Bioelectricity
Prof. Mainak Das
Department of Biological Sciences and Bioengineering
Indian Institute of Technology, Kanpur

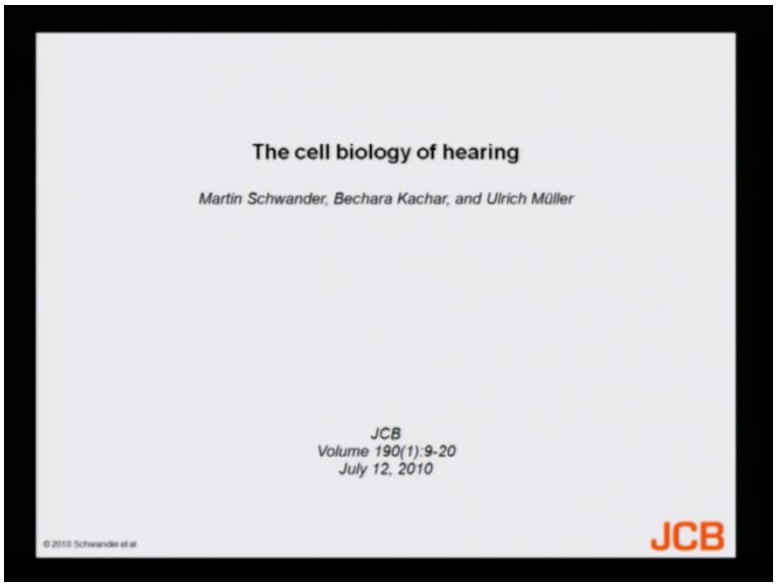
Lecture – 27

I have already introduced you to the basic structure of the ear, and the eyes. So, in this lecture, what I will try to do is that I will just go do a recap in the form like you know initially when I showed you this drew all the figures of the hear cells or the rods, and the cones. So, in this lecture, I will give you the actual picture like I have collected all this from different journals, and I will give you all the references, please go through them. And eventually we will be talking about how this actually this hearing prosthesis or the cochlear implants or the camera in front of the eyes are being fit.

(Refer Slide Time: 01:00)

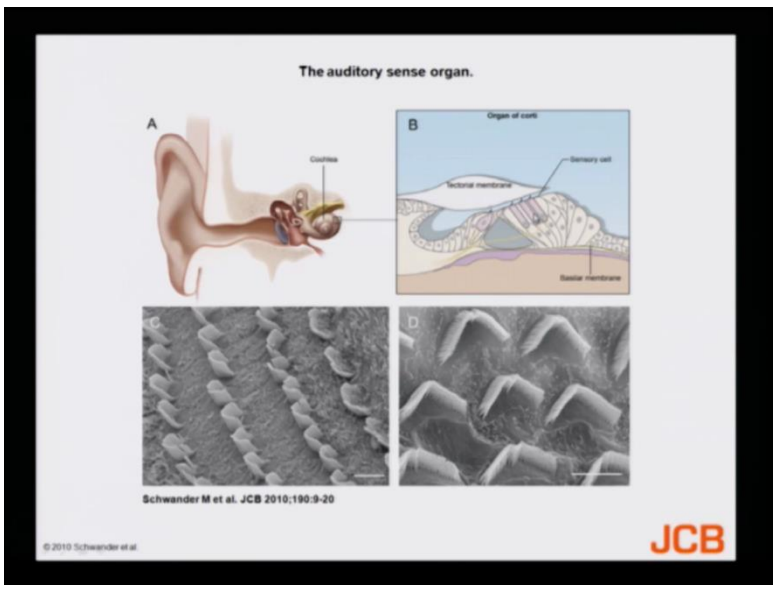
So to start with, so where there will be two classes which I will be taking consecutively. This will be the section of the implants man-machine interface, and the implants, and all those things. So, the title of this class is biology of hearing, and the cochlear implant; this is part one. There will be, then eventually we will move onto the vision, and then we will move on to the brain.

(Refer Slide Time: 01:25)



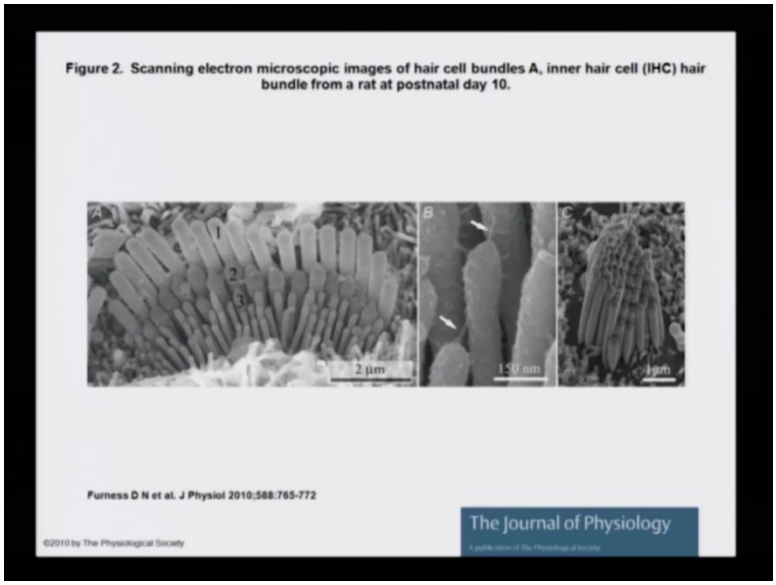
So, this is the reference I wish all of you to kind of consult, The cell biology of hearing by Martin Schwander, and Kachar, and Muller. This was published in journal cell biology in the Volume 190, part-1 that are the issue one from page 19 to 20, kindly go through this, this is available online. So, this will be a big help to understand to this following paper the cell biology of hearing by Martin Schwander, and Kachar, and Muller which is published in journal cell biology in the Volume 190, issue number one in the year 2010 will be a big aid to understand some of the structures, which I have already discussed with you in one of the classes. So, here I want you to go through it.

(Refer Slide Time: 02:18)



So, coming back to the structure of the auditory sense organ; so if you look at this structure, you will find that this is where what I have already showed you that the outer ear. You could see the outer ear out here,, and then you see the inner ear, so the middle ear, and all the three bones, and here is the inner ear. And I told you that there are hair cells which are present. So, these two micro grasp what you see out here underneath there are four pictures out in this picture; these two pictures - this one, and this one. You could see these are the arrangement of the hair cells, which is shown like this. So, they are in array, and they are actually sitting out here inside the cochlear what I have drawn.

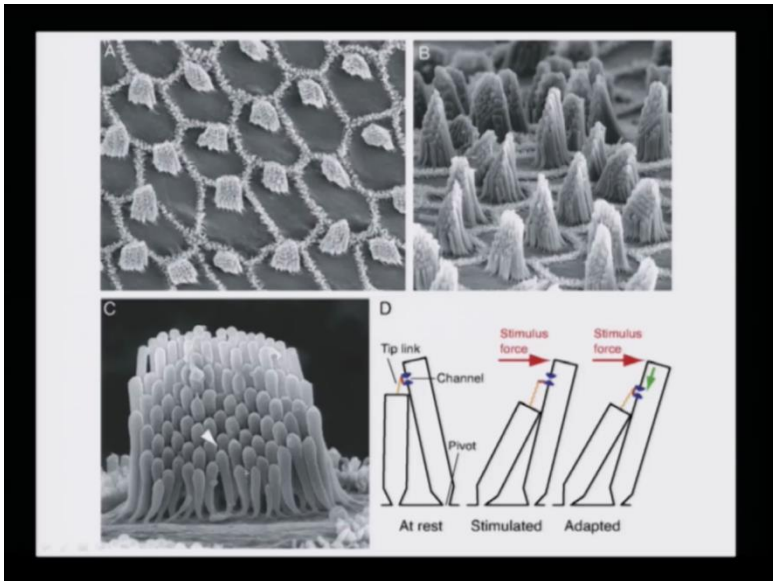
(Refer Slide Time: 03:08)



Now, if you look at this picture at the further resolution, they are if you kind of see the dimensions of the individual cells that will give you an idea how small these structures are which are sensing ear different frequencies. And this reference again this is another reference which I want you people to go through is by Furness D N Furness in journal physiology in the year 2010, which was in the issue 588. Please go through these things where you have a scanning electron microscopic image of hair cell bundles with the inner hair (IHC) cells from the part of the rat postnatal day 10. Please go through this, and that will kind of give you an idea at these are the nano machines of the body which helps us to decipher wide range of signal from sound, light, smell, taste, and so on, and so forth, touch likewise.

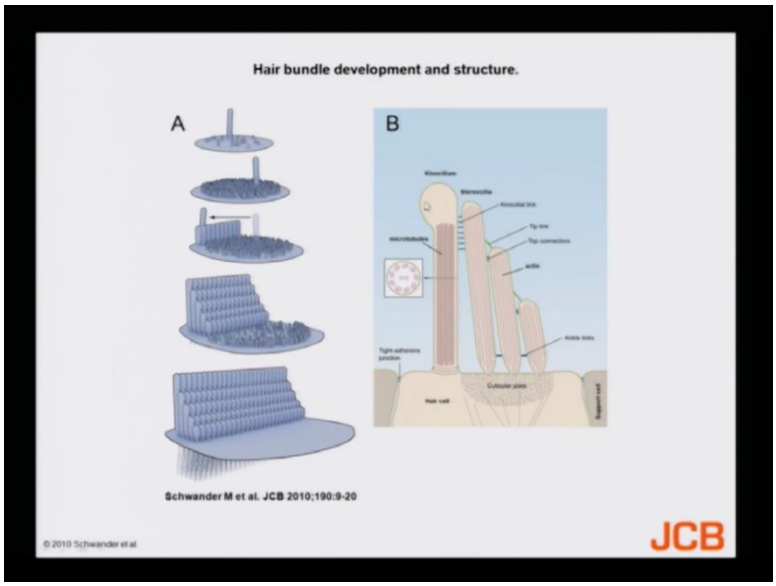
So, these are those specialized structure that is the reason why I am taking this special lecture where I wanted you guys to expose to those specialized structure which are translating the physical signal of nature into electrical signals. These are really some of the profound machines, which has evolved over the course of evolution of thousands, and thousands of years.

(Refer Slide Time: 04:45)



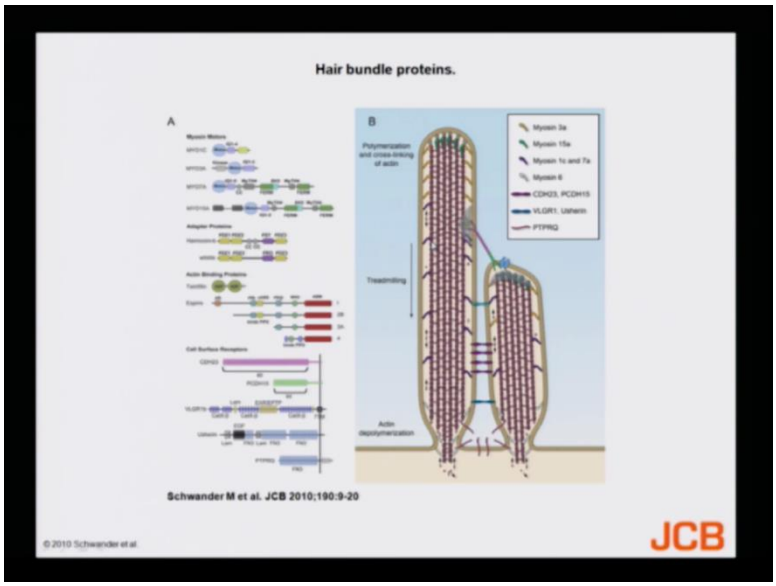
So, now look at this one, if it moves in one direction, then it will pull all of them in one direction, and I will show you that. So, if you look at it, they are arranged in a height as if like staircase, they are arranged in a staircase. So, if you look at the slide now with this, so look at this, they are almost arranged like a staircase model out here.

(Refer Slide Time: 05:05)



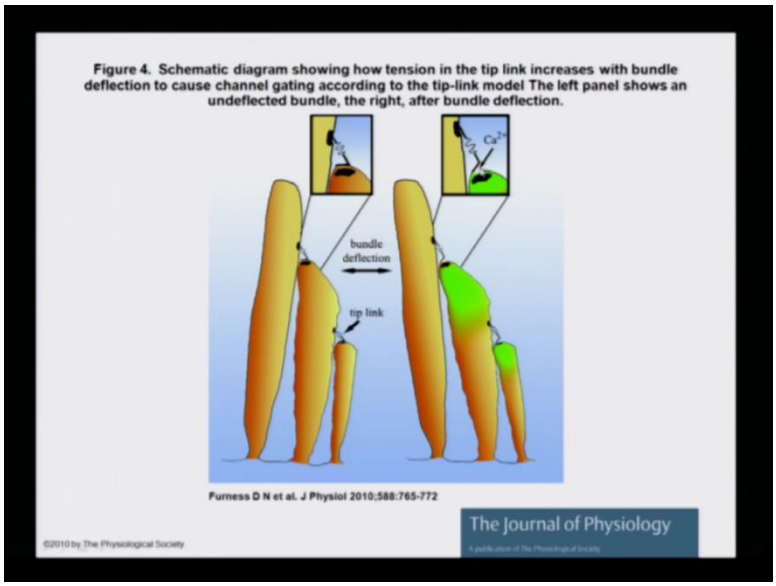
So they are all now if you look at this cartoon, what has been drawn out of those pictures. So, as if you are sitting in a photo session look at this picture; as if these cells are sitting in a photo session, and the cameraman is sitting here, it is almost like that. So, this bigger one which is called the kinocilia, and all these are the steriocilia, they are connected with a connector linking the tip link you could read that tip link out there. And the tip links, and here you have another set of links, and these are all eventually connected to these cells. So, if this kinocilia moves on the left, then the rest of all the connectors will move to the left. If the kinocilia move to the right, then everything will move to the right. Sepending on now if you look at this image, depending on which direction they are moving if the sides had what kind of current it is going to conduct, where I will be inhibitory or excitatory.

(Refer Slide Time: 06:02)



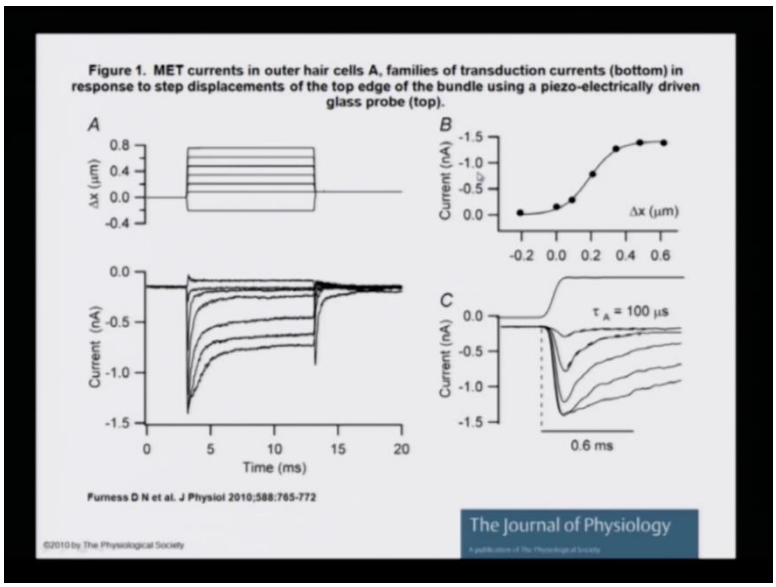
So, from here, so this is the molecular architecture. So, this is all consists of different kind of myosins, if you could see, and please I request you go through this reference. So, these myosins are basically they are also called the myosin motors, these are the molecular motors of the protein motors what is involved, and there are actins. So, those of you have please go through the basics of actin-myosin integration in order to you know results in a movement of the sliding movement. So, you are having this actins, and the myosins, the adoptive proteins, and ligand, and so forth. So, this is how the molecular architecture looks like. It is a very complex, and beautifully met structure if you look at it. So, you see this wonderful super coiled proteins which are forming the base or the framework, they are connected with each other, and they have a whole range of sub types.

(Refer Slide Time: 07:05)



This is the schematics, again for this schematics you have to refer to this journal that journal of physiology D N Furness article. So, if you look at this, this is where the channels are setting. So, if they pull in one direction, the gate opens, and the calcium enters. So, if you look at this this micrograph, and look at the look at this micrograph, so this is how the calcium entry is taking place. So, there is a pull, so it is almost like a hinge of the door, there is a pull on the left, it pulls on the left like this, and the channel opens.

(Refer Slide Time: 07:40)

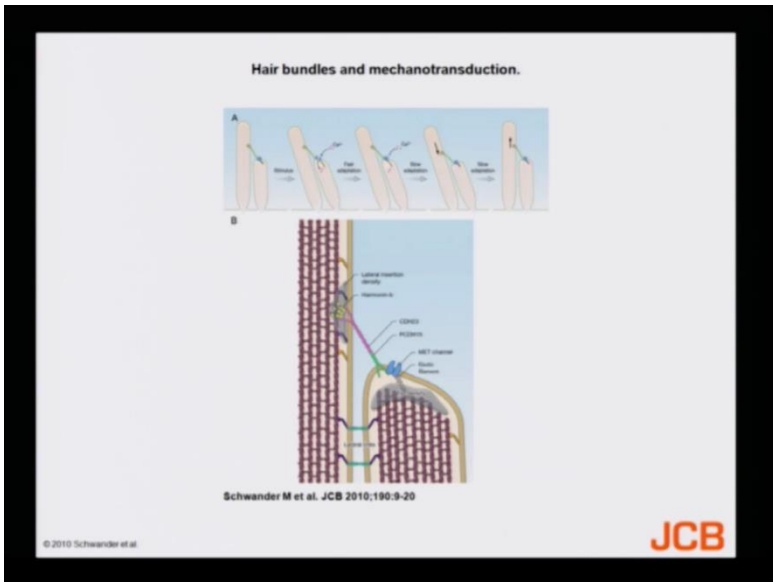


This is how this structure functions this is while I was drawing it, it was really tough for people to visualize exactly what is happening that is why I decided that I will give a special lecture, where I have all this figures. The schematics, which will help you to appreciate how this whole process is taking place, and followed by this if you come to. So, these are called MET, MET currents mechano-transduction in current basically.

So, if you come back to this one. So, this is where the current is being generated you see this green green patches. So, that is showing that these are calcium influx where the calcium current, and this is how you are recording those currents in terms of the nano amperes, and if you go back to the previous loads. You will see, and these are the different deflections which are taking place delta x is showing in the terms of micro meter where deflections which are taking place, and these are the currents which are generated with respect to the different kind different level of delta x.

So, this is the functions. So, x axis is showing you that delta x or which is the deflection, and on the other hand the y axis is plotting the current. So, here also you can see the different currents different a, and different time points. So, this is how all these nano ampere currents are being measured, and these are very small currents, but good enough to code a piece of information what is being processed by the hair cells.

(Refer Slide Time: 09:13)



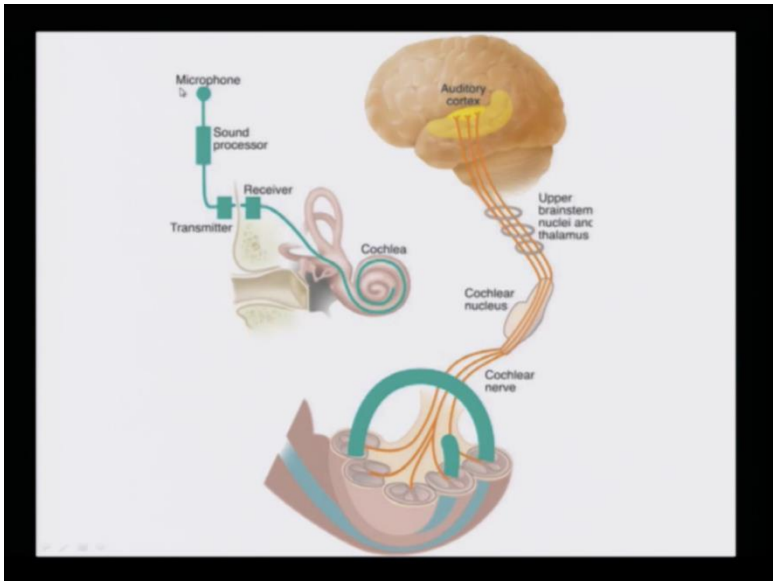
So, coming back. So, these are the hair bundles, and the mechano-transduction what is taking place. So, as I was telling you it is pretty much their repetition of it. So, there is an

stimulus they move in one direction. So, you see in this situation this is all moving towards the left one second one second one's they move towards the left the calcium channels pulled, and calcium channel open, and again there's an adaptation, and they come back to their original position.

So, if you follow this diagram very carefully, then the whole mechano-transduction will be very clear to you people, and this is how they are attached this is believed how they are attached there is a spring there is a tip density if you look at it, and this is that spring which is pulling this pink color spring attached to the partly green color spring plus green color this thing. So, this is what is pulling. So, if this one moves on the left. So, it automatically this will make the whole structure move to the left.

So, after giving you this overall outline, I will move onto the cochlear implant. So, how the cochlear implant really looks like as a matter of fact at once the cochlear implant as I have mentioned earlier it was the first one which was the success story of mankind in terms of neural engineering or neural prosthesis.

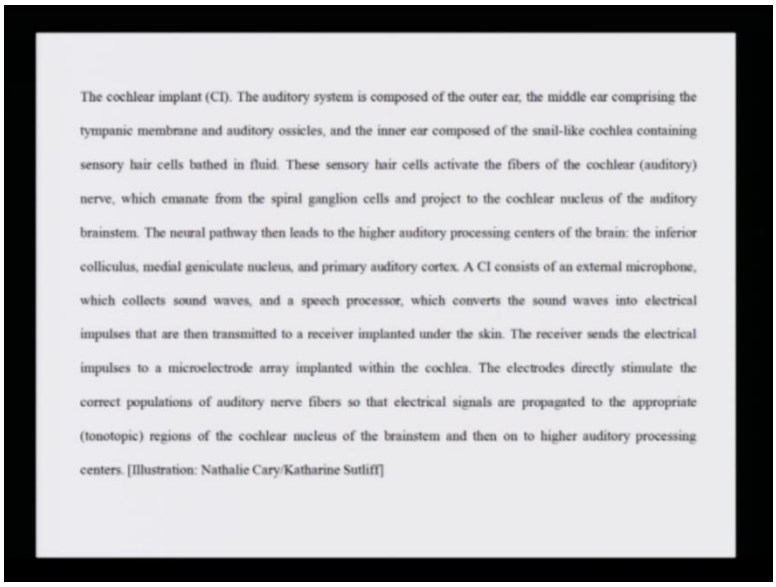
(Refer Slide Time: 10:29)



So, this is how the cochlear implant works you have a microphone there is a sound processor there is a transmitter, and there is a receiver, and from here this signal is fed into the cochlear in the cochlear there are these are these are connected this whole thing is connected to the cochlear nerves, and this cochlear nerves carries the signal to the auditory cortex.

So, essentially what you are doing you are ruling out say for example, if these cells of yours these hair cells of yours are all damaged. So, what you do you fed the direct information the sound sound information directly to the cochlear nerves, and the cochlear nerves, and take the whole information through the cochlear nucleus to the auditory cortex of the brain, and where it is being processed. So, you are bypassing the whole cochlear, and this is what I wanted to highlight in one of the previous lecture.

(Refer Slide Time: 11:21)



So, this is how it looks like the cochlear implant the auditory system is composed of outer ear this is the summary of it, and the middle ear, and the comprising the tympanic membrane, and auditory ossicle ossicles, and the inner ear composed of the snail like cochlea containing sensory hair cells bathed in a fluid. So, this was what we discussed.

These sensory hair cells activate the fiber of the cochlear nerves which emanate from the spinal ganglion cells, and project to the cochlear nucleus of the auditory brainstem the neural pathway that leads to the higher auditory processing center of the brain the inferior colliculus medial geniculate nucleus, and the primary auditory cortex

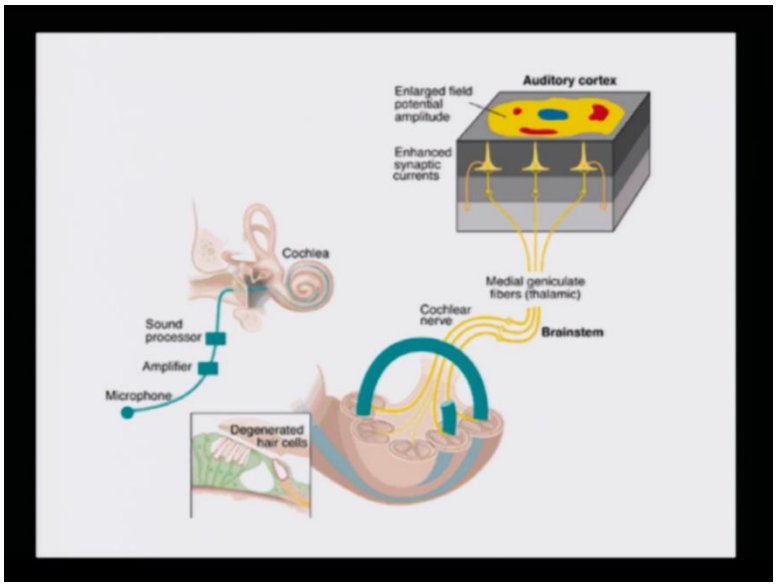
So, if you go through this, then this will give you an idea about how these signals are being processed, and if you read through here. So, what is happening is that a c I consists of an the cochlear implant c I stands for the cochlear implant consists of an external microphone which collects the sound waves. So, look at it which collects the sound waves and. So, this is what is collecting the sound waves, and a speech processor which

converts the sound waves into electrical impulse. So, here is the speech processor sound processor.

Then next one which converts the sound waves into electrical impulse, and then transmitted to a receiver implanted under the skin here is the receiver which is underneath the skin. So, after the receiver implant the receiver sends the electrical impulse to the micro electrode array implanted within the cochlear. So, here within the cochlear the micro electrode array which are. So, all these m e what we have studied from the beginning. So, this is where they are finding their applications why they m e has to studied in order to understand how this whole cell electrode interface is. So, very important criteria before all these kind of implants will be successful.

Now, coming back to the slide. So, so this is where micro electrode array implanted within the cochlea the electrodes directly stimulate the correct population of auditory nerve. So, that electrical signals are propagated to the appropriate tonotopic regions of the cochlear nucleus of the brainstem, and then on to the higher auditory cortex. So, from here this is going to this specific part, and from here it is moving to the auditory cortex. So, this is the overall summary of the cochlear implant what I wanted show you people ok

(Refer Slide Time: 13:55)



From here this is another cartoon which is showing the same thing a micro microphone amplifier the sound processor the sound signal arc where they need the electrical signal,

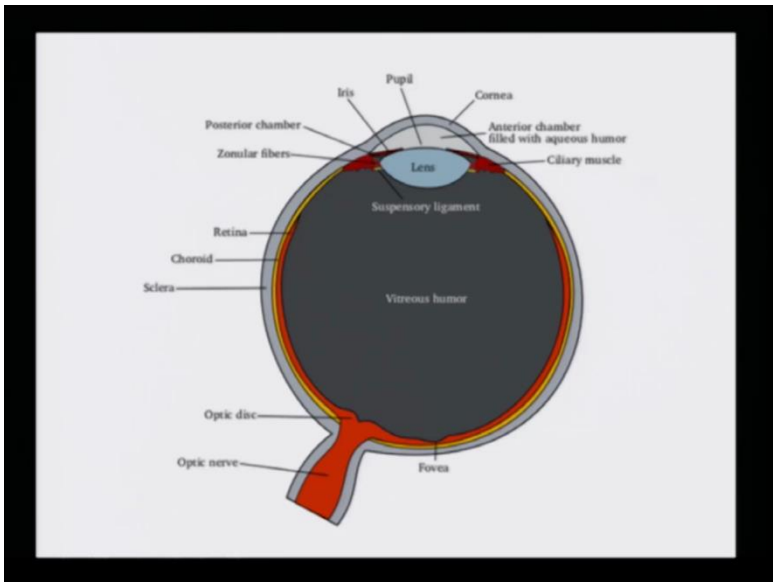
and then through the cochlear. So, this is where the cochlear nerves to the medial geniculate fiber or the thalamic fiber thalamic region of the brainstem from here it is moving to the enlarged field potential amplitude in the auditory cortex, and enhanced synaptic currents

So, this is the situation when you are hair cells or what I showed you those wonderful mechano sensing cells are getting degenerated. And there are no other option, but to resort to neural engineering techniques in order to restore your vision these are the extreme situation, but this is one of the big success story of mankind era of last hundred hundred fifty years of man's the quest to interface machine with its body parts. So, from here, the stimulating hearing auditory neural pathway from the cochlea to the inner ear to the auditory cortex of the brain. So, hearing can be restored in the congenitally deaf kittens this is this is where it was done with an electrode that stimulates the auditory nerves in response to environmental sound relayed via a microphone, and sound processor it is pretty much the same thing what we just went through.

So, electrical discharges of the neurons in the auditory pathway results in a strengthening of intra cortical synapses that was the synapse strengthening. If you look at it enhance synaptic currents, this is what it is meant results in a strengthening of the intra cortical synapses. And an enhancement of the neuronal response to sound the area of the auditory cortex which over which electrically evoked field potential can be registered is enlarged in cats with early implant red, and yellow compared to deaf cats which is in blue. So, this is how it looks like. So, here is the blue showing you the deaf cat the red, and yellow are showing in the implanted cat.

So, this is what? I wish you people go through, but carefully from here I move on to the next one which is the eye or the retinal visual or retinal prosthesis. So, this is I have already discussed with you people the structure of the eye I will give you an part of the idea about how you place the camera in front of the eye. So, here I have decided to show you some of the real time pictures which will help you to appreciate the subject much better as compared to you just mean drawing out here on the on the screen. So, just the same way as we have walked through with the hearing or the ear prosthesis, I will walk you through with some wonderful pictures out here that will help you to understand it better.

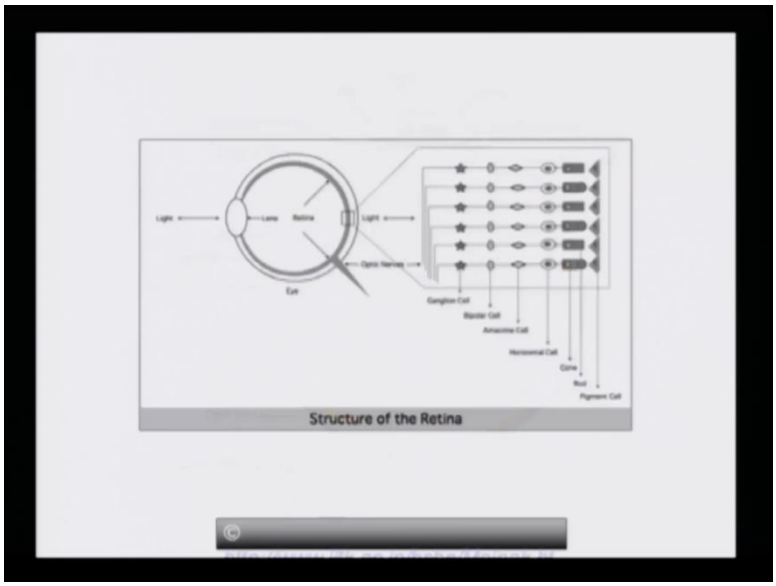
(Refer Slide Time: 16:50)



So, this is the overall this I have already discussed with you people. So, the structure of the eye the cornea the lens, and here you have the retina, and here you have vitreous humor. So, the light travels all the way through, and I have already told you that the there could be either a corneal blindness where basically say that somebody has donated a eye basically it is the cornea which is being taken out from an deceased individual, and implanted with the another individual, and the cochlear has very little blood supply. So, the compatibility of the tissue my compatibility or in human reaction is very least, then comes the blindness of the lens which is essentially the cataract.

So, you replace this lens with a synthetic lens, and now comes the retina, where if there is a damage in the retina, then we need something deliver it more than cornea or lens implants what is that that is what we can discuss.

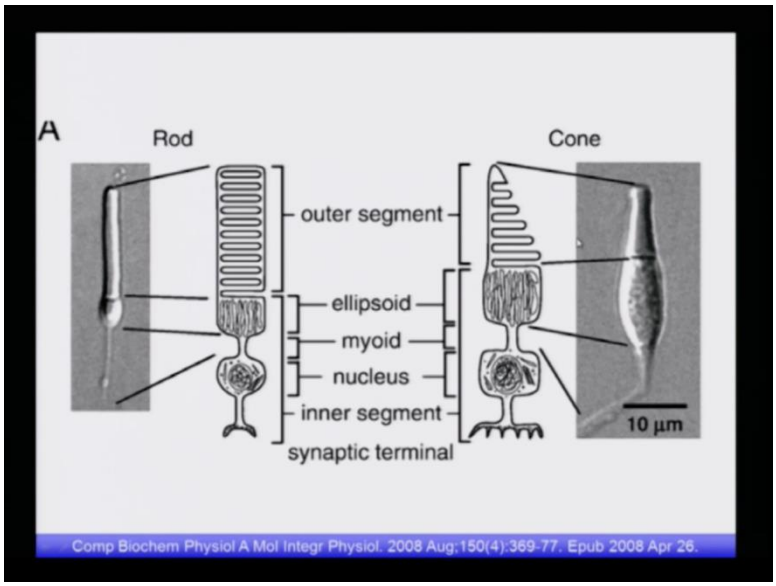
(Refer Slide Time: 17:55)



So, this is the overall structure of the layout the pigment epithelial cell the rods, and the cones layer, then any of the horizontal cell the amocrine cells the bipolar cells, and the ganglionic cells. So, this is the complete layer which is dealing with the whole eye prosthesis. So, the whole structure of the eye, and this is you know much more kind of you know blown up picture where you have the pigment epithelial cell sitting at the base on top of that. You have these violet, and black shaped rods, and the cones, and then you have the horizontal cells, then you have the bipolar cells here. You have the amocrine cells out here go through it, and here you have the retinal ganglion cells, which are carrying the message to the brain. And this is how the light falls light falls from this side actually as a matter of fact all you remember light is falling.

So, essentially here the first layer what you see this red could divided the first layer is the retinal ganglion cell layer, but since neither of this layer this layer or this layer l six l five l four l three has any kind of photo receptors or any kind of light sensing proteins in them. So, the light is only sensed by the photo receptor layer, and beyond that there is an optic layer of the pigment epithelial cell which is essentially the absolute the back of the eyes, these two lines this front is retinal ganglionic retinal ganglion cell. And the bottom will be the pigment epithelial cell which is basically helps in having a cushioned effect.

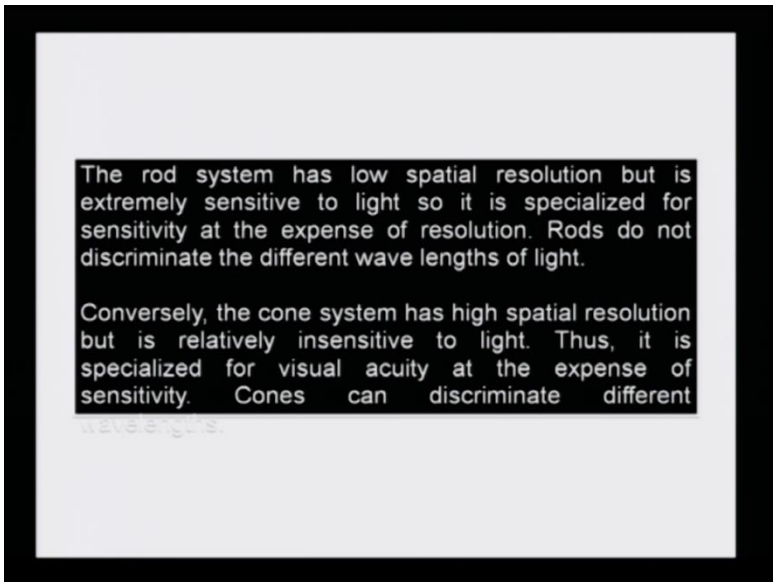
(Refer Slide Time: 19:52)



So, this is how a physically a rod, and a cone looks like. So, these are from the fish retina, and the reference is given here please go through this if anyone of you is interested to really to see how they look like, and how they are being isolated from the fish retina. So, it is a paper in comparative biochemistry on physiology part a in molecular integrated physiology in a eighty thousand eight in the month of august this is volume one fifty eight, and issue number four. So, these are the rod cells physically that is how they look like this is where the outer segment of the rod cells this is the inner part inner segment of the rod cells this is where all the light sensitive proteins rhodopsins are sitting, and this is from where the impulse is being sent. So, all the dark current which are measured it is measured here.

Similarly, here is the cone. So, this is the outer segment where the specific rhodopsins are sensing r g b red green, and blue color they are sitting here, and then out here from here this signal moves, and look at the dimension they are in even their thickness is less than ten ten micron. So, this is the kind of dimensions we are talking about, and you know in the lens there'll be hardly thirty microns.

(Refer Slide Time: 21:09)



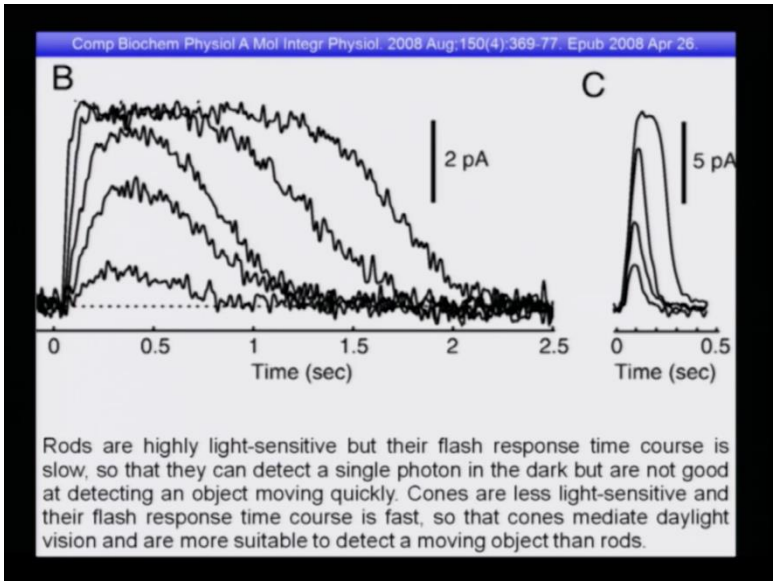
So, the rod system has low spatial resolution, but is extremely sensitive to light. So, it is specialized for sensitivity, and the expense of resolution rods do not discriminate different wave lengths of light conversely the cone system has very high resolution, but is relatively insensitive to light that thus it is a specialized for visual acuity at the expense of sensitivity cones can discriminate different wavelengths always remember this.

Now, this is even a much more well kind of you know almost giving you a three dimensional look about the rods, and the cones. And this is the reference from progress in retinal eye research published in two thousand nine in the month of July in the volume twenty eight, and issue number four. Please go through it I am just little these pictures the whole reason to show you these pictures that that will give a overall a idea of a bit of an appreciation about how wonderfully. All these different kind of structures have evolved over a period of thousands, and thousands, and thousands years of a longed on evolutionary you know evolutionary time scale.

So, coming back. So, this is how the rods, and cones are distributed. So, distribution of photoreceptor in the eye. So, please again you should go through this progress in retinal eye research in the yaer two thousand nine. So, distribution of the photoreceptor in the eye overall rods outnumber the cones by a ratio of twenty is to one or greater in the retina; however, in the fovea the cone density is the highest, and is correlated with visual

acuity. So, this is the fovea region. So, these are the those are the different areas of the retina. So, fovea is rich in your cones.

(Refer Slide Time: 23:08)



So, now moving on to the different kind of currents, which are being measured. So, rods are highly sensitive. So, you can this is where I am the comparative biochemistry, and physiology are of the integrated molecular physiology in the year two thousand eight please go through this. So, rods are highly sensitive light sensitive, but their flash response time course is slow. So, that they can detect a single photon in the dark, but are not good at detecting an object moving quickly cones are less sensitive less light sensitive, and their flash response time course is fast.

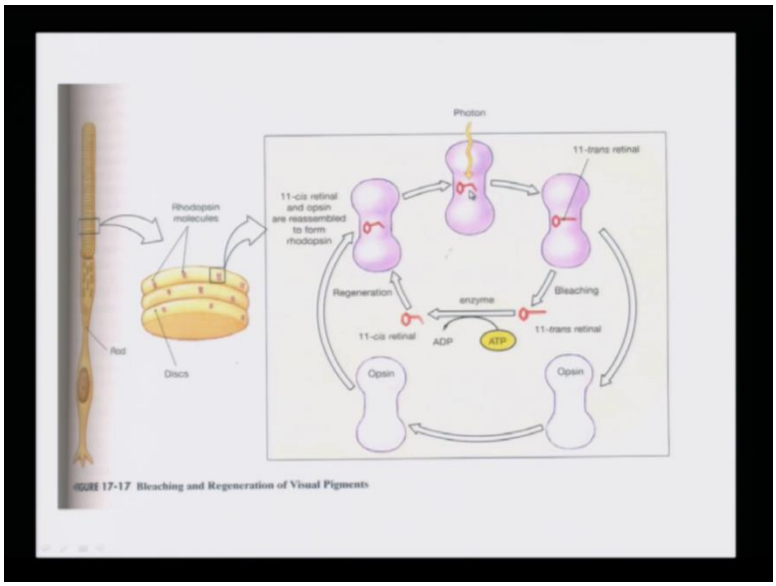
So, that cones mediate daylight vision, and are more suitable to detect a moving object than rods this is very critical thing which I wish to highlight, and this is what is called the flash response time. So, the flash response time of the rod cells. So, something moves like this the cone can detect it that something like this a cone can figure that out rods would not be able to, because they need bit of a time to adjust, and understand a flash of light. So, this is a very very interesting for you people to really look at carefully that. So, if you look at this slide again a little bit carefully you see the time window what is the most important here look at the time window the response time how much time it takes each one of them to respond.

So, after this, so this is about the cones all the different cones the blue cones the green cones, and the red cones, and the different wavelengths they could perceive this is how an there are several species which are different other wavelengths which they can perceive the fishes could perceive another color. So, this is how one's they are isolated in the cell culture this is how they look like how these are the rods you could see these rods a rod like, and their get more purified area of the rod cells, and here are the cone cells this is how they look like in a culture dish. So, that is why I wish you people should have a very clear idea, and how they kind of you know look in the culture dish, and how they grow from here.

So, photoreceptor hyperpolarize on light stimulation was a great surprise to the neurobiologists, because it was an exceptional case that a neuron shows a hyperpolarization not a depolarization on stimulation well this you will read just note it down hyperpolarization not a depolarization on stimulation. So, this is where I was trying to show you the dark currents you remember I was telling you about the dark currents. So, this is the outer membrane, and within the outer membrane this is how all those different proteins which are involved in this phosphodiesterase, and cyclic g m p, and all those things. So, this is the disk membrane, and this is the outer membrane this is how they are arranged out here. So, and this is the picture of how the dark current is measured. So, you have a electrode in the presence of light in the presence of light what you see is the minus seventy milli volt out here, and where there is darkness you see minus forty milli volt.

So, essentially, it was that whole concept of dark current what I have been introduced to you, and what exactly is happening. So, when the light is binding to this membrane. So, what it does. So, this is the one second, let me.

(Refer Slide Time: 26:43)

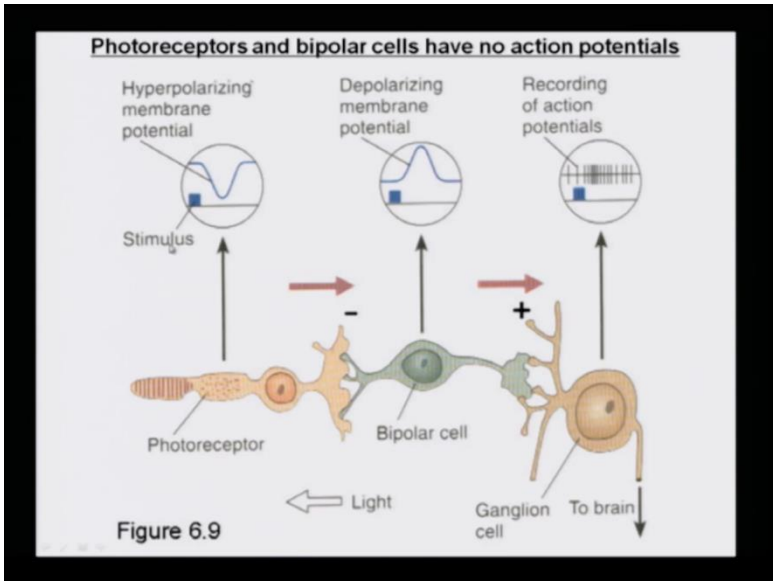


So, this what is happening, and light is binding. So, this eleven cis retinal which is present there along with opsin which is forming the complete rhodopsin moity split up into. So, the first thing happen when the photon goes these eleven cis retinal become eleven trans retinal, and then eleven trans retinal detaches from the opsin. So, this is a detachment which is also called bleaching. So, then what happens this eleven trans retinal through an enzymatic process transform maybe a cis retinal, but in the mean time the opsin does certain few other things and that will be coming what opsin is doing in this slide opsin activates a protein called transducin, and the transducin activates something called phosphodiesterase, and this phosphodiesterase remove the cyclic g m p gating of the sodium channel which ensures the entry of the. So, if you look at the slide very carefully you will see a cyclic g m p declines, and the gated sodium channels closes. So, this is the three is very important for you to look at this is that step three which is very very important. So, this is where phosphodiesterase is binding, and removing this gate. So, if you look at this picture it is a cyclic g m p which is holding this sodium channel up here where I am circling.

So, one's the light falls what happens is cyclic g m p out here is being removed from that binding side by phosphodiesterase, and the phosphodiesterase removes it thus this channel closes, and once this channel closes the current flows through the through the sodium channel stops, and this is how the signal transduction within a eye takes place.

Now, this is a much more complex picture what is happening light is falling rhodopsin is photo activated from this you know activated followed by phosphodiesterase activation hydrolysis of cyclic g m p cyclic g m p decrease in the cytozol, and the sodium channel close, and the signal moves. So, this is what is the light cascade the first is this is the basic overall structure of the rod cells followed by a photo excitation, what is taking place where eleven cis retinal is transformed into eleven trans retinal. And this leads to the bleaching process, and then comes the what is happening in the rhodopsin moity all the arrangement the rearrangement within it cyclic g m p has transmitter of vision.

(Refer Slide Time: 29:17)



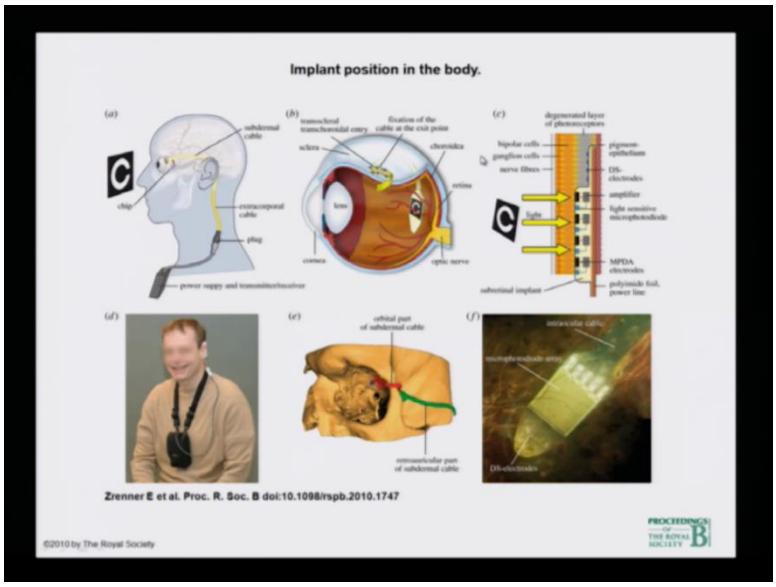
So, this is another cartoon showing the photoreceptor. So, so this is something very interesting which I have not highlighted previously the photoreceptor bipolar cells had no action potential they do not really should action potential. It is only the current which is generated which moves onto the next one hyperpolarizing membrane potential generates that current which moves on to depolarize the bipolar cells, and then followed by the ganglion cell via the action potentials are being generated.

So, this is how the signals are moving if you follow this very carefully. So, please remember photoreceptor, and bipolar cells have no action potentials hyperpolarizing membrane potential, then reading to the depolarization of the bipolar cells, and then at the ganglionic cell layer is all the process is taking place. So, essentially what we meant

by that if you look at this picture go back. So, all the action potentials are generated in this layer sorry in this layer at the l six layer retinal ganglionic epithelial cell.

And coming back to the and. So, this is another picture where we are showing you the phosphodiesterase is sitting which is converting the cyclic g m p into g m p, and there by closing the sodium channels. And if you look through it this is how the phosphodiesterase is sitting quiet it is unable to act till there is an activation from the transducin protein, and this is how where arranged along the membrane. So, these are all g protein coupled systems, and this is the summary of it the bleaching, and the regeneration of the visual pigment where it is again a getting regenerated. And again the eleven cis retinal which is through an enzymatic process from trans becomes cis, and the cis again gets incorporated into the opsin moity, and again gets back to the membrane.

(Refer Slide Time: 31:14)



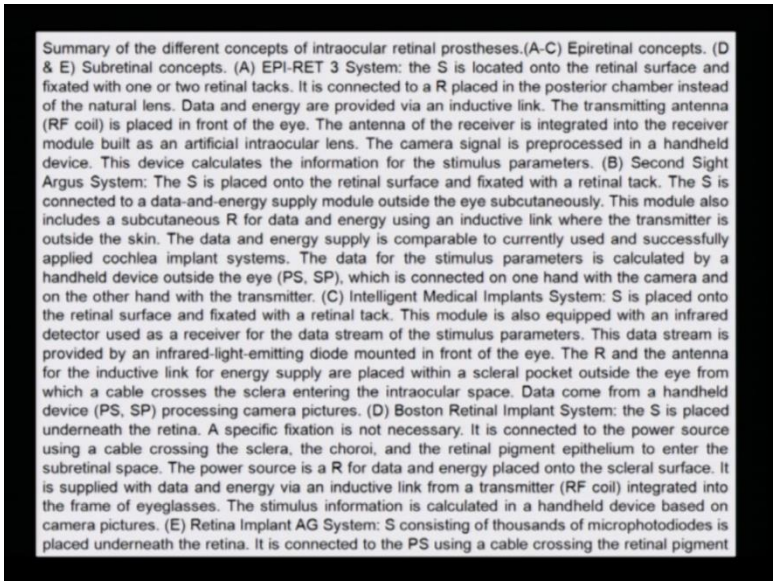
So, now coming back to the implant position in the body. So, this I have already discussed, and now I want you to show you the exact picture. So, this where you can put an implant either you can put something out here in front of the eye, and this is how it looks like. So, this is a cornea this is the lens, and this is where you can put you can put an implant here either you put something in the front of the eye a camera or you could have a implant here where you see this c.

So, this here is the retina here is the chordial, and the fixation of the cable at the exact point, then you have the trans sclera trans chordial entry, and the sclera you can do it on

the sclera. So, this is how to work. So, this is the implant actual implant which is sitting out here this where the light is falling the light, then separate micro photo diodes, then they have the amplifiers which are sitting there you have the d s electrodes, and from here there's signal is being is sent all the way to the brain. So, please go through this reference by zrenner e you could see this, then the proceedings of the royal society at b which was published in the year twenty twenty thousand twenty ten please please go through please mark this reference, and go through it.

Now, this is how most of those implants look like these are the complete. So, these are the basically the light sensitive micro photo diodes which are sitting there, and this is where the image plate is all, and all the electrodes are connected underneath. So, you have the see there the photo diode electrodes, and the contact holes this is how they look like physically. Please please go through this reference that will give you an idea about how they look like, and these are the different spots where you can really make all the connections, and there is a reference which is given expert rev in ophthalmology published in the year two thousand nine. So, p s is the power supply r is the receiver s is the stimulator, and s p is the signal processor. So, this is how these different cameras are being put, and different implants are being placed. So, there are different regions where they are being placed.

(Refer Slide Time: 33:31)



So, and if you look at the summary of it, please go through this summary of the different concept of intraocular retinal prostheses, and this is either it could be a epiretinal concept or it could be a subretinal concept. So, these are those detail which those who are interested you need to understand the different system. So, there is something called a Boston retinal implant system please go through it, and there you have intelligent medical implant system, and you have this second sight argus system. So, these are the different people who have over the years have kind of you know developed these different prostheses regime, and they are the ones who are come up with different models in order to you know for people to understand that how these different prostheses takes place.

So, what I wanted you people kind of a take home message from this though I mean this is very, very tricky, and a challenging area in terms of the fact that I am repeatedly telling in this course. Whenever I am talking about animal electricity that how successfully we can implant an electrode without really disturbing the cellular assembly where we are doing the implant there will be of course, some degree of disturbances. But how we could minimize the immune reaction, how we could ensure over the period of longer period of time the electrode fidelity will be maintained. These are some very very challenging problems which mankind is going to face for years, and centuries to come, because this is long run thing. This is not something like you know it is possible it is how much we can fine tune how far we could be innovative enough to take to that level where this becomes a routine thing.

So, it is a journey, and please go through these references, because after this once I have done these two prostheses I will be moving on to about the man machine interface where people have tried you know really to implant a trained monkeys, I will be coming to that after this. So, I am closing on this one. So, please go through these references, and try to philosophy it in your system, because it is something which you have to think a lot this is not something, because we know what could be done, but what are the innovative ways.

Thanks a lot.