence is offered by the brain tissues, your current will not change. And you know what happens with the voltage as impendence changes the current through that will change.

So, if the current changes, then the charge will change. So, most preferable thing is constant current sources are used. So, can I use whatever the current that I want? No,

correct. So, what happens is generally at the brain interface whenever you excite this by using some current, inevitably you are throwing some charges, you are throwing some charge on to the interface.

When I say throwing means whenever you excite this with current source there will be a charge distribution that takes place here. Here, if you are familiar with electrochemistry, then how this charge gets converted and then transferred to this medium depends on two things. So, you have capacitive reaction that is taking place at the interface, or you have Faradaic reaction that is taking place or both anything could have happened.

You can have a capacitive reaction, a Faradaic reaction or both will be taking place at the interface. Now, that will decide how much current can go inside and how you can retrieve it back, when I say how you can retrieve it back is this.

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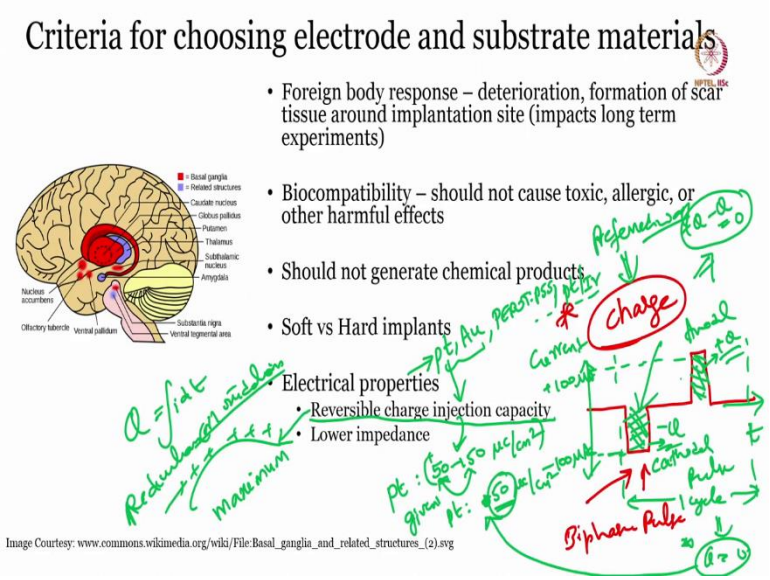

So, whenever you excite something, whenever you excite the membranes, brain membranes, when I say excite means you are inevitably charging, charge your transferring, through something like through capacitive means or faradaic means or both.

So, what you are doing is, you are giving this kind of current pulse. So, this is a biphasic pulse, this is anodal pulse, this is a cathodal pulse ok. So, sorry this is the other way. So, this is a cathodal pulse, this is anodal and the x axis it is going to be time, on y axis it could be current for example.

Now, let us say this is one cycle, let us say this is minus 100 microamperes; you are generating plus 100 microamperes. Now, we know that charge is

$$Q = \int idt.$$

So, when during the cathodal pulse you are transferring some certain charge. Let us say this is -Q, during the anodal pulse we need to retrieve that charge, so that during one cycle I have net charge +Q -Q = 0.

Why means, suppose if there are any charges that are left over on the brain, then some kind of reduction oxidation reactions may take place, reduction or oxidation reactions takes place and that will impact the brain. That may damage the brain, that may damage the electrode, so many things will take place.

So, this is a most preferred way of transferring the charge. So, what happens is when you are doing this let us say electrical properties we are discussing right, let us say some of the metals that we use are platinum, gold, these are also called as noble metals.

Then we can also use conductive polymers like PEDOT, PSS, then you can also use alloys, platinum iridium alloys and so many other things are possible. Every material has something called as reversible charge injection capacity, to be precise this is maximum reversible charge injection capacity.

That means, in a normal term I do not want to go into the details about the maximum charge, but I will just want to give you some example. So, first what is the idea? You have to pump the charge and you have to retrieve the charge.

So, finally, after the end of one pulse you have to make sure that the total net charge that is transferred is 0. So, now, in this process there are some material let us say for example, platinum; if you take platinum has a range ok.

So, 50 to 150 micro coulomb per centimeter square. So, this is the charge injection capacity, means if you are sending at the rate of plus 50, you can receive at the rate of minus 50, for a particular material ok it varies. Why sir this is 50 to 150? It you know depends on lot of parameters, because I told you that is why it is such a complex thing, I

do not want to get into the details of all these because I had to explain everything from there.

If you are interested, you can see some articles on electrochemistry about the cyclic voltammetry and we can understand that. Means for a platinum let us say for example, for a given platinum material it has plus 50 or it is not plus, I will just use micro coulomb per centimeter square, this is the charge injection capacity.

So, if you use 50 micro coulomb per centimeter square capacity, you can retrieve also at the rate of 50 micro coulomb per capacity. Suppose if you have induced more charge during this time. So, let me take some number and then explain it.

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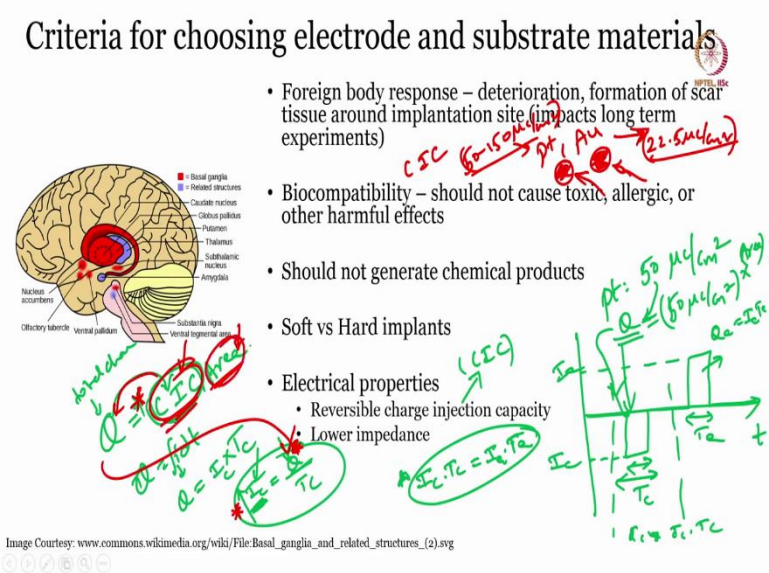

So, let us say for a given platinum you have charge injection capacity per centimeter square, let us say you take this wave form, you have induced the charge, you have injected here.

So, 50 micro coulomb per centimeter square alright, and you have a time here. So, for this 50 you multiply this 50 micro coulomb per centimeter square with respect to the area, you will get the total charge that you can transfer in a particular cycle. In this cycle, this is the maximum charge that you can transfer.

Now, you got the total charge, total charge is let us say or this I can call it a CIC, Charge Injection Capacity into the area. Now you got the total charge. So, what is Q?

$$Q = \int idt.$$

Now anyways i is a constant

$$Q = I \times T$$

this is nothing but a cathodal pulse you know T_c, I can call it a T_c this is T_a this is I_c, this is the maximum amplitude right.

Now, you can calculate the maximum current, it is the maximum current that you can pump. Similarly, you have I_c I_a here right I_a. And what is Q_a?

$$Q_a = I_a \times T_a.$$

What is this Q_c? Charge induced during the cathodal pulse is

$$Q_c = I_c \times T_c.$$

So ideally, we need

$$I_a \times T_a = I_c \times T_c$$

this is the charge balance equation right.

So, what is the maximum current that you can supply depends on the Q, this Q depends on the CIC. Now you understand the relation, your maximum current; let me take red pen and highlight the flow ok. You no need to remember or by heart all this, this is very simple mathematics I am doing.

Your Q, your maximum I_c is decided by Q and Q is decided by the CIC because, if you take two materials let us say platinum or gold with the same surface area, what is decided is CIC. CIC will decide what is a Q and Q will decide what is the I.

So, that is the reason your platinum has the range of 50 to 150 micro coulomb per centimeter square, this is the CIC and for a gold it is around 22.5 micro coulomb per centimeter there are different numbers, I am just giving roughly these are the numbers.

Means, if I use Au, I can apply lesser current when compared with the platinum because same surface area right. Assuming that area is same what varies is CIC. This CIC properties you can deduct from something called as cyclic voltametry curves.

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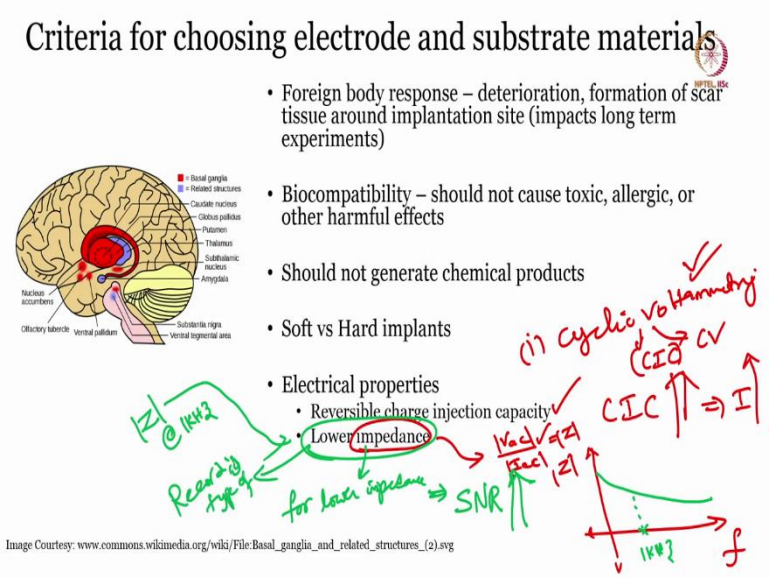

There is something called a cyclic voltametry using which you can deduct CIC, they are also called CV character. There are so many other things also right which is one of the important.

Now, you understand the importance right of CIC, if you want to apply larger currents you have to go for materials which has larger CIC, this results in larger currents. So, understand this, this is the importance of this one, then lower impedance.

What is this is you already know you give impedance when you are talking about sinusoidal signals, you give sinusoidal voltage divided by the current that is produced between the electrodes, then you will get something called as impedance.

Now, this impedance can be plotted with respect to frequency; and how does that curve generally look like? Something as drawn here. So, one of the characteristics is in the research field we look at the impedance at 1 kilohertz. What is the impedance offered by the electrode at one kilohertz? Ok, this we call it as a characteristic impedance or generally impedance.

Now, any guesses whether the impedance is more or less? So here for the electrodes with lower impedances it is observed that your SNR, signal to noise ratio is high. So, this is one of the requirements and this is I already discussed, this is for a recording type of electrodes, this is one of the important things. Not only that there is something called as chronopotentiometry which I have not discussed because that is beyond the scope right now.

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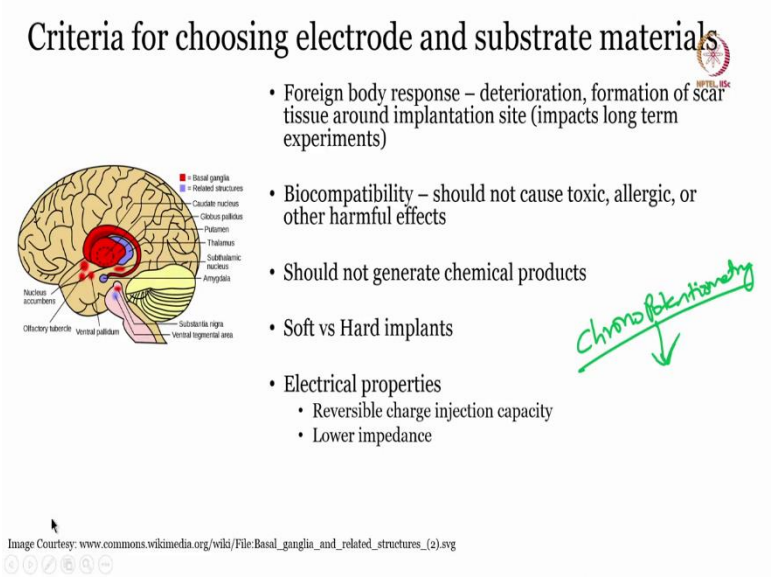

But you can also go through that electrochemistry articles on chronopotentiometry which from there you can decide on you know what is the maximum current that you can apply, such that you know it should not fall beyond the safety limits of the particular electrode electrolyte interface right. So, there are so many other things are involved in that actually.

So, that is how I am just concluding it, because if I go on discussing about this, we can discuss a whole day on that. So, that is why I am telling these are the different criteria's for choosing electrodes and substrate materials and whenever you are talking about electrode properties, you need to go for electro chemical methods.

And electro chemistry background people may understand this more and if at all you are in the neural research field you need to know more about this electrochemistry as well, electronics is not alone sufficient.

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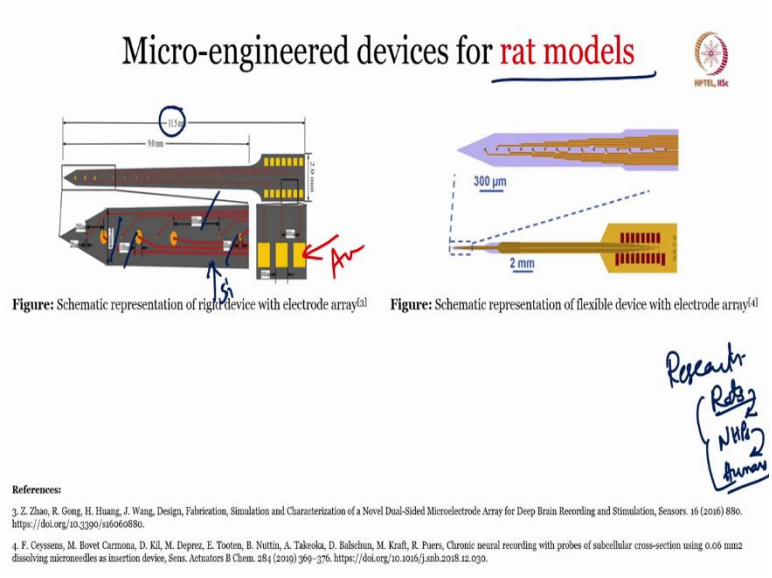

So, next thing is I wanted to show you some of the devices that have been developed for rat models. Then people may ask we are discussing about human brain, suddenly what is this rat thing coming up. So, generally the research goes like this, in research suppose let us go back to the brain. So, let us say that I am working on Parkinson, and this is found to be the effective target right. So, how should I prove it.

If I tell I have to prove it, I cannot work on humans directly. So, what I should do is first work on the rats, then go for something called non-human primates, NHPs, then you go to humans like NHP, like monkeys. So, this is the cycle of research, that is why a lot of research is going on in the rats.

Now, for a Parkinson disease I said that subthalamic nucleus could be the reason for it, but it is also observed that there are side effects that are associated while stimulating the subthalamic nucleus region, there are side effects that are there. So, now, people are moving towards some other targets in the brain; maybe if not subthalamic nucleus what else could have been the reason? All those things have to be initially studied in the rat models.

So, most of the microfabrication techniques use it to fabricate miniaturized devices. So, that they can implant in the rat's brain. You know you can understand our human brain, how big it is, and you would have seen the rat, how small the entire body is. And you can see the brain is hardly you know 1 to 2 centimeters; the length of the brain is.

In that you have to identify the particular region and you have to you know stimulate the particular region and you have to devise the electrodes, all those things in that particular range.

So, generally in the order of you know micrometer range or nanometer range, that is where the microfabrication techniques come into picture. So, look at the slide now. So, what are we doing? Here if you look at these electrode dimensions, see they are all in the range of micrometer.

The entire device if you see just 11.5 mm right very very small and this is the substrate here, they used silicon. So, you can see the references I have given in the slide and then if you are more interested you can go in detail about what are the materials that they have used. So, I remember this is gold that they have used. And this is the specialty of these devices, it has electrodes on both the sides.

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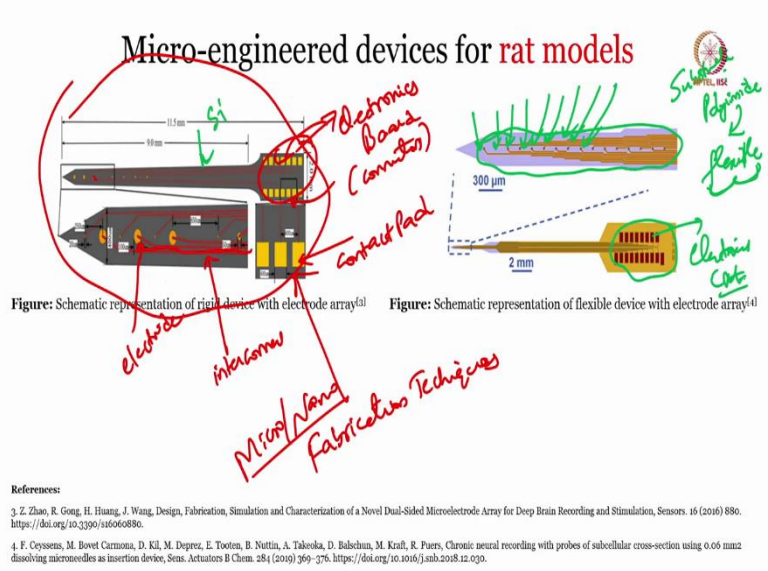

Now, you see this here, now let me erase this. So, this is electrode, and here it is a contact pad and these are interconnects, the red color things, these are interconnects which are connecting the electrode to the contact pad and here the electronics will sit.

So, now this you take it to the electronics pot or electronics board. There are some kind of connectors that are available for example, FPC connectors, then you just clip in that FPC connector to this and that connector will go to PCB and all those things.

So, let us not discuss more about it. I will just show you some pictures in the following lectures. So, this is how generally anything is fabricated, then how it has to be done? How this structure has been created using something called as fabrication techniques? That is what we are mostly interested in. Fabrication techniques, precisely micro or nano.

These are the ranges; it could be micrometer range, or it could be nanometer range and this is one example of rigid substrate. Rigid substrate means the substrate that they have used is silicon and this is a silicon substrate. Now here if you see, this is something different, they use the substrate as a polyimide. I already discussed, this is a polyimide, and this is very much flexible.

So, you can fold it just like that. So, if there is a flexible material how are we going to create these kinds of structures over there, see the flexible material is a little tricky, first of all the material that is used for a flexible substrate comes as a liquid. So, that has to be solidified or cured. You spin coat that particular material and for one of the examples for a polyimide I am saying.

So, how to get a polyimide? It is like it will come as a poly amic acid. So, that is a liquid that has to be cured. So, where will you cure it? You will take a silicon wafer; on the silicon wafer you drop quest the polyimide liquid and then we spin coat it and once you spin coat it you do something called as curing. You do 80 degrees curing or 250 degrees or 360 degree whatever the process requires or at whatever temperature it must be mandatorily cured.

So, that particular thing you can take and now you have a silicon, on top of it there is a polyimide right, there is a polyimide material which is all over. Now that you have to take it for whatever the next steps are.

So, if you want to deposit metals like titanium or whatever, you can use a PVD technique or CVD techniques, maybe CVD you cannot use for metals. I am saying for example, you can do any technique and deposit whatever the material that you want, then you go for creating patterns, that we are going to see the example next.

So, this is how you can do micro fabrication techniques by using that. At the end what we will do? You take the peel off that polyimide; I mean once you take off the devices you

need to peel it off. Now that device is slow flexible. So, it is like this curving, it is not like solid, like a silicon, it is like a curve.

So, now this cannot be inserted in the brain because it is so flexible that there is some buckling effect. Buckling effect is something like this, you can see this right like this. You cannot insert it properly; this is the challenge with the flexible materials. The advantage is you have mechanical properties that are matching to the brain, the disadvantage is there is something called as a buckling effect.

So, to overcome this what do generally people use is a mechanical shuttle around this. So, you put a hard substance along with that and try to insert it, once the insertion is done you take out that shuttle. Are you getting it? Or some other form of shuttle like biodegradable materials you can use because biodegradable means it is going to degrade over a period of time. Are you getting it?

So whatever the material that you use like a polyimide along with biodegradable materials for example, PLGA, poly-lacti-co glycolic acid, that acid you can use that is a biodegradable material, but that is a little stiff.

You can insert it properly. After a week's time or 2 weeks' time, that is going to dissolve within the body with minimal or with least side effects. And whatever polyimide substrate that you have inserted it will be there and it is the contacts whatever are there or electrode contacts that will be in touch with the brain.

So, in any way you can, that is a tricky challenge with the flexible materials. So, now, you can look at the slide. So, you can see the electrodes here. These they use the platinum and iridium oxide electrodes and similar the same structure, you have a contact pad, and this goes to the electronic circuit board.

So, the story remains the same. So, if I want to conclude it, this is how the story goes. So, for every material that you are choosing, it has to satisfy different criterions. We have seen foreign body response criteria, then we have seen biocompatibility criteria, then we have seen it should not generate the byproducts, means your material should not react with the electrolyte or with the neighbouring tissues. No, that is also not acceptable.

Then second thing is mechanical property, whether it is soft or hard then other one is electrical properties and we have also seen what the challenges with the flexible materials are, because they are so flexible you cannot insert it properly. This is something called buckling effect that is involved. So, these are all the challenges that exist with the flexible.

So, what is the challenge with the hard materials like silicon? I told you already there is a local irritation that triggers immune response, again local trigger immune response and there will be different things also there. Are you getting? So, you have advantages and disadvantages of both and based on that you have to play around. So, in the next part we will see the electronic systems and other aspects of brain stimulation.

Thank you.