Introductory Neuroscience and Neuro Instrumentation:
Cellular Structure of the Central Nervous System
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Lecture 1

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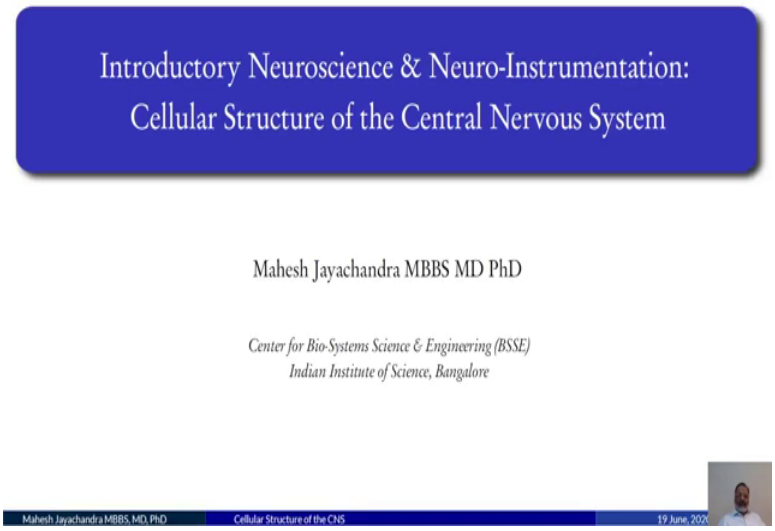

Hello, and welcome to an overview of the cellular anatomy of the nervous system.

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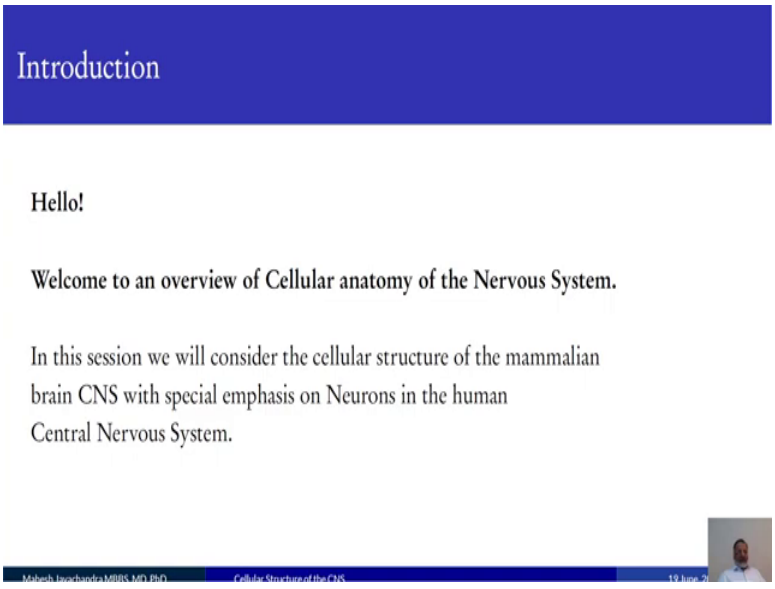

In this session we will consider the cellular structure of the mammalian brain of the central nervous system with special emphasis on Neurons in the human central nervous system.

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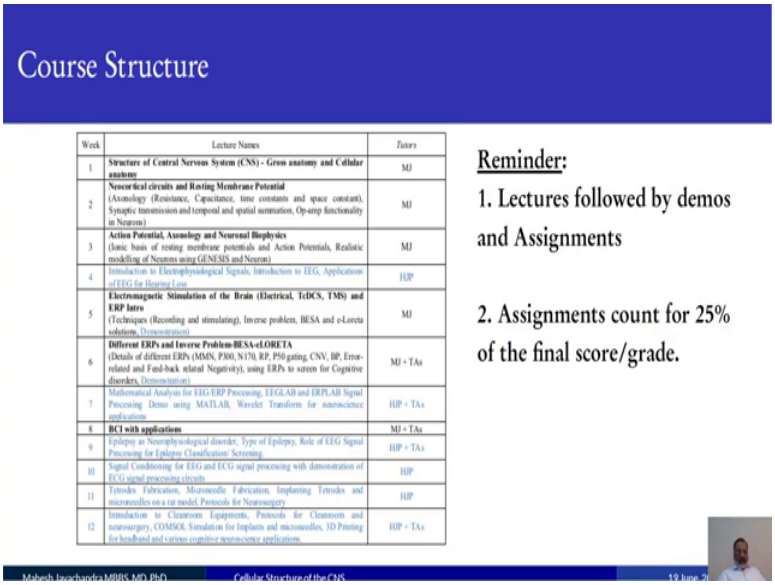

The course is structured as follows. Half of it is neuroscience, neurophysiology and the other half is neuro-instrumentation. The neuroscience part of it will be conducted by me and the neuro-instrumentation part will be conducted by Professor Hardik Jeetendra Pandya, the Department of Electronic Systems Engineering at Indian Institute of Science, Bangalore.

The lectures will be followed by some demos and assignments. These are weekly assignments, and they count for 25% of the final score or grade. Remaining 75% is the final exam, and you get two credits if you pass. You are free to audit the course and just sitting through without paying anything.

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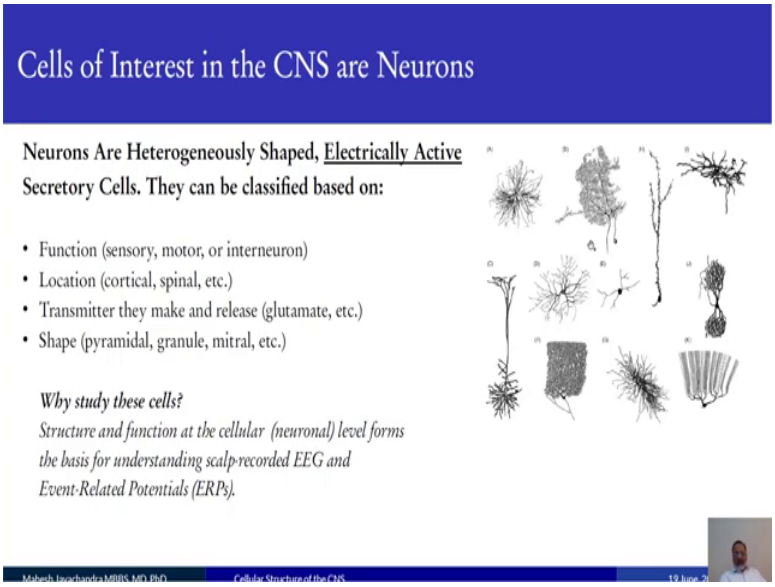

Okay, so the main cells of interest in the central nervous system are neurons. So why study these cells at all? One of the foresay of this course is to give you an exposure to event-related potentials. These are scalp related potentials and recorded from the scalp like EEG.

Now, to appreciate the origin of the event-related potential, it is important to know or have some idea of the structure and function at the cellular or neuron level. This helps us to understand the potentials on the scalp much better.

Okay, so having said that, so neurons are heterogeneous, they come in many shapes, many sizes and different structures, but the main thing is that they are electrically active, and they have membrane potential between the extracellular fluid and the interstitial fluid and so, they have a membrane potential of anywhere from -70mV to -90 mV. And this is perturbed momentarily by spikes or action potentials. And all of them display this property neurons.

So they can be classified on basis of their function. Whether they are sensory, whether they are used in perception of feeling of touch of temperature, et cetera or there could be motor where they use for movement, it could be involuntary movement or it could be voluntary movement like moving your hands, involuntary like the moving of the diapher.

They could be classified on basis of their location, whether is on the cortex, which is the brain proper, there in the spinal cord or in the peripheral nervous system. They can further be classified by the neurotransmitter they make all of them make neurotransmitters. This is the way they chemically conduct, chemical conduction occurs between neurons.

These neurotransmitters can be glutamate or cholinergic or various other possibilities and finally, they can be classified on basis of their shape. They could be pyramidal cells like shape like pyramids, or granule cells just like small little granules, so on and so forth. So, on the right I hope you can see this, there are pictures of different neurons, essentially they are pyramidal neurons, and we will talk about them in more detail later, but straightaway, what strikes one is the varied structures they come in. And it has something to do with their function.

I mean, it would not stay in evolution, it would not be conserved unless there is function. And we will explore some of the possibilities in the next slides and lectures.

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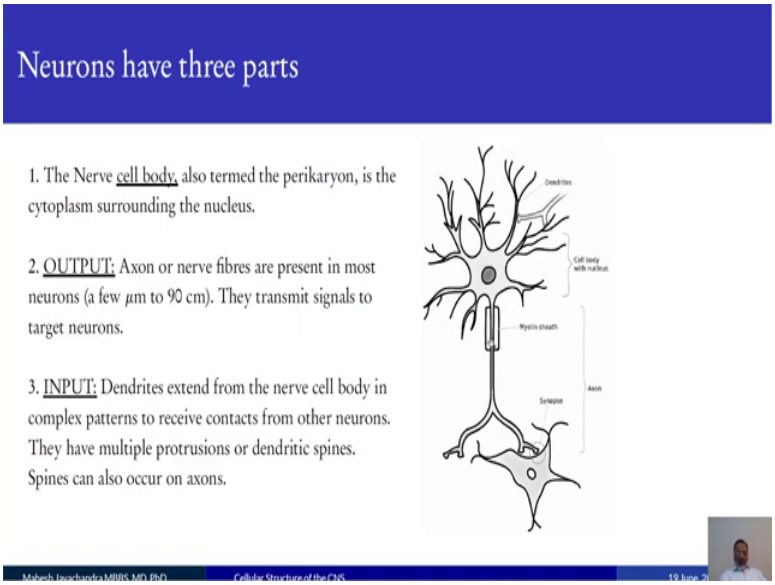

Okay. So coming to a neuron, a canonical neuron. Now, the neuron is basically what you studied in high school. In fact, what you need for this course is if you have 12th standard high school from India, it will do just fine. So you just get more detail, but the fundamentals remain the same. So the neuron that consists of a cell body with a nucleus, that is also called the soma of perikaryon and so cytoplasm surrounding the nucleus.

So it has inputs and outputs. So the outputs are the nerve fibers, which come out from the neuron. They are present in most neurons, and there can be a few microns that is one millionth per meter or they can be as long as 90 centimeters from the motor cortex to the spinal cord and they transmit signals what I told you about this membrane fluctuations and stuff like that they transmit that stuff to other target neurons.

And the inputs of these neurons are like the branches of a tree they are called dendrites. And they get inputs from connections from other neurons. And there is a microscopic structure over here where they have spines, they are called dendritic spines, and that is where contact is made from other neurons. We will get into more detail subsequently.

One thing to note is the connection between one neuron to another it is not continuous, generally. So there is a distinct space over there, and it is called, the whole connection area is called a synapse. This long structure over here is the axon, which transmits the impulses, which result from processing in the neuron by all the impulses coming from the dendrites, the output is over here.

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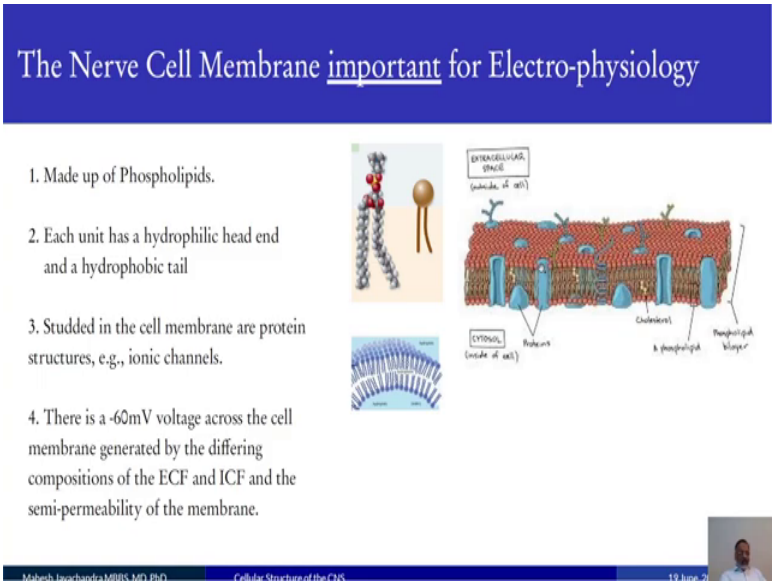

Right. Now, we will get into some cellular details about the axon and the sub-cellular structures in the axon. But the most important structure in the neuron is the cell membrane. As I mentioned briefly earlier, there is an extra cellular space that is basically sea water, really, lot of sodium, lot of chloride and then there is an intercellular space of cytosol. And you have this membrane. This is a piece of the cell membrane of a cell, and you have this membrane and between these two sides, there is this voltage.

The structure of this, this is made up of phospholipid. So typically you have hydrophilic head and a hydrophobic tail. Now so this is a hydrophilic head, so the head is outside so is in contact with water all the lipids, the hydrophobic tail, it is basically lipids, fats that is in between and then you have another hydrophilic head over here.

Now floating, and it is a very mobile moving kind of a structure. It is not rigid. So floating in the lipid membrane, are ionic channels. It is best to visualize them like icebergs that are floating in the arctic sea. And these also are not fixed. They move around. And these are studded in the cell membrane, and they allow ions to transfer from outside to inside and from inside to outside to maintain the cellular concentrations of the cytosol that is intercellular fluid and income in relationship to the extracellular fluid.

So as I mentioned, that is -60 millivolt potential across the cell membrane, and this is generated by the different compositions of the intracellular and extracellular fluid. And the fluid, the membrane is also permeable or semi-permeable, it is semi-permeable to certain ions. We shall see, get into more details subsequently.

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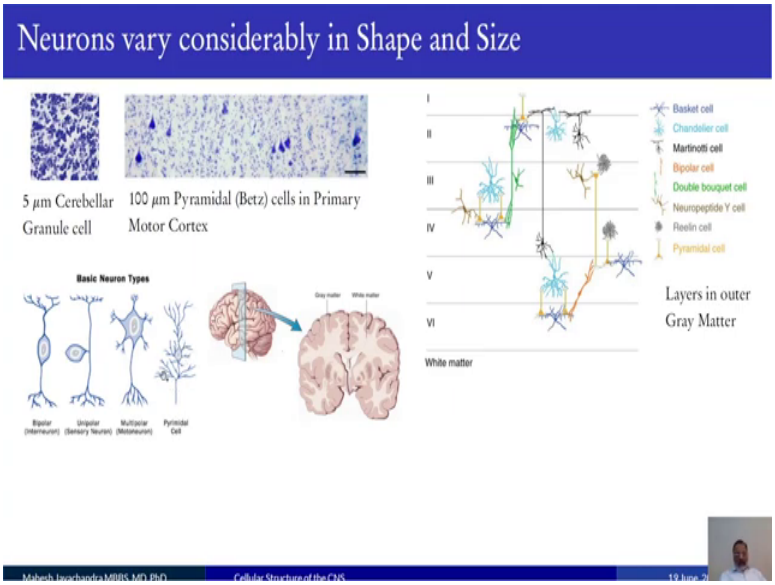

Okay. Now coming back to the neuron the shape and the size. Now, they vary vastly depending on the anatomical position, they are in the brain. For example, in the cerebellum, and we will get into details in the next course of the microscopic anatomy of the brain.

You have cells, neurons, which are as small as 5 μm or 5 microns, they are called granule cells. And then there is another place in the brain called the primary motor area, the primary motor cortex. And there you have some of the biggest largest cells, pyramidal cells in the brain that easily reach 100 μm and they could be 120 μm very, very big. These scales are different. So you have a wide variety size.

And you also have wide varieties and shapes. If you look on the left, on the right over here, basically in the brain just to give you a quick overview, preview of what I am going to talk of the macroscopic brain. This is the human brain. And if you take a section like this and you look at it, there is a central white area it is called the white matter, and that is where all the nerve fibers.

And it is surrounded by a gray area, the gray matter, and this is where the neurons and all the different brain cells pretty much are located. Now this area, and I keep coming to this repeatedly, the gray matter the outer gray matter, it is divided into six layers 1, 2, 3, 4, 5, 6 and it has a distinct structure in different parts of the brain. Like the sensory areas of a particular structure, the motor areas have another structure, so on and so forth.

And you see the varieties of different shapes of the neurons and the different dendrites over here. And they are named very evocatively after their shape, like we have basket cells and you have chandelier cells. And then you have bipolar cells with just two axons coming.

So the cells also, the neuron types can generally be divided into a bipolar neuron where it has two distinct processes coming out at either ends or it could be unipolar which then divides or it could be multipolar where you have a single axon giving multiple branches, or it could be a pyramidal cell, which has a distinct apical tuft and a basal tuft and we will get into that.

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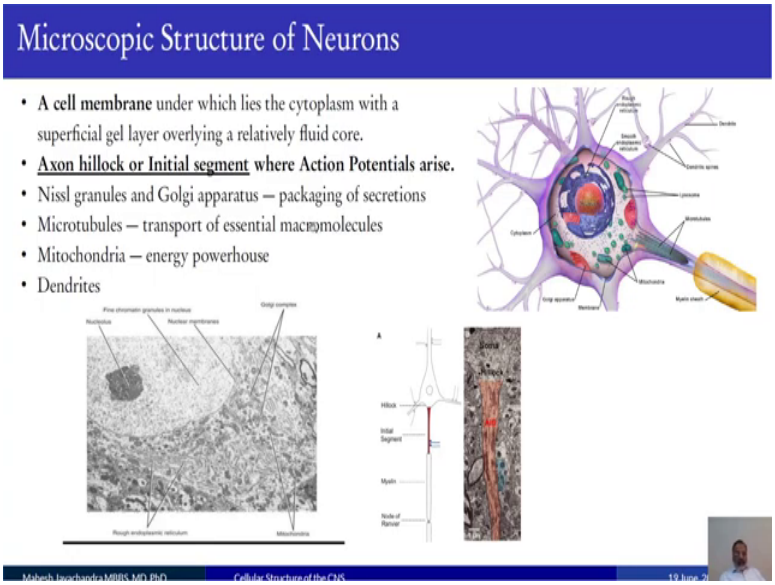

Now moving on to the microscopic structure of neurons. This is not really relevant to the electrophysiology that much, but for two reasons I have included it. One is that there is a continuity from what you have studied in the, your last biology courses to this. And the other thing is, there is stuff which happens over here, just as regular cells secretory cells, cells which are not neurons, but which do other things like secrete hormones or enzymes, so on and so forth. And the neurons are similar to cells that where they have a very similar structure with some distinct differences.

So you have a cell membrane we just talked about that. All cells have that though they do not have those floating icebergs of sodium channels and semipermeable properties and the cell membrane, it overlays a cytoplasm which is the superficial gel layer. And there is a relatively deeper core.

And one interesting difference and it has all the usual things. The mitochondria, which is the powerhouse of the cell where all the energy is produced, it has got microtubules, which is for

structural properties, as well as for transmitting substances to and through different parts of the axon and the cell. And, of course, it is got dendrites.

But one thing I want to draw your attention to something called the axon hillock, so the axon arises from the soma or the perikaryon and this is where it arises from. And here you do not see these small little dots, it has not been labeled the small blue dots that is called the Nissl substance or the Nissl granules. And then and the Golgi apparatus, they package the different things made by this cellular factory.

Now they are absent over here. Now this is kind of important because when you are doing histology, you can identify the axon and one of the ways to identify it is it can because in electron microscopy, it can get pretty difficult. You can identify it as a place where there are no granules, these Nissl granules, they are blue, so usually you are staying into something called cresyl violet, it is called the Nissl strain and they blow you can easily make out.

This is a schematic over here, where you have a canonical pyramidal cell and then you have the initial segment from where the axon arises and then you have an axon. And this is something called myelin, which is an insulation for the axon. And this is the electron microscope equivalent of the schematic, here you have the soma, and then you have the axon initial segment.

Now, why is this relevant this initial segment, this is where the action potentials or the spikes, the way which neurons communicate, this is where it is initiated at the initial segment. The reason is, there are a lot of sodium channels over there, and we will get into it. I will repeat that there are a lot of sodium channels over there, and we will get to it subsequently.

The rest of the cell is pretty much a standard biological cell. There is no big difference except when specifically the secretions and what they package otherwise, it is not very different. The difference in neurons is this whole electrical activity, it is inherent electrical properties.

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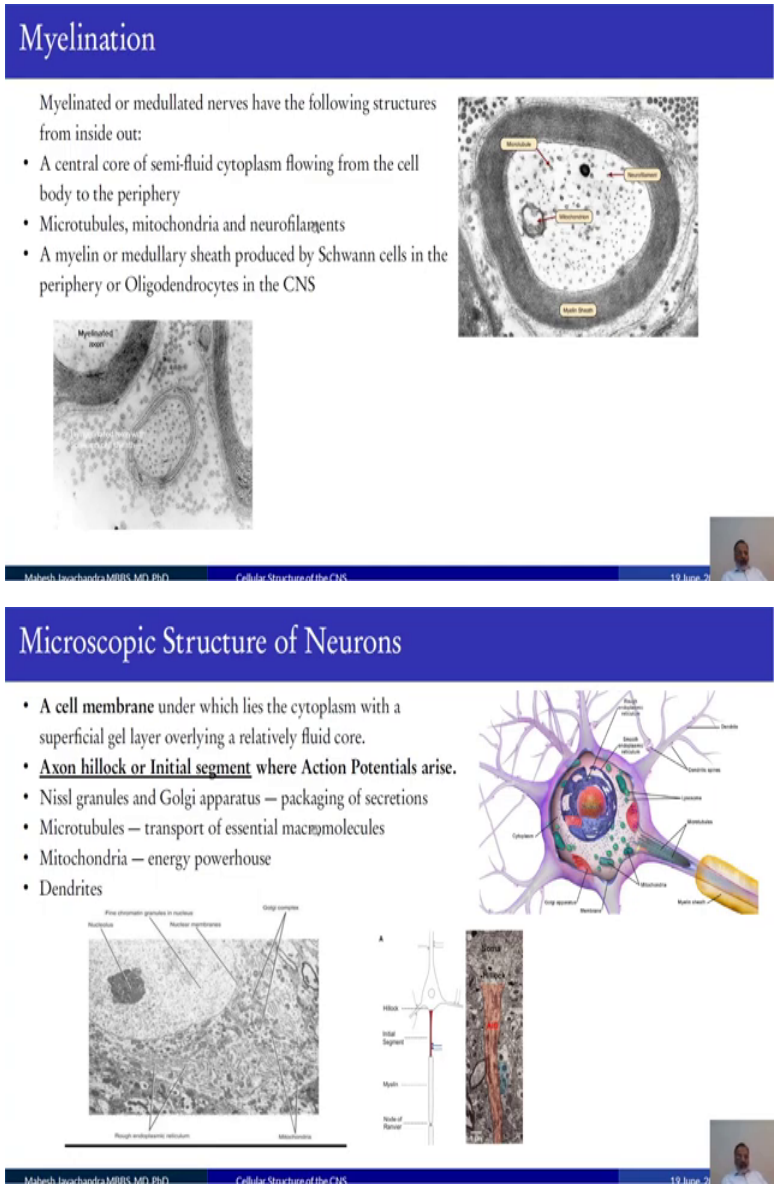

We mentioned, let me go back, first you see this myelin over here. Now this myelin it is a insulation, it is like insulation for your electrical wire, slightly different, but same principle. It is separated from other myelin areas by a node a place where there is no myelin it is called a node of ranvier.

And these are the electron microscopic photographs of axons. So, this is a central part of the axon, the place which arises from the initial segment and goes and transmits information to other neurons. So, there are microtubules over here, which are needed to transport stuff. There is mitochondria over there because you need some energy over there, but you will

notice there is no cellular apparatus of the nucleus or endoplasmic reticulum or Golgi thing like that. And over here you have a photograph right here, it is a little difficult to see it is faint, but this is a myelinated axon and this is an unmyelinated axon where there is no myelin it is just kind of the negative cell membrane, the phospholipid cell membrane, it is just in contrast.

Now, which the axons do not produces. So this myelin sheath is produced by the Schwann cells, it is a name of a cell in the peripheral nervous system or in the central nervous system by a particular cell called Oligodendrocytes, another name. So you will see the importance of the myelination subsequently.

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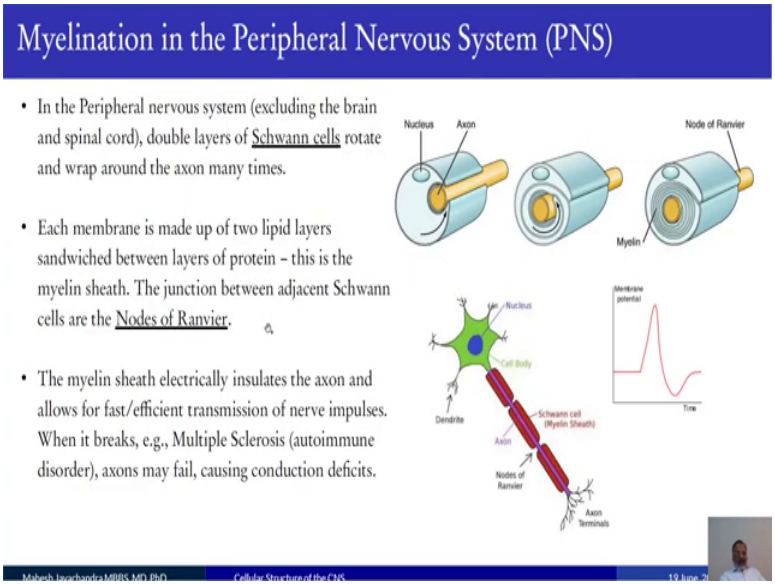

So how does it happen? So all cells have that phospholipid membrane we talked about earlier of the hydrophilic heads and tails. So one cell just takes its membrane and wraps it around an axon during development. And as it keeps wrapping it around, you have this double layers, which by virtue of their wrapping provide electrical insulation.

So, each cell or Schwann cell in the peripheral system will wrap up one area and in between two areas as we have mentioned in the previous slide is the node of Ranvier. Again, this is a place where there are a lot of sodium channels.

So, this is a canonical sketch of a neuron, and the axon conducts the impulses or the electrical activity of the soma downstream and this is how it looks. You have the membrane potential and there is a deflection and then it comes back to baseline. We will explore this in very great

detail in subsequent session, but this is just to give you an idea that while this impulse is being transmitted, the myelin sheath affords electrical insulation and makes it very efficient.

And one thing to bear in mind is that in some diseases, the myelin sheath can breakdown, and the classic disease where it happens, demyelinating diseases, multiple sclerosis where you can have sudden loss of different sensations.

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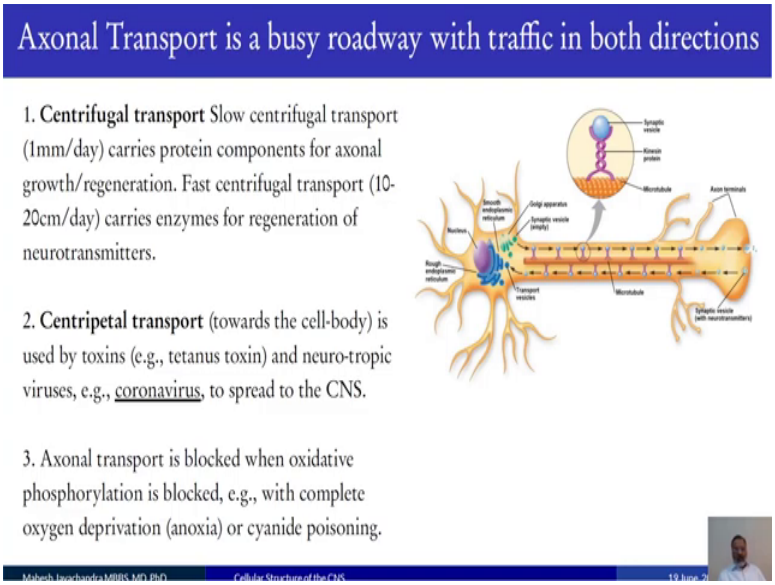

While we are in the zone let us talk about axonal transport. We will be focusing on electrical activity, but it is good to know some of the underlying physiology, which is happening in the axon. So basically you need two things. One is, I mentioned about neurotransmitters is going to be made and transmitted right till the synapse. And then secondly, you have the neuronal structure itself, it undergoes wear and tear. So, there are elements of it which have to be replaced.

So all this secretary stuff and making structural stuff is done in the cell body and then it is all packaged into vesicles and then there is actually a trolley kind of a system, which takes it right till the end to the synapse. And you have two kinds of transport, stuff which is going outward from the neuronal cell. From here it gets made and goes outside.

So this is called slow centrifugal transport it is about 1 millimeter a day and then it carries protein components for axonal growth and regeneration. You also have a fast centrifugal transport 10 to 20 centimeters a day which carry enzymes to regenerate neurotransmitters, that needs to be done, quicker.

Besides this movement from the soma to the synapse, there is also reverse movement centripetal movement towards the cell body. And it is a common thing used by pathway, used by toxins for example, tetanus toxin or neurotropic viruses for example, the coronovirus to spread to the central nervous system.

This process requires energy and anything which poisons or blocks the energy production at a very fundamental level ATP, ADP that level we need free phosphate anything which blocks it will block axonal conduction, and you also get it, for example, decreased oxygen, anoxia or with cyanide poisoning, that blocks this whole transport system and the axon and subsequently the neuron begin to die.

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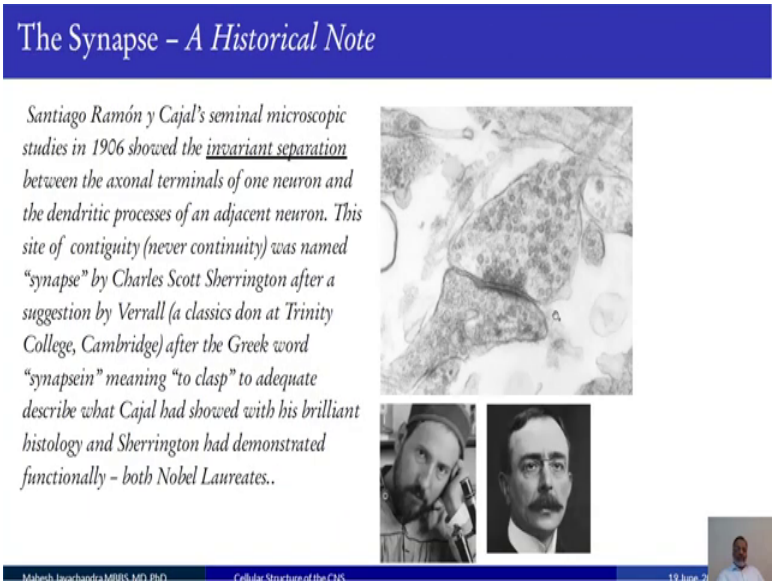

Okay, we have a small historical digression. So there was a lot of controversy about 100 years ago on how neurons actually communicated. One school of thought at that time was it was a continuous flow from one axonal sheet with no breaks in between, and that is how they communicated.

But there was this really brilliant anatomist Santiago Ramón y Cajal from Spain, who did a lot of path breaking stuff on neuroanatomy. And in fact, he won the Nobel Prize for it. And some of his drawings are still unrivaled, for the kind of detail they brought, and neurophysiologist finally had a structural correlates of the central nervous system to work with.

And they found out that, specifically Cajal that in between axons, there is this thing called the synapse. It was named by a classic scholar from Cambridge and it means that you have

contiguity, so there is contiguity it is close to contiguous to each other, but there is no actual physical continuity. There is a distinct break over there. So Charles Scott Sherrington also won the Nobel Prize for physiology. And he named the synapse off of this suggestion, by this Cambridge scholar Verrall.

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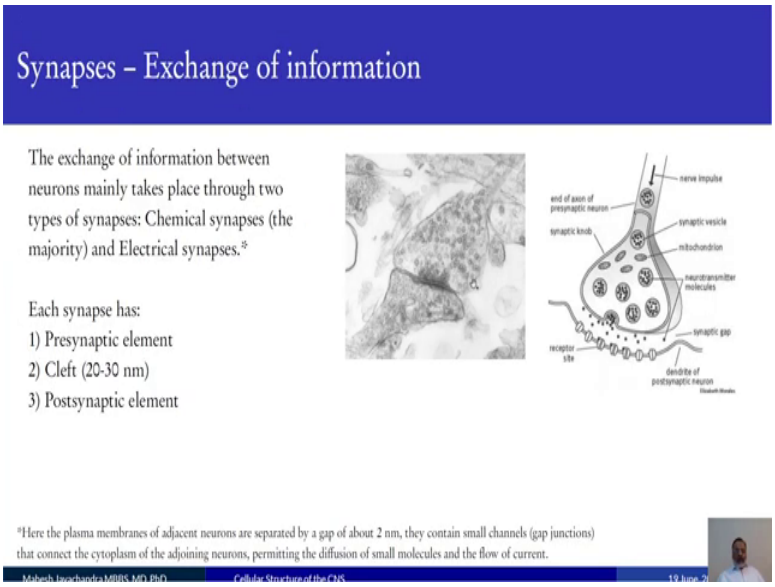

So exchange of information between neurons occurs mainly via synapses, and the synapses are chemical. I will explain that in a minute. There are another kind of synapses where it is electrical, they are very few. So generally the vast majority of synapses are chemical and each synapse as a presynaptic element coming from axon, and the post synaptic element, which is going to the cell and then there is a divide or a cleft in between and this cleft is about 20 to 30 nanometers.

So there is a presynaptic element, there is a cleft and there is a postsynaptic element. So how does information get transferred? So if you notice, there are a lot of these round things over here in the presynaptic knob as it were, and these are, these contain neurotransmitters.

So when an impulse, you saw that deflection that red little drawing in a previous slide, when the nerve impulse comes to the synapse, it triggers off a series of processes, where all these, little vesicles they are called, synaptic vesicles they begin to fuse the membrane and throw out all their contents, these are molecules.

These are neurotransmitter molecules they could be glutamate, they could acetylcholine. So these molecules travers cross this cleft and they attach to receptors on the postsynaptic membrane. So this is the presynaptic process and this is the postsynaptic membrane. And

once they attach to these receptors, they cause ionic changes and depolarize this membrane and giving rise to deflections on actual potential spikes in the postsynaptic element. This all happens very fast. Not as fast as an electrical transmission, but order of milliseconds, this transmission of information, approximately 1 millisecond. So impulses which come here, 1 millisecond delay and they are transmitted over here.

Now just a word about electrical synapses, there you have adjacent neurons which are separated by a gap of about 2 nanometer1/10th the size of this and they contain small channels they are called gap junctions that connect the cytoplasm of adjoining neurons to each other. This permits the diffusion of small molecules between one neuron to another and also the flow of electrical current, but the vast majority are chemical synapses.

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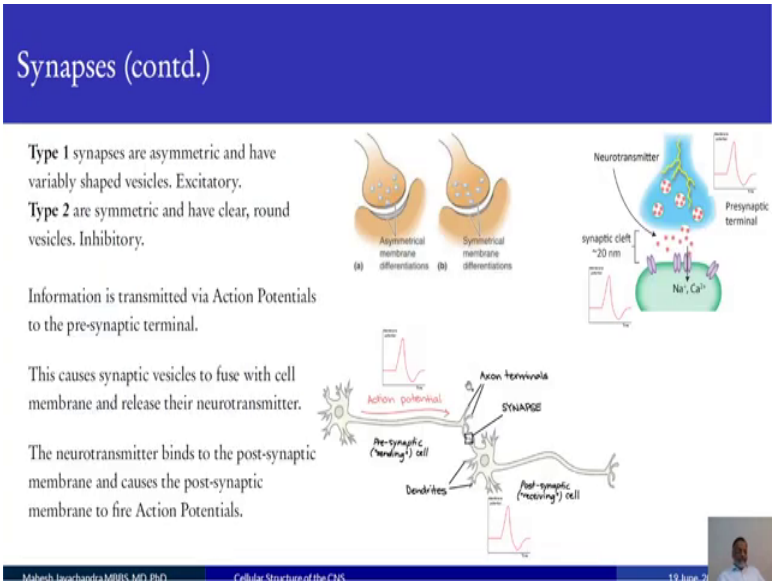

So, they can be divided on basis of this structure or morphology into type 1 and type 2 synapses. So, type 1 synapses are asymmetric and have variably shaped vesicles. Type 2, so this is the asymmetric part, this is thinner than this, type 2 are symmetric more or less same and they have clear round vesicles. And these tend to be excitatory and these tend to be inhibitory there are two possibilities.

One is, information comes and excites the cell or information comes and inhibits the cell. So information is transmitted via action potentials to the presynaptic terminal. So, this cell fires action potentials, this is what an action potential looks like this is the way information is transmitted. So, these can come singly or they come in bursts or they can come at a steady rhythm, it is different for different cells. So, that comes all the way to the synapse.

And then as soon as it comes here, just to reiterate from the previous slide, all these vesicles the neurotransmitters are released, they go bind to their receptors on the postsynaptic element and allow sodium and calcium inside the cell. And once enough of this happens, you get an action potential over here and that is transmitted via the axons node of Ranvier so on and so forth.

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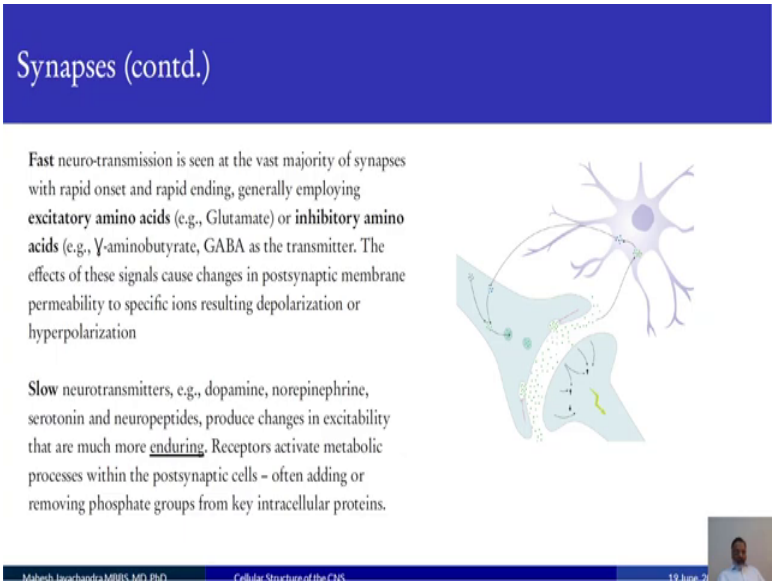

So, now we can talk about different kinds of synapses. So you have two kinds of synapses depending on the amino acids, which are released, the neurotransmitters released in the terminals. One causes excitation and that is usually glutamate. This is an important point bear this in mind. So neurons, which have glutamate project they release glutamate and that causes excitation in this subsequent neuron downstream or it could be inhibitory, which is gamma aminobutyric acid or often called GABA and that inhibits.

So a neuron, which is being bombarded by excitation and inhibition, it will fire or transmit action potentials only when there is a balance between these two excitatory and inhibitory possibilities and the excitation is more than the inhibition.

So depending on which neurotransmitter is released it can cause as I said excitation inhibition. So, speaking of it in electrophysiological terms, it can either depolarize or hypo polarize the postsynaptic membrane. We will get into exact detail about depolarization, high polarization and the action potential resting membrane potential lectures. But this is just to give you an idea of the terms so that you get familiar with the jargon.

So also synapses generally what we have been talking so far, work very fast. I said 1 millisecond the information is transmitted. So, this is a classic fast neurotransmission, but you also have another variety of neurotransmitters which is much slower, but the action occurs over tens of seconds, minutes and sometimes even hours.

And these are different set of neurotransmitters, we would not be chatting about it too much, but just to give you an idea of the names dopamine, norepinephrine, serotonin, neuropeptides and these have enduring effects. And many of these, for example, are implicated in mood disorders. So when you feel down or you feel excited, you feel excited for some time or you feel down for some time and much of that is presumed to be induced by the slow neurotransmitters.

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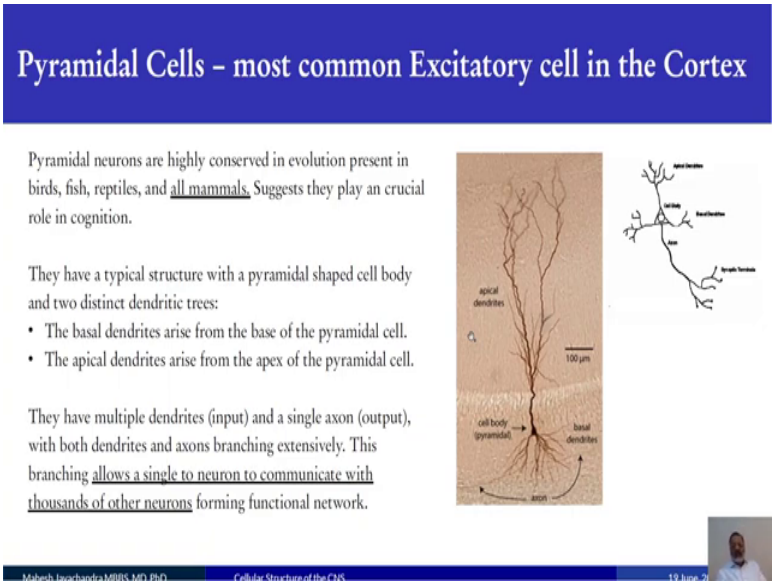

So, moving on. So, pyramidal cells. So these are the most common excitatory cells in the cortex, the cortex is the brain for now. So they are highly conserved in evolution, which means they are present in birds, fishes, reptiles, and all mammals. And when something is conserved in evolution it means that it is significant.

If it is, if something is, and it is functional, if you do not use something, then evolution dies out, it is not used. So, this suggests that pyramidal cells play a crucial role in brain function, especially higher mental function or cognition.

So they vary greatly in shape, size and their dendrites, their branching like structure, but they all have some fundamental things in common. They have apical dendrites these branches. If you think of a tree or a plant so you have a stem, and then you have these apical dendrites

like branches, and then you have roots and one guy call the axon and it is like a tap root, you cannot, you can barely see it over here. Sometimes it is not prominent, but most pyramidal cells have this canonical structure, where you have these apical dendrites, and you have a cell body and then you have a basal dendrites.

So the apical dendrites arise from the apex of the pyramidal cell. This is the canonical pyramidal cell circuit so these are the apical dendrites and the basal dendrites arise from the base of the apical dendrites and the basal dendrites. And then these, the axon takes all this information and transmits it to via synaptic circuits to other axons.

So this branching allows it to, there is a lot of branching and this branching allows you to increase the surface area majorly. And also a single neuron can connect with thousands of other neurons forming a network.

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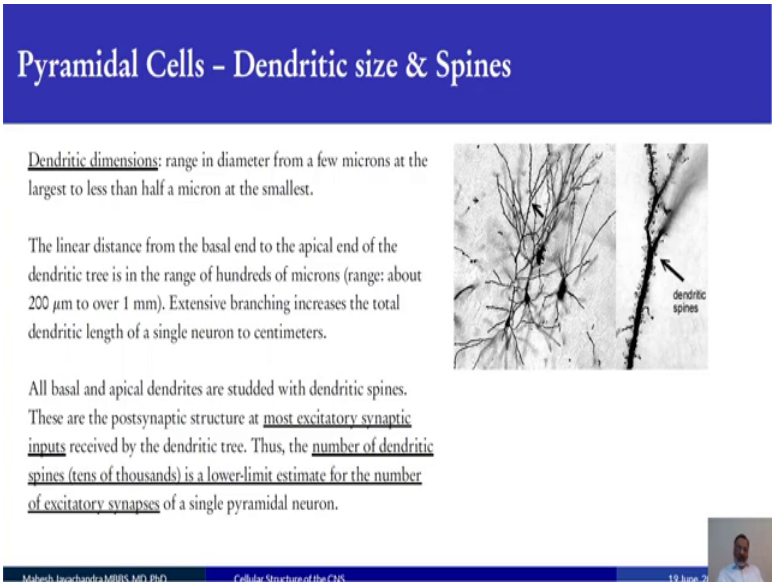

So, coming in a little more detail of dendritic size and spines, so these dendrites, they can in diameter, they can be a few microns or they can be in diameter, those are the largest ones or they can be much smaller to half a micron. And what is the spread? So the linear distance of a dendritic tree. How big is it?

So it is about one fifth of a millimeter to about 1 millimeter, and that is pretty vast compared to the size of the actual cell. And again, this extensive branching increases the total dendritic length of a single neuron to centimeters.

Now, all these dendrites, all these dendrites are studded with something small protuberances called dendritic spines. So these are the postsynaptic. Remember, we talked about presynaptic, synapses and post synapses. So these are the postsynaptic structures at most excitatory synaptic inputs. So in fact, if you can count the number of dendritic spines, you can get a lower level estimate for the number of excitatory synopsis on the cell of a single pyramidal neuron.

Now, why is this important? Now this is important, both the dendrites and the spines because a lot of computation occurs over here. When I say competition, I mean it in a very basic way not exactly the computer stuff, what you have in standard hardware software. This is basic computation, you can compare two different inputs, you can compare two different outputs in that sense.

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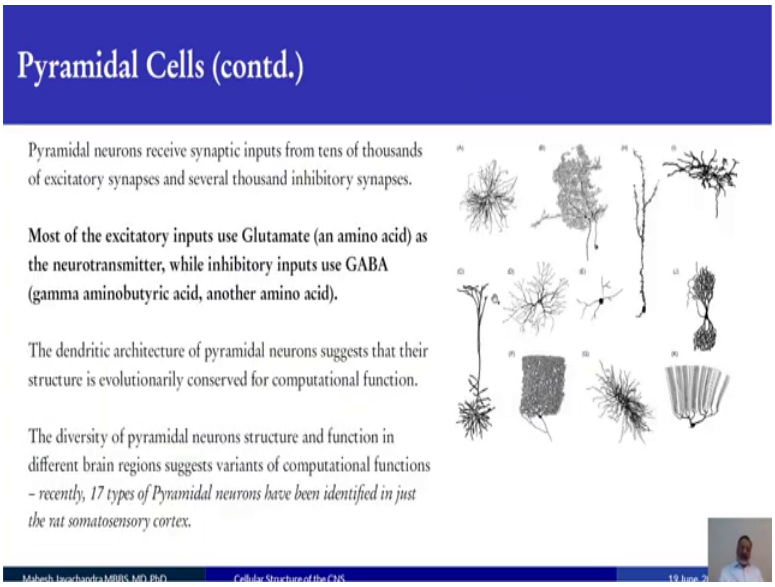

So, continuing, so this is a slide which we saw earlier, this is just to give you an idea of the different kinds of pyramidal dendritic trees. Now, you understand about dendrites. So it is like plants, there are tons and tons of different plants and it is like that this is just a metaphor. Now, pyramidal neurons through the dendrites, they receive synaptic inputs from tens of thousands of excitatory synapses, but you also have inhibitory synapses.

So excitation makes them, depolarizes them and they start transmitting action potentials. But there is a process which occurs in the reverse way, and those are inhibitory synapses, and they use GABA as mentioned earlier. So, the balance between this excitation and inhibition, allows the soma to reach depolarization to fire action potentials. So again, to reiterate, most

of the excitatory inputs use glutamate. And by the way, glutamate and GABA are amino acids, very basic chemical compounds.

And looking at the dendritic trees and seeing the way most of these cells are conserved in mammals. We just have one or two so far cells which are been found in the human brain which do not occur in non-humans otherwise everything else is common to all our brains from rats, cats, dogs, elephants.

So the structure true, so again to reiterate, the structure is conserved. So it is probably conserved because of all the different computational functions, which neurons do. And there is a diversity of pyramidal tract structure, I am sorry, pyramidal neurons structure and function in different brain regions. So this suggests there are a variety of computational processes possible. And just in the rat somatosensory area, this is the area where the rat feels the world through its whiskers. There are 17 different kinds of pyramidal neurons just in the rat touch area.

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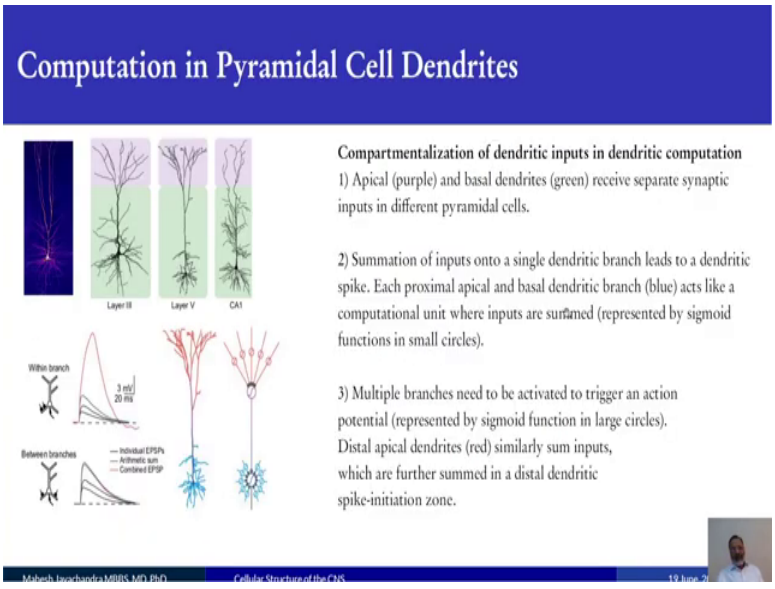

So just to get an idea, how could one compute using a neuron? Many, many people have worked on this and there is lots of data on this. This is just to give you an introduction. So consider a pyramidal neuron. And there are different kinds, remember I told you layer 1, 2, 3, 4, 5, 6. This is a pyramidal neuron from layer 3. This is a pyramidal neuron from layer 5 and this is from the hippocampus, CA1 neuron pyramidal neuron, and they have very distinct trees dendritic trees.

So, you have the apical tree, which is in purple and the basal dendrites, which is in this green zone, they receive separate synaptic inputs, excitatory inhibitory whatever, but they receive separate inputs in different pyramidal cells. So, these inputs all sum into a single dendritic branch.

Now, these inputs can be very close to each other and they will temporarily sum so that, together if they fire close you have a huge response, or they can spatially some they are further apart and then it is not such a big effect.

But the summation of this causes the depolarization, depolarizing over here. And you can represent each proximal and apical dendritic branch with different colors over here. So you have the blue and the pink, and each of them can be the dendritic inputs can be represented as a sigmoid function.

And once it reaches depolarization, then it fires the axon and it can fire it over here, or once the sigmoid functions over here from the basal dendritic inputs you can fire it over here. So they all have to sum up. And once it reaches a certain threshold, then it starts firing. But you can easily see that, for example, you could think of a differential amplifier, you are having one input over here, another input over here and then it does its differentiation and compares two input so on and so forth.

Now, just bear in mind that this is at a gross level. All these things can also occur at the dendritic spine level.

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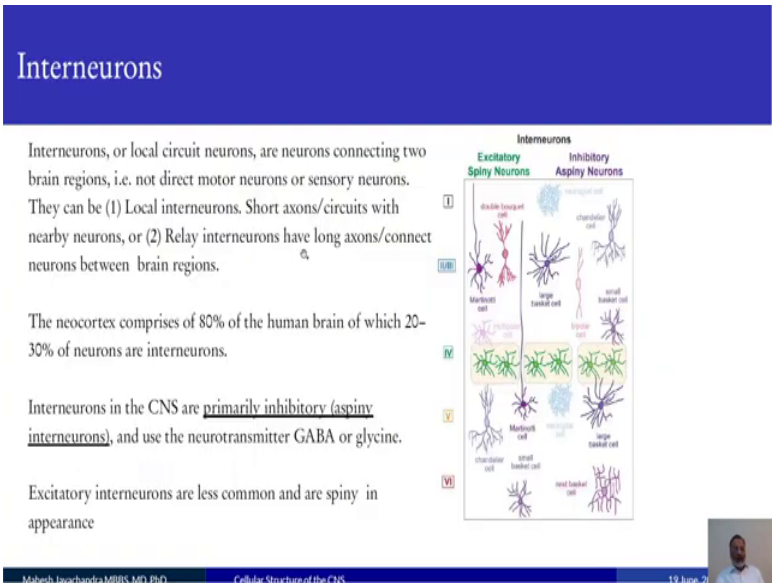

Okay, so we talked about pyramidal cells, they are the main excitatory cells in the central nervous system. So let us talk about interneurons, which are the other neurons, which are electrically active in the brain, central nervous system.

So, these 20% to 30% of neurons are interneurons, and they are called local circuit neurons also, and they usually connect two different brain regions. So they do not directly involve themselves in sensory or motor activities, but they do the connections between these neurons.

So, they can be local and these are short axons and circuits between nearby pyramidal cells or rather interneurons or they can be relay interneurons with long axons and connect between brain regions. So, these cells are primarily inhibitory. So the pyramidal cells are excitatory, interneurons are primarily inhibitory and they use the neurotransmitter GABA, gamma aminobutyric acid or glycine.

There are excitatory interneurons, but they are less common, and they tend to be spiny. So they have spines. So again, remember the layers 1, 2, 3, 4, 5, 6. So these are different interneurons, which occur in the different parts of the gray matter of the brain. And again, they are kind of very evocatively named based on their dendritic structure, for example, this is a double bouquet cell, this is a large basket cell, this looks like a chandelier, so it is a chandelier cell, so on and so forth.

So these are the A spiny guys which are excitatory which are not common, this is a bipolar cell. And these are excitatory, which is by far the majority. And if you think about it, you need inhibition, because if you have only excitation then you will probably have epilepsy or non-stop reverberation. So you need inhibition too.

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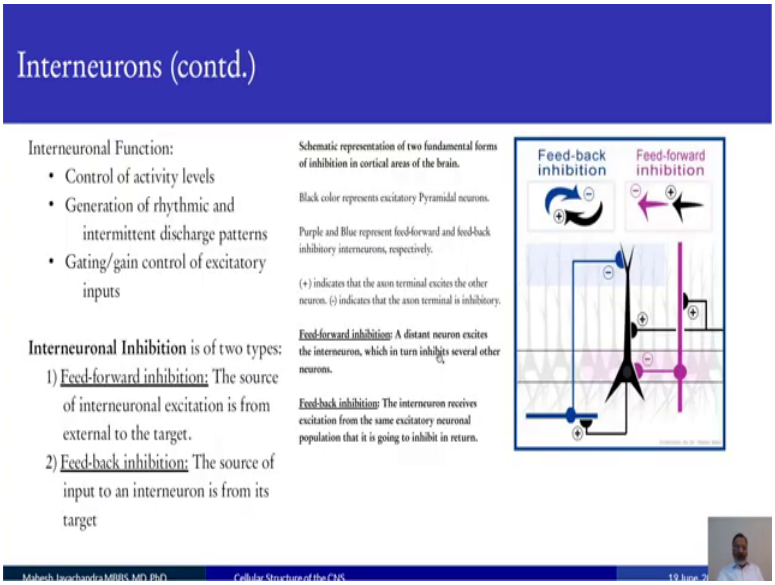

So this is for all your instrumentation, engineers over there, a little more detail about what interneurons actually do. So one is they control activity levels, and they can inhibit pyramidal cell and preventive from firing or they can depolarize it and make it fire.

It could also, there are also important to generation of rhythmic and intermittent discharge patterns, because most of the patterns we can think about generally are found in the brain, the ways neuron fires, where it fires and bursts, whether it fires rapidly and adapts, whether it fires slowly, all these things have generally been seen in different parts of the brain. So interneurons are very important for that.

And finally, gating and gain control of excitatory inputs so that you do not have run away the excitation. Again you are run away excitation you get epilepsy. So the inhibition it does is of two kinds. You have a feed-forward inhibition or a feed-back inhibition. So the feed-forward inhibition the source of the interneuron is excited. It is excited by a neuron from outside an external neuron.

Now feed-back inhibition is the source of the input to the interneuron is also its target. So here if you look at the schematic just briefly the black color represents the excitatory pyramidal cell, the purple and the blue represent feed-back and feed-forward inhibitory neurons. So purple is feed-forward, this is purple, so you can see that it is getting inputs from an external neuron and then it inhibits the pyramidal cell.

And this is the feed-back guy, and it inhibits the pyramidal cell, but it also receives input from the pyramidal cell. So these are the two main kinds of inhibition the interneuron does

and a balance of this plus and minus inputs does the, search the threshold for the pyramidal cell to fire action potentials and communicate with other neurons. So this is a fundamental concept, feed-forward and feed-back inhibition. And remember, excitation is done by glutamate and that is from pyramidal neurons and inhibition is from interneurons and they use GABA of glycine.

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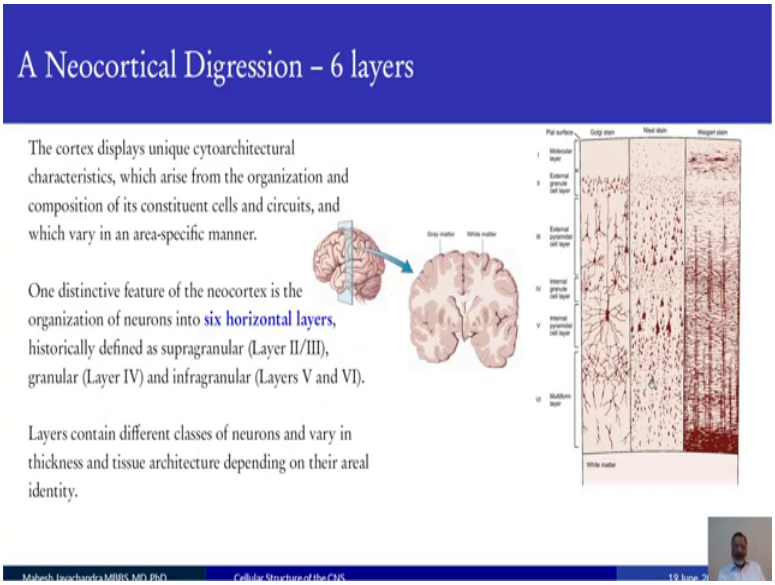

So now I want to do a small digression and talk about the neocortex, the human neocortex, so this is the brain, the human brain. Now consider taking a section like this, a slice and looking then at it from the cut side. So it has a gray matter on the outside and it has white matter on the inside, and the white matter is all the nerve fibers which transmit information from one part of the brain to another, but we are interested more in the gray for now.

And as I mentioned there are 6 layers, 1, 2, 3, 4, 5, 6. And generally, layer 4 is the granular layer because the cells look like granules over there, and because of that it is easier in sort of layer 1, 2, 3, we talk of the granular layer and we have the supergranular, infragranular layer.

Now these, this is a same section, but we have used different stains. Here we use the golgi stain and it was created by Camillo Golgi, and it is a silver stain, it is a very interesting stain. It just stains 1% to 2% of the target cells so actually the density is 99 times more than what you see over here, but whatever it stains, stains completely if you see the whole structure.

So you can see the full cell body and the dendritic structure. The Nissl stain only stains the cell bodies principally and there is another thing call the vguard stain which stains all the microfilaments and fibers and stuff. So you see there is a district structure over here. And this

6 layered structure is conserved in evolution so all mammals generally have it all the higher mammals anyway.

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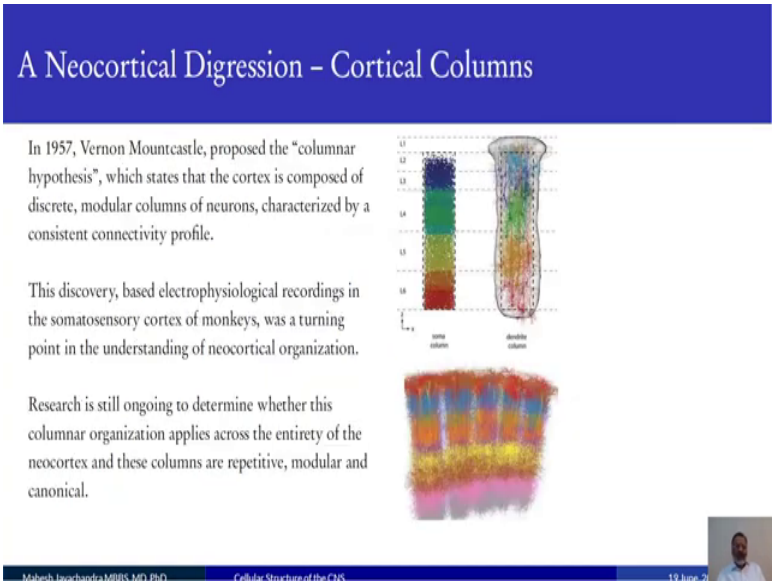

And in 1957 Vernon Mountcastle one of the greatest neurophysiologist of his generation, he proposed the columnar hypothesis, and he based his hypothesis on recordings from the touch area of weak monkeys. And he proposed that besides these 6 layers there is also a vertical organizing principle in the cortical columns, and it is about 300 mu in diameter one-third of a millimeter in diameter and has a specific kind of structure and function.

And it is concern in mammals right through. So just like the horizontal layering, this vertical layering is concern. And we still do not know whether the applies across the entire neocortex and these are modular and repetitive and or they can be changing. They can do different things with different inputs. A lot of research is going on, but this is the fundamental computing unit of neocortex.