

Neural Science for Engineers
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Lecture - 32
Introduction to Brain Stimulation

So, welcome to the course on Neural Science for Engineers. I am Sreenivas Bhaskara one of the TAs of this course. And we have been looking at the Brain Stimulation. And we have seen, what is brain stimulation? Why brain stimulation? How brain stimulation can be done? What are the different criteria for choosing a material? Then we have always also seen some overview of how a fabrication process flow looks like.

So, now we are looking at electronic systems that are required for stimulation. And we have also seen why wired systems are not preferred over wireless systems. And now we have discussed because we are talking about you know movement related stuff if you put a wire on top of the head then the rat may not walk with the natural movements.


So, there is always a pull from the wire. So, that is the reason to go for a wireless, but the problem with the wireless is the rat has to carry all those things. So, you have to make sure that the weight of this particular electronics module should be as tiny or as small as possible so that the rat cannot feel that there is an overweight on the head, so that is how it is.

And with the wired channels there are wired. So, wired means there is a connector that is coming from here and then the wire will go to the electronics box, I mean to the computer wherever the supply is coming from. You have no problem with the bandwidth or electricity and all those things, that is advantage, but the disadvantage is natural movement will be affected.

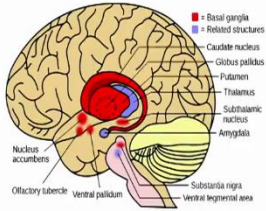
With the wireless natural movement is achieved but the problem is the battery and all that you have to use that should be carefully chosen, otherwise the electronic systems will take off all the battery that is required.

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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:

- Seth F Oliveira, The dark history of early deep brain stimulation, The Lancet Neurology, [https://doi.org/10.1016/S1473-4422\(18\)30237-0](https://doi.org/10.1016/S1473-4422(18)30237-0).

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

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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].


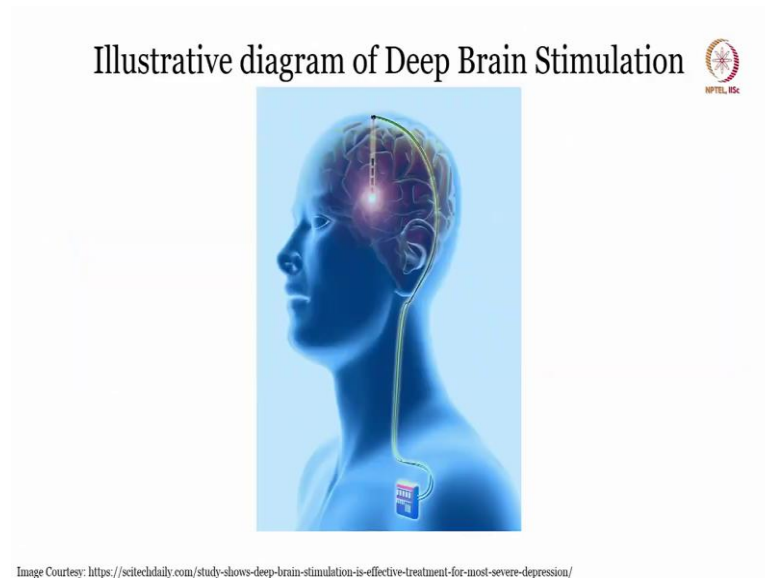


Image Courtesy: www.thegoldenconcepts.com/blogs/health/parkinson-s-disease-spotting-symptoms-preventative-measures

Reference

- K. Sen and R. Bonita, "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.

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Criteria for choosing electrode and substrate materials

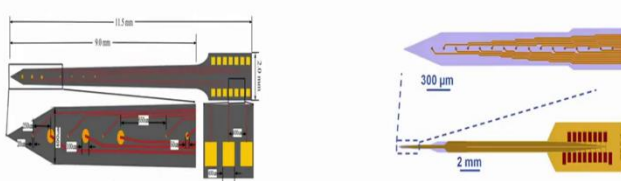
The diagram shows a cross-section of the brain with various structures highlighted in different colors. A legend on the right side of the diagram lists the following structures: Basal ganglia (red), Related structures (blue), Caudate nucleus (green), Globus pallidus (yellow), Putamen (orange), Thalamus (purple), Subthalamic nucleus (pink), and Amygdala (light blue). Labels on the left side of the diagram include: Nucleus accumbens, Olfactory tubercle, Ventral pallidum, Subthalamic nigra, and Ventral tegmental area.

- 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)

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Micro-engineered devices for rat models



The figure contains two schematic diagrams. The left diagram shows a rigid device with a long, thin, tapered shaft and a wider base. Dimensions are indicated: 11.5 mm for the total length, 10 mm for the tapered section, and 1 mm for the thickness of the base. The right diagram shows a flexible device with a similar tapered shaft but a more pronounced curve. Dimensions are indicated: 300 μm for the thickness of the shaft and 2 mm for the length of the base.

Figure: Schematic representation of rigid device with electrode array^[3] **Figure:** Schematic representation of flexible device with electrode array^[4]

References:

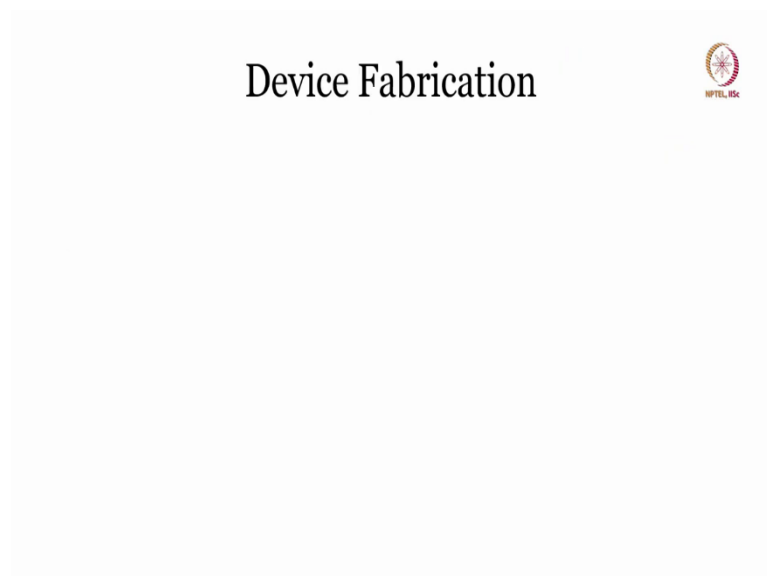
3. Z. Zhao, R. Gong, H. Huang, J. Wang, Design, Fabrication, Simulation and Characterization of a Novel Dual-Sided Microelectrode Array for Deep Brain Recording and Stimulation, *Sensors*, 16 (2016) 880. <https://doi.org/10.3390/s16060880>.

4. F. Ceyssens, M. Bovet Carmona, D. Kil, M. Deprez, E. Tooten, B. Nuttin, A. Takeoka, D. Bubschun, 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>.

So, look at the slides now. We have seen all these things in the previous lectures.

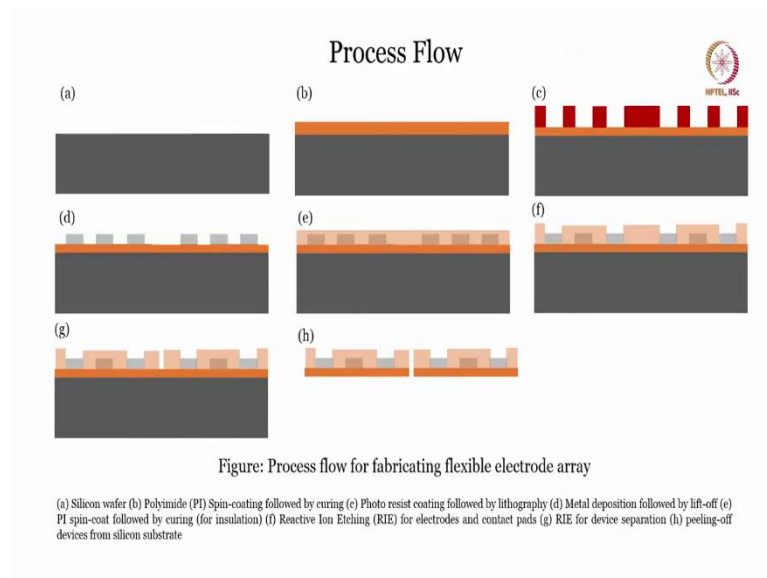
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Device Fabrication

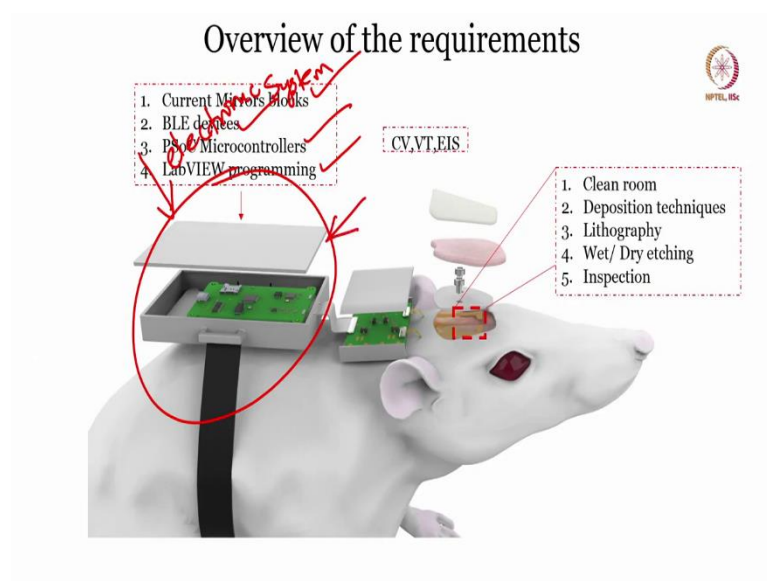


The slide is mostly blank, with the title 'Device Fabrication' centered at the top. In the top right corner, there is a small circular logo with the text 'NPTEL, IISc' below it.

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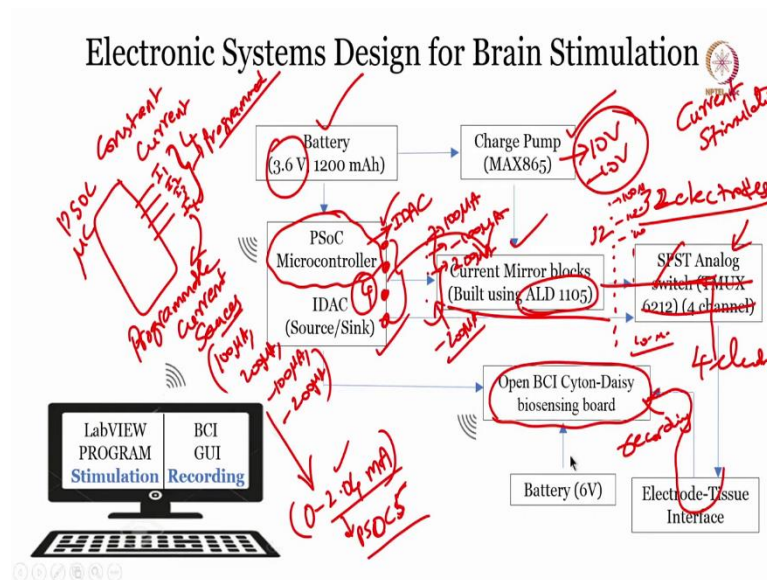


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Now, we are talking about this electronic systems part. And we have also seen these are the different requirements and we need current mirror blocks, BLE, these are I told you, but why we need it?

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So, now whatever this part is there in this. Now, look at this I just gave some random examples, you need to have a battery, yes of course, and that battery also should have low weight and it should have a stability, so many requirements are there.

And you need to have a charge pump because of the current requirements, you cannot just work with the 3.6 volts, you may need to work with 10 volts, -10 volts so that you can have a lot of supply of currents, wide range of currents that can be possible right.

And there is something called PSoC microcontroller, there is a reason for choosing this PSoC microcontroller. In this work finally, you need to supply current. I can also say current stimulation.

So, these microcontrollers have something called as IDAC blocks, current digital to analog converter blocks. They will supply constant current. This PSoC microcontroller have the blocks that can supply constant currents I1, I2, I3 and I4 and these can be programmed. So, I can say that they are programmable current sources.

So, if you want 100 microamperes, you want 200 microamperes, you have -100 microamperes, you have -200 microamperes, so there is a range. Generally, for this you can go up to 0 to 2.04 milliamperes because we are talking about PSoC 5 family series. PSoC 5 family can support up to 0 to 2.04 milli amperes ok.

Now, how many such things are there? These only 4 are there, 4 current sources. These 4 currents and you have let us say 32 electrodes for example, your requirement is 32 and you have only 4 and that is a maximum available. So, you cannot connect these 4 to the 32. So, what will you do? We do something called as current mirroring.

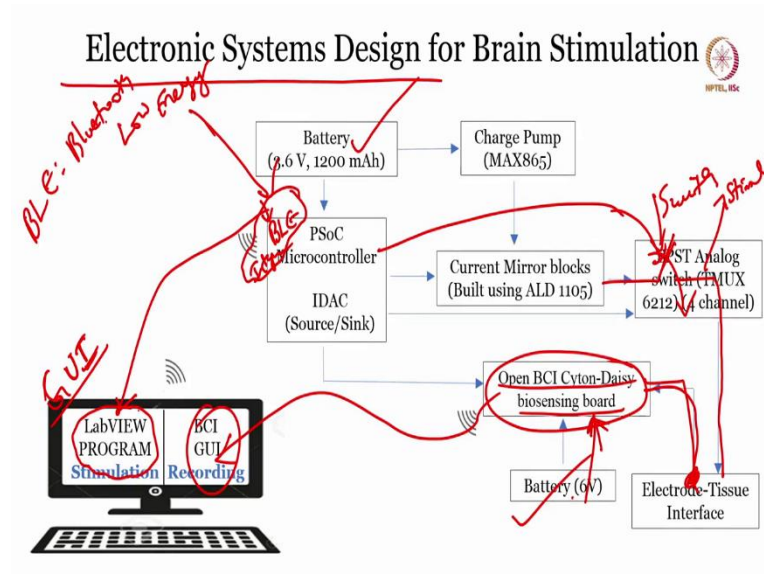
So, what current mirroring blocks will do is you have 4 this; 4 I can make it as 32 outputs like this and this is one of the IC's that we are using here. So, you are doing the same thing current mirroring same 100 micro amperes can be converted to 100, 100, 100, 100, 32 to 100s something like that.

So, that is the job of the current mirror block. So, it is not that only 100 you need, you may need -100 also at the same time and you may need some other different current 200 you may need, this is -200 you may need. So, these 4, the requirement why we chose only 4 is because we have to stimulate the surface target and we have to stimulate the deep brain target.

So, surface target needs different current, deep brain target is different current. So, that is the reason why we are going for current mirror blocks, because see if you have only 4 electrodes for example, you have only 4 electrodes then you these 4 you can connect to those 4 and then you can program and then do that kind of thing, but now it is not the case.

And this SPST analog switch, do not worry about these numbers and all those things. This switch is for making sure that whether you are going for a stimulation or a recording; when it is in stimulation this switch is connected to this guy and if it is not stimulation, the switch is off so that this electrode is always in this contact. So, that it will go to the sensing board. This is for recording. So, just let me iterate this point not to confuse you.

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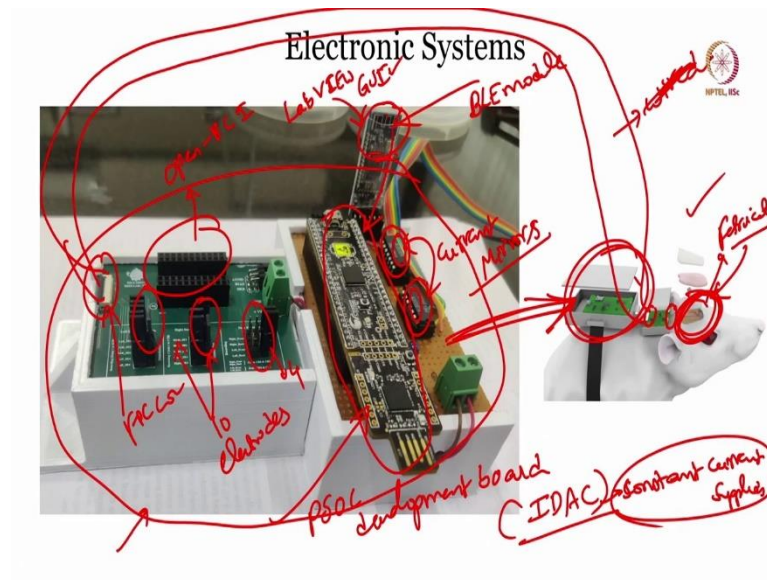


So, there is this switch, this is one of the requirements of our design. So, this is a switch here, you can program the switch from the microcontroller only if you close it, then you can go for stimulation if you open this then it is automatically into recording. So, what is this guy, open BCI Cyton-Daisy biosensing board, it will sense the potentials here and wirelessly transmits the signal to the GUI provided by the BCI.

So, for stimulation also we have a module here called BLE, integrated BLE module. So, the microcontroller that we are using does not have the inbuilt BLE, so BLE stands for Bluetooth Low Energy. So, this BLE, work on low Bluetooth Low Energy and this we are wirelessly connecting to the LabVIEW.

So, LabVIEW is a software where you can build your GUI. You can create your own GUI and you can start stimulating whatever the currents and different requirements that you have. This is just a rough understanding or just a brief understanding about the kind of things that are involved in designing electronic systems. Battery is required for powering up and again this battery is required for this open BCI Cyton-Daisy board and these are the things.

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I will just show you how does it look like. So, if you look at this is a BLE module, like a transceiver. And this is a PSoC development board where we are using IDAC, I told you already right constant current to digital to analog current.

I do not want to confuse you with the terminologies and all. Then this goes for an open BCI Cyton-Daisy board and this is a FPC connector. After the operation is done these connectors will come here, there is a big connector, from that connector the wire will come like this.

So, that is an FPC connector now you understand, now you can correlate the things. So, this guy is wirelessly controlled by using this guy and this guy we are supplying the inputs using LabVIEW GUI. So, based on the programming, the microcontroller decodes and everything these are ALD 1105 you can see this here, by using this we have built current mirrors.

So, this is a basic prototype. So, we have 10 electrodes support, there are 4 more additional electrodes that it can support. So, this is how overall it looks like. It took a lot of time to understand and study various things that are available and then come up with this and this we know already we have done, we have talked about fabrication.

In the fabrication you know after once you have enough idea about fabrication you can fabricate the devices, then the devices are connected. Now I talked about wired. If you

look at this system this is so big and heavy weight also. This thing has to be translated like this.

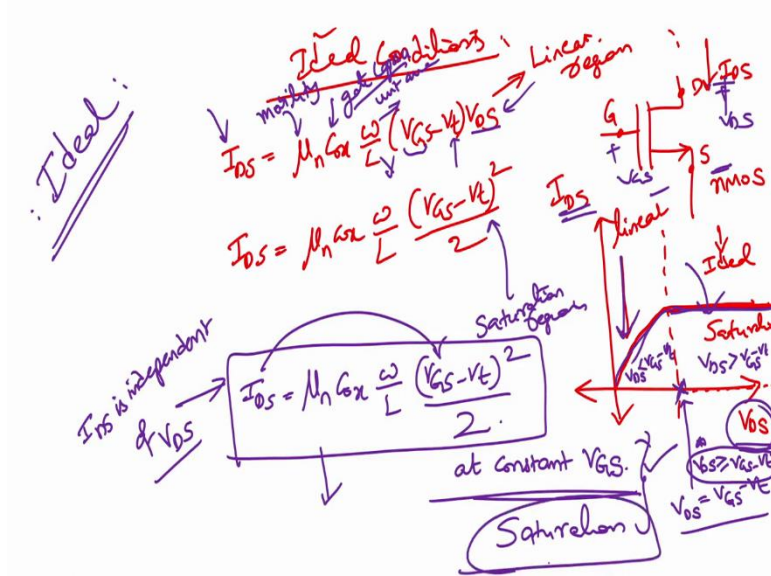
So, we have to do a research more on this kind of components that are available, many things are there to optimize such that I can go for this. So, this is also one of the research exposure area.

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So, now for our understanding or for our discussion we talk something called current mirrors. This is utmost important for electronics engineers. So, first what we do is we will see what a transistor is, I mean basics of a transistor how does it conducts and all those things or current to voltage relation from there we can see how we can achieve current mirroring and from there we can also see how the current multiple out, you know multiple current outputs are generated by taking care of one by using one current source. So, for understanding we will take a basic transistor.

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So, we all know there is something called NMOS, PMOS. So, this is a NMOS transistor, so you can say this is a drain gate source. So, here we will not derive all the current equations, voltage equations, how the transport happens and all those things. We will assume that you know the current relation, current to voltage relations, all those things and then we will try to use that relation and then see how the mirroring can be achieved.

So, I am not going to derive all those basic equations. So, let us look at the slide what happens. So, this is the general relation or you might have seen this plot there is a current that is flowing through this I_{DS} , I assume that there is external circuit and all is there. This is V_{DS} , if I plot the graph of I_D versus V_{DS} , generally it looks like this. This is in the ideal scenario, there are exceptions to this.

Now, initially till some point current seems that increasing linearly with respect to V_{DS} and it will saturate here, saturation, means even though whatever the V_{DS} value you are increasing your current will be remain constant.

So, under ideal conditions what happens is your I_{DS} if you write it is nothing but,

$$I_{DS} = \mu_n C_{ox} \frac{W}{L} (V_{GS} - V_t) V_{DS}$$

it is when it is in linear region. There are so many other exemptions, I just mentioned as ideal conditions.

So, the other one is

$$I_{DS} = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS} - V_t)^2}{2}$$

let's understand these terms and what they represent. So, this is the current flowing from drain to source, this is a mobility. Now, NMOS the majority of the carriers are like electrons.

So, mobility of an electron in that particular transistor from drain to source. This is gate capacitance per unit area and you have width of this transistor and you have a length of the transistor and V_{GS} is voltage applied between the gate and source and t is nothing but the threshold voltage and V_{DS} is the voltage that is applied between drain and source.

Now, this is in linear region, this is in saturation region. Do not get confused here your

$$I_{DS} = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS} - V_t)^2}{2}$$

Now, this is V_{DS} not V_{GS} , you look at this I_{DS} versus V_{DS} means at constant V_{GS} , I_{DS} is independent, you know independent of V_{DS} .

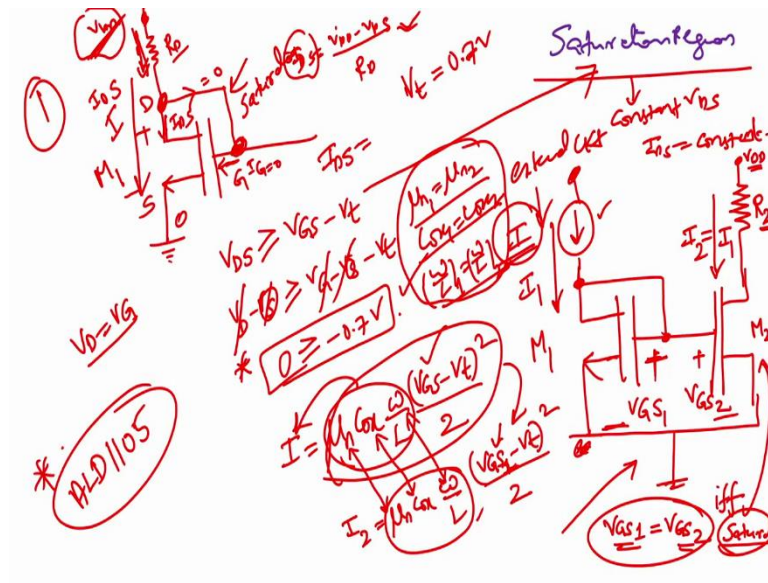
If you maintain your V_{GS} constant, your I_{DS} depends only upon this V_{GS} and V_{GS} is constant more or less I_{DS} independent. If you look at this curve, this is always constant, but that is not the truth, but I am just discussing about the case so that you understand the current mirrors. So,

$$I_{DS} = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS} - V_t)^2}{2}$$

Now, the same concept I can use it for the current mirror.

So, the only requirement is you have to maintain constant V_{GS} and that should be in saturation, these are the two requirements. As long as you maintain this your I_{DS} , again I remind you we are having an ideal discussion. There are variations, saturation effects and all will be there, but we are just excusing them right now. We are not discussing much about that.

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So, now, first you have to keep the transistor in saturation region. So, if you look at this guy. So, there is a point here, this point is nothing, but where your $V_{DS} = V_{GS} - V_t$, this is $V_{DS} > V_{GS} - V_t$ and this is $V_{DS} < V_{GS} - V_t$.

So, whenever $V_{DS} \geq V_{GS} - V_t$, if you can maintain this much of voltage across the drain and the source, you are pushing the transistor in the saturation region otherwise it is in the linear region. Our requirement is it should be in the saturation nature.

So, the basic requirement is it should be in the saturation region. So, if you maintain constant V_{DS} your I_{DS} is going to be constant. First, we will generate this constant current then we will just discuss about saturation, then we will go for current mirroring, how it happens? So, you let me take the transistor here, so let me call this as M_1 .

I put a resistor here, V_{DD} some R_D this is a drain, this is the source, this is the gate and whatever is the current flowing through is going to be I_{DS} . So, the current entering this terminal through the gate, nothing can enter. So, this I_G is 0 means this current is 0, so whatever is the current flowing here that should be the same current.

So, I can write like this $I_{DS} = \frac{V_{DD} - V_{DS}}{R_D}$, because this is a voltage developed here divided by R_D . So, one can use this condition just to find out I_{DS} , there is one more condition for I_{DS} . What we do for this kind of cases, you see this is very simple thing. Now, let us check

whether it is in saturation or not condition is what $V_{DS} \geq V_{GS} - V_t$, if this condition is satisfied this is in saturation.

So, what is V_{DS} , the voltage difference between drain and source means $V_D - V_S \geq V_G - V_S - V_t$. So, V_t for example, I will take 0.7 ohms right. So, here if you see drain and gate are connected. So, means $V_D = V_G$. So, V_D , V_D gets canceled V_S is at 0 so 0 here 0 here they are canceled. Now, 0 is on the left-hand side ≥ -0.7 ohms, this holds good.

So, means this transistor you are always pushing it into saturation. By default, if you connect the circuit like this. So, you are pushing it by default into saturation. Now, here you are just supplying the voltage V_{DD} and R_D . What other way is you are using a voltage source constant, voltage source I can use a constant current source also. This could be any way, anything else. Some external circuit, some current I.

For this current source this is in series, this transistor M_1 is in series. So, same current has to flow in the series; obviously, enough V_{GS} will be developed such that this current

$$I = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS} - V_t)^2}{2}.$$

So, the V_{GS} will be developed such that this entire thing is balanced to I.

So, here what you are doing in the case 1, you are applying some constant voltage based on that you are generating a current I. Here you are pumping the current such that it will generate a constant voltage here. So, now, this is very nice, and this is the fundamental thing for our results.

Now, how to do current mirroring? I have to generate one more source like this. What do I do is, I will put one more transistor let us say this is M_2 , I will connect the sources, I will short the sources, so this is V_{GS1} , this is V_{GS2} . Now, from looking at this $V_{GS1} = V_{GS2}$ and you take the resistor and you give a voltage supply V_{DD} or whatever it is and this is a load of transistor 2.

If proper choice of V_{DD} and R_2 is chosen such that if M_2 is also in saturation, if there is a condition if and only if this M_2 is also in saturation. What is I_2 ?

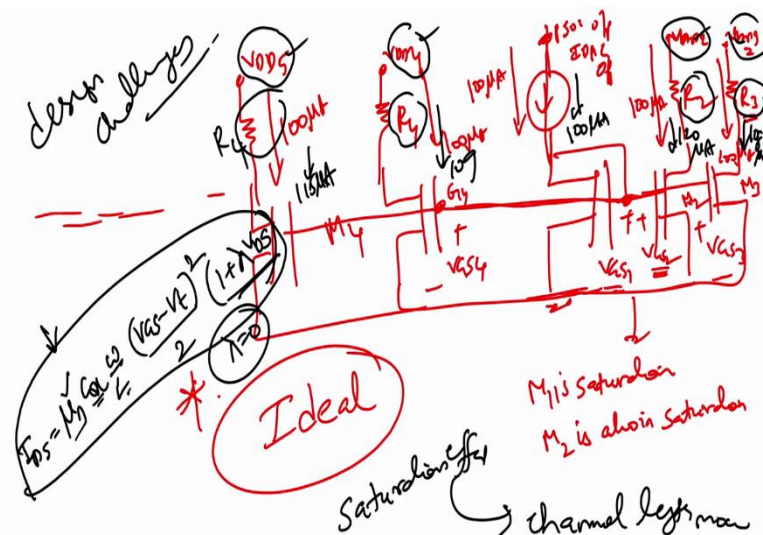
$$I = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS2} - V_t)^2}{2}$$

and we already know that $V_{GS2} = V_{GS1}$, means whatever is the current that is flowing here I_1 and the same current will flow here also your I_2 that $I_2 = I_1$.

So, if you can have right choice of I_1 and I_2 . So, you can have, I mean if you have a right choice. What are the things that are matched here is, I have just broadly categorized this and then I just over simplified this. I wrote μ_n as same C_{ox} as same $\frac{W}{L}$ as same, if you maintain all these things $\mu_n, \mu_{n1} = \mu_{n2}, C_{ox1} = C_{ox2}, \left(\frac{W}{L}\right)_1 = \left(\frac{W}{L}\right)_2$, then only you can achieve this and also you have to maintain the saturation.

If you maintain all these things, this is also called transistor matching $\mu_{n1} = \mu_{n2}, C_{ox1} = C_{ox2}$, why do we think that we just chose 1105 that is because of that reason.

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So, you have taken this transistor connected like this by pumping the current right you have generate you have generated the V_{GS1} that V_{GS1} you reflected on the another transistor ok that is nothing but V_{GS2} source are shorted and you have chosen R and D; R and V_{DD} in such a way that it is in also in saturation M_1 is by default saturation M_2 is also in saturation.

Then you can take one more transistor, do the same thing this is V_{GS3} this is R_3 this is V_{DD3} chose your R_3 and V_{DD3} such that this transistor M_3 is also in saturation. Now, what else also I can do? Again, one more transistor I can take I can give the supply like this is M_4 now this is V_{GS4} . And again, I am shorting this because whatever the potential that is

available at the gate I am giving to this gate also ok get G4 right and again I will choose R_4 and V_{DD4} .

Similarly, I can have one more transistor V_{DD5} correct, this is V_{DD2} V_{DD3} this is coming from PSoC output that is it one of the IDAC outputs. So, one of the IDAC output terminal supplies the current that current will flow through this transistor creates V_{GS1} that V_{GS1} is replicated to V_G another transistor then same current will flow.

If you are pumping 100 microamperes you will get 100 micro amperes, you will get 100 micro amperes, you will get 100 micro amperes, you will get 100 micro amperes here you have get like that you can have whatever you want, but all this happens ideally. Exceptions are like this what are the exceptions first problem is maintaining these many stable voltage sources and to exactly see how much resistance and all.

And we are talking about the brain we do not know exactly what kind of resistors will be there, that is also one of the criteria. These are all design challenges, there are so many design challenges I am talking about right. And there is something called saturation effect nothing but a channel length modulation. What do you mean by channel length modulation? I wrote

$$I_{DS} = \mu_n C_{ox} \frac{W}{L} \frac{(V_{GS} - V_t)^2}{2}$$

but this is not the case, the real equation is $(1 + \lambda V_{DS})$.

This I have neglected; I have considered $\lambda = 0$ and I explained everything. Now, when this comes into play now what happens is you are pumping 100, here it could be 120, here it could be 108, here it could be 109, here it could be 115 because μ_n 's are not exactly even though you take a match transistor μ_n 's cannot be exactly same C_{ox} may not be exactly same $\frac{W}{L}$ some variation will be there and V_{DD} variations are there.

These are all several design challenges that we have, but to understand let me conclude. This is how a basic current mirror designs can be done, there are lot of challenges that are involved. So, this is the brain stimulation, it is not that easy. This is one of the concepts of generating different from few current sources, you are generating many current sources.

But I told you about lot of challenges that are involved in that, so many techniques that people use h bridge, z bridge, so many things are there. So, this is one of the challenge and we have seen so many challenges that in the current mirrors. So, this is from pure electronics point of view.

So, if at all I have to conclude this, for brain stimulation first of all you are starting with the fabrication, choosing the materials, materials have lot of challenges and we have to satisfy all the criteria. Then we have gone for characterization techniques, then we have to come for electronics, then wireless communication, then this electronic signaling part, signal processing part.

So, many things are there, so that is why this is a trend in biomedical electronics field that you have huge challenges to solve. So, this is about the brain stimulation and different perspectives in terms of engineering we looked at, how brain stimulation can be done, what are the challenges that one can solve in this process and next things will be covered by our colleagues in the next lecture.

Thank you.