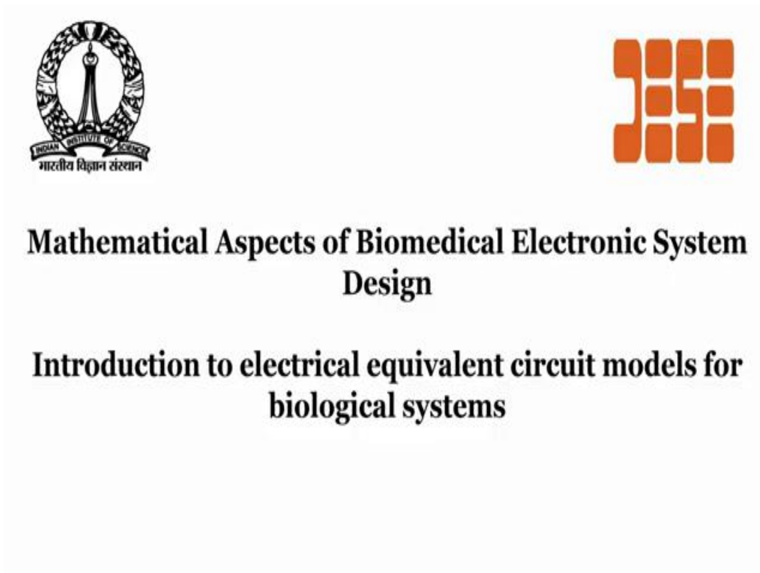
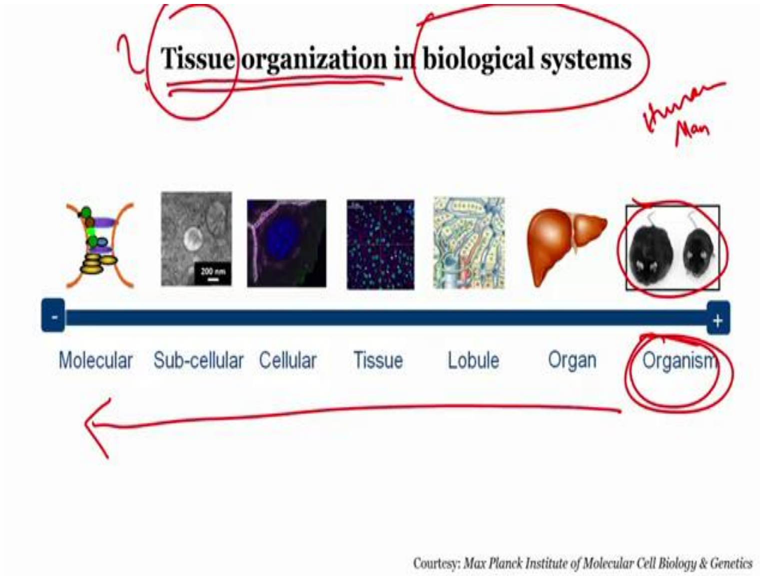
Mathematical Aspects of Biomedical Electronic System Design
Lecture 08
Introduction to electrical equivalent circuit models for biological systems

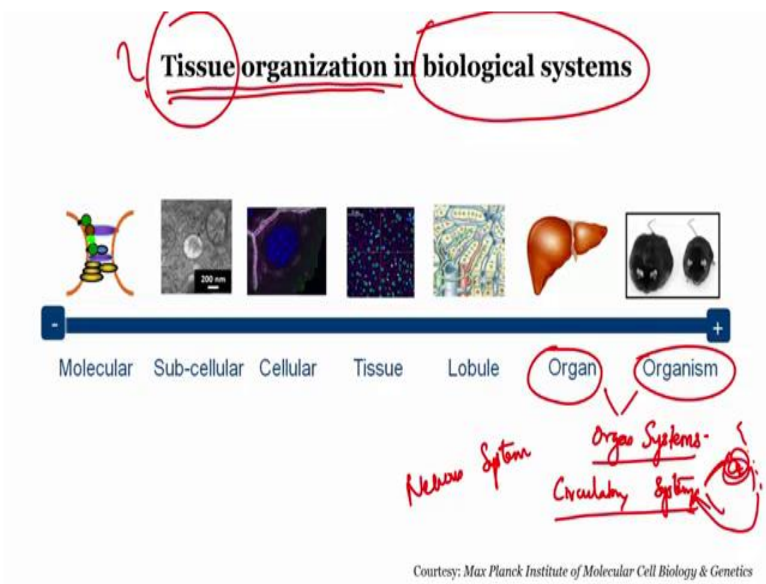
(Refer Slide Time: 0:32)



Hello everyone, welcome to this new module on the course, mathematical aspects of biomedical electronic system design, this is a TA session, my name is Anil, I am a TA for this course, Professor Chandramani Singh and Professor Hardik Pandya has already covered the several fundamentals of the mathematical aspects of how to design biomedical systems. In this session, we will take a deep dive into, the introduction to electrical equivalent circuit models for different biological systems.

(Refer Slide Time: 0:59)





So, before we start off, we need to understand, how tissues are organized in the biological system. So, this is a very interesting graphic, which we have borrowed from the famous Max Planck Institute of Molecular Cell Biology and Genetics. So, what is tissue organization, that is what we have shown here, what is tissue organization, for that matter what is a tissue and how do tissues make biological systems?

So, before we delve into electrical equivalent models of biological systems, we need to understand, how these systems come together, how they assemble and form organisms. So, let us go back from the bigger abstraction, to the smallest unit of the whole organization. So, all of us know, that we are all organisms, man is an organism, human being is an organism.

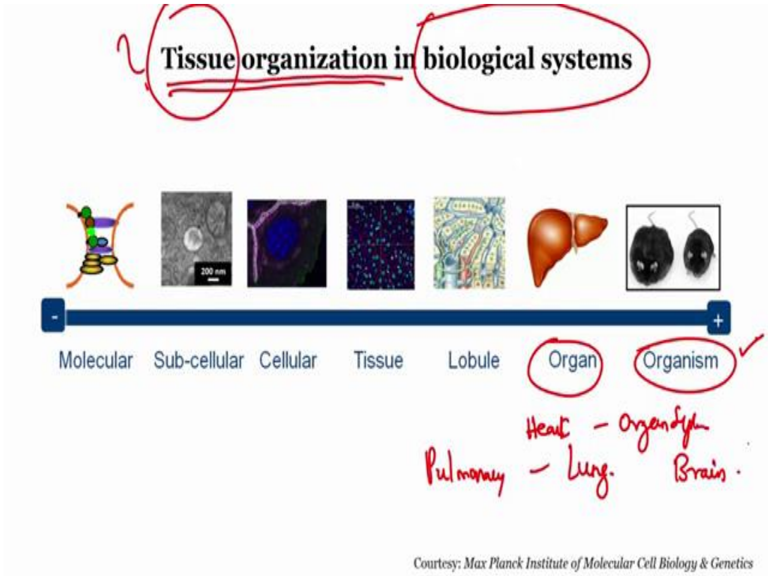
This mice and rat shown here, these are all organisms, they are capable of independent existence and depending on their level of development of their brain function, some and some members of this organism are also capable of making decisions of their own. So, these are aspects, where we identify certain entities as organisms.

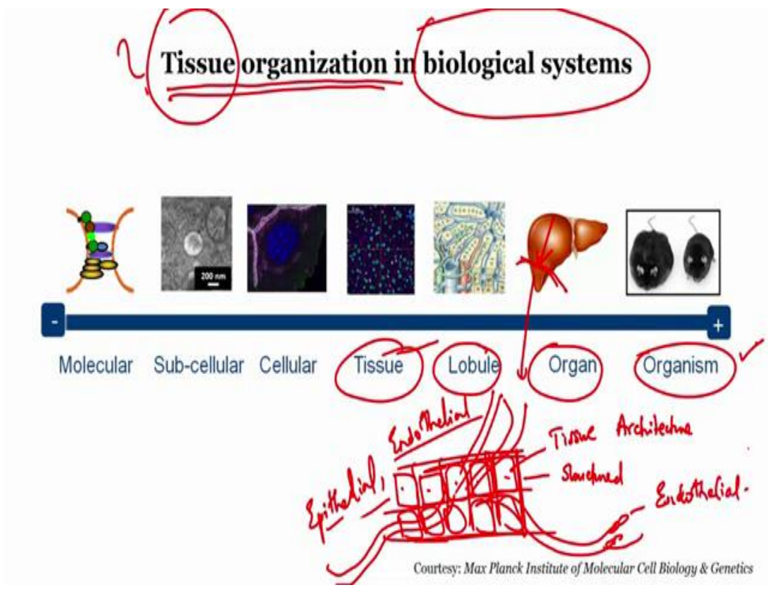
Now, coming down so organism like, let us say human being, human being is composed of different organs, this we have this is basic high school biology, all of us have learned about this basic high school biology.

So, each organism is composed of different organs, so organs and organ systems actually, so in between organism and organs, you have actually organ systems, all of you might have studied. So, what is organs, organ system, let us say our circulatory system is an organ system, the nervous system is an organ system. So, what is an organ system? Organ system is a, is a collection of organs within an organism, that can perform a set of functions.

Let us say circulatory system if you take, it can perform pumping of blood and oxygenated blood is pumped through the body, then the different parts of the body used this oxygen and then it is circled back to the circulatory system, where the deoxygenated blood is again revitalized with oxygen pushed back into the body. So, that is the circulatory system. So like this, we have different organ systems.

(Refer Slide Time: 3:37)





Now what are these organ systems made of? Yes, these organ systems are made of organs, let us say, if we again takes a circulatory system, it is made up of heart, heart is an organ. If you take pulmonary system, lung is a very important part of it. If you take nervous system, brain is a part of it. So these are all organs, individual organs. So that is a next level of abstraction below the organ system.

So first we have organism, then we have organ system, then we have an organ, okay? Now, what are these organs composed of? These organs are composed of a specific structured arrangement of cells, along with blood vessels, which supply nutrients to the cell. So those are the Lobules and tissues.

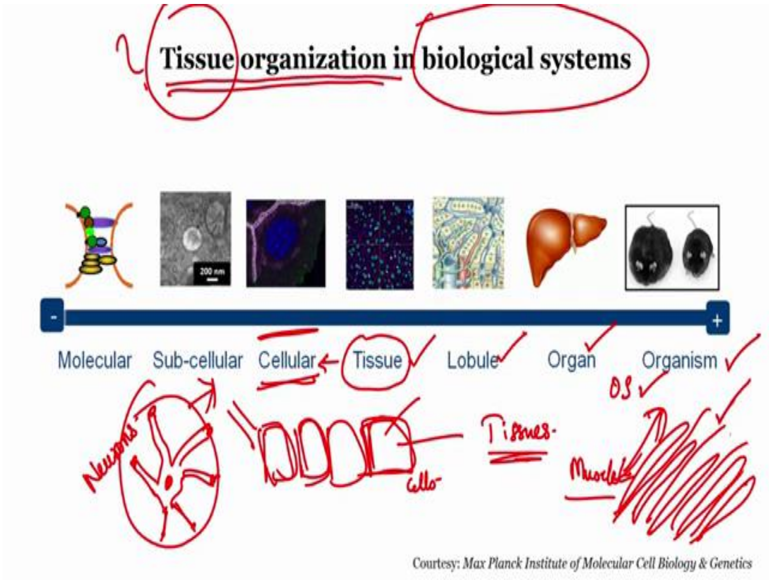
So, let us say I make a very simple abstraction of this organ. Let us say I am taking liver as an organ, and I am cutting a part of it. Let us assume that this is liver, and I am cutting a part of this organ here. And if we try to see it from a cross section point of view, what we see is an organization of cells, which are the basic units of life cells, arranged in either a structured order, or a non-structured order, depending on the organ they may, or may not have a structured organization. And then between them you have actually something called as matrix, which holds these cells together.

So, this organization is called tissue, or tissue architecture. Now, just these cells usually these are called epithelial cells, epithelial cells, there are endothelial cells, different types of cells are there, which come together to form tissues. Now, these cells alone cannot survive, they need nutrients to survive. Who brings the nutrients? The nutrients are brought together by vasculature, or the blood supply into the tissues.

So, it is a very complex arrangement, it is brought together by blood supply into the tissues, these are also tissues actually, these blood cells or blood vessels, are also made up of specific types of cells called endothelial cells. I might be going into this, you just consider it as general awareness, so that we understand the next part of the course. So, this is just a general understanding about how organs are assembled by tissues and Lobules.

So, cells themselves in a structured arrangement cannot exist on their own, they need to be supplied by nutrients and those nutrients are supplied by these vessels like blood vessels, lymphatic vessels, etc.

(Refer Slide Time: 6:31)



So, now we have covered organism, we have covered organism, we have covered organ system, we have covered organ, we have reasonably covered Lobules, we have covered tissue. Now, how do as I said, how do these tissues come to exist, these tissues come to, come to exist, when cells come together, cell I think all of you are aware. So, cells are kind of like the individual functional unit of, of a living being, individual independent function unit of a living being.

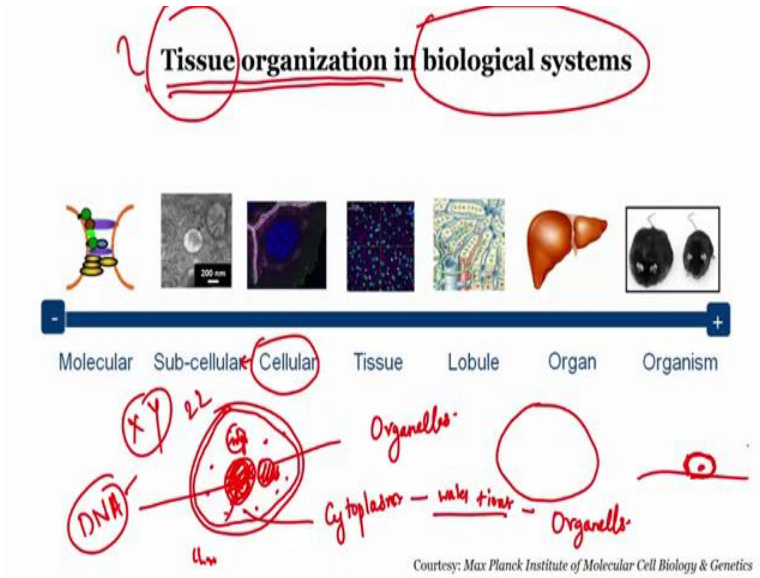
So, cells can come together arranged in a particular form and form tissues as we said before. So, the way the cells come together, and the kind of function that the cells perform will dictate what kind of tissue this is. So, let us say we take muscle tissue here, the actually the cells are not like this square shaped, they are actually more spindle shaped. These are called muscle fiber cells, they are shaped like this evolutionarily they have come to attend the shape. So, that they can expand and contract to perform the muscular functions.

So, that is why they have this striated, is called striated epithelium, there are different types of muscle tissues, just for example, I am telling you. For another example let us say we take brain, brain has lot of different types of cells, but one major cell which you all might be aware of is the neuron, neuron has a different structure like this, with nucleus and these dendrites, these are used for conveying the electrical signals to the next cell. So, these are neurons.

So, as I said this cells do not necessarily have one particular shape, the shape is dictated by function, there is an important dogma in biology called form dictates function. So, the form of this neuron dictates its function, which is to transmit electrical signals for brain function. The form of this muscle cells dictate its function. So, that it can expand and contract and perform muscular functions.

So, that is what cells, that is how cells come together to form tissues. And the shape of cells will be different for different types of tissues. And these, this change in shape, size, and organization will define, what is the end function of such tissues.

(Refer Slide Time: 9:07)



So, now we have covered that, cell as an abstraction, cells as an abstraction come together and form tissues. Now, what is inside these cells, that is the next part, that is a sub cellular. So, all of you this is basic, I will only go into the basic details of 10th standard biology. We all know that, cell is there, cell has a nucleus inside, cell has a cell membrane. And there are other parts of the cell called mitochondria, then Golgi bodies, the different, different organelles are there. These individual units inside the cell are called organelles.

So, nucleus is often called brain of the cell, you would have all learned in 10th standard, then there are other small, small organelles in the cell, which is beyond the scope of this course. So, what you need to understand here is that, this cell membrane defines the structure of the cell. It is like so in all your dimensions, in all the drawings you see cell as a 2D, or oblong structure.

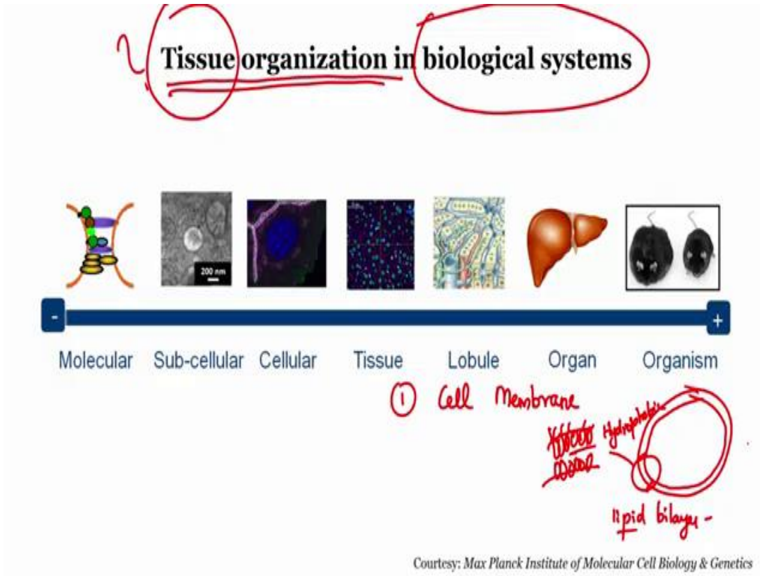
But I actually what is the cell? Cell is actually a 3D ball, it is actually an 3D ball, which is it is like a you can consider it like a droplet of water that is found on top of this lotus leaves, hydrophobic, in hydrophobic surface, if we imagine water many of these cells are shaped like that, it is a 3D, 3D, or what you call a 3D volume with this, which is optimized for the surface tension and it will be circular, or it is 3D circular volume in shape.

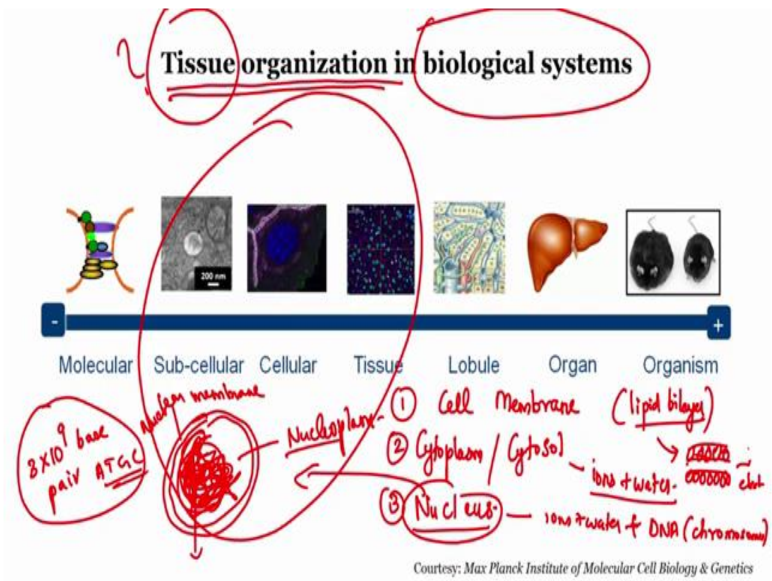
So, within this, the nucleus is contained and you have the cell membrane. But this the inside part of the cell is called the cytoplasm, inside par of cell is called cytoplasm. And for our important our understanding, the main thing to note about cytoplasm is that it is mostly consisted of water and ions, different types of ions are the major constituents of cytoplasm along with the other organelles.

So, the nucleus is very interesting, nucleus is what contains, is important because it contains a DNA the deoxyribonucleic acid which is like kind of like the software program for our overall functioning. So, nucleus hosts the DNA through chromosomes, all of you might have heard about the XY chromosomes, 22 pairs and alright these are all basic knowledge. And the cell membrane limits the shape of the cell and makes it stick together as a single entity.

So, this is a basic structure of the cell, this is important because, we this will define how we understand the electrical equipment model of the cell. So, I think this is clear to you. So, this is the structure of the cell.

(Refer Slide Time: 11:59)





So, what are the major, major, major components that are needed to be understood and in order to electrically model a cell are these, one cell membrane, which is the outer membrane, it is, it is usually consisted of a what is called as a lipid bilayer, lipid bilayer lipid is basically fat, it is a fat bilayer, if you zoom in how it looks like is, we have two walls, two layers of the membrane, there are two, two sets of lipids here.

This organization is there, because inside this it is a hydrophobic surface that means, it is afraid of water, because this serve this inside is hydrophobic and these parts are hydrophilic, it helps the cell to get its structure, because the cell attains a volume of minimum surface tension and just like water droplet is formed on top of lotus leaf. But depending on the surface and kind of organization that is there, So, cell membrane is mostly considered a lipid bilayer, please note this, this is really important, when we model the electrical equivalent circuit.

So, what I told cell membrane is consisting of lipid bilayer conserve lipid bilayer. So, that is basically like there are two layers and in between there is a void kind of situation, just keep this in mind, it will become interesting when I tell you what this translates to electrically, this is lipid bilayer. The next important thing is obviously the cytoplasm, or sometimes called the cytosol, this is the intracellular space, the space inside the cell. This is mostly consisted of ions and water, I am just telling the major components of it. This is required for electrical modeling.

Then we have the nucleus, another so the nucleus as I told consists again kind of like with ions and water, but it also contains the genetic material, or the DNA in the form of chromosomes. Now, the nucleus is interesting, because nucleus is again like a cell, nucleus by itself also has a nuclear membrane. And the portion inside the nucleus is again called nucleoplasm, like cytoplasm, it is called nucleoplasm. I think many of you might have understood read about this in your high school, but I am telling this again, because these are all, these are all contribute to how we model it electrically.

So this is nucleoplasm, again we have nuclear membrane, which is again a lipid bilayer. Only thing is the nuclear, nucleoplasm is very densely packed with the genetic material, the chromosomes, the 22 pair of chromosomes are densely packed here.

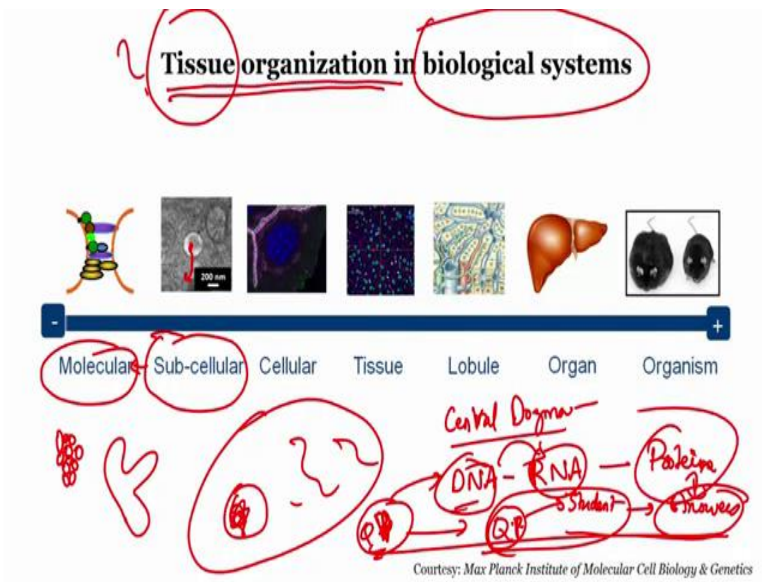
Why am telling densely packed is because our DNA material, is just it is a very interesting fact which I wanted to bring to your attention. Our DNA material consists of 3 billion, 3 into 10 raised to 9 base pairs of nucleic acids, which that is basically ATGC pairs, you can read up about it. These are nucleic acids. This is what constitutes our DNA.

This if you try to linearly put this 3 into 10 raised to 9 base pairs in a linear fashion, it will I do not know exactly, but it is said that it can go around the Earth two times, I am not sure. So it is very long. So, to contain it within the very small micron, or even nano dimensions of nucleus, it gets heavily condensed. So, it is a very dense layer, this nuclei genetic material is very densely condensed inside the nucleoplasm.

So, that is a thing and the nuclear membrane is much smaller as compared to the cell membrane. As you can see, if I draw the cell on top of this, the nucleus will be very small portion of the whole cell membrane. So, the nuclear membrane, if you go for a first level simplification, nuclear membrane is almost negligible. If you just keep this in mind, it will be importantly electrically modeled.

So, these are the different constituents of the cell, which are important to us, from our biomedical system, mathematical model, mathematical modeling point of view. So basically, it is cell membrane, cytoplasm, organelles, organelles do not contribute much to the electrical properties, I will come to that soon. Then nucleus, nucleus again consists of nucleoplasm and nuclear membrane. And obviously, the nucleoplasm consists of the genetic materials.

(Refer Slide Time: 17:02)



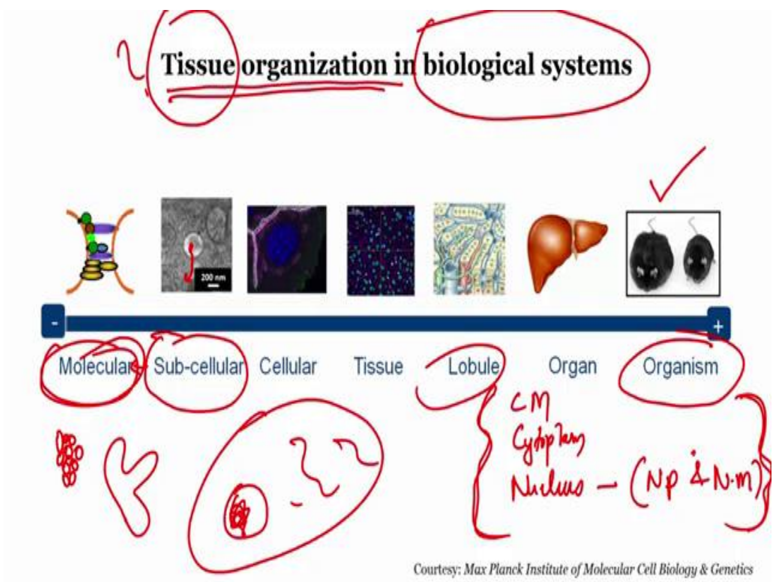
So this is the sub cellular description of the cells. Now, within the sub cellular space, there are a lot of proteins. Proteins are can be considered as how do we say it is this, they are, they are assembly of nucleic acid molecules, or different types of molecules. And they, depending on their shape, they are able to perform a particular function. I think that only we should cover here, because if we go into detail, it is an entire field in itself. Only thing is the DNA, that is inside the nucleus, actually determines what all proteins get made. And these proteins that are made reside in the cytoplasm.

So a copy of the DNA, this is called the central dogma of molecular biology, it is a defining principle of entire field of biology, where the DNA, a copy of the DNA is made as RNA, which is ribonucleic acid, which is then convert it to proteins.

So, it is just like you having one master copy of your question paper, and then you make xerox copies of the question paper. And these xerox copies are distributed to students. And the students, who know the correct answer to the questions, write the answers, correct answers. These correct answers are the proteins, the each question paper given to the student is RNA and the original question paper is the DNA.

And it is very important that, students do not make any changes to the original question paper. Then the whole chain gets disrupted. That is why in the cell first that a copy of the DNA is made called RNA and using the RNA we make protein. So, that the fidelity, or the faithfulness of the DNA is not compromised. So that is how proteins are made. Now, this was just a brief deviation from our core area, but these are interesting points. So I wanted to cover that.

(Refer Slide Time: 19:05)



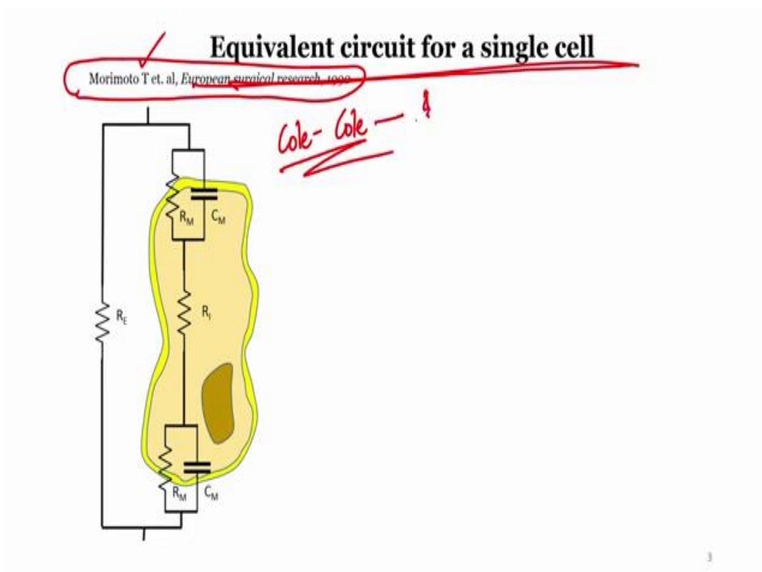
So, this is a central aspect of biology, and that is how these molecular species come into existence. But to be honest, for our consideration, the proteins do not contribute much to the electrical equivalent model of the cell. So we would not go into details of it.

So, for us, the main thing is again, I will repeat, I will keep repeating it, because it is very important cell membrane, CM, cytoplasm, and nucleus, you need to remember only this, nucleus again consists of nucleoplasm and nuclear membrane. Just consider these three things for now. Cells again, then come together to form tissues, tissues, along with vasculature, or lobules come together to form organs, organs, organs come together to form organ systems, and organ systems come to form independent, self-aware organisms. That is how the whole life comes into existence.

So, this is a brief introduction to overall tissue organization, I hope all of you are clear, if you have doubts, you can always post questions in the forum. Now, we will go into the main aspect of this lecture, which is, so we wanted to make sure that you understand the whole beauty of biology.

So, that you can appreciate the electrical model also and it does not become like a rote learning, or by hearting as such, because you understand all these things automatically, if somebody asks you, you can automatically by default, intuitively come up with the electrical equivalent circuit of any type of cell that is given to you. That is why, we went into detail about tissue organization and what, what constitutes a cell, what constitutes the sub cellular components of a cell etc. Now, let us get into the interesting stuff.

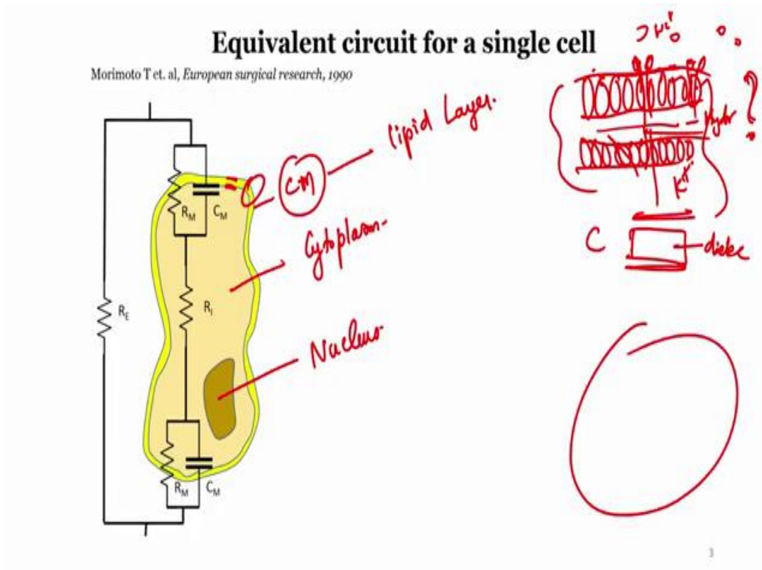
(Refer Slide Time: 20:49)



Now, what is, so now we will see the equivalent circuit model of a single cell. Let us start with the basics, once we know the single cell, we can always bring the cells together and form tissues, bring the tissues together and form organs. Now, so this equivalent circuit model has been in place for a long time, I think even from 1960s people, used to have the idea of an equivalent circuit model.

But this kind of model is was very in detail explained in this paper by Morimoto T et, al in 1990. This is often called the cole- cole model, you can read it up, there might be minor modifications. We will take a separate lecture, where we go through each of the different types of models that are there in literature. So, that you have a good understanding about different, different models. But now we are let us not think about who which scientists did what and all. Let us just try to understand what is the model.

(Refer Slide Time: 21:44)



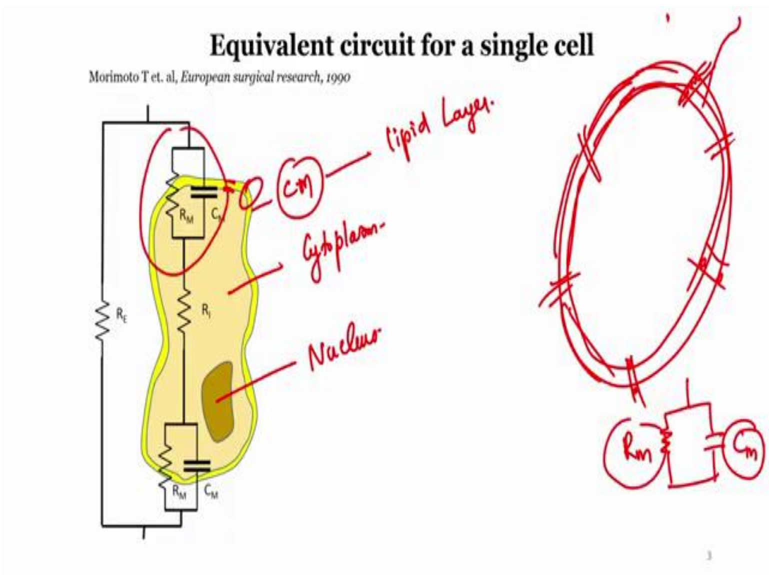
Now, this is the cell, as we have described, so this is a cell membrane, like just now we covered, this is the cytoplasm, this is the nucleus, this is clear. Now, what did I tell? I told you that, cell membrane is a lipid bilayer. So, that is why these two layers are here. Now how was the lipid bilayer, I will zoom in, lipid bilayer is like two layers of fat, I am if any biologist hears how I am explaining it, they might scold me, but because this is, this is an electrical engineering course I am simplifying it.

So lipid bilayer is like two layers of fat separated by a void, this void becomes hydrophobic and this edges become hydrophilic. Now, what does this look like to you? How what does this look like to you? Yes, this looks like a capacitor right? We have two parallel plates separated with a dielectric membrane, that is our capacitor right? So this is like capacitor only.

But then there is a small catch here, this lipid bilayer is not always continuous. In some locations, there might be openings, that opening why is it opening there? It is interesting, why is an opening there in the lipid bilayer? Obviously, it should be there, because how else will the cell take in things that are outside the cell so that it can survive.

So, it needs to have a ion imbalance, so there is a sodium potassium balance equation that is done, sodium ions come in, potassium ions go out and what some nutrients come in. So, those these things happen, the cell cannot exist on its own, it needs nutrients from outside. So, these small, small ion channels, these are called ion channels, allow some things to come in and go out through the cell membrane at specific locations in the overall membrane.

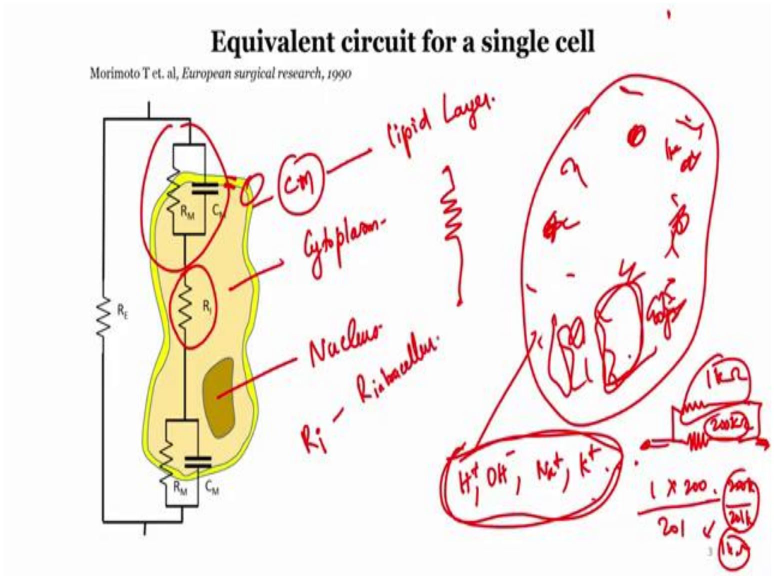
(Refer Slide Time: 23:36)



So, if I draw the membrane here, let us say I draw the membrane here as a big entity, there are two layers right? If I draw the membrane here, there will be random openings here and there, not many. So, what would these random openings be then? They will be like a resistance, they will be like a low resistance path for an electric current to come through.

Because all in only other places, it is just like a capacitance, in some places, there is a direct path. But it is not a direct path like a shot, but it is a sufficiently resistive path. That is why you can model the cell membrane as a parallel combination of a resistor and a capacitor, you can name it a Cm and Rm, membrane capacitance and membrane resistance, that is way Cm and Rm, that is what is shown here. So, that part is done, you have understood. So that is the electrical equivalent model of the cell membrane of the cell. Now, that is done.

(Refer Slide Time: 24:41)



Now, what, what did we see next? What did we see next? Is that we have the cytoplasm. Here as you can see, the cytoplasm is modeled as a simple resistor. Now, you will obviously ask me, how can that be there? Cytoplasm has lot of organelles, there are a lot of proteins running around the cytoplasm. There are the mitochondria, there is Golgi bodies, lot of things that you have learned, there are some things like the suicide bags of the cell lysosomes, liposomes or something, we used to study right in school.

There are a lot of things, there are a lot of, it is a site of Indian factory, there are a lot of things happening in the cytoplasm. Then how can you model the cytoplasm as just your assistance? How can that be happening? Yeah, this is where our basic circuit understanding needs to come in, what did I tell you, the cytoplasm is mostly consists of the liquid power part or the cytoplasm mostly consists of ions, water, basically a water needs ionic state H plus and OH minus and other ions like sodium ion, potassium ion a lot of ions will be there.

Now, imagine a circuit, where you have a low resistance, low value resistance, let us say one kilo ohm resistor connected in parallel with very high resistances, like 200 kilo, 300 kilo ohm etc. Now, what is the effective resistance? Let us say we are just, just simplifying it, we are just connecting it with a very high resistance and a low resistance. Now, here this low resistance is the ions, because ions as you know are quite conductive.

So, they will have very less resistance, let us say this 200 kilogram is from the organelles, because they are like they contain this, like this lipids and proteins and all, they are heavy molecules and they will have high resistance. Now, what will be the effective resistance of this parallel combination? Will be 1 into 200 by 201, R1, R2 by R1 plus R2, simple, simple first, first year engineering topic.

So R1, R2, by R1 plus R2 kilo ohm. So, what this will be? This will be 200 kilo ohm by 201 kilo ohm, basically it will be less than 1 kilo ohm. So, what that means is that, the effective electrical nature of the cytoplasm is dictated by the heavily conducting, is dictated by the heavily conducting ions, inside the cytoplasm. That is why no matter what all things are there, no matter what all things are there inside including the nucleus, it is not going to affect the, affect the electrical property or the cytoplasm.

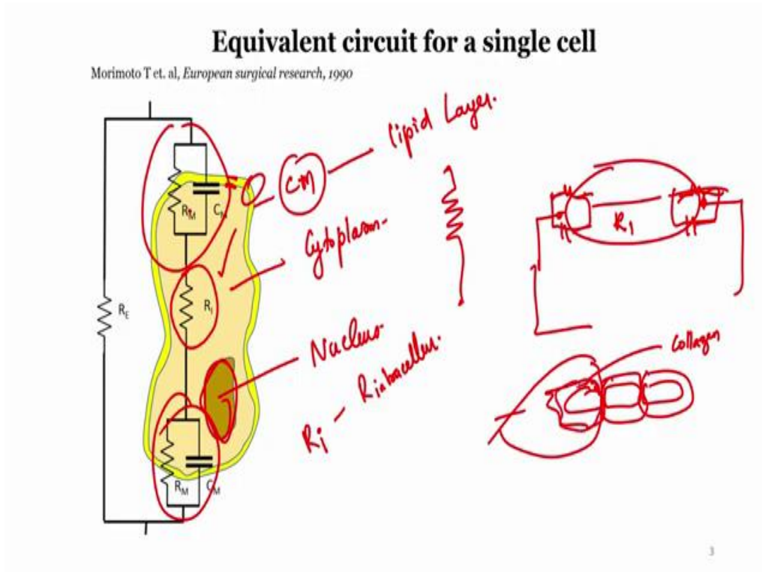
Because, it is overpowered, or it is what we call majorly dominated by the highly conducting ions in the cytoplasm, that is why it is modeled as a resistor, this Ri means, ionic resistance you can tell intracellular resistance, you can call it in different ways. So, this is R intracellular inside the cell.

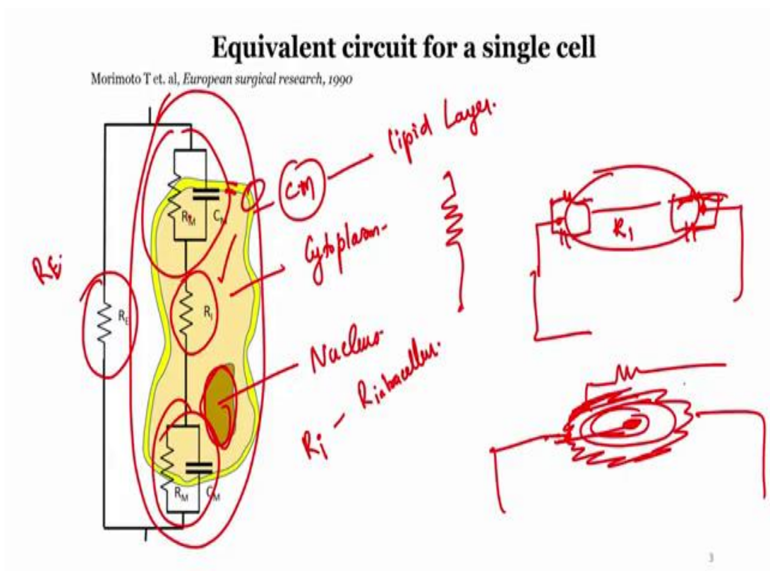
So, this is clear right, these are very important conceptual understanding, this is not very in detail covered in not recovered in any of the curriculum, actual physical curriculum in the country. So, these are things that we have come to understand part of our research, that we are sharing with you, I hope this is useful and you can appreciate the importance of these things.

And more than appreciating it, I think you can understand the, the beauty of it and the how interesting this whole thing is, how biology our basic unit of life is getting modeled as, as abstract resistances and capacitors, which we only play around with in break boards.

So, that is the reason why the cell membrane and the cell membrane is modeled as the capacitor and resistor parallel. And you understood the reason why the cytoplasm is modeled as a resistance.

(Refer Slide Time: 28:25)





Now, for simplicity, because if you are let us say you are taking a cell, single cell, it is a very hypothetical situation, it is very difficult to apply current to a single cell. Though there are now technological advancements, where we can do that, but let us say we are applying current through a single cell, current has to enter from one point and exit from one point. So, the cell membrane is can be modeled as two, two set such interfaces of resistors and capacitors, that is a simple thing.

So two, it is two such interfaces of resistors and capacitors. So that is what we are seeing here these two and it goes through the cytoplasm, which is Ri, note here that the nucleus is not at all coming into picture, but why we have, why we have drawn the nucleus, I will come to that. Now, the cell does not exist on its own, I told you many times, cell cannot exist on its own, it has to structurally arrange itself around something called as a matrix.

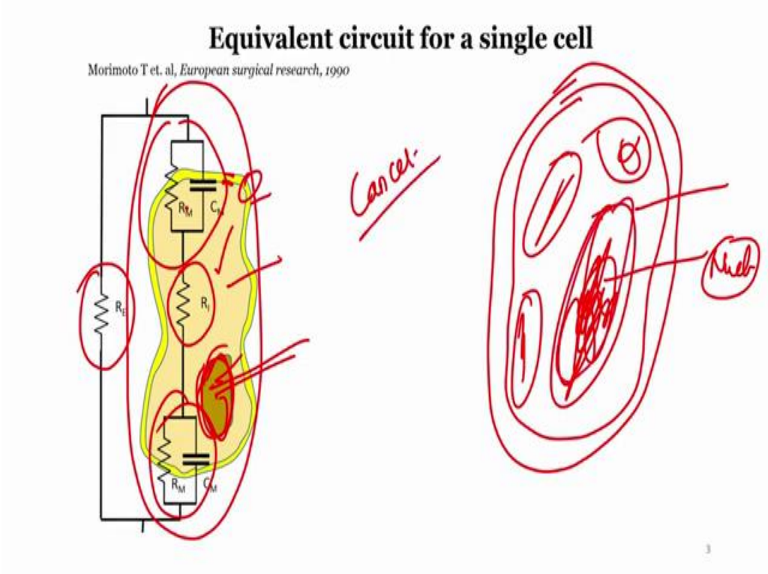
Now, this matrix is usually consists of many different materials, but mostly it is called extracellular matrix is mostly consisted of fibers you can say like, collagen fiber, it is called, but you can just think it has fiber. So, these are like nonliving entities and they are like resistances only, like you take a very high resistance resistor and you are just connecting it, is like fiber just fibers.

So, that is why this collagen will come, let us see now I take the I remove this part of the tissue, where I take one cell along with its associated matrix and keep it aside. It is a very hypothetical explanation.

So I take a cell and I take it is associated fiber, this is cell and then I apply current through it, what will happen, so this current through will go through this resistance in parallel with the effective model of the cell that is this part. So, effective model of the cell and the Re, what is Re, Re is extracellular matrix, resistance of the extra, extracellular matrix.

So, that is why Re is there. So, Re will come in parallel, because you can see, Re is coming in parallel with the effective model of the cell, that is that will define how a cell and its matrix responds to the electric current. So, this is the basic equivalent circuit of the cell.

(Refer Slide Time: 30:36)



Now, you have understood, then you are like obviously asking why, why do I have a drawn the nucleus, it is not even participating in it. One thing is sense for a sense of completeness without the nucleus the cell itself does not have any purpose in existence, because the whole genetic material is inside.

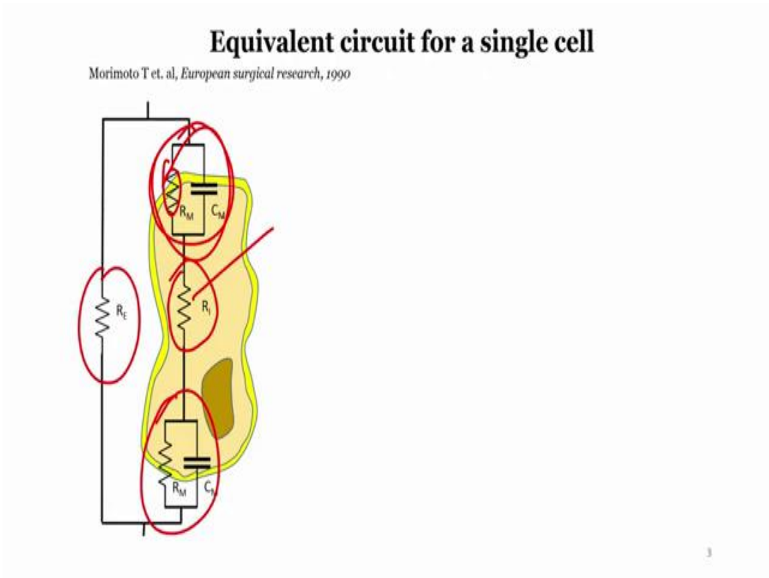
But for our electrical modeling, it is not contributing, but there are conditions like gene cancer and other diseases, what happens is the nucleus becomes extremely large and also becomes multi nucleated, or multiple more than one nucleus comes in conditions of disease. What, what is this course about? This course is about designing biomedical systems. Why are biomedical systems designed? Biomedical systems are designed to diagnose diseases to help in surgery for different biomedical applications.

So, in disease condition, what happens, I will simply tell you I will not go into detail, what happens this nucleus no, this small nucleus might become this big and it might become multinucleated, like this and along with the membrane, in this condition it may not be a good assumption to omit the contribution of nucleus, we do not know, it may not be a good assumption, that is why the nucleus is there, that we have to go in a case by case basis and see.

So, that is one thing, because the nucleus also has nucleoplasm, which is again quite conducting, but it is not as conducting as cytoplasm, because it is a dense region with a lot of genetic material. So, this is very complex modeling, this is the thing of research. These are the things that people doing mathematical modeling research in biomedical systems do, I am just introducing you to this flavor get to, get to get a flavor of all these things.

So, that is why the nucleus is still shown, because there are conditions like in cancer, where the nucleus might become bigger and contribute to the actual effective equivalent circuit of the cell. So, I think this is very clear for you, as I described earlier only thing that you need to think about is the cell membrane, the cytoplasm and the extracellular matrix nucleus to some extent.

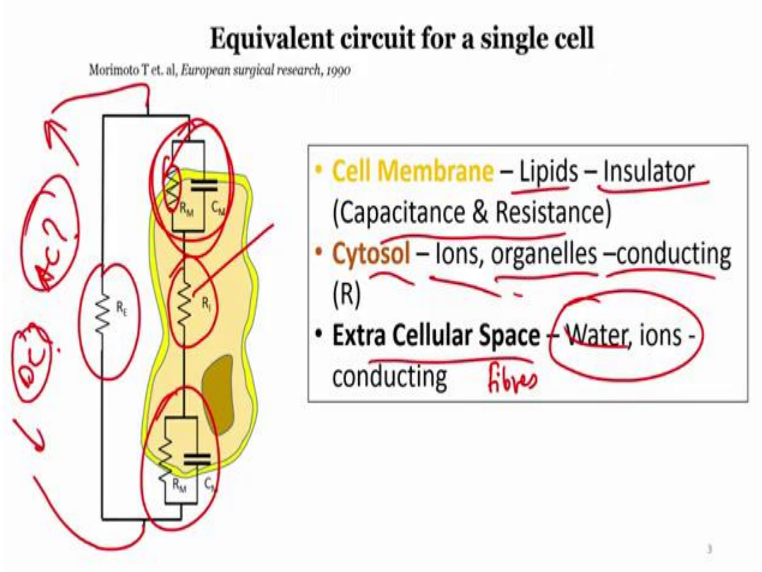
(Refer Slide Time: 32:35)



So, cell membrane is a parallel combination of a resistor and capacitor the Cm and Rm, membrane capacitance and membrane resistance, you understood why this resistance is coming. And then the intracellular space consists of Ri, the intracellular resistance and you understood why it is only a resistance, why it is modeled as only resistance, you understood why there are two pairs of resistor capacitor parallel combinations for the membrane. And you understood what is the extracellular matrix and why it is modeled as a resistor.

This is the basic quite exhaustive way of looking at the equivalent circuit of a single cell. Actually, this is all what you need to know, once you know this, you can always build on this and may come up with new, new circuits, where different cells come together.

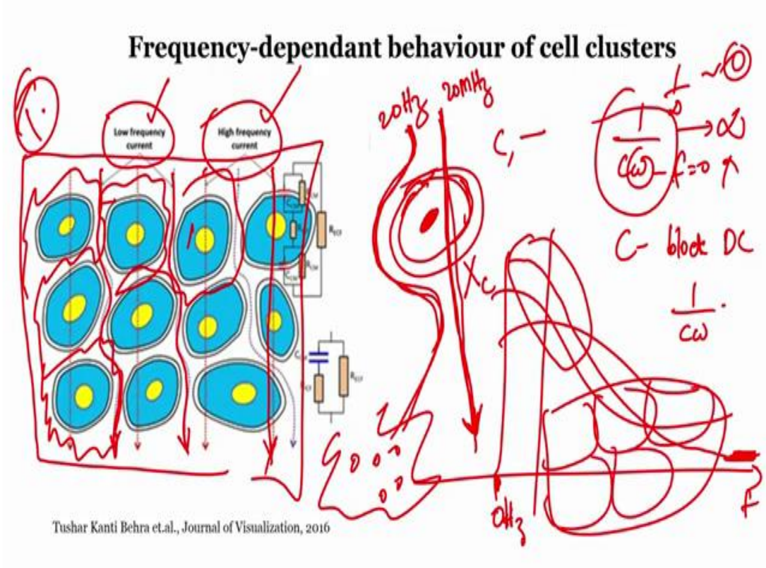
(Refer Slide Time: 33:26)



So, we'll see some examples, so again this is just a repetition of what we have told, lipids, lipids are insulators, capacitance and resistance and then cytosol are ions and organelles conducting, extracellular space is water ion and fibres, extracellular space also has water, by the way. So, it is also that is why it is also resistive.

Now, this, this is like we are just seeing what a, how can we see, how can we model the cell as resistor capacitor combinations, mathematically how can we have a equation equivalent circuit physic with this physical significance. Now, we only model it how what, but what are we applying it across this? Are we applying a DC voltage? Are we applying an AC voltage? What if we apply a DC voltage? What if we apply high frequency AC voltage? What if we apply a low frequency AC voltage? How does it change? That we will see next slide.

(Refer Slide Time: 34:20)



Now, once you understood the basic property of the cell, which we just covered, these things should come to you automatically. Now, I will help you out, but by the moment I explained, it will be very obvious to you. Now, what did I tell you? The cell membrane is capacitive, C, so what is the nature of a capacitor, the capacitor, what is the impedance of capacitor, let us say

$$= \frac{1}{C\omega}$$

that is the impedance of capacitor, ω is what the frequency.

So, what that means is, when frequency is zero, the capacitor offers infinite impedance, basically capacitor blocks DC correct, and very high frequency, capacitor almost becomes close to 1 by infinity, which is roughly 0, it becomes very small value.

So, what that means is that, at low frequencies, let us say I take the spectrum, this is very high frequency, this is low frequency, this is DC 0 hertz, what that means is, at very high, at very high frequencies, let us say this is the impedance of the capacitor, at very high frequency, the capacitive impedance is low, at very low frequencies the capacity of impedance is very high. That means, it is very difficult for the current through, current to pass through at lower frequencies. Because, of this $\frac{1}{C\omega}$ relation, which is very obvious, I think all of you understand.

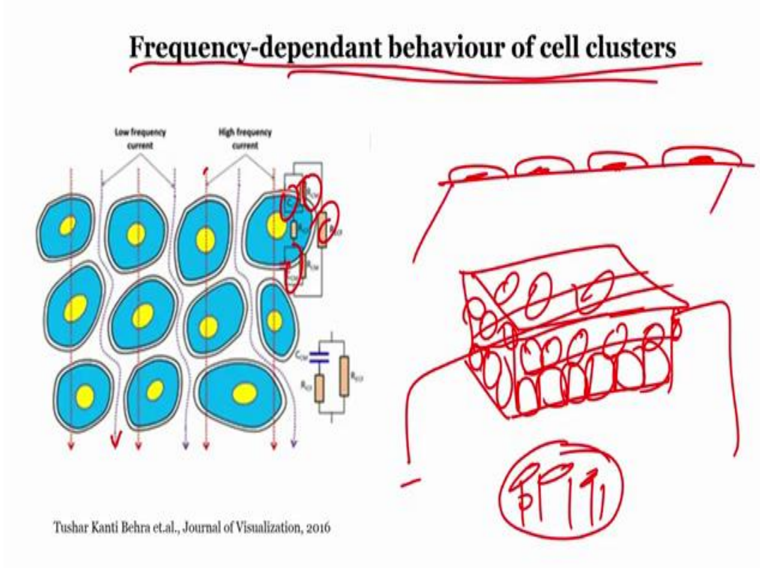
So, because of that, what happens that means, at the moment of first instance, when the cell sees the alternating current, if the alternating current is of a very low frequency, let us say 20 hertz, which is very low frequency, the membrane itself offers very high amounts of resistance, or impedance to the flow of current in the effect that, the current skips the cell and goes around the lower resistance part. Because this is just a resistance, outside the cell it decides to go around the cell at lower frequencies.

But in higher frequencies, what happens? The capacitor the membrane, the capacitive lipid bilayer has very the capacitance of the membrane has very low impedance, so it will allow. Let us say the instead of 20 hertz, it is 20 mega hertz, very high frequency, the current can pass through, because it is a lower resistance path now, low impedance path now. This is the frequency dependent behavior of cells that are clustered together, that is what is shown here, this is from a paper from Journal of visualization, we have adopted it from there. So, that you can understand it.

So, what this is what is shown here, see high frequency component the current is able to pass through the cells directly, the low frequency component tries to avoid the cells like this and tries to pass through the matrix, this has very important implications of how a tissue. What, what will this be? These are all matrixes here, as we told, this is all matrix around the cell, full matrix. So, this matrix and cells coming together is what constitutes tissue.

So, this behavior defines how the tissue responds to low frequency excitation and high frequency excitation, that is how the impedance response changes and depending on different kinds of tissues, the way the cells are arranged, the percentage of matrix and cells in the tissue, some, some tissues might have lot of matrix and very less number of cells. They will behave differently, some tissues may have very less matrix, mostly cells only they will be there, they will behave differently. So, you will be when somebody tells you, this is the structure of my tissue.

(Refer Slide Time: 38:00)



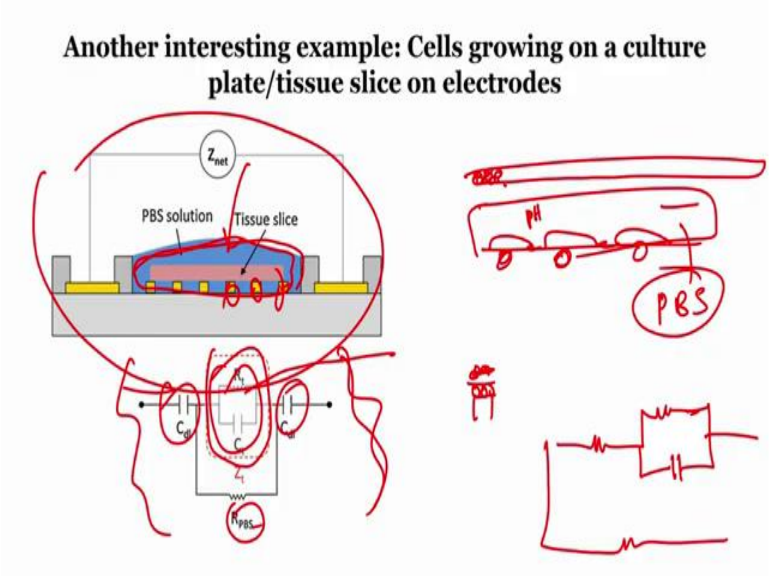
Now, tell me what will be its equivalent circuit model and how will it respond to an AC signal of so and so frequency. Now, you should be able to intuitively tell them, that how it will respond you may not be able to tell exact values of what impedance will be there, at what frequency.

But you will always be able to tell, it will have very high resistance to flow of current at this frequency, but at this frequency it will be low. Those frequencies you can get by the equivalent circuit parameters, these are Rm, Cm, Ri, Ca parameters of the tissue. So, this is the frequency dependent behavior of cell clusters.

Now, one last thing is, let us say this is 3D, we are seeing a 3D volume of cells, arranged in a tissue, cells are there like this. This is a 3D volume of cells and you are applying current correct. So this is what we saw. And we saw how low frequency will bypass it and high frequency will go through the tissue and all right.

Now, let us say imagine that we have a plate, where cells are grown 2D plate, and we have electrodes below it. And it is a two single mono layer of cells that are growing, it is like a surface where one one layer of cell only is growing like this nucleus, and this is these are electrodes. How do we model that?

(Refer Slide Time: 39:22)



That is what is modeled in this model, this is from Professor Pandya's, one published paper, we can share the link to that paper, you can go check it out. So basically what that means is this tissue slice, a tissue slice will also be a mono layer, or a few layers of cells, one, or two layers of cells, that is a tissue slice with matrix and a culture of cells will have just single cells with some matrix.

How can we model this? Now, you are unless you have understood things. Now you know how to model things. So you can always put effectively put the effective impedance of the whole tissue as one resistor in parallel with a capacitor. And let us say the tissue is kept in a solution called PBS, PBS is, is the phosphate buffered saline, it is what is used to maintain the PH.

So, that the cells do not die, so that is a again a salt solution. So, it has a resistance, so RPBS and these electrodes that are there, below the cells, they offer a double layer capacitance at the interface between the because there is a interface of metal and the lipid bilayer, of the cells. So, that is basically a double layer capacitance, that is why it is modeled like this. A double layer capacitance, effective cell model, is a very simplified model of the whole tissue, you can always improve it, improve on it. And the solution that is in, this solution that it is in is the RPBS.

So, this is I just wanted to tell this to you like you given a scenario, how will it model it in a very simple way, you can always make it more complicated, you can put a resistance in the path of the cell and tell like that it will be like this, not like that.

So, many things you can do depending on what kind of cell it is and you can improve, keep improving the model. This is one interesting example. This is how you model, different types of cell organization for different biomedical applications, this is a biomedical application, where we trying to measure the mono layer of cells on an electrode.

And seeing and if let us say we add some drug to kill the cells. How will the electron measure the impedance, how will it is change? This is how biomedical systems can be built from first principles. And the first principles we have covered now, all the first principle frequency depending behavior, DC behavior, how what is resistor, what which part of the cell is a resistor, which part of the cell is a capacitor all these things we have covered.

So, I hope this gave you a very good introduction to basic electrical equivalent circuit modeling of cells, and how they come together to form tissues. And in the next lectures, we will see other interesting aspects of mathematical modeling of biological systems, stay tuned for upcoming modules. And if you have any doubts, please feel free to post in the forum and we will be more than happy to help you out to understand the concepts. Thank you and see you in the next module.