Introduction to Cell Biology
Professor Girish Ratnaparkhi
Professor Nagaraj Balasubramanian
Department of Biology
Indian Institute of Science Education and Research, Pune
Biology of Cells – Part 1

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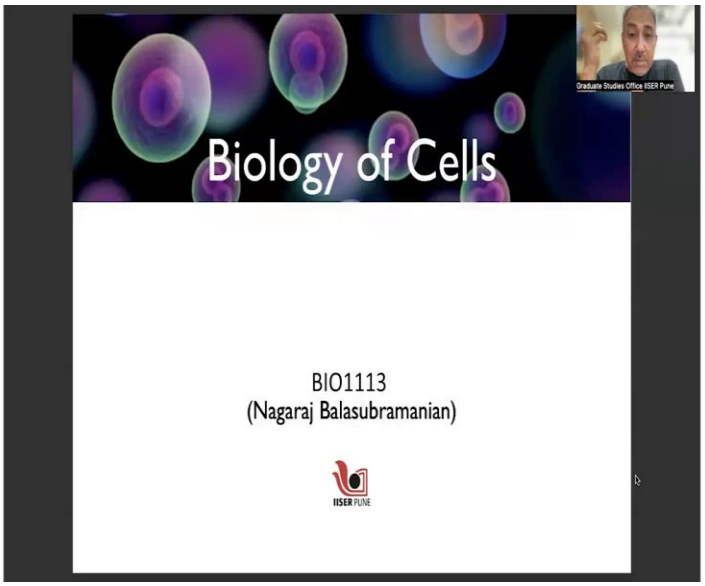

So, we continue with this series of lectures. We are actually beginning this series today. Last time we spoke a little bit about microscopy.

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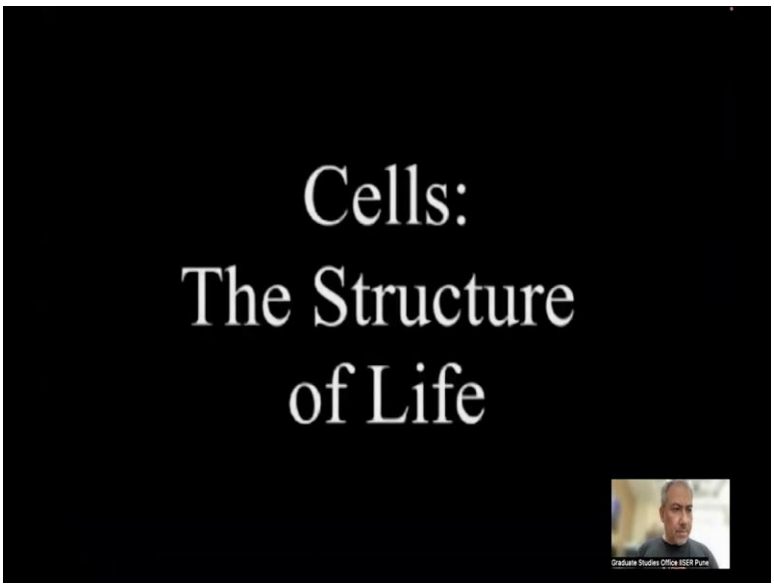


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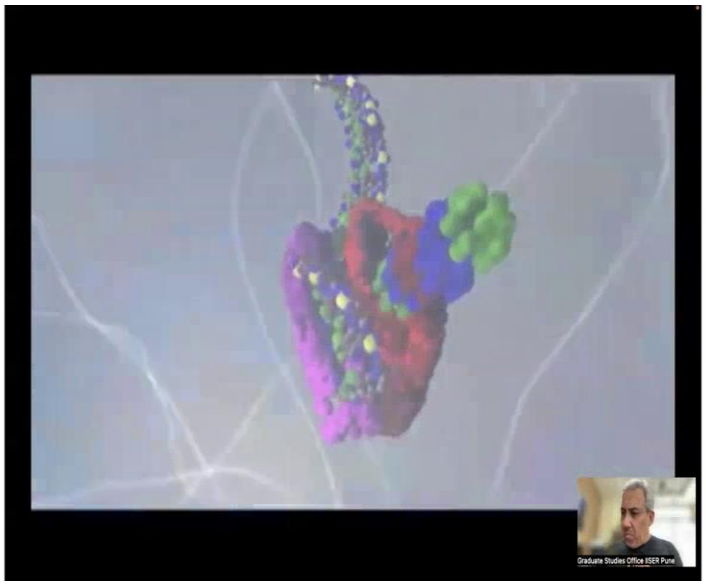

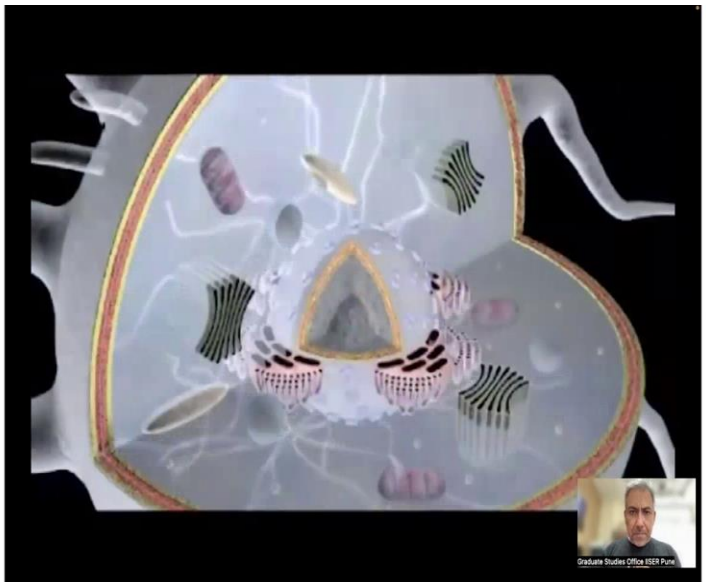

Narrator: All life on Earth is made up of cells, the smallest units of life. Cells carry out all the processes of life, taking in energy and nutrients, growth, responding to stimuli, and reproducing. A cell membrane controls the flow of materials in and out of all cells. Inside the cell membrane lies the cytoplasm, a rich reacting chemical soup of proteins, fats, nucleic acids, carbohydrates, ions and water. Structures called ribosomes synthesize the proteins found in cell cytoplasm. Structures like ribosomes that carry out specialized functions in cells are called organelles.

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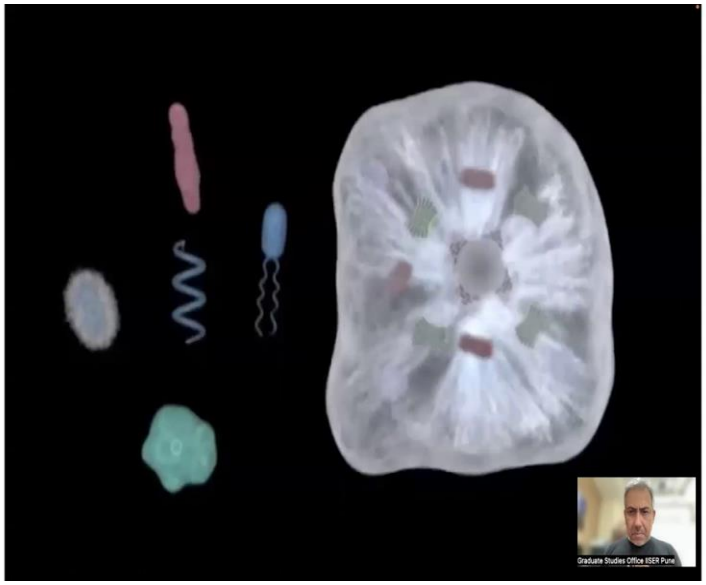

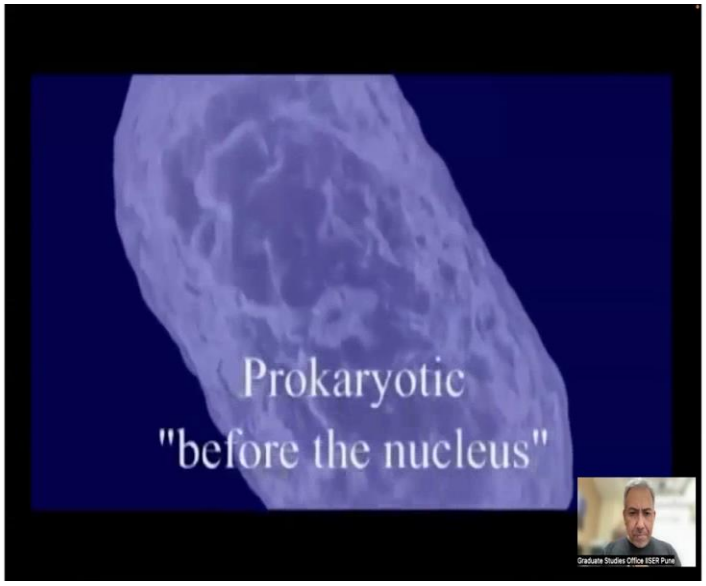


Eukaryotic
"true nucleus"
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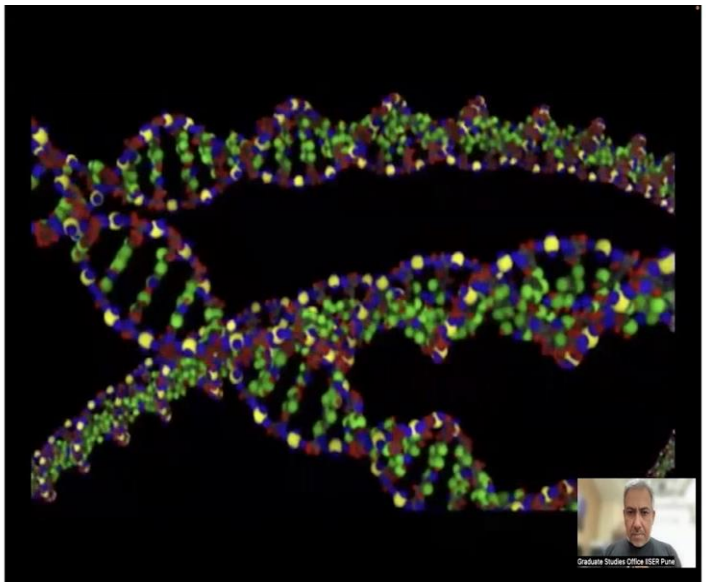
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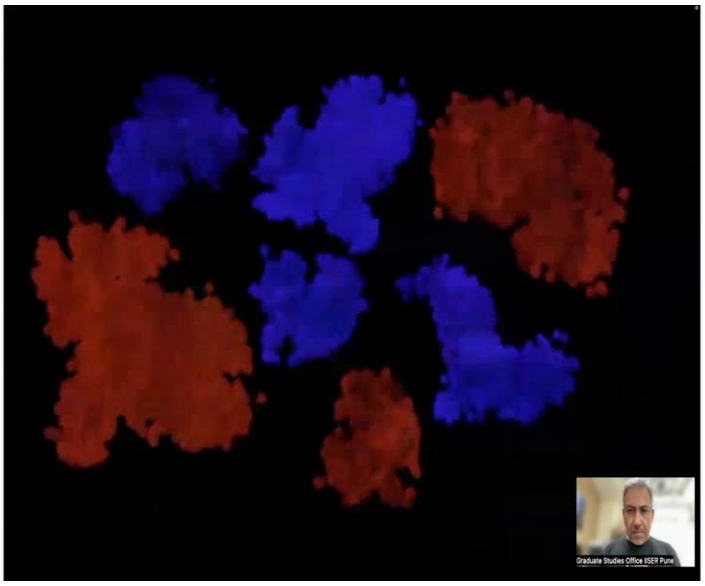

Cells are divided into two categories, based on whether they have one particular organelle, a nucleus. Cells lacking a nucleus are called prokaryotic, Greek for before the nucleus. Cells having a nucleus are called eukaryotic, Greek for true nucleus. The nuclei of eukaryotic cells contains DNA, the genetic material of all living organisms, and several types of proteins enclosed in a double membrane, called the nuclear envelope.

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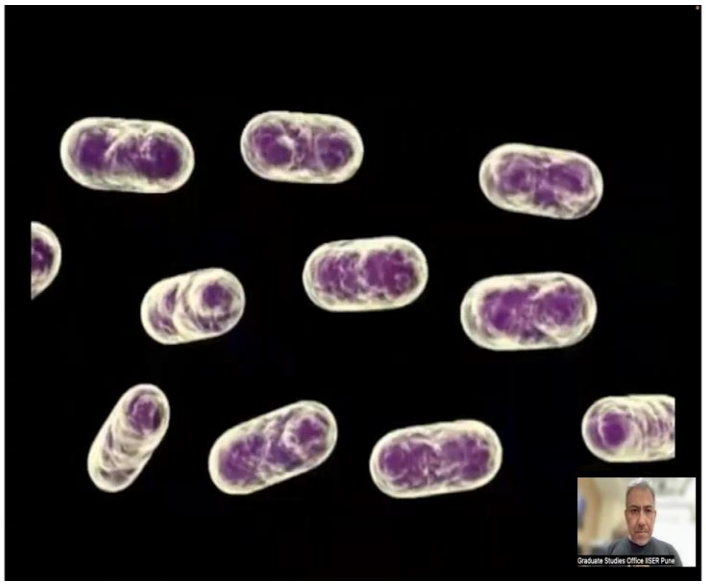
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No membrane encloses the DNA of prokaryotes, which is usually attached to the cell membrane and concentrated in a region of the cell, called the nucleoid. Nucleoids are only distinguishable and that they are somewhat darker than the rest of the cytoplasm. Several other differences exist between prokaryotic and eukaryotic cells.

Prokaryotic cells are usually no larger than half the size of the smallest eukaryotic cell, and have you if any organelles other than ribosomes. Eukaryotic cells, on the other hand, usually have at least six or seven different organelles in their cytoplasm. Another difference is that prokaryotic cells are found only in the form of simple single celled organisms, like bacteria. Eukaryotic cells

are found in more complex single celled organisms like paramecium and euglena and all the multi-cellular organisms on Earth, including humans.

Because of their greater complexity and because they are the building blocks for complex multi-cellular organisms in the rest of this program we will focus on the structure of eukaryotic cells.

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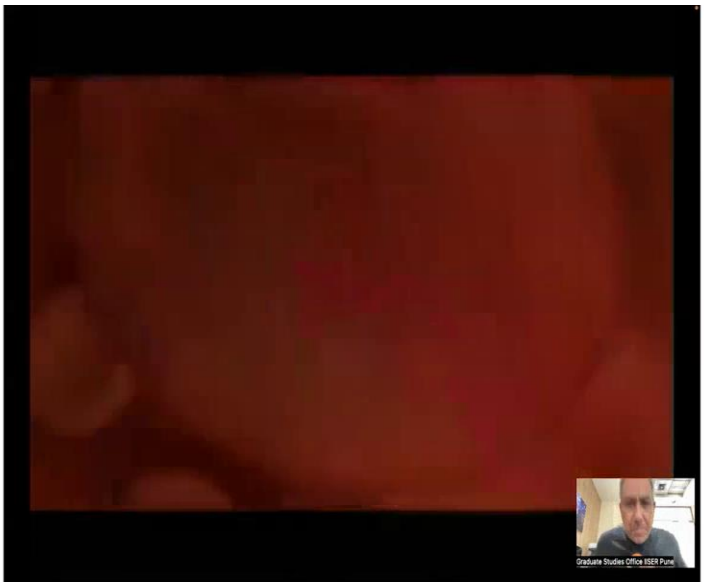

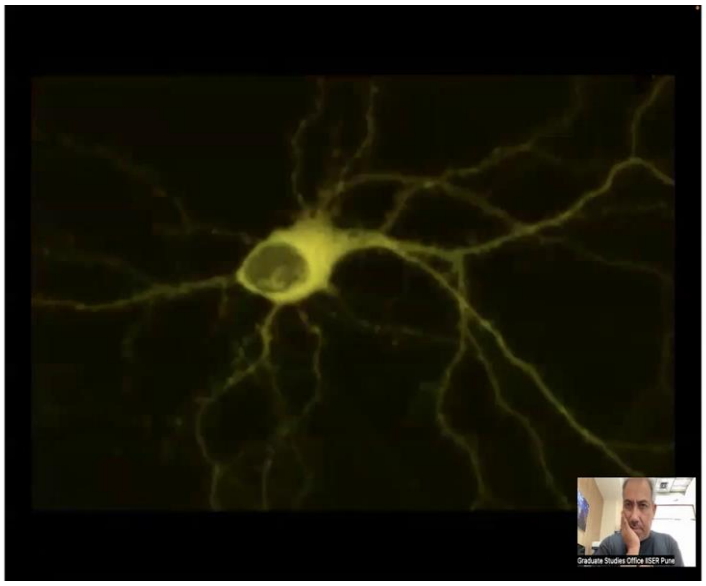

Eukaryotic cells can take on a large number of shapes, sizes, and functions. For example, in our own bodies, round dimpled red blood cells carry oxygen, while long thin nerve cells that transmit information between the brain and the rest of the body, branch out at either end and can measure several feet in length.

In the world of single celled organisms, the slow, constantly changing shape of amoebas allow them to trudge through their environment and capture prey, while their single celled veteran, the paramecium and euglena, are built for speed.

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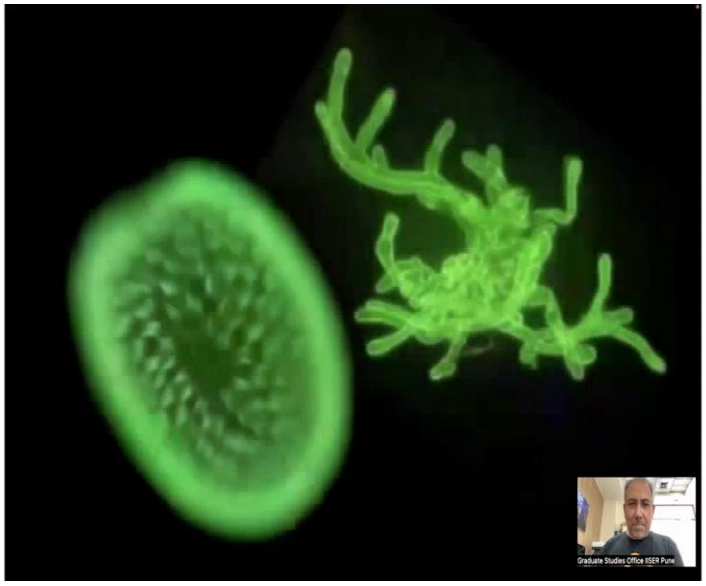


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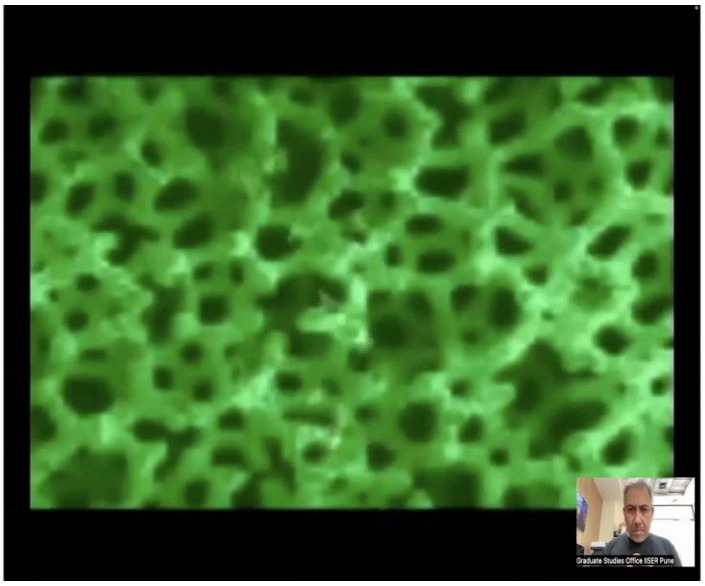

Stiff non-living coating called cell walls covered the cell membranes of plants, fungi and certain protests. The cellulose cell walls of plants and chitin based cell walls with fungi provide members of these kingdoms with a structural support necessary to stand erect on land. The protective coatings approaches such as diatoms, which like glass are largely made up of silica are some of the most beautiful structures in nature.

Besides being strong, cell walls are porous, allowing the passage of small molecules such as minerals, amino acids and sugars to the cell membrane, which actually controls the flow of materials in and out of a cell.

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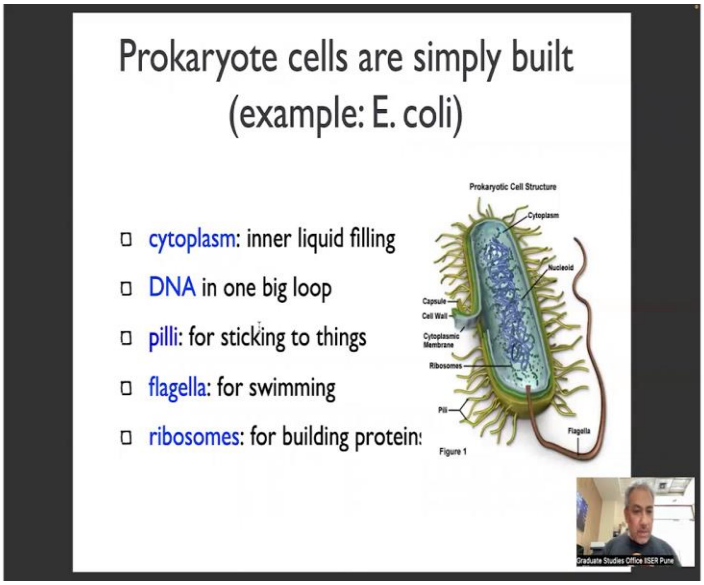

Professor: The critical thing to consider here, when you are thinking about prokaryotes and eukaryotes, and do not worry about the other details that were discussed in this particular video, it is meant to be an introduction and it is something that we will come back later and there are going to be things that we are going to very specifically discuss individual aspects of this as well.

The important distinction to remember between prokaryotes and eukaryotes is, of course, the fact that there is a nucleus that is present in eukaryotes that is not present in prokaryotes. Prokaryotes have nuclear material, but the way it is organized and the way it is processed is very different. The size of cells is distinctly different between prokaryotes and eukaryotes. And that is an important factor to consider when we think about what could have led to the evolution of more complex eukaryotic cells.

One of the things to keep in mind is the fact that these cells have indeed become significantly bigger. And that complexity or what exactly is actually going to allow for the cells to get bigger and develop complexity is an important question for us to think about. So, when you are comparing prokaryotes and eukaryotic cells, you have the presence or absence of the nucleus. You have the fact that these are cells that are bigger as compared to the other that eukaryotic cells are significantly bigger and are more complex as compared to prokaryotic cells.

There is also this point that was raised that eukaryotic cells actually give rise to more complex organisms. So, when it comes to making up of tissues and more complex multi-cellular

structures, eukaryotes have done significantly better and are able to put these structures together in a way that prokaryotes might not be able to. So, prokaryotes are simple. They have a cytoplasm, they have DNA which is present in the form of one big loop, they have structures like, they could have structures like pilli or flagella, and importantly, they have ribosomes as building blocks for proteins.

So, it is a very basic unit of the cell. It is a unit that has a simple set of players. The more important thing is that these simple set of players are able to allow for prokaryotic cells to replicate, to divide, to multiply, as the case may be, and allows them to procreate and pass through multiple generations.

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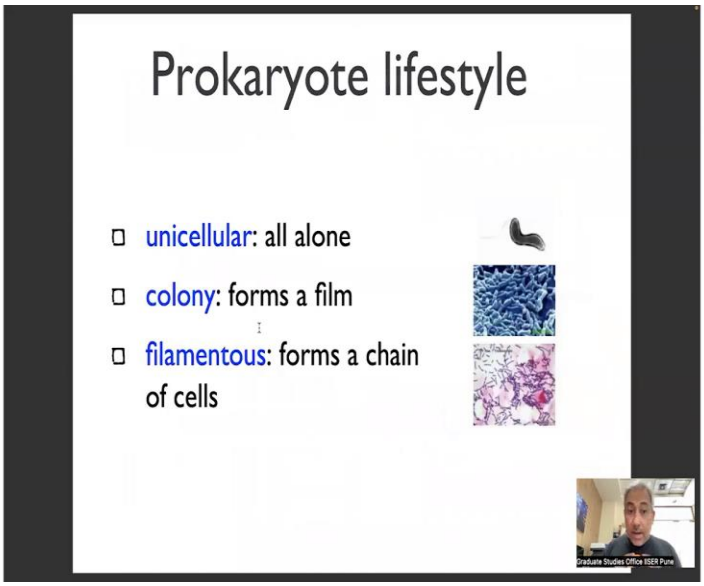

Prokaryotic lifestyle is largely unicellular, and this is again, very distinct difference from the eukaryotic organisms. They could make colonies at times. And in some cases they can form filamentous structures as well.

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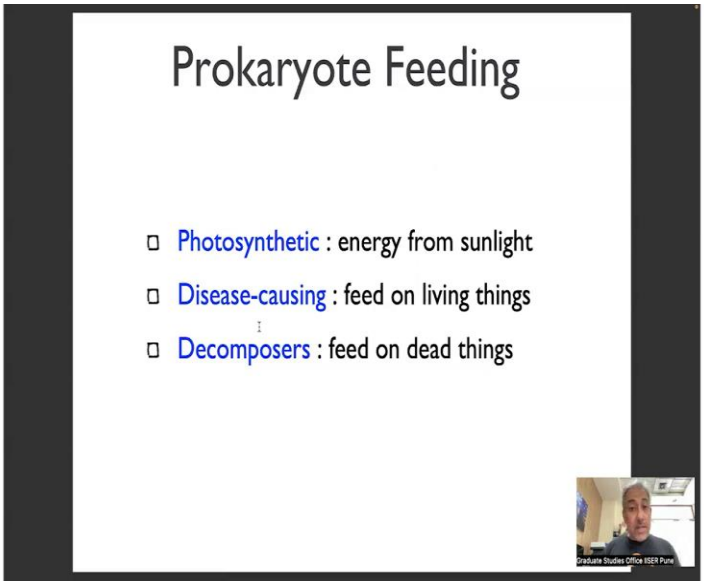

As far as prokaryotes are concerned, their ability to feed is driven by multiple different pathways. They could use something like sunlight and use photosynthesis. In case of disease causing prokaryotes, they could feed of living things. And there are decomposers that could feed off dead things as well. So, their mechanisms for intake of food are distinct.

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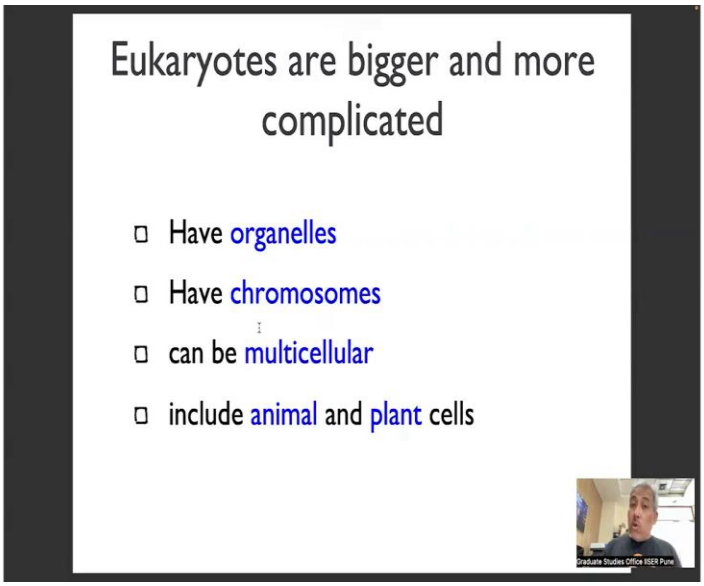

Eukaryotes, on the other hand, as I mentioned, are bigger and more complicated. They have organelles. And when we come to cellular organelles, we will discuss what the relevance of presence of these organelles means. The fact that there is compartmentalization, which is an

interesting idea in cells, that different things inside the cell do different things for the cell and cellular organelles are built largely to achieve that.

The presence of the nucleus obviously, I alluded to earlier, eukaryotes also have their DNA is organized in very distinct structures called chromosomes. And so the way chromosomes are assembled and put together also is a very distinct characteristic of the nucleus that is present in eukaryotes, which is very distinctly different from prokaryotes. They can be multi-cellular and cells such as animal cells, we, cells in our hands, brain are all eukaryotic cells. Plant cells are eukaryotic in that sense. And so this distinction does exist between prokaryotes and eukaryotes.

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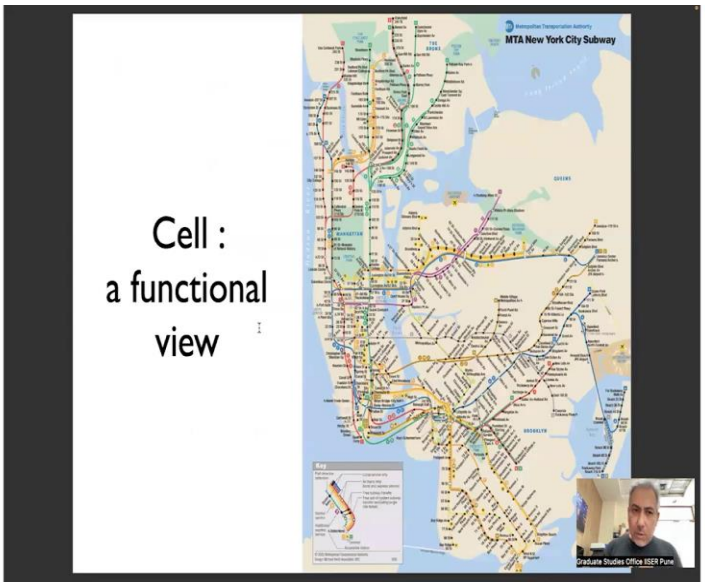

One of the important, as I said, characteristics of how cells are assembled is the way different aspects of the cell are required to make it function optimally. So, when you think about a functional view of the cell, my favorite example is this map that is for the metropolitan subway system in New York, and you can see how the architecture of this railway system is built. And there are very distinct aspects of this railway network that all work together to ensure that not only the trains are moving from one place to another as required, but also people are carried along with it from one place to the other.

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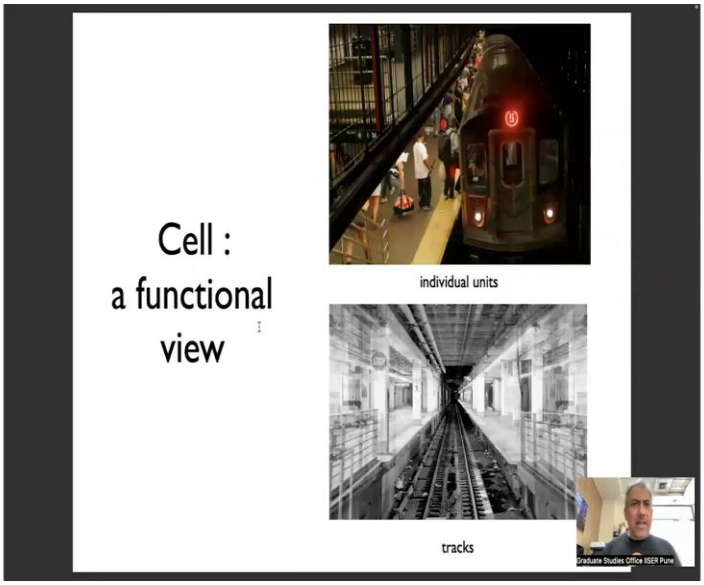

And there are very distinct aspects of this system that we will encounter even when we think about cells. So, this is just a very generalized view that allows you to think about how cells are put together. One is the presence of these individual units. So, just as you have train compartments, and individual trains that are able to move along these distinct tracks. Cells have very distinct structures that are able to do this as well. So, the presence of these individual units and how these individual units are used is an important aspect that we will come to when we think about cells. Like the train system cells have tracks on which things can be moved around and we will come to what those tracks might be for cells and how they are used.

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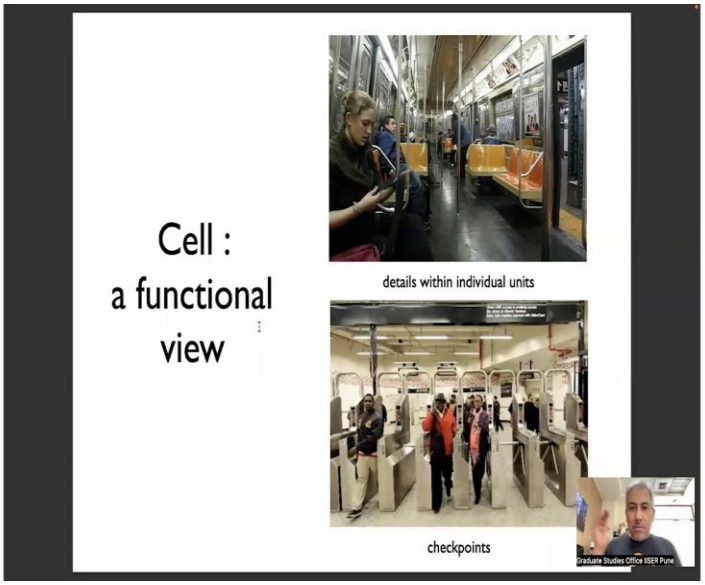

Each individual unit has very distinct details. So, compartment has doors, has handlebars, has seats to sit and this could vary depending upon the kind of compartment that you are looking at. So, these individual structures that exist in cells also have their own distinct characteristics or properties. And that allows them to do what they are required to do. This particular unit may be very different from another unit, because their functionalities are very different.

There are very distinct checkpoints that are present in any train system across the country. And those checkpoints exists even in cells as well. The checkpoints are built to kind of ensure that entry is regulated, that you have the right ticket to get into the right place, it makes sure that those who cannot get into a particular area, which is restricted for any reason, are not able to get there, all these checks and balances exists in cells as well, right. And so checkpoints are very vital also.

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And like with any other train system, there are distinct command centers from which all this network is watched, is regulated, is commands are sent out to say this particular train needs to stop and be delayed for a certain amount of time to allow for other trains to pass through. This individual compartment or train may not necessarily know that it needs to stop at that particular point. It is this command center that looks at everything and ensures that there are no clashes that are happening and make sure everything works on fine, works fine in this network. The same is true for cells. There are very distinct command centers that actually do this. And when we think about cells, we are also going to think about these command centers and what they mean.

The other interesting thing that a network like this has, which again cells themselves also carry, is that they have very distinct information cues. So, when you look at a subway system, the different kinds of trains, the railway station has a particular name, the train has a particular number. And so, this information cues are vital for many reasons. It ensures that somebody who is a passenger who is getting in knows that they are taking the right train. It allows them to know that this particular train will travel on this particular track.

So, the information that is provided in these cues helps you decide, helps you make decisions, the command center is able to visualize these trains based again on what train they are looking at any given point. This also means that they are able to regulate the system based on these information cues.

So, within the cell as well, whether it be cellular organelles, whether it be trafficking vesicles, they all carry this kind of information cues. And the information cues may not be written down, but there are, they have their own codes, which can be read by the system that is operating inside the cell. So, for you and me, being able to see that this is an A train or an R train might be information that we can process and make a decision. The cell uses very different information cues, but it uses it to the same effect. It uses it for the same reasons or purposes, so to speak.

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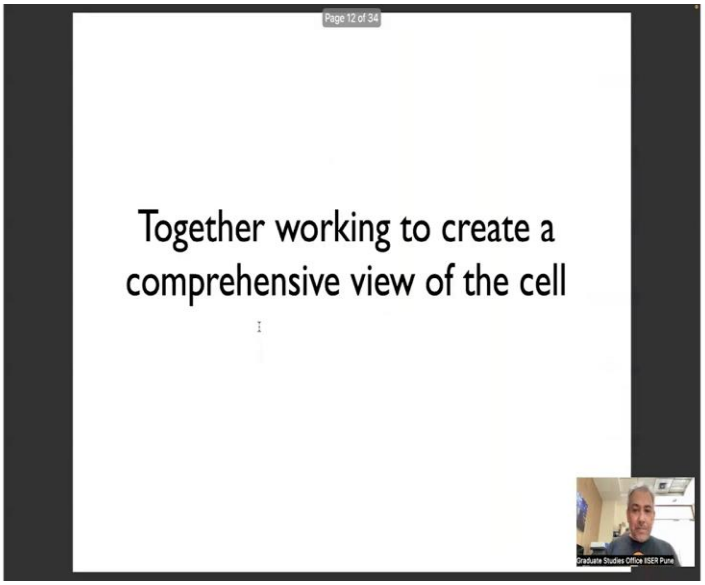

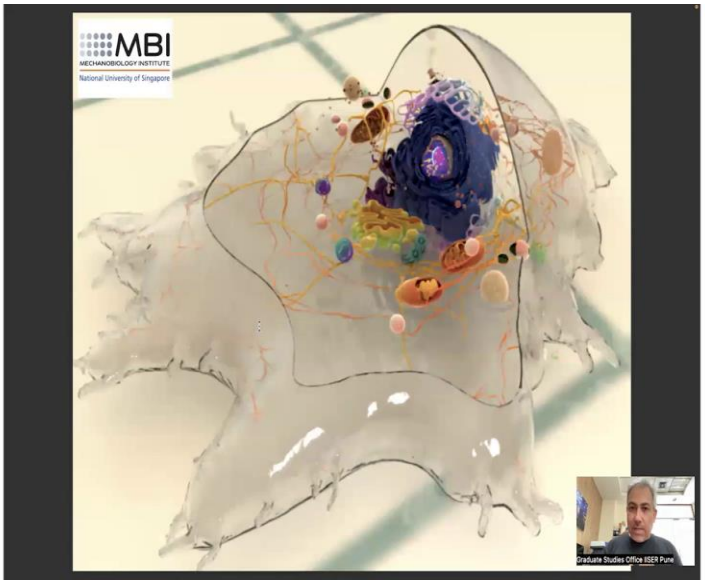

Together, all of this comes together to create the comprehensive architecture of the cell, and also drive the comprehensive functionality of a cell. So, remember, when you are thinking about

cells, you have to consider that there are all these multiple aspects that have to get integrated, have to talk to each other, in many cases, influence each other and together determine what the cell does at a particular point of time.

So, if you are thinking and we will begin with the cellular membrane, which is the boundary of the cell, which is what talks to the external environment, and you go all the way into the nucleus, which is the innermost core of the cell, everything that happens on the outside is reflected or is affecting, not just the plasma membrane, but all the way into the nucleus. And all the players that are present in between are contributing in one way or the other to drive this outcome.

So, when a cell has to respond to something, be it a neurotransmitter, be it, you have a cookie and there is this intake or increase in your blood sugar level and cells have to respond to the sugar intake that has happened, everything is determined by this complex network and is determined by how this complex network comes together or works together to drive the behavior of cells.

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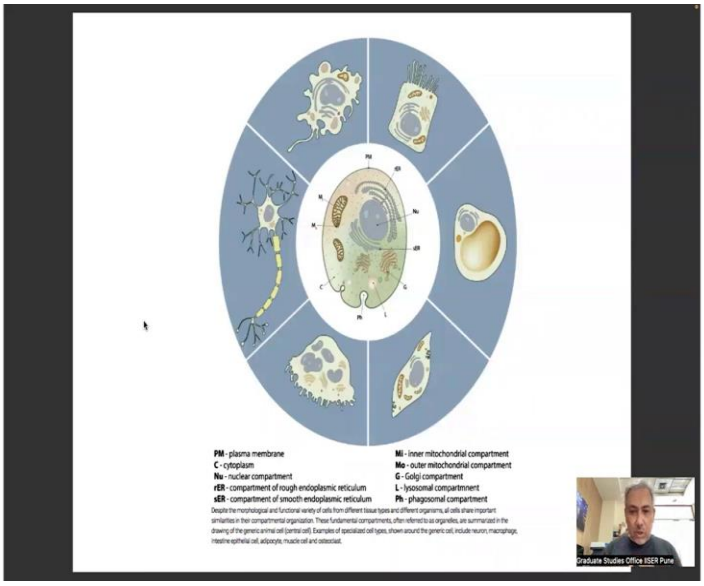

So, all these players are coming together to essentially drive the behavior of the cell and to determine how the cell actually works eventually, and that complexity is what we are going to try and understand and we are going to try and figure out how exactly this is brought together.

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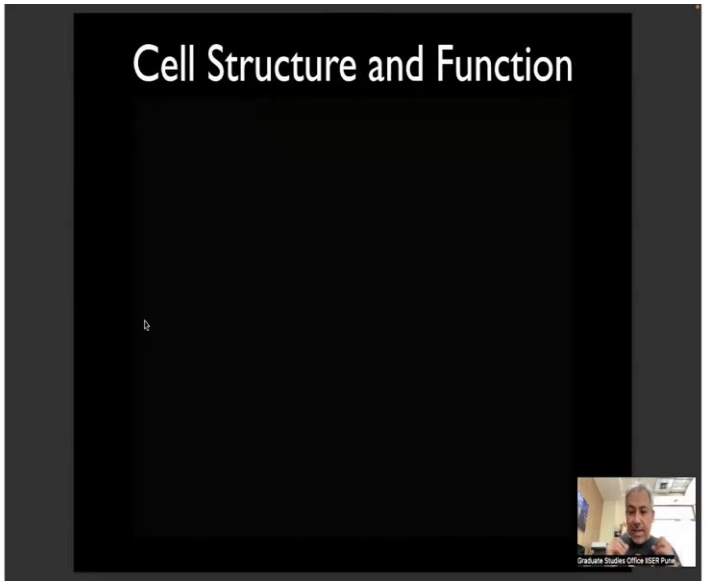

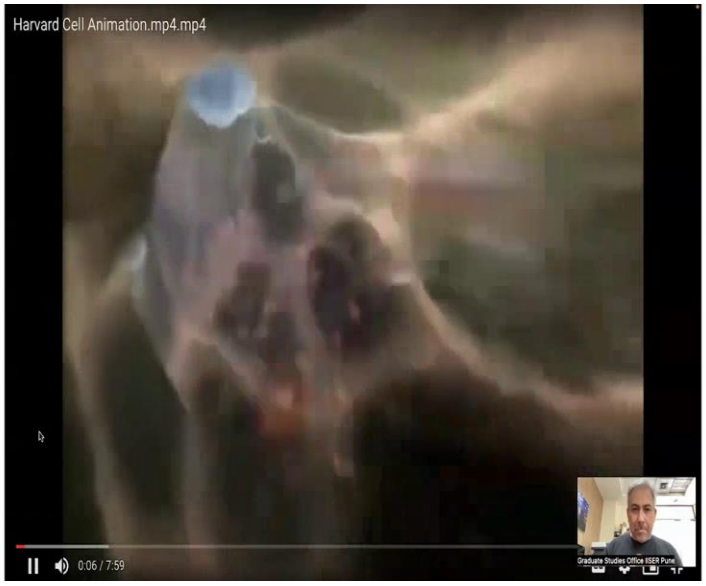


P-selectin
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Leukocytes
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The video I am going to show you next is a video that essentially captures all these players. It is a fairly complex video. So, do not worry if you understand, do not understand everything in that video. At this point of time, you are not expected to. We are going to keep seeing that video at regular intervals in this class. And the idea is, with time you will be able to see and know more of those players that are involved in cellular function.

So, this video essentially captures cellular response or behavior. And it tries to tell you if a cell has to react to something, how many different things have to happen or to take place to allow the cell to do what it is supposed to do. It is very beautifully animated and everything is put together to scale, which is what makes it particularly interesting to see.

Narrator: While red blood cells are carried away at high velocity by a strong blood flow, leukocytes rolls slowly on endothelial cells. P-selectins are endothelial cells interact with PSGL-1, a glycoprotein on leukocyte microvilli. Leukocytes push by the blood flow adhere and roll on endothelial cells because existing interactions are broken, while new ones are formed. These interactions are possible because the extended extracellular domains of both proteins emerge from the extracellular matrix, which covers the surface of both cell types.

Professor: So, just to kind of give you a sense of what you are looking at, you are looking at the surface of the cell. So, there is a boundary now, and the cell and the receptors that are present on the surface, things that are poking out from the membrane and are actually feeling the

environment and they actually bind to a network or a mesh that is present around the cells which is called the matrix.

And like the movie this matrix is present everywhere and it essentially controls everything that the cell feels. And this is a good example of something that is present outside the cell that the cell can come and bind to, and can influence things that happen inside the cell. So, the movie begins with cells that are actually moving in blood vessels. And as they attach to the matrix, you are going to see how exactly information is passed on from, as a result of that binding of receptor to the matrix into the cell.

As I said, again, do not worry about the complexity that appears here. The conceptual parts are what you need to pay attention to. So you are looking at a cell, that is binding to the matrix, and now the receptors on the surface are binding the extracellular matrix, and now this is causing the cell to respond or react. We will see what happens.

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Harvard Cell Animation.mp4.mp4
lipid raft
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Cholesterol
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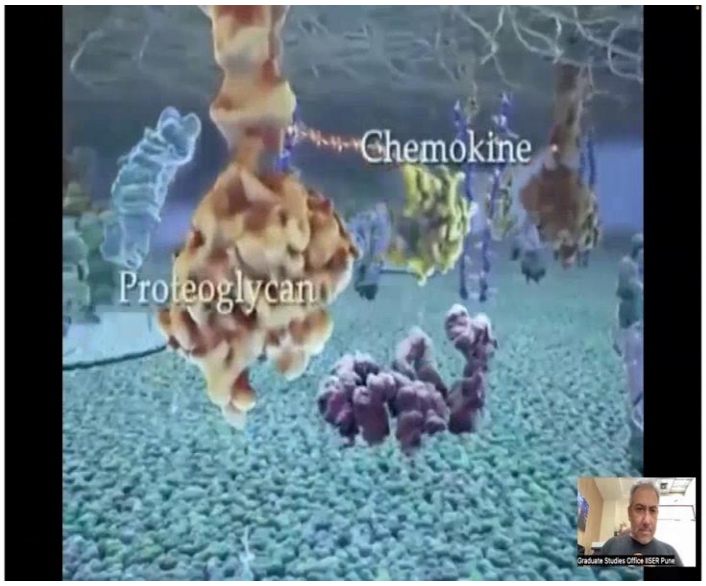

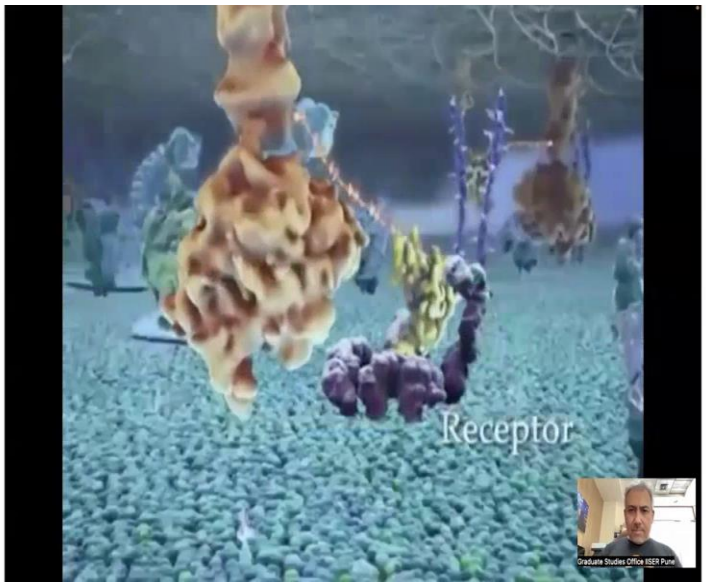

Narrator: The outer leaflet of the lipid bilayer is enriched in sphingolipids and phosphatidylcholine. Sphingolipid rich rafts raised above the rest of the leaflet recruits specific membrane protein.

Professor: So, this floating see that you can see of lipids is the cell membrane. And these are receptors that are floating in the cell membrane moving around. And there are these regions of organization, if you want to call it that, in the cell membrane, where the lipids are arranged into more compact structures, which are called lipid rafts, and you can see receptors that are enriched in these lipid rafts.

Narrator: Rafts rigidity is caused by the tight packing of cholesterol molecules against the straight sphingolipids hydrocarbon chains. Outside the rafts kinks in unsaturated hydrocarbon chains and lower cholesterol concentration result in increased fluidity. At sites of inflammation, secreted chemokines bound to heparin sulfate proteoglycan on endothelial cells are presented to leukocyte seven transmembrane receptors. The binding stimulates leukocytes and triggers an intracellular cascade of signaling reactions.

Professor: So, that was a receptor binding to something on the surface and now triggering a reaction within the cell. And all of this is happening on this jiggly membrane. And remember the membrane is a very fluid structure and we will come to it when we talk about the cell membrane, and this is your first introduction to what the membrane is likely to look like. And as I said, everything here is done to scale. And everything is done with the information that exists in literature at this particular point of time. So, it is important for you to see it that way.

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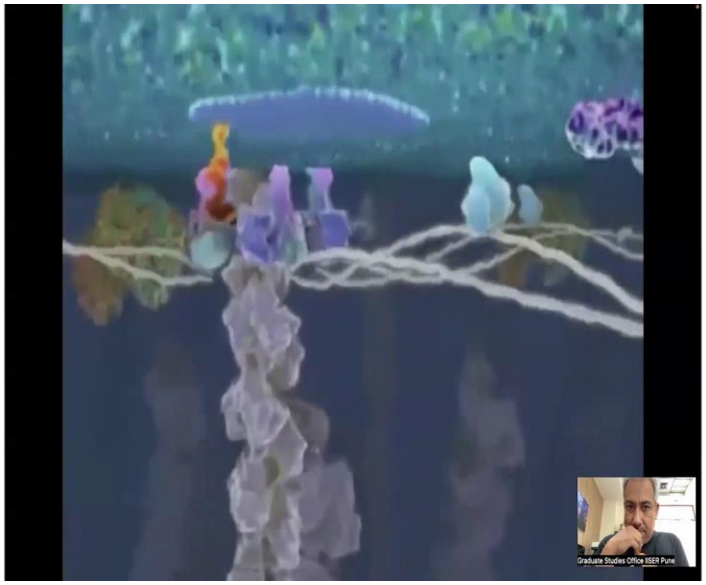

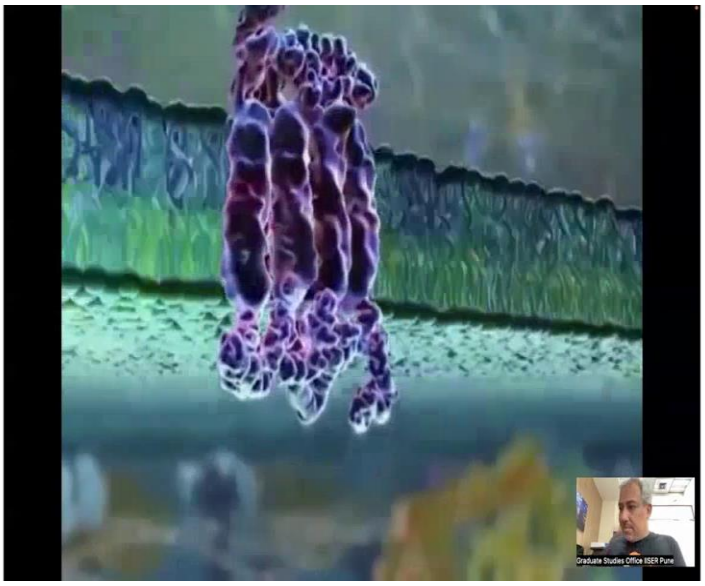
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Spectrin tetramer
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Actin filaments
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Harvard Cell Animation.mp4.mp4
Severing
protein
3:05 / 7:59
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Microtubules
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Vesicle
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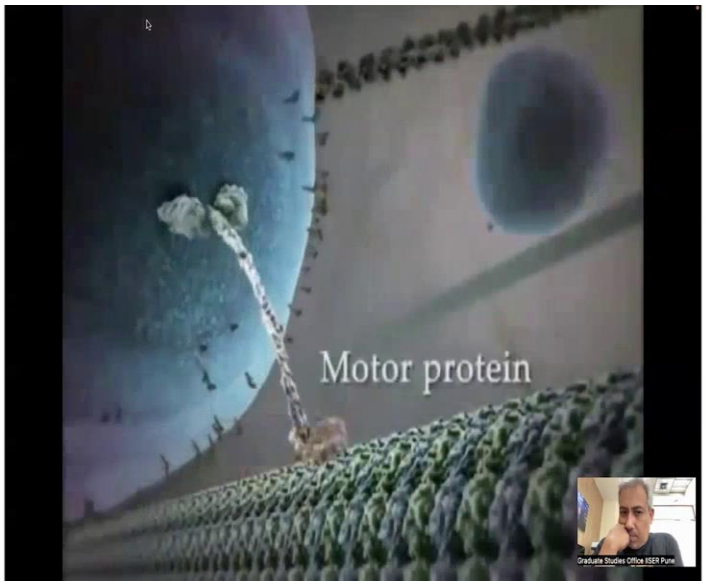

Narrator: The inner leaflet of the bilayer has a very different composition than that of the outer leaflet. While some proteins traverse the membrane, others are either anchored into the inner leaflet by covalently attached fatty acid chains or are recruited through non-covalent interactions with membrane proteins. The membrane bound protein complexes are critical for the transmission of signals across the plasma membrane. Beneath the lipid bilayer, spectrin tetramers arranged into a hexagonal network are anchored by membrane proteins. This network forms the membrane skeleton that contributes to membrane stability and membrane protein distribution.

The cytoskeleton is comprised of networks of filamentous proteins that are responsible for the spatial organization of cytosolic components. Inside microvilli actin filaments form tight parallel

bundles, which are stabilized by cross linking proteins. While deeper in the cytosol, the actin network adopts a gel like structure, stabilized by a variety of actin binding proteins.

Filaments capped at their minus ends by a protein complex grow away from the plasma membrane by the addition of actin monomers to their plus end. The actin network is a very dynamic structure with continuous directional polymerization and disassembly. Severing proteins induce kinks in the filament, and lead to the formation of short fragments that rapidly depolymerize or give rise to new filaments.

The cytoskeleton includes a network of microtubules created by the lateral association of protofilaments formed by the polymerization of tubulin dimmers. While the plus ends of some microtubules extend toward the plasma membrane, proteins stabilize the curved conformation of protofilaments from other microtubules, causing their rapid plus end depolymerization.

Microtubules provide tracks along which membrane bound vesicles traveled to and from the plasma membrane. The directional movement of these cargo vesicles is due to a family of motor proteins linking vesicles and microtubules. Membrane bound organelles like mitochondria are loosely trapped by the cytoskeleton. Mitochondria change shape continuously and their orientation is partly dictated by their interaction with microtubules.

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Centriole
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Harvard Cell Animation.mp4.mp4
Pores
4:31 / 7:59
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Ribosome
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Translocator
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Endoplasmic reticulum
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Golgi apparatus
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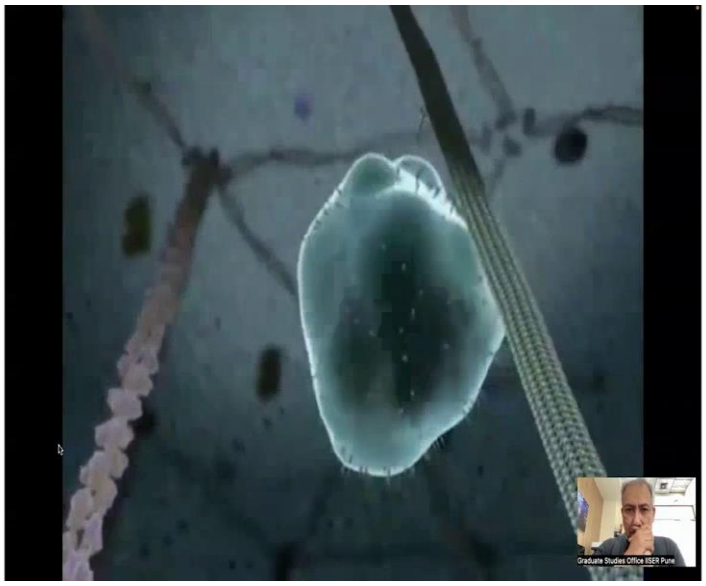
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Plasma membrane
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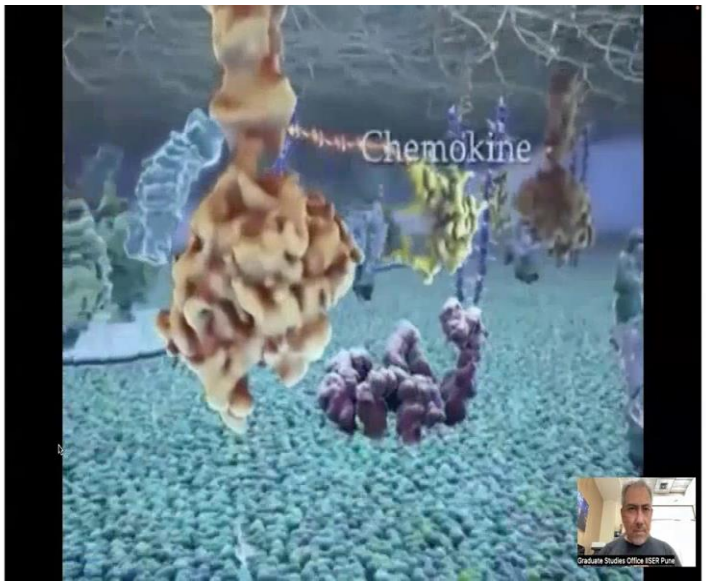
Chemokine
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G-protein
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Integrin
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I-Cam
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All the microtubules originate from the centrosome, a discrete fibrous structure containing two orthogonal centrioles and located near the cell nucleus. Pores in the nuclear envelope allow the import of particles containing mRNA and proteins into the cytosol. Here free ribosomes translate the mRNA molecules into proteins.

Some of these proteins will reside in the cytosol. Others will associate with specialized cytosolic proteins and be imported into mitochondria or other organelles. The synthesis of cell secreted and integral membrane proteins is initiated by free ribosomes, which then duck to protein translocators at the surface of the endoplasmic reticulum. Nascent proteins pass through an aqueous pore in the translocator.

Cells secreted proteins accumulate in the lumen of the endoplasmic reticulum, while integral membrane proteins become embedded in the endoplasmic reticulum membrane. Proteins are transported from the endoplasmic reticulum to the Golgi apparatus by vesicles traveling along the microtubules. Protein glycosylation initiated in the endoplasmic reticulum is completed inside the lumen of the Golgi apparatus.

Fully glycosylated proteins are transported from the Golgi apparatus to the plasma membrane. When a vesicle fuses with the plasma membrane, proteins contained in the vesicles lumen are secreted, and proteins embedded in the vesicles membrane diffuse in the cell membrane. At sites of inflammation, chemokine secreted by endothelial cells bind to the extracellular domains of G

protein coupled membrane receptors. This binding causes a conformational change in the cytosolar portion of the receptor and the consequent activation of a subunit of the G protein.

The activation of the G protein subunit triggers a cascade of protein activation, which in turn leads to the activation and clustering of integrins inside lipid rafts. A dramatic conformational change occurs in the extracellular domain of the activated integrins. This now allows for their interaction with ICAM proteins displayed at the surface of the endothelial cells. These strong interactions immobilize the rolling leukocyte at the site of inflammation.

Additional signaling events cause a profound reorganization of the cytoskeleton, resulting in the spreading of one edge of the leukocyte. The leading edge of the leukocyte inserts itself between endothelial cells and the leukocyte migrates through the blood vessel wall into the inflamed tissue. Rolling, activation, adhesion and trans-endothelial migration are the four steps of a process called leukocyte extravasation.

Professor: So, do not worry if none of that made sense. It is not meant to make sense right now. The only thing, the only reason that video comes right at the beginning is so that you have a sense of appreciation for how complex everything that is happening in the cell at a given point of time is. And it has essentially captured everything that happens in the cell. And it is, everything that is happening at a particular point of time, which is this particular cell, when you have a wound and leukocytes are a class of cells that have to go to the site where the wound has happened and they are trying to actually move towards that particular site.

So, everything from the surface of the cell two things that are happening in intracellular organelles is coming together to allow the cell to get from point A to point B. And what you can, I mean if this is an example of something that is taking place, you realize how many different steps need to happen for the cell to actually do something that looks very intuitive and simple, which is get from point A to point B.

And so that is what this video is essentially capturing. What we will do is as we go along further and we discuss each of these components and we will bring this video back and we will play only those sections so that you have a sense now of, okay, these are the things that are happening at the plasma membrane, this is what is happening at the Golgi. And once you looked at the Golgi, you have an understanding of what exactly the video is trying to say. So, the hope is, at

the end of this lecture series when this video is played at the end, you have a better sense of what all different things that they are talking about here.