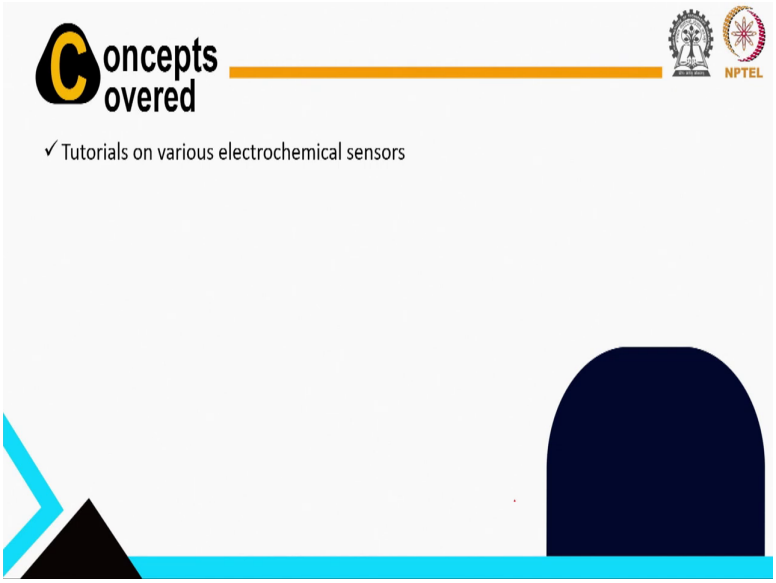
Nanobio Technology Enabled Point-of-Care Devices
Prof. Gorachand Dutta
School of Medical Science and Technology
Indian Institute of Technology, Kharagpur

Lecture - 36
Tutorial - 03

Ok, dear students, let us show you in this Tutorial some new and advanced some problem based on this problem you can correlate the whole story that I taught during my whole courses.

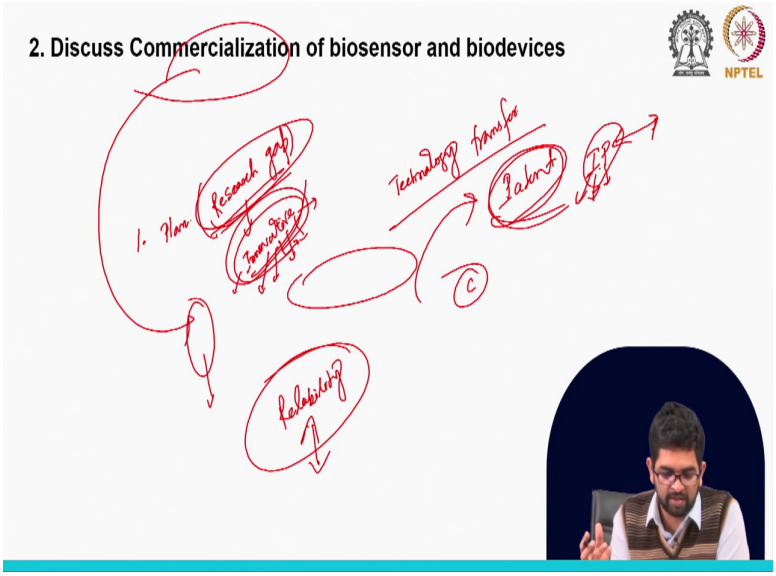
(Refer Slide Time: 00:49)



So, today's tutorial mainly for the various electrochemical sensors that can help you, can guide you to understands the all the problems you can face during the development of

biosensors. This is mainly see this course is very much related to your practical applications, your independent thinking, that is why I plan in this tutorial.

(Refer Slide Time: 01:07)



Let us discuss some commercialization's of the biosensors and the bio devices. How we can commercialize of a biosensors and bio devices and kind of problem you may face during the commercializations process, clear. See I just taught the development of biosensors during the whole class.

Suppose you got some idea and you wrote your project and then you have to start your work and based on your result and your development if you want to start your own startup, right. If you want to commercialize that technology, you have to bring the technology near patient immediately, you have to bring the technology in the market.

So, how you can commercialize? So, I am just going to tell you very briefly some points that you should keep in mind before the commercialization of your biosensors or any bio devices. This is not only applicable for this is very general thing and this is equally applicable for any technology transfer.

So, mainly it is technology transfer. So, you have one device, right. So, please try to remember the points. So, 1st point you have to plan, like which area you want to develop a new device. But this plan should be very much innovative that I already taught you during the writing of the proposal.

So, there should be should have a research gap, right. Based on this research gap your plan should be innovative. So, when you are going to commercialize. So, your innovative idea should not be leaked means it is better do not discuss your whole innovation plan publicly. Even generally it is recommended do not bring your new concept in the confines of somewhere before coming to the market. So, it is everything your own copyright kind of things.

So, with whom then you can discuss? Do not you should not discuss the all the plan. Rather with your collaborators or with some others like suppose you are developing a device. So, you should discuss with your collaborator or with some like a medical doctors and other engineering you have discuss the possibility.

The possibility means how we can solve the you know your innovations, your research gap how we can solve, that you can discuss with them. Then try to summarize the whole idea in how we can solve, those problem you should not openly discuss, ok. Before the then only you can make the patent, if you want to make the patent.

So, your ideas should not be openly discuss to other is someone else should not be I mean someone else should involved for this work. If it is your own copyright means try to keep inside your group by in your research and try to complete this work and file the patent.

So, in every issue they have the IP section I means your in that property that is your intelligent property that they can protect or if you do not have maybe you have to approach the proper sections. And you have to file your work and ask them to copyright you have to copyright your innovations.

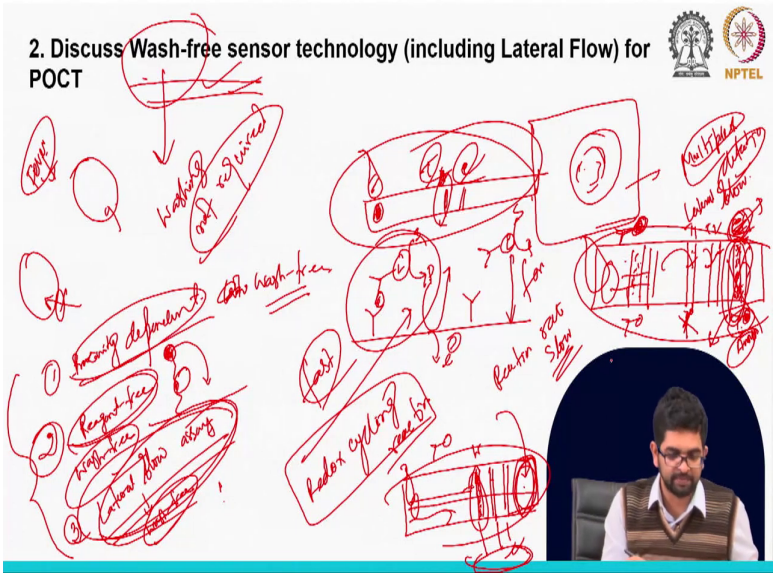
Then what we will do? Then after the patent filing and once it is done, then you have to think about how you can bring these innovations, then you have to contact to the industry or someone that they can help you. And that is definitely there should be some sharing of your like your profit.

So, the industry people they can help you like some fabrications of your sensors they may check like the reproducibility of the sensor because it is really reproducible or not then only they will bring this innovation in the market. So, your innovation should not be only inside the laboratory based, right.

So, as you are going to use this one for commercial agent purpose. So, it should be very much reproducible. Means it is that little to the reliability of your sensor reliability without this reliability you cannot commercialize. Because your sensor may be stored for the very long time outside the environment and if it not so the reproducible data then you cannot bring this device specially this kind of device for the solutions of this current problem. So, you need to think about the reproducibility always, ok.

So, this is the things that I am going to tell you when you are thinking for the commercialization of the device of your sensor. First, just try to think about the innovation technique should not openly discuss and make it like your own copyright your patent and then approach how, you to the industry and then try to make your product and bring to the market.

(Refer Slide Time: 07:12)



Second thing Second topic today today's tutorial I want to discuss that is the wash free technique, how we can bring for the point of care that I already taught you, but finally, as we are end of this course. So, let us think how we can bring this all the innovations or whatever you learn to the market, right.

So, wash free is the best method, because you do not need many step washing basically washing not required, right. If you do not need the washing then it will be useful for handling by end user. Because end user what they will do, they will just drop their sample like the glucometer available in the market, right.

Just they will you have the chip here there is a you can drop the sample here you can drop your on blast on drop of the blood, then this one you can inject with the potentio stat, right.

There is electronic part and you will see the electronic your digital value on scale something like this.

So, this kind of innovations is very very important for commercializations, ok. So, in this case in this kind of cases it is you can see this is their wash free. Why we need washing you know already to wash out all the interference spaces? To wash out that is you do not need or they can increase the background current you have to remove them for that you only wash it. But if you can develop some washing free technology that I taught many washing free technology right, can you remember one is the proximity dependent wash free, right.

What is this proximity dependent wash free? Just I just summarizing you again like, if you have your surface a target and if you do not have a surface a target, if you have surface a target then your secondary antibody will be bind and it will be it will have a label, right.

And this label a substrate can react it can form product and this product can react very close to the surface, it will transfer the electron or when you can incorporate in this surface a redox cycling reaction right, you can incorporate redox cycling reaction. So, if this redox cycling reaction is very close to the surface then your electron transfer rate will be much faster.

Because of the very closer to the surface that is called the proximity dependent wash free means you are just dropping your all the reagent on the sensor surface and because of the close proximity you will get the faster electron transfer. So, this is the very fast process. So, you will get the higher current. And if you do not have target then your label everything your all the reagent everything will be very far from the surface.

So, because of the far so, your reaction rate your reaction rate will be slow, right. So, this is the wash free concept you can apply for a device development. And this I taught already right, and 2nd wash free technique you can I think you should remember that is the reagent free the reagent free and they can change the conformation. So, in a in this case wash free proximity case they are not changing the conformation, but suppose you have a DNA or aptamer it will have some tag electroactive tag, right.

So, if it wind with some target then it will change its conformations and it will come to the close to the surface right, that I taught you. So, this is also kind of wash free concept you do not need washing and also, we do not need many reagents also, that is why the reagent free or at the same time wash free.

This kind of concept you can apply for the commercialization's of your technology. Try to focus more in this kind of technology. If you want to bring something, it should be very simple that is the main concept. Why and that is the explanation like you can compare with the glucometer, just drop wait for few second and see the data people want something like this device.

But if this is included was washing steps then only expert persons or in the dielectric centre, they can do Layman no not possible, ok. So, that is why if you really want commercialization think about this kind of washing free technology. So, I taught you like proximity dependent reagent free and number 3 is the lateral flow, number 3 is the lateral flow is it. I think you can just try to remember. Lateral flow case also it is kind of wash free some pregnancy test kit kind of things already available in the market.

So, they are the kind of lateral flow or wash free technology they are also same thing just drop the urine sample and you will see the color one is the control and another is the so first line the test and second line is the control. So, test and control you can see just color change or I already taught in my course that is the electrochemical change. So, here in the right if you have like a paper strip here you are dropping the sample.

We so, here you can working counter reference you can fabricate, ok. And accordingly means if it is your like working electrode and here all of your reagent will be immobilized and I mean if you have that target and secondary antibody they will bind here and you can add these things with the potentio stat and you can measure the very small number of change.

And I target you can get you may get the signal right here. So, this lateral flow basically see this is because of the capillary flow of this paper it has this property if you drop it flow

through this and here we are (Refer Time: 13:59) region when here all the excess things will be I mean stored.

So, you get your target I mean your whatever you want, like in the working electrode case you want your wanted to see maybe color change or maybe signal electrochemical signal change whatever. In pregnancy test kit kind of thing, you may see the color change.

And if you want the electrochemical signal change then you have to design like working counter different electro fabrication you will do that, I already taught you. So, that you can predict right, just I am guiding you today like how you can predict, how you can think some new innovation for the commercialization.

So, this kind of technology is very much important if you want to think about the commercializations, ok. So, lateral flow case I just want to discuss little more why? Because it is very much useful nowadays if it is in the COVID time also so, people develop so many lateral flow based like rapid test kit.

So, this kind of test kits really important. Suppose like a paper strip here you can make like see some like multiplex detections. So, I will recommend let us go the multiplex detection instead of go in instead of a single detections. Why? Because based on the multiplex multiply and (Refer Time: 15:34) detections you can easily predict, when doctor can easily prescribe some medicines.

Otherwise based on only single detection it I mean it can be sometimes misguide. Suppose like a fever case I told you know fever. So, it is due to what? It can be virus; it can be bacteria, right. That is I told, if you can develop some multiplex chip one is the virus case one is the bacteria. So, if it is virus related then doctor will not prescribe the antibiotic. So, if it is bacteria then doctor say ok, it is not related to the virus. So, you can go for some antibiotic, something like this.

So, development of multiplex system and wash free technology is really important for the commercialization hm. So, this kind of scope you can think. And definitely just try to think

that very simple step, simple technology not many steps. If you have any solution, think about the simple let us, drop and the sense kind of thing. This is the one of summary for this course. And yes, now let us come back this lateral flow again. So, you can design like test 1, test 2 and some control.

So, why we need control? I already told you that if I mean your strip is working fine or not, suppose see here this is the sample pad here. So, you add some sample and here you will have all the basic reagent that we need for the detections. Then it will your all the region will dissolve and if target one comes, then you will get that target will bind with this. Suppose you have the antibody this target will bind and secondary antibody or if you have here that also will bind.

And it will show the color here. But if you do not have this target then it will not bind it will not show color. But if you do not have target still your secondary antibody they should come in a controlled region and they should bind. And this level mainly we are adding the gold nano particles. It is a pink color and it will means come together it will show some pink or reddish color you will see.

So, if they are really ok, means they are not denature they are somehow not damaged then definitely it will come and bind here and it will show the color. See suppose if you do not have control line.

So, your secondary antibody that conjugated with the gold it is not binding T 1 it is not binding with T 2. And you may think that you do not have the target means you are I mean its negative result. But if somehow your secondary antibody is damaged denature not working properly all you have target, but it is denatured. So, it will not bind with the T 1 or T 2.

But if you have control line it will guide you that if you denature then control line also will not show the color. So, it means your strip is not working. So, based on this you can I mean confidently tell that yes, you are getting false positive or false negative that you can tell some means if you are getting when generally you are saying the negative result I mean no, or it can

be a false negative. That false negative data you can definitely say based on the control the c control data right that is how we need this control line, ok.

So, just try to think to design this kind of lateral flow sa also wash free technology and lateral flow sa, ok. So, in the exam now let us come during the exam time I may ask this kind of the questions like design a wash free biosensors and try to means say use this kind of wash free technology for commercialization's.

So, so maybe in this NPTEL course like exam may be MCQ type, but this kind of (Refer Time: 20:12) table you should prepare so that you can readily answer it. Not only the I will recommend means not only you have you should not write like the whole story very precisely very you can summarize the story like this way I am just telling you, ok.

(Refer Slide Time: 20:32)

The and next questions today's tutorial either nanomaterials for diagnosis. See my whole course I taught you the different different nanomaterials, right. So, now if I ask you to summarize the nanomaterials that you have learn in this course what is the utility, what is the benefit of the nanomaterials, why we need the nanomaterial now if I ask you the end of this course what is the answer?

So, I can summarize 1, 2, 3, 4, 8 the first thing is that nanomaterials say suppose you have a surface right, this is the transducer surface. So, you may want to increase the electron transfer rate in this case you can use some nano particle, right. So, nano particle like gold nano particle something like this. So, they can enhance the electron transfer rate and second thing they can, so one is the conductivity you know improve another is the surface area.

So, you may ask and why we need to improve the surface area? It is very much needed because which calibration plot you are getting, I just taught you all the measurement of the calibration plot from the low concentration to high concentration right, you are getting the calibration plot. So, here is the concentration of your target and here is this output signal.

So, if you can detect a very large range of the concentrations then your sensor surface will be very much applicable to detect very low limit to very high limit of detections. Why we need the sometime very high limit detections? Because in some disease cases the target level can be very very high. And suppose some cancers like prostate specific antigen this cancer biomarker it can be sometime maybe microgram per ml. But your sensor may be can detect the nanogram per ml and it can stop working.

So, if some patient has the very microgram per ml so, may your sensor can detect only nanogram. So, you may think that your say this patient may count an only nanogram, but no it is contain very high. So, we have to take some first precaution that is why your sensors should have the very broad detection limit, how you can improve this broad detection limit, their nanomaterial can help, ok.

So, why I am reminding you again at the end of this class? Because then only why you are planning some proposal then at the very beginning you have to think this all the major criteria for the development of the sensor. So, you should mainly try to think to make a broad range of the sensor. So, suppose if it is a planar surface and you are immobilizing the your antibody, right. So, how many anti body you are immobilizing? Just thing so, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 so here you have the 10 antibody, right.

But now, if you immobilize your sense same sensor surface with some nanomaterial. So, it is something like this see your why I am saying the surface area increase? Because they actually it is the if you measure like the radius of the surface, it is the same, your planar surface area is the same, but actual surface area you can (Refer Time: 24:26) actual your active surface area for the sensing.

See this is the what is the actual active surface sensing area? Is this one see so, ok. So, this is the your actual active surface area. See it is far better and very much higher than this one, ok. So, here you can immobilize your antibody see how many antibody you can immobilize here, here, again here see. So, here you immobilize 10 here may be here you can improve more than 100. So, you may improve the 10 times sometime 100 times you can improve the I mean number of the this is by receptors you can immobilize.

So, if more by receptor see, now this sensor surface can be easily saturated right, saturation may come very fast. But in this case the saturation may not come very fast because if you increase the target concentration. So, nanogram to micro, micro to like it can attract the analytes right.

That is why you may go like from nano to micro also micro gram per ml, that is why nanomaterial can help this thing. And another things that I already I think I already taught you in this class that is the functionalization right, functionalizations also very much important.

Easily if you have some nanomaterial surface you can functionalize the surface like I say carbon based or preferable material is a carbon based nanomaterial, right. Carbon based

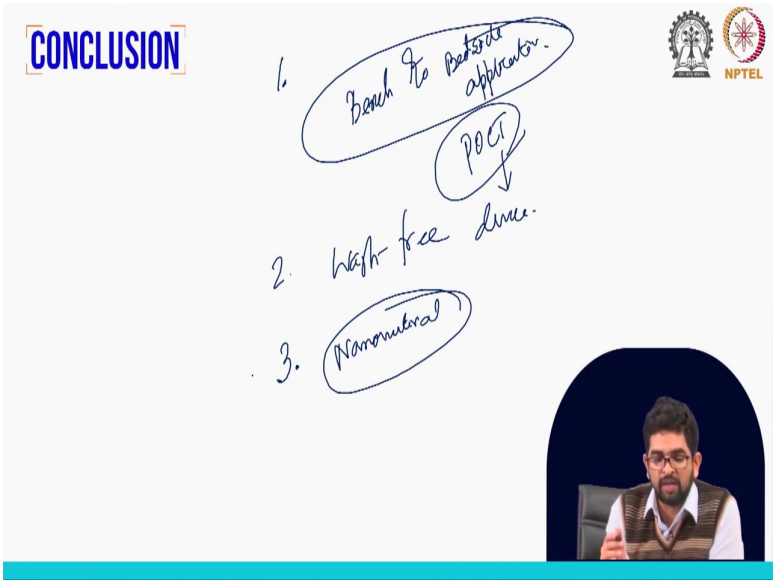
nanomaterial they have many functional group you can easily functionalize carboxylic group, right.

So, if you have the carboxylic group on the surface and your bio biological stuff has the amine group and what you will do then? This is your biological stuff it has the amine and carboxylic amine the amide bond you can form with the help of EDC MHS right and easily your surface can be covered with some biological molecule, that can nanomaterial can help.

Also, you can easily tune as a tuning property that I taught you know you can easily tune the surface catalytic activity with the nanomaterial the tuning can be done easily, right. So, for the all the things that is why you need some nanomaterial for the diagnosis it has the.

So, so many other properties also main things I just again I just summarize before end of this course. So, that while you are making some plan just try to remember this kind of all the story for the nanomaterial so that easily you can bring those concept and you can make Nobel idea, ok.

(Refer Slide Time: 27:48)



So, what is the conclusions of the this tutorial? So, I taught you mainly just try to remember to make some very good technology that can easily transferable or you can bring easily to the market.

So, I can say whenever you will focus some research, this research should not be only in the lab you should bring this one to bench means bench to bedside applications, right. So, bench to bedside application is very very important mainly point of care testing's device only can I mean bring your technology to the market easily.

And for the all the commercialization that I taught you how to make your patent and how to you can bring the technology in the market that I just mentioned in this lecture. Then second

things I taught just try to make some wash free device not the washing base. So, wash free device can help easily so, the Layman can use easily the drop and sense kind of technology.

And number 3 is the nanomaterial. Nanomaterial is the very very important for the biosensor development it has huge like properties you can use like surface the main the very basic properties is the conductivity, surface area you can tune easily those are things that it has so many other like the functionalization.

So, many other types of properties you can use for the sensing development, ok. So, these tutorials helps you to summarize maximum the concept I taught. Again, the next class I will again I will summarize and I will briefly cover all the courses next slide and then I will try to complete this course.

Thank you. Thank you student.