**Compliant Mechanisms: Principles and Design**
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**Lecture - 68**
**Miniature compliant mechanisms as cell-manipulation tools**

Hello. We are going to discuss our second case study which is a grasping a biological cells. Here is where compliant mechanisms become very useful to have a very distinct technique for handling single biological cells.

So, let us look at this second case study where compliant mechanisms go down to the micro-scale and are able to manipulate single biological cells. And also try to measure the forces being acted up on them. This work was done with my former students Santhosh Bhargav, Annem Narayana Reddy and Deepak Sahu who was the one first made the gripper in our lab to hold biological cells, and the two PhD students Santhosh and Reddy did a lot. And there are a number of other students who contributed to this work and in fact this list may not be exhaustive.

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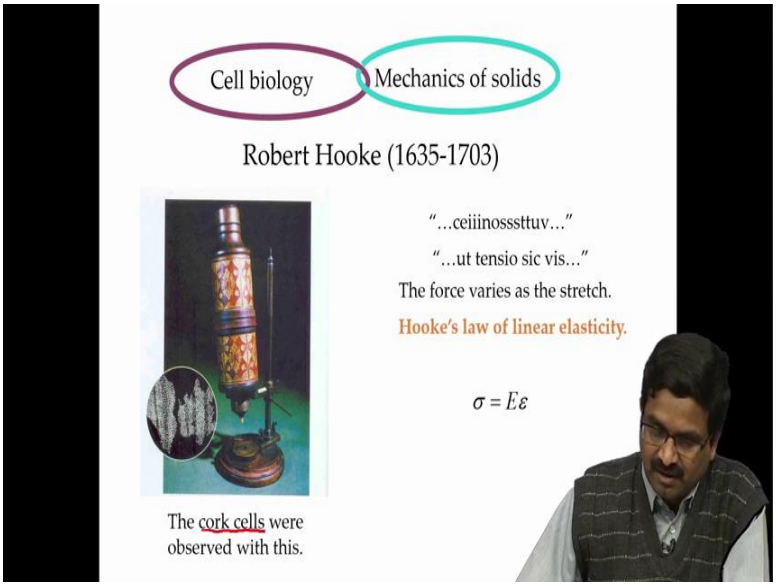


So, always start with this microscope image. To say that it was Robert Hooke, one of the pioneers in two fields cell biology and mechanics of solids because the Hooke's law that we talk about today is credited to Robert Hooke who said using an anagram in Latin "ut tension sic vis" which means the force varies as the stretch that is what he had observed.

He had also observed the cork cells under the microscope and realized that living organisms are made up of building blocks which are cells. As we know biological cells they are of the micron size.

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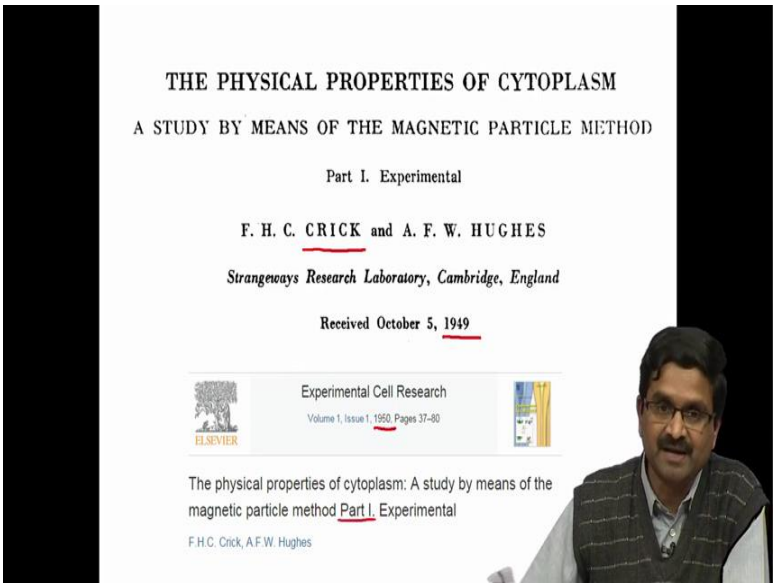


So, cell biology and mechanics were linked at their very inception. It is actually quite interesting today when we work on mechanical engineers work on biological cells and biology it is not at all surprising, because the very originate of a in a way from both fields cell biology and mechanics Robert Hooke had done that; one man. It is also very interesting to note that Francis Crick; the Crick and Watson fame, Watson-Crick fame in 1949 had published a paper in 1950 another paper. So, there are, received here and published there.

There are two parts. So, this is part one and part two; where we are talking about physical properties of cytoplasm. So, he is talking about using a mechanical method for probing biological cells. In fact, it is interesting this year 1959 to 49 because just a few years before he discovered along with Watson the double helix structures. He was interested in mechanics of cells so long ago.

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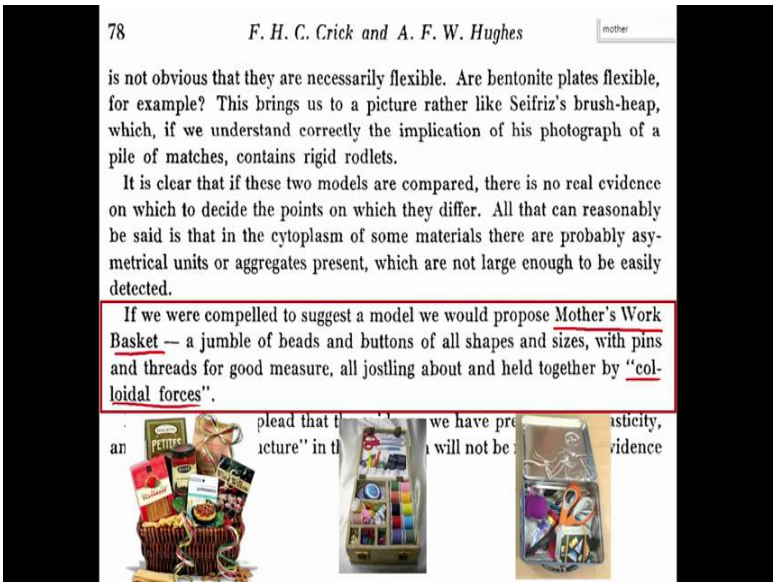


And we had one papers that are go back to 1938 and so forth as well. So, Crick's description of a biological cell is important as you listen to a mechanical engineer talking about biological cells. He talked about a cell as if it is a Mother's Work Basket in his time I guess mothers used to sew things and there where jumble of beads and buttons of all shapes and sizes and there are pins and there are this threads and so forth. Those are all jostling about inside the cell due to colloidal forces he himself put it under quotes.

So, basically cell is a complicated thing. And understanding it from mechanical viewpoint is what many people are doing under the name of or by mechanic sub cell or mechano biology of the cell.

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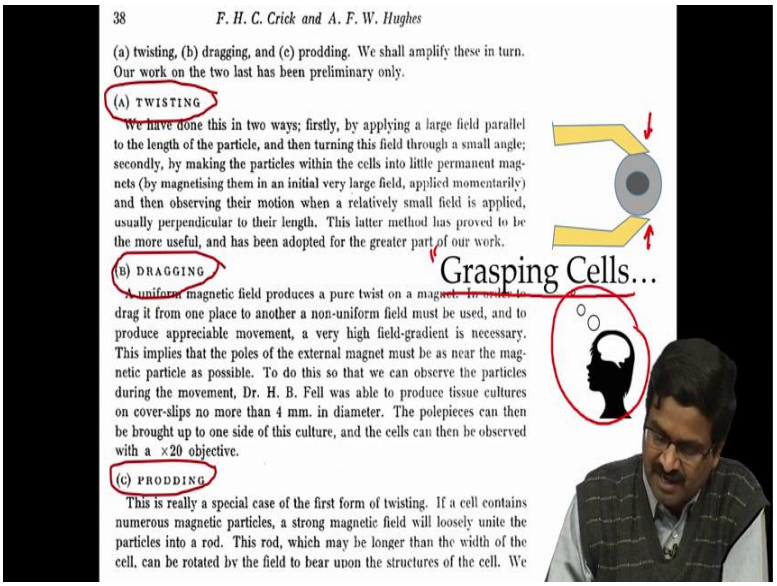


What is of importance to us now is that Crick had devised instruments for twisting, dragging and prodding cells in order to understand these are taken from his paper the (Refer Time: 04:23). So, when we say grasping cells we literally mean that we want to grasp it like a gripper, but what we actually mean is thinking about cells and understanding how cells behave from the viewpoint of mechanical; both are there in the word grasp now it has a fun is intended.

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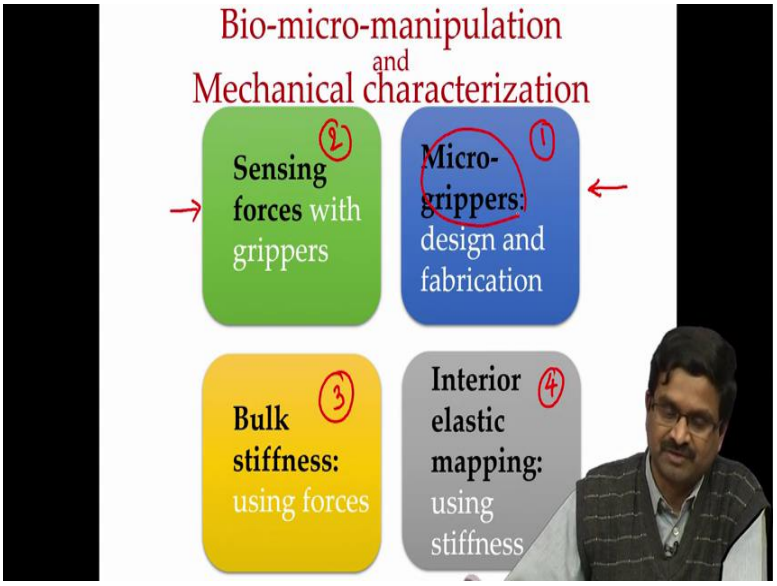

So, there are lot of things that are needed for this. First we need these miniature grippers that are what we will focus on in this lecture, but we also need to sense forces which also can be done using compliant mechanisms. Compliant mechanisms help in this one and also two. And then with these things we can do three, we can measure bulk stiffness. We can also measure their interior properties which is this four. So, compliant mechanisms play an important role in this particular field. You can manipulate cells in many ways, but there is an advantage with the compliant mechanisms when you do this grippers you do not use any other field; meaning that there is no electrical magnetic a Crick had used magneto twisting (Refer Time: 05:33) as it is called today.

So, you do not have any other energy field affecting the cells because, what all things affect a cell is not known people are still trying to figure out figure figuring that out. So, if you have a mechanical one you do not have interference with anything it is no thermal if you use laser tweezers there could be temperature changes in the cell. That might also make cell behave differently. So, here we are using purely mechanically and in what are environment of the cells.

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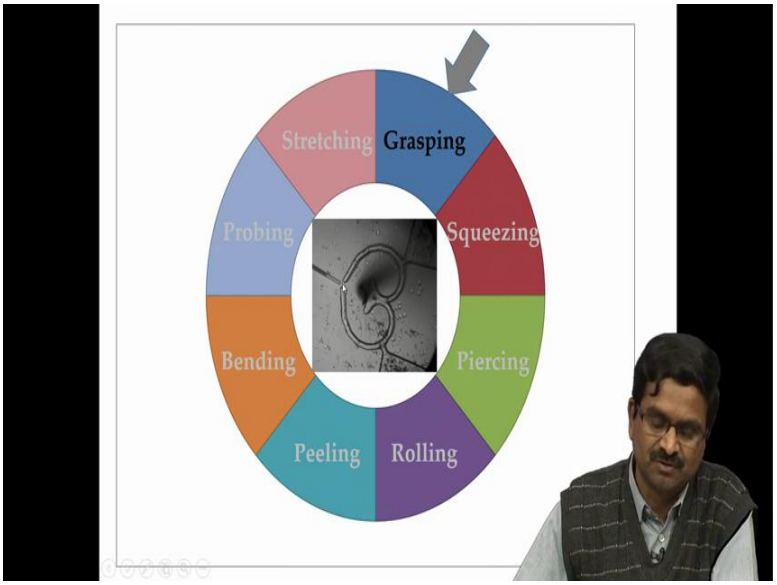


So, without going into the details first I am going to show you a few movies or video clippings of doing all kinds of these manipulations, grasping, squeezing, piercing, rolling, peeling, bending, probing, and stretching; so all the things just to get an updation for this. Again this lecture all the case study lectures have a lot more information in the

slides than what we have time to discuss all these. Just let us see what compliant mechanisms can do.

First is grasp; what you see here is a compliant mechanism. There are number of cells here these are MCF seven cells these are mammary gland cancerous cells there is a small pipette which is used only to position the cell and does not do anything there is a dark shade here that is the probe that is actually going to push this here. This is fixed here as well as there and this is made of SU-8 polymer and it can hold this single cell. And this is made of SU-8 and this dimension is about 5 or 7 microns the cell itself will be about the same size, so about 10 microns in size.

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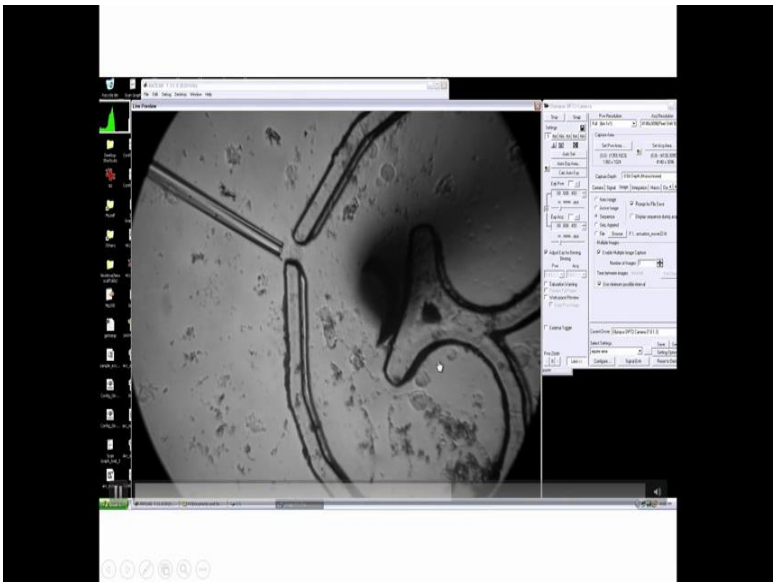

You can see that in the movie. So, this is just positioning it and this one is holding it and you will see when it comes into focus the cell actually being grasped and squeezed a little bit also. So, that is why the cell is. So, with this is only is there to position and it is able to grasp it and do this as this one input is there. So, we can do that now with compliant mechanisms.

And next thing is squeezing; this squeezing is really squeezing a lot as we will see.

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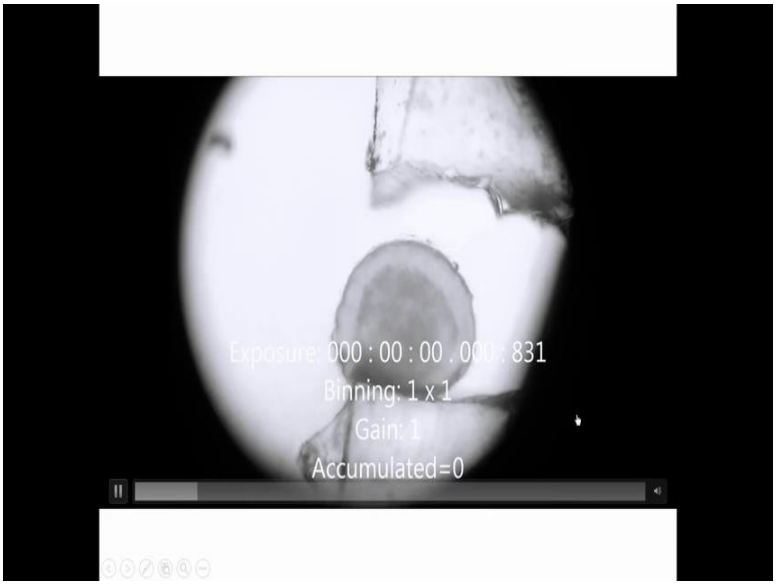


And these also done with compliant me grippers where you are going to see the jaws, it is actually squeezed it and let it relax real time, so it takes a while. So, you can see it when we play it again when you apply force somewhere else this compliant mechanism kind of squeezes it. So, it should play. Let us do this I think it has to go back it just squeezes and then it just recovers and stays there.

But you can also pierce and inject things into it; here we just calling it piercing because we are not injecting anything into the cell just to show that we can actually do this.

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And in fact, here it is a zebrafish embryo that you can also do with the single cells, with a pipette we are piercing it and a compliant mechanism is holding it in place while it is being done.

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And we can also roll a cell as we will be seeing in the next textures movie. We can actually make it roll as if it is in between your fingers. And number of mechanisms word designed, recently also one I showed in one of the previous lectures we can grasp and roll using one single or two input that are coordinated.

And you can peel a cell. It is a particular special type of cell where you can peel them off their substrate. And here you do not see the compliant mechanism, but what you do not see are these two probes to which a micro-Newton force sensor was attached which we will discuss in another case study.

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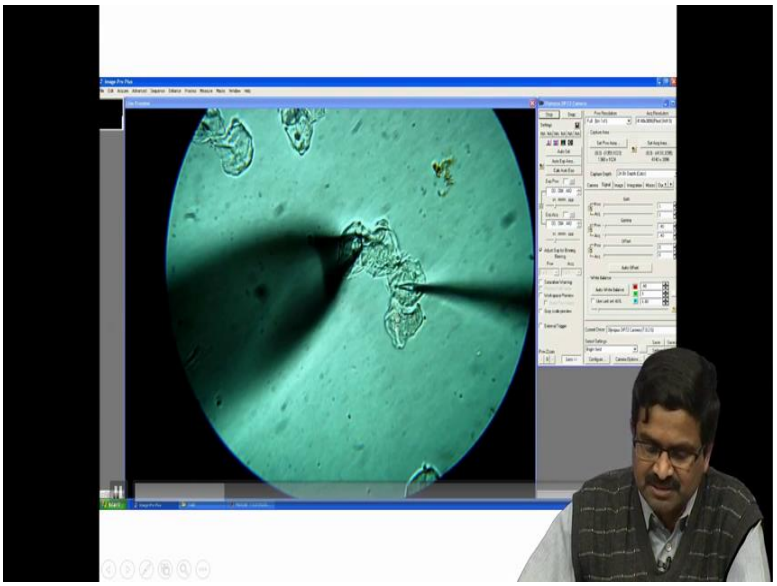

So, it is more of manipulation capability with the probes and the probes are attached to a compliant mechanism that measures forces. We can peel one cell which attached another one by just tearing them a part.

And you can also bend a cell. Most of the cell bending of a cell does not make a whole out of sense, but for some cells it does matter as we see in this video. These are particular type of cells they are very special type of cells where they are flat and you can actually bend it here. So, you can see this with probes, again probes are attached to the force sensors which are again compliant mechanisms, so it is a bent now.

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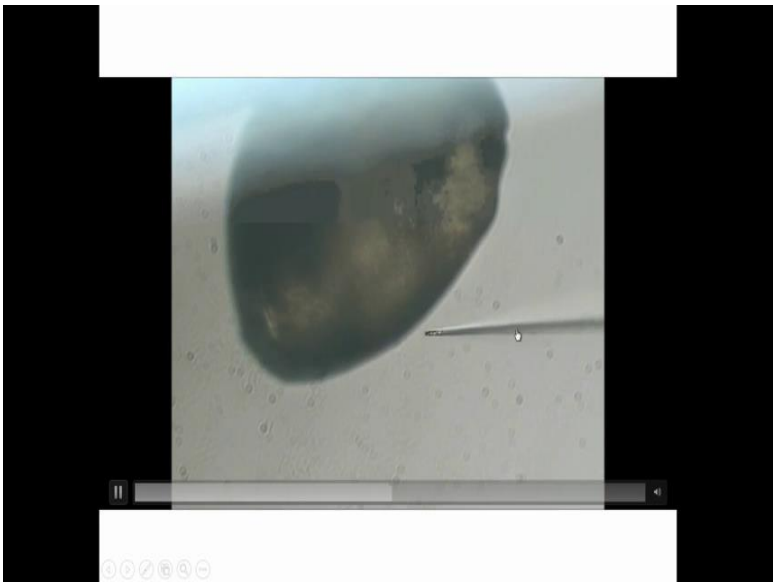

And you can probe it; so here you can see this needle that is probing is very flexible it is bending so much more compared to the cell itself and all these forces can be measured.

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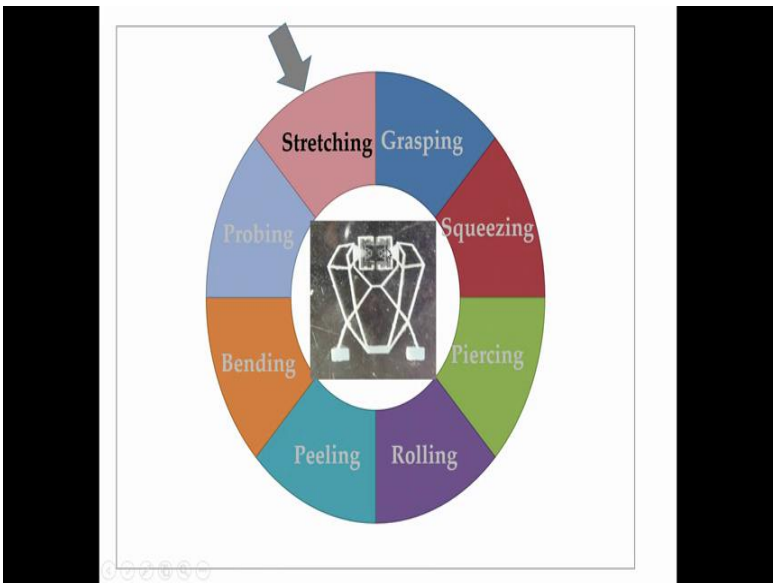


And stretching we had already seen. One point to notice here is that the material of this mechanism under one insight they are different. So, the reason is that if you use lithography and make the micro compliant mechanism here it is suppose to grasp something and then stretch you need to have very tiny beams. So, those tiny beams

making something this big is not possible. The process that makes big compliant mechanism cannot make this.

So, what we have ended up doing is in this composite compliant mechanism. So, to speak composite meaning the two of them are together not this made of composite materials. So, we have three d printed this, this white one and if the small one is SU-8 made lithographically made and put it into that. So, that is how it is done.

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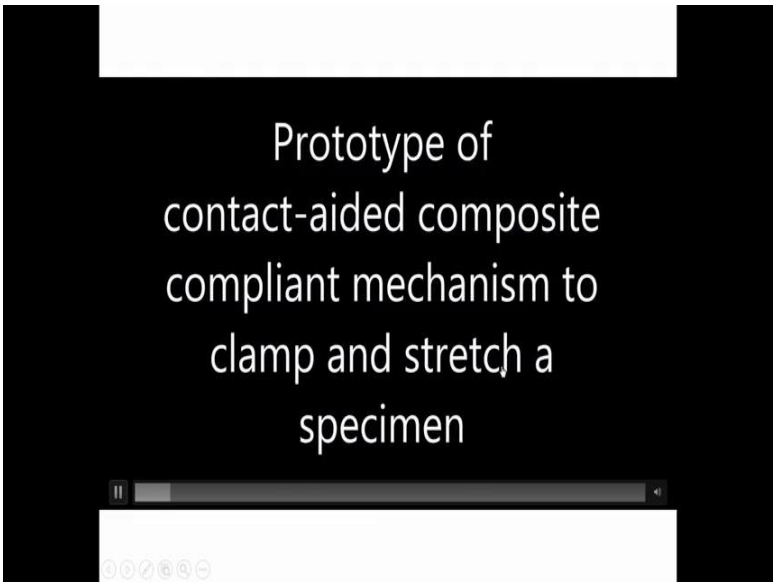


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And this video of this we have seen earlier how we can use a single input where you can open up things over here you put a little thing there it can grab it or also stretch it. So, this video shows that.

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So, how when these two (Refer Time: 11:53) also a contact aided compliant mechanism when these things touch that is when these things open up. It is all one single piece it opens up. Now you put something remove your force then it will hold it and keep it.

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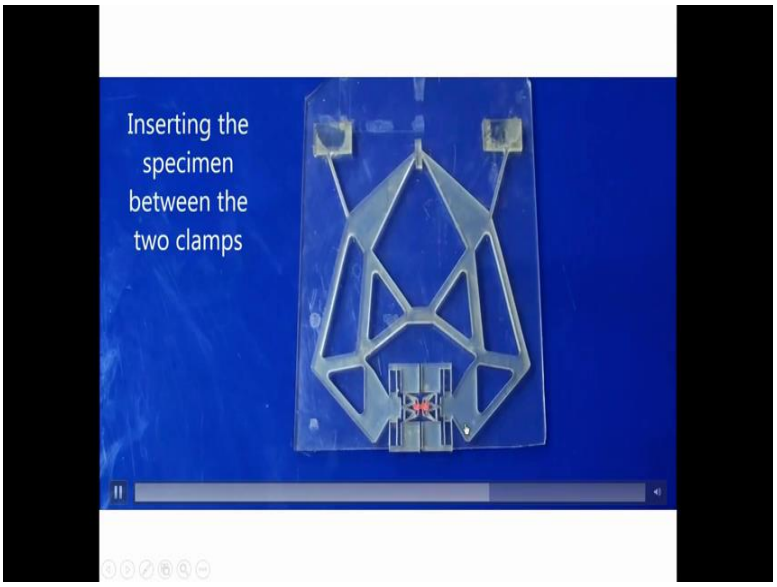


After that when you press it, it is going to actually stretch it; as you can see.

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So, once it is placed now when you pull it the other way this starts stretching. So, things were coming together when you push when you pull they go apart. So, we can actually in grab something and then stretch. Their micro version of this is of course as I said it has to be made of two parts.

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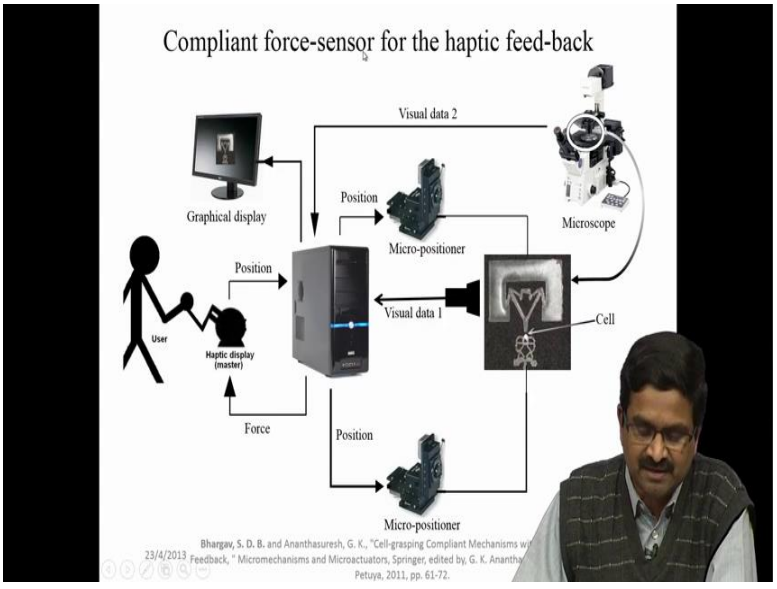


With all of these things force sensing can also be done compliant mechanism; not only manipulation but also force sensing which we will discuss in another lecture. But what we will focus on here, in fact this is the force sensor compliant mechanism. There is a

compliant that grabs the cell and this one whatever little force is there it will amplify the displacement over there which you measure using a digital microscope and you have a force sensor as well.

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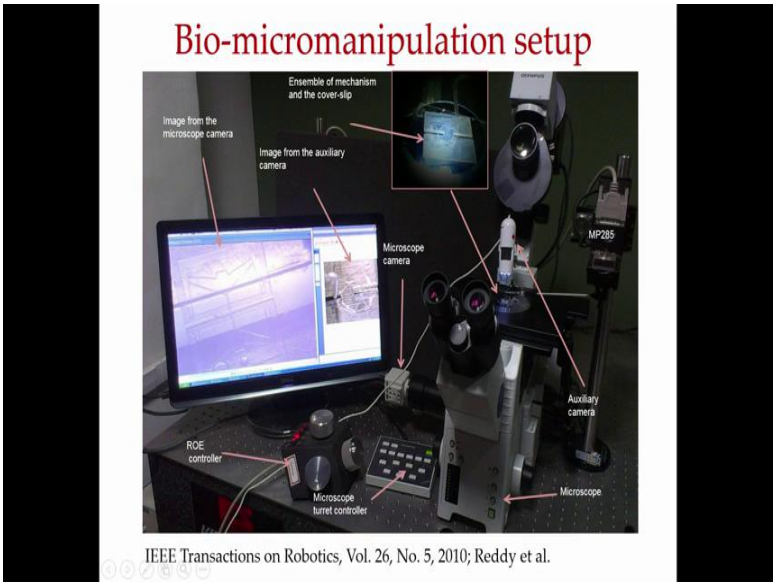


This is a set up in our laboratory. This is a digital microscope that measures the output displacement and gives us the force, while compliant mechanisms are actually manipulating the biological cell

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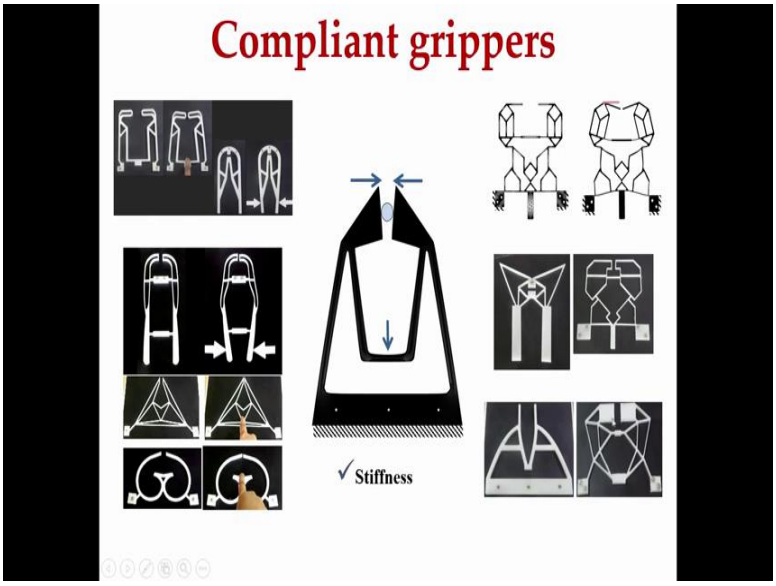

If we look at the design aspect; we looked at a number of grippers and each gripper has it is own characteristic. If you see in fact the other day when we looked at our database there were two dozen or so grippers in our collection. All of them have we saw this gripper just now holding a cancer cell here; best cancer cell and these are lot of other ones. So, this is something that we just saw in another movie when this will come together. In this empty space we put DACM's so we can measure the force as well.

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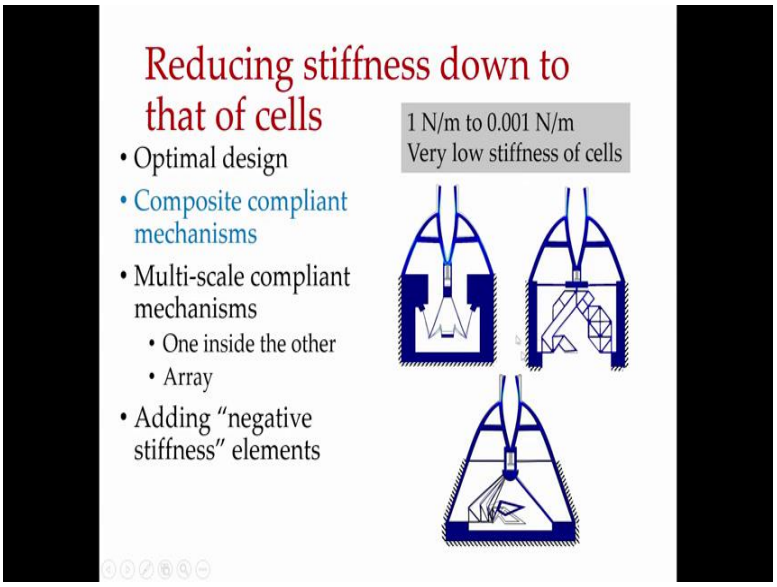


And this reducing the stiffness down to the stiffness of the cell which can vary anywhere from 1 Newton per meter all the way to 1 milli Newton per meter; so it is a very very low stiffness that biological cells have. So, if I want to handle them gently without causing damage to them you have to have this range of stiffness to your mechanisms also that is why lots of tricks were played out one is just optimal design first you make optimization topology shape or whatever and then composite you put one inside the other.

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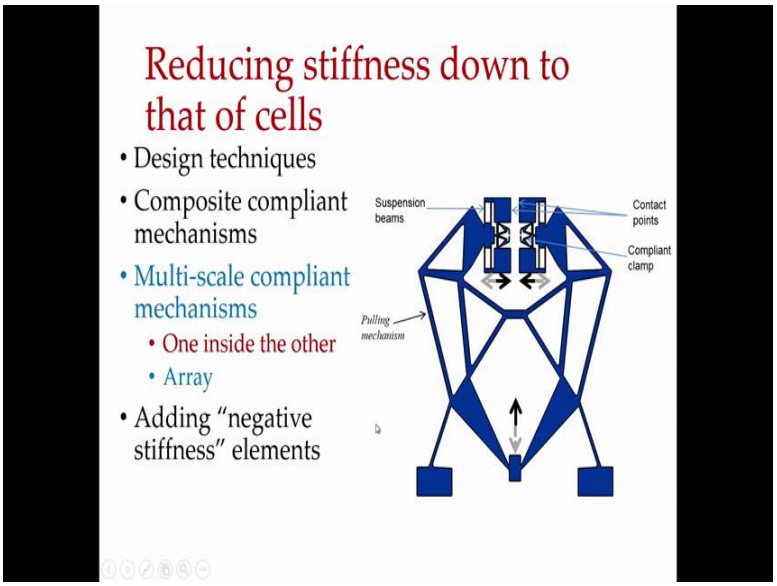


And you also add occasionally we had tried to add negative stiffness elements by that what I mean I will show a picture later. So, one inside the other as we just saw definitely makes a lot of sense.

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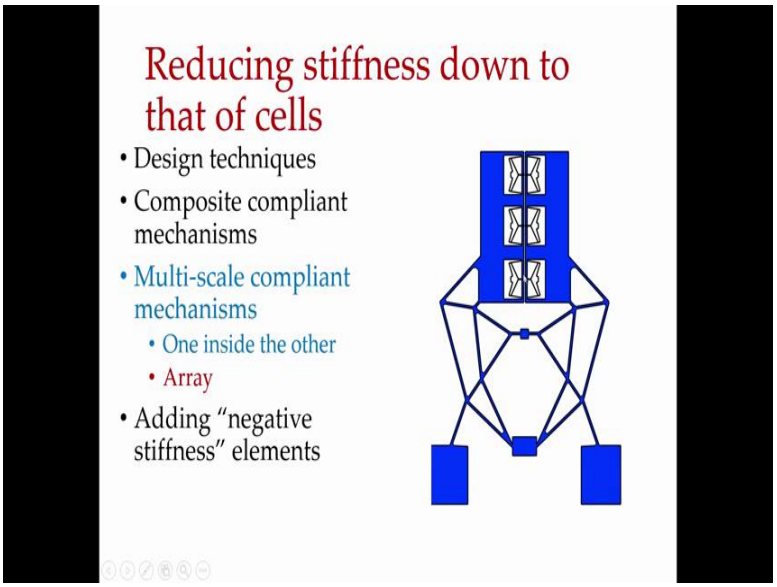


And we can put an array of them. So, not one many cells can be grasped with the same time.

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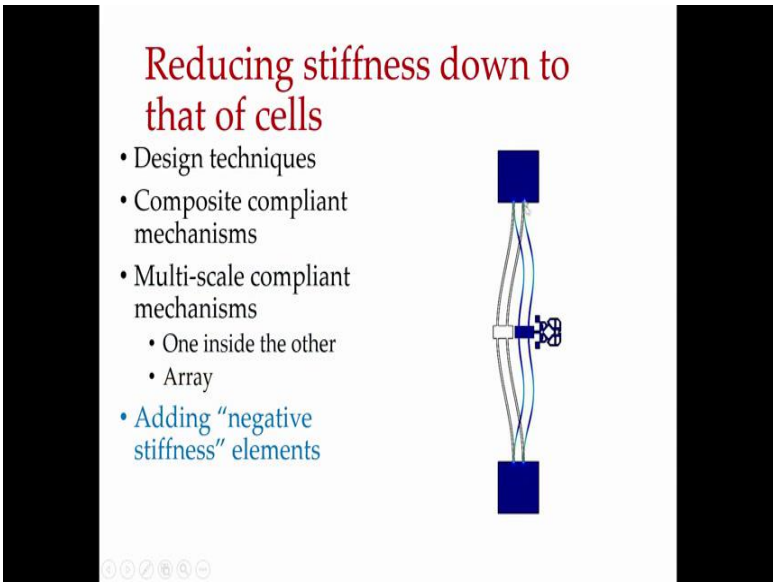


Negative stiffness is we have talked about bistable elements. Bistable elements over a small range they have negative stiffness. If we attach that preloaded along with the gripper then the gripper overall has some positive stiffness. This has negative stiffness over a small range you put them in parallel overall the stiffness would reduce; that is the idea we will reduce by even order of magnitude, so to get down to that level.

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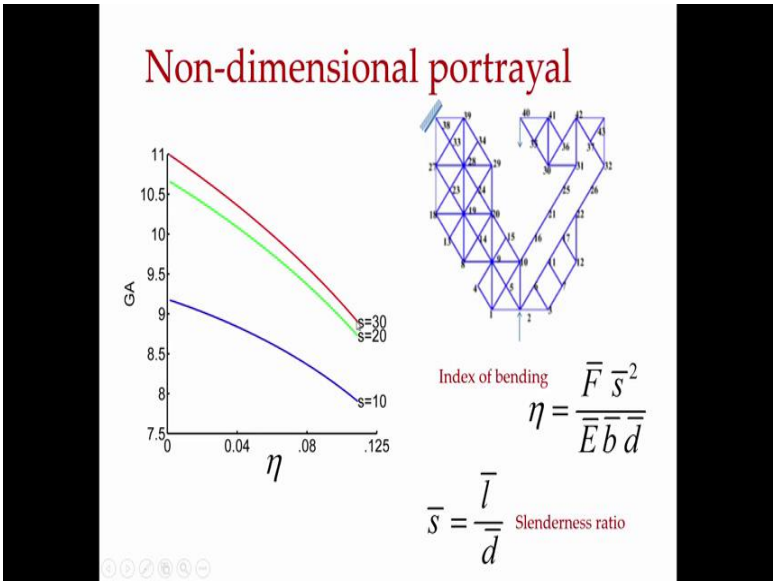

And we also use these non-dimensional maps to understand the capability of geometric advantage, mechanical advantage and the force requires stresses and so forth in doing this.

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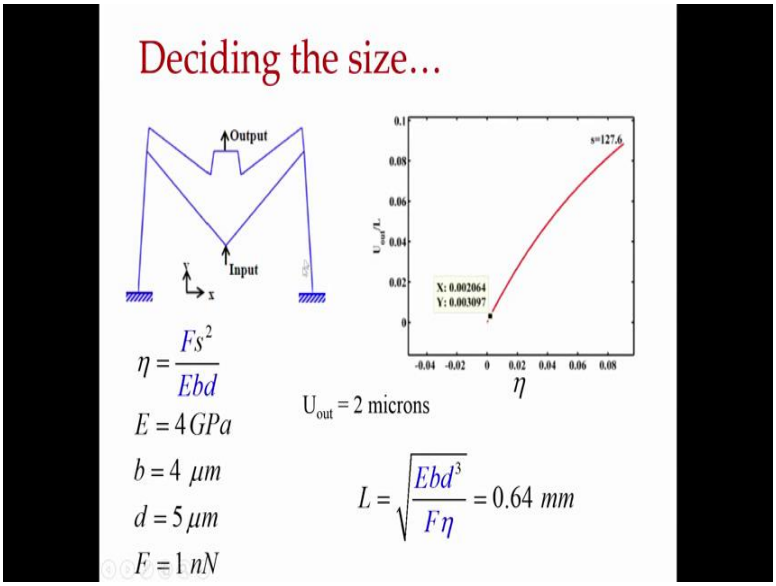


And sometimes we can use these maps to decide the size as we had discussed once. So, what should be the size of this? So, we have the characteristic length L; let say this one is L from here to here how much that should be in this case it (Refer Time: 15:38) be 640 microns based on your fabrication capability this is the thickness, b in this case is out of plane thickness, d is in plane width that is 5 microns. Somebody says with fabrication they can only make 5 micron beams we can put that if you want to measure 1 nano Newton force and from this map you can get this eta and assume in this case it is SU-8 materials 4 Giga Pascal's Young's modulus. If you want to have at least two microns to see under microscope measuring this displacement smaller than that if you think it is difficult. 1 nano Newton giving the out output displacement 2 microns it says that size should be 640 microns.

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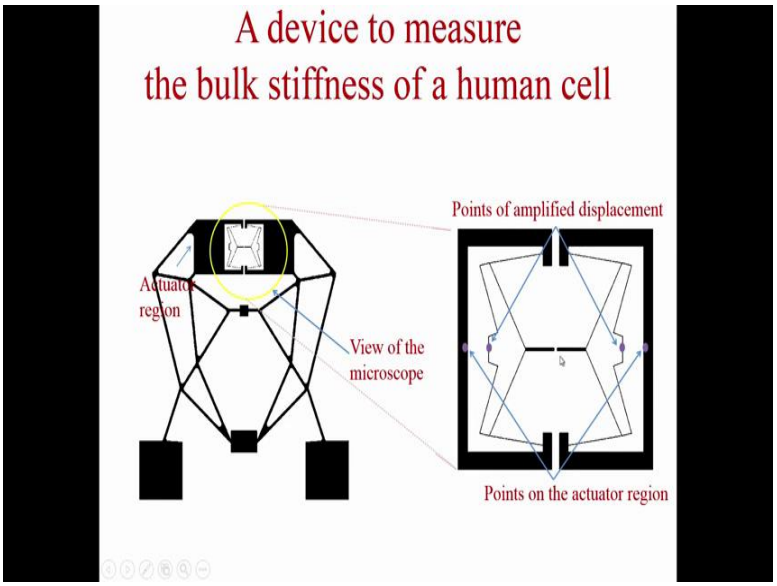


Accordingly you can design and putting one inside the other we already talked about where you have one mechanism that gives the parallel jaw motion and within that we put two DACM's. And this is where the cell is going to go. So, this tiny space is where the cell is going to go these beams are only 5 microns wide. And the cell as we can see that is also a few microns.

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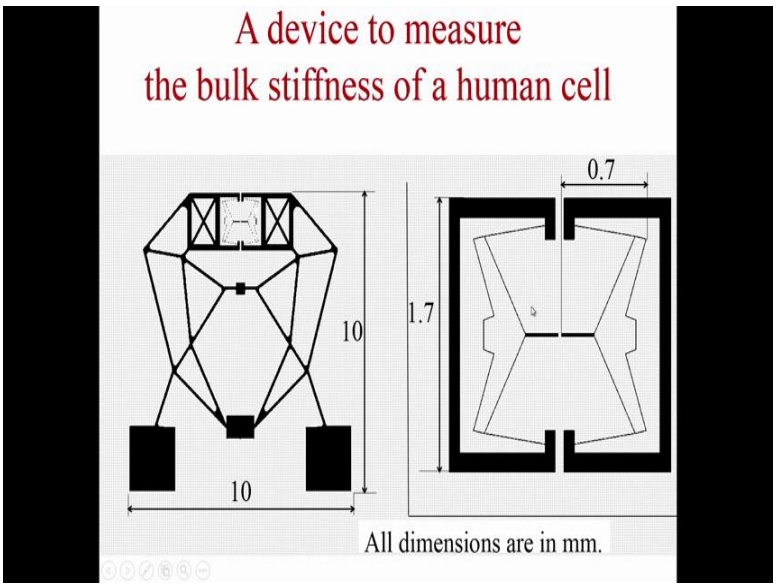


And this 1 is 10 millimeters by 10 millimeters, this big mechanism. Within that there is only 1.7 by about 1.7 so about 2 millimeters thing and these things are very small. They

do not break we make sure that stress are small and range of displacement here is only to squeeze by about 10 microns.

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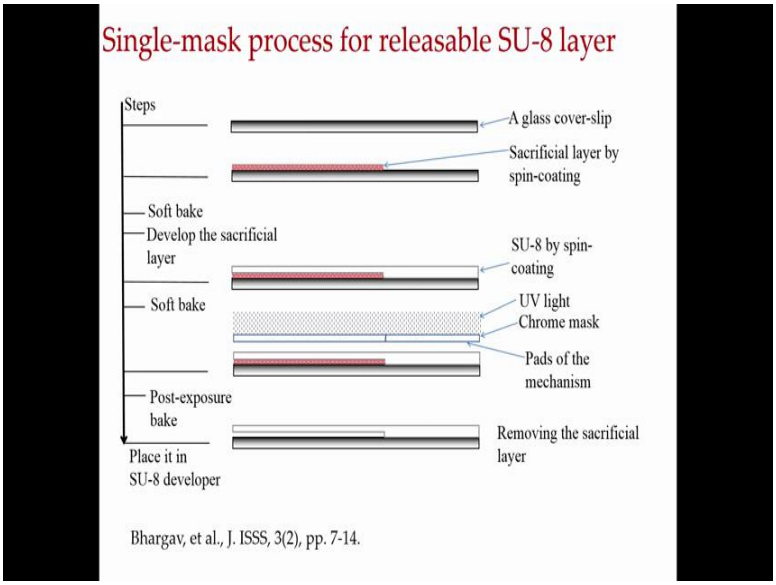


There is a process that was developed that is also very important. And what material we are using here we are using SU-8 and then lot more difficulties in this. It is not just the designing compliant mechanism when you try to put it in water sometime the buoyancy force makes them go out up, while the cells are sitting there these things will go up like this. So, we have to play with a lot of parameters even in fabrication to make this.

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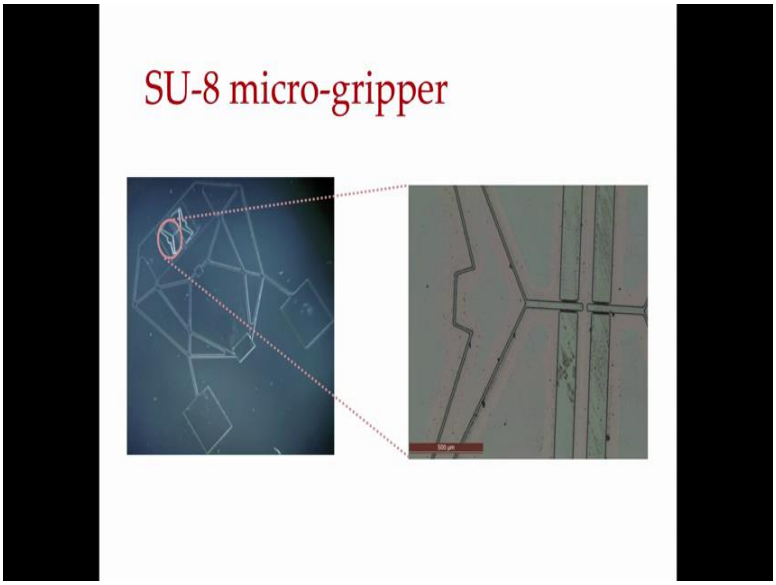

Finally, when we do that we have the mechanism and this little mechanism over there that is where the cell would go and grasp. So, a compliant mechanism can be used to manipulate a biological cell in many ways. So whatever you think of and including tearing now we can actually tear a cell apart with mechanical tools. One can use this beams, but then compliant mechanisms themselves are made up of beam segments. So, we have to arrange them in a way that the manipulation that we are interested is obtained here.

And in the next case study we will see how compliant mechanisms can be used to measure force as well.

Thank you.