Electronic Systems for Cancer Diagnosis
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Lecture – 05
Clean Room Equipments Contd…

Hi welcome to this particular module and this is the part of next lecture which is focused on what is a clean room? And why the clean room is required for tissue culture? And what a class of the clean room, along with that we would also see what should be or what are the possible equipment that one can have in the laboratory to run experiments related to bioengineering. When I am talking about bioengineering that is the combination of engineering, combination of biology, combination of some of the chemistry, as well or you can say biochemistry as well ok.

So, let us see in next few minutes what exactly clean room means right and then we will continue this model as a part of lab experiment where I will actually show what are the equipment within the clean room right. So, if you see the slide what you see is that.

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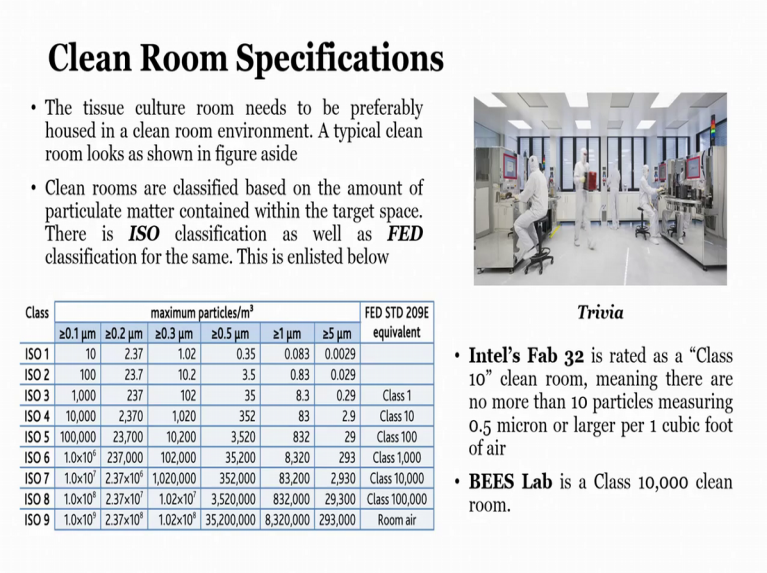

The tissue culture what do we have learned until now cell and tissue culture. So, the cell and tissue culture room needs to be preferably housed in a clean room environment. A typical clean room looks as shown in figure aside you look at this figure when and see what exactly you can see in this particular figure.

So, if you see this is a clean room, that you can see and the personnel within the clean room they are wearing thick clean room gown, this is to avoid any contamination within the clean room. Now when you talk about clean room what exactly clean no means, clean rooms are classified based on the amount of particulate matter contained within the targeted space right.

So, how many particulate matter is there within a given targeted space based on that we can classify the clean rooms and there is a ISO classification, already there as well as FED classification which is listed below and you can see there is a class ISO 1 to ISO 9 and within the class ISO 1 to ISO 9 now you can see what kind of maximum particles per cubic meter should be there for the clean room to be classified as class ISO 1.

Let us talk about class ISO 1, you can see 0.1 micron or greater only 10 particles per meter cube, while 0.2 is about 2.37 greater than 0.3 should be 1.02 greater than 0.5 would be 0.35, 1 micron can be 0.083 and greater than 5 micron would be 0.0029, with this stringent you know classification or the amount of particulate matter, you can say that this is classified as ISO 1.

Generally what you see is ISO 10 kind of ISO 4 kind of clean room where it is class 10 FED STD 2 or 9 equivalent, where you see that ISO 4 there can be 10000 particulate matters or maximum particles per cubic meter when we were talking about 0.1 microns while when you are talking about 5 microns it should be 2.9 particles per cubic meter when you want to classify the clean room as class 10 ok. So, this is very important point that you need to understand.

Same way when we talk about our laboratory environment; laboratory environment is somewhere around ISO 9, but if the laboratory has positive pressure module which we will see in the following slides and I will show you actual positive pressure modules with HEPA filters in my laboratory that we can bring the class down to class 10000. Now the one that you see right in the screen is the class thousand kind of clean room and the clean room classification also depends on something called HEPA filter H E P A, HEPA stands for High Energy Particulate Air and filter is a filter. So, HEPA filter and the number of HEPA filters you install in a HEPA and how many times you are circulating the air so, circulation per minute right, that defines or that helps to maintain the class of the cleanroom.

So, there is a conventional clean room when the HEPA filters are used on the along with the clean room, in the clean room facility where then we talk about non conventional class of clean room then you will see the laboratory which we will show you as a part of this course where there are positive pressure modules and the positive pressure modules are connected with HEPA filters and we require air conditioning unit to circulate the air and keep the environment constant. That means, that we require the temperature to be at 27 degree centigrade, we require the RH to be let us say 45 or 50 whatever we want to have in a controlled environment, if you perform experiments in a controlled environment the repeatability the accuracy would be high. I have told you to look at repeatability accuracy resolution.

So, now you should have the understanding what exactly the difference between all 3 of those terms are if you talk about Intel's Fab 32. So, Intel Fab 32 is rated as class 10 clean room, meaning there are no more than 10 particles measuring 0.5 micron and or larger per 1 cubic foot of air, while the laboratory that is my laboratory is a class 10000 clean room right, that is what we have discussed and this is how the ISO classes are there.

Now the requirement for the cell culture, for the tissue culture if you do the tissue culture in a preferably housed or if the tissue culture is housed in a preferably clean room environment then the contamination would be sufficiently or substantially low compared to when it is not kept in a clean room environment. So, there is a reason of having a clean room.

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When I generally see a clean room conventional kind of facility 1000, 10000 or 100 you will see that there are several equipment placed within that facility and those equipment are as few of those equipment are shown here. If you see from the left one the left top left one is the LP-CVD Furnace or you can say it LP stands for low pressure, CVD is chemical vapor deposition furnace ok. So, this kind of furnace can be used to grow thermal to grow a silicon dioxide, the process is also called thermal oxidation and the temperature that is used for growing silicon dioxide would be close to 1100 degree centigrade.

Again within the oxidation there are 2 types of oxidation there is a dry oxidation, there is a wet oxidation. So, we will see if the time permits because our focus is more on developing the electronic system for cancer diagnosis. However, when you are talking about developing a system the system would consist at some point some microchips or micro sensors and those micro sensors we can fabricate with the help of equipment shown here and in the clean room facility.

The next one is a PECVD and PECVD stands for plasma enhanced chemical vapour deposition, this is used to grow silicon dioxide and silicon nitride, but the advantage of PECVD over LP-CVD is that the temperature used for the reaction is very low. When we say very low compared to LP-CVD temperature is about 400 degree centigrade and in the PECVD I was talking about 1400 degree centigrade. Now viton PECVD we have to

use if the LP-CVD can be sufficiently good for us to grow oxides, why low temperature is required. So, I will give you a quick example if you have a aluminum layer.

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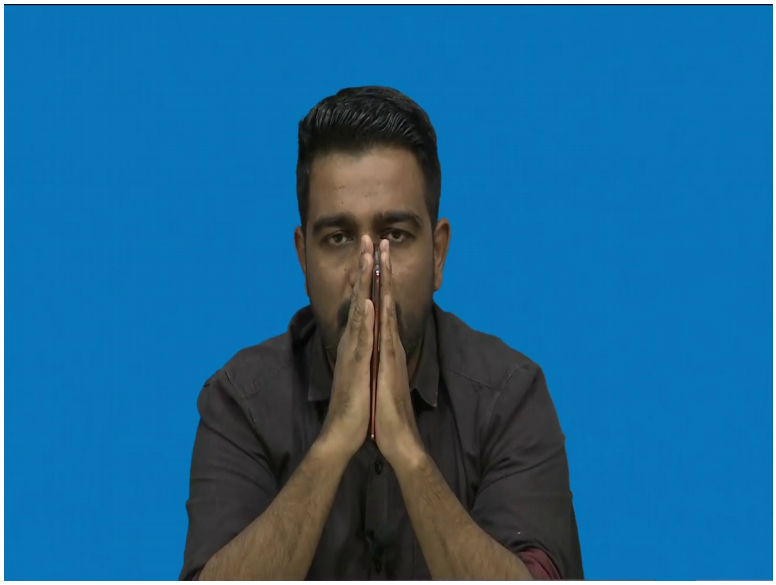

Let us say my mobile is an aluminum layer and my hand is a silicon substrate and on this I want to grow another oxide. So, like this is a sandwich type silicon aluminum silicon dioxide right. So, if you see this is silicon this is this one is your metal which is aluminium and this one is silicon dioxide.

When I want to grow silicon dioxide on metal on this metal my temperature if it is 1100 degree centigrade the melting point of aluminum is extremely low. So, it will melt when you are growing silicon dioxide onto the onto the aluminum, but if we can grow silicon dioxide on aluminum at 180 degree centigrade 100 degree 200 degree centigrade then there is no issue of melting of aluminum that is the advantage of plasma and hence chemical vapor deposition over LP-CVD.

However, every time there if there is a system which has some positive points there are some limitations as well. So, what are the limitations of PECVD over chemical vapour deposition which is LP-CVD this also is coming up in deposition is just plasma enhanced that is a low pressure.

So, the thermal oxidation gives a better quality of film compared to PECVD. So, if you require a film quality to be extremely good then you had to rely on thermal oxidation, for

devices such as the micro electromechanical systems based sensors you can use PECVD as a intermediate layer or as a insulating layer between 2 metals or metal and a semiconductor. So, I will talk about that at some point then you see is a CVD system which is from Tystar equipment. Next one is the Chemical Mechanical Polisher the CMP machine is used to polish the wafer. So, generally we may I will show you the silicon wafer in next few classes and you will see that there are 2 types of silicon wafer, when you talk about from the roughness point of view one or polishing point of view, one is single sided polished wafer and one is double sided polished wafer.

On a polished wafer which is single sided and if the second side is rough if I want to polish it and make it as smooth as this is the front side I had to use chemical mechanical polisher and like I said once I show you these silicon wafer you will understand more about how the CMP machine can be used. Next one you can see that dicing saw once you have a wafer with chips, how can you dice it up. So, let me give an example if you can see here right now in my hand is a keyboard.

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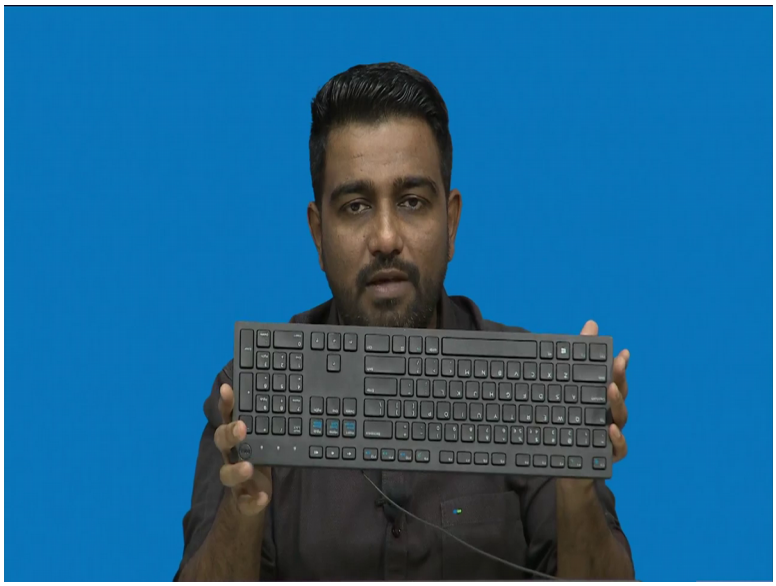

Can you see yeah this is a keyboard right assume that this is a silicon on which there are multiple chips multiple chips I want to slice each of the chip how can I slice it.

So, I had to rely on the machine which is called dicing saw micro actuation or micro automation where it will slice it individual chips in the dimensions or in the with the (Refer Time: 11:50) that I want hm. So, from one chip to second chip I can monitor it, I

can put the values into the system. So, that it will cut the chip without harming the next chip next to it ok.

So, dicing saw is something very important equipment when you are talking about a micro chips that you need to play cut out of the wafer. However, if you consider this is a silicon wafer the there is you can use a diamond cutter it is like a pen with diamond tip and you can if you just scratch it off like this that and you and you press it then what will happen it will break into piece.

So, there are like, but that is not a good way of cutting of the chip from the silicon wafer. So, we had to rely on a standard method which is your silicon or saw dicer ok. So, that is what you can see is saw dicer in the slide. Next one is the EVG 501 Bonder can you see in the slide EVG 501 Bonder. So, that one is used to bond silicon to silicon EVG bonder silicon to silicon, 2 silicon wafers when we want to bond, we can use a EVG bonder. Next one you see is a Metra Thermal Evaporator. So, metra thermal operator is used to evaporate the metal onto the and to deposit a thin film of a metal onto the substrate. We will discuss more about thermal evaporation in the lectures.

Next one we have is a parylene deposition system, parylene deposition system is used to deposit polymer on the substrate on the silicon. So, parylene is like a thin plastic. So, if you want to grow a have a parylene layer on the substrate silicon substrate or oxidized silicon substrate then you can use the parylene deposition system.

Next one we have is a AJA sputtering unit and sputtering is another phenomenon by which is a part of physical vapor deposition, where we can sputter the metal and we can deposit the metal on the substrate we will see again most of this equipment in the part of the lecture notes in the future. We will see next one what we see is an E- beam evaporator it is an electron beam operator again to use the metal using the E - beam technique.

The advantage of a E-beam or why we had to go for a E- beam over thermal you operator is that in the E- beam you can deposit a metal which is having a high melting point, while thermally operator has a drawback that the melting point of the metal is not too high you cannot thermally evaporate it we will discuss what exactly; that means, when we discuss about thermally evaporate. Next one is your Denton E- beam thermally evaporator followed by Photoresist Spin Station. So, when we look at the

photolithography you will understand what is a important of photoresist spin station as well as the EVG mask aligner. If you see headway EC 101, next one is a photoresist from laurel, next one is spin station, but next one is the EVG 620 mask aligner, followed by you have MJB 3 mask dual side mask aligner, there is a single side mask aligning, dual side mask aligning we will discuss in detail.

Next is when we had to bond PDMS, PDMS is a silicone, SILICONE and to that if you want to bond a glass then we have to do a oxygen plasma. How can we do a oxygen plasma? We can do oxygen plasma with the help of March Jupiter 3 O2 this is one of the equipment there are many equipment available in market. This one system where you can show that we can do oxygen plasma system, then when you want to etch a metal or a semiconductor or a silicon we can use wet etching bench. We have next one is RIE which is a hard or dry etching chlorine and dry etching fluorine. Finally, we have a Deep RI which is deep reactive ion nature and that is for etching silicon, but the deep reactive etching is much faster compared to reactive energy system.

So, as you see this there are so many equipment within a convinced and cleanroom, but if it is 100, 1000 or 10000 and as a part of this course we will go through most of the equipment quickly. So, that you understand that how it can be used to fabricate the sensors, once you have fabricate the sensors then we had to develop a system in which the sensor can be placed you have a mechanical jig or you have a press fit context instead of shouldering or wire bonding, because shouldering and wire bonding will cause a damage sometimes and it is difficult to you know replace the chip.

So, can we come up with a different technology where we just use a plastic contact to the chip and every time we do not want the chip we can just remove the contacts we can throw the chip put load another chip. So, that is our about the mechanical design along with the electronic chip, but how entire system will look like that is our idea and how it can be used for diagnosing cancer. So, we will we will look at that particular things.

Now if we just talk about how a lab has to or should have different equipment, when you are when you want to work at the interface of engineering and biology, engineering and medicine, engineering and chemistry.

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So, if you look here in the slide, what I am going to show you is equipment from left to right, the first one on the top left is your thermally operator followed by pathology of oxidation, then we have 3 D cell culture, we have BSL 2 which is biosafety hood 2, we have cell imaging microscope and then we have spin coater which is a then we have peristaltic pump the one that you can see on the next line peristaltic pump is with the wires right with the wires over here and then we have the upright microscope followed by fume hood, which is a bio base you are written here, which is a fume hood, then we have micro manipulator.

We had to discussed micro manipulator in the last module and then we have a CO 2 incubator which we have discussed, we have oven, we should have a DI water plant and we have oxygen plasma system.

So, these are the system or equipment which are basic equipment that one should have or if it is there in the lab it is easier for a person to work at the interface of biology, medicine and engineering.

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We here are looking at another set of equipment the top left here you go from top left the first one is Wet bench with the solvent acid bench and solvent bench are different followed by a mask aligner, then we have towers with HEPA filters I like I said these towers can be placed into the laboratory to bring the environment down to class 10000 depending how many towers we are bringing in and these are high energy particulate air filters which are HEPA filters installed into these towers, followed by we have a vacuum oven, then we have wet bench, we have high resolution quantitative phase microscope, we have autoclave and we have a microtome, we have discussed most of the things; however, the one that we are not discussed we will discuss in the following lectures ok.

So, these are the equipment that will help researcher to work at the interface of bio engineering.

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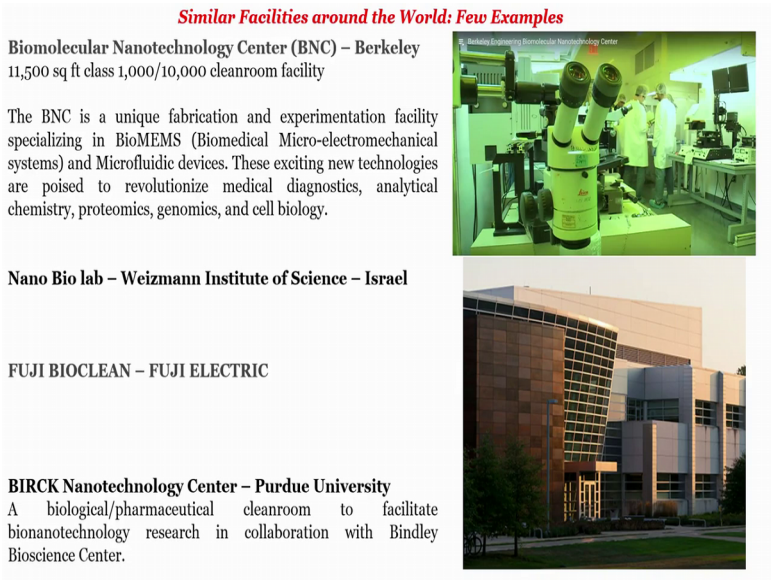

Now, when we talk about why these kinds of facilities are important or is clean room really important that should be a question right. So, yes when we see the top universities involved including Israel, we have Fuji electric, we have Berkeley and we have Stanford, we have BIRCK an endocrine center at Purdue. They have a dedicated whole you know a center for performing or to facilitate Bionanotechnology as well as MEMS based , BioMEMS based devices, micro fluidic systems, medical diagnostics genomics, proteomics, cell biology you know.

So, we require this kind of center or a clean room environment and with that particular purpose here at IIS, we have a center for nanoscience is a sense in engineering which is right in the campus it has all the facilities and most of the equipment that we are talking about as a part of the center facility for the student. They also have a very beautiful program called INUP program through which people from other part of our country can come and can learn as well as it is a free training program.

So, as far as I know you had to go through the department website and understand more about those things, but when you are talking about engineering and biology I will show you how the lab that we have right over here in the department of electronic systems engineering and Indian Institute of Science looks like and what exactly equipment are there and how it will help us to work on this interface right. So, with this approach our institute also have started working towards this kind of facility, where we are talking

about bioengineering we are talking about interdisciplinary research and whatever I am teaching today or the part of this whole course is a interdisciplinary research.

So, how to use an engineering knowledge to come up with a novel solution regarding to medicine or biology right, now let us see one more slide talking about HEPA filters and we will end our lecture or this particular module right over here and then in the following lectures we will talk about other topics. So, if you talk about just a HEPA filter you can see here in the slide.

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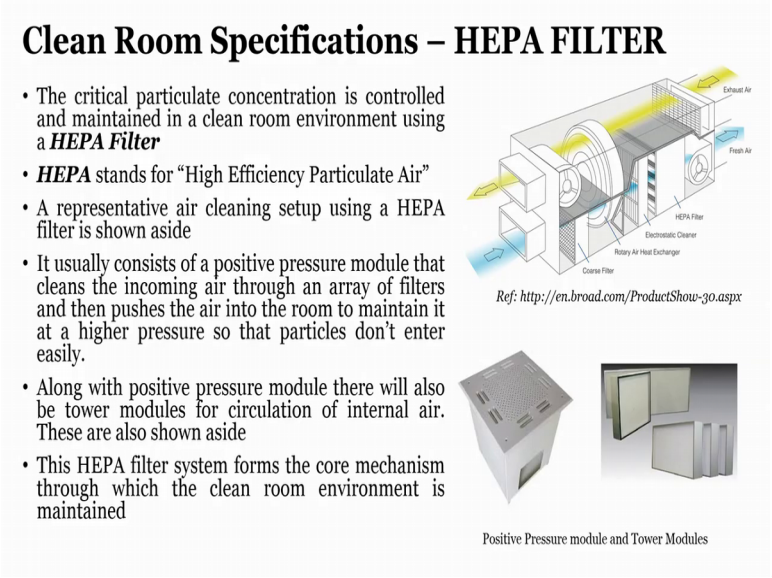

That the critical particular concentration is controlled and maintained in a clean room environment using HEPA filters, like I said HEPA stands for "High Energy Particulate Air". A representative air cleaning setup using HEPA filter is shown here, you can show this particular system right where there is a coarse filter, there is a rotary air heat exchanger, there is a electrostatic cleaner, there is a HEPA filter and there is a fresh air this is an exhaust air so, this is the circulation of the air. And if you talk about positive pressure modules and our modules, it looks like this we will actually see these modules in the lab class.

It is usually consisting of pressure positive pressure module that cleans the incoming air through an array of filters you can see here and the pushes the air into the room maintained it at a higher pressure so, that particles do not enter easily. Along with the positive as a model there will be also at our modules for circulating the internal air. And

the finally, the HEPA filter system forms a core mechanism through which the clean room environment is maintained right. So, it is an extremely important component for any clean room laboratory right.

This is the last slide for me for this particular module. So, we will discuss more about other modules in my next class till then you just go through this lecture notes, this is more like an information and we will see how can we actually interface our engineering knowledge which requires really basic engineering, but with the idea of how to use these devices or that engineering knowledge to form an entire system right.

Not always you require a top level of understanding or knowledge to develop a system, you require a right approach, you require understanding about one particular subject in detail right and then along with your friends, along with the colleagues, along with the persons who are expert in their own field you have to start collaborating, that collaboration will give you an actual thing to work right.

So, how we will use so, we will see a 3 D printer is a part of this course right, have not I said that, I said that why 3 D printer. So, how did is ready to electronic engineering it is not, but 3 D printer is used for making the mechanical casing and it is used exclusively. So, it is good to know how 3 D printer will work right, there is the idea the idea is not to just learn a specific subject, but also to understand what other subjects or what part from other subjects can be used to develop an entire system.

Of course, you require a thorough knowledge when you will develop an entire system, but what I am saying is that with the pre requisites of basic electronics you can you will see and you will learn how to use it too for solving a particular problem in a medical domain right.

Till then you just take care and I will see in the next class.