Bioelectricity

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Lecture - 19

Welcome come back to the lecture series on Bioelectricity. So, this is lecture number nineteen. So, in the previous lecture, we talked about the basic structure of the retina and the eye and there we talked about the complex layer of different cell types in the retina which insures that the image which is formed on the retinal blade is conveyed correctly to the brain and the decoding takes place. So, our eyes human eyes can distinguish light wave length from the range of 400 to 700 nano meters.

So, if you recollect your previous lecture, where I have shown on the retina on the bed of the retinal pigment epithelial cells, you have this rod and the goon cells. The rods are the ones which could distinguish the different intensity of light, whether it is in during the dark conditions or during heavy light conditions. Likewise and the cone cells are the ones which could distinguish the different colors. So, essentially cones have cones are of different types it could be a red crone cone it could be a blue cone it could be a green cone depending on the specific ability of that cone cell to distinguish a specific color type.

So, today what we will do we will be talking about the electrical activities of this rods and the cones under one broad heading photo receptor electrical activities of the photo receptors and then we will be talking about the current stage of the prosthesis where people have lost their complete vision or partial vision.

So, essentially there are two kind of blindness those I have previously described either the blindness could be at the level of the lens. Where there is the damage at the lens and the lens has to be replaced by lens artificial lens, those are curable blindness. But there is a another level of blindness which arises at the level of the photoreceptors. The photoreceptors gets damaged either because of old age or because of some birth defects or because of some injury or some other patho physiological situations.

So, let us first of all discuss the structure of the rods and cones and then we will talk about the electrical activity in terms of the dark current which are gen and why these are

called dark currents and then we will briefly talk about some specific aspects of the cones and then we will talk about the prosthesis.

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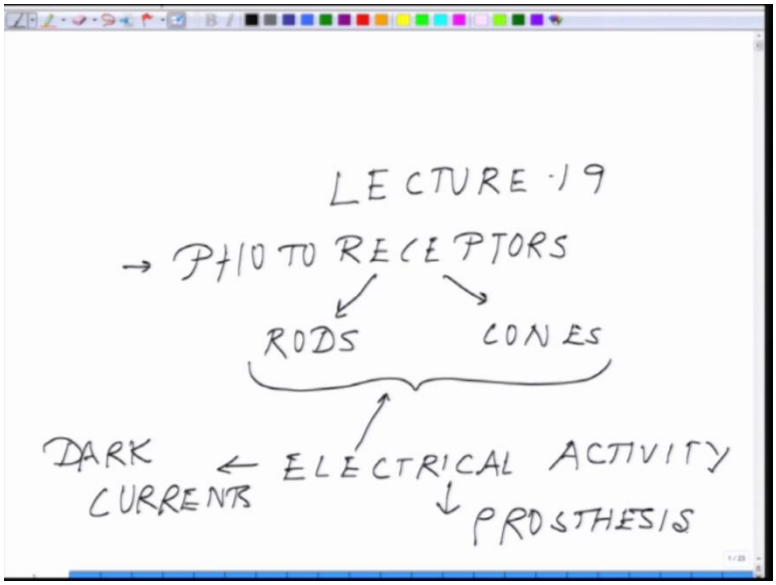

So, we start off with. So, we are into lecture nineteen. So, basically we will be dealing with the photo receptors and within the photo receptors we have the rods and the cones and their electrical activities and the concept of the dark currents and followed by that we will moving on to the prosthesis. So, moving on to the next slide. So, let us talk about the structure of the rods and cones. So, these are the very unusual kind of a structure these are almost like you know clearly elongated structure like that a cone pretty much a cone looks like this. So, this is the part say for example, if you look at his pen. So, you could see there is this kind of you know light black color or ash color body and underneath there is a lighter color. So, this the part essentially where all the light receptive pigments are present and this is the cell body. So, if

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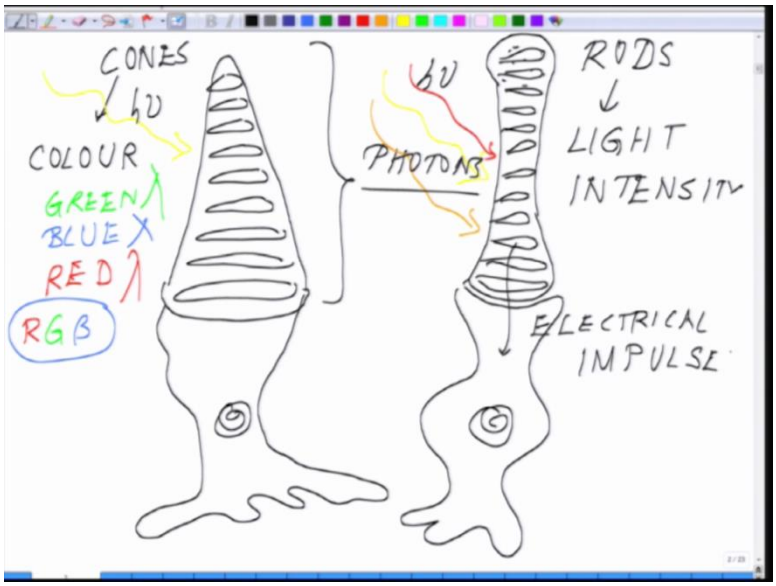

I draw it looks something like this. So, for example, cones because of their whole structure they are more like the structure which is similar to this and this is the classic structure of the cone like cell and within this structure you have these what you see this cap like structure which I have just now drawn for you. So, this is where all the light sensation or different wavelength distinction takes place where else if you look at the rod they are more like almost like a rod only and then here you have.

So, this is where. So, they are called cone they are for color perception. So, these are the cones here for the colors and these are the rods for different light intensity. So, this is where they have the nucleus and the way it works is this is where the light falls. This is the one the cone the cone is the one, which could distinguish between you know the green it could be a green cone it could be a blue cone or it could be a red cone almost like you know r g b coding. So, the different coding of the wave lengths of these these could distinguish yeah. So, these are the different wave lengths of the specific cones are of a specific type they could be excited. So, that they could emit they could they could absorb light at the blue wavelength or they could absorb light at the red or they could absorb the green wavelength.

So, for example, this kind of color vision in only functional in high intensity light because if you walk in the dark you realize that you cannot distinguish color. What is you essentially see a shade of black and white, so that means, the cones are only active

when you are in a bright light and where you could distinguish the different color red green likewise. And there are people who suffer from color blindness where they could not distinguish this different kind of color; that means, such individual suffers from certain genetic disorders where their color distinction specific types of cones which could distinguish color does not develop properly or mal deformed of mal formed. So, there is another kind of blindness which is called as night blindness which is essentially as it becomes darker you are unable to really distinguish objects properly that essentially happens.

Because of the rods and it is not genetic disorder it is mostly because of the malnutrition of lack of vitamin a in the food and we will come to that where it exactly happens in the case of rods if you look at this structure. So, to here any kind of like you know lights which are falling here and they respond to the light. So, essentially what happens when the light falls. So, these light or these photons binds to specific sites on the membrane and the ones ba they bind to the membrane this light energy is translated into electrical impulse this is what essentially happens

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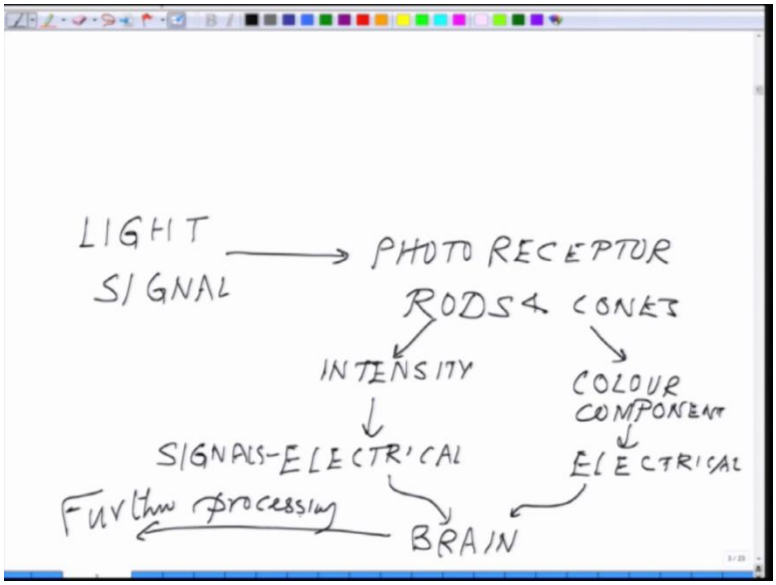

So, here you have the light signal falling on photoreceptor which includes rods and cones depending on the situation it could distinguish the color component and if it is dark it is not going to do. So, and the intensity and these are coded as electrical signals electrical signals and these electrical signals are essentially send to the brain for further processing

and in between rods and the cones are the whole network of amocrine cells horizontal cells which ensures that the exact depth of the object what we are looking at the exact the movability and all these features are being added to this. So, what the brain receives is a complex electric signal which has to you know distinguish in terms of colors intensity depth frame and all those things.

So, coming back again coming back to the structure how this electrical signals are being received. So, it is very interesting that on the photoreceptor we there is one term which i am going to introduce is called dark currents

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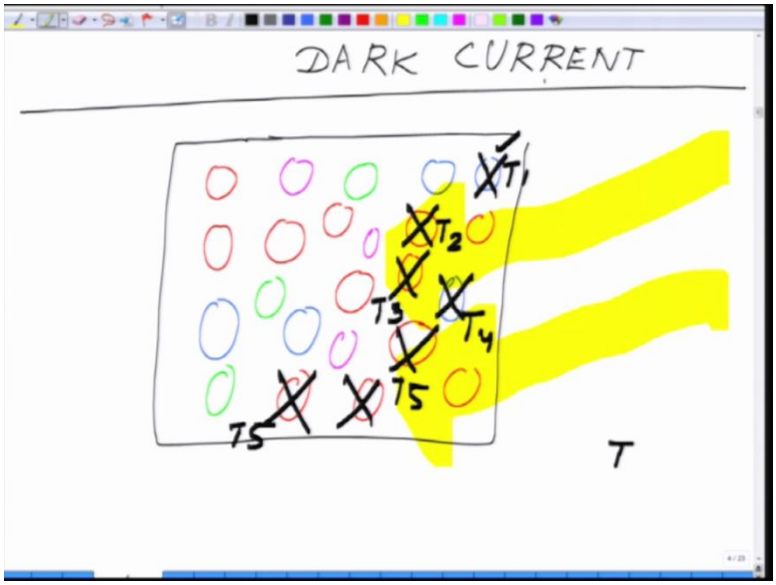

So, what does dark current means. So, there is a common way we look at it. So, we believe there is a intense some signal is coming our sensory cells respond to that and generate action potentials ok. And this action potentials eventually is conveyed to the brain and we test it for the object what. So, ever we are looking or we decipher the information fine in the case of rods and cones this thing is just reversed something like that when the light falls in the photo receptor layer. They do not generate any signals and where the light does not fall they generate signal it is just the reverse it means when the light is not falling suppose my eyes are closed.

So, actually conveying the signals. So, essentially what happens suppose you have the matrix like this this you have to conceptualize in your brain then only you are going to understand for example this is the matrix of say you know say for example, these are

different matrix of rods and cones which are sitting there. I am just putting different colors of your understanding.

So, imagine this is the photo receptor layer and these individual circles are different photo receptors. So, say for example, let me just I want extra thick fair enough when the light is falling here like this and this is the wave of light which is falling . So, when the light is falling differentially some point this will on second at one point this one will get shut off and then in the next point this one will get shut off and this one will get shut off this one will get shut off, but this all shutting off is taking place if this is taking place if this is taking place t one this will take place at t two this will take place at t three t four t five likewise you know.

I am just randomly putting all the different numbers and t stands for the different time. So, essentially what is happening you are getting a matrix over a period of time, where initially this one switched off, there is one frame you are getting where on say for example, think of a flood light one light goes off there is one image. Next light goes off, next three lights goes off, you have another image. Next four lights goes off, you have another set of image, and essentially what is happening, you are recording this frame by frame. And eventually the whole image is formed in front of you or say for example, in a city you are looking from the top all of a sudden, I you know switched off all the lights. In such a way that you make a figure I just selectively put some lights on and switch off all the lights and then I change the figure and I gain switched off certain lights and gets a figure.

Likewise I can really frame by frame I can actually convey the message this is exactly how some of these the retina actually this kind of a analogy how it works. So, for example, the frame one if you talk about the frame let us let us try to you know

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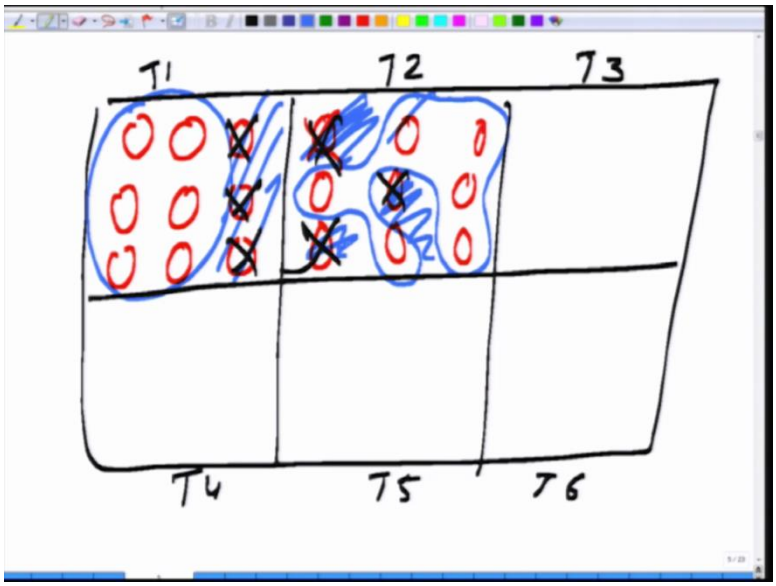

Let us draw six frames this is what is happening. So, this is say example time t one this time t two this time t three this is t four this t five this t six and this is let us assume this is our. So, the first when the first part of light comes this on this one this one goes off then next frame. So, for example, sorry this one this one and this one goes off. So, now, within these two you'll see initially you saw a image like this what.

I am circling like this with a contrast here there is contrast here then you see a image like this with a contrast here you are seeing you are kind of seeing a shape now. Likewise frame by frame and this is all happening within a frame of you know nano or symto seconds you have lot of frames then this frames are the ones which eventually form the image this is very very essential for you to understand before I go to the individual at the cellular level. So, it is the frame by frame images which are formed by because of shutting off of say one photo receptor or or some population of photo receptors.

The other photo receptors are active then another set of photoreceptor is active the other set of photo receptor goes off likewise. So, whenever you have to imagine think of a flood light in a in a bellodrom or on a stadium where if one light goes off one frame. Then few lights goes off you have another frame few lights goes off another frame or you can like think of a somebody is showing you the sky and slowly one by one you know showing you the stars follow the stars it is almost like that one switch off switch on switch off switch on. Likewise something of that or you are seeing a city from the top all

the lights are on than somebody switch a ways of a light and make a figure then switches of the light makes a figure switches of the light makes the figure and then that whole image will come exactly that is how retina functions. Now, coming at the cellular level what is happening. So, so I can use the this. So, what we can do what I'll be doing actually now I will give you the membrane structure here

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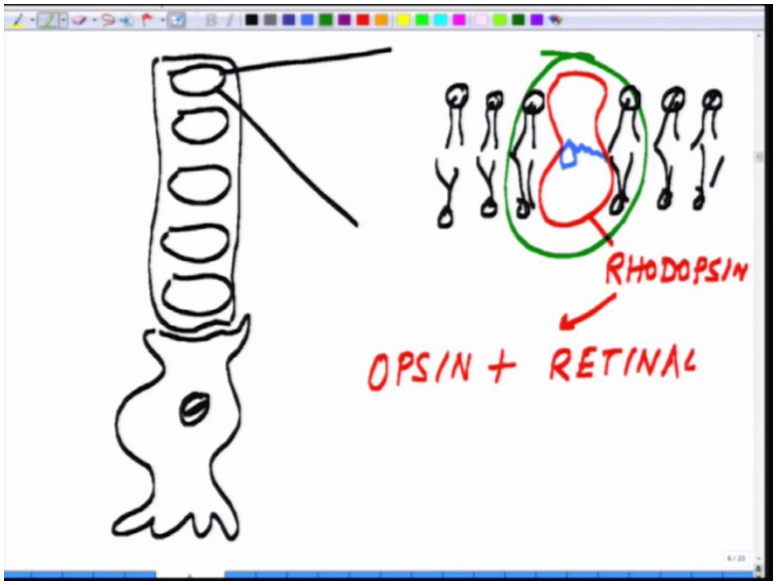

Now, let us see the structure of the membrane we will be talking mostly about the rods this time rods I mean the signal processing is fairly the same . So, here the here the rods. So, if you really ha blowup this image it is almost like this this is the membrane stricture you remember in previous one of the previous lectures we have talked about the membrane this is the lipid by layer and on the lipid by layer you have the something like a protein sitting there which I called rhodopsin protein ok.

The rhodopsin is a huge molecule rhodopsin which is essentially made up of two one is called opsin the other one is called retinal and the retianal fragment is sitting somewhere i will just put it in the blue now some where here the retinal fragment is sitting. So, this is how it looks like. So, there is an opsinuety and there is this retianal molecule. So, this is the key molecule which ensures or this is the one which receives the light. So, it receives the light. So, this has light this is the light sensitive protein it is this molecule which ensure it has variants of course, which ensures that at different intensities how it will

function with different wave length how it is going to function. So, this key molecule now we will be talking about what exactly happens with this molecule in the next slide

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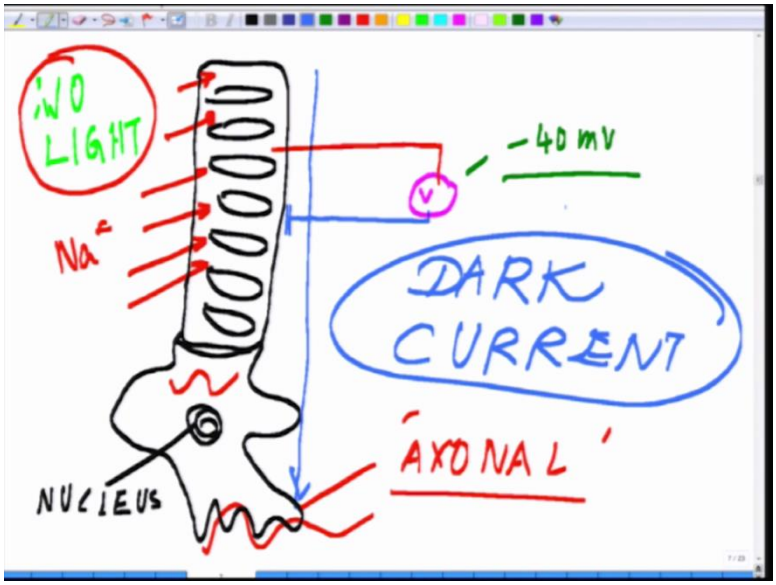

So, next slide what I will do I will talk about. So, let us again get back to the structure of let us take example of a rod. So, here you have all those rhodopsin molecules are sitting here and ok here you have the nucleus. And now say for example, you put an electrode inside the cell and then you put another electrode of course, outside the cell like this and you have voltammeter sitting here what will you see.

So, initially what you will see when there in no light falling in this . So, at that time your voltammeter reading will tell you around minus forty mill volt this the situation when on second there is now light let me put that there is no light. And at that point, there is the flux of the sodium which is getting in as the sodium is getting in it is ensuring all the sodium irons are ensuring that these electrical impulses are been transmitted.

So, this is the kind of the axon axonal end of a rod or a cone cells because when the light is falling oh when the light is not falling sorry. So, mark it it is not falling there is profused entry of the sodium ions and this ensures that is generates action potentials which are transmitted to the next layer what you could see well let us take that the electrical signal is travelling like this now when the light falls. So, this is basically what is term as what is was trying to discuss with you is dark current there is no light yet it is generating action potentials now next let us go to the next situation .

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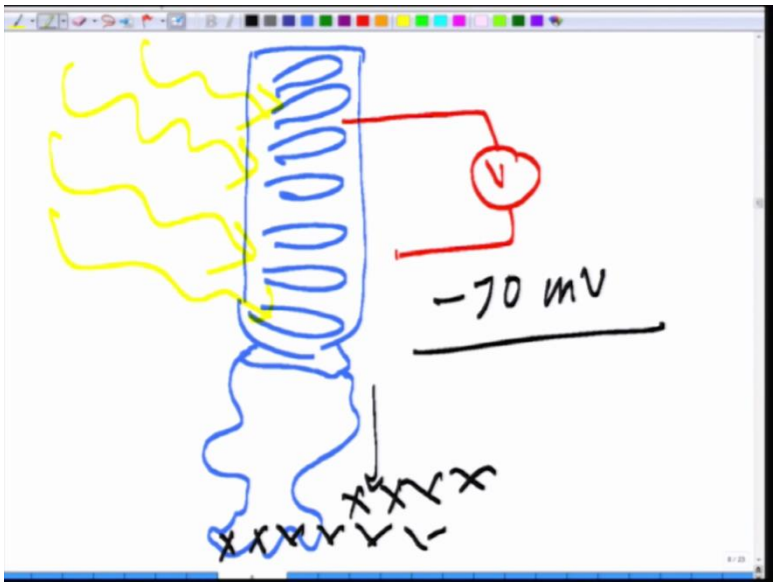

In the next situation, what is happening, here we have again the rod cells. Now again the same way, you have a electrode inside, you have voltammeter sitting herem and then you have the other end of the voltammeter. Now light is falling on this, when light is falling on this, what you see the membrane potential goes to minus 70 milli volt. Now what is happening here when minus 70 milli volt is up here. It means, it is no more sending any signal out here. Just reverse to the situation where during no light, it was sending signal and you see without light. So, basically these signals are being there is no signal what exactly happen this is a very very interesting phenomena.

So, let us dissect the problem at different level first of all when the light was falling sodium channel no was not falling sorry excuse me when the light was not falling sodium channels are open when the light started falling sodium channels were closed. So, what is regulating the sodium channels first question and how that regulation is modulated by light because when the light falls sodium current stops. So, it means light and the gating of sodium channel is linked.

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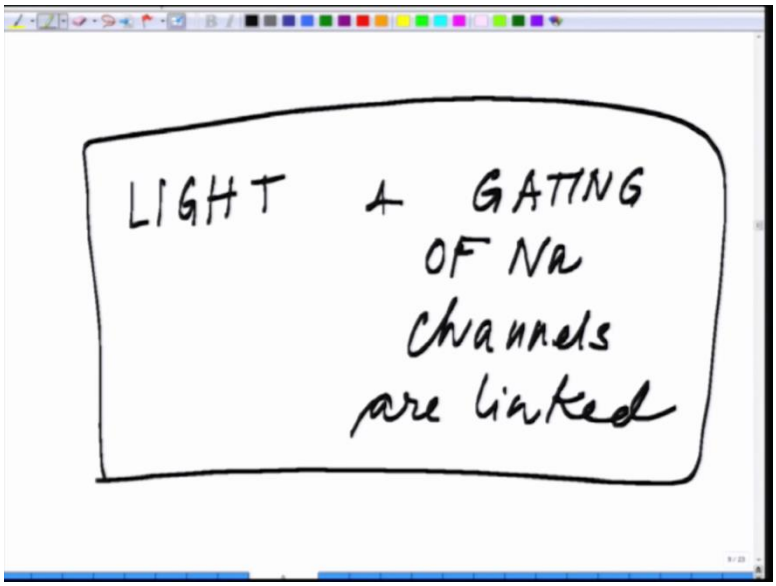

So, these are the two things which are now we will be discussing light and gating of sodium channels are linked and now what we will do will establish that linkage what essentially is happening.

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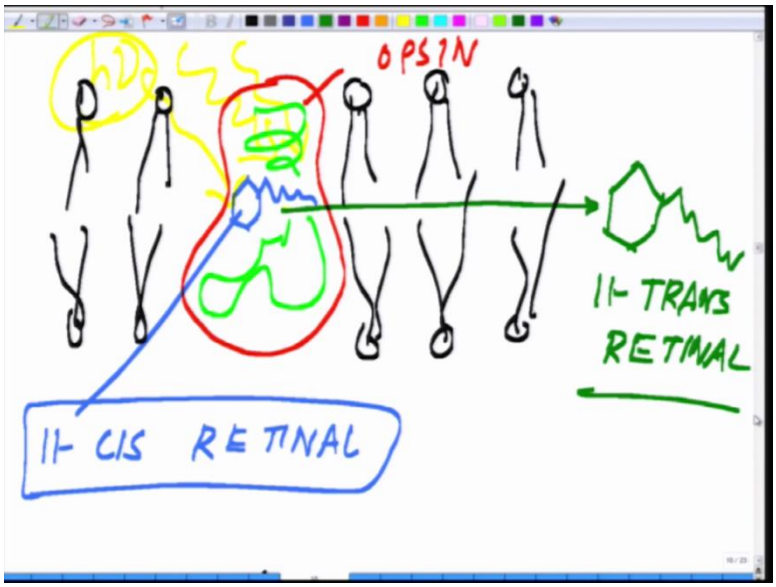

So, there are two things which are happening out there . So, the first thing what happens is now let us go back to the membrane structure what is happening remember. So, here in the rhodopsin molecule here lipid by layer rhodopsin molecule sitting out there with its opsin muity and the retinal muity. So, I told you some where here retinal fragment is

sitting and this is the protein which is with its complex structure out there which is shown it green now when the light falls. So, this muity what you see here is retinal muity this remain as eleven cis retinal with the (( )) group this is in this stage and of course you have the opsin one second opsimuity and all together ceradopsin.

So, now, the light is falling at this stage there was no light now here the yellow thing what you were showing h new is the light is falling the light is falling what happens is this eleven cis retinal what you see here transformed into eleven trans retinal. So, the cis bond becomes the trans bond when the light falls on it. So, now, what we see there is a change in the molecular architecture of that retinal molecule what are the consequences of that change this is the first change. So, within the rhodopsin having this opsin and the retinal muity attached on it it is it is a complex protein when the light is not falling on it the retinal muity remains in eleven cis retinal form when the light falls on it this retina becomes eleven trans retinal, but then what happens next. Let us move on to the next slide one we save it.

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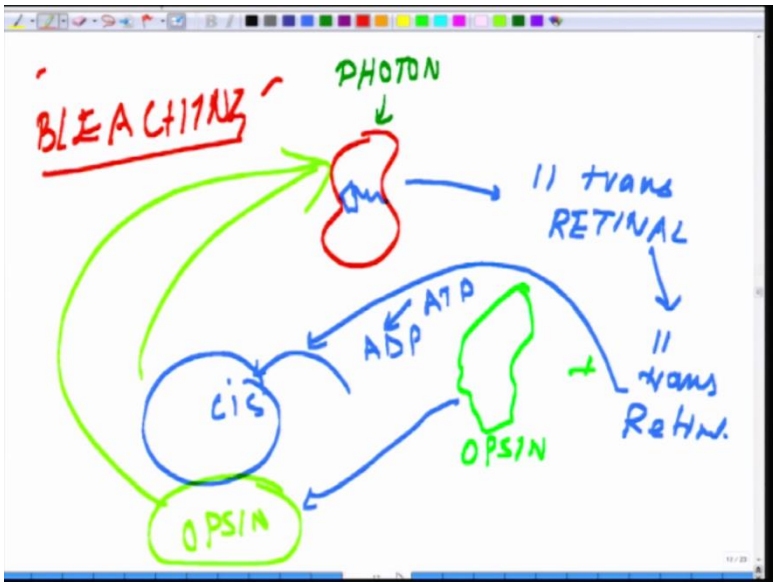

so the next thing what happens is this when the eleven cis retinal is formed. So, let us go back. So, here the photon is falling on hmm here is the muity sitting there. So, photon has formed now you have eleven trans retinal this eleven trans retinal then disassociates from this structure. So, your left with is now you have this opsin protein coming out plus you have eleven cis sorry eleven one second let me just rub it off and you have this

eleven trans retinal now this opsin protein now remain pretty much orphan at this stage and whereas, it eleven trans retinal through a enzymatic action again become cis ok.

So, there is an complete enzymatic action where a t p is being used to convert it into eleven trans cis retinal now this cis form again assemble with the orphan protein or the orphan component which is opsin and again from this stricture. So, this is basically what it is being called a bleaching phenomena there is kind of continuous bleaching taking place with in the eye, but during that process something else has happen that is what we are going to discuss how the channel remains open

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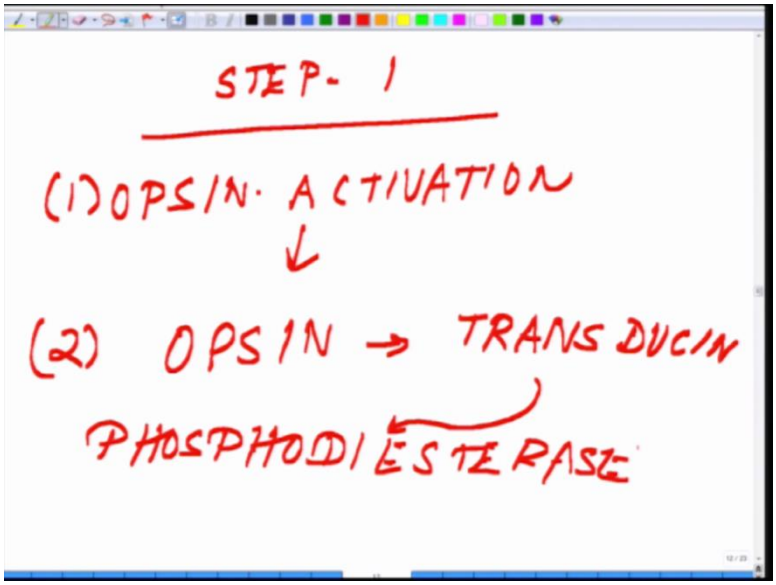

So, what essentially happens in step one we come back to step one step one was opsin activation because when the light falls I told you the opsin becomes opsin comes out and the eleven trans retinal disassociates ok.

Then what the opsin does in step two is opsin does something very interesting opsin activates a second enzyme called transducin and this tranducin which intern activate another enzyme called phosphodiesrase and this phosphodiesrase then does something very interesting what it does is

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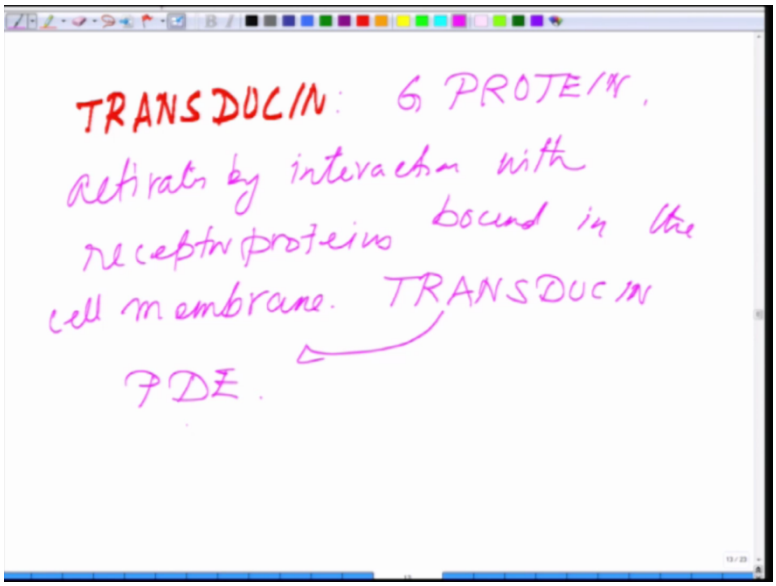

Now, just before that little bit about that transducin what is exactly just give me one minute hmm transducin transducin it basically a g protein it is a series of protein g protein it is a membrane bound enzyme and it activates by activates by interaction a receptor proteins bound in the cell in the cell membrane in this case what tranducin does transducin is of course, is activate by opsin and transducin intern activates phosphodiesrase.

What I have talked about and phosphodiesrase what essentially does is very interesting phosphodiesrase disintegrates the molecule called cyclic g m p then where what is the role of cyclic g m p ok

So, coming back to the slide now you have phosphodiesrase i am showing by p d e this p d e then acts on cyclic g m p. So, what is the role of cyclic g m p in this whole context of things what I was trying to tell you. So, let us come back to the first question here out here the question what we ask one second let me go back to that slide where we talked about the dark current introduced you to the dark current

Yes when there is no light I showed you this picture when there is no light you could the sodium channels are open up to this concept is clear then what essentially happens when the light falls sodium channels become closed. So, the fundamental question comes here we asked two fundamental questions on was this one light and gating od sodium channels are linked we will take it up from here in this slide

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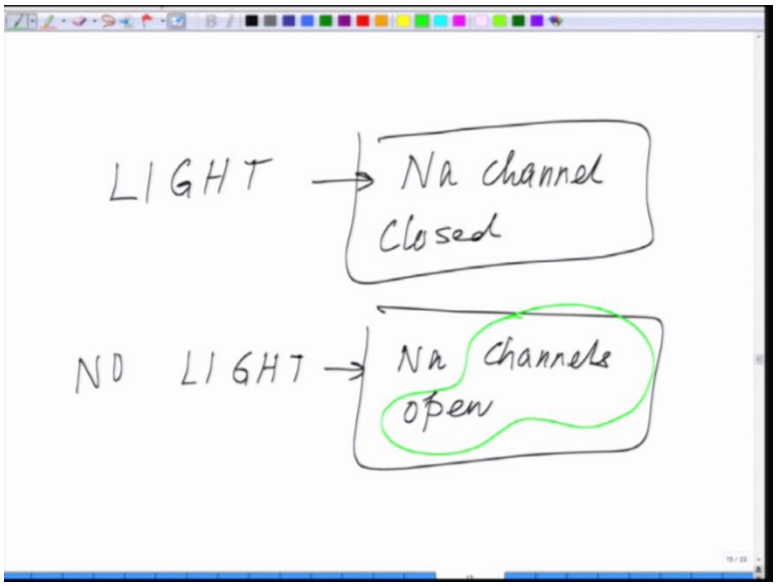

let us see. So, light it is two situation no light sodium channel and sodium current sodium channel closed no light sodium channel open fine .

Now, the next challenging question was what keeps this sodium channel open at this stage as if a door is kept open. So, how you keep your door open there are three ways how you can keep your door open think of a room where ever you are sitting and listening to this lecture you can keep the door open by using like something under the door stopper or you have something by which you keep the door like this. So, these molecules are something like door stopper molecule and the door stopper molecule or the door opener molecule of sodium channel is cyclic g m p, in other word what is essentially happening.

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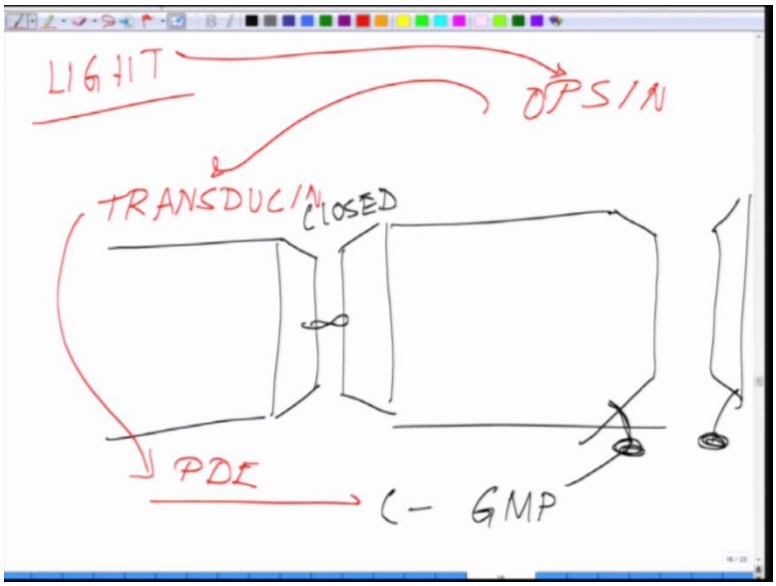

Say for example, this is let us take as analogy you know this a door of a room this is the wall and this is the door which is locked. So, this there is cyclic g m p if this is this is say for example, the sodium channel and this is in closed state or this is door now this could be kept open like this by holding it with something like this you have to hold it which could be a door stopper or anything in the case of channel you have the cyclic g m p setting. So, cyclic g m p acts as a door stopper keeps the door open. So, now, the door will only close when you remove that door stopper that door stopper cyclic g m p is removed by the molecule called phosphodiesrase which is activate by transducin transducin is further activated by opsin and opsin is disintegrated in the presence of light does it make sense

So, when the light falls. So, lets summarise what exactly happened ok

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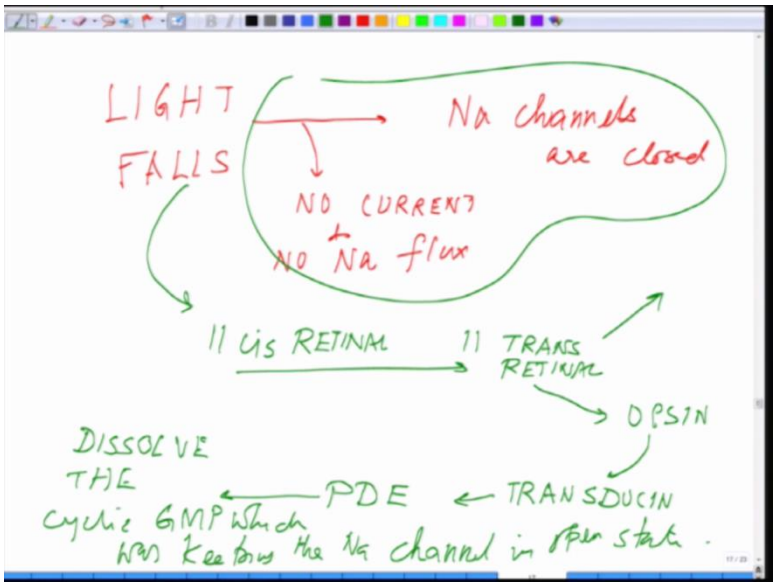

Now, coming back to the next slide. So, light falls on the retina what you essentially see no current and no sodium flux. So, it means sodium channels are closed. So, what is happening at the molecular level during this whole thing light falls eleven cis retinal becomes eleven trans retinal on the mrudopsin molecule, molecule eleven trans retinal dissociates out. And this process dissociate the opsin molecule this opsin molecule then activates a protein called transducin this transducin further activates a molecule called phosphodiesrase, phosphodiesrase then dissolves the cyclic g m p which was keeping.

The sodium channel in open state this is exactly what is happening in this whole process of signal transaction within the rods, and the cone. When the light falls the electrical signal ceases and when the light is not falling the electrical signals passes on, and that is why this is called dark current, which is also called cyclic g m p regulated current and depending on the wave length of the light. In the case of cones these electrical currents are being stimulated or you now stopped. So, this a very fundamental concept which.

I wish or wanted that you people it should be clear to you it is this layer which is most critical one. So, say for example, now somewhere or other if this layer. So, let us go back and see the global picture out here. So, out here let me let me give me on minute

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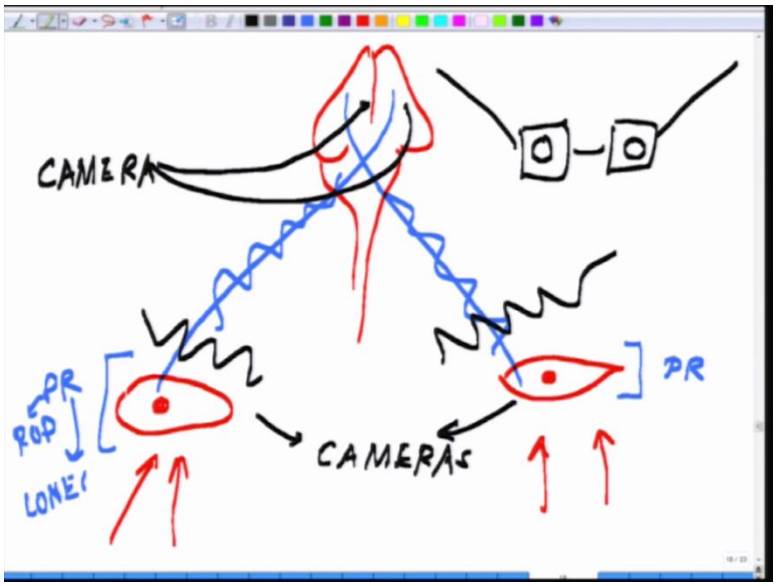

So, here you have the brain spinal cord here you have the eyes. So, the electrical signal moves like this left to right right to left now at this level at first level where the image processing takes place the p r or the photo receptor layer which is essentially the rods and the cones. So, the electrical signals are travelling from the eyes all the way to brain and the processing takes place now imagine somewhere or other rods and the cones layer goes bad what will happen

So, now there would not be further image processing taking place they will see it, but there would not be any further message going on this is all blocked what intervention can happen. So, one option is that if you could replace this eyes with a camera or with two camera's on two sides. So, or you have a goggles like this you know something like this where you have the camera sitting out here and this goggle is connected interfaced at directly to the brain. So, camera instead of this now they are directly cross talking with the brain this is the approach which inspire people for one century that could we reall y bypass the whole vision by putting camera's instead of eyes. So, basically what is happening this circuit is no more functional this is a defunc circuit out here. So, what you are doing you are interphasing the camera with the brain. So, images which are forming analog images are digitize and the digitized signal in the form of electrodes are being fed to the brain. So, in this context

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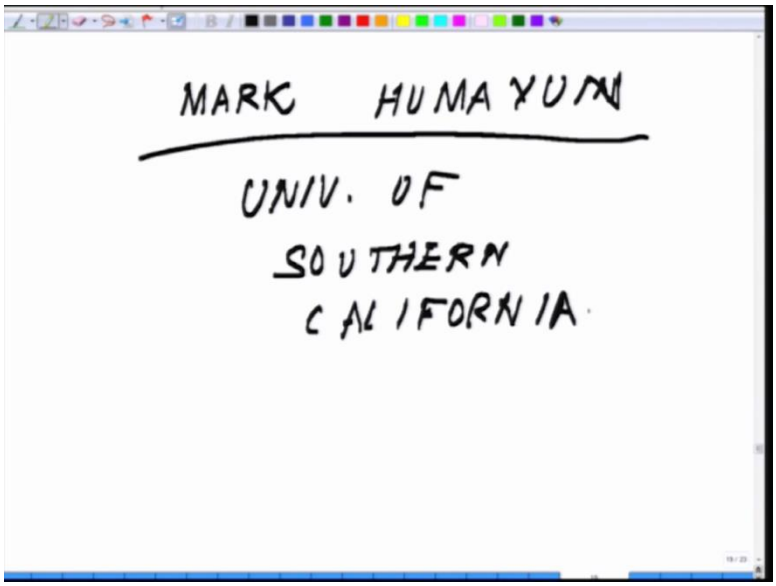

I will recommend you to read some of papers and of course, at the end of the course i will be providing all the references which I with. So, one of the person who have made really good contribution is from university of southern california you should read his Mark Humayun spelling may be wrong sorry his paper from university of southern california u s a he has made some very interesting camera's where he has interfaced them with the brain and this is really interesting piece of work which is going on. So, where prosthesis has kind of a successful process, but there is lot of improvement which has to be done. So, what i will be essentially doing.

I will be giving these references of Mark Humayun and I expect you to read through them because that is where lies most of the future of prosthesis. So, again to tell you what is the major challenge in this game in this game the major challenge how he interphase the electrodes with the brain because you are putting some foreign material in form of electrode. So, that has to be biocompatible not only it has to be biocompatible it has ensure that all the signal over a period of time continuously reaches because you cannot continuously open the system fix the electrodes it has to be done.

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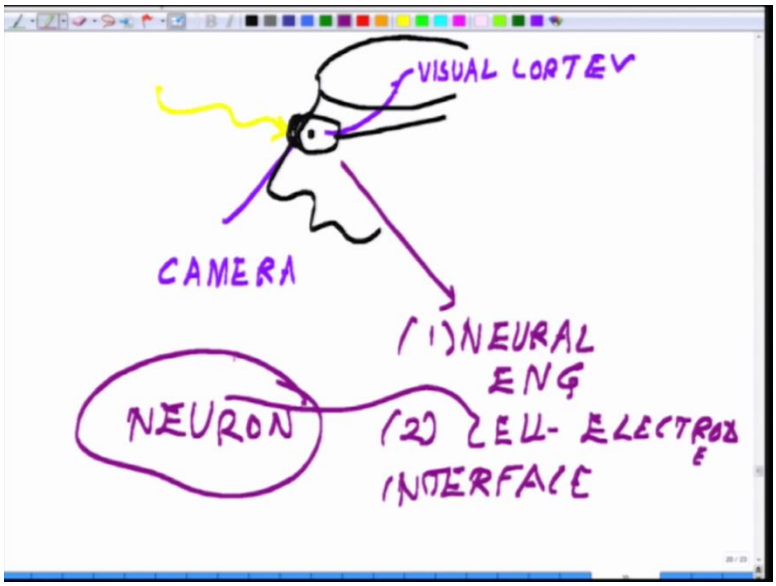

Say for example, here what we are talking about is the individual and if this is the brain. So, that is you are saying is essentially if this person has this goggles they are put in. So, here is the retina which is receiving the light and this goggle which is a synthetic retina is essentially interfaced with the visual cortex out here in the brain. So, there is enormous amount of electrode implantation, which has to be done to ensure all the message reaches the brain at the visual cortex.

And then of course, this person will be able to you know visualize if this person is unable to see, but this needs not only I mean of course, the camera technology is very well advanced, but the interface technology which is the whole area of neural engineering. Or you know you can talk in a much more specific way the cell electrode interface or neuron electron interface. This is in terms of the cell here this is the very very challenging area where lot of research is going on for last one century that how really we can develop extremely high biocompatible material which will convey the signal and help in this prosthesis business.

So, I will close in here with this and in the next class we will talk about the ear and the ear prosthesis and so on and so forth. We will finish this prosthesis part with the basic structure. So, there also we will be following the same strategy, and I will be adding all these references for you please kindly go through some of the work of Mark Humayun that is very inspiring pieces of work which is happening across the globe.

Thank you.