Introductory Neuroscience and Neuro-Instrumentation
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Lecture 65
Recent Advances in the Neuroscience and Neuro-Instrumentation
Microelectrode Arrays and Deep Brain Stimulation

Hello everyone, welcome to the course Introductory Neuroscience and Neuro-Instrumentation. We having going through the recent advances in the field of neuroscience and neuro-instrumentation. I have discussed about epilepsy classification in the last week's module. So, far what we have seen mostly is non-invasive recordings of brain waves.

So, for this particular lecture, we will be touching upon a very interesting topic that is an invasive brain-computer interface, what basically we will be doing is, I will be discussing about how we can or when should we go intracranial or when should we go, when can we open our skull and take recordings for better insight.

So all this thing we are going to discuss in this one short module, along with that we will be discussing about I will show you one more concept which is known as Deep Brain Stimulation, when some particular electric pulses, so far what we were doing is, we were recording electric potentials or we are recording biopotentials from your scalp.

Now, what we will be doing is, we are providing the small current to your brain and observe the response. So also this entirely one more huge area of research, which is known as Deep Brain Stimulation, so or direct brain stimulate, Electrical Current Stimulation, Direct Electrical Stimulation, et cetera.

So let us see first step by step, why should we go for an invasive EEG? What are the different implications of that? When should we go for the invasive EEG? When should we go for the, until which point on your head we should open, like inside your head, in between your scalp and brain, there will be many layers, there will be Dural and after that, there is a cortex and then inside that there is a brain, so till which point you should go and when you should go.

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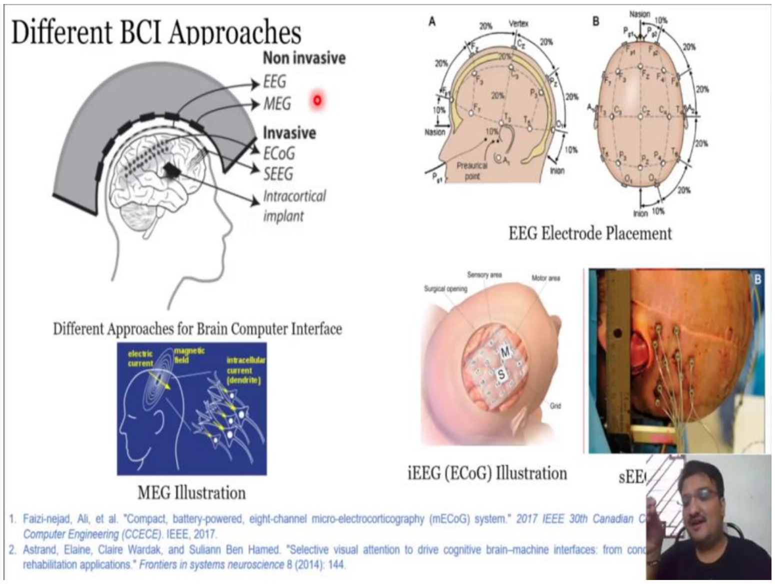

So, all this thing we are going to discuss in this lecture. So first, let me just give you an idea. So these are all the different BCI approaches which we have seen so far. So this is basically a non-invasive approach in which on your scalp, you will put some electrode and opting. This is known as a normal conventional base EEG.

Now there is one more term MEG. So MEG is Magneto Electroencephalography. So we would have studied in our initial in a plus 2 or before that, that when some change in current happen that magnetic field will get induced. So similarly, when currents will pass through your, inside your head or the neuro-electric pulses, there will be a small magnetic field above your head which you should be able, which if we can sense that particular magnetic field, then we can it will give us some idea about the activity going inside your head.

So this is a somewhat a principle, one of the motivation behind FMRI as well. So there are Magnetometers or SQUID using which you can obtain the intensity of magnetic field and conclude more about the, it compared to EEG it has excellent spatial resolution and it is been used. So just I will just show you quickly illustration of MEG.

So this is basically a illustration of MEG as I mentioned some electric current happens as a result of that magnetic field will get induced and we are measuring that as simple as that; whereas, this is a bit 10, 20 system or normal EEG recording which we have seen so far. If we go further, deep inside your head, in that case, we will be dealing with; we are taking a recording from somewhere this line near to your cortex or the surface of your outer surface of your brain that is called ECoG.

So with nothing but electrocorticography, in other words, it is, it is also known as iEEG stands for intracranial EEG. So if you see this image, it shows how intracranial EEG, from where it is being recorded. So your skull it is your skull will be opened, it is minimally invasive process, then some electrode will be placed and further we can record the response.

Now, this is for iEEG, if we go further deeper inside the brain to take recording, it learns something called sEEG, which stands for stereo EEG, stereotactic EEG, in which what we are doing is this kind of incision would be made inside your head and further electrode will be placed even deeper.

If I talk about how, till how much it would be said, it will be somewhere like here as you can see further, if we go even or deeper inside the brain or there is one more study a field of study to put bioresorbable implants inside your head. So what does bioresorbable implants or bioresorbable electrode does is, if you place this bioresorbable sensors or electrodes inside your brain with wireless transmission capacity, it can give you an idea about the neural activity happening inside your brain in real time continuously.

So, just for any subject with a brain disorder be it epilepsy or anything, we are not able to record the responses so that recording time is limited, you cannot put electrodes on a subject and record throughout, it is inconvenient, and you cannot record it for a longer duration of time. Whereas, if you can play something like an Intracortical implant with a bioresorbable material.

Very important thing, that material which you are using is bioresorbable otherwise, it might result in some form of infection or it may hurt, it may damage some of the tissue and as a result of that you might loss your sensory system or you might also poor in implantation or when you go inside your body and putting something very important thing that it should be biocompatible bioresorbable.

So I hope this different approaches the first two approaches are non invasive and the next two approaches are minimally invasive sEEG is invasive. Basically now, we will see when this approaches are used. If you think like we are measuring or we are recording using easy, it is simple, you are not supposed to open your skull anything, even once you have one proper headband or any kind of device, it was very, very easy for even a semi-skilled person to take the recordings and check it further.

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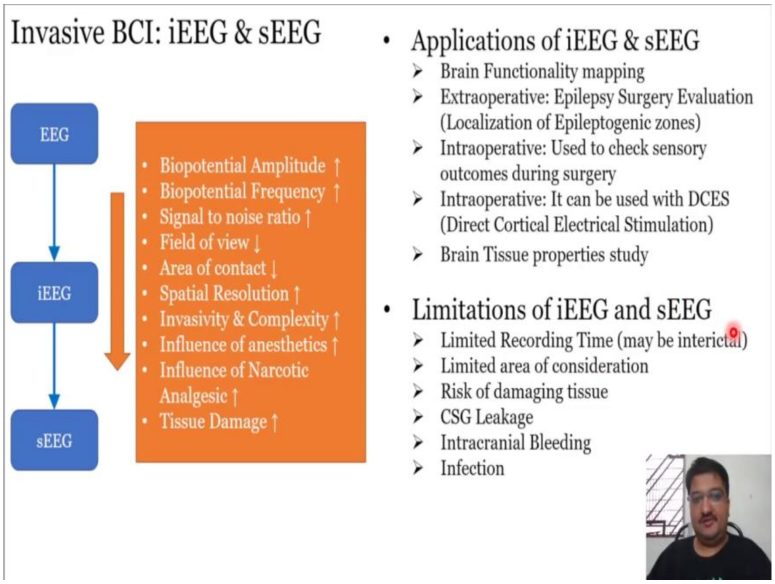

So why should we go? Or why should we open the skull and go interracially? Or why should we go even deeper into your brain to measure the response. So all this thing comparison behind these three techniques and why should we go for iEEG and sEEG? Additionally, how the parameters are affecting things will change. When you go from EEG do iEEG to sEEG? So we will discuss this thing. So it is very important analysis are points which I have noted down.

So consider this is your EEG. This is the, like evolution right, from EEG to intracranial EEG to sEEG. It is very clear now that EEG will be recorded from the scalp, ECoG will be somewhere near to your cortex and sEEG would be deep inside your brain. So now let us see how it differs? So first, when we go from EEG to intracranial EEG to sEEG, the amplitude will increase.

So very simple why because it has been already noted down that you have many layers before your brain, between your brain and scalp, so whenever you go inside there will be some of the layers will, can act as an attenuator for biopotential. So whenever you go deeper inside your brain, then this your biopotentials amplitude will increase.

Additionally each layer works as a low pass filter. So whenever you go deep inside your brain, that action of low pass filter or finally your cutoff frequency, after which that skin layers will stop allowing the biopotentials to go out of skull. So the cutoff frequency will get increased as a result of that you will get even higher frequency component.

So these are the first two point, one more thing is for EEG you will find it is a recording from scalp. So, you will find more noise, it also has this atmospheric dependency as well. Whereas, if we talk about intracranial EEG and stereo EEG, there are compared to and there are two things one is that you are going deeper inside your brain, so you will get a prominent response amplitude frequency would be higher and noise also would be lesser.

As a result of that you will be obtaining a very nice SNR signal to noise ratio. Further if I talk about a field of view or when I think about electrical design there should be area of contact defined, like basically electrode is nothing but a metal body which will acquire or which will allow some biopotential to transmit from your brain, that neural response from your brain to finally signal conditioning or calibrating units.

So, the area of contact whenever you go from your scalp to your deep inside your brain, there is a lot of cortical columns plus there are so many like you have to consider brain anatomy while placing electrodes inside your brain. So that area of contact for electrode if I talk about electrodes, there is a cross section or patch, so that patch of the electrode will get reduced additionally the region or site of observation when you are like will get reduced as well.

Further as you go deeper and deeper your field of view and area of contract will decrease as well as your spatial resolution will get increased because your source, you are getting closer to the source. That is the most important thing when you grow intracranially or you are going for stereo EEG intracranially. It is also known as Electrocorticography.

So Electrocorticography and stereo EEG, you are going deeper inside your brain; you are going to near to the generator of your biopotentials. That is why your spatial resolution will increase but and one more thing why this is one of the reason why sEEG is used was video EEG for brain surgery and brain tumor detection because you exactly need to verify or exactly need to go to a particular tissue which has a tumor and you have to remove it.

One more thing, before going for brain surgery or brain tumor removal fMRI is advisable because that will provide you an exact location of where your trauma is. Further you can go deep inside or go to deep inside your brain and remove the tumor using sEEG but when you go, as I mentioned deeper to your brain, it is advisable to first have an image or a spatial distribution and you should be exactly aware, you should be exactly able to locate your, a tumor or lesion inside your brain so you can remove it properly.

Another point is that tumor or lesion should be removed by some experienced a neurosurgeon, because even a small change in terms of your movement or even a small change in electrode may hurt or may result in lifelong adverse consequences. So when I go from a EEG again to iEEG and sEEG, the invasivity, the incision everything will increase.

Another point is complexity that is experimental complexity when you go from EEG to iEEG to sEEG, experimental complexity will increase like for EEG if you want to set up your experiment, you can do it in 10 minutes provided your system is ready, whereas for iEEG unit to open it and it might take some time as well as it needs expertise and for sEEG unit to place electrodes you should have stereotaxic equipment which will precisely move your electrode across the skull.

So when you go from EEG to iEEG to sEEG your invasivity and complexity increase. One more thing is for iEEG and sEEG are opening the skull. So you need to provide some anesthesia. So now the influence of anesthetics or some pain removal drugs that is narcotic analgesic, will be higher when you go from EEG to sEEG.

Now, your EEG or scalp EEG also, will vary with respect to your when you apply any anesthetics but for scalp EEG you do not have to give any kind of anesthesia because it is a non-invasive process. There will not be any kind of pain felt by a subject. So for the other two techniques like iEEG and sEEG, whatever the response you are obtaining that would be in influence of anesthetics and analgesic but there are different kind of anesthesia available, which makes sure that suppose there is a case when you need to get an idea about the sensory system or get an idea whether a subject, you need to make sure that subject is not losing any kind of sensory system during the surgery.

So in some of the complex surgery, you might have to take and check the functionality of sensory system during the operation. So in such intra-operative checks, what you can do is, you there is a specific kind of anesthesia available, which will prevent some of the functionality of your sensory system but making sure that other remains intact.

So designing or working or setting an experimental protocol, setting the proper drug for a brain before brain surgery, during brain surgery setting a proper drug for anesthesia is also an important task and all this thing like your timings, your because every anesthesia will have its own recover time.

So your entire brain surgery should be planned in such a way that subject will not be, it’s sensory system will not be harmed, it will not have any adverse consequences as well as the subject will not feel any kind of pain and operation should be carried out properly. So anyway, there is no for a, anyway for a students or any of the doctoral students here, after anesthesia, Dural anesthesia is also a super specialization when specifically they will be taught only about anesthesia related to brain surgery.

And last but important point along with tissue damage, there will be a lot of infection. So when you put your electrode inside your, inside your brain, then there will be a or even for mostly for stereo EEG, the tissue will come into contact of your electrode. So all this thing must be checked before I perform, taking recordings and all that, that interface between your tissue and your electrode must not harm the tissue itself.

But yeah, the chances of tissue damage is higher when you come, go deep inside your brain. So now, let us quickly see what are the applications and limitations of invasive EEG techniques. So first and foremost, brain functionality mapping, second is extraoperative means when like anything which has been done, when operation is not under progress, but interoperative means wide operation you can check sensory outcomes yours of sensory outcomes whereas in case of extra operative thing, you can evaluate any surgery or epilepsy surgery evaluation or brain tumor evaluation.

Further, you can also check I have told one term Brain Stimulation. So there is something similar, Direct Cortical Electrical Stimulation during the surgery. So you will give a specifically pre designed stimuli that is nothing but a small electric current and as a response to that your brain will show some response.

So basically, this all our applications mainly for when you have a critical case of epilepsy, you need to remove some of the particular tissue of your brain or you found some brain tumor which is can be life threatening all these things can be removed with the assistance of invasive EEG techniques.

So now, what are the limitations of invasive EEG techniques? So first thing is recording time is limited. So you cannot place your electrode and open your skull and keep it there for a longer duration of time. Additionally, you cannot you know make incision or you cannot put electrodes in your entire skull, that should be a specific region.

So whenever you perform any kind of surgery or this kind of recording your focus should be defined, that your site of generation should be defined. So further there is a risk of damaging tissue I already mentioned that it might hurt the tissue as well. There are a leakage of cerebrospinal fluid as well as it might happen that you may receive some form of bleeding as well as infection. So all these things will be considered when you go from noninvasive to invasive EEG.

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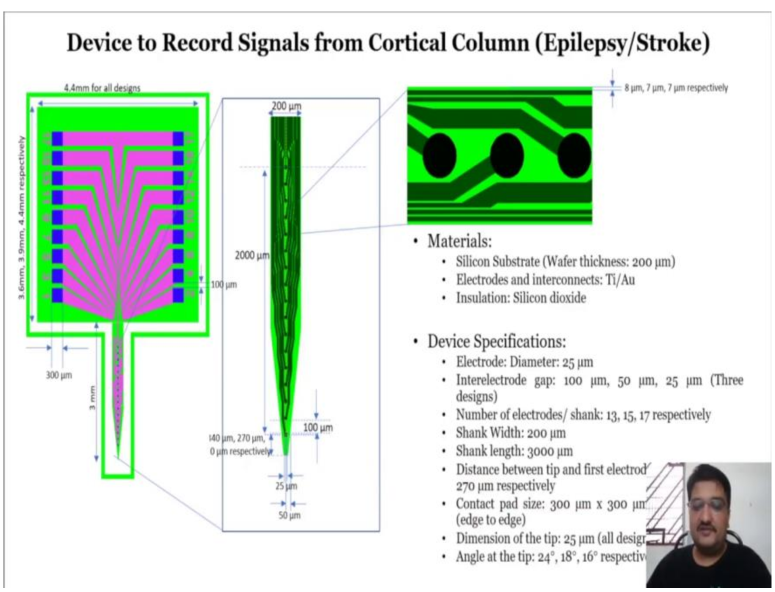

So now, we will see how to realize this kind of recording and what are the devices, instrumentation required to get this kind of recording. So I already mentioned that area of contact or the site which we are observing, which be much much less so, that dimensions of your electrode would be in sub millimeter range. So it would be few tenths of micrometers.

So now, so far you have been taught a lot about microfabrication, like what are the thin film deposition techniques, how photolithography works, what are the characterization techniques? A few of the things have been touched up by a Professor Pandya. So this all this thing will taken into consideration when you are designing any of this kind of application.

I will quickly tell you about what this device look mean and what does it look like? So first of all, idea wise this is the entire one microelectrode. This is known as Shank, so further this is a zoomed in view of this shank here and additionally, this is the final view of how this electrodes will be placed. So this Shank will be inserted or this Shank will go inside your brain when you are taking intracranial or stereo EEG and all this pads are your metal plates.

So, from metal pads you can take output from this new square and then you can analyze your bio potential. But all this thing is possible when you know what are the fabrication for that, there are microfabrication techniques, which has thin film deposition which is thin film deposition basically has a physical vapor deposition and chemical vapor deposition.

For physical vapor deposition, thermal evaporation and e-beam techniques and all techniques have been already explained in the course for etching there are different kinds of etching for CVD is a chemical way to deposit any kind of baton on to Silicon or any substrate. So this is actually a mask using which we have fabricated some of the microelectrode arrays to for diagnosis of epilepsy and stroke.

So these are the materials which has been used as I mentioned on silicon substrate of 200 micrometer, we try to pattern this electrodes and which metal is used either you can use gold or titanium. So that separate study you can perform considering material property but conductivity as well as heat resistance all this thing is very nice when it comes to your gold or titanium and there should be insulation layer of course.

When a microfabrication technique you should be having one insulation to separate out silicon from your patterning layer and these are the design specification. We will not go into the detail of the design specification, but from numbers you will get an idea that a few micrometers are is the gap between two electrode. So further, if you go into the detail, you should be able to know that this is one Shank.

You can have multiple Shank here as well. But the idea is you should also know in which side you are going to place this electrode because inside your brain your anatomy should also be taken into consideration because that has its own shape, things are placed when you go inter-perennially inside your brain, already there is a lot of nerves and the thing is there is a very small gap, it is in few millimeters like, 2 millimeters, 4 millimeters not more than that between the nerves which are going and even a small incision or even a small damage to that nerve, as I mentioned can result in lifelong disabilities.

So this distance is between free space, I should say inside your brain is very, very small. So considering all this thing the Shank's dimension should be designed, should be designed dimensions should be finalized as you can see here. The Shank's width is around 200 micrometer, so 0.2 millimeter and such devices exist and people have able to fabricated obtained responses using that.

So in our lab we are also aiming to get this kind of devices, this is just a one of the devices which I have shown here which is having 18 electrodes, multi micro electrode area I should say and this all the dimensions I mentioned this is a Shank width, the Shank length is 3 millimeter or you can just know this is your Shank, you can operate your Shank on which direction you want it to move using stereotaxic equipment, which has a precision of very, very you know in terms of few micrometers.

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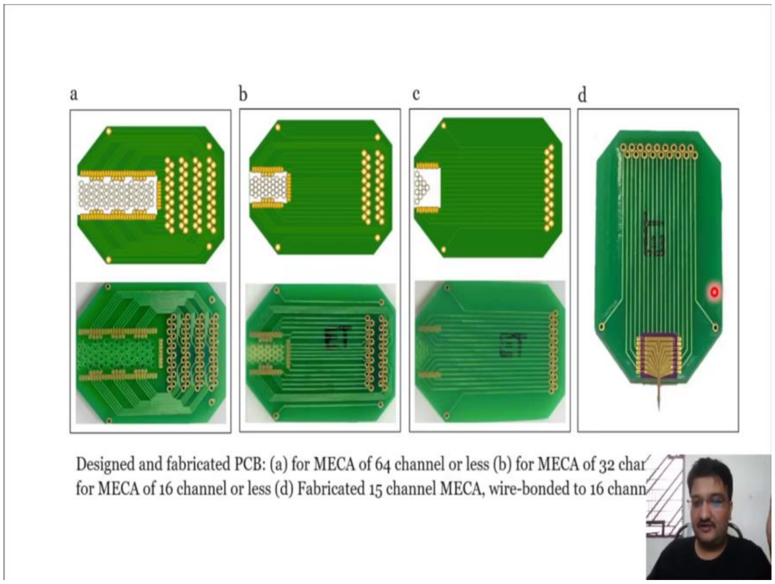

So that will make sure that you will not touch any of the nerve or any of the tissues or damage or infect any of the nerve and tissue. So additionally this all our analysis like you can, what is the angle at the tip and all this thing once you go into the detail of the design of microelectrode array. You can consider all this parameter. So now, I will show you some of the designs. So this is basically you can see, we have seen microneedle.

This is a microneedle with one Shank say microneedle is placed here; wire bound it in some of the PCB. So this is a next step, once you fabricate your device, that particular thing will be wire bounded and on into some of the PCB. This PCB will have a signal conditioning circuit to acquire a particular biopotential. So as you can see here, there is already wire bounded PCB.

Now further how the entire microelectrode assembly will look like or what are the rest of the thing required to finish the loop? What microelectrode does, it will record the biopotential from a deeper region of brain. What PCB will do? It will perform as a signal conditioning circuit but after that, how you are going to transmit your biopotential from your PCB to the real world for finally any kind of conclusion where you are going to see all this thing?

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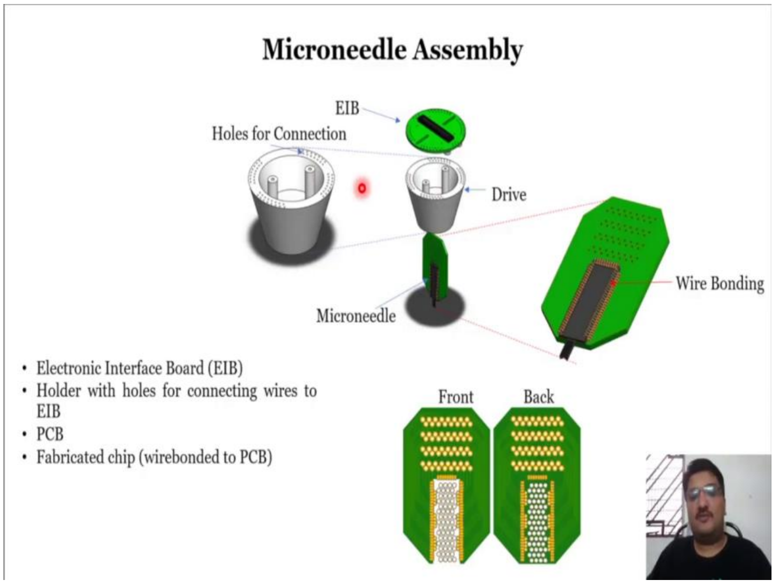

So that is basically the entire system based on microneedle, microelectrodes. So I will quickly show you the system or microneedle assembly. So it is something like this. So this EIB is Electronic Interface Board. So this is basically your microneedle, black part whereas this is your PCB, wire mounted PCB and the rest of the thing drives and Electronic Interface Board is to acquire the potential from your PCB to the real world and that should be provisioned to precisely move your microelectrode.

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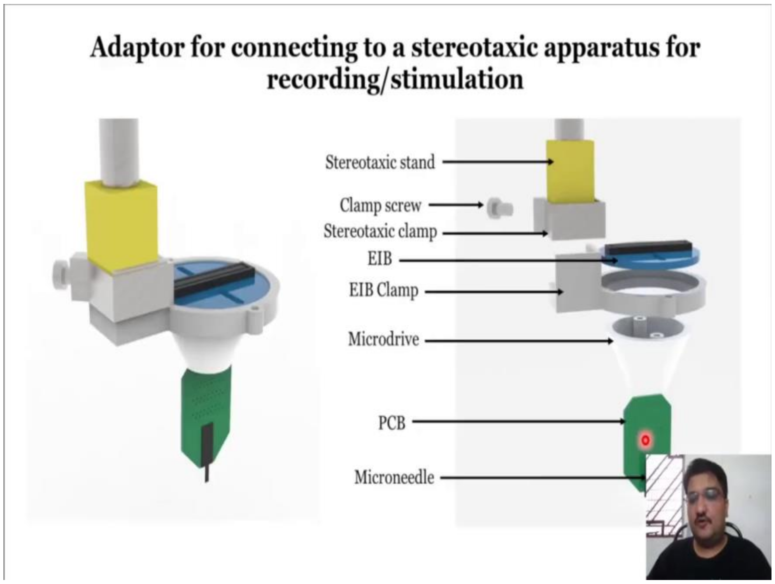

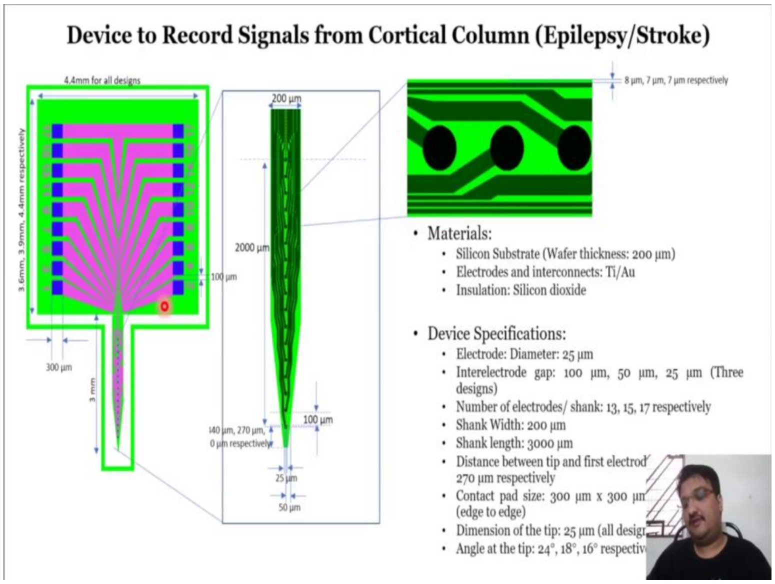

For that, we will be having a Stereotaxic stand and this is actually the system on which is been used for microneedle recording. So you have a PCB microdrive, Electronic Interface Board and you have a stereotaxic stand. So this stand will be this would be connected to your stereotaxic equipment and then once you move it in our direction, particular direction you should be able to navigate your microelectrode accordingly inside your deep brain region.

So this is basically an idea, but as I mentioned, the key part remains, this fabrication of your micro needle. The rest of the things are already existing in real world, but you should be able to know that how you can get this kind of design for a which all the basics of microfabrication is very important, so that you can pattern a desired way or desired number of electrodes with proper contacts, in order to get the desired by microelectrode arrays.

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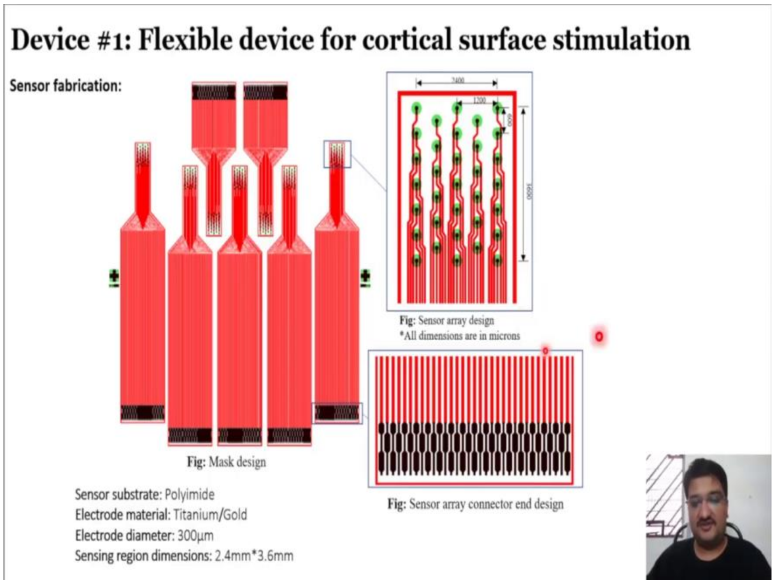

So I hope this microelectrode Portion is understood and clear. Now, we will touch upon another very important topic that is I mentioned brain stimulation, deep brain stimulation. So again the acquisition part of microelectrodes remains the same, you can see this is one of the design or of mass design I should say for the fabrication of your electrode, all the images are shown this part basically is your electrode, again the dimensions and all are provided whereas the bottom part this part is nothing but your contact pad.

You then you can see the length of your electrode differs here. So you can go based on the length of your electrode, height of your electrode, you can go in a particular region, so you have to decide how deeper you want to go inside your brain and you can think about it. So here the substrate which has been used as polyamide and material is used titanium gold. What is the diameter of electrode is 300 micrometer and this is the sensing regions dia dimensions.

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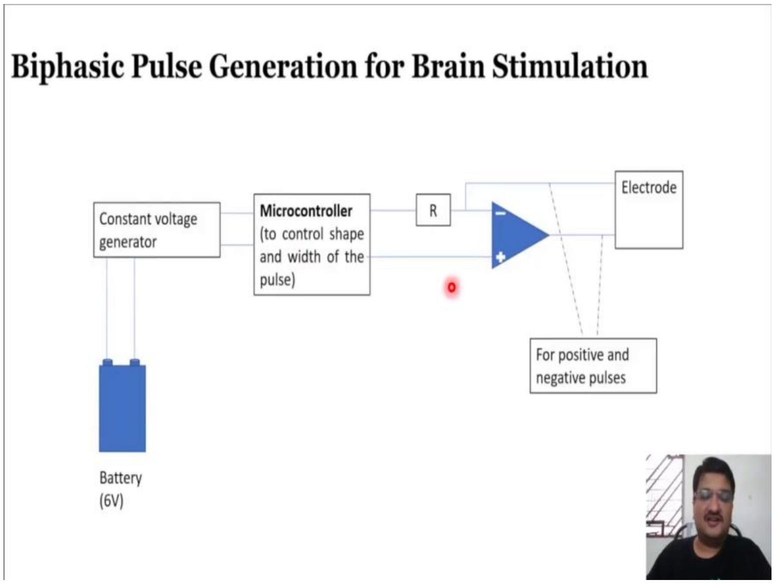

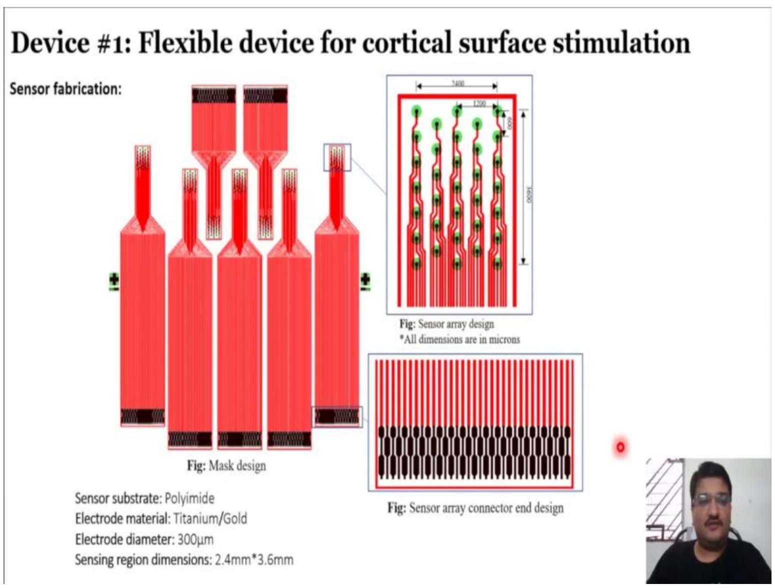

So further this is the actual fabricated image which we are I was talking about and once you fabricated any kind of device, you should be characterize it properly like you cannot fabrication microfabrication as it suggests, that it will be a precision in the micrometer range. So you cannot directly say and evaluate any of the fabricated device.

So for that you must do some what characterization. So basically there are many techniques for characterization, electron microscopy like SEM or if required TEM, if your final precision is in a few nanometers range you should go for TEM but in mostly in this case if you go for SEM or if you want to see the consistency or if you are making some kind of trenches and you want to see the consistency of that how the uniformly it has been deposited and all of you should go for optical profilometry.

So there are many characterization techniques to evaluate a fabricated device. So this is basically a fabricated device, you can see here and this is actually images of SEM. So I have already shown you before that this is the target or is the mask we are using, which will be used to pattern the device. So similarly, here you can see the same kind of structure has been obtained using a fabrication technique.

So this is just to provide you an idea that whatever has been taught in the course of the this particular topic, this particular subject that neuroscience and neuro instrumentation has a lot of you know importance in even a process like microfabrication has a lot of importance in the field of neuroscience and neuro instrumentation. So I this is basically add one more point that characterization is as important as the fabrication process, because that will give you an idea of how successful your fabrication process is.

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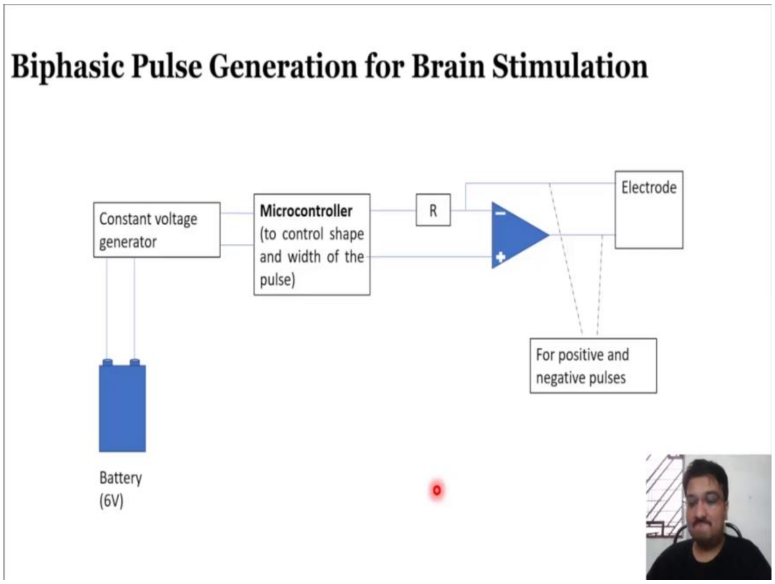

So finally, which kind of current should be given, this is just an illustration that some it is basically a combination of your microcontroller and your op amp. So op amp, using op amp you can generate any kind of pulse offers but yeah in microcontroller you can program it from the inbuilt timer. So based on your requirement with some preliminary label electronic design, you should be able to generate a stimuli which can be used for your brain stimulation.

I already covered auditory stimuli and visual stimuli in one of the previous module, the similar kind of approaches here there we are using some software which has an inbuilt timer, here we can use some general-purpose microcontroller and program your device and obtain the desired electrical stimuli or periodic electrical waveforms to obtain a particular brain stimulation.

It has been, studies have shown that if you provide any particular kind of stimuli electrical stimuli, you will be getting, you can navigate or you can make a person or do a particular thing like for example, if biophysical electrical stimuli is being inserted into rats brain, you can able to navigate the rat in a particular direction.

So if we talk about the application a lot of application exist not only just to check whether a person's sensory system and everything works fine during the operation, not only intra-operative but extra operative as well as in real life as I mentioned, you can able to move rat in a particular direction.

Similarly, you just place a camera or something, micro camera on the rat's head and you can move it you can use it to for spying purpose or any other thing. So there are a lot of application of dream based simulation. But the idea of this particular module is to inform you or is to glance through the topics of multi microelectrode area or microneedles as well as with the slight change slight modal additional modality in microelectrode easily getting a response which is in response to a particular stimuli.

So I hope these two topics are microneedles or microelectrode arrays and brain stimulation is clear to all of you, you can feel free and explore more about the topics to get a better idea. If you have any questions, feel free to ask us in forum. I hope this is clear and it will help you and you will be able to obtain more and more literature about this and you can go through it and as I mentioned feel free to ask questions regarding this in forum. Bye. Take care