Microfluidics

Dr. Ashis Kumar Sen
Department of Mechanical Engineering
Indian Institute of Technology - Madras

Lecture - 01
Introduction and Scaling

Welcome to this course on Microfluidics, from the title micro and fluidics intuitively you may think that this is fluid mechanics that we know at microscale or in microchannel, well in some situation this may be true, but in many situations this may not be applicable. For example, if you consider flow between two parallel plates separated by 1 micron distance, and if you consider that the fluid is liquid.

Then we can go ahead and apply the governing equations and the boundary conditions that we know from fluid mechanics to obtain the flow solution, but if the fluid between the plates is gas, then use of you know the equations and boundary conditions that we know are questionable. So you know in microscale many flow situations, we need to modify the boundary conditions or modify the governing equations and the entire approach could be different okay.

So what happens that microscale is there is a modification of different forces that are involved, for example surface forces like surface tension become very dominant, and this is because of the high surface to volume ratio at microchannel. And the volume forces or the body forces like the weight of the fluid becomes almost negligible okay, and the modification of these forces bring an interesting and unique effects that are only realizable in microscale flows.

To give you another example of how microscale flow is different from that of microscale, if you consider let us say mixing of two fluids at microscale we know that if you increase the Reynolds number of the flow you know the two fluids will talk to each other better, and the mixing will be more effective. At micro scale in small channels exactly the reverse happens, because in micro channels the mixing is diffusion based.

And here if you increase the Reynolds number the diffusion time scale goes down, so the mixing becomes less effective as we increase the Reynolds number. Similarly, there are some special effects like a electroosmosis, electrophoresis, diaelectrophoresis and these effects are only realizable at microscale, at microscale such effects are almost negligible, you know this new and unique effects.

And combined with the modification of different forces that are involved bring in you know unique characteristic to microscale flows and that can be exploited to design and develop microfluidic devices for different applications, for healthcare diagnostics, for chemical and biological applications, for drug delivery and drug discovery, and many more different applications are possible.

In this particular course our focus would be to understand the fundamentals and the principles of fluid flows at microscale, we would also look at how we can design different you know microfluidic components, how we can analyze them. But we will restrict our discussion to the component level microfluidics, towards the end we will talk about few applications of microfluidics where we would bring in different microfluidic components to build microfluidics systems.

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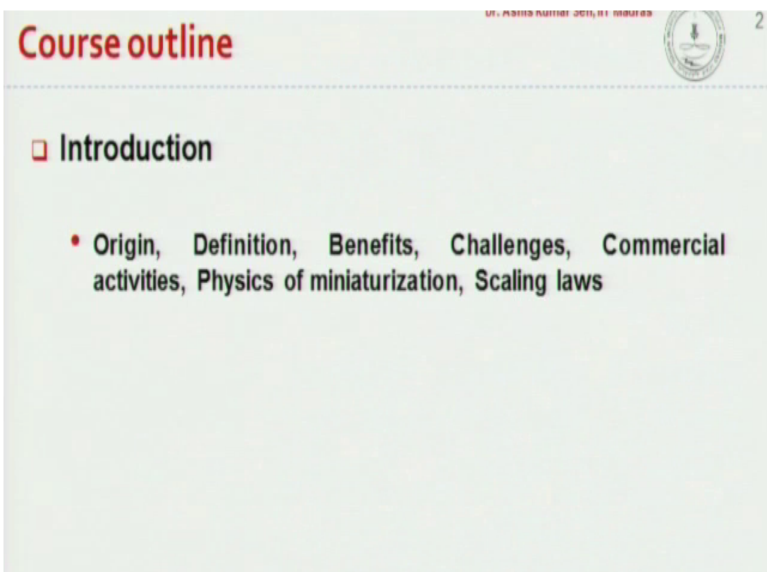

So with that let us look at the course outline. So we would first start by talking about the origin of the microfluidics, how microfluidics evolved, we will define what microfluidic is, we will talk about some of the benefits and challenges in microfluidics, and look at some of the commercial activities that are going on in microfluidics. Then we will look at the Physics of miniaturization as we reduce the length scale, how the physics is going to be modified, and we will discuss that in the context of scaling laws.

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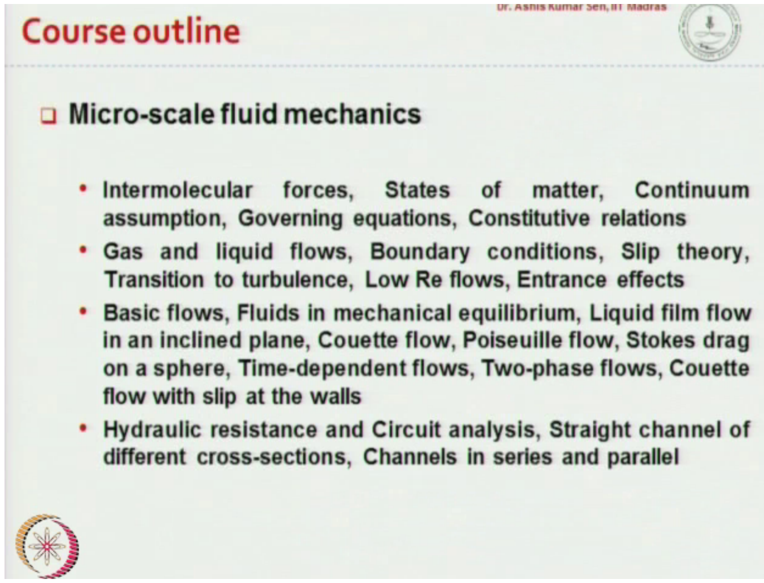

In the next chapter, we would talk about fluid mechanics in micro scale or in microchannels, here we will be talking about you know the intermolecular forces, the forces between molecules, and how that can help us understand the different states of matter solid, liquid and gas. We will talk about the continuum theory, and then discuss the governing equations and constitutive relations for gas and liquid flows.

We will discuss you know the boundary conditions both for liquid and gases. And here we discuss the slip theory, then we will go about the transition to turbulent, how flow can transit from laminar to turbulent, and we will also discuss the low Reynolds number flows and entrance effects. Then we would discuss some of the basic flows and we will try to obtain the solutions, and we will take very simple case fluids in mechanical equilibrium.

Then we talked about liquid fluid flow in an inclined plane, and then we will go over Couette flow, Poiseuille flow and then discuss stokes drag on a sphere. We would also briefly cover about the time dependent flows and two face flows, and then we would consider Couette flow with slip at the walls. Then we would talk about hydraulic resistance and we would use that to analyze basic circuits, and we will discuss that in the context of straight channels of different sections, and we will talk about channels in series and parallel.

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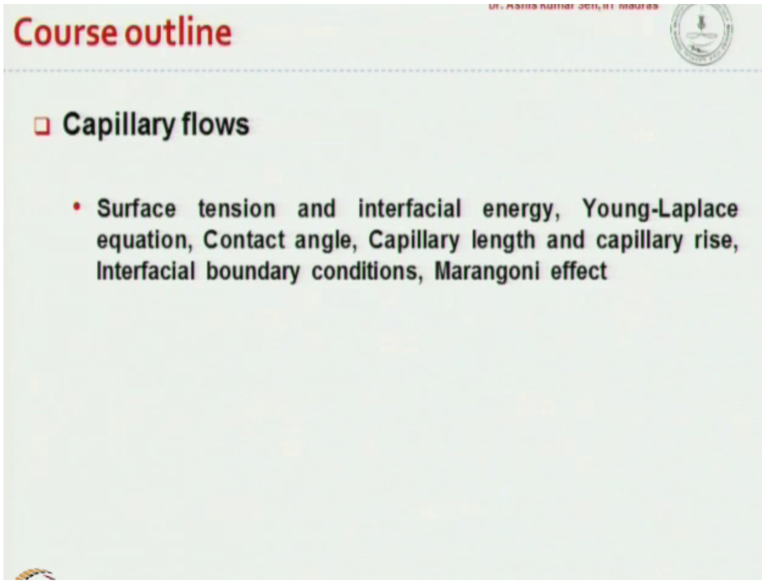

In the following chapter, we will talk about capillary flows, flows in small channels or capillaries, where we would talk about surface tension and interfacial energy. We will discuss the Young-Laplace equation which basically drives capillary flows, and introduce contact angles, capillary length, capillary rise, interfacial boundary conditions and Marangoni effect.

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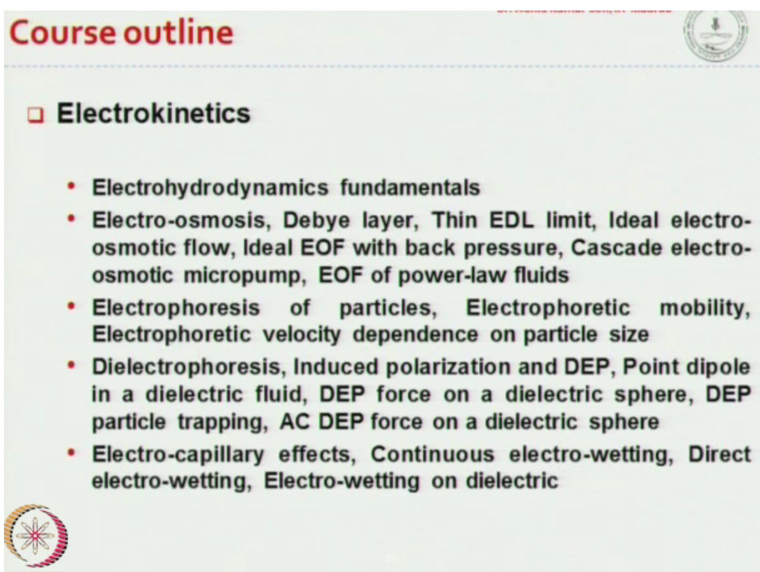

In the following chapter, we will discuss electrokinetics here we would start by talking about the fundamentals of electrohydrodynamics, and then go over electroosmosis, electrophoresis, dielectrophoresis and electrocapillary effects. So we will talk about all of this electrokinetic effects.

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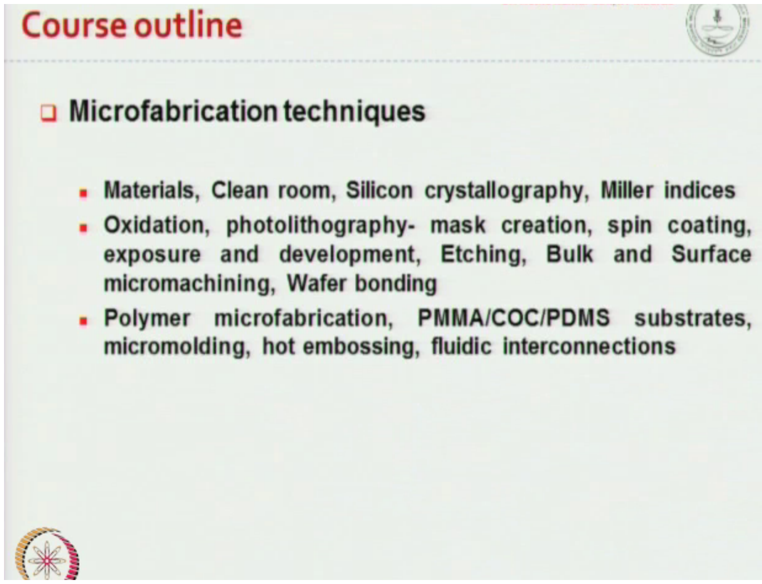

Then we would move on to talk about microfabrication techniques, here we would talk about both you know Silicon-based as well as Polymer microfluidic device fabrication. We will start with talking about materials, clean room where these microfluidic devices are fabricated, and then discuss briefly about the silicon crystallography, and Miller Indices. In Silicon you know microfluidic device fabrication we will talk about oxidation, photolithography, etching, micromachining, bulk and surface micromachining, and bonding of wafers.

So this is what we will talk about to fabricate silicon microfluidic devices. Then we will talk about polymer microfluidic device application, where we would talk about different substrates, the PMMA, COC and PDMS substrates. And different established fabrication procedures like micromolding and hot embossing would be discussed, and then we will briefly talk about fluidic interconnections.

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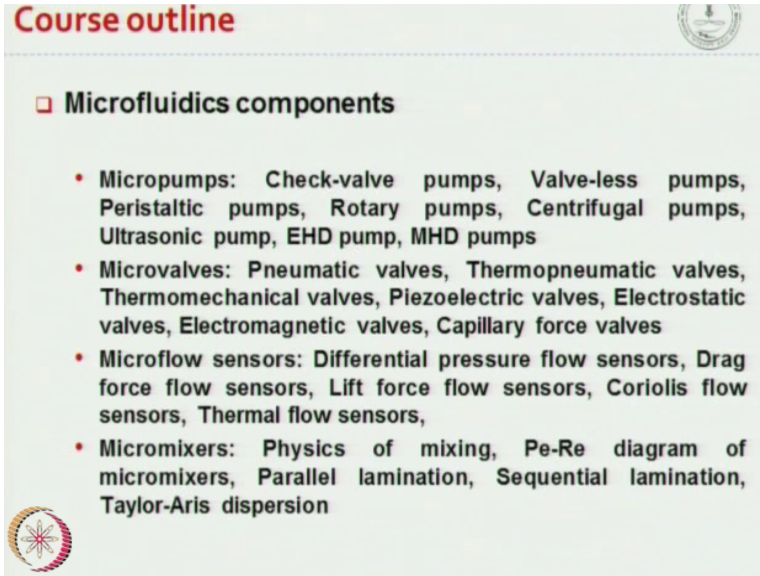

In the following chapter, we will talk about microfluidic components, different microfluidic components like micropumps, microvalves, microflow sensors and micromixers. Micropumps are components that is used to drive fluid through microfluidic devices, microvalves are used to manipulate flow in micro devices, microflow sensors are used to measure flow rate in microfluidic devices and micromixers are used to mix fluids in micro devices.

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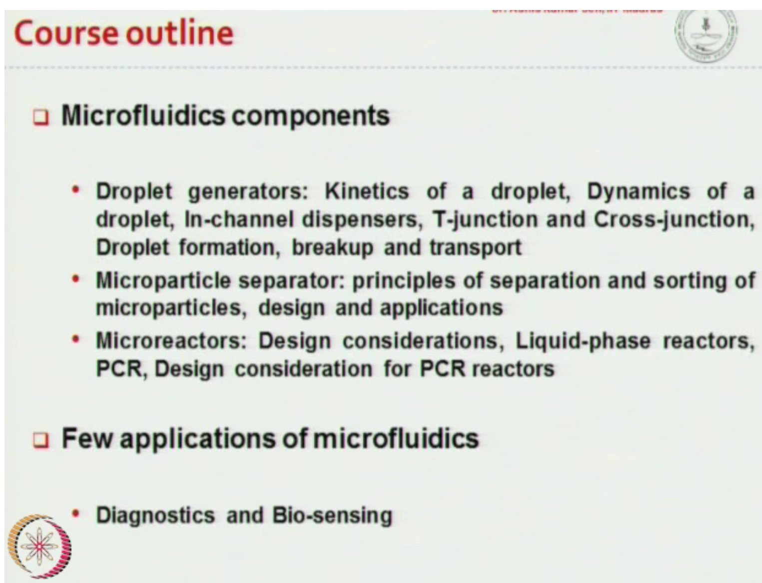

Then we would talk about droplets generators, discrete droplets in microchannels has formed at different area of microfluidics called digital microfluidics, and then we would also talk about microparticle separators and microreactors. And the last chapter would be on the applications of microfluidics, where we would talk about you know its applications on Diagnostic and Bio-sensing. So that is regarding the course outline or the syllabus.

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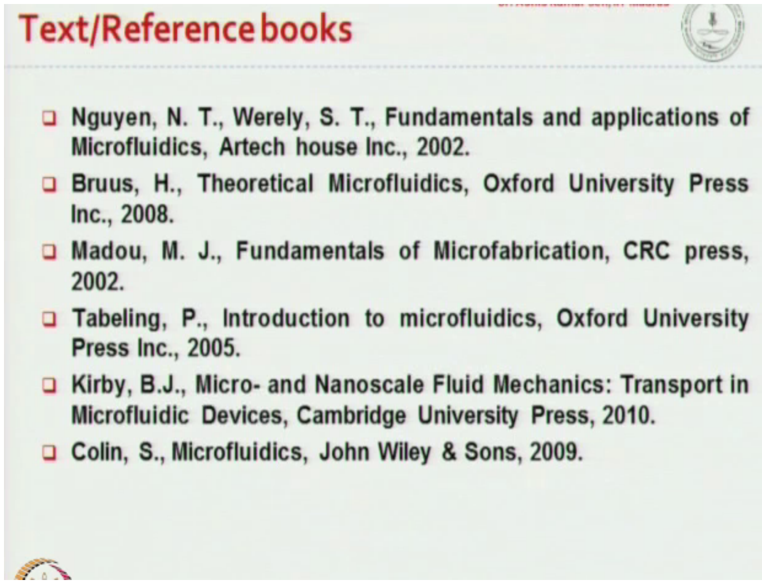

These are different text and reference books that you know for this course it is relevant, and my lecture would comprise materials from these books as and when it is appropriate from different books, all these books are equally important. The first book tis on Fundamentals and Applications of Microfluidics by N T Nguyen. And the second book is by Henry Bruus, Theoretical Microfluidics.

The third book is on fabrication Fundamentals of Microfabrication by Madou. And the next book is on Introduction to Microfluidics by Patrick Tabeling. The next book is Micro and Nanoscale Fluid Mechanics by Brian Kirby. And finally we have Microfluidics by Stephen Colin. So all these books most of these books have Indian edition, so you can actually buy them.

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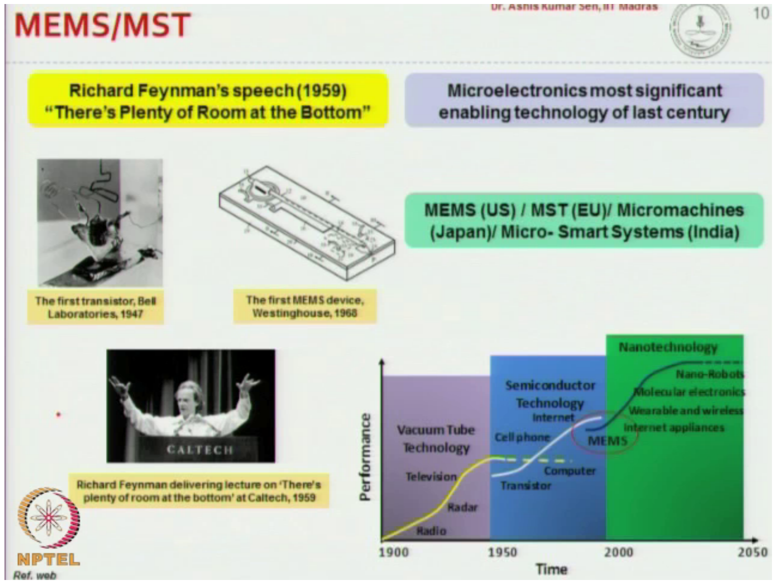

Okay, with that let us get introduced to what microfluidics is, microfluidics originated from a larger area all MEMS or microelectromechanical systems, here if you look at the evolution of technology in the previous century, the first half of the previously belonged to vacuum tube technology where we talked about radio, radar and television. And the second half belonged to semiconductor technology, where we started with transistors coming in which was invented in the Bell labs in 1947.

And then came computers and there was cellphone evolution, you all have seen what has taken place in the second half of the previous century. In the next 50 years or so, the nanotechnology era is going to come, and where some of these applications we have already started to see you know internet appliances, variable and wireless molecular electronics and nano-robots. MEMS is considered as the path and link between semiconductor technology and nanotechnology.

The area of MEMS that recognized in 1959, where you know Richard Feynman said there is plenty of room at the bottom, what he indicated was a lot could be done by looking at the lower end of the dimensional spectrum namely the nanoscale and microscale. So the area gets organized and a lot of efforts were put to develop MEMS devices, the first MEMS device was fabricated by Westinghouse in 1968, and then you know many more new MEMS devices were coming up.

As I said the semiconductor technology was considered as the most enabling technology of the last century, and MEMS got developed in parallel with the semiconductor technology. So the area of MEMS as it is called in the US, and in Europe it is called microsystems technology, in Japan it is known as micromachines, and in India the area got recognized about 6-7 years ago and it is called micro and smart systems.

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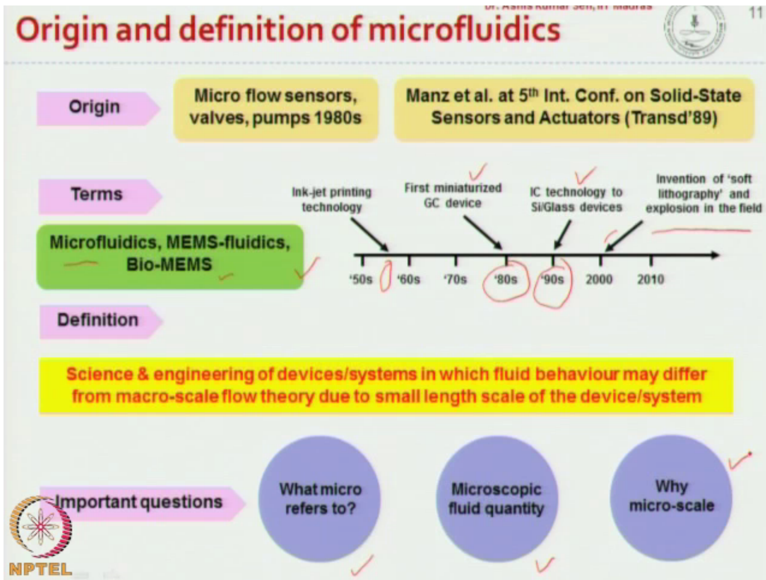

So now let us talk about how microfluidics originated, if we look at here the origin of microfluidics can be traced sometime in 1960s around here, where the ink-jet printing technology was developed, and around 1980s the first gas chromatography device came up, which can be used for you know chemistry chemical applications.

And the real thrust to microfluidics came around 1990s after the 5th international conference on transducer 1989, where Manz et al told that life science and chemistry are two important applications of microfluidics. The lot of you know tremendous amount of effort were put to develop microfluidic devices, to around 1990s you know IC technologies was used to develop microfluidic devices.

And then in the year 2000 soft lithography was invented by a different research groups including Whiteside's group at Harvard University, and followed by invention of subtle lithography there was an explosion in the field lot of you know work was done to develop microfluidic devices using subtle lithography for various different applications. When you talk about microfluidics there were different competing terms.

For example, since it came from MEMS and the fluidic part of MEMS it was named as MEMS fluidics, and then there was term Bio MEMS which is basically area of MEMS applied to bio applications, but you know title microfluidics prevailed okay and it is widely accepted. Now if we you know how we can define microfluidics okay, so microfluidics can be defined as a science and engineering of devices or systems in which the fluid behaviour may differ from that of in the microscale flow theory due to small length scales of the systems okay.

Now when we talk about microfluidics there are 3 different important questions that has appeared. The first question is what micro refers to in microfluidics? Okay, how small is micro in microfluidics? Is it referred it to the device size or it is referring to the actual fluid quantity. The second important question is microscopic fluid quantity; how small the volume of the fluid can be in microfluidics? So the third question is why microscale? Okay, why we need to go to micro scale?

So in this lecture we try to answer the first two questions, whereas the third question is a much bigger question and a major part of this course would be trying to understand the third question okay.

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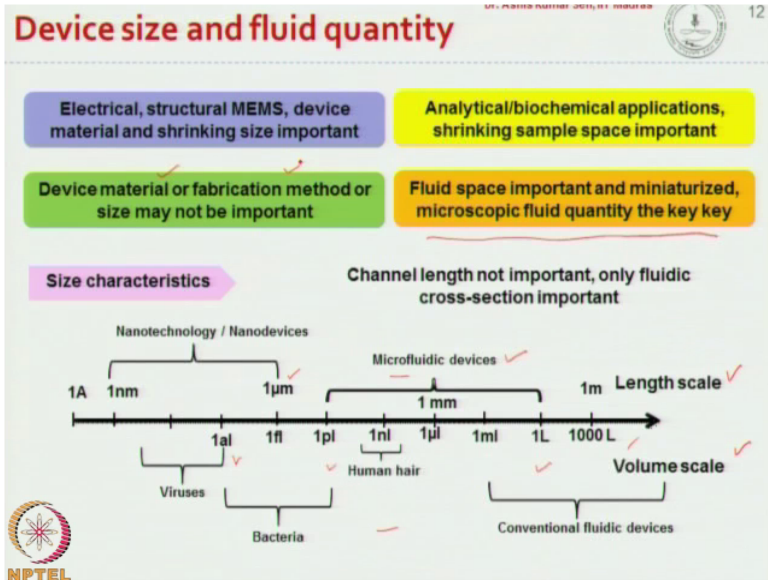

So here we try to understand what micro refers to in microfluidics? If we look at here in this you know here, we have length scales and volume scales. We have length scales from 1 angstrom to 1 meter in an interval of 2 orders of magnitude, and we have volume scales from 1 attoliter to 1000 liter in an interval of 3 orders of magnitude. If you talk about devices that have sizes, you know >10 millimeter.

And our volume which is >1 milliliter it is categorized as conventional fluidic devices, our human hair is of the order of 100 micron in size and the typical volume is 1 nanoliter. Biological objects like viruses and bacteria, viruses have volume < 1 attoliter and bacteria have size between 100 nanometer to about 10 micron depending on which dimension we are talking about, and they have volume between 1 attoliter and 1 picoliter.

Devices that have size < 1 micron okay they are known as nanodevices, microfluidic devices have size between you know 100 micron to about 100 millimeter okay, so that is the size of the microfluidic devices either it can be channel size or it could be the overall footprint of the device, and they have volume between 1 picoliter to 1 liter. So this is you know we understand now what we referred to micro in microfluidic devices.

So in microfluidics the length of the channel is not important, the length of the channel could be as long as few meters, but the actual fluidic space is going to be important in microfluidics okay, so this is very important to understand. If we talk about electrical MEMS structural MEMS means for example a cantilever sensor, if we reduce the size of the cantilever we can expect that the sensitivity may go up okay.

But in microfluidics we are not after the increasing the sensitivity reducing the size of the device, we are after miniaturizing the fluidic space, so it is actually the miniaturization of the fluidic space which brings in new effect, and these new effects are exploited to design develop new devices. So in microfluidics the device size is not important but the microscopic fluid quantity is going to be the key. In microfluidics also the device material or the fabrication method they are not going to be important.

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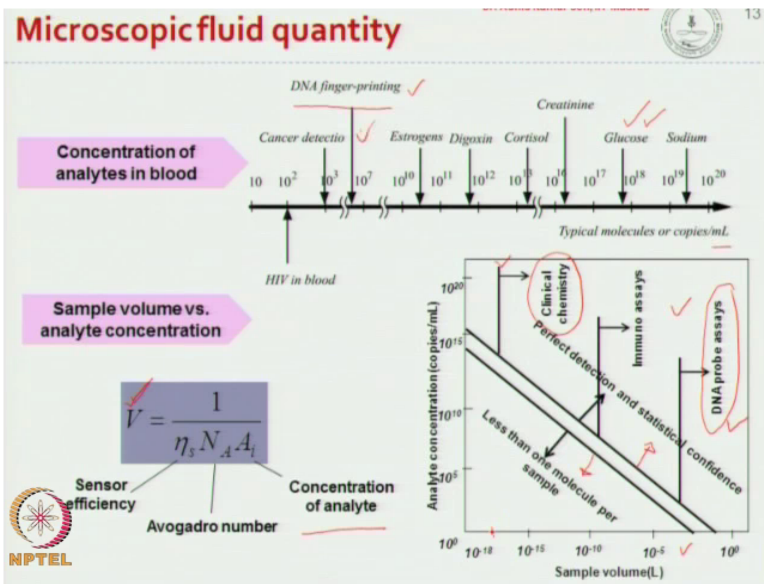

So here we try to look at how small a fluid quantity could be in microfluidics, so the fluid quantity volume okay the volume of the fluid that we use in microfluidics would depend on the concentration of the analyte that we want to detect for example in life science application. So here you would see the typical volume of typical concentration of different analytes in a milliliter of blood.

So you can see the concentration of sodium glucose you know the analyte that we need for fingerprinting and many other analytes, and you can see that the volume of the sample that you need to detect certain analyte is inversely proportional to the concentration of the analyte. For example, here since the concentration of the glucose is in the blood sample is very high the amount of volume that we need to detect glucose will be less as compared to if we are to detect DNA fingerprinting.

So this is what is shown here, in this plot here on the x-axis you have the sample volume, and in the y-axis you have the analyte concentration, now any point which is below this line has <1 molecule for sample, so the detection is not possible. Any point which is above this line you know in that case perfect detection is possible with statistical confidence okay, so you have enough number of molecules to do the detection.

If you compare DNA assays with clinical chemistry in case of DNA assay, the concentration here is very low as compared to let us say you want to detect glucose okay, so since the concentration in this case is low you need a larger volume of sample to do the detection, whereas here since the concentration is very high you need low volume of sample for the detection right.

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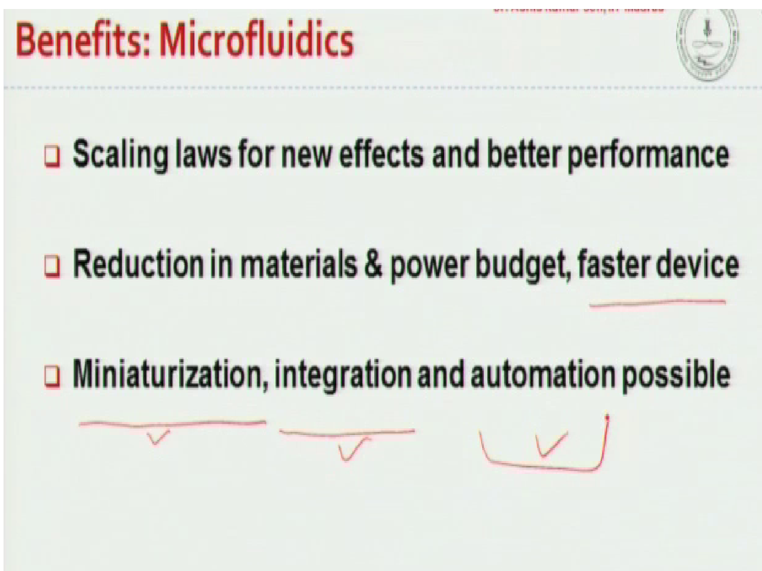

Now we talk about some of the benefits of microfluidics, the first benefit of microfluidics is the scaling laws, the scaling laws bring in new effects okay new and unique effects that are only realizable at microscale, and which provide better performance. The second benefit is in terms of reduction of material, since we are talking about you know device of smaller size there is saving in terms of material.

And since we are talking about you know different functionalities coming together in a smaller space we are talking about smaller power budget okay, also it leads to faster devices okay, because all the functionalities are done over a small space it the performance or the speed of the device goes up. The third set of benefits is miniaturization, integration and automation, since we are talking about using microfabrication to make microfluidic devices miniaturization is very well possible.

And integration is possible in microfluidics we can integrate fluidics with optics and electronics, automation is possible we can automate you know the way we want to perform different functionalities in a microfluidic device using a software interface like (()) (24:31).

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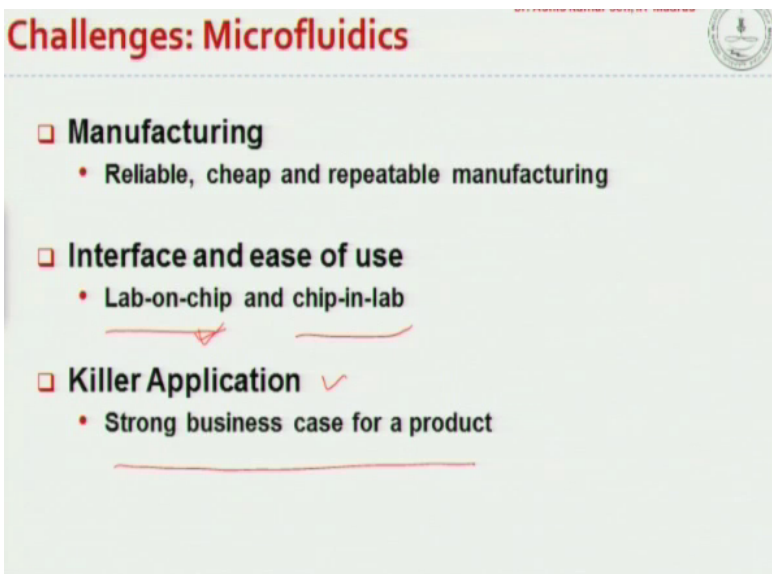

Next we look at some of the challenges that exist in microfluidics, the first challenge is the is manufacturing in terms of manufacturing after about you know three decades of development in microfluidics, we have yet to see a manufacturing method that is reliable, cheap and repeatable okay. The second challenge that exist in microfluidics is interface and ease of use okay, in microfluidics we talk about lab on chip concept okay.

Where you know we tried to bring in different operations that we do in a typical lab, for example in a pathological lab you want to analyze blood, and we have you know various equipment present in the lab, when to bring in all the equipment the functionalities that can be achieved using the equipment into a small chip and that would be called as lab on chip okay the lab on chip concept.

But till now the chip is very small but it is the peripheral equipment like you need a pump to drive fluids through the chip, and you need a detection system that make the chip very bulky okay, so until now what we have seen a chip in a lab rather than lab on chip which we would like to achieve. The third and important application the challenges is going to be finding the right kind of applications, so we are yet to find a killer application that will create a strong business case for a product which will give a thrust to the area of microfluidics.

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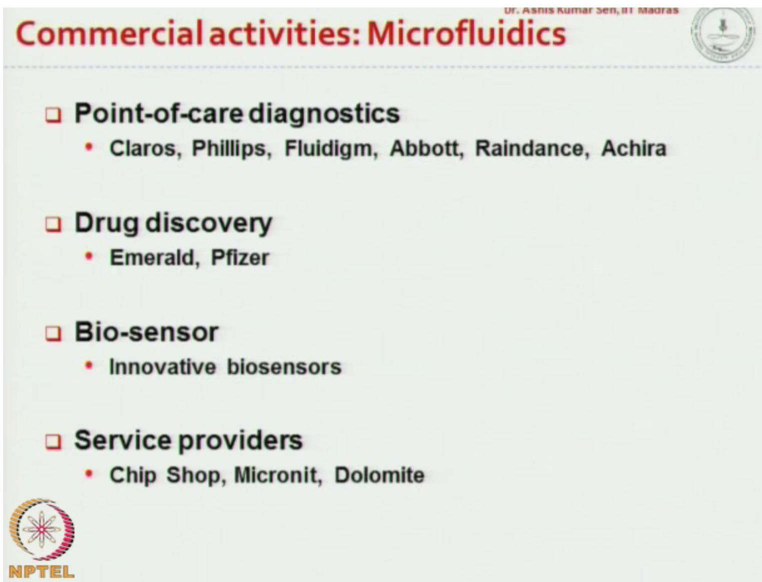

Next we talk about some of the commercial activities in microfluidics, it is happening in different sectors in point of care diagnostics, in drug discovery, in biosensors and also in terms of providing services. In point of care diagnostics, we have companies like Philips, Claros, Fluidigm, Abbott, Raindance and we have a company called Achira Labs in Bangalore which is also trying to develop a point of care diagnostics.

In drug discovery we have you know companies like Emerald and Pfizer, where they are trying to use microfluidic technologies to you know do drug screening multiple drug screening. Then microfluidics can be applied to biosensors applications companies like Innovative biosensors are working on developing biosensor based on microfluidics. And then there are some commercial activities going on in terms of providing services okay.

Let us say you want to fabricate microfluidic devices from a vendor, there are vendors like Micronit, Chip shop and Dolomite, who can actually design and fabricate the chips for you.

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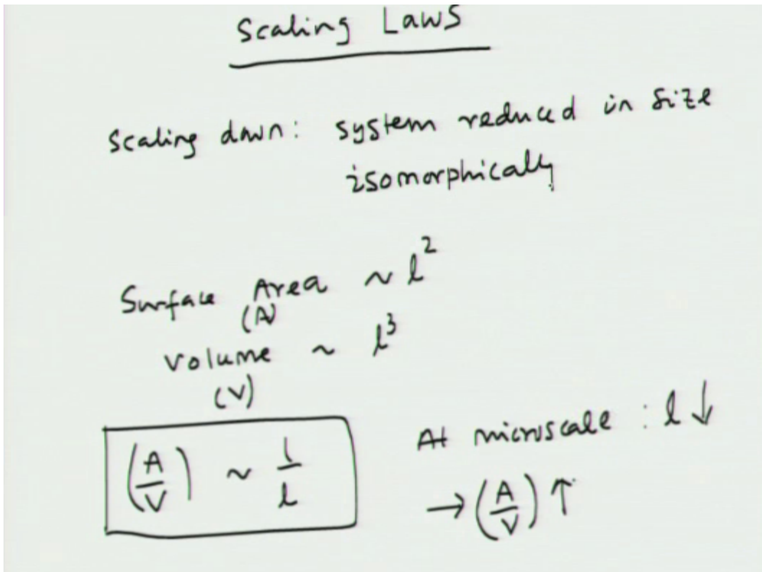

So let us talk about the scaling laws before we talk about scaling laws, let us try to understand what we mean by scaling down? Scaling down means we want to reduce the size of a device or size of a system isomorphically equally from all directions. So scaling down means system reduced in size isomorphically, if you consider you know surface area of a device surface area scales as l square and volume scales as l cube okay.

So this is the surface area we can say A and the volume is V, so the surface area to volume ratio put scale as 1/l. Now at microscale l is small and that gives the area to volume ratio goes up, so at microscale the surface area to volume ratio is very high, so the surface effects become dominant okay. But how we can see you know the effects of high surface area to volume ratio we have to consider few examples.

Before we you know consider a few microsystems let us discuss this in the context of some of the objects that exist in nature okay. So for example the first example that we would see is you know how small or how big animals could be?

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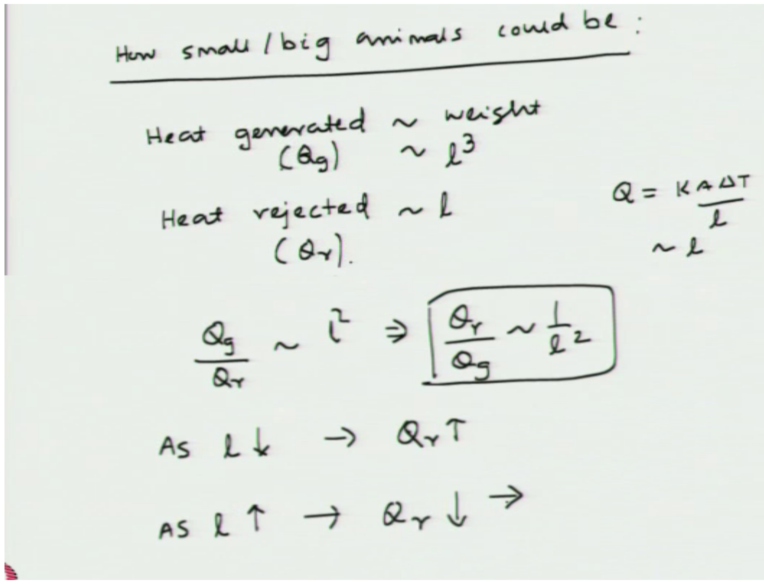

So we try to see how small or big animals could be okay, now this we can find out by considering energy balance okay, so if we can find out how much heat is being generated by an animal and compare that with how much it is being rejected. Now the heat generated is proportional to the body weight okay proportional to weight, so that means proportional to l cube, and the heat rejected we can say that is being conducted from inside the body to the surface.

So that is by conduction and by conduction heat transfer we can write K A delta T/l, so this scales as l, heat rejected would scales as l, so this is let us say you know heat generated Qg and this is rejected Qr. Here, we see that Qg/Qr is going to scale as l square right or Q rejected/Qg would scale as l/l square, so you know as l reduces Qr is going to increase. So you know smaller animals will lose heat constantly and their heat rejection is much more significant as compared to the heat generated within their body.

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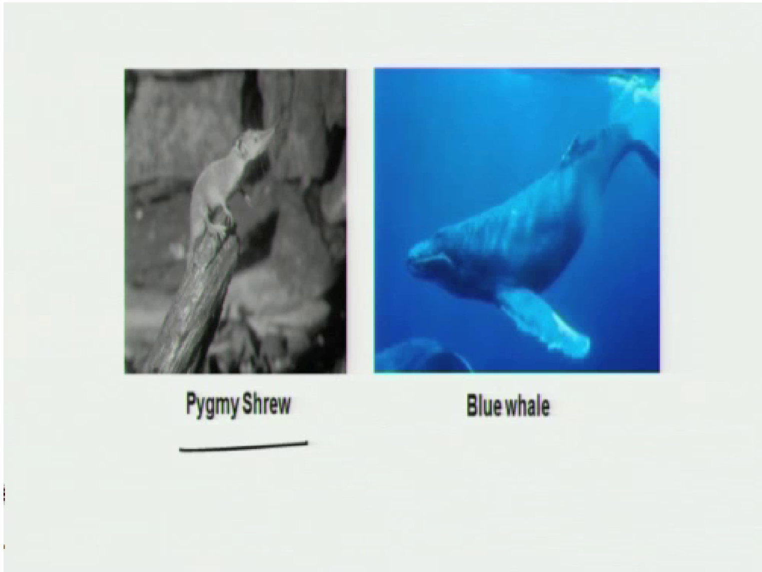

So they need to eat continuously to generate enough amount of heat to server and this is in fact the case in the case of Pygmy Shrew okay, Pygmy Shrew is the smallest one blooded animal that is found and it needs to eat constantly to maintain its body temperature okay. Whereas the other extreme Blue Whale is the largest animal that is possible okay. So here if you see as l increases then heat rejection will go down.

So far larger animals heat rejection becomes an issue, and that is the reason why there is a limit on the maximum size of the animal okay blue whale is the largest animal possible, and in them heat rejection is the major issue, and that is the reason when hunter actually kills a whale because you know in typically the heat from the inside of the whale gets transported to the surface because of the blood circulation.

And when whale is killed, the circulation blood circulation stops so the heat is actually trapped inside the body, so as soon as the whale is killed, its meat gets cooked. So there is the maximum size on the you know animal which is blue whale, and there is a minimum size of the animal which is the Pygmy Shrew. Now let us look at another example where we say that you know why it is possible you know for an animal which is very small in size to walk on water why insects can walk on water, while human cannot walk on water.

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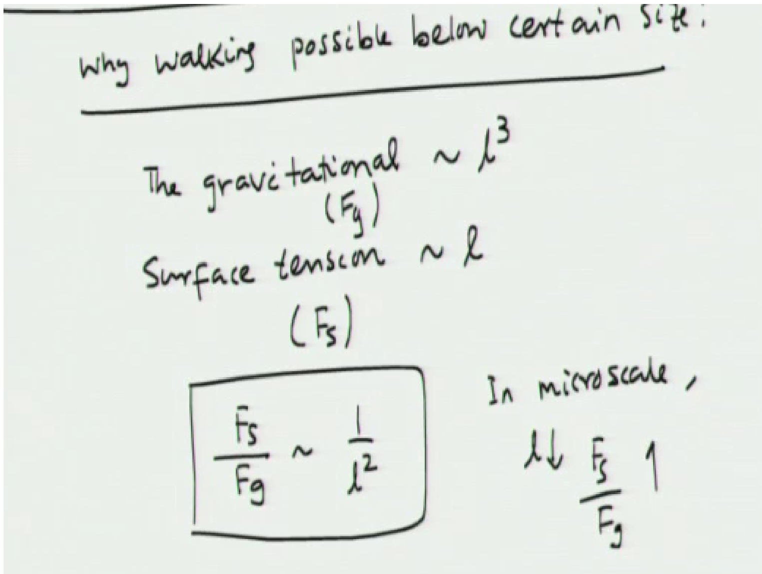

So why walking possible below certain size okay, now here we can say that the gravitational force which acts downward direction is proportional to l cube, and the surface tension force which tries to balance the gravitational force, surface tension scales as l, so this is let us say Fg and surface tension force is Fs. So Fs/Fg scale as 1/l square okay. So as in microscale l is small, so the surface tension to the weight of the body is very high.

So there is a high probability that you know smaller creature can walk on water and that is the reason why insects can easily walk on water, because the surface tension force is much higher compared to the body force the gravitational force while we cannot walk on water, and this also explain why we are you know it is easy to spill coffee from a cup, but it is not possible to pour water from a capillary okay.

So with that, you know we continue our discussion on vertical trimmer equation okay, Trimmers vertical notation.

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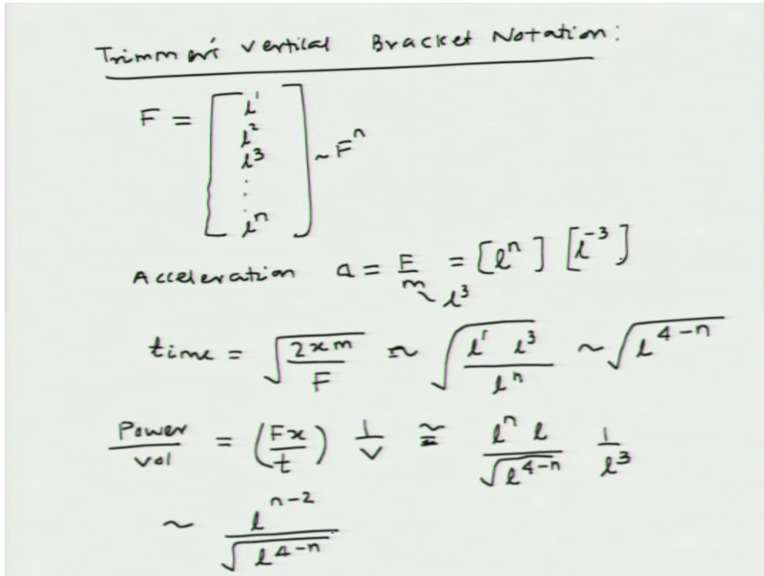

So we look at Trimmer's vertical bracket notation, so using trimmer's vertical bracket notation if we know how you know different forces scale with length scales, it is possible to find out how acceleration time and power to volume ratio would scale okay. So if you can generalize let us write some force F scaling as l1, l2, l3 up to l to the power n okay, so we can generalize it as F to the power n. Then we can say that acceleration a=F/m, so l to the power n* m is l to the power l cube, so l to the power -3.

Similarly, we can find time is 2x m/F square root, so that is scaling as l to the power 1*l to the power cube/l to the power n so square root so this is scaling, so that would scale as l to the power 4-n square root okay. Similarly, the power to volume ratio you know power is work/time so Fx/t*1/V so that will be l to the power n, so this will scale as l to the power n x is l and t is l to the power 4-n square root*1/l cube okay. So that would scale as l to the power n-2/l to the power 4-n square root.

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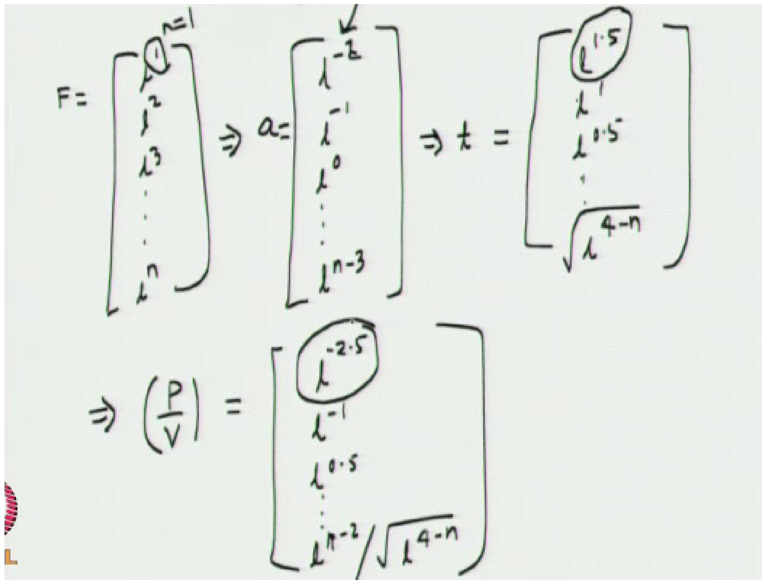

So we can you know generalize if F is l1 l2 l3 l to the power n, then implies acceleration can be generalized as acceleration l to the power -2, then l to the power -1, l to the power 0, l to the power n-3. And time t could be generalized as l to the power 1.5, l to the power 1, l to the power 0.5 up to l to the power 4-n square root. Similarly, the power to volume ratio can be generalized as l to the power -2.5, l to the power -1, l to the power 0.5, up to l to the power n-2/square root of l to the power 4-1.

So you can see here you know for force if you look at different elements, this is the first element so l to the power 1 so n is 1, then the acceleration by this formula is going to be l to the power n-3 so this is going to be -2 okay acceleration will scale as l to the power -2. And you know the time is going to scale as l to the power 4-n square root so that would be 1.5 okay, so this would scale as time would scale as l to the power 1.5.

Similarly, for power to volume ratio we have this formula here okay, if n=1 we would get the power to volume ratio to be l to the power -2.5, so you know from the trimmer's vertical notation we observed 2 interesting things one is.

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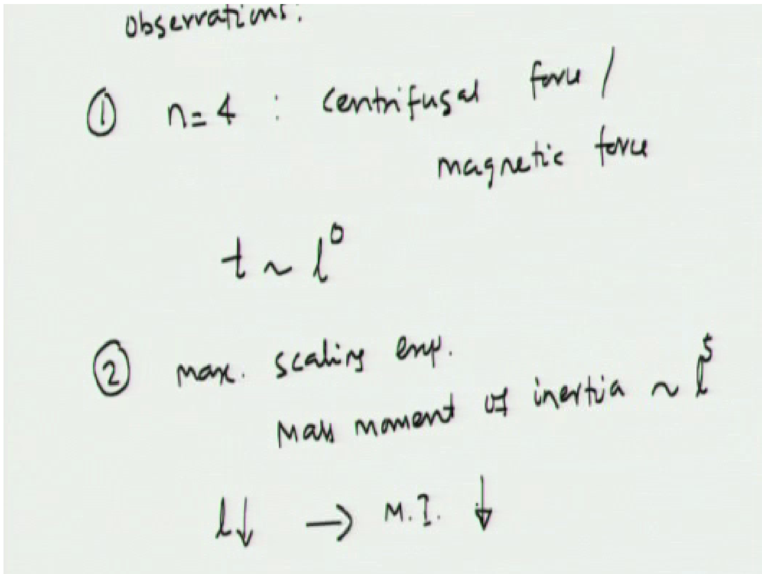

So we have 2 important observations, one is when n=4 which is the case for centrifugal force or magnetic force, then the time would scale as l to the power 4-n square root, so this would scale as l to the power 0, so for centrifugal force and magnetic force the time is independent of the length scale okay, and this is contradictory to our normal observations or intuition that smaller things tend to be faster.

The other important observation is the maximum scaling exponent force is possible for you know for not force but moment mass moment of inertia, which would scale as l to the power 5. The maximum scaling is possible for mass moment of inertia which would scale as l to the power 5, so in that case you know what it means is as l reduces then the mass moment of inertia goes down significantly, so what that means is that smaller motors would achieve the maximum speed much faster as compared to larger motors okay.

So that is the conclusion we can make, with that let us stop here.