**Cellular Biophysics**
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**Introduction**
**Part: 02**

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Hi, so, as we were saying, why questions of biophysics are important. But it is as fascinating to also examine the what, what are we going to study in this course, you see this guy here, some of you maybe have better eyesight than I do. This is a lizard. It is a leaf tailed Gecko. That is its eye over there somewhere. Its arms are somewhere here, and the body is up there. And what this Gecko has done is what all nature seems to do, it adapts to its surroundings.

So, this adaptation is critical for survival. And this is not an ecology class. But ecology affects biology and biology affects ecology. So, it is important to know what comes from where.

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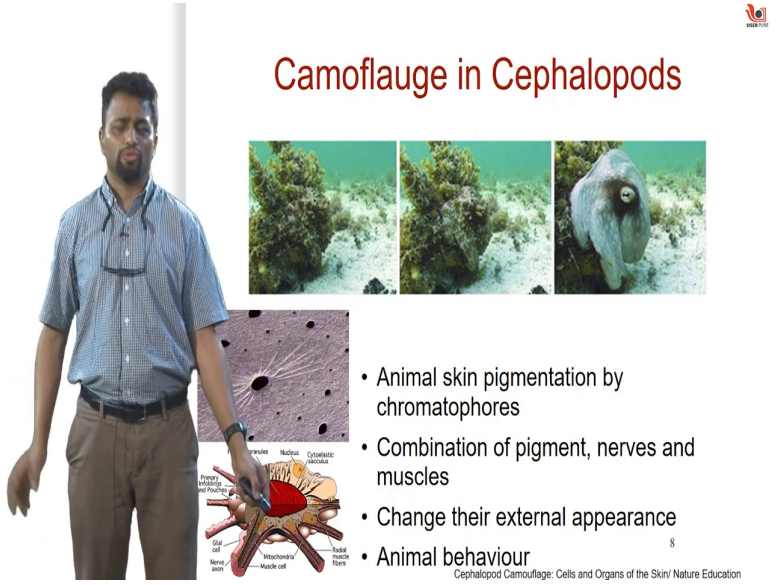


In this context, when you will go underwater, and you look for animals that are classified as Cephalopoda the head and the brain are in the same location. The classic example is an octopus. And what you are looking at in this image here, is some seaweeds and some corals. And this is the sandy bottom of the ocean.

What you do not see right now, or maybe some of you already know the answer, and therefore you have picked it up, is that if you wait for bit, this animal was always there. So, maybe if you go back to the first picture in this video, which I grabbed from the internet, this one this guy here, was camouflauge to adapt to his or her background.

And eventually, once detected, it changed color and tried to escape. So, camouflauge through animal skin pigmentation in octopi. And cephalopods in general, is driven by chromatophores. And a combination of neuronal sensing through nerves, muscles, and pigment control. In a way, the final pigment controls the so called machine, the engine that creates this change in color is due at a cellular scale. But the sensory part is due to a higher order function of the eyes, the brain and the nervous system.

So, we are going to focus on the part of the microscopic detail at the cellular scale. These guys, these dark spots you see here are chromatophores inside a cell, what you see in this sort of stellate like cell is that those cell those chromatophores have aggregated to the center, what drives this aggregation who controls this aggregation? These are some of the questions in the later part of this lecture, we are going to actually have opportunity to discuss.

The irony is that in any complex problem, you can, of course, try to study the whole problem, I mean, but it will not suffice for you, as an individual, alone to try and address everything, even as a field as a discipline, we often break things into small parts, so that we can see the parts, make sense of them and talk to each other and put it all together so that we have a big picture.

So, any kind of science is in a way interdisciplinary, the more complex it is, the more interdisciplinary is an animal behavior, while I put it at the bottom is in some ways linked to such cellular biophysical properties of chromatophores and the energy balance model molecular motors, cytoskeleton and so on and so forth. And this again comes to what we will study and why in terms of larger context of biological problems.

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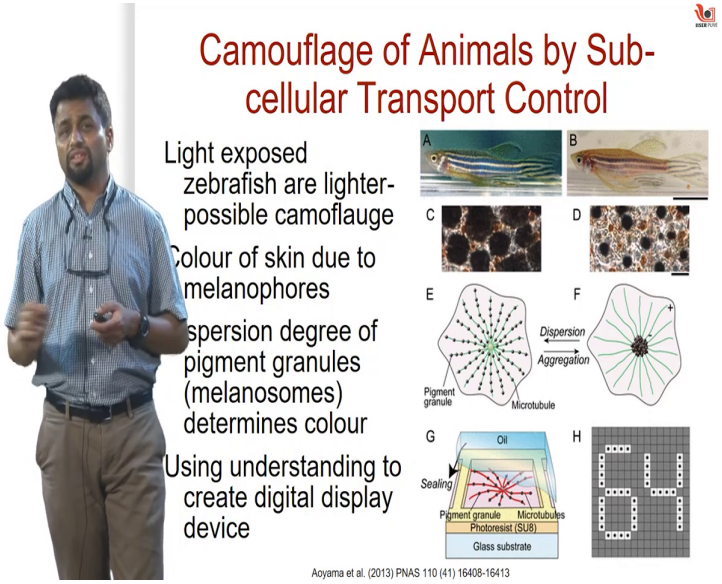


So in some senses, this behavior also shows up in other animals. Light exposed zebrafish are lighter, possibly due to camouflauge, the color skin is due to melanophores and the dispersion degree of pigment granules and melanosomes determines the color. We will use this understanding and we will see how some people have then used it because in the spirit of what some people call synthetic biology, if you understand the principle then you should be able to make something with it. The simple example is the automobile.

Because we know Newton's laws and because we know how simple objects move when given a thrust, we can design an engine to do exactly what we please. Now is this true of biology? Now, a lot of people are really pushing the frontiers of this and this Japanese group. In this particular case developed a system using the molecular motors that we are understand

now very well to produce a digital display like your, like the old fashioned Casio watches, or the ones that you see at the railway station.

So, the point I am trying to make is that understanding and engineering or bioengineering, they can go hand in hand, they may not be by the same person, but by different labs by different groups. So, just understanding for its own sake is not necessarily a stopping point for us, we can actually do more with it.

And this is only possible when we find general principles. And by principles, I do not mean saying, you know, Red Ant is better than a black hand because it can sting. But I mean, equations, equations that can predict predictions that we can test and make new things out of. So, that is what the aim of biophysics is. And that is why we are going to deal with these kinds of systems.

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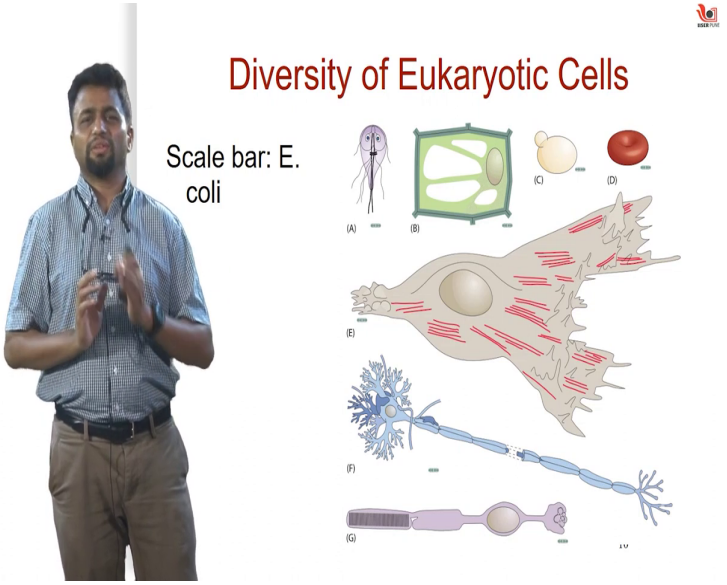


So, we said it is cellular biophysics. And we are going to touch upon a couple of different cell types. And this would have been a quiz question for me. What are these cells that you see over here, maybe some of you recognize some of them, all of you have blood in you. So, you recognize the red blood cell. Maybe many of you recognize the neuron without which none of this would be possible, our brains would not be working. And those are the retinal cells, therefore, you would not be able to see me without the presence of these.

Now, what has not been commonly thought of is the fact that you have a little scale bar here, somewhere down here, you should see this little line that Smudge is nothing but an Escherichia coli, gram negative bacterial cell. Why did I put it there? You remember high

school physics, where we talk about units, dimensions, mass, length, time, sometimes charge. And the fact that these are basic for us to be able to make sense.

Now, for some reason, a lot of biology has had a very hard time trying to make sense of numbers, or quantification. And a large focus of this course is going to be on exactly this quantification, but any quantification especially units, if you remember, your physics is based on relative numbers. I mean, after all, unit is nothing but relative to something.

So here, we are going to say that we are going to measure sizes relative to E Coli. Why E coli? Okay, good question. And I am going to ask you this in one of your quizzes, but one of the simplest reasons is that we know a lot about it, we know how it behaves, we know how much of it is there. We know how fast it divides, we know its size, we know its dimensions, and we have some fairly accurate estimates of its mass.

So, if we have that as a standard, then we have a chance at quantitating. Life in diverse eukaryotes. Incidentally, this is Giardia intestinalis, this is a plant cell, and this is fibroblast, so called skin cell.

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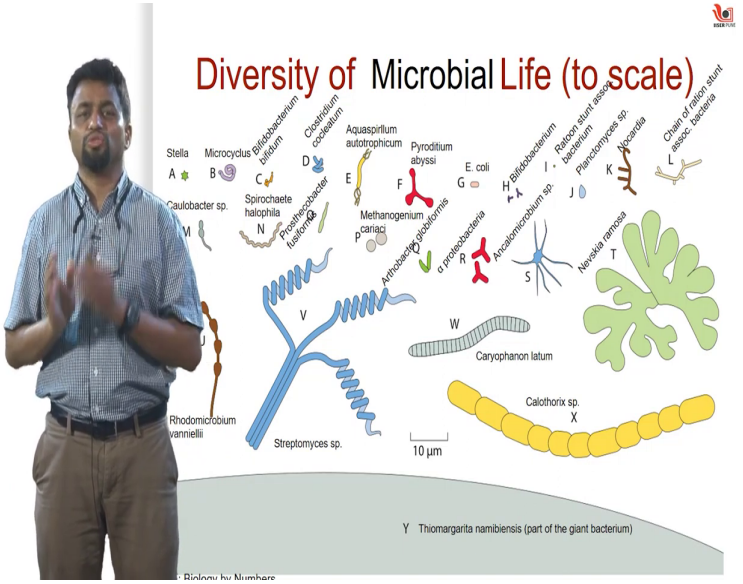


But diversity of life at cellular scale is not just present in eukaryotes, we also have microbial life, also called prokaryotic life. And if you sit around trying to compare these things, so you have a scale bar down here, which is 10 micrometers, E coli is approximately 2 micrometers in length, so it is already 5 times as much. And you see that bacteria prokaryotic microbial life can extend in all of these sizes, hundreds of times of the size of an E coli cell.

And if you plug in back the species names, you will see that there are all kinds of funny bacterial names. Many of these you may never have heard of. And if you are not a microbiologist, you probably never will. I am not expecting you to remember these names, but it is to tell you that there is a diversity. And I hope I have conveyed this to sufficiently that even at a cellular scale, there are all kinds of different cells, there is no such thing as a single cell in other words, and yet, we are going to have to simplify in order to make sense and talk about a single cell.

Now, those of you remember high school chemistry and physics, remember we always talk about a hydrogen atom. So, for us the equivalent of a hydrogen atom in biology at the cellular scale is going to be a E coli cell an E coli cell.

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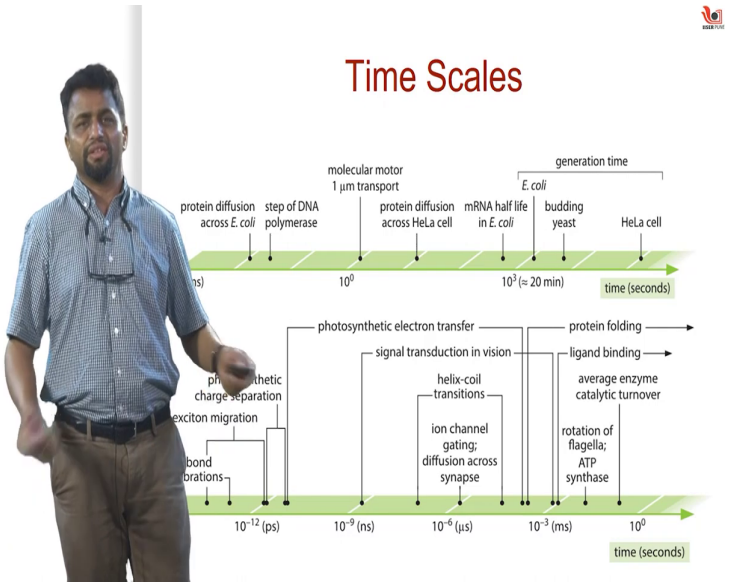


So, along with size, we also have differences in time. And this is sort of a rough idea for you to see that all the way from $10^{-3}$ milli second, all the way to seconds cellular scale can exist. And indeed that this time can extend all the way up to flagellar beating in 10s of seconds and even minutes timescales. In fact, cell division of bacteria, simple E coli like bacteria is 20 to 30 minutes depending on the growth conditions. And this would suggest to you that one thousandth of a millisecond to 110s of seconds, I am sorry, 100s of seconds is the range of timescales that we are likely to see at a cellular scale.

Mycobacterium tuberculosis incidentally, which causes TB and which a lot of humans are affected. India is one of the higher highest burden countries at the moment, is a very slow growing bacterium. So, how does all this the mechanisms of the internal behavior and the

timescales of cellular behavior, how do they integrate, and these are things that we are going to discuss in parts of this course when we talk about dynamical systems, gene expression networks, and try and see if we can make sense of it.

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So, when we look at cell motility. So, far, we talked about space separately and time separately. Now we combine these two, we look at space and time. And in such a case, what you are looking at is a swarm of bacteria that are spreading like crazy throughout this region, and completely filling it, this swarming behavior has been described in an earlier paper. This is from the old work of Howard seabag. And I am going to touch upon his work quite a bit, because it has been pioneering in the sense of the kind of revelations, the application of physical logic and experimental techniques has revealed to us the nature of bacterial cellular life.

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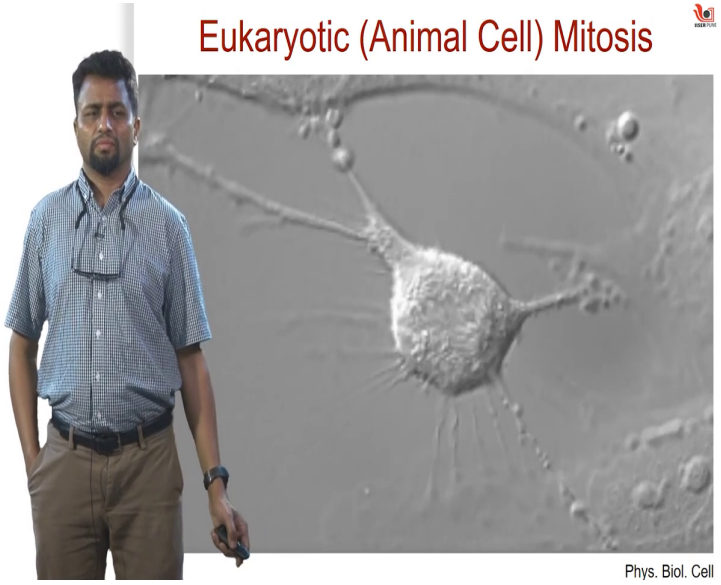


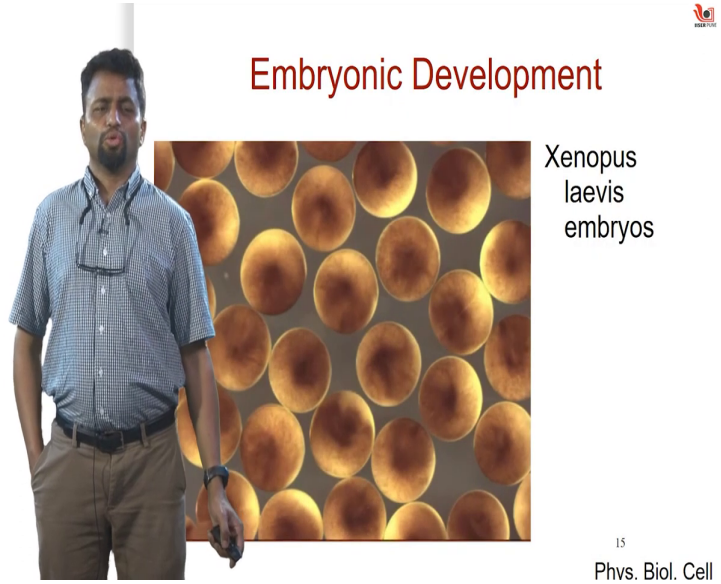


(Video): This video sequence shows some of the events of the eukaryotic cell cycle for an individual mammalian cell growing in tissue culture.

Professor: So, this is mammalian cell culture and its division.

(Video): This living cell is observed using differential interference contrast microscopy.

Professor: DIC is label free label free, you do not need to put a dye so you can see.

(Video): At the start of video sequence, the DNA has finished replication, the chromosomes have condensed, and they have all lined up in the middle of the cell. Shortly after the video starts playing, the chromosomes split into two equal groups and move to opposite sides of the cell.

Professor: This you know this part is in fact nothing but mitosis. And mitosis. I mean, many of you remember the words mitosis meiosis, you can probably recite the stages of miotic subdivision. But for us, the interesting part is that if I want to take a chromosome, let us say, this is my chromosome, and I want to move it from this part of the cell to this part of the cell somewhere here. What do I need to do?

I need to exert some kind of a force, I need to push it or pull it or do something. I mean, if you do not do that, an object at rest continues to remain at rest. And this we know from Newton's laws. An object in motion on the other hand continues to remain in motion, which is the law of inertia.

The problem with that is do even the simple laws of inertia apply at the cellular scale. It is a good question. And I would like to tell you that weird things happen inside cells. This is not because biology is different, but because the physics is different. And I hope that you will learn such fascinating things that you will look at your biology course and your textbook for the different perspective after you finish this course.

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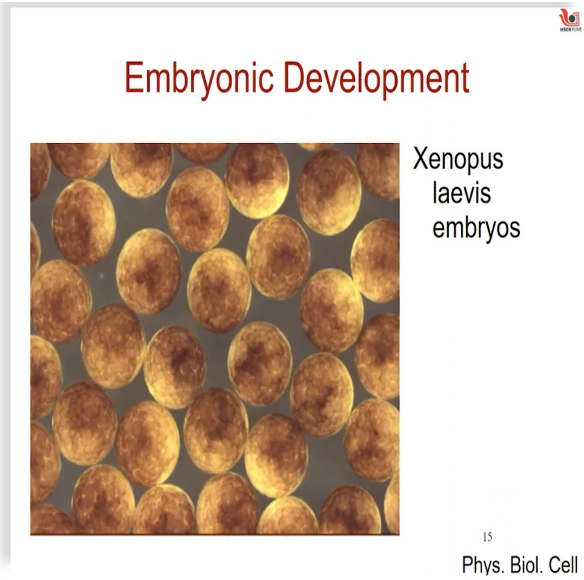


(Video): This video shows the remarkable.

Professor: Now, embryonic development as I said to you earlier, we were all one egg, right one egg, ek unda usmai se bana ek chicken, chicken ko khaya, no more chicken, no more egg. But in this kind of a situation, life itself is reproducing itself. In other words, embryos, when they are formed, they divide they grow into adults, they, in this case of frogs, they will sexually reproduce, form new embryos and they will continue the cycle of life.

The process by which an egg divides and become such this complex organism is fascinating and the early division in Xenopus, laevis, South African clawed frog is amazing because it is so synchronous meaning to say that there is no higher power telling these embryos now you divide, now you divide there is a clock. That clock is something that we are going to discuss in the later lectures about the genetic program of cell division.

Because if something is so regular, then what is the law that governs it? How does the timing get maintained? And all of these questions are fascinating. And it is important, however, to also know what the biology is, in order to make sense of the questions and the answers that we get out of them. So, I am going to continue playing this video and I hope you enjoy this beautiful movie of Xenopus embryos dividing.

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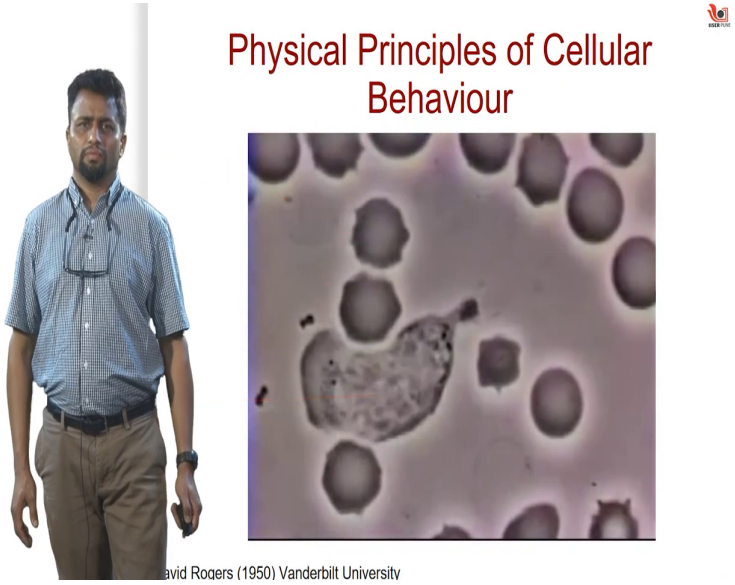


(Video): This video shows the remarkable synchrony of the early embryonic cell divisions for the quad frog Xenopus laevis. About 25 frog eggs were fertilized simultaneously in this petri disc and then filmed over the first dozen rounds of cell division. Each cell division cycle takes about 25 minutes in real time.

Professor: So, 25 minutes is pretty much close to bacterial cell division.

(Video): Not only do all the cells in each embryo divide simultaneously. But the entire disc of embryos maintains essentially the same clock time, over several hours after fertilization.

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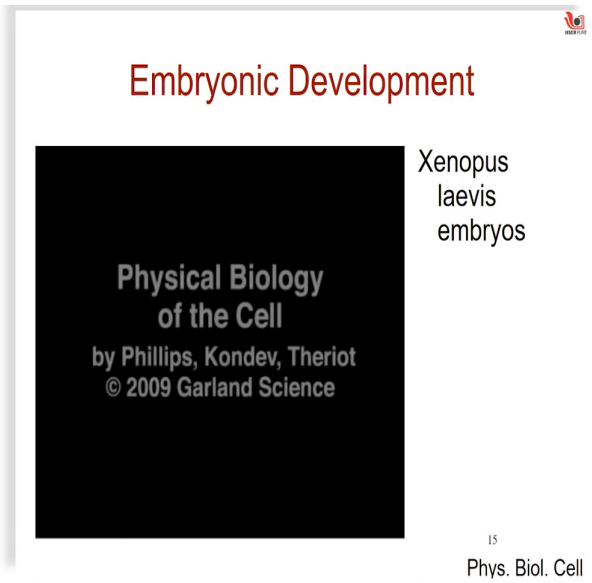


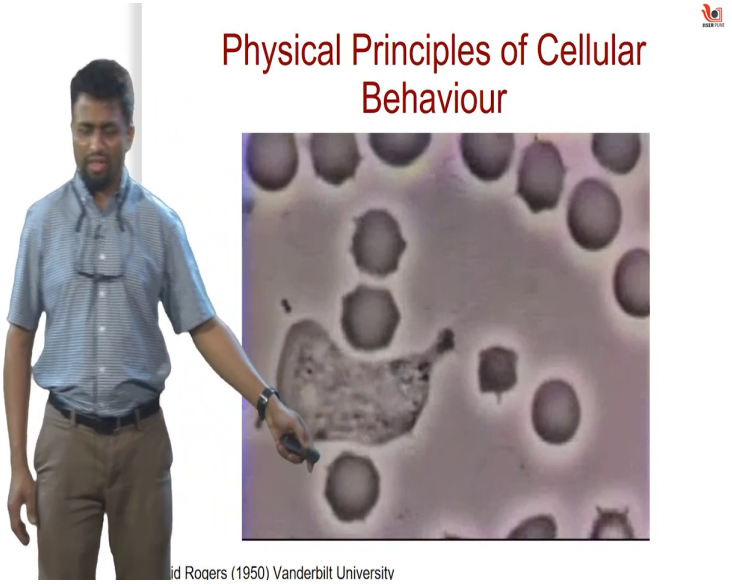

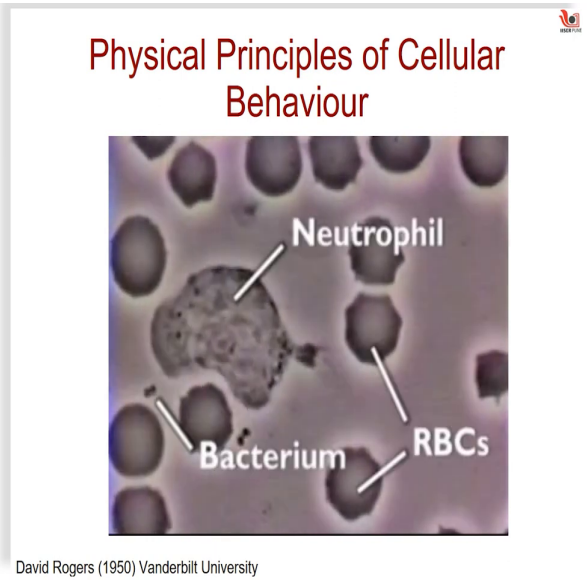


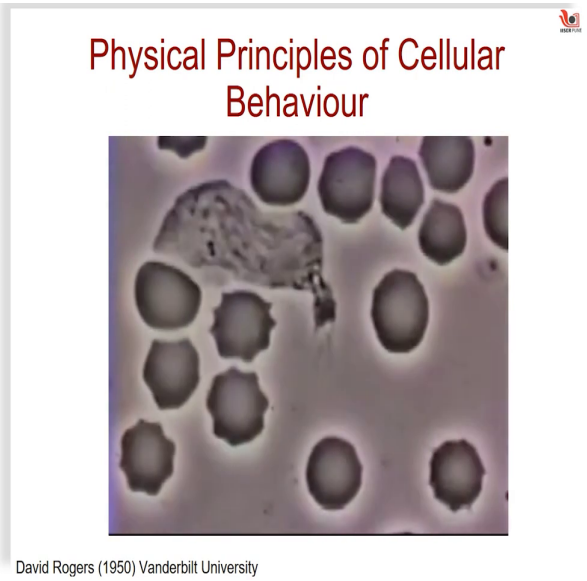


Professor: So, I have one more video to show you, which is related to the idea.

(Video): This classic movie was made by David Rogers at Vanderbilt University.

Professor: So, what I am going to show you now is a video that I just started. And it is an ancient video. I mean, by today's standards, it was made in 1950. And yet this video illustrates something really dramatic illustrates the migration of a cell, which is inside us. This is inside our blood cells. What you are looking at here are red blood cells. This is a neutrophil this is a white blood cell  in other words, or type of white blood cell.

And these little guys here, they are bacteria. They are Staphylococcus aureus bacteria, which ordinarily if they were in your blood, you will be in trouble there will be septicemia of some kinds. Now, what you will see is nothing but predator prey behavior, just like the cheetah

running in the Savanna chasing a deer, you will see something like that, and I am going to let them speak and then we will discuss a little bit about what that tells us.

(Video): This classic movie was made by David Rogers at Vanderbilt University in the 1950s. It shows a neutrophil, a type of white blood cell chasing a bacterium through a field of red blood cells in a blood smear. After pursuing the bacteria around several red blood cells, the neutrophil finally catches up to and it gulps its prey.

Professor: So, it is important to note that this bacterium is behaving like a large animal. But the back I am sorry, the back neutrophil is behaving like a large animal and bacterium like a prey food for the large animal. But these are not large animals. They do not have brains. So, what is going on? How are they sensing each others presence? How is the bacterium trying to escape? How is the neutrophil trying to catch?

What causes it to finally eat it up? What happens to the others? Does it have any memory? All these questions are things that we think that the kinds of things I am going to talk to you about in the coming lectures are a part of, they are going to help you understand the broader context of this behavior.

(Video): This classic movie was made by David.

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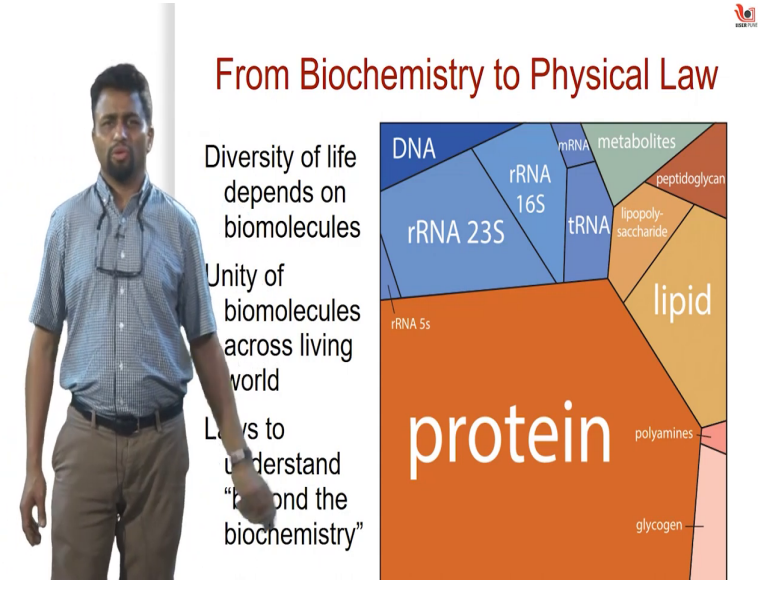


So, along with that, we have the problem that if you are a molecular biologist, you are familiar with this kind of a map. And what this map depicts to you is the diversity of molecules or biochemical components inside a cell, it tells you that the unity of biochem biomolecules exists and that proteins form the largest diverse group in terms of biomolecular

life. But what it does not tell you is how these relate to each other. And it does not tell us what the physical laws are, that may be limiting what we see in terms of the diversity of biomolecular life and biochemistry.

Now, if you want to study biochemistry, you should take a biochemistry course evidently, whatever you talk about is how these fit into each other how at a systems level, they integrate.

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And finally, in terms of answering the why again, that even after you learn such a course, even economists, the journalist called the magazine is called the economist, so I assume a economist, have been intrigued by the question, when you have a transcriptional response event, which is to say DNA is interacting with a protein and resulting in the change of chromatin state, resulting in gene expression changes.

This is like finding a needle in a haystack. I think many of you may be familiar with the terminology in the English language. And those of you who are not let me explain this, you go to a farm, there is a bunch of dried stalks of rice or wheat inside that someone put a needle. Now you do not know where they put it, how do you find it. And this is a search problem. This is an actual formal search problem. And we do not know how cells solve it. We will talk about some of the possible ideas that may explain the data.

But if we understand the algorithm by which cells and biology is working, then we can design better search algorithms, you can be the new Google basically, you can build a better search engine, you can discover new things. And these are some of the benefits of kind of this sort of research, which in fact, relates to some older ideas of Shannon's information, entropy and DNA as an information storage device.

So all in all, I hope I have convinced you that this subject is exciting. This subject is modern; this subject has relevance to economics, to the basic sciences, and even maybe to our broader understanding of life. So, I am going to pause here, and we are going to return when we discuss a little bit more about the structure of this course.