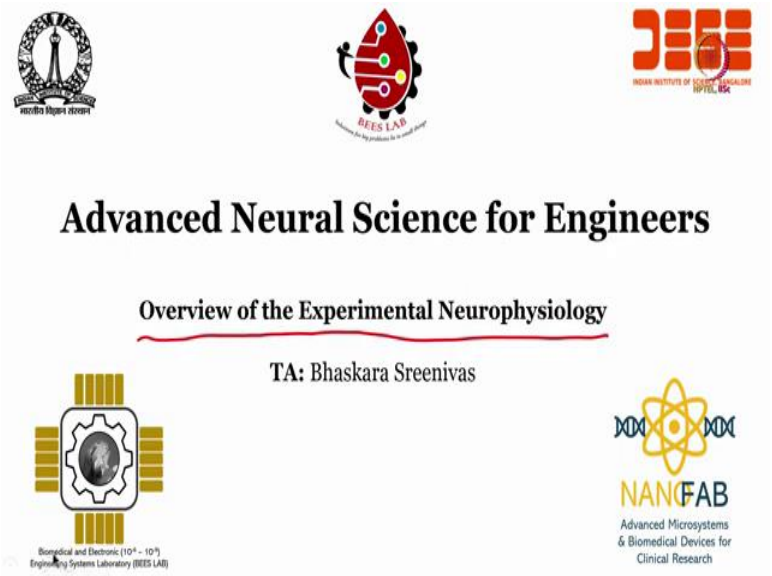
Advanced Neural Science for Engineers
Professor Hardik J. Pandya
Department of Electronic Systems Engineering, Division of EECS
Indian Institute of Science Bangalore

Lecture 29
Overview of the Experimental Neurophysiology

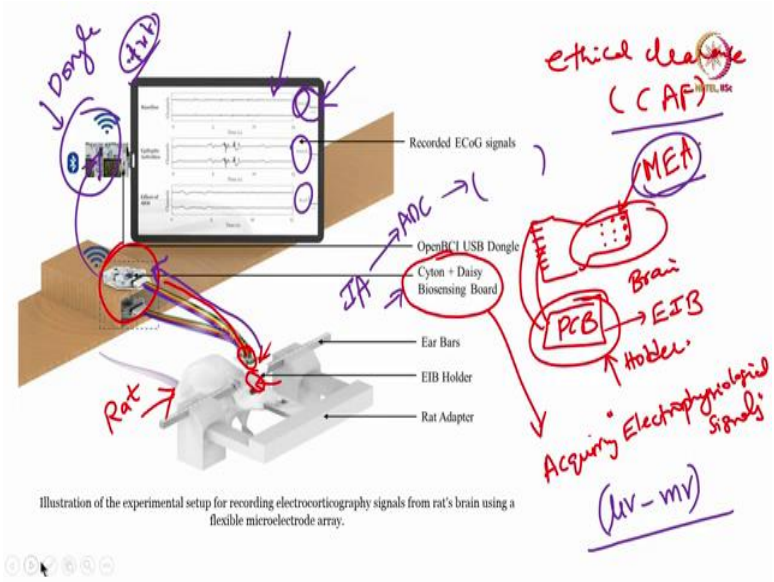
Greetings, everyone. Welcome to the course on Advanced Neural Science for Engineers. Myself, Sreenivas Bhaskara. And I am one of the TAs of this course. Let us look at the slide now.

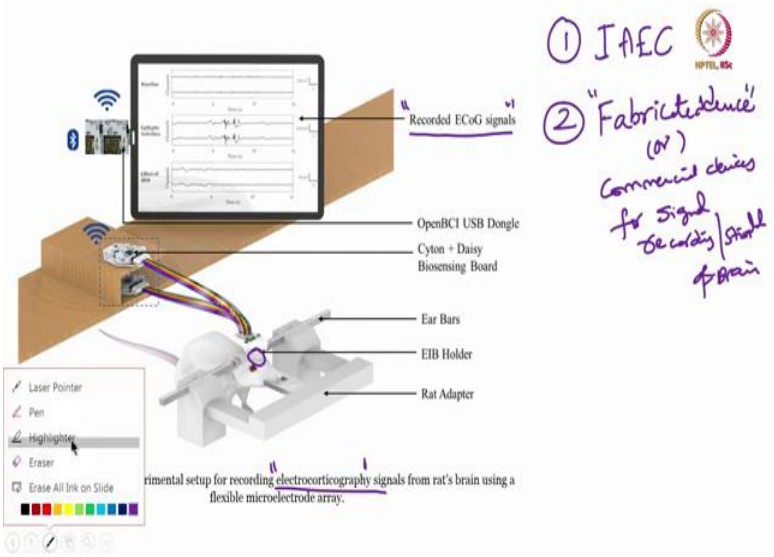
(Refer Slide Time: 00:13)

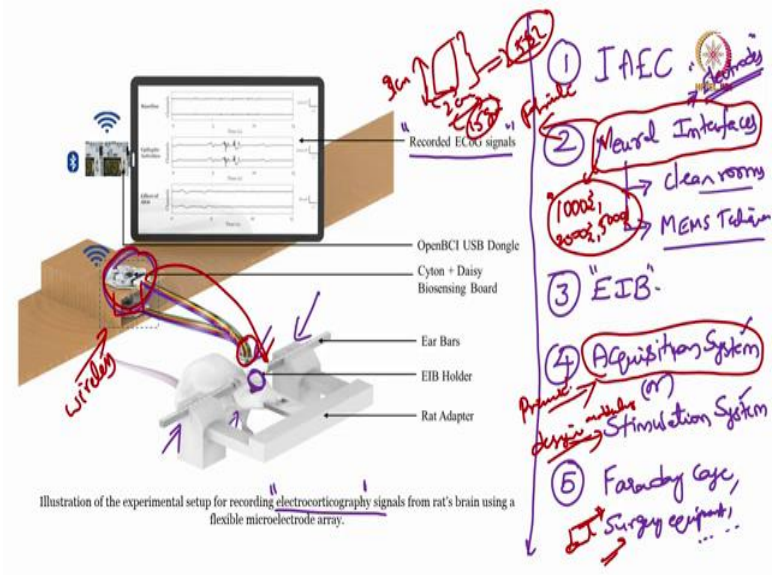


So here in this lecture, we will see something on experimental neuro physiology. So when I say I just want to make it simple, when I say experimental neurophysiology, what I am referring to is how the brain signals are accessed from animal models and then how the brain stimulation is performed and all those things. So let us get started. So, let us go to the next slide.

(Refer Slide Time: 00:46)







So, if you look at this slide, here, if you see here, there is a rat, again, this is like we call it as a let us say, rat. And for experimental neurophysiology lab first of all, we also need to look at what kind of rat that we are looking at are we looking at wistar rat, are we looking at a long evan rates are different kinds of breeds are available, first of all to perform all these experiments, one should have an ethical clearance, this is called as ethical clearance and that should be obtained from central animal facility that we have on IAC.

So that is one thing. Second thing is first of all, you need to identify the which variant of the rat model that you are looking at once you finalize that, then let us look at what happens here. Now, you look at this here. So, this is a EIB holder, EIB stands for electrode interface board. And here if you look at inside. So, just look at the slide in here actually, there is a sensor and which you cannot see right now and we will discuss in detail about that later on and that sensor is attached to, you can see some bit of green color here right that sensor is connected to that PCB and that PCB through which the connections are taken out.

So, the electrodes that are present on the brain, let us say brain, let us say this is brain typically and we have some electrodes that are running on the brain and there is a sensor here this we call it as micro electrode array. The other end of this micro electrode array is connected to our PCB let us say this PCB. Right now, that PCB is covered with the EIB holder. This PCB is called an EIB electrode interface board and there is a holder which connects and then sits and head up the rat. Why it is required?

Because once the rat comes out of anaesthesia after implantation, it is going to throw the things out unless otherwise they are strongly bounded to its head. That is why we need all this setup. We will just look at some of the perspectives in detail some in brief whatever I could do my best I can do it in a given time for me and you can see this once the electrodes are coming out this system if you look at it, this is called Cyton Daisy biosensing board, this is for acquiring the bio potentials What is this for?

Acquiring electrophysiological signals. The electrical signals from the brain are sensed using these electrodes that are there in the MEA. So, let me take my laser pointer what am I referring to. So, here I told you already I showed you the electrodes from there you can sense it then through the PCB, through the electrode interface board, you get the electro I mean that signal out and that signals we are connecting it to biosensing board and that biosensing board has analogue to digital converter I mean amplifiers in the first stage like instrumentation

amplifier to amplify the signals because the brain signals typically are in the order of can you get some number.

Meanwhile, I will take my pen. Typically, they are in the order of micro volts to milli volts. Micro volts to milli volts. And these signals you have to process, that is where these biosensing board come into picture that will have something called IA instrument and amplifiers then followed by ADCs, then it will be streamed to this laptop via a dongle here. There is a dongle here. So, I am just giving you an overview of how it works and you can see this picture, this is just a schematic.

So, we are just showing how the signals and waveforms look like if you look at the amplitude here, which is a look at the scale 200 micro volts, 1000 micro volts and 80 micro volts are in the order. And this is one of the paper published from our lab and then the schematic I have taken it from the paper. So, you can look at it these are the various aspects. First of all, what is this first you need to have a rat and to perform the experiments you need to have ethical clearance then you need to have an electrode array, are you getting it.

Then you need to have I mean this microelectrode array then from the micro electrode array the signals will go to the system I mean while your potential acquisition system from this system the signals were converted to digital and then they are sent to the software a GUI and this here the signals will be like whatever the signals that are there stored in dot txt file or whatever the file format is compatible with then you can use those files and then start doing processing for many other analysis like we generally do for Spectrum Analysis, time frequency analysis and also you can compute various other things which your application demands.

Now, if you look at this to have all these things in place, let me erase all ink, what are the things that we need actually, so what is this one more thing here recorded ECoG signals electro, what is this ECoG electrocardiography signals. Why we are saying? Because now we kept the sensor only on the cortex of the brain we did not go deep brain right then there is a concept of LFPS action potentials all those things comes into picture many other things are there now this application is demanded recording ECoG signals. So that is why we use this this is nothing but electrocorticography.

First of all, you need to have ethical clearance from animal facility. We have Institutional Animal Ethics Committee. Then second one is you have to have a device or I can say a fabricated device or if it is a commercially available you can buy commercially available

device, commercial devices, for what? For electrophysiology signal for signal recording stimulation of brain.

Now let us put a name to this, instead of writing all these we call this as with a simple name, let me erase this, I just want to tell you what we are doing. I will give a simple name to that. Can you guess a name to that? This is called as new neural interfaces. These devices are called as the whatever it is whether use for call signal recording or stimulation. So, these are called as neural interfaces. So, here is the concept of clean rooms and MEMs techniques, you might have seen many MEMs technique, deposition techniques, etching techniques, all those things, lithography all those things.

We also see some of the things in detail. So, first you have neural interfaces for these you have a clean room and MEMs are techniques where when a MEMs fabrication techniques and all those things. So, once you are done with the rat then then you know neural interfaces, then third one the most important component is a electrode interface board and how to fix it? Then there is something called acquisition system. Acquisition system. Acquisition System, now here we are just recording the signals from the brain.

If you are stimulating if you send electrical signals, then you need to have stimulation system. Now, whatever the neural interfaces that you have fabricated has something called electrodes, active electrodes. Now, these electrodes are the material that is used for the electrodes must be compatible either for acquisition our stimulation accordingly, so we will discuss it in detail. Now that is what characterization of the device. Whatever the device that you fabricate, how do you know whether it is feasible for recording or stimulation? Are you getting it? So, the fifth one could be.

So, we also need to have something called as a Faraday cage this all comes under the logistics not in detail, many other things are there. So, you need to have a Faraday cage then you can see here some people might be wondering what is this this is called as stereotaxic operators for doing the surgery. How do you do neurosurgery for the rat? Correct? Then the you need to have surgery equipment.

Faraday cage. Why Faraday cage? Because you do not want interference to takes place because the signals are in them in the range of micro volts and all those things, et cetera. So, many things are required for this, this is like end to end. Now, let us look at the other perspective. So, the other perspective is this. For example, if at all most of the labs what

people do is they procure the neural interfaces. Now, if you guessed the number, you know that cost of the neural one device is in the order of 1,000 dollars, 2,000 dollars, 5,000 dollars.

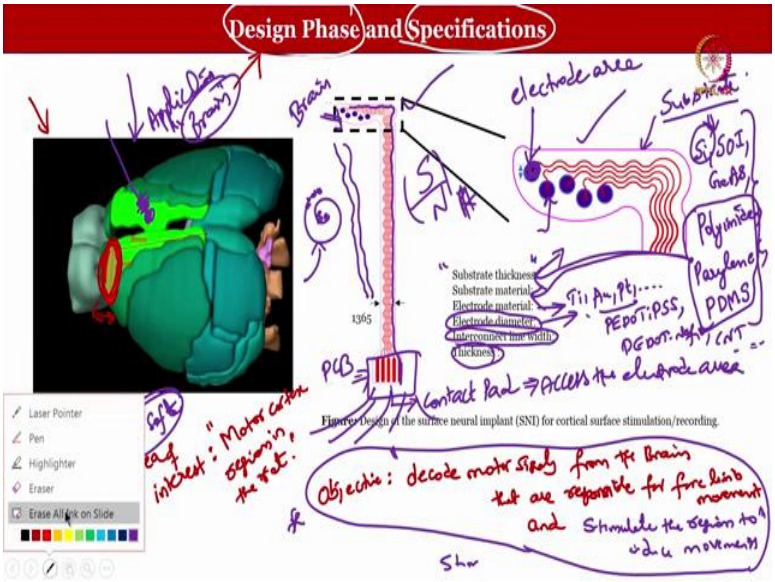
You can convert it Indian rupees and then just think about it how much costly that is going to be, it just roughly can calculate 5000 into some around 85, 90 rupees if you take around 450,000 rupees or 500,000 somewhere around that is the cost of that particular device. And this acquisition systems you have something called a wireless acquisition system and we have wired acquisition system.

When you look at the commercially available what in the my knowledge I am not saying this is what it is, in my knowledge, the one which we tried to procure was around 20,00,000 or something, if it is wireless wired is 20,00,000 if it is wireless, it is going to be around 50,00,000 or something which can wirelessly sit. Now here it that the point here is if you look at it, it is also wireless actually.

But if you look at it, you need to have this board and there is a battery that comes here because it needs to be supported by 4 AA size batteries which is very bulky for the rat to put it on the head. So, there is very small device let us say you know, 1 centimeter by, I think 3 centimeter by 2 centimeter big device, which has the battery and everything ASIC based designs and all those things which can sit which can fit here that is it like a crown, very small 3 centimeter with 2 centimeter the weight is around hardly 15 gram, the entire device and this is costing around 50,00,000.

So, something like this, if at all, someone wants to run these kinds of labs, these are the things that you want to start from your own. If at all, we what we do here in IISc is we fabricate this. We do not procure anything, this we fabricate. And acquisition system is procured, and stimulation system we are designing and developing a wireless stimulation system and these we are making, we are also developing this surgery, Faraday cage we are making surgery things and all our procured it. Whatever the engineering perspectives that we have from our side we are trying to do to develop indigenously, all those things. Now, I am going to discuss some of the perspectives of how to get started.

(Refer Slide Time: 14:05)



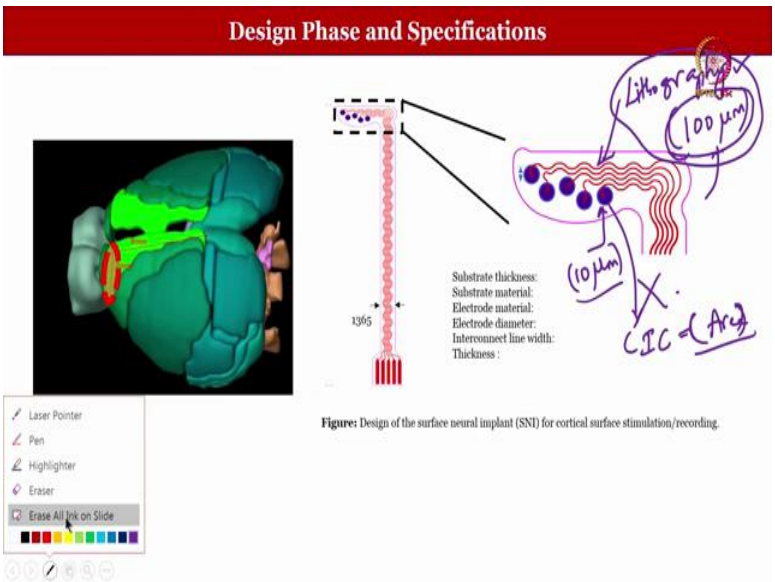


Figure: Design of the surface neural implant (SNI) for cortical surface stimulation/recording.

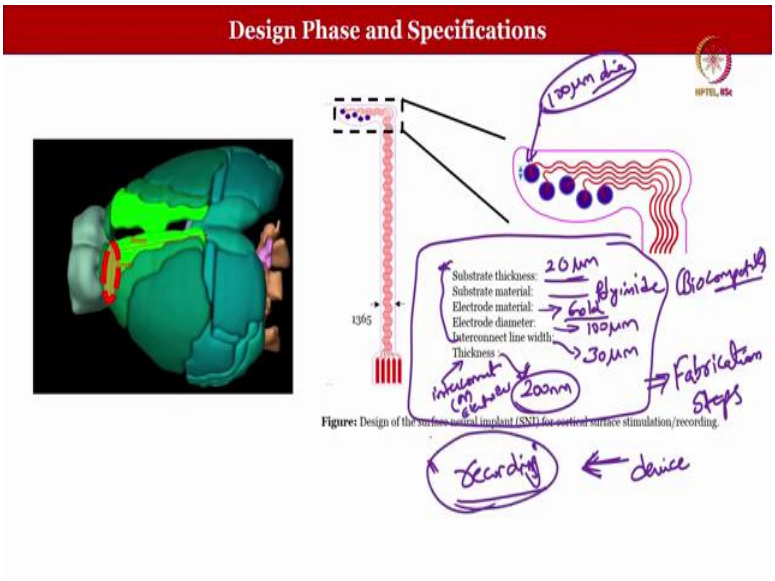


Figure: Design of the surface neural implant (SNI) for cortical surface stimulation/recording.

So, look at next slide, first thing is to design a device what is this is important? This design phase. So, let me change the color look at this the first thing is your design phase and specification which should be very much clear. What are the design when I say design phase, what does it include, what does it mean? This means, what is the area of interest? What is the area of interest in the brain?

Now, for example, one of application that I work with I just give you with the flow, let us say motor cortex region, motor cortex region in the rat. Why we are interested in motor cortex? Because we want to decode the signals whenever rat moves and the motor cortex is responsible for firing up of course the signal flows from other areas to motor cortex and from motor cortex to the limbs it will move but the thing is the idea is to just to decode the motor signals from the brain just understand that much so far.

Now here is the representation of that motor cortex if you look at the left picture, this one. Here this is the area of interest and that area is around this area is around 1 mm by 3 mm something like that. Now, I know this is the area that I am looking at. Now, the objective. One is objective is what, objective is decode motor signals from the brain that are responsible for fore limb movement and one more objective is there. What is other objective is?

Sometimes we want to stimulate that region, stimulate the region to induce movements. That means, what happens here is you can decode the signals from the brain when the rat is moving voluntarily, otherwise, if you want to stimulate that particular area, so that you can tell the rat where to move left or right or forward or something, I am just giving you in a layman language to understand. So, our electrode should be able to decode or stimulate. So, the objective is fixed.

Now, once you know the area, 1 mm area, then you can decide which array that you need to take. So, once you decide which array to take, then you know which, once you decide the area you can have an architecture like this something like this, where every dot here represents an electrode something like that. I am just giving a schematic of how does this look like. So, now one need to decide what is the diameter of the electrode and all those things.

So that is a tedious thing, it is a brief it is not a brief exercise, it will take some time. So, what one need to do is these are the electrodes now where the electrodes will sit the electrodes will sit down some kind of substrate. So, this is a substrate. On the substrate these electrodes will sit now you can see it you can see here these electrodes are connected to there is a wire here

micro wire and coming all over to here, why this goes to the brain and here this side, this is called as contact pad.

This is an electrode area the one which with a circle this electrode area and the one with the kind of rectangle is the contact pad through which you can access the signals, access the electrode area. Now, this will be connected to connector on the PCB and then that is how the signals will go to the other acquisition system or stimulation system or something. So, once you have once sort of there are a whole lot of other things to do.

So, when I say design phase and specification for several objective has to be fixed then you need to go for specifications. So, what about the substrate? Which substrate can I take, we can have we can have you might have seen silicon, silicon insulator, gallium arsenide so, many substrates many are there. Now, along with that there is a substrate called as polyimide, polyimide and then there is also a substrate called as parylene C, then there is substrate called PDMS. Now out of this which substrate to be fixed?

That depends on where you are using it the application, now what is this application you are implanting it in the brain. Implanting in the brain and the brain tissues and if you look at a silicons Young's modulus is this is in the order of giga pascal somewhere, but brain tissue is very soft what happens is when you put a harder material on a softer material, it is going to rupture it and it has to be there for a long time. So, whenever the rat moves, and this is going to rupture the brain, the tissue.

Let us say you put a silicone here in this and whenever the rat moves, it is going to rupture the nearby tissue what happens because of that there is something called as glial scar formation, and means that you end up damaging the tissue and you do not have an access to the tissue because right now, the scar layer has already formed and the recordings will not be proper.

So, since the brain tissue is very soft, when I say very soft when compared to silicon, people use something called flexible materials which are polymer, polyimide, parylene C, PDMS these are all flexible materials. You can choose one of them for the brain application. That depends actually it is not like I am unnecessarily forcing it, but you can think in that way which material I can choose.

I mean, substrate material I am saying. Then substrate thickness, how much thick the material is going to be. So, I will give an example where when we when we the thickness is very

small, then when you use polyimide as a substrate, then there are a lot of curling effects applied, this is not will be like this, this device will be curling like this. Here the electrode contact pads are there here the electrodes will be there like very deep, very difficult to make it linear and then put it on the brain very difficult task for the doctors to do that.

And if you use too much thick, correct again the effect is going to be then it may not be in contact with the tissue. So, one has to play a role there deciding the substrate thickness. Then there is something called an electrode material. Now, we have a lot of electron materials that are available, we have titanium, gold, platinum, these are all materials that are available. And recently these materials are coated with something called as PEDOT PSS poly ethylenedioxythiophene polystyrenesulphonate PEDOT PSS and PEDOT Nafion, carbon nanotubes so, many other things that are medicines are also available.

Coating materials are available, metals are also available, CNTs are available. According to the application means when I say when you are going for only recording then what is required is just the interface impedance has to be as small as possible for having high signal to noise ratio. To make it high your impedance of the electrode offered is going to be less. If it is stimulation there are so, many other parameters like charge injection capacity all those things has to be satisfied.

Now, once you characterize that device, then we go for then we can decide whether we can be it can be suitable for stimulation or recording something. Then of course, the electrode diameter is decided by the stimulation and recording things then interconnect line width. If you look at this, there are five electrodes. So, how much will be the interconnect line width between two lines?

And the thickness of these interconnects, very much important. All these are decided by the either of process. Let us say for example you might have known by now let me clear all the things you might have known by now that to form this kind of pattern, you do something called lithography.

And let us say the lithography system that we have is having the resolution of 100 micrometer let us say 100 microns, but your feature says here this electrode size is going to be 10 micron, that is how you have designed it, but when you went to do that a lithography and then when you started working on the lithography system, then you realize that 100 micron, this is the maximum resolution the lithography can give, but you are looking at 10 micron.

So, is it possible to get this kind of structure? Not possible. Are you getting it? So, the point here is so, many other parameters also will decide here. Some of the things I am discussing are you getting it, and also electrode wire diameter is decided by the charge injection capacity what is the charge injection capacity because it is somewhere I mean it is a function of area and also it is a function of it also decided by whether the lithography can limit this or not which the process flow.

If the lithography cannot allow you to go less than 100 microns then obviously you cannot go for this. So many other parameters are defined. Let us first you have to fix these things. So let us say for example, you have fixed all these things, some numbers or all these like substrate thickness you have, let us say you are taking it as 20 micron, then substrate material you have finalized as a polyimide because this is one of the best material that we can use, one is it is compatible with fabrication for MEMs based fabrication processes.

And other thing is it is a bio compatible material. First of all, that is very very important. When you are implanting something in the brain something in the body, it should be, bio compatible and it has very good chemical resistance. So, means, you will be using lot of chemicals in the process, of chains and all those gold chains, titanium chains all those things in the process.

So, this polymer should not be etched away in the process. Are you getting it? So, then let us say for example, your electrode material is going to be gold for a discussion and electrode diameter somewhere around let us say you can say 100 micron, this is 100 micron dia and assume that lithography supports. Then interconnect line width you can say 30 micron or something and that the thickness is around again 200 nano meter, means what thickness I am talking about this interconnect.

Interconnect thickness or electrode thickness. I just talked about electrode dia, I did not talk about thickness. This is substrate thickness, this is very important all these things. Are you getting it? So once we have finalized with all these things. Now what we will do is we will try to see, so what are the fabrication steps that are involved for this particular device. And this device what we do is we limit our discussion to only recording, I am not going in detail about the stimulation and all those things.

Let us see. Suppose if I want to use this device for recording gold material, it is more than sufficient. And this thickness is also more than sufficient. This diameter it is also more than sufficient. Do not worry, this is compatible for recording. Let us assume like that.