

Neural Science for Engineers
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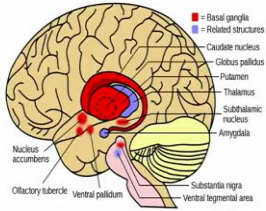
Lecture - 31
Brain Stimulation Device Fabrication

Hello welcome to the course on Neural Science for Engineers this is Sreenivas Bhaskara one of the TAs of this course and if you look at the slide, we have been discussing about Brain Stimulation.

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What is Brain Stimulation?

- Controlling abnormality in a particular brain region by applying electrical signals
- Clinically accepted surgical treatments are already available for conditions such as Parkinson's disease, Essential tremor, Dystonia, Epilepsy, Obsessive-compulsive disorder
- Stimulation of either Cortical surface or deep brain structures such as the subthalamic nucleus, pedunculopontine tegmental nucleus (PPTg), etc.
- Origin of Deep Brain Stimulation is dated back to 1980s in dealing with Parkinson's disease ^[1]



References:


1. Seth F Oliveria, The dark history of early deep brain stimulation, The Lancet Neurology, [https://doi.org/10.1016/S1474-4422\(18\)30237-0](https://doi.org/10.1016/S1474-4422(18)30237-0).

Image Courtesy: [www.commonswiki.org/wiki/File:Basal_ganglia_and_related_structures_\(2\).svg](http://www.commonswiki.org/wiki/File:Basal_ganglia_and_related_structures_(2).svg)

And we have seen what is the brain stimulation.

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Why Brain Stimulation?



- Neurological condition like Parkinson's disease is generally treated
 - using medication, diet (Primary stage)
 - **DBS** (for advance stage)
- **Prevalence:** 10 million people are estimated to be suffering from Parkinson's disease which makes it difficult to do their day to day activities^[2].

Key Symptoms of Parkinson's Disease




Image Courtesy: www.thegoldenconcepts.com/blogs/health/parkinson-s-disease-spotting-symptoms-preventative-measures

Reference
2. K. Sen and R. Bouita, "Global health status: two steps forward, one step back," *The Lancet*, vol. 356, no. 9229, pp. 577–582, Aug. 2000, doi: 10.1016/S0140-6736(00)02590-3.

Then we discussed why brain stimulation.

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Illustrative diagram of Deep Brain Stimulation



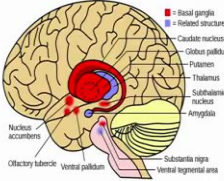


Image Courtesy: <https://scitechdaily.com/study-shows-deep-brain-stimulation-is-effective-treatment-for-most-severe-depression/>

Then we have seen how the deep brain stimulation devices looks like.

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Criteria for choosing electrode and substrate materials



- Foreign body response – deterioration, formation of scar tissue around implantation site (impacts long term experiments)
- Biocompatibility – should not cause toxic, allergic, or other harmful effects
- Should not generate chemical products
- Soft vs Hard implants
- Electrical properties
 - Reversible charge injection capacity
 - Lower impedance

Image Courtesy: [www.commonswiki.org/wiki/File:Basal_ganglia_and_related_structures_\(2\).svg](http://www.commonswiki.org/wiki/File:Basal_ganglia_and_related_structures_(2).svg)

And the criteria for choosing electrodes.

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Micro-engineered devices for rat models

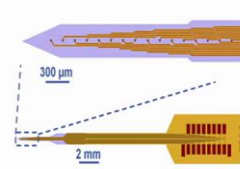
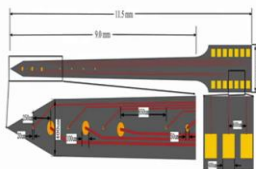


Figure: Schematic representation of rigid device with electrode array^[3]

Figure: Schematic representation of flexible device with electrode array^[4]

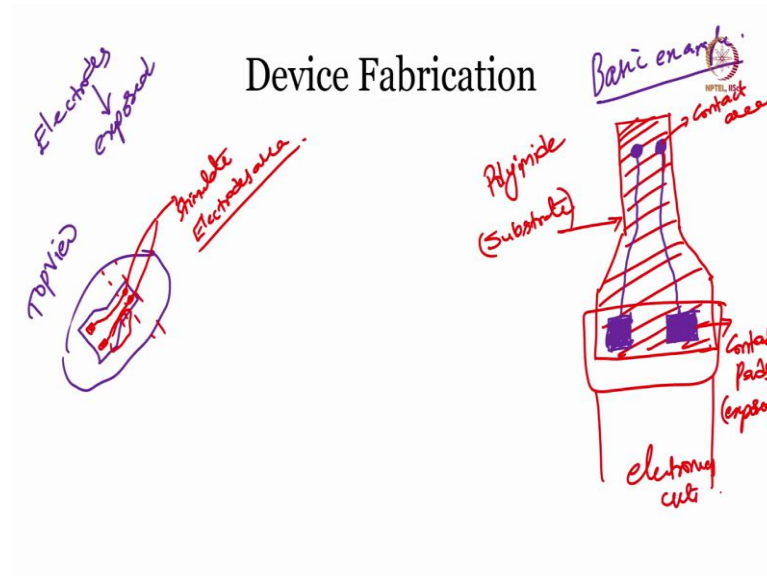
References:

3. Z. Zhao, R. Gong, H. Huang, J. Wang, Design, Fabrication, Simulation and Characterization of a Novel Dual-Sided Microelectrode Array for Deep Brain Recording and Stimulation, *Sensors*, 16 (2016) 880. <https://doi.org/10.3390/s16060880>.

4. F. Cryssens, M. Boret Carmona, D. Kil, M. Deprez, E. Tooten, B. Nuttin, A. Takeoka, D. Balsehun, M. Kraft, R. Puer, Chronic neural recording with probes of subcellular cross-section using 0.06 mm² dissolving microneedles as insertion device, *Sens. Actuators B Chem.* 284 (2019) 369–376. <https://doi.org/10.1016/j.snb.2018.12.030>.

These all I have extensively discussed and we have seen hard versus soft materials or it can be rigid versus flexible devices, we have seen advantages and disadvantages.

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So, now let us talk about device how generally it is fabricated. Now for us to understand in detail I will take a very basic example as follows. So, let us say I have to fabricate a device like this, let us say this is a substrate. So, means this is not a hollow shape, everywhere material is there.

Now, for our understanding I consider this as a substrate polyimide. Now this is an insulator, polyimide does not conduct. So, where are the electrodes? So, let us say I have one electrode here at this area and I have one more electrode at this area.

Now, for our understanding I have just simply considered 2 electrodes. I have a contact pad like this and I have a contact pad like this. So, these have dimensions. So, these are square, rectangle or whatever it is and there should be contact interconnects. So, interconnects like this from here to here, it could be in any fashion depending on the application of whatever we are talking about.

So, for this is a basic example. We can have different architectures depending on the application. So, because there is a lot of research going on, people are talking about omnidirectional.

Now, here one part one should understand is wherever the electrodes are there, those electrodes only need to be exposed because on the brain. So, let us say this is the brain top view. So, you put the device, how does this device look? Like this.

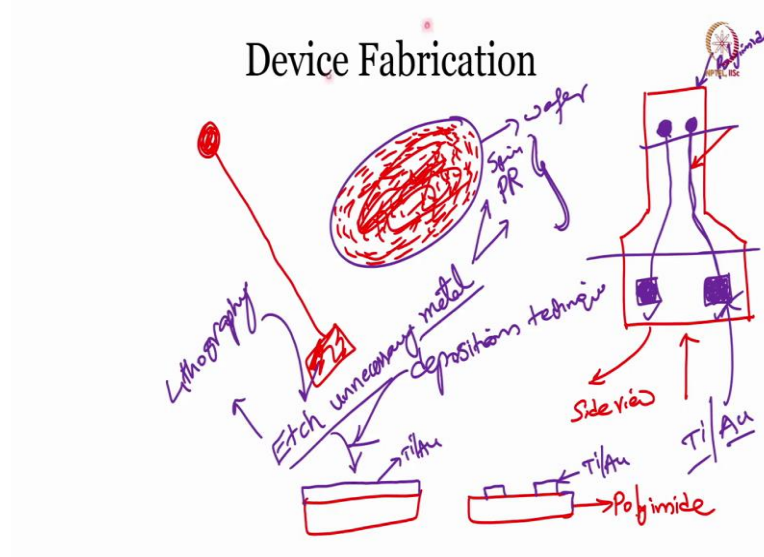
Now, here my region of interest is only this area, only this particular area has to be precise, this area that is it. Only that particular area we need to stimulate, remaining areas we do not want to stimulate or record. So, only that area needs to be exposed, only the electrodes area needs to be exposed.

If you see this is electrode area whatever I am pointing right now, that area should be exposed, this area this interconnect line is there you know this area should not be exposed; what will happen otherwise?

So, if I draw like this, this is how it looks like. This area gets exposed, if everything is exposed means everywhere the stimulation takes place. We should not stimulate the unnecessary area, unintended area, wherever it is intended that area need to be exposed that is called contact area. Contact area only needs to be exposed, interconnects and all should be should not be exposed.

And this area, these contact pads also need to be exposed, why? Because this has to go for another electronic circuits right electronic circuit board. So, let me erase everything and I will redraw and now you have understood the requirement.

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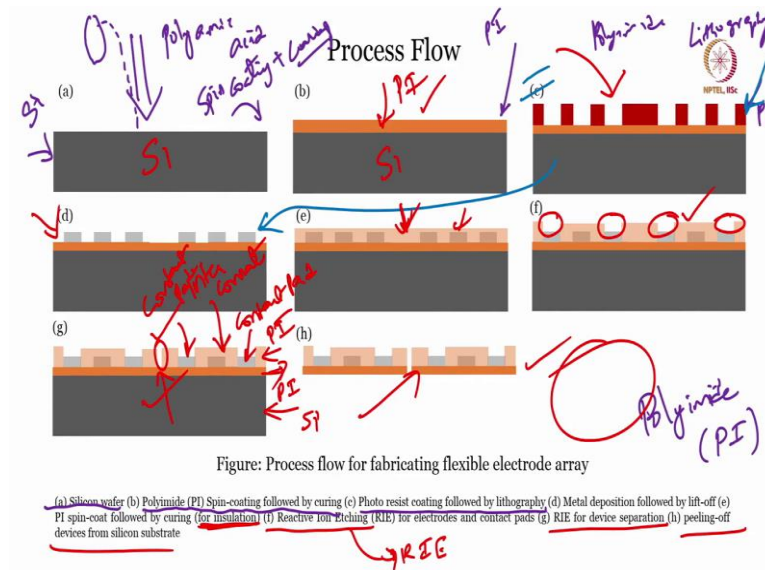


So, we have a device something like this right on the device. So, there is an electrode here, here and there is an electrode here and these are the interconnects, this should not be exposed, keep that in mind. This is an interconnect area, should not be exposed. So,

how the device fabrication happens is this entire thing is a contact or a let us say for example I told you that this is a polyimide.

This is I can say for example gold, generally we cannot use only gold we can use titanium or gold. So, let us see how the process flow looks like.

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So, I talked about polyimide and this polyimide does not come just like that, this comes as a liquid. So, what is that? Liquid polyamic acid. So, directly we cannot work with the liquids, we have to make them like a solid or solidify it or cure it. The terminologies cure it then we have to go for process steps.

So, now you take this silicon, first step is considering a silicon wafer. So, here second step what we do is over this silicon wafer we drop cast the polyimide. So, you have a polyimide bottle, and you drop cast it and then you spin coat it. Spin coating you do, then followed by curing, at some certain temperature. Like for example, some processes we can do at 80 degrees, 250 degrees or 360 degrees. Whatever the requirement is, then it will become like a solid, it will stick to the silicon wafer. So now, your polyimide is ready.

So, polyimide instead of writing all the time like this I just write PI. So, that is what is the point mentioned here, polyimide spin coating followed by curing. So now, what is the next step, now here if you see photo resist coating followed by lithography. So, let

me go back to this part. So, what happens is for example, when you use any deposition technique. So, if I take this wafer. So, the gold or any material that you want to deposit, will be deposited everywhere.

So, this is how the entire gold will be deposited everywhere, all over it will be deposited. But I do not want it all over the device, I want only this kind of structure only this electrode here and there is an interconnect line here and there is a contact pad here. Only this part I need, I do not want all over this, like this whatever I have shown here in the wafer.

So, what we do is generally in terms of side view, let us discuss this in the side view. In the side view what happens is from this angle if you look you have a polyimide. This is polyimide right on top of that. So, let me change the color on top of that, you have two contact pads, this I cannot show everything, I can also show like this, but let us just restrict our discussion to only this one, I do not want to make these things complicated.

If you look at this from this side, let us assume that you know you are not seeing these electrodes, just see this contact pads only. So, that is very easy to understand. So, this is a metal, or this is whatever I was referring to titanium or whatever the material that is. So, initially what will happen after deposition once you use deposition technique, so you will have a polyimide and along with that everything will be deposited.

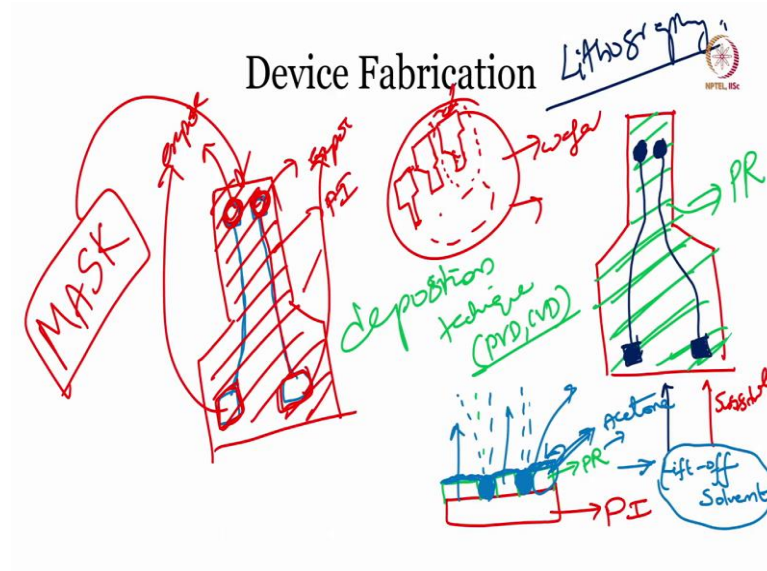
So, what people can do is, if you deposit everything then you have to etch unnecessary metal, you have to etch it. So, first you deposit photo resist or spin coat the photo resist then you need to do baking there are a whole list of steps involved in that. So, how to etch anything is first you should do something called lithography, first you do lithography, create a pattern then you can etch it.

So, I am just simplifying the things. Understand that these are not the ultimate steps, I am just simplifying, so, that we just need to see how these are fabricated just as an example. So, what you do is this is a photo resist right. So, photo resist has been spin coated and you perform something called lithography.

So, assume that you know the steps of how to create lithography. So, lithography is nothing but process of transferring the pattern, that is it. So, you want to create this

pattern. So, you do not want the entire gold to be deposited everywhere. So, what you do is initially you coat this with a photo resist all over.

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So, this is the structure, this is the substrate that I am looking at, on the substrate now what you do, you spin coat the photo resist, now use spin coat everywhere. Now this green color thing is a photo resist and there is a process like prebaking and all that should be done.

For example, if you have not understood, that will be covered. So, there is a photo resist that is deposited now you want to etch the photo resist from some areas. So, in some areas wherever you do not need photo resist means you want the gold to be there.

So, this is the area. So, wherever I am showing understand that photo resist has been removed, there is a photo resist developer, what you do is you need to remove. Just like that you cannot remove it, there is a process, you should do something called lithography, this is what I am referring to.

Now, photo resist is removed at this areas wherever the black is there, you know wherever the black regions are there in that area photo resist is somehow removed. Now you look at from this angle, what will be there? Now if I write the side view, the bottom layer is polyimide, then I have some photo resist because I did lithography on this photo resist. So, there are a lot of steps that are involved in this.

Now, I wanted this black pattern that is exposed. Now you can do any deposition techniques. So, you can go for PVD technique or CVD technique, whatever the process allowed and then deposit. Now what will happen? Now let me take another color. Now you want to deposit the gold. So, when you deposit, this gold will come and sit here. So, in this place gold will come and sit and gold will be coated everywhere, here also.

So, then what you do after this you do not want the gold to be all over right, now this you keep it in a lift off for this process is also called lift off, solvent. So, then this part will be removed because when you put this in acetone or photo resist stripper or techno stripper whatever it is, this photo resist will be etched over this, photo resist already gold is there, automatically this also will be etched, this also will be etched, this also will be etched what is left is this pattern remains same. So, let me draw it neatly here. So, what is left is I have this device.

So, if the photo you after dipping it in the lift off solvent means for example, acetone if you keep it, then what will happen? Everywhere this photo resist will be removed, what is left over? This pattern will be left and everything else is removed, this is how you achieve it. This is also called as a lift off. There are many methods of creating this kind of patterns but understand this, we are talking about lift off technique.

So, what you do here is this is the c step. So, first you deposit the photo resist then create a pattern and because for that mask many things are required, I am not going in detail about it, I am just trying to explain the brief overview of how the process takes place. Then we go for something called as you deposit the metal and then do lift off. So, once you do lift off you will achieve this. This is what we have discussed in the last slide, once you do lift off, you will achieve whatever you wanted.

So, now one more thing is what I said now you just did lift off, but this metal is exposed. This entire thing is exposed, interconnects are exposed, what we should do is we have to insulate them. So, how to insulate them because we already know that photo resist is a insulator. So, what we do is again spin coat, similar step whatever you have done here, spin coat with respect to this.

Now, with that what happened is again all over photo resist, I mean polyimide has been deposited all over coated. So, what you should do, you need to expose these areas this

particular area has to be exposed. So, that we can do by using something called as reactive ion etching, RIE.

So, we have something called as wet etching techniques where we use chemicals and all other things in liquid form and we have something called dry etching techniques, where we use chemicals in gaseous form. Now I have created, I have exposed by using RIE this area and this area I have exposed during RIE.

Now, what is the other step here, there is something called as you see this RIE for device separation, see whenever I fabricate the devices I will not go for only one device you know because I have an entire wafer, on this wafer I have n number of devices like this, n number.

So, many like that will be there depending on what is the size. So, I will have a mask using which I can do lithography. So, there is something called mask using which we can transfer the pattern and do lithography.

In lithography one of the most critical things is a mask. Design of a mask that has to be designed properly. So, using that mask we can create the device separation and finally what is the device that you need is a polyimide. Now if you see you have a silicon here, now you have a polyimide here, now here again you have a polyimide, and these could be contact pads.

Now, if you look at this guy, this is covered within the insulation. What do you think is that interconnect? I am just showing the side view, you know that could be interconnect, this could be again a contact pad. So, then there is something called as peeling off devices from the silicon substrate.

So, we can peel off or we can cut it nicely by using a surgical blade kind of thing, it depends on whatever it is. So, to iterate again, we have silicon wafer here and silicon wafer we spin coat, we are drop casting polyamic acid and we are doing spin coating and curing, then we are going for lithography to create the patterns and now the patterns are created.

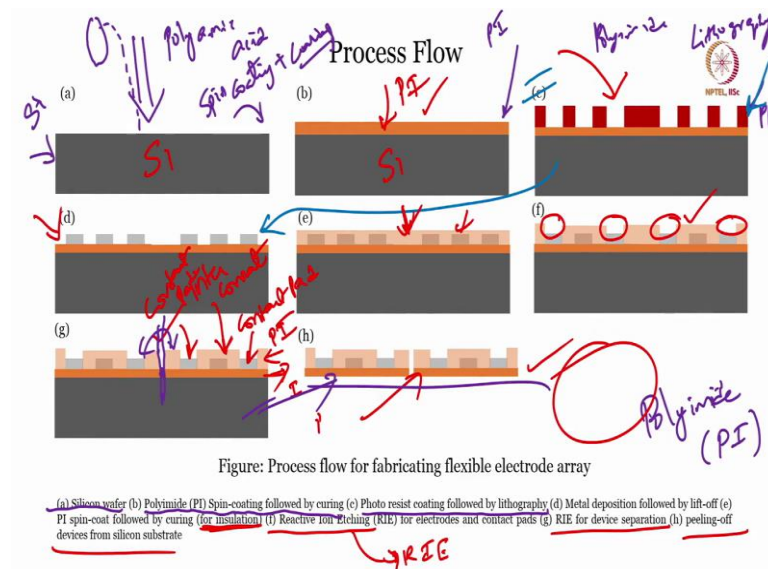
But I do not want to expose the entire electrodes or entire electrical contact like this. What I mean to say is this entire thing like from here to here, I want to expose only the

electrode area and the contact pad area. So, what I do again, I use an insulation layer. So, this is what is mentioned here, this is for insulation. Then once you are insulating, you are insulating everything, you are insulating electrodes also, you are insulating contact pads also.

So, I do some kind of etching, in this case RIE etching, to remove this particular polyimide in this area, so that these could be connected to the electronic circuitry later on. So, this is what is explained again here, and this is for device separation, because I told you that you cannot fabricate a single device, we can go for a few 10 to 100 of devices at a stretch in a single silicon wafer.

That is why a device separation step is required and then you can peel off that particular device. We can separate the devices or we can peel off the devices from the polyimide substrate. So, but here if you look at it there is a small mistake which I am pointing out. So, make a note. So, here if you look at this, when you peel off, what we generally do is we can take a fine surgical knife and then we can cut this.

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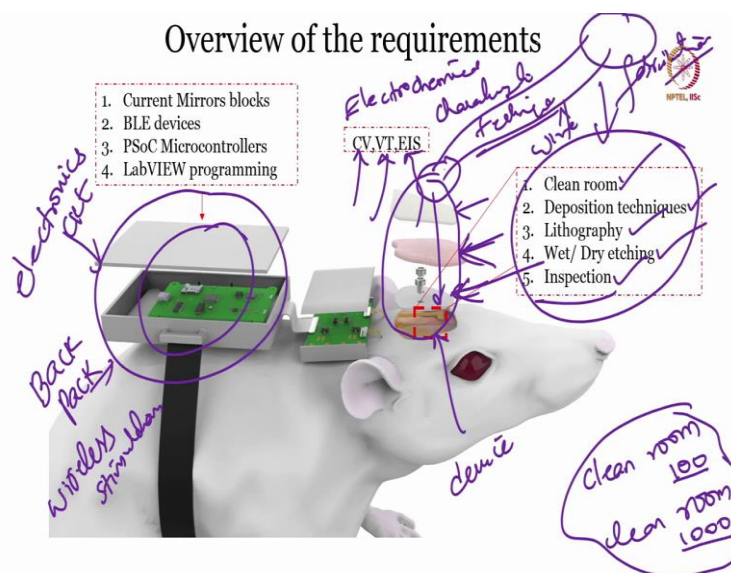
So, that we can cut the entire thing, so here it looks like there is a connection but there is no connection as such. So, what I mean by this is there is no connection as such. So, you are peeling of the entire thing, I mean that is you are separating between the devices. So, there is no polyimide here, its empty.

So, it is like that. So, then you peel off the devices, means taking out or taking off from the silicon wafer. So, that is how this process flow is. So, I have just discussed about different steps that are involved in the process and we have not gone in detail. So, that will be discussed later on.

But the point is I wanted to tell you that these are the different steps that are involved. So, lithography is a whole complete step and spin coating, there are different steps that are involved. In that RPM is there, I mean how fast with what speed you are rotating the spin coater and all those things. So, many things matter. Mask is there in lithography, so many things are there.

So, I just bypassed all those things and then briefly touched upon what exactly it looks like. So, I want just to give a feel of how a device can be fabricated so that you can keep in mind. And next step is once this device is ready then we have to go for electrical connection. So now, I will just give you what is the overall requirement if at all you want to work as a Neural Science Engineer or you want to work in this kind of biomedical related work. So, what are the requirements that you need?

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This is the device that we are talking about, whatever is the zoomed in area, that is a device and for fabricating that device you should have first of all, there is something called clean room. And this is the place where the categories depends on let us say for example, I say clean room 100, clean room 1000.

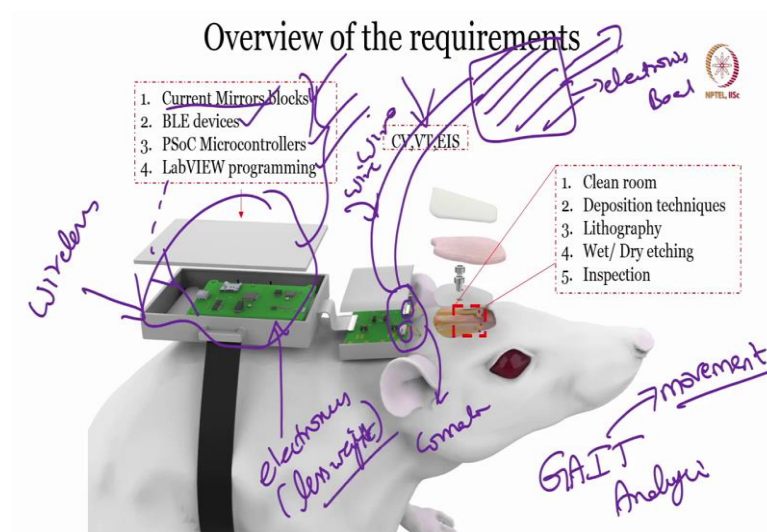
So, what does it mean is, it shows the purity of that room with respect to some dust particles or particles of some size which are less than 0.5 micron or greater than 0.5 micron. There is actual lot of things about clean room and there are different deposition techniques we discussed about, I mean not discussed like we just briefly touched upon PVD, CVD and all those things. Then we talked about lithography is required, etching is required, inspection using a microscope, you inspect those sizes and all those things.

So, with this if you have knowledge about all these things then we can fabricate. Then after the fabrication we have to characterize it. So, this is a cyclic voltammetry, voltage transience, electrochemical impedance, spectroscopy, we have discussed briefly about that also. These are electro chemical characterization techniques, we have discussed already. Why is this so important to do?

So, next is if this is done, these are the real electronics circuit. Now if you look at this diagram or representative picture, you have these electronics connected to a backpack and we do wirelessly. This enables wireless stimulation.

Generally, what happens is we can have a connector here, now this is just to represent the surgery of what it takes. Which is like a skin then this dental cement and this is a skull bone. Now, there is a connector to this and then it will go through a wire, then it will go to the electronics board. So, what I mean to say is now you have electrode here and there is a connector here, the contact pads are here.

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Now, you put a connector to this, using this connector, there is a wire here. This will go to the electronics board and this board is controlled, you know you are using a computer, and this is a wire. So, what happens with the wire is we are going to do something called as gait analysis, gait is related to something called as movements. Like how fast it is moving and how slow it is moving and all those things.

When there is a wire then the problem here is it cannot move properly, because when somebody ties some rope or something like that, you cannot move freely, that is how it is. So, the idea is people are going for a wireless stimulation where there is some kind of communication happening wirelessly.

And of course, it is very complex circuitry, a lot of research is going on in this area as well. While designing these different blocks. So, in some of the works that we found out we can use the current mirror blocks. Why current mirror blocks and all we will discuss and we have BLE devices and we have PSOC microcontrollers and we have lab view programming.

We need to use all these things to set up this particular guy, then electronics board and this electronics board will be very less in weight such that the rat can easily carry that while doing a behavioral analysis. So, we will briefly look into the current mirrors in the next lecture.

Thank you.