Introduction to Mechanobiology
Prof. Shamik Sen
Department of Bioscience & Bioengineering
Indian Institute of Technology, Bombay

Week - 01
Lecture - 01
Need to study Mechanobiology

Hello, and welcome to our first lecture of the course Introduction to Mechanobiology. So, what is mechanobiology? As the name suggests you have a mechano and a biology component. Mechano probably have indications that there is some amount of mechanics in biology.

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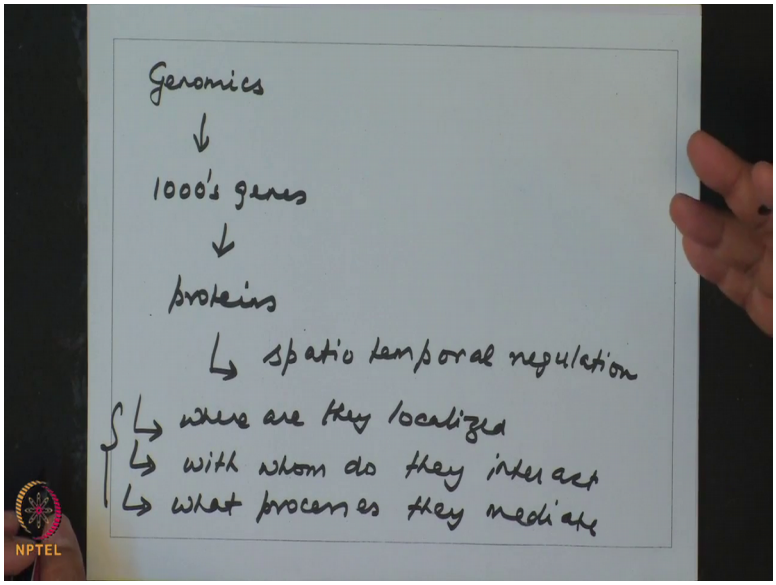

So, if you have to break down mechanobiology I can break it into two terms mechanics plus biology. So, this might mean an approach where you try to understand how physics or mechanics is relevant to biology or how you can make use of physics to engineer biology for different applications.

So, why is mechanics important in biology? So, since the dawn of genomics you have access to information about thousands of genes which encode for proteins, but these proteins are not always present in cells and you have a spatio temporal regulation. So, where they exist, where are they localized, with whom do they interact and what

processes they mediate are all important to reconstruct our picture of how these proteins might be participating in various cellular processes ok.

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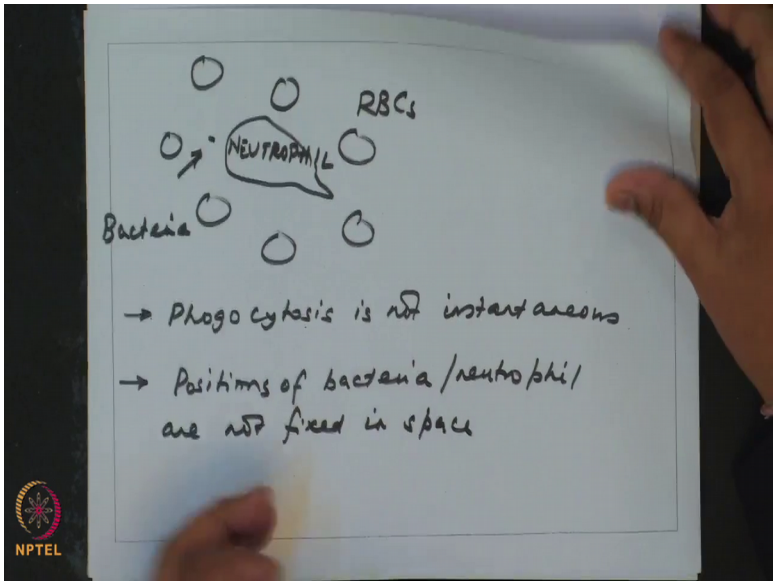

So, let us take a simple example you know from your immunology studies, that you have neutrophils which actually eat up foreign bodies' right like bacteria. So, if you go to YouTube and you search for videos of it is a neutrophil eating bacteria, you will come across various movies keeled come across various movies you start any one of them. So, what you would find is pictures somewhat like this you have a neutrophil you have a tiny bacteria and surrounded by these are RBCs, this is your neutrophil and this is your bacteria.

So, if you play the movie you will see that this phagocytosis is not instantaneous. So, what you will find in these movies is neither the position of the bacteria or the neutrophil positions of bacteria are not fixed in space rather what you will find this is the bacteria tries to escape and the neutrophil chases the bacteria.

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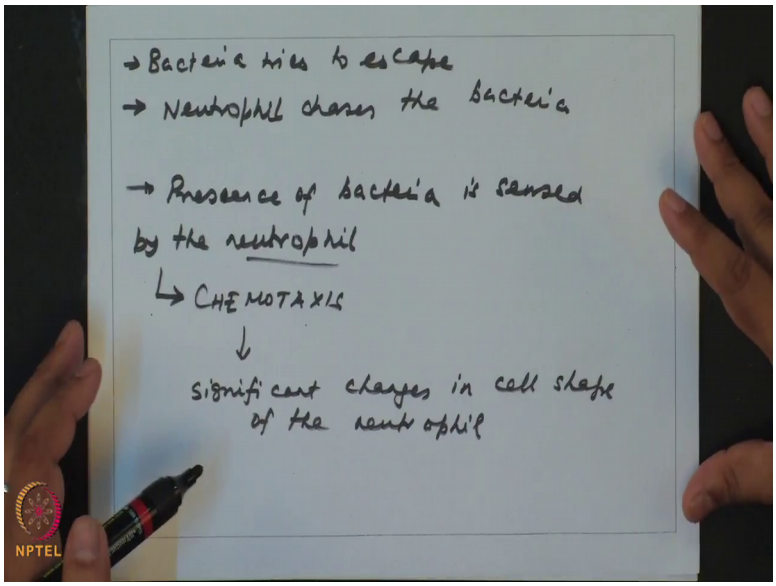

So, the process literally in acts like a cop chasing a thief ok. So, how is this process we happening it turns out that the presence of bacteria is sensed by the neutrophil and this induces chemotaxis. So, the bacteria actually sensed out some chemokines which are sensed by the neutrophil and the neutrophil moves in the direction of the chemical field and. So, this chemotaxis involves significant changes in cell shape of the neutrophil. So, there is lot of dynamics or mechanics at play which is participating in the biological process at well. So, in a nutshell your mechanobiology, it us an interdisciplinary field ok.

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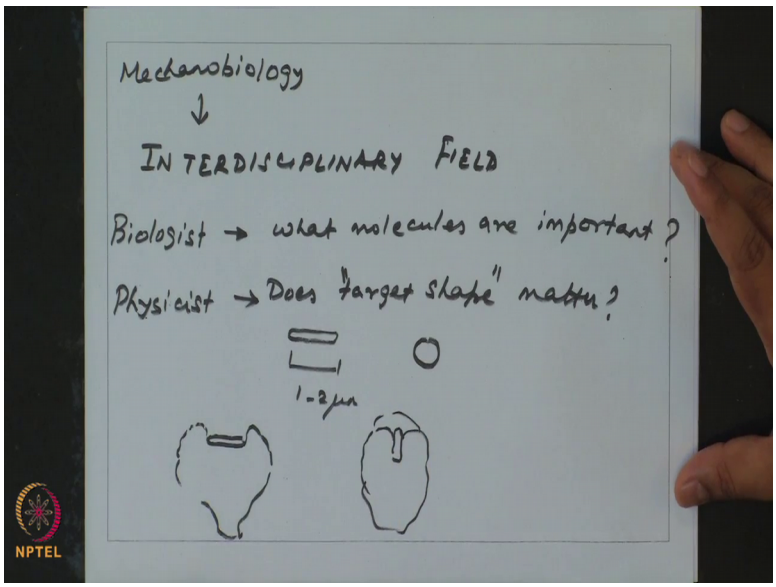

So, for a traditional biologist the question of relevance might be what molecules are at play, but a physicist might ask the question that instead of a bacterium which has a shape like this you typically have one to two microns in length if the target size was round. The physicist might be interested in asking does target shape matter and one would imagine that it does matter. Because if you look at the phagocytosis long time you would see if this is the bacteria the phagocyte the neutrophil does not eat up the bacteria in this configuration, rather you have a configuration like this in which the neutrophil sends out it covers and eventually it gulps it ok.

So, the process in which target shape comes into picture during the process of phagocytosis is of course, interesting.

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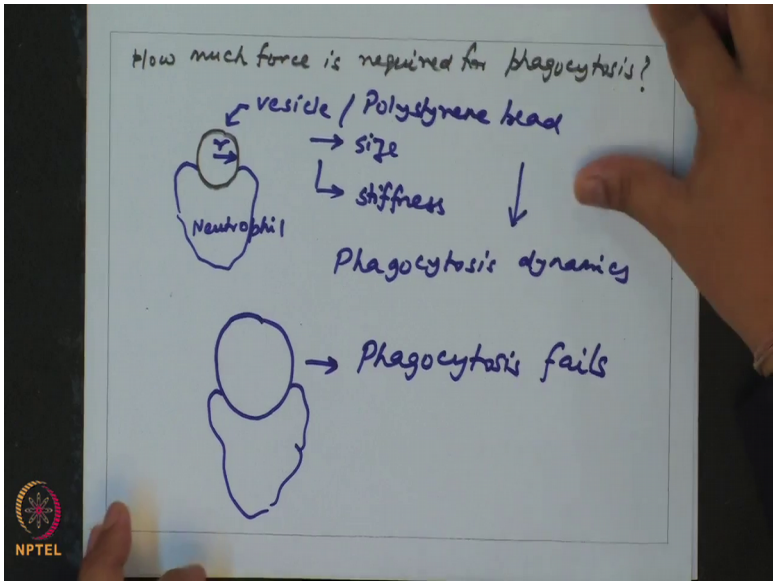

You might also ask that how much force is required for phagocytosis. So, if you do an experiment in which you take a vesicle and you track its phagocytosis dynamics by a neutrophil. So, you will understand that depending on the size of the vesicle. So, the size of the vesicle as well as its stiffness in other words instead of a vesicle if you had a polystyrene bead, the phagocytosis dynamics would have been different and experiments have been done. Where if you take a bead which is huge at some point the neutrophil actually gives up, your phagocytosis fails you might also ask that what is the effect of confinement.

What do a mean by confinement?

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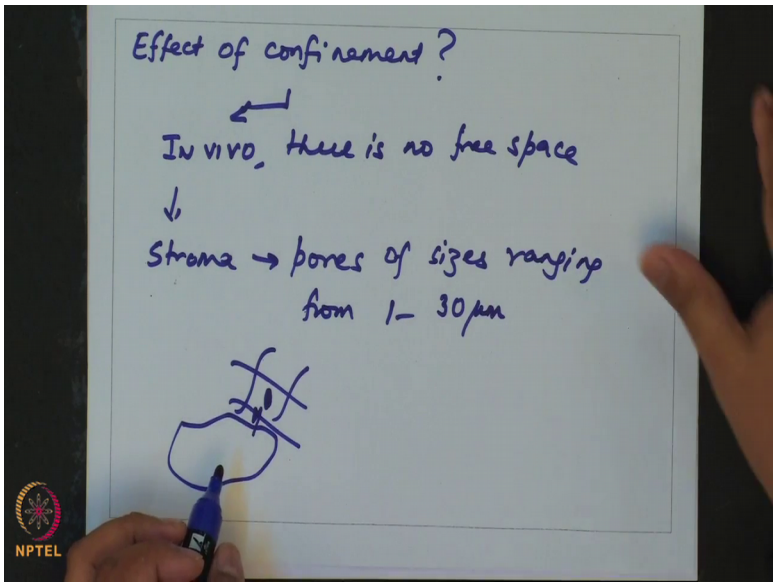

So, in vivo there is no empty space, the same process will happen in the presence of in inside in some ecm or the stroma which has pores of sizes ranging from 1 to 30 microns. So, how the process will happen when the cell is actually tracking the bacteria through this matrix where the cell has to actually squeeze through this confinement. One might also be interested in asking that how is this chemotaxis unfolding ok.

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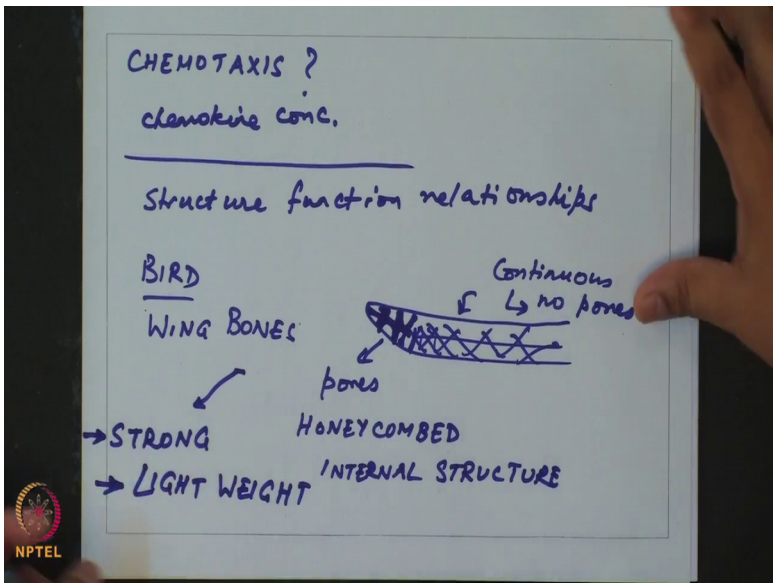

So, how does the chemokine concentration matter in terms of how fast it takes the process to complete, you can also make use of mechanobiology for understanding

structure function relationships. If you take the example of a bird and you look at its wing bones, you would have a structure where which is. So, this portion of the bone is continuous in other words there is no pores, but the way I have drawn here you have pores. So, what or rather you have a honeycombed structure. So, what the bird is trying to achieve is that the wing bones must be strong another same time light weight ok.

So, two objectives which are counted to each other typically we associate strong with more material, but if the material if you have too much of the material the material it might be strong but it is very heavy, which will really compromise the ability of the bird to fly. So, this is another example, but structure and function are intimately linked.

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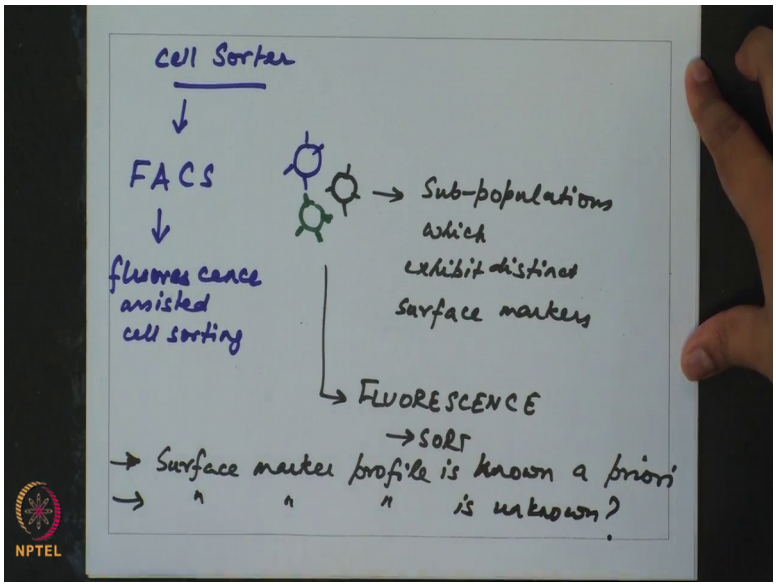

If you think of another application I will talk about a cell sorter, why is the cell sorter? So, what does the cell sorter do? So, you have heard of FACS right fluorescence assisted cell sorting ok.

So, what FACS does is if you have two populations of cells, where the surface markers are different, you can label these individual subpopulations which exhibit distinct surface markers. So, I can make use of fluorescence to sort these populations to sort; however, this process will work if I know the surface marker profile, but what if you surface marker profile is unknown, instead what you perhaps have is information pertaining to their deformability.

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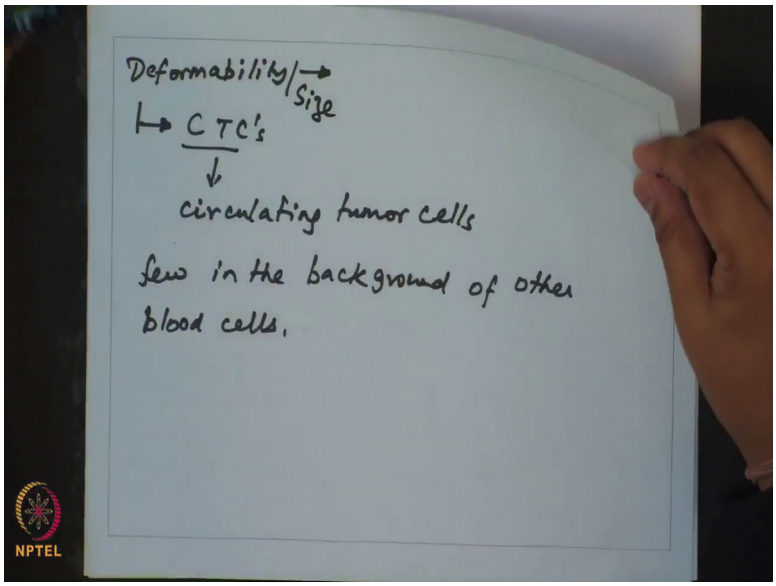

So, as an example we know in that in cancer. So, there is a population of cells call CTCs. So, this is short form for circulating tumor cells now CTCs are very few. It is a very few in the background of other blood cells. So, how do you isolate these circulating tumor cells is the question. So, one approach which occurs which lot of researchers have taken you used to use a strategy where populations are separated based on that deformability or deformability or size. So, let say I have a devise.

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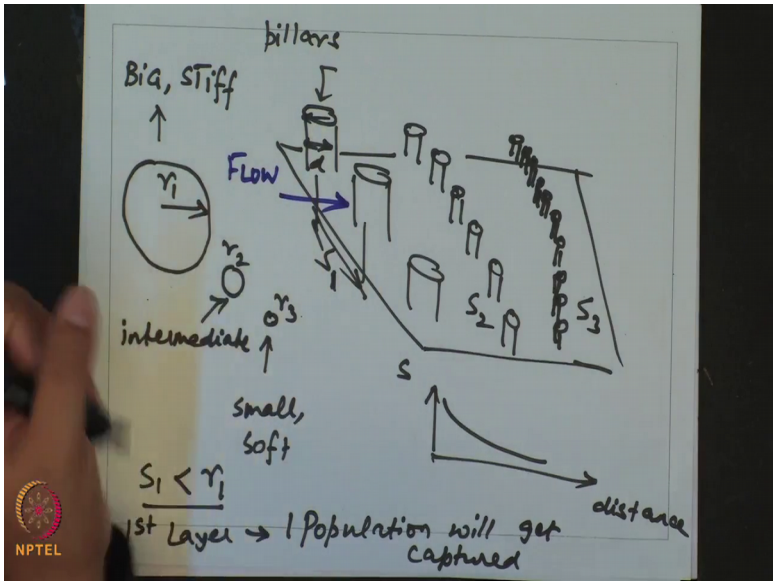

So, you have a device. So, these are pillars and what you are changing is the size the diameter of these pillars d and the spacing between this pillars s. So, the spacing decreases; if I were to draw the spacing as you go ahead your spacing decreases as a function of distance you are spacing decreases. So, if you have two cells imagine if two big populations of cells. So, there is big and they are stiff, it means they are not much deformable and this is small and soft and you have another population intermediate both in terms of size and in terms of stiffness ok.

So, you can use these devices where you flow them horizontally through these devices. So, you would appreciate that if this size. So, let us say these radii I are r 1, r 2 and r 3. So, you have three layers. So, if s 1 is less than r 1 and this cell is stiff then in the first layer one population will get captured; similarly in the second layer you will have this intermediate population which might get captured second or third layer and the smallest ones will flow out. So, this is a way of separating multiple populations which have sub populations in them, if these deformabilities or size are practically different ok.

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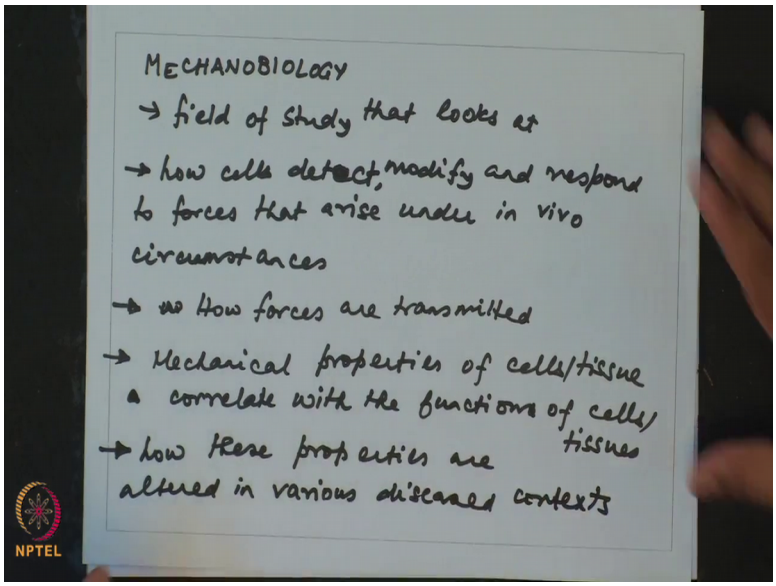

So, to summarize mechanobiology is a field of study that looks how cells detect, modify, and respond to forces that arise under in vivo circumstances. How forces are transmitted and how mechanical properties of cells and tissues correlate with the function with the function of tissues cells and tissues, and how these properties are altered in various diseased contexts ok.

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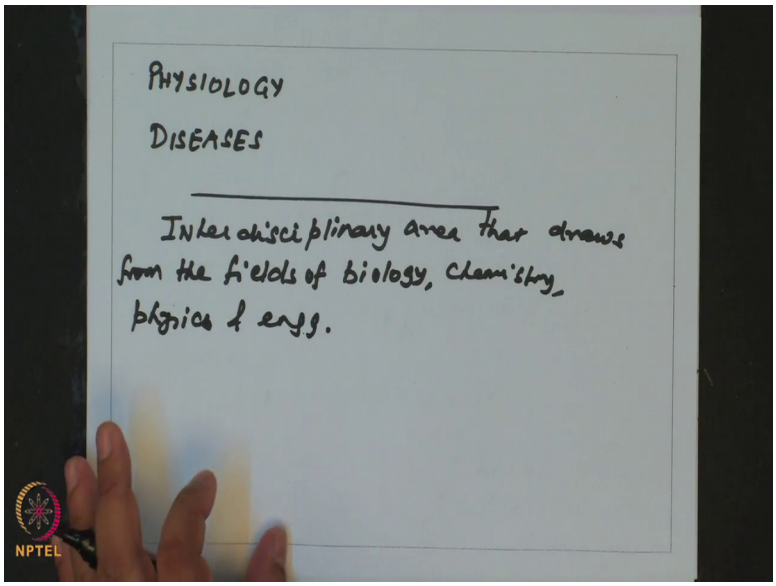

So, this field is relevant to both physiology as well as diseases and it this is an overall is an interdisciplinary area that draws from the fields of biology, chemistry, physics and engineering. So, in terms of course what will you learn? So, we will focus our focus will be on biophysical and bioengineering aspects of mechano transduction.

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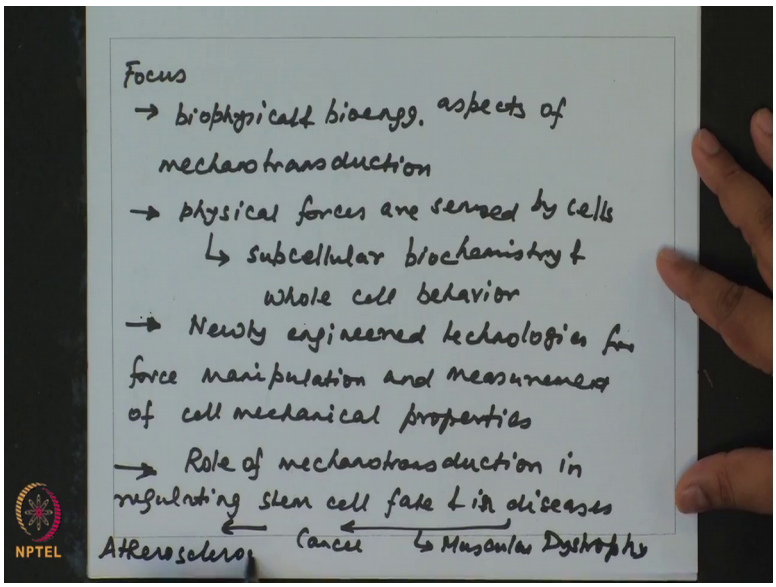

So, I will discuss how physical forces are sensed by cells and how it alters sub cellular biochemistry, and whole cell behavior. We will also discuss about newly engineered technologies for force manipulation and measurement of cell mechanical properties, and

we will discuss the role of mechano transaction in regulating stem cell fate and in diseases. On the disease will discuss about cancer muscular dystrophy and athero sclerosis as three examples of this course is research oriented.

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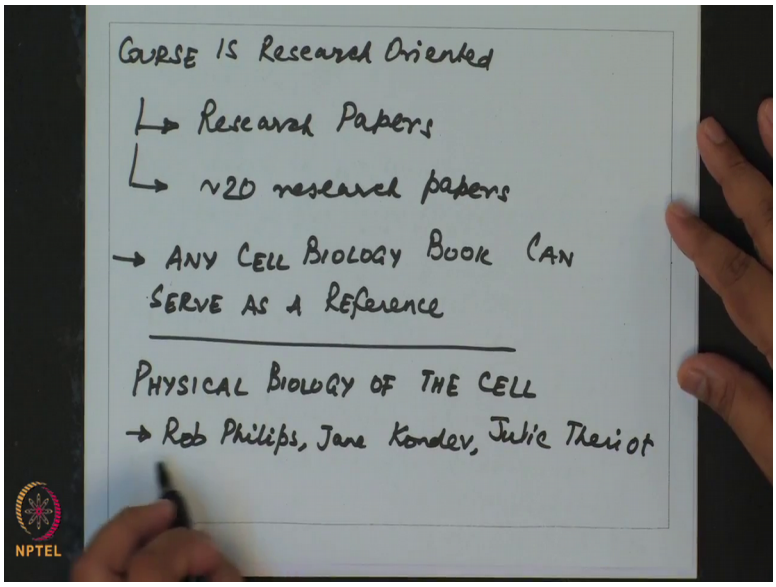

So, I would like to reemphasize the course is very research oriented. So, most of the course material will come from research papers that you will have to download and read. So, over the course over the entire course you will probably read order 20 research papers and any cell biology book, can serve as a reference. So, for example, bruce alberts a car or loodish any of these, I would also like to give the reference of some of the more recent biology books which have been written one of from a more physics point of view, one of this is physical biology of the cell by Rob Philips Kondev and Julie Theriot.

So, this is a very good reference book in terms of evaluation.

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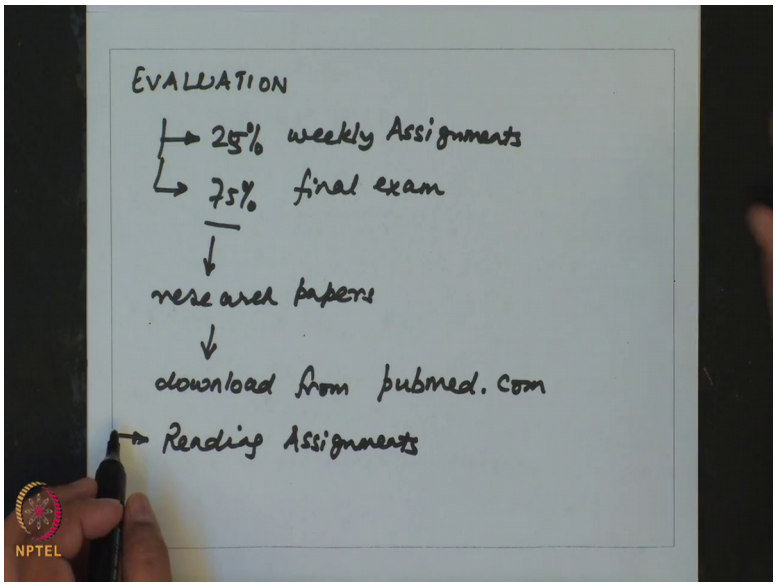

You have 25 percent from weekly assignments and the rif 75 percent from the final exam. Again most of the questions for the final exam will be based on the research papers.

So, I would reemphasize that if you do not read the research papers if you do not find time to read the research papers very soon you will not be able to follow the course. So, most of it would be research papers, you will have to download most of these research papers pubmed dot com. So, as we go forward at the end of every lecture I will give you reading assignments. So, these reading assignments are will be from multiple research papers.

With that I thank you for your attention, and I look forward to teaching you about and introducing you to the field of mechanobiology.

Thank you.