Introduction to Cell Biology
Professor Girish Ratnaparkhi
Professor Nagaraj Balasubramanian
Department of Biology
Indian Institute of Science Education and Research, Pune
Plasma Membrane: The Boundaries of Life

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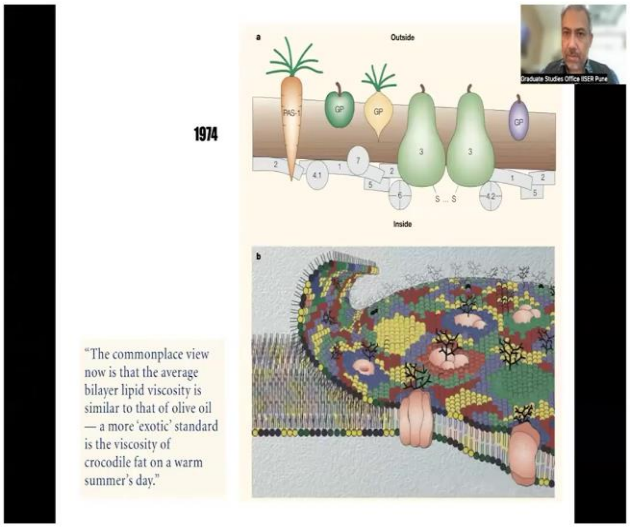

Among the things that we were thinking about, at the in the last class, is we were thinking about the fact that there is a boundary that these early cells, including cells that we know of today need to have, and the importance of this boundary. And one of the questions that I had raised for you guys, is to think about, what that boundary could do?

And what kind of advantages or disadvantages you see for generating a boundary? Now, one of the early thoughts to have here is the value of such a boundary, and how that boundary could effectively have defined this early architecture of a cell. And this boundary in cells is, is rather vital, simply because it helps define what is outside and what is inside.

So, the nature of this boundary is hugely important to how, cells were created, and the idea of cells were created. So, the idea of a cell is essentially a bag in which all these components exist, and talk to each other and work with each other and function. And so that boundary becomes that much more important.

And as life progressed and evolved, and, prokaryotes became eukaryotes, this boundary became more and more intricate, it became more and more functionally relevant to the point that when we now look at cells in eukaryotic cells, this lipid membrane that we think about, is extremely closely tied to everything that the cell does, to, what the cell does, how it does it, all of this is dependent on this boundary?

So, that is how vital the boundary is an example of, this relevance of this boundary, this lipid bilayer stems from the fact that so much of that interface, so much of proteins and other components that line that surface, or that membrane are integrated are either bound to the plasma membrane on the outside or on the inside, are integrated into the cell membrane.

And their functionality, these proteins have now all evolved in such a way that they work best in the lipid bilayer. For a long time, people did not think much about the lipid bilayer, they thought, Okay, well, it is just a sea of lipids and things float around in them, and that is about it. That it is a boundary, it has no functional relevance, really, it is just a way to kind of separate outside from inside.

But as we have thought more about it understood this better, what we now know, is that, that there is a huge role for these lipids in defining the functioning of cells, so this sea of lipids, if you remember the movie, the inner life of the cell, you saw this thing, essentially, a wobbly, very flexible structure into which these proteins are all present.

This sea of lipids also is not just a uniform layer of lipids with time, we have understood that this sea of lipids is actually more complex than that, the sea of lipids has many kinds of lipids. Some of these lipids actually come together and make, compact lipid floats on the plasma membrane. So, these are like tiny islands of lipids that are floating in the sea of lipids.

And these islands are referred to as lipid rafts. So, they are regions where proteins can come sit together, talk together, function together. So, the lipid is no longer considered a very, naive or even inert boundary of the cell. It is a very active boundary. And it is, this edge is hugely important for how proteins in the cell work and how the cell eventually works itself? So, that is the amazing thing about the membrane.

And there are many models that have been proposed. I am not going into these, because this is really beyond the preview of what we are discussing today. Of how this membrane should look? There is something called a fluid mosaic model and if you want please go look this up which is one of the most common accepted models or the best accepted models for how this lipid bilayer could look and function.

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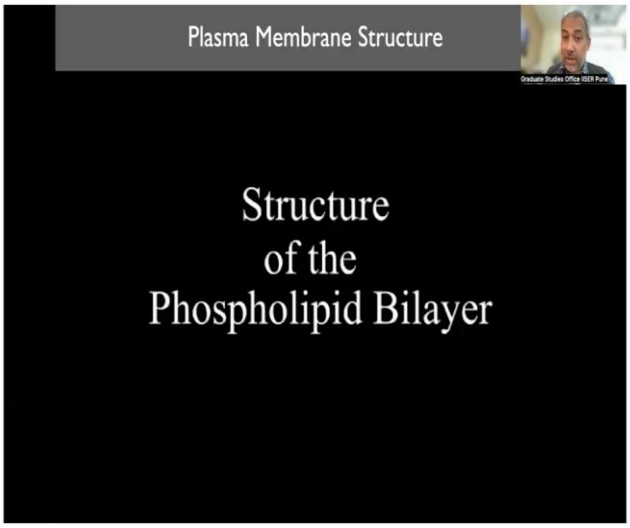

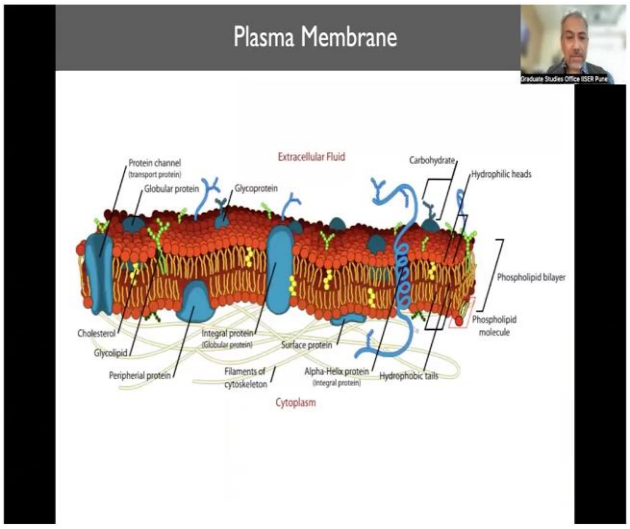

We will come back to the two movies that, that we want to look at the end, this architecture now looks like this, and now, this is a cross section. So, you have an outer leaflet and inner leaflet which are coming together. And the outer leaflet has a mixture of lipids. So, it is not one kind of lipid, it is different kinds of lipids, the inner leaflet has a mixture of lipids.

The outer leaflet and the inner leaflet now, we think could have slightly different compositions as well. And this will matter to the functionality of the cells, there are many kinds of lipids that can be part of such a bilayer. So, when you look at different, membranes inside the cell, the plasma membrane and other cellular membranes, you know that the lipid composition now could be variable. And this is, again, something that has been characterized.

Proteins could be things that are integrated only in the outer leaflet only in the inner leaflet. There are proteins, some proteins that go through which are transmembrane proteins. But they all work to kind of allow the outer environment to be distinctly different from the inner environment, and also allow for the membrane to be able to communicate what is happening outside to the inside of the cell.

So, when we come to receptors and signaling, we will discover how something happening on the outside is communicated as a change in the structure of the receptor to the inside of the cell. And that is outside in signaling. And similarly, things happening on the inside can be communicated outside, which is inside out signaling in cells.

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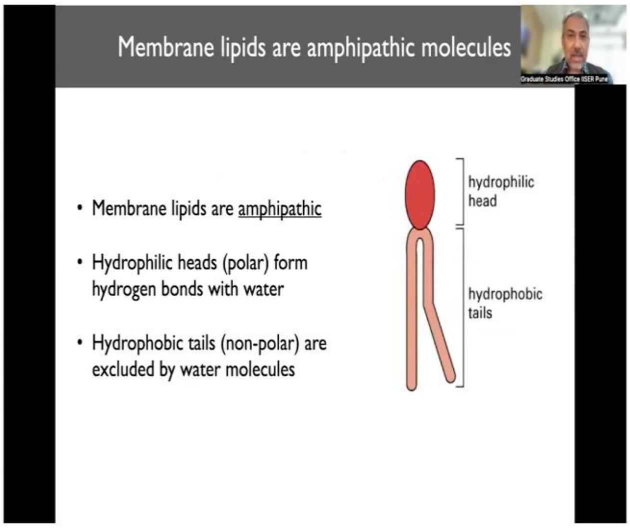

The lipids as I, as we talked about yesterday, they have a hydrophilic head and a hydrophobic core. And that is the architecture, depending upon the kind of lipids the nature of that hydrophilic head and hydrophobic core could vary, the kind of kinks that they have, or how straight the lipids are, could make a difference to how they are packed together.

The really nice thing about lipids in an aqueous environment is that they can they have the energy to come together to as molecules and maintain this architecture. So, when you see a sea of lipid that floats as a boundary, inherently this is coming, because of the kind of interactions that these lipids have with each other, allowing them to stay together and create a boundary, the advantage of this boundary is this boundary, can be broken, it can be modified, it can be bent. And all those become very valuable.

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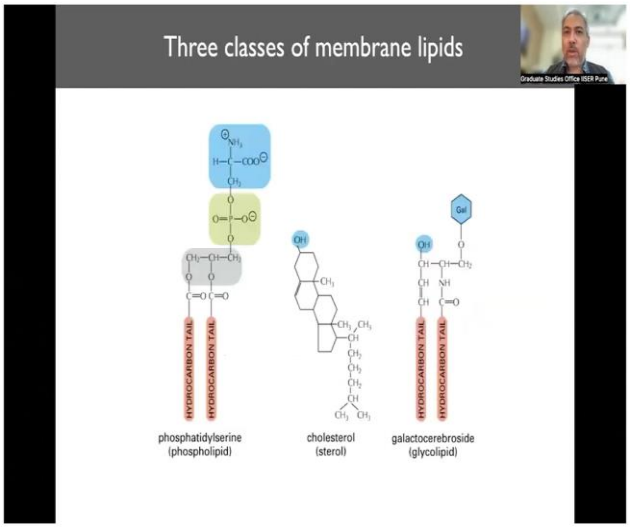

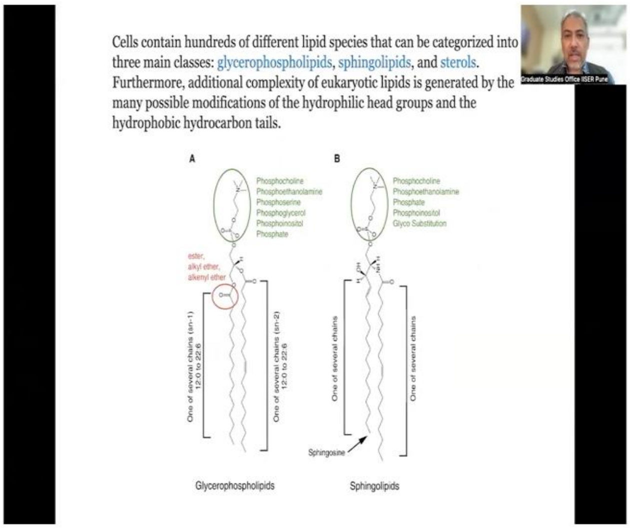

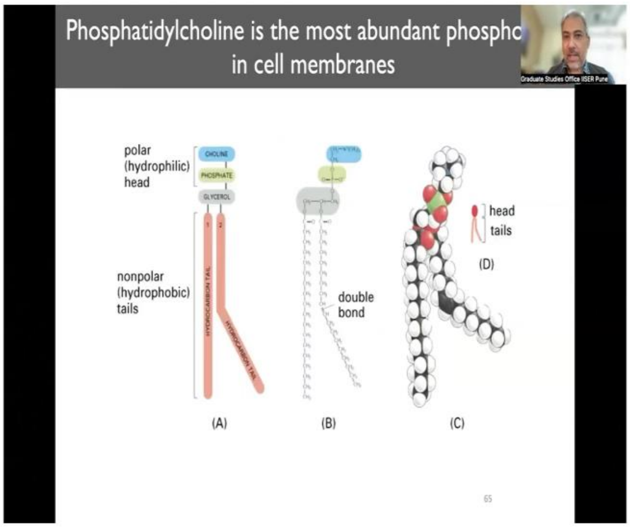

When you think about the functions that the lipids do. There are different classes of lipids there are, Phosphatidyl serine, there are glycolipids, there are sterol like cholesterol, and the architecture of these lipids makes a big difference to, how they are assembled, how they are put together? You do not have to know all the details about the lipids at this point of time, you just need to know the fact that there are multiple lipids.

And they could be assembled this way in to make the membrane. So, as I said, the nature of this tale of lipids makes a big difference to how they get packed. And molecules like sterols like cholesterol have very flat tails, which means they can be packed more tightly, which is one more reason why they can come together to create a compact kind of float this lipid draft that we talked about in cells.

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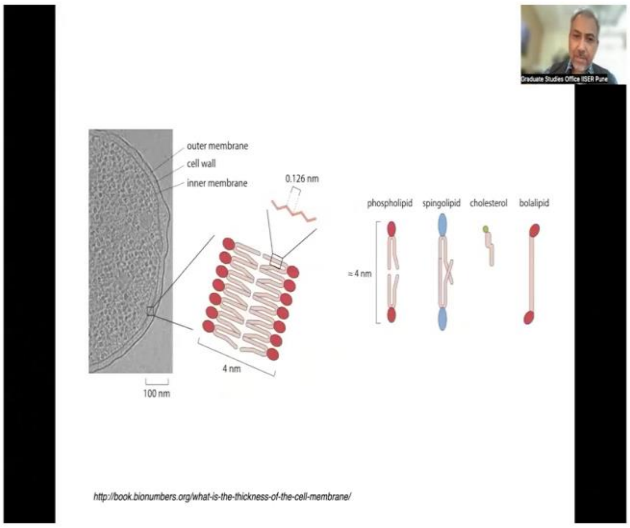

So, this is the assembly we are looking at. And as I shown here, this has a very defined thickness, it has a significant amount of flexibility, it also has a significant amount of strength. So, it is not something that can very easily be ruptured, unless and until a certain amount of force is applied.

And there are innumerable number of proteins that have learned over evolution to modify the membrane and this is the really remarkable thing, everything from the bending of the membrane to creating folds, proteins have found a way to work with this lipid membrane and do things with it.

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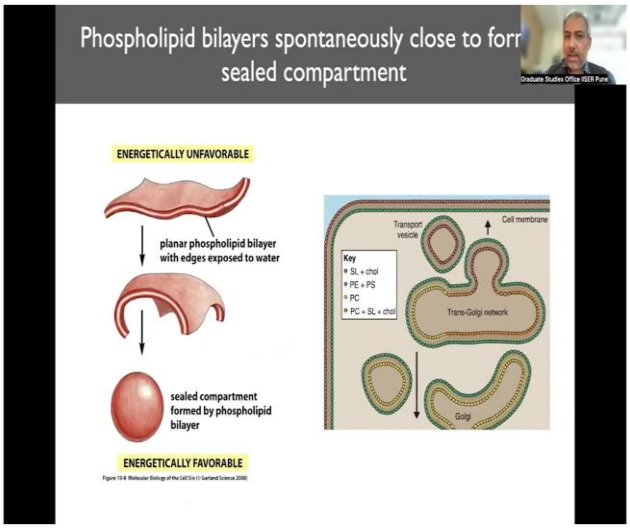

As I mentioned, that there is the other really nice thing about lipid membranes is that, when they self-assemble, there is a tendency for them to make an energetically favorable arrangement, that inevitably is in the form of a sphere, which, when they come together almost immediately defines an outside and an inside.

And this could be one more big reason why this membrane or the origin of the cells, as we know, it could have began with a lipid bilayer, because of their ability to assemble into these energetically favorable structures. And as this image shows you, there are many components in the inside the cell that are made up of lipid membranes. And the fact is that the composition of these lipids in these different membranes could also be variable.

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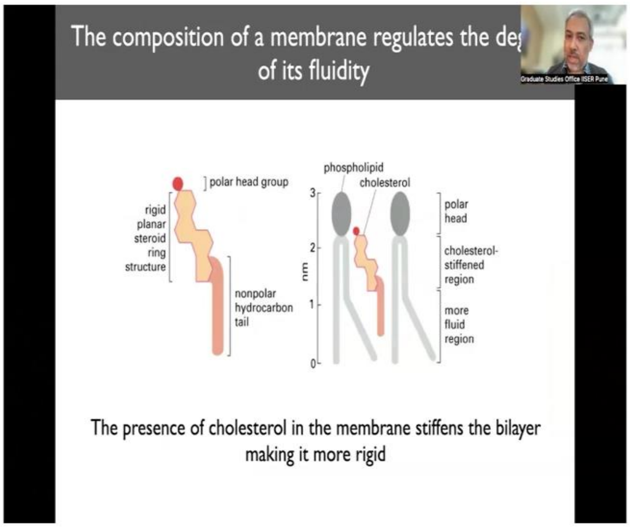

This is again to show how cholesterol can help pack lipids better, and create more tighter structures, which are more rigid. And so, they have a slightly different fluidity and a slightly different architecture than the rest of the membrane, which is the reason why these become islands of signaling, islands where receptors and other things can come and park themselves and do things inside the cell membrane.

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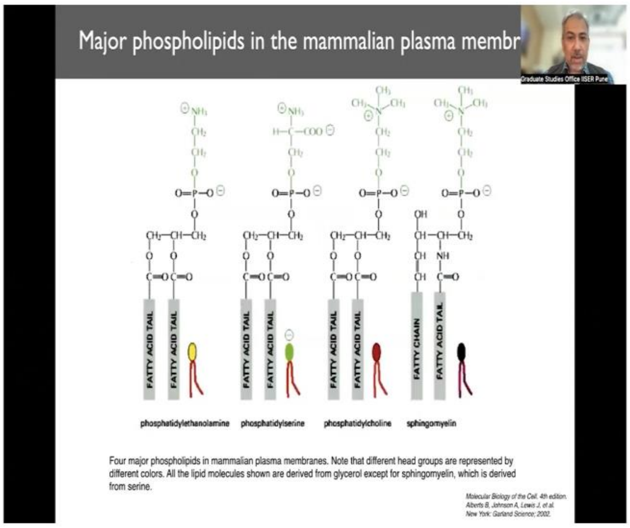

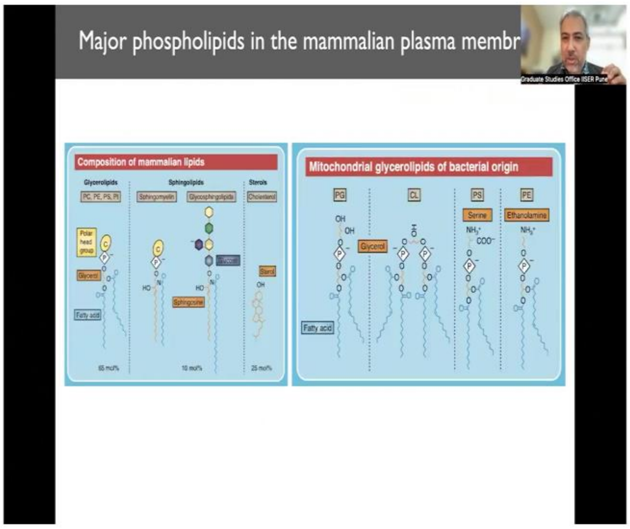

Again, just to kind of give you a sense of all the different types of lipids how their tails will be variable, you do not have to remember these things, this is just matter of information. The composition of lipids, as I said, the relative ratios are also very important.

In mammalian lipids, you have glycerol lipids, which make about 65 percent, 10 percent sphingolipids and sterols make about 25 percent. The one of the, because we talked about the micro mitochondria, I just added this here, that the mitochondrial glycerol lipids, interestingly, among the characteristics, that allow us to think that the mitochondria could have had a bacterial origin, or a prokaryotic origin.

Is the fact that the mitochondrial glycerol lipids have an origin that makes them seem like bacterial lipids, is not that fascinating that, along with the fact that they have a double membrane, the composition of those lipids is also indicative of the fact that this endosymbiotic theory may have actually been, been true.

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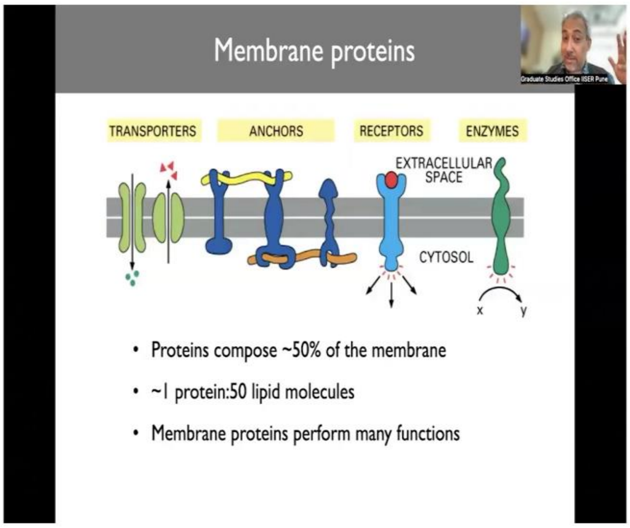

And, as I said, different kinds of proteins, proteins make up almost 50 percent of what is on the membrane now, initially, this may have evolved as only a lipid boundary, but now the proteins have integrated into the lipids, and these proteins are all designed with the lipid in mind, not just on the plasma membrane.

But even inside the cell, in the different organelles, where proteins work with lipids, the interesting thing is these proteins now all work in the lipid environment, the best, which means they have evolved in that environment in such a way that now that is what, their architecture, their interactions, their functionality is all dependent on this lipid. And that is the beauty of this system, so to speak.

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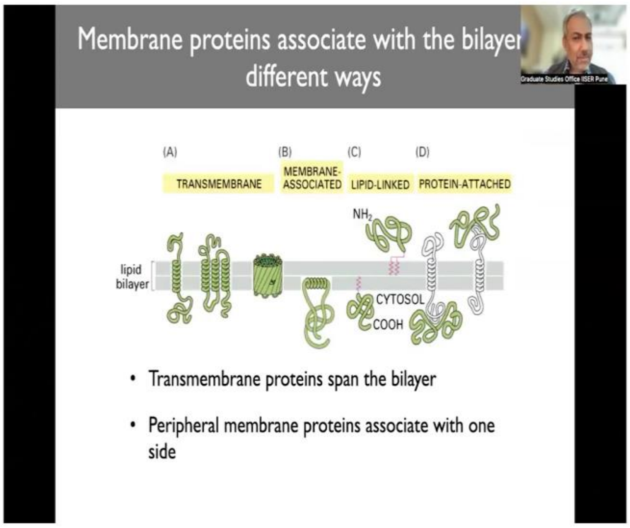

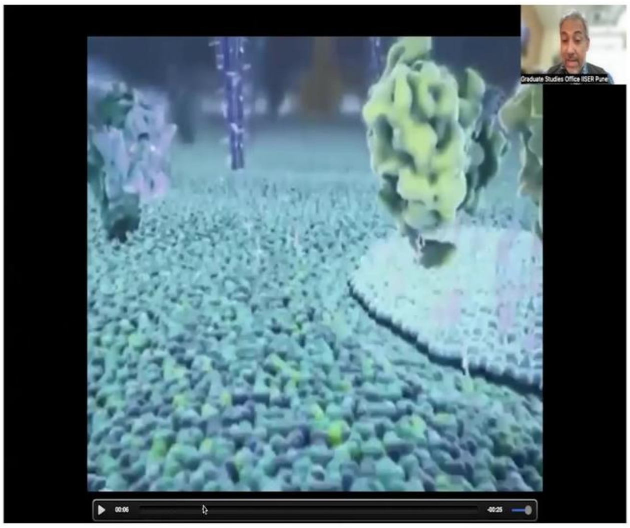


Lipid raft


Cholesterol

But proteins are present on the outside on the inside transmembrane proteins, all of which are present on the on the membrane. So, by layer is enriched in single lipids, so, I am going to just play this part of the movie, the inner life of the cell, before we go ahead and look at the other stuff. And now, you know a little bit about the membrane, now you have a better understanding of what these lipids mean, what are these things that are floating around.

You have a sense of what this floating island is, it is an island that is made up of lipids and cholesterol, which is called a membrane raft, you can see that island that is now floating around. And then, these are moving around and remember, look at the lipid that is present here, as I move this back and forth, you can see it is like a sea, where it is constantly bubbling around. And so, the lipid can be modified, bent, moved around in different ways.

This is a cross section. And this is a beautiful image, because, it really lets you see everything I spoke about the outer leaflet, the inner leaflet, their composition being slightly different. The lipid cholesterol rich lipid domains, which have a slightly different organization, which is distinctly different from the rest of the membrane, the fact that receptors can go through and are anchored in these domains the way they are, all of this is contributing.

And as I move it back and forth, you can see how everything is jiggling around, moving around in a way that allows these lipids to hold these proteins and allow them to function. So, now when you think about a cell, you are not thinking about a flat line. Because that is how we drew a cell. But now you are thinking about something that is constantly changing, constantly moving around, that can be bent that can be curled that can be pushed through corners and spaces, which is all possible, because of this lipid boundary.

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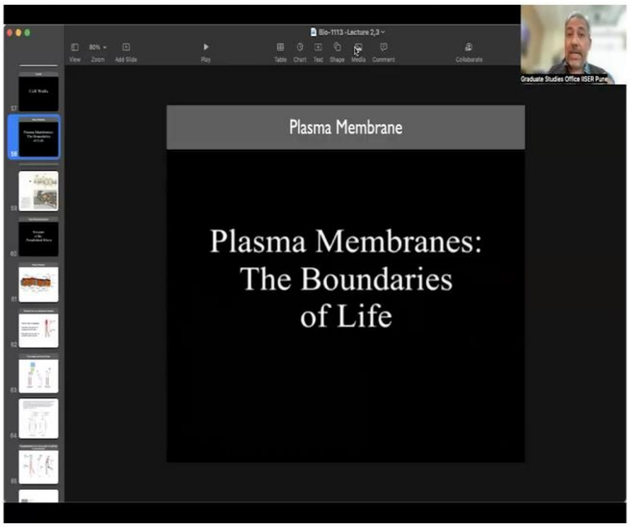

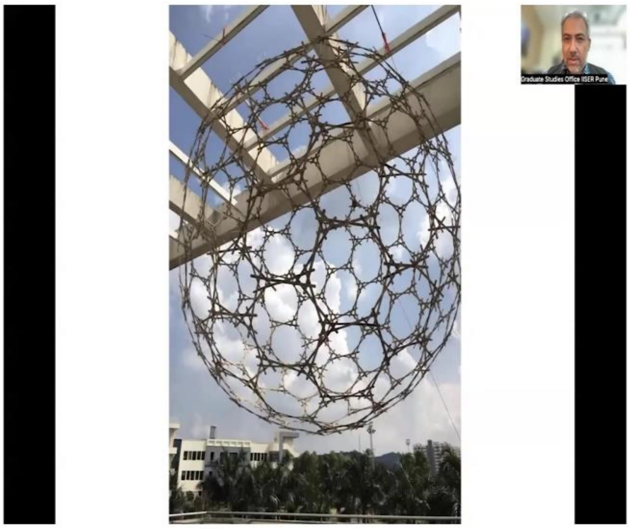

The next class, we are going to focus on something that looks like this. This is actually a geodesic dome that was built at IISER a few years ago, and this was part of a project, that was done here. And this is all assembled using, sticks, bamboo sticks and rubber bands and ties. And, and this kind of architecture, this geodesic dome always reminds me of the cytoskeleton because that is the kind of architecture.

The cytoskeleton, this kind of architecture and this kind of arrangement, in terms of what it does is what the cytoskeleton is about. So, where we are headed is towards the geodesic dome, the structural dome that is inside the cell that kind of keeps or holds this floppy membrane that is floating around. So, that is what we will get to in the next class.