Fabrication Techniques for Mems-Based Sensors: Clinical Perspective

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Lecture - 28
Microchip for Rapid Drug Screening

Hi. In the last module what we have seen? We have seen how we can design drugs screening device using micro engineering right. So, if you recall, we have seen how to draw a process flow using photolithography for fabricating a micro heater. Over the micro heater, there was an insulator. Over insulator, there were interdigitated electrodes. And over the interdigitated electrodes, we created using a separate process a mold to form channels in PDMS.

And we have done the bonding of this PDMS with channels over the interdigitated electrodes below which there is a insulator, below which there was a micro heater. So, how the chip will look like, and how we can use this chip to understand the or to evaluate the efficacy of different drugs.

Let us see today right, and we will take some examples that what kind of cells or cancer cells, we can load into this chip. And what when we flow the drug, what kind of diffusion occurs and because of diffusion if the drug is effective, whether cancer cells dies or not. And if it dies, what kind of electrical response we obtain right that is idea. To create an engineering device that can be used to understand the efficacy, the performance of the given drug. And the application here is cancer ok.

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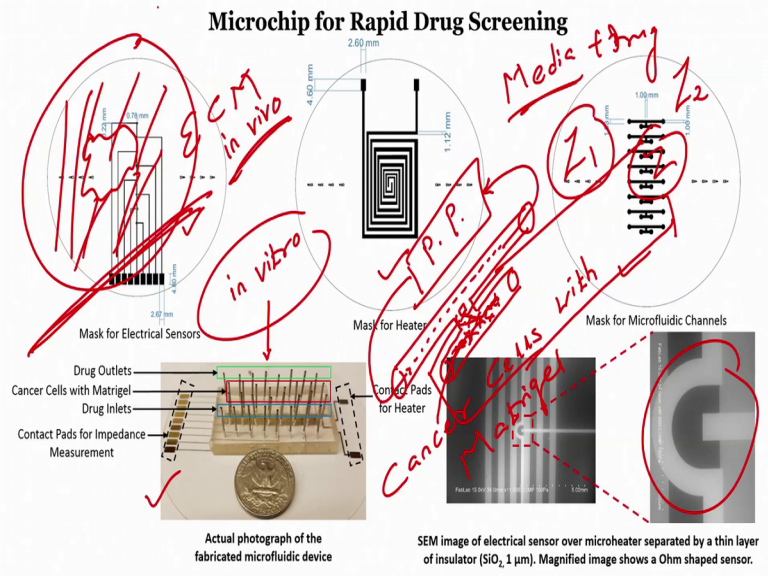

So, if you see the screen what you see here is last time we have seen how we can fabricate or the process flow for fabricating heater, process flow for fabricating interdigitated electrodes, process flow for forming channels in PDMS. Then we have sticked the PDMS through the interdigited electrodes, and the final microfluidic chip will look like the one shown in figure here. This is a actual photograph of the fabricated microfluidic device.

So, like last time we discussed right that in if you if you see this one, right take one single channel what we have, we have a longer channel, and we have a shorter channel, here we have a pillar. Now, we will load we will load cancer cell, cancer cells with matrigel right.

If you remember, what we have discuss that a cancer a tumor is surrounded by extracellular matrix ECM that provides nutrition's and required things for tumor to sustain and in fact grow. So, how can we replicate this in vivo situation, this is in vivo within the body all right. A onto the in vitro platform, this platform is called in vitro or in vitro. This is what happens within the body is called in vivo or in vivo ok. How you pronounce does not matter, it is written as in v i v o in v i t r o ok.

So, inside the laboratory if we are growing a cell, so if you are going to tumor, if you are performing experiments, which are trying to mimic the actual situation, which happens within the body, then this is called in vitro system. And microfluidic chip mimicking the

in vivo system here, we are looking at it. So, what we have to do? We have to add cancer cells within the with matrigel into this shorter channels ok.

So, now we have lot of cancer cell with matrigel. Then what we will do, we will flow the drug. So, we have peristaltic pump peristaltic pump, so there is a reservoir from which the drug will come in and the drug that goes out will again go back to the reservoir right. This is where it stores the drug within the peristaltic pump, we can store the drug with media. Of course, you cannot just flow the drug right, whatever we may flowing a drug, when we take the drug, it will by flow through the it will mix with the blood and flows with the blood right.

So, the role of the blood here, we are replacing media as a blood, and we are adding drug to the media right. So, when I just flow media in this channel in this particular channel like this right, and the media will diffuse into the matrigel with cancer cells. And I may get let us say impedance Z 1. If I am measuring the impedance, why can measure impedance, because there are electrodes in this area right like this there are electrodes in this area.

So, I can measure I can measure impedance Z right. So, what happens, when I flow the media, then I will have impedance Z. If I flow media with drug, then the cancer cells may die. If it dies, then the conductivity would increase. If the conductivity increases, impedance decreases, so I will have a different value of impedance Z 2. If the value of Z 1 and Z 2 are significantly different, there is a statistical significance then I say that my drug is effective, so let us see.

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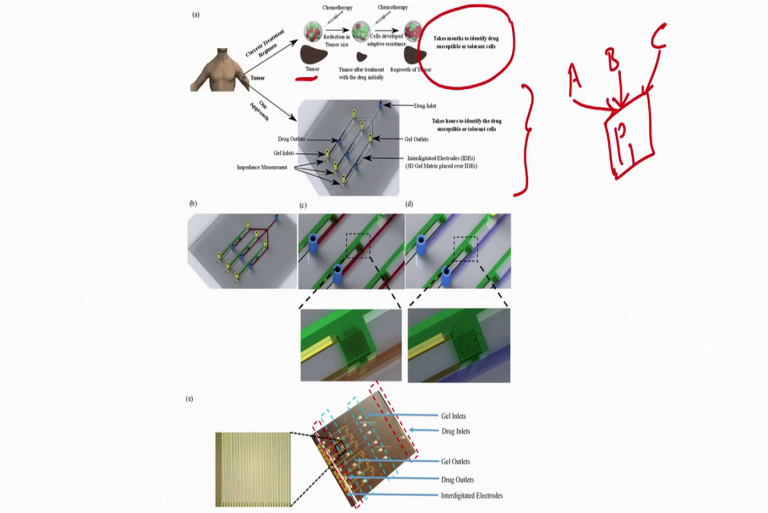

Figure: Lab-on-a-Chip for chemotherapy drug response screening. (a) 3D schematic of the presented platform for multiplex drug susceptibility testing, (b) Cancer cells are placed in a 3D matrix in a separate microchannel (green) that is connected to a parallel microchannel for drug flow (red), (c) Cancer cells are intact and viable in the 3D gel structure and before the introduction of drugs. In the presence of effective drug flow, the cancer cells respond (lyse), (d) We observed that the number of intact cancer cells reduced after introducing effective drug flow in the chip, (e) Image of a fabricated device. The chip involves interdigitated electrodes with 10 μm width and spacing.

So, this is what our concept is right. Our concept is that the current regiment the current treatment regiment is you give the chemotherapy right for a given tumor, you give the chemotherapy wait for certain time right. And if there will be reduction in tumor size, if the chemotherapy is effective right. But the cells develops adapt adaptive resistance, and there is a regrowth of tumor.

Now, this whole process to know whether chemotherapy is working or not takes ideally few months. So, the problem here that we are addressing is that how can we design a device that can tell, which drug would be effective from a given number of drugs for given number of let us say A, B and C drug for a particular patient P 1, which drug would be effective A B or C right.

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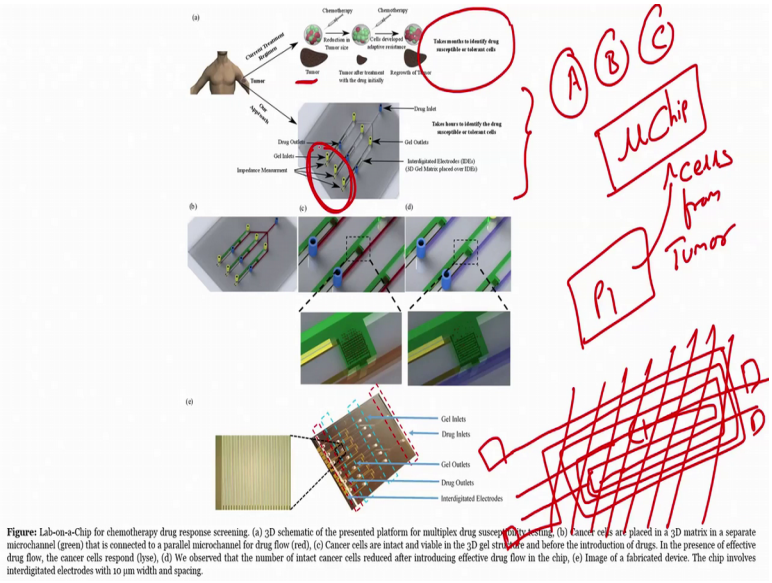

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We do not know and current techniques takes about few months. So, how about we create a microfluidic chip right from patient 1? We take the cells right, we take the cells from tumor region right. We load into the microfluidic chip, and we test A, B, and C separately A, B, and C separately. And we can then find whether which drug is effective based on the electrical properties of the cell.

So, if you see here, there are gel inlets, drug inlets, impedance measurement, because the idea here is that now, how can you when you load the cell should die right, because it is not at 37 degree centigrade that is why the bottom is the bottom of the chip is nothing but our heater right. The bottom of our chip is our heater. Over the heater, there is insulator right. And then we have electrodes right we have electrodes a different electrodes right. So, 1 electrode, 2nd electrode, 3rd electrode, and 8 electrodes. So, we can have here 8 electrodes, you can see here impedance measurement right. So, the help of electrodes, we can measure the impedance.

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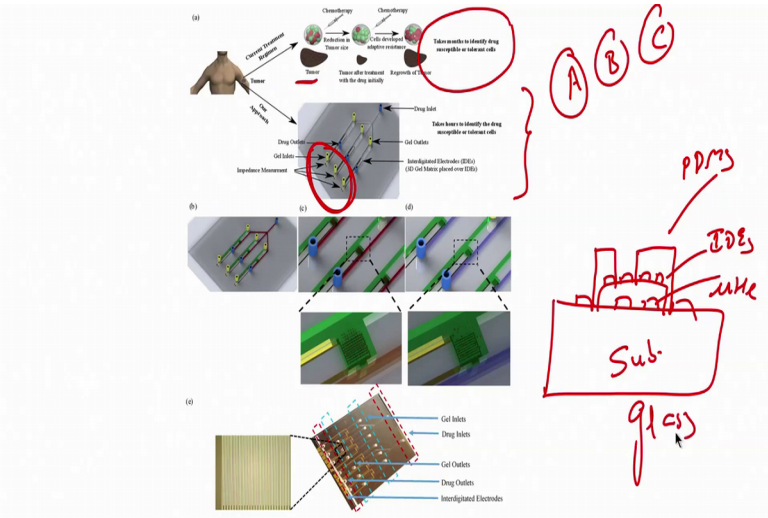

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Now, when you load the when you bond the PDMS, which channels onto this microfluidic chip. So, you assume like this, there is a microfluidic chip with heater. There is an insulator, there are electrodes right. And you are bonding this chip with PDMS. PDMS, interdigitated electrodes, micro heater, and this is your substrate, substrate is glass right.

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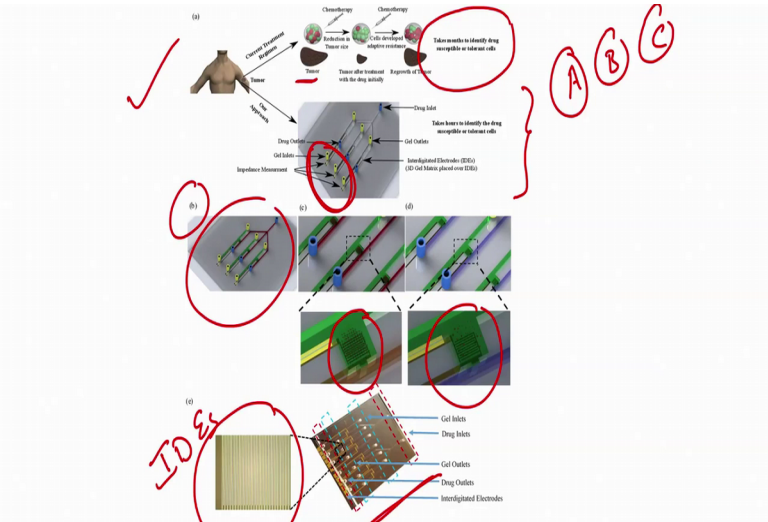

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So, when you do this, when you do this what will happen? So these are you can also form interdigitated electrodes using this particular pattern all right. So, you can see here

3D schematic your a would be a 3D schematic of the platform for multiplexing drugs susceptibility testing. b would be the this one would be cancer cells are placed in a 3D matrix right in the 3D matrix.

c would be cancer cells are intact and viable in 3D gel structure, you can see here cancer cells are intact, and viable in a 3D gel structure, before introducing drugs. d would be the intact cells are reduced after introducing, you see here the number of cells that we are presenting are reduced after introducing the effective drug flow right. This is actually fabricated device, and this is the interdigitated electrodes, E is interdigitated electrodes on to the device right.

So, the point that we are making here is that this is a conceptual diagram a 3D schematic diagram of what of telling our hypothesis that if we have this structure, and if you load the cells with some gel, and we introduce a drug right, so a where b is our microfluidic chip, c is where we are introducing these cells, d is where the we are introducing drug and the cells are dying right. And if the cells dies, then our we can see change in impedance. This is our schematic representation.

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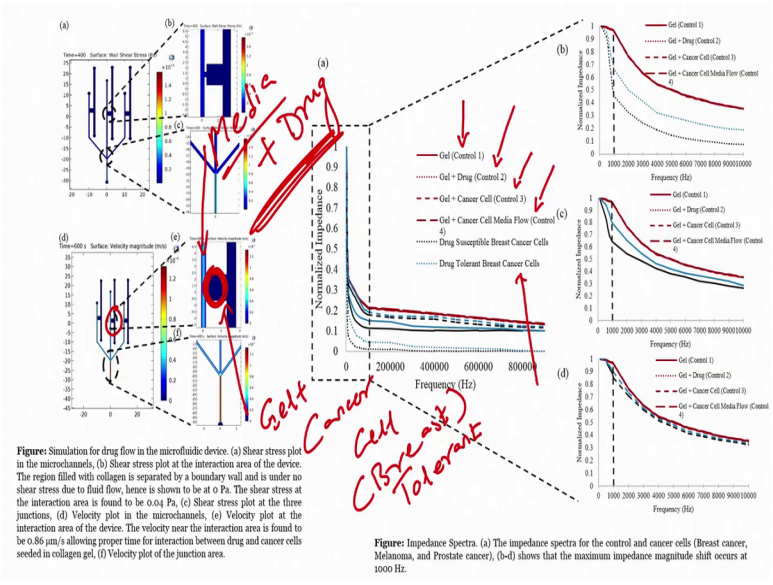

Figure: Simulation for drug flow in the microfluidic device. (a) Shear stress plot in the microchannels, (b) Shear stress plot at the interaction area of the device. The region filled with collagen is separated by a boundary wall and is under no shear stress due to fluid flow, hence is shown to be at 0 Pa. The shear stress at the interaction area is found to be 0.04 Pa, (c) Shear stress plot at the three junctions, (d) Velocity plot in the microchannels, (e) Velocity plot at the interaction area of the device. The velocity near the interaction area is found to be 0.86 μm/s allowing proper time for interaction between drug and cancer cells seeded in collagen gel, (f) Velocity plot of the junction area.

Figure: Impedance Spectra. (a) The impedance spectra for the control and cancer cells (Breast cancer, Melanoma, and Prostate cancer), (b-d) shows that the maximum impedance magnitude shift occurs at 1000 Hz.

So, now let us see actual experiment actual experiment. Now, always remember whenever you create or whenever you fabricate or whenever you want to fabricate a microfluidic chip always, you need to perform simulation. Why simulation, you need to understand how is your flow right. So, to understand microfluidic chip in detail, you

need to understand lot of things like a Reynolds number, one of the example is a Reynolds number right. What is the shear stress within the microfluidic channel right, what is the velocity right whether the flow would be smooth or not ok.

So, so lot of things you need to understand, and that is why we perform a simulation. Now, after performing simulation, you see here the plot the plot of normalized impedance versus frequency. Now, what I said is we will measure the impedance that is why you require impedance analyzer ok.

And we will be looking at all the things that we are talking in the in the series of lectures like impedance analyzer, peristaltic pump, microscope right. Different kind of microscope whether it is inverted microscope or it is a metallurgical microscope, but it is a stereo microscope, we will look at it. We will look at the micro manipulator right, we look at the incubator. We will see PDMS bonding on to the electrodes, on to the glass right.

So, this process we will actually see in this particular course right now. Let us understand, how this device, how this chip can be used for testing the drugs. So, if you see here, we have several controls, three controls in particular. One is just gel, when you introduce into this smaller channel when you introduce, so if you see this particular thing right, then when you introduce just gel in this channel, what is the impedance ok.

Then when you just introduce gel plus drug, so there is there is no cell ok, there is no cell. Thus gel is there, and you are introducing here drug, so gel plus drug, what is impedance. Now, you have gel plus cancer cell no drug. So, here the 3rd case will be gel plus cancer cell right control three, what is the impedance, these are our controls ok.

Now, 4th control we have used four control I am sorry we are used four control not three. So, 4th control would be gel plus cancer cell and media flow. So, now we are flowing just media, no drug no drug ok. 5th would be now we have cancer cell, which are breast cancer cell breast cancer cell. And we are loading media plus drug what is impedance, we are flowing media plus drug. And here it will be gel plus cancer cell, which is breast cancer cell.

Next test would be, if it is a tolerant breast cancer cell right. One is susceptible, which will die with the introducing different drugs. Another breast cancer cells are tolerant to it

resistant to it, but resistance you cannot say, we can here say that it is tolerant to the particular drug. So, when we treat the breast cancer cells with a drug, and leave it for some time it becomes tolerant. So, instead of susceptible, we will use breast cancer cells, which are tolerant right. So, gel plus breast cancer cell, which has tolerant breast cancer cell. And we will flow media plus drug, and we will see the change in impedance.

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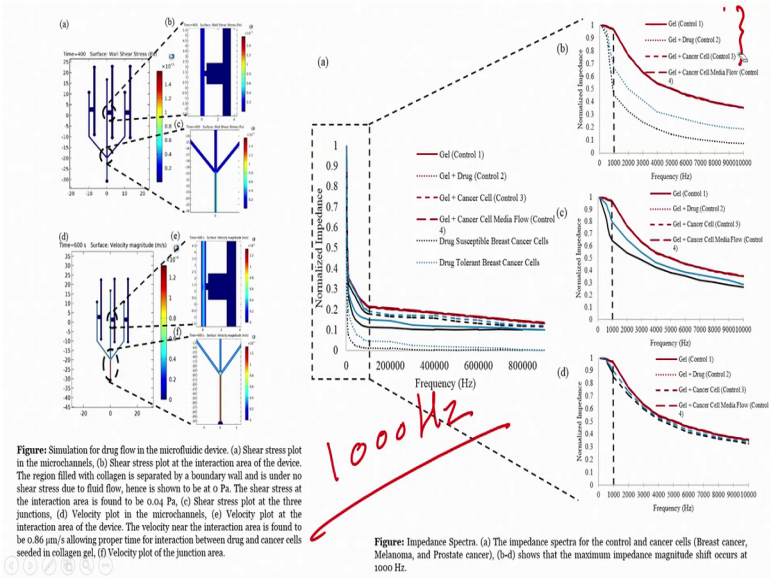

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So, when we will when we perform this experiment when we perform this experiment, what we found is that at 1000 hertz. We could see maximum difference between control and cancer cells between control and actual experiment that is our drug susceptible breast cancer cells. When we flow the drug and breast cancer cells tolerant one, when again we flow the drug.

So, if you if you magnify this right if you magnify this, we can clearly see here that there is a difference between all here four controls right, these are four controls. So, cancer cell plus media flow you can see here. Then you have gel control four here right control 1, control 2, control 3, and then we again have gel 1, control 3, control 4 right.

So, what we see here is that the maximum impedance magnitude shift occurs at 1000 hertz. We just were interested understanding at what frequency, we can see the maximum change in the impedance magnitude. So, what we found is 1000 hertz is what we have to use.

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Now, we also need to understand, why we cannot use a steady platform. So, what I what do I mean by steady platform. Steady platform means, if I have a well, if I have this micro heater right, if I have insulating layer, and over the there are interdigitated electrodes, can I just put matrigel with cancer cells right, and I will get Z 1. And if I put drugs drug one let us say with media right drug one plus media, then after some time let us say 24 hours. I would be able to see a difference Z 2, if the drug is effective correct.

So, this is a static study. Static way of measuring the change in impedance. Why I cannot perform this experiment or why should I not perform this experiment right, there is a question. So, the answer could be that because our body is dynamic and not static, we should try to see what happens in a dynamic situation compared to a static platform right, because here the drug plus media is in continuous contact with your cancer cells that are loaded inside the matrigel.

So, static platforms will give us a different response compared to dynamic platform. And we should be looking at dynamic platforms, because our body is dynamic right. So, that is why, we are understanding this microfluidic chip for a rapid drugs screening.

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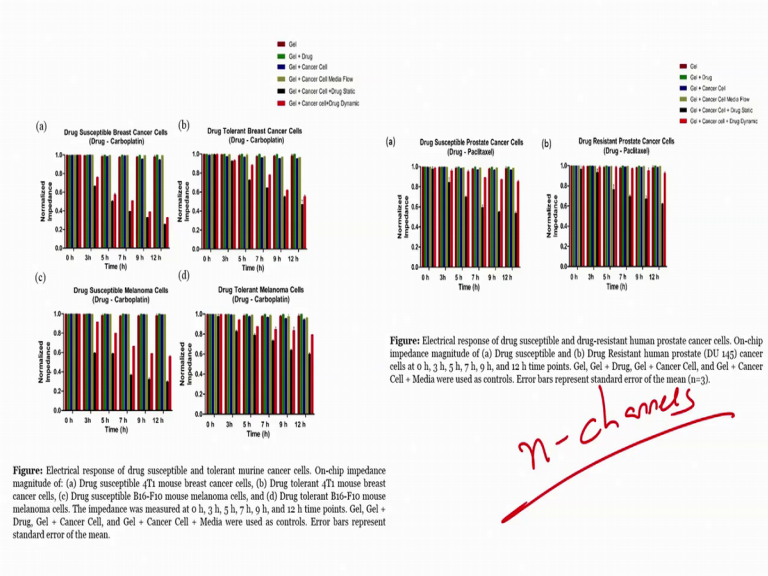

Figure: Electrical response of drug susceptible and tolerant murine cancer cells. On-chip impedance magnitude of: (a) Drug susceptible 4T1 mouse breast cancer cells, (b) Drug tolerant 4T1 mouse breast cancer cells, (c) Drug susceptible B16-F10 mouse melanoma cells, and (d) Drug tolerant B16-F10 mouse melanoma cells. The impedance was measured at 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h time points. Gel, Gel + Drug, Gel + Cancer Cell, and Gel + Cancer Cell + Media were used as controls. Error bars represent standard error of the mean.

Figure: Electrical response of drug susceptible and drug-resistant human prostate cancer cells. On-chip impedance magnitude of (a) Drug susceptible and (b) Drug Resistant human prostate (DU 145) cancer cells at 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h time points. Gel, Gel + Drug, Gel + Cancer Cell, and Gel + Cancer Cell + Media were used as controls. Error bars represent standard error of the mean (n=3).

Why I said rapid, because you can have eight different channels you can have, n number of channels in reality. So, you can test at a time several drugs for a particular patient right. And within 24 hours range, you should be able to tell, which drug when is effective for that particular patient. So, we are we are designing a patient centric platform, we are designing a rapid drug selling platform, which is patient centric right. So, if you see this screen, what you see here in the screen is that we have, we are looking at electrical response of drug which is susceptible as well as tolerant right for murine cancer cell.

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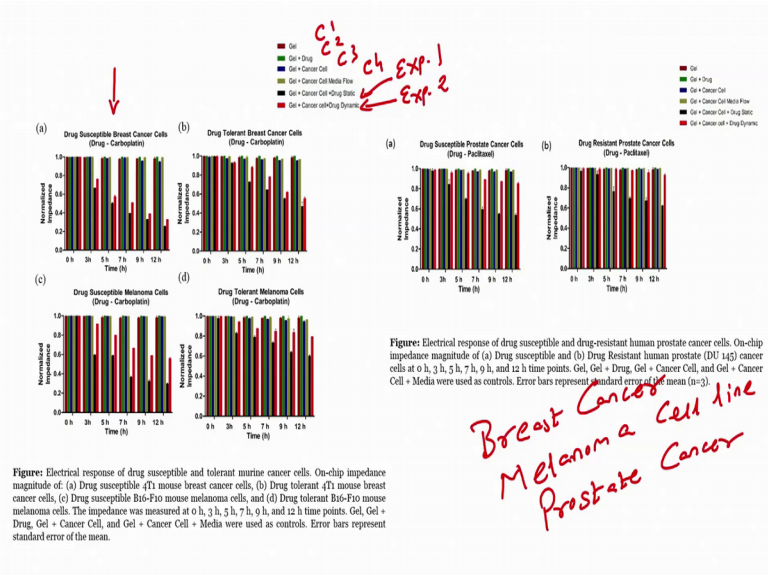

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So, if you can see the screen, we are talking about murine right cancer cells that are taken from the mice ok. Now, what we see here, we have control 1, which is gel. Control 2 gel plus drug, control 3 gel plus cancer cell, control 4 gel plus cancer cell media flow. This is experiment 1, this one is our experiment number 2 right. So, what is our experiment number 1? Gel plus cancer cell plus drug in a static situation, experiment number 2 is gel plus cancer cell plus drug in a dynamic situation all right.

So, first let us see drug susceptible breast cancer cells. Here we have tested three different cell lines was first one is breast cancer cell line, second one is melanoma cell lines melanoma is skin cancer, third one is prostate cancer cell lines ok. So, three different three things we had tested breast cancer, melanoma, and prostate cancer.

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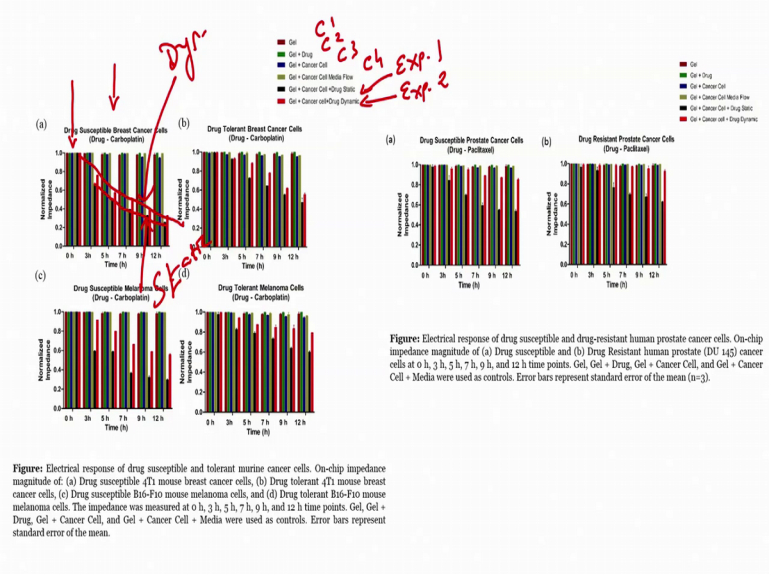

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Now, let us see so if you see at 0 r a 0 r right, there is the impedance is almost one, which is normalized impedance right. And as you keep on increasing the hours from 0 to 3 to 5 to 7 to 9 to 12, you can see a change in impedance for our experiment, which is static which is here and dynamic. So, this top one is dynamic, the bottom one is static right. We can clearly see that a dynamic experiment shows us different result compared to static experiments right.

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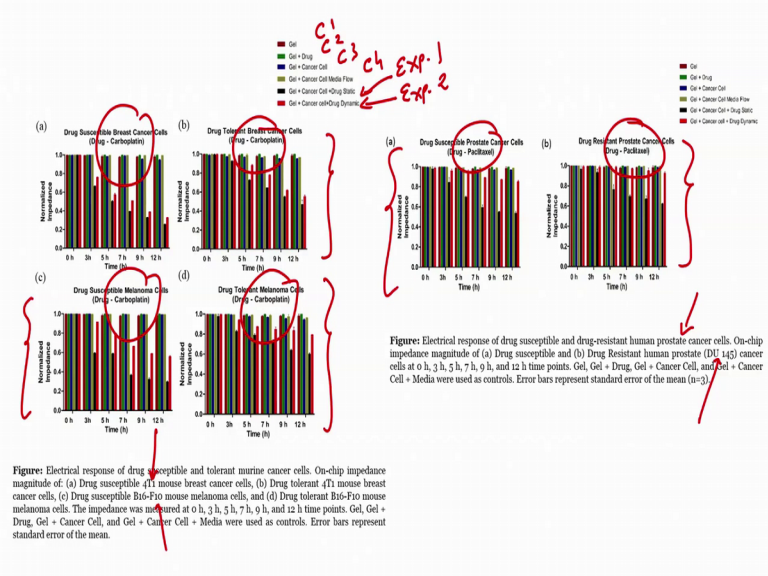

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Now, what if we have drug tolerant cells what if we have drug tolerant cells, in that case also we could clearly see a signature at 1000 hertz this impedance right. And we can see that the static results are different than dynamic, however we can clearly understand effect of drug for using dynamic platform. What if we are using melanoma, in melanoma also we can see a signature. What if melanoma is tolerant, tolerant melanoma cells also so we can see a particular signature, you can you can very easily see right.

So, you have different signatures for breast cancer cell, which is susceptible breast cancer cells, which are tolerant right, melanoma cells which are susceptible melanoma cells, which are tolerant. Now, you will see we have used a particular drug chore carboplatin carboplatin carboplatin carboplatin correct. So, for breast cancer cells and melanoma cells generally platinum based drugs are used for chemotherapy platinum based drugs are used.

While for prostate cancer textual based drugs are used textual base drugs that is why, when we go for prostate cancer cells to understand the effect of drug, we are using paclitaxel paclitaxel right. So, anyway this is just for understanding that platinum drugs generally are used for breast cancer cell in melanoma, while textual based drugs are used for prostate cancer right.

And we our interest is not to really go into details why textual based drug, why platinum based drug our understanding for this subject lies into the fact that can we design or can

we fabricate a device that can perform rapid drug screening for a given number of drugs. And can tell for a particular patient, which drugs to which drug to administered or which drug to give. So, again for prostate cancer cells, you have a different signature.

Now, there is one more thing that is interesting. So, the thing in the impedance for tolerance cells is different than change in impedance for susceptible cells right. From here, it may not be easily visible right from here it may not be easily visible. But, we can see in the next slide that you can clearly see a difference between impedance normalized impedance, when you are considering susceptible cells, and when you are considering resistant cells. So, for the present study these plots are obtained using 41 mouse breast cancer cells B16-F10 mouse melanoma cells. And DU 145 drug resistance human cells or post prostate cancer cells DU 145 prostate cancer cells ok.

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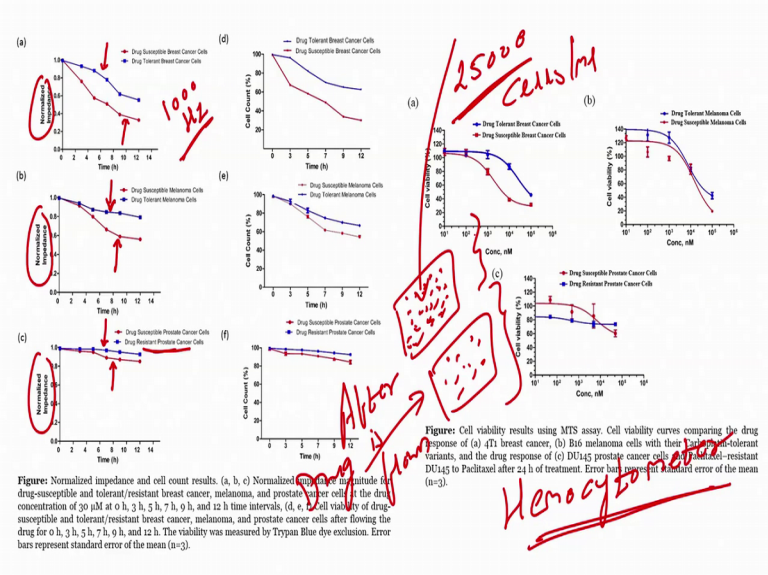

Figure: Normalized impedance and cell count results. (a, b, c) Normalized impedance magnitude for drug-susceptible and tolerant/resistant breast cancer, melanoma, and prostate cancer cells at the drug concentration of 30 μM at 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h time intervals, (d, e, f) Cell viability of drug-susceptible and tolerant/resistant breast cancer, melanoma, and prostate cancer cells after flowing the drug for 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h. The viability was measured by Trypan Blue dye exclusion. Error bars represent standard error of the mean (n=3).

Figure: Cell viability results using MTS assay. Cell viability curves comparing the drug response of (a) 4T1 breast cancer, (b) B16 melanoma cells with their Taxol®-tolerant variants, and the drug response of (c) DU145 prostate cancer cells and Paclitaxel-resistant DU145 to Paclitaxel after 24 h of treatment. Error bars represent standard error of the mean (n=3).

Now, if you see here what we obtain? We obtain a clear signature we obtain a clear signature, when we are plotting normalized impedance versus time for impedance measure at 1000 hertz, because there is our optimized frequency. When we plot normalized impedance versus time for drug susceptible and drug tolerant breast cancer cells, measure at 1000 hertz frequency. We can see that the drug tolerance cells the impedance change is less compared to drugs susceptible cells. Red one is drug susceptible, blue one are drug tolerance cells all right.

Same thing goes for melanoma drug tolerant, which is this one blue one. And drug susceptible, which is red one. Same thing also goes for prostate cancer, but one thing that we need to understand is that prostate cancer cells particularly resistance are very difficult to kill. The resistant drug resistant both cancer cells are extremely difficult to kill in general prostate cancer cells are difficult to kill with paclitaxel.

And we could see, so these are all electrical measurements right a, b, and c a, b, and c all three are electrical properties of a cell that we are interested in measuring for different drugs correct. And what we can see here that a, b, c normalized impedance magnitude for drugs susceptible, and tolerant or resistant, breast cancer, melanoma, and prostate cancer cells at the drug concentration of 30 micro molar at 0 hours, 3 hours, 5 hours, 7 hours, 9 hours, and 12 hours time interval right. So, this is for 30 micro molar concentrations.

Now, what are this d, e and f? We have to understand whatever signatures we are obtaining, whatever methods we are using are correct or not. So, how can we test it? So we can test by understanding whether the cells are dying or not. So, if the cells are dying, then the cell count will reduce right if the cells are dying the cell count will reduce. So, what we can do, we can extract the matrigel with cancer cells after the drug is flown.

So, let us see this is cells with matrigel right. And these are cells within matrigel, after the drug is flow. How many cells have died, how many cells have died right in terms of percentage. Now, how we will know how many cells have died. So, we know when we initially load into this well, how many cells we are loading. So, is it 25,000 cells per milliliter 25,000 cells per milliliter or it is 40,000 we know right whatever number we are loading, we know. So, this would be our 100 percent.

Now, when we recover these cells, after a drug is flown after drug is flown. If we recover these cells, and counted using hemocytometer hemo cyto meter hemocytometer is used to count cells life or dead. So, using hemocytometer we can count number of cells.

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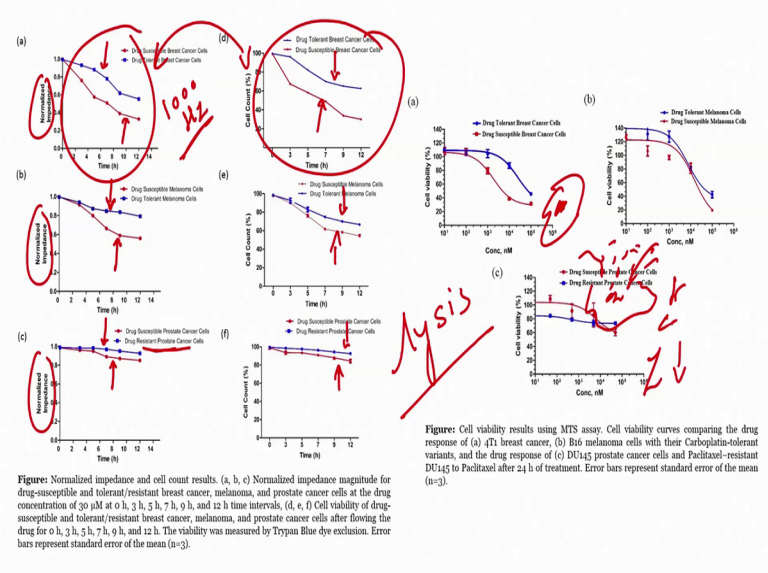

Figure: Normalized impedance and cell count results. (a, b, c) Normalized impedance magnitude for drug-susceptible and tolerant/resistant breast cancer, melanoma, and prostate cancer cells at the drug concentration of 30 μM at 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h time intervals, (d, e, f) Cell viability of drug-susceptible and tolerant/resistant breast cancer, melanoma, and prostate cancer cells after flowing the drug for 0 h, 3 h, 5 h, 7 h, 9 h, and 12 h. The viability was measured by Trypan Blue dye exclusion. Error bars represent standard error of the mean (n=3).

Figure: Cell viability results using MTS assay. Cell viability curves comparing the drug response of (a) 4T1 breast cancer, (b) B16 melanoma cells with their Carboplatin-tolerant variants, and the drug response of (c) DU145 prostate cancer cells and Paclitaxel-resistant DU145 to Paclitaxel after 24 h of treatment. Error bars represent standard error of the mean (n=3).

So, when we perform this experiment of counting number of cells, after the drug is flown. Then we found that you see here clearly drug susceptible cells and this is dropped tolerant, and this is drug susceptible. Drugs tolerant and drug susceptible cells, it reduces as time increases for when the drug is flown in the channel right.

Same thing goes for melanoma and prostate cancer. And we can we can see that this signature number of cells dying right, corresponds to the impedance is not it that means, whatever impedance we are measuring has a correlation with the number of cells dying. Because, when a cell dies, the conductivity would increase. When we lies the cell for lysis lie lying or lysis, when you lies a cell or when lysis offences cell, which nucleus will rupture will rupture. So, the content within the cells will come out, what are these content can potassium, can be calcium, can be other proteins right, and be can be different things.

Now, because the contents of the cell will come out the conductivity, conductivity would increase and impedance would decrease right. Now, this particular technique is not so sensitive that it can measure the one cell dying, it cannot measure single cell die ok. Group of cells should die, and then we can we have to understand how many cells are dying, have to understand the sensitivity of the platform.

However, for the given study, we could clearly see that there is a correlation between number of cells dying and impedance changing. So, here what d, e, and f shows; d e and

f shows cell viability of a drug susceptible n tolerant, resistant, breast cancer, melanoma and prostate cancer cells, after flowing drug for 0 hours to 12 hours right in an interval of interval of 2 hours first is 3, 5, 7, 9, 9, 12 2 to 3 hours.

So, when you load the cells in hemocytometer, you to mix the cell with trypan blue trypan blue dye right to understand which cells are dead and which cells are alive. This is a very basic technique in biology to understand or count the number of cells. Now, after doing this, we can also test our results or we can compare our results with a goal standard, which is our MTS assay cell viability cell viability you see here this is cell counting, this is cell viability ok.

So, here the cell viability how can we understand using a technique called MTS study MTS assay. So, when we perform cell viability, we can again see that the there is a signature, when the drug tolerant cells and drugs susceptible cells are measured right for different concentration of drugs the measure for different concentration of drugs. And there is as you increase the drug the cell starts dying cell starts dying.

So, when we perform all these experiments, we can say that we can say that the impedance measurement impedance measurement can be used to understand whether the drug is effective or not correct, from this all these experiments we can say that impedance measurement can be used to understand whether the whether the particular drug is effective or not.

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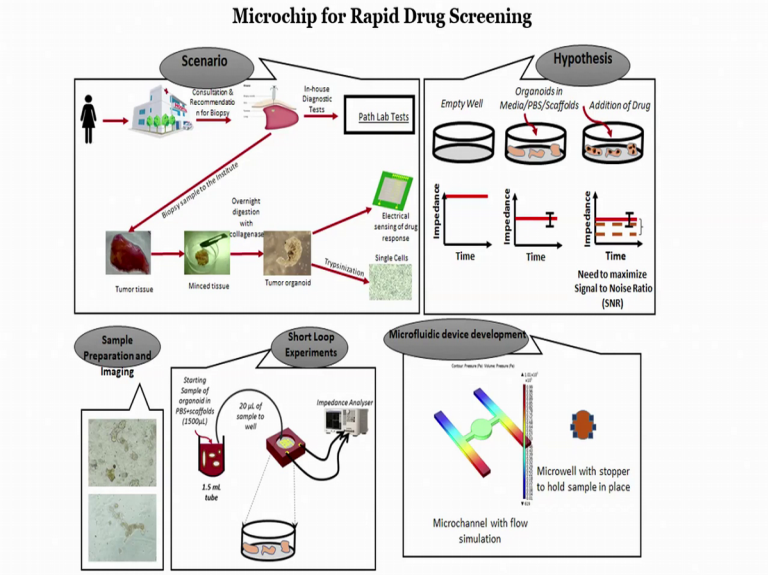

So, let us quickly recall, what we have studied in this particular class right. We have concentrated on developing a microchip for rapid drug screening. So, the idea is can we develop us drug screening tool, which is present centric. And we can we can see the change or we can understand the efficacy of drug within 12 to 24 hours.

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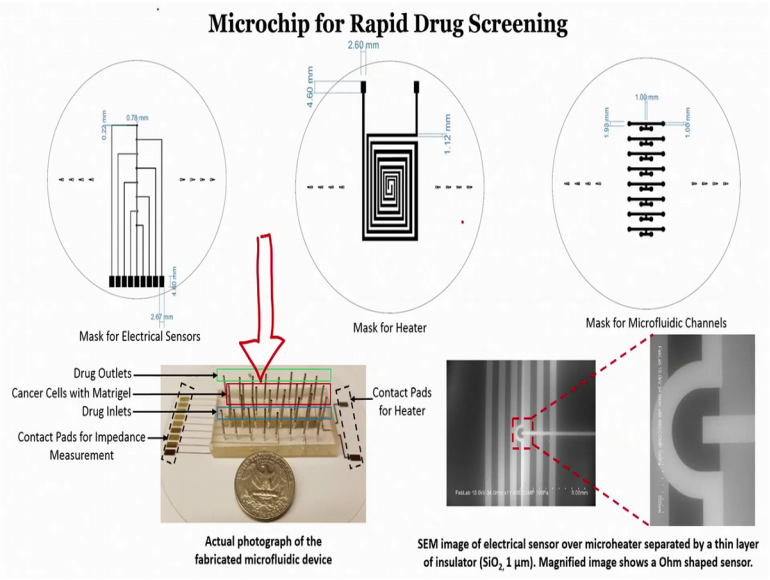

For that we have seen, how we can draw a process flow for fabricating a microchip.

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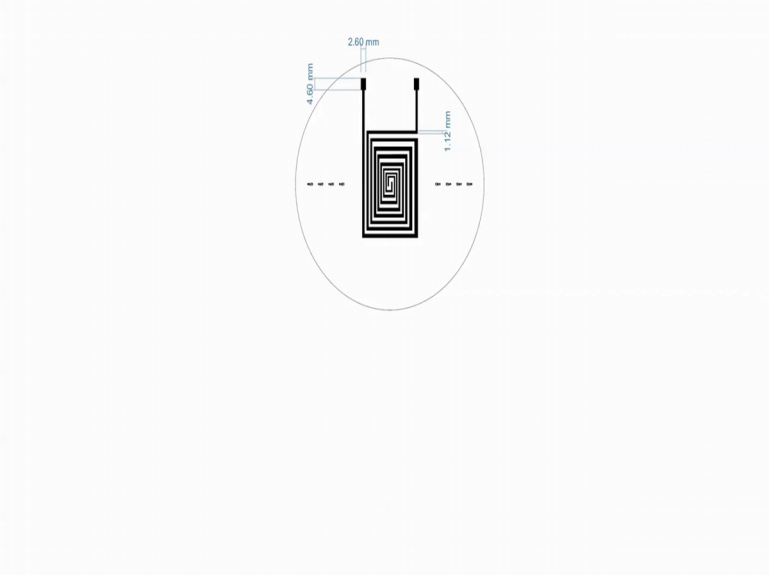

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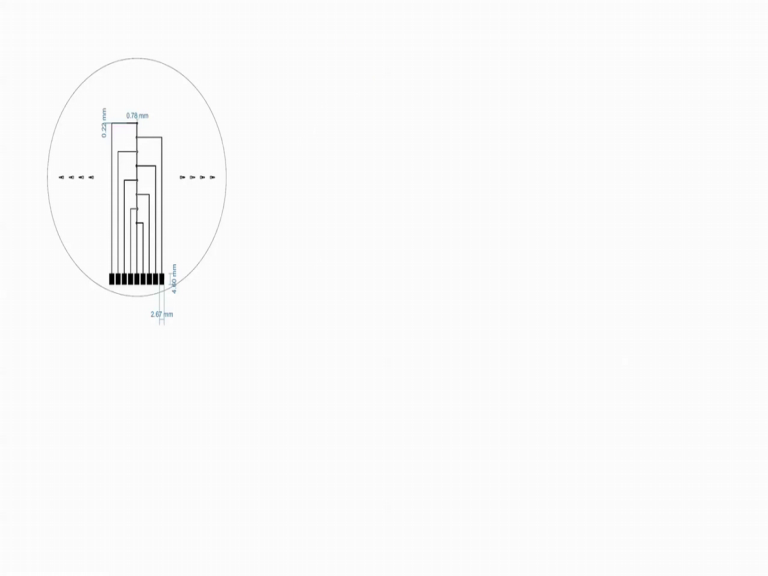

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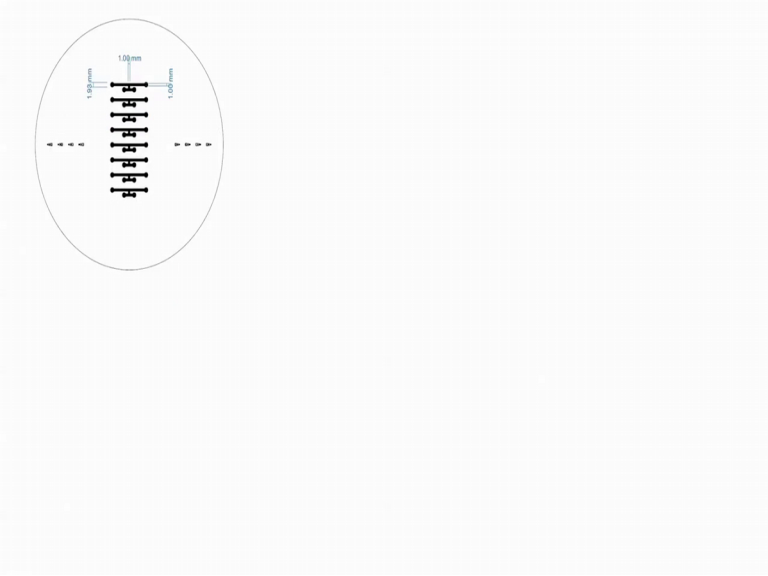

We have seen process for individual components starting from heater, then we studied interdigitated electrodes, then we studied how to create a PDMS channel using a mold. And here we have considered SU-8 then when we have all three together right, how it will look like right how it will look like when we have all three things ready. And when we bond it, when we bond the PDMS with glass right, how it will look like we have seen this right, which is our in vitro platform to understand or to measure or to evaluate the efficacy of given drugs right this platform. After that, we understood what how we can

plot a 3D schematic to convey our message what and why this technique we are using, and what is our hypothesis.

Then we have seen actual results, and we found that 1000 hertz is an optimized frequency for our experiments. Then we have seen that for given controls and given experiments right how the impedance normalized impedance changes with respect to time right. And here, we can clearly see that the results obtained from static platform is different than results obtained from dynamic platform right.

Also we have seen that we can measure not only the breast cancer susceptible cells, but also breast cancer tolerant cells and same thing for melanoma susceptible and melanoma tolerant cells. We also tested prostate cancer cells, which are human prostate cancer cells and number is DU 145. And prostate cancer cells there are resistant to drug, which is envious in the plot. Similarly, for breast cancer what we are seeing breast cancer cells, we have used 41 mouse breast cancer and for melanoma B16-F10.

So, here if you see the signature, we can clearly see that as if the drug is effective right for a given drug, we can clearly understand that the difference in the impedance right for when we when we pass a drug for about 12 hours. And we can also see that the drug resistant cells particularly prostate cancer, we do not see that much change in impedance, because it is very difficult to kill prostate cancer cells using paclitaxel right. We have also performed and we have seen how the power plot will look like for cell counts using hemocytometer.

Finally, we have understood cell viability study using MTS assay right. So, if now if we are given, if we are given, so the if you are given what exactly you will be you, what kind of what kind of experiments you will perform or what kind of device you will design right, then you can now tell you can now tell that yes for cancers, for chemotherapy, we know a microfluidic platform can be a potential answer right a microfluidic platform can be potential answer.

Because, we can we can measure different drugs at a same time by measuring the change in impedance that is we can now design a patient centric platform using our knowledge of micro engineering. How to measure the efficacy or performance of drug by loading the cells into the well below, which there are electrodes and passing the drug, and this

cells are with it matrigel and when we when the drug diffuses through this matrigel, it will kill the cancer and you can see the change in impedance.

Now, as you can do for one channel you can do for eight channels, which we have seen in this in this example that means, eight different drugs for one particular patient, you can use and you can say, which drug to give to that particular patient or eight different patients, eight different cancer cells right or eight different patients suffering from a particular cancer. You can load you can their cells from the patient; you can load into this microfluidic platform, and pass a particular drug and see, whether the drug is effective for which patient. Again you can save the time right.

The idea of understanding or proposing or you know performing research in this area is can we can we reduce the time can we reduce the time, which is currently used to administered a particular drug regarding chemotherapy for a given patient right. Can we reduce this window, can we bring it to 24 hours can we bring it to 48 hours and can we propose a particular drug right?

So, you will be learning this kind of interesting microfluidic chip. I hope, it is interesting to you. I hope, it is new thing for you to learn that this micro technology is not only meant to understand micro sensors that can be utilized in your in your in your display, in your iPad, in your in your android or in your laptop right or even in satellites magnet technology can also be used for clinics.

Micro technology can also be used for creating novel biomedical platforms that is the beauty of micro engineering right that it is not limited to a particular area or field of focused. It can be utilized for several applications. If I want to make a guess sensor, I can make it. If you want to make a accelerometer, you can make it. If you want to make a pressure sensor, you can make it right or you want to make a microfluidic chip, you can make it, because you know the basic the understanding right of micro engineering.

So, we will take another topic, interesting topic and what we will be covering in these lectures right. This would be I think it is not available some somewhere, most of the topics are not available in some particular book. So, the examples are the current research area, which lot of people are interested in and a lot of people a lot of groups are working in all right. Along with that we will be keeping our focus on to the understanding micro engineering. And we will be taking you to the laboratory, and show

you few of the equipment that I discussed in this particular module. Till then, I will see you in the next class, take care. Read the lecture, if there is any question, you can ask us in the forum. Bye.