Cellular Biophysics
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Solids vs fluids

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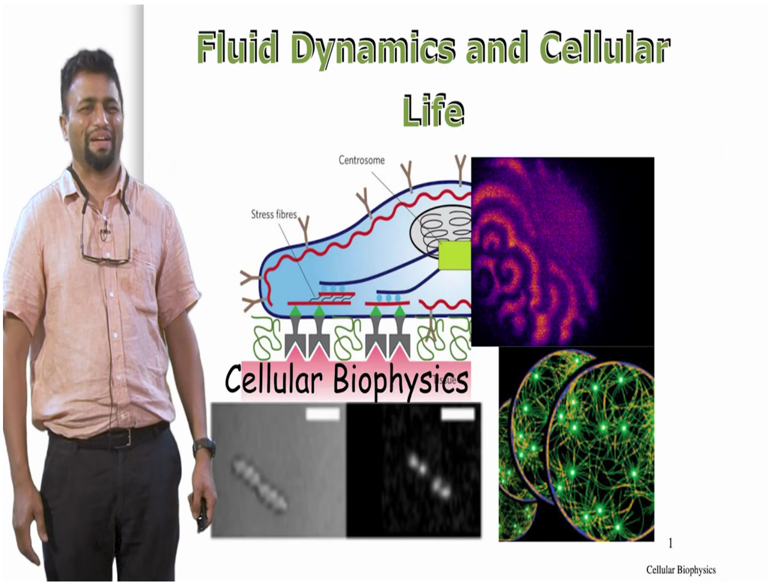

Hi, welcome back. This is cellular biophysics. And after our introduction on the broad outline of this course, I am going to dive straight into the topic that we want to discuss today, which is fluid dynamics and cellular life, we are going to take you on a journey to ask and answer the questions about what aspects of fluids and water in particular, makes sense to us from the perspective of physics in biological systems. We will deal with it at two levels. We will start with the sort of larger overview in terms of what we can call continuum approaches.

And then we dive into some so called molecular approaches. We will not of course, again, like I said in the introduction, not focus on molecular dynamics and atomistic interactions, because those are sort of beyond the scope of this course. Those are indeed more appropriate for us molecular biophysics course. But why study water itself is, to me an intriguing question, and perhaps obvious to most people studying biology, because we know that water makes up the largest bulk property of any biological material, we are made up of roughly, give or take 70 percent water in mass.

Why not other fluids? Why not other solvents? Why not methanol, why not ethanol? Why not ether. And one can make arguments about this. But remember that life on Earth is the only one we know of. But I mean, until we find it, we do not know if there is life on any other planet. And on other planets, maybe other considerations apply.

And maybe one can speculate that this may happen. And one of the things we talk about, often about the validity, the reason perhaps why water is the solvent in which life exists on earth may have something to do the chemistry of it may have something to do with the physics of it. And we will focus on the latter.

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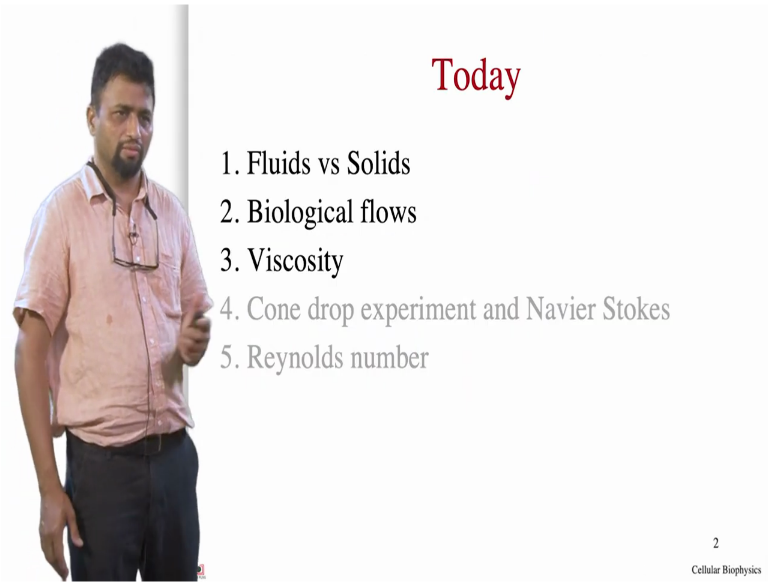

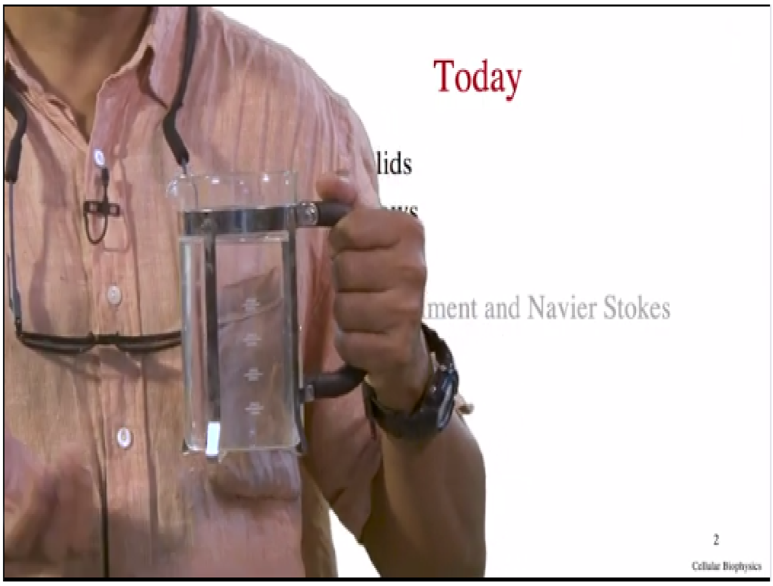

So, for today, we are going to talk a little bit about the contrast between fluids and solids, something that maybe you are very familiar with. So, it may be a revision in some senses, then biological flows, and we will end with viscosity. And I am going to continue onwards to the cone drop and fluid drop experiment, Navier stokes equations and Reynolds numbers. So, here, I have with me a jar of water. And it has gradations on it 100 ML gradations.

And if I were to pour it into another vessel, yes. So, these gradations if I pour 100 ML, one volume unit into another vessel, you know this, that it is going to take the exact same volume into the other vessel volume will not change, yes, but what will change is the shape because now if I put it on this table, which my studio people are gonna get really upset about, but it will not be in this form of a cylinder anymore, correct?

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Because water, this is intuitive knowledge to all of us, but something that we learned over centuries of physics that it takes the shape of the container in which it is classical fluids, at least, also maintain volume. So, volume is maintained, they are not incompressible, in other words, and in that sense, there are some contrasts between solids and fluids. And the properties that we are going to talk about is indeed the contrast the kinematic and dynamic viscosity is not drag forces.

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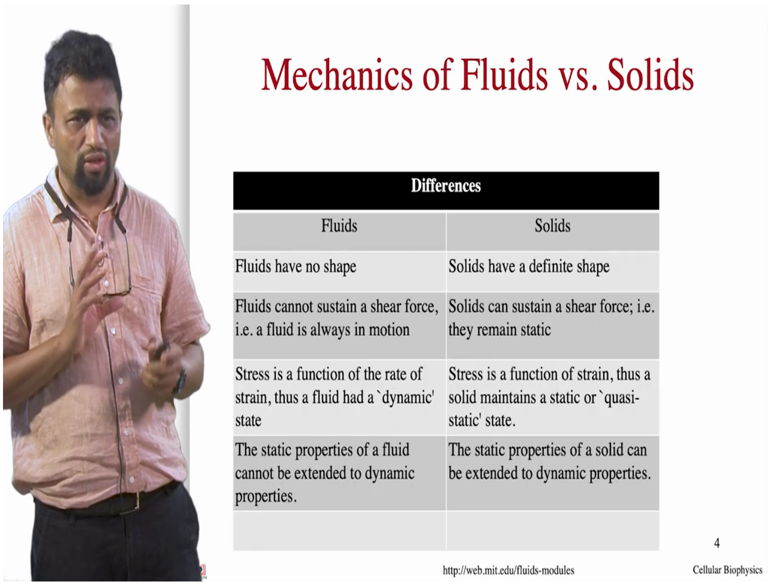

But the only thing I want to highlight over here is there indeed, like I was saying, fluids unlike solids have no shape, when we say they cannot sustain a shear force, it means that if I, if I take my water and start doing something to it, moving it around, it will not be able to sustain it will not resist it. On the other hand, if I try to bend my jar in which this thing is concerned, this can sustain a force. That is what it means that it cannot or it can sustain a shear force, because the solid by and large remains the same until it gives it breaks.

In the case of fluids, stress and strain have a relationship which is dynamic. And I will elaborate more on this, because this requires a bit more some little bit of arithmetic. But suffice to say, stress as you remember from elementary high school physics is nothing but force per unit area. Strain is the relative deformation. So, the relationship between stress and strain is a defining feature of materials. For solids, the stress strain relation is connected by young modulus, the proportionality constant, which is characteristic of that solid.

For fluids, the strain and stress are not related directly, they are related by their first derivative effective, can we talk a little bit about this, the static properties of fluid cannot be extended to the dynamic properties, whereas for a solid they can. And again, these are things that are mathematical, and we will have to dive into those equations in order to make more sense of them.

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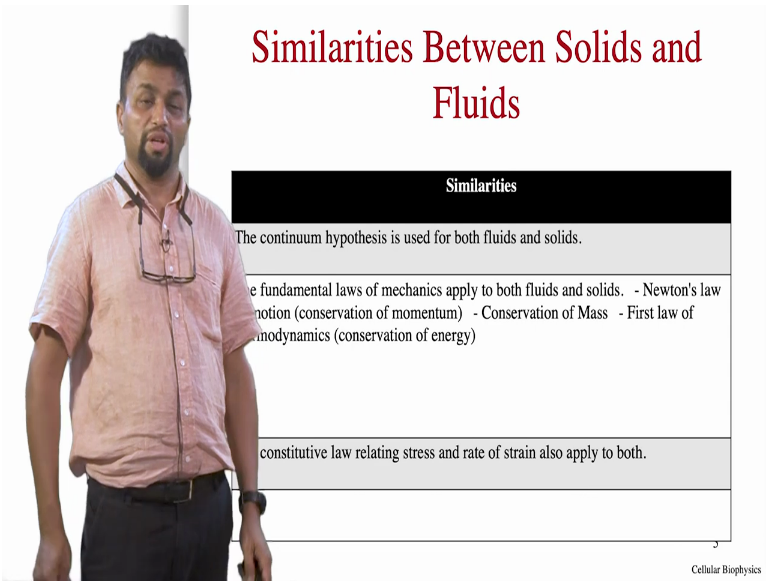

But there are similarities also, and those similarities pertain to what we can do with solids and fluids. In, for example, we can use the continuum hypothesis. For both of them, we can actually assume that we can ignore the molecular detail and consider them to be a bulk like, like as if you say that there are many people in this room, but we consider them to be a population of this classroom.

So, that is what it means to go from molecules to continuum. We can do this for solids, we can do this for fluids, the fundamental laws of mechanics, especially Newton's laws apply to both, that is to say, conservation of momentum, mass and the first laws of thermodynamics the conservation of energy.

This is important, because, as we will see, fluids, of course, have certain properties that, modify them. It is not that the laws do not apply, but there are special ones that apply. And this becomes interesting because, like we said, at the beginning, life is made up of water, and life has water in it and molecules are in water. And so these become very important to understand in detail.

Finally, the constitutive laws relating to stress and rate or strain apply to both by which I mean that conservation of stress and rate of strain apply to both and we will again have to write out models and equations for that, to make a little more clarity or one. Suffice to say that there are things that are common between fluids and solids. The distinctions are what we are going to be interested in.

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But one of the things that fascinates me most about fluids and water in general, is that it is in motion. And anyone who has had the good fortune of coming to going to a beach knows this, that there is always motion of the waves. Now, we agree all of us that the motion of the waves is due to other factors and mostly gravitational, at a planetary scale. And you know this when your moon phases change, and you see it also in the fact that the ebb and flood tide, the OT and Bertie, as they are called, in some languages change with the time of the day.

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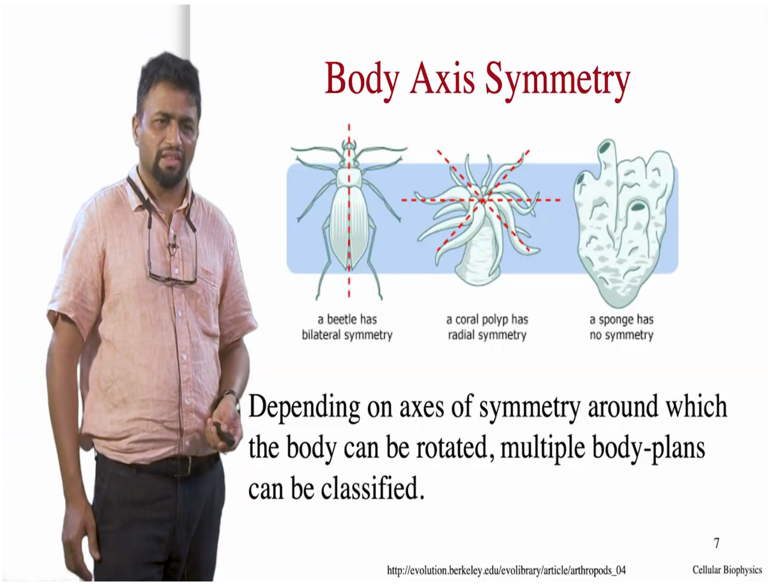

But, at a molecular and cellular scale, it begs the question, Does any of this matter? I mean, there is no do we even have to consider the effects of gravity. And one of the things that is very fascinating for me, in terms of biology is what we see as body axis symmetry. Any organism you look at plant or animal it has, most of them seem to be symmetric, like, look at yourself. I mean, if you have got to cut yourself into two halves, the left and right externally at least I mean, luckily, most of us have two pairs of why a pair of eyes, the nostrils are halved the arms are halved this is part of the Vitruvian Man drawing of Leonardo da Vinci.

And this is true of a Beatle and which has a bilateral symmetry, as we call it. That is to say along one axis, we can mirror the two parts, we put them on to each other, they are more or less similar. This is a fascinating topic for me symmetry, because they are not identical. But and in fact, there is a lot of work in sociology and neurobiology, about aesthetics of asymmetry. And we would not get into that. But I think those are fascinating questions. And if you want to learn more, please read.

On the other hand, there are organisms which we may call more primitive or simpler evolutionarily earlier than us, like corals, which have radial symmetry, and sponges which have absolutely no symmetry, so that depending on the axis of symmetry around which the body can be rotated to multiple body plants clan can be classified. But these body plans, where do they emerge from? Now one idea is that of course, all of this emerges from our genetic bow plan the so called genetic program of development in embryogenesis.

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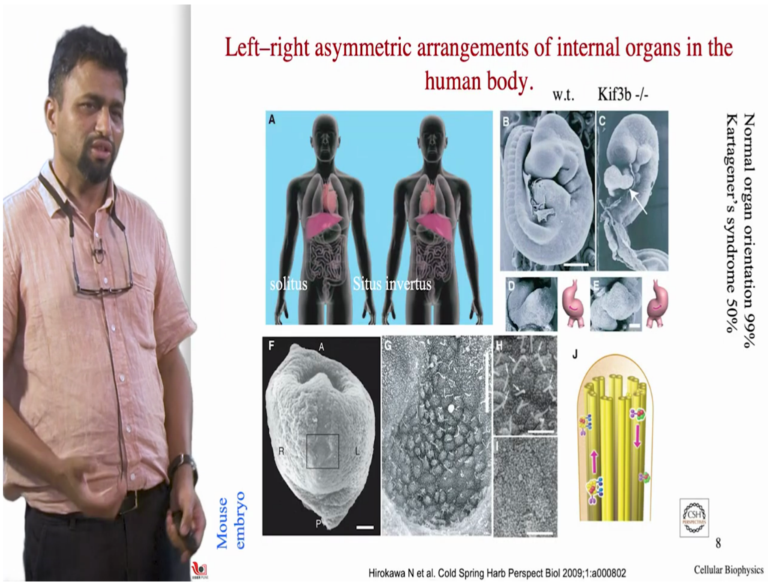

But there is an additional factor in it. And with humans, we know this, our heart is in the one side of our cavity, and our liver is oriented in a certain way. Our organs take a turn in one direction, or large or small intestine. And all of this seems to defy this simple bilateral symmetry idea we see from the outside. So, what drives it is something that is fascinating because it comes from the time when we were embryos when we were some 1000 cells, 500 to 1000 cell stage.

In the case of mouse embryos, where these experiments are possible to do when people were trying to investigate? Why a certain set of humans and there is a very small percentage where there is what we can call organ orientation issues. And this is 99 percent of humans, our hearts are in one side and livers on the other side in something called Carter gainers syndrome 50 percent have it flipped. So, right is left. I mean, right is wrong in that case.

So, the reason for that has always baffled people, it has been something that has been fascinating, because other words, when the majority is like this, and why do some of these people have 50-50 flipping of the organs. And it turns out that it is heritable, it is genetic. And after decades of work, it was found that the genetics can be nailed down to one gene, particularly kinase protein Kif3b. Kif3b when mutated in mice, shows that in the embryo, you get a 50-50 litter of pups who have their organs flipped.

Some have it right, some have it wrong. So, what is going on, and when people went and investigated this further, they found that in the mouse embryonic development, there is a stage at which the organ positions are determined these organ positions are determined by fluid flows. So, you know, I talked about the ocean flows being driven by gravity, what drives these flows. So, the flows here are determined by tiny organelles or structures that are made up at a cellular scale called cilia.

These cilia are in embryonic tissue in a particular region, as you see in the sort of middle of my slide in G. In this work by Hirokawa and company, along with Nonaka, they showed that if you are mutated, if the animal is mutated for Kif3b, then the synchrony of the ciliary beatings is destroyed, which means that there is no coherent flow generated. If there is no coherent flow generated, then it appears that the organs get randomized.

Now, there may be likely a negative inhibitory role if one organ is placed in one way that the other one goes the other way, which would explain why there is a 50-50 randomization, as opposed to when there is flow. Another really open question remains, which is why do we need organs in one place? And I would argue, I do not know the answer, but I would argue with me have evolutionary basis.

And the answer to that question is very hard, very, very hard. And I am not going to try to answer it right now. Again, I really encourage you to read the literature more, because there is a lot there. As I keep repeating these, why questions in biology are very easy to ask very hard to answer. And some of these groups have spent decades doing this and they are still nowhere near the answer.

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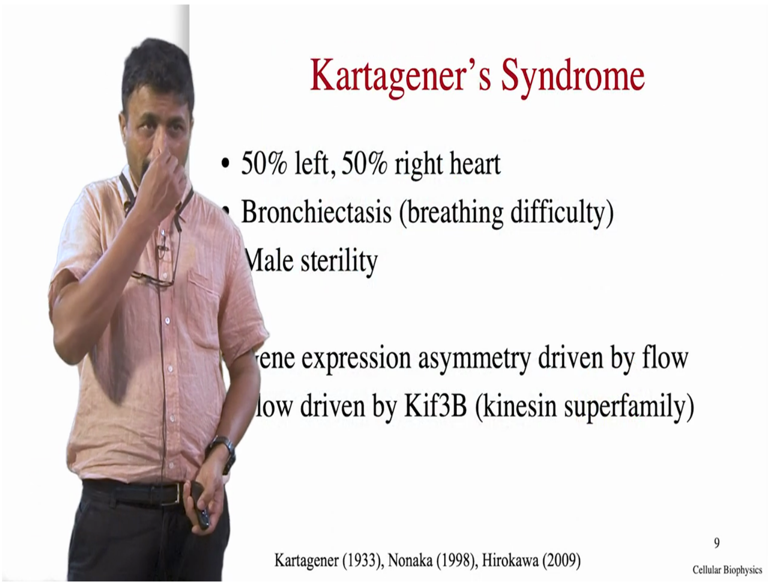

So, suffice to say that this 50-50 left, right is not just a quirk, it is not just that one, you are left handed right handed this is really serious, because people with the Flipped organ positions have breathing difficulty and may lead to male sterility again, because the kinesin protein is also involved in the sperm swimming behavior. So, the way by which these flows interact with the biology is by generating gene expression asymmetry, and the process by which it happens is this ciliary beating, but the event that needs to be triggered is fluid flow.

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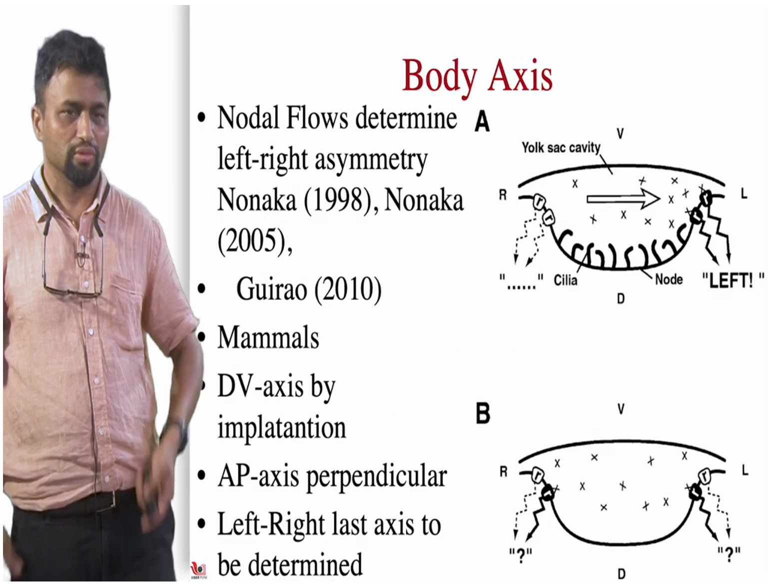

So, that was sort of my point over here. And these fluid flows are called nodal flows. And in a series of studies, the Japanese groups of Nonaka and company together with Hirokawa showed that you could would put tracer particles and could actually observe in early embryo mouse embryos, that this is indeed the case and more recently, it has been also shown in mammalian embryos.

This sort of idea that there is a an interaction between gene expression and the fluid mechanics and flows is a very recent idea that has taken seed in a lot of people's minds in terms of embryology and developmental biology. And you could argue that part of the reason why this has taken so long is because, while these fluid mechanics concepts have been very old and around, measuring them and finding evidence for it has been much harder experimentally.

So, my hope is that we will actually now use this as a motivation to I understand theory for fluid mechanics, which dates back to the 1900s, even earlier at times. And I hope you will then see at the end of this section that this connection is very important to make. And there are more things to be discovered in the coming days.

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Some other places where fluid flows are very important, and we are still going through a pandemic at the moment is 2022. We are not done yet, is blood flow. And I talk about blood flow simply because we know that many of our currently important diseases are diagnosed with blood sampling, and blood flows can themselves be measured in living animals.

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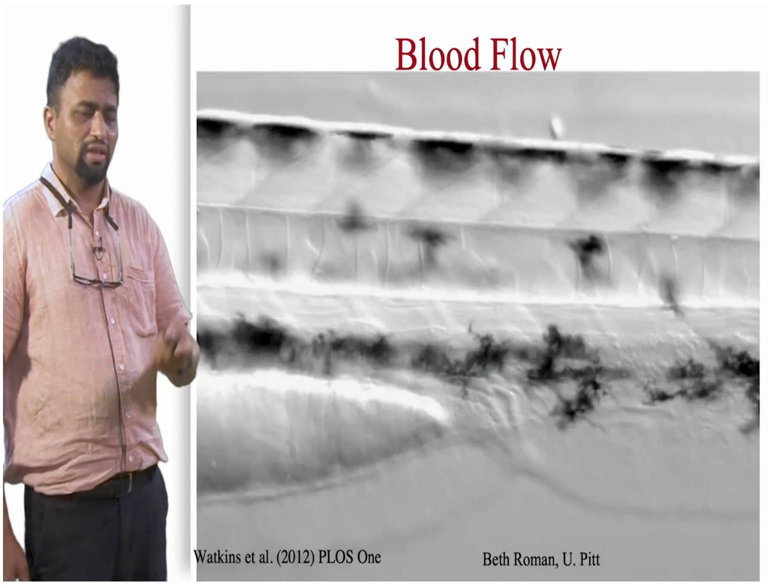

And in this example, the images taken of a transparent zebrafish embryo were red blood cells provide enough contrast in bright field microscopy, that you can actually see single cells flowing past, large number of medical defects arise from faulty flows. In fact, one of the ways by which COVID has now started to be identified, is to look at the elasticity of the red blood cell as it squeezes through narrow channels.

Apparently, the correlation exists right now of lack of elasticity of red blood cells with COVID infection, what the causation and the mechanistic basis of that is, is unclear. But this also tells us that in a way, the blood is always a good reporter for our general health status, which is why most of you when you enter a new organization have to do a blood test. This is the so called complete blood count that you do, there is a good chance that the biophysics of red blood cells or other cellular components may become important in the coming days as an additional measure.

So, you will see a little extra tick in your CBC in your complete sense, complete blood count in future. So, this is my hope, in some senses, there is a very beautiful paper by Jochen book, you are welcome to look at it, I am not gonna site it here, I will add it at the end.

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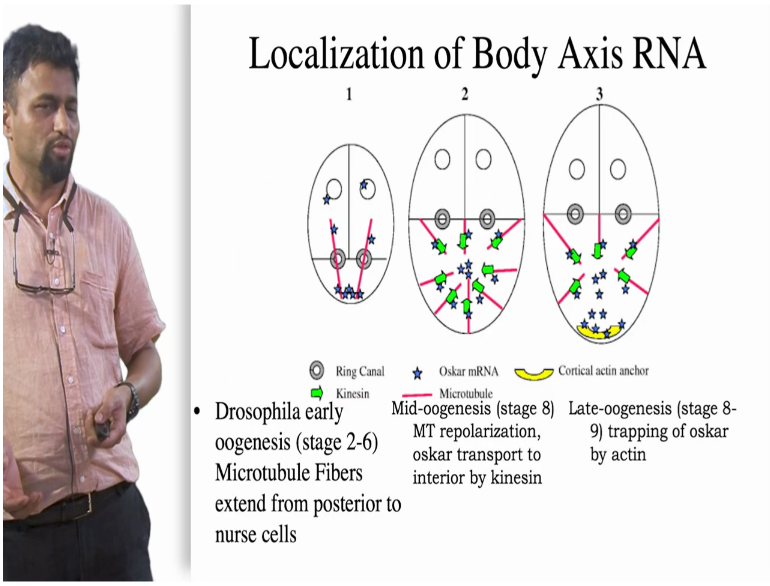

So, in terms of body plan determination, this is important also in fruit flies. And in this particular case, in Drosophila oogenesis. It has been shown that microtubule fibers extend from the posterior to the nerve cells. So, you are looking at it in the panel 123. And the RNA of a factor called Oskar, which is an mRNA is transported as granules into the center. And this in the late who Genesis is then trapped and forms cortical anchor, which then eventually leads to differentiation.

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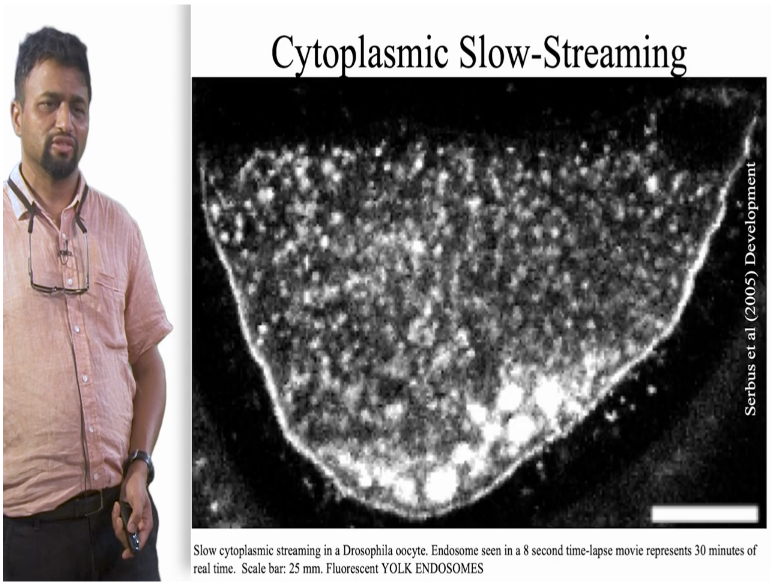

This determines the body axis through the RNA transport, and its transport itself of these granules, which are labeled suggests that there is a coherent streaming of some sorts of these granules. The question in many of these cases is often does this streaming motion have any functional role? Do these things need to move? So, the only answer to that question from a genetics perspective we have right now, is that if you do not have it, you have defects in your axis symmetry, but the cause causation, linkage, mechanistic linkage is still under investigation.

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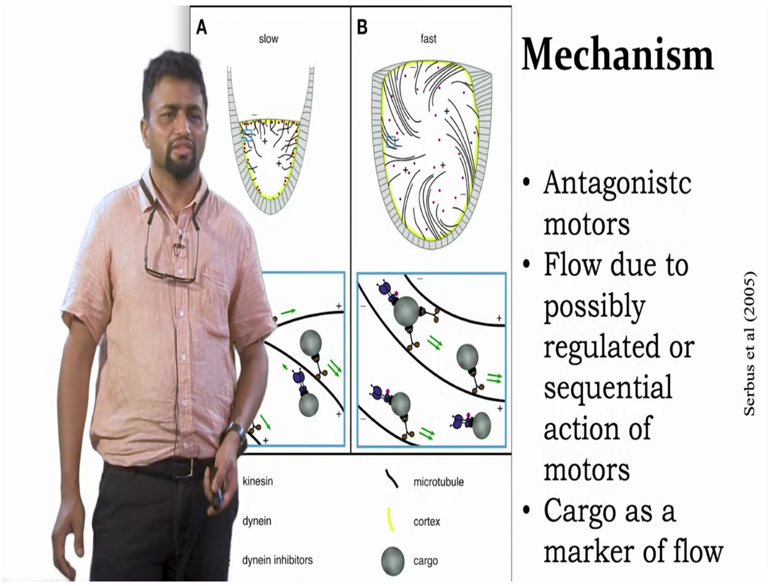

And currently the mechanism by which the flow itself is generated remember, we were talking about biological fluid flows is that there is an antagonism of molecular motors. With sequential actors, actions of cargoes and motors, and the cargo itself can be used as a marker of flow.

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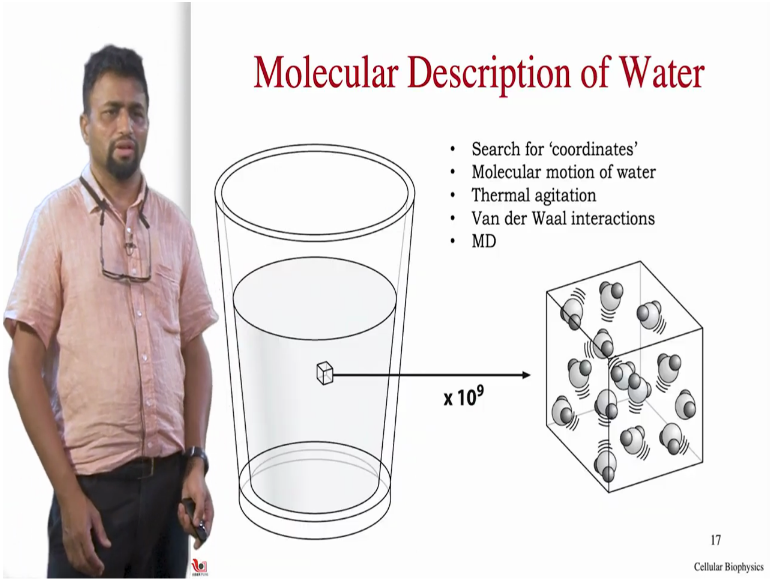

So, I hope I have made it evident to you that knowing not just the static nature of water, which we can consider the sort of physical chemistry of it, but also the dynamics of it makes some sense.

Now, of course, when you look at water as a chemical component as a chemical entity as a compound, it is evident H2O is the composition these fat box blobs in this box on the right are nothing but your oxygen molecules and the two small dots on it are the hydrogen and those dashed lines indicate the hydrogen bonds that form between water. In a small parcel of water inside my mug here, there could be up to a billion molecules of water right and by small parcel I mean millimeter by millimeter by millimeter cube.

And you can actually calculate this exactly, even more. So, with fast computers these days, we can do explicit molecular dynamics, calculations of water dynamics, making and breaking off temporary bonds, Van der Waal interactions and their thermal agitation. Now, this is an approach that has proven to be quite productive. People are using these kinds of calculations to understand everything from corrosion dynamics, better, better, better movement of ships and submarines to water to understanding how the heartbeats.

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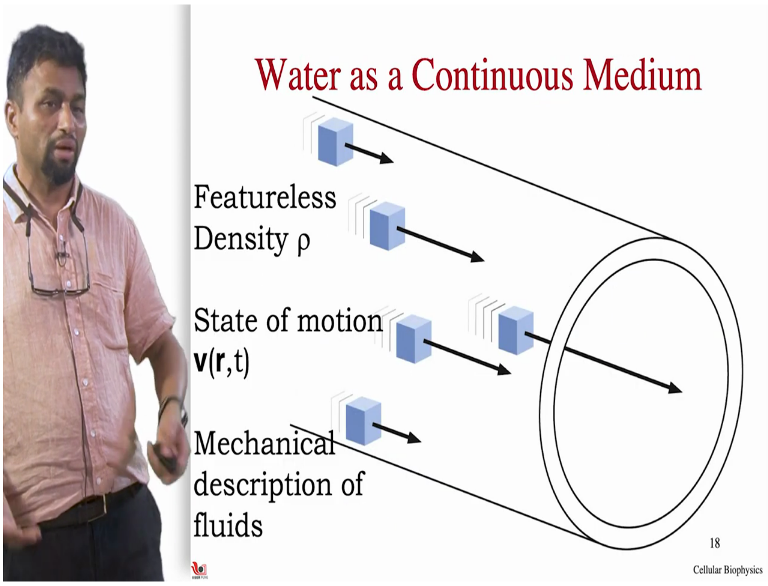

But for us, we are going to today restrict ourselves to what we call the bulk nature where we consider water to be a continuum medium. Featureless, meaning we zoom out, it is like taking a lens and Defocusing it in a camera. And there, we see that we can just simply say that there are density, there is ρ, there is a state of motion that is a vector v, which has coordinates, the position vector r and time. And this becomes our mechanical description of a fluid.

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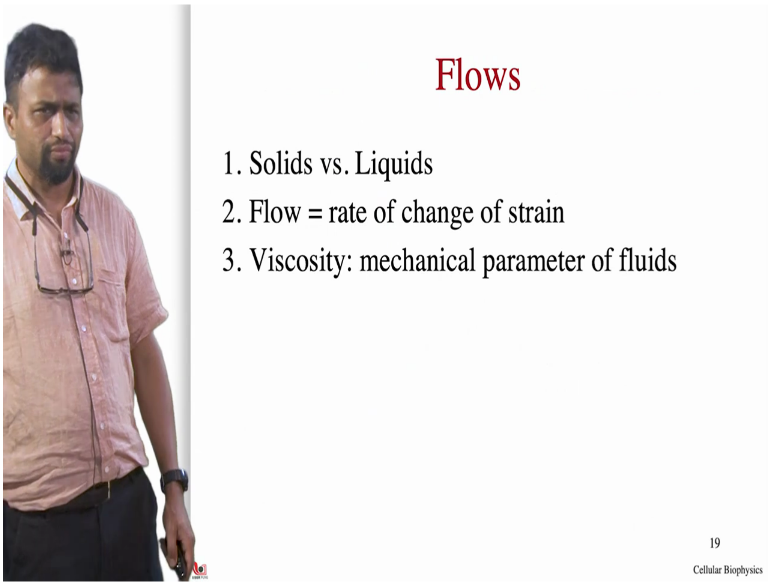

So, in that sense, flows can be compared between solids and liquids. And the flow itself is some kind of rate of change of strain. And viscosity is a mechanical parameter.

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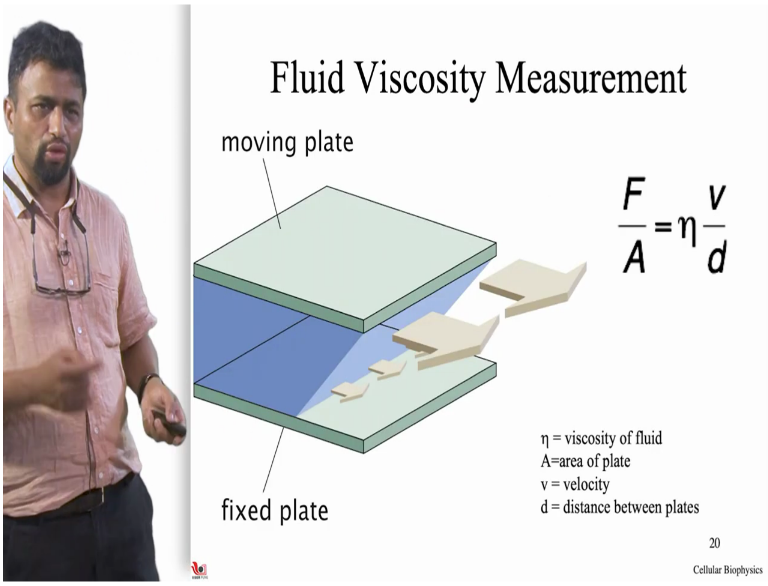

Now, viscosity measurements of fluids can be made based on this equation. And this equation is an important equation that I am going to end with for today, which is F by A is your stress, v by d is the gradient of velocity. So, whose velocity are we talking about v over here indicates the velocity of the moving plate meaning to say there is a fixed plate, there is a fluid connecting the two plates, and you are sharing it.

So, this is nothing but a shear viscometer. In some words, the area of the moving plate is A, the force you impose with those big fat arrows on top is the driving force, v is the resultant velocity of the fluid. And d is the position in terms of height from the fixed plate going in the z direction in the upward direction.

So, as you go upwards, you expect that your velocity will change. And this gradient is that slope that you see. Now, these kinds of measurements are doable, and there are measurement instruments for it. But a much simpler measurement device is one that involves a prop here, so I have here with me a ball. You see this steel ball. Now I am going to drop this steel ball into my jar of water. Now, as I drop this ball, I am going to bring it as close to the surface of the water as possible, it is evidently going to fall.

You know this, why, because gravity, but the rate of which it falls. And this is very quick, as you noticed, is going to be determined by at least two things, the fluid nature of the water, and gravity. And in that fluid nature of water, you will remember probably, there are a couple of things that are going to take an important role. And those are going to allow us to estimate the viscosity. And this because of what I just did is nothing but the principle of the ball drop viscometer and we are going to talk about this in the next lecture. But suffice to say for now, I am going to stop and we will take a little break.

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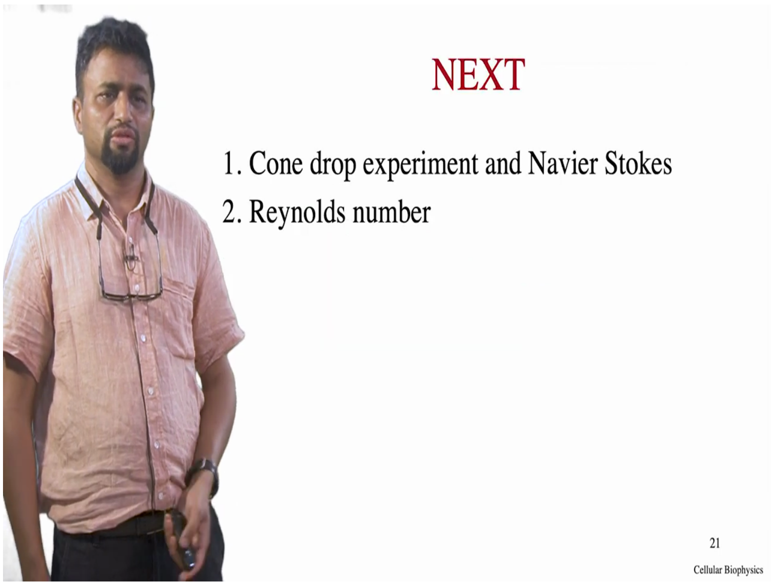

So, cone and ball drop experiments, Navier Stokes and Reynolds number are the next topics. Thank you very much for listening, and we will see you next time. Bye bye.