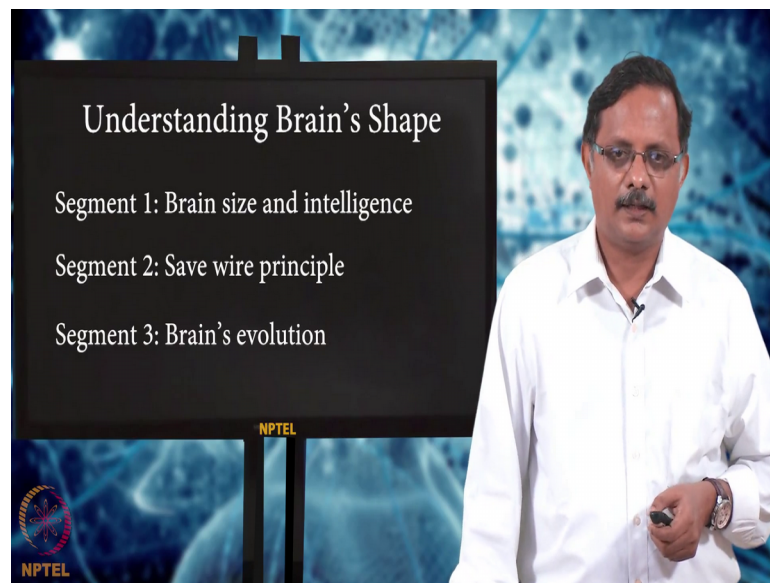


Demystifying the Brain
Prof. V. Srinivasa Chakravarthy
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture - 03
Understanding Brain's Shape - Segment 2 - Save Wire Principle

We have been discussing we have been trying to understand brain shape.

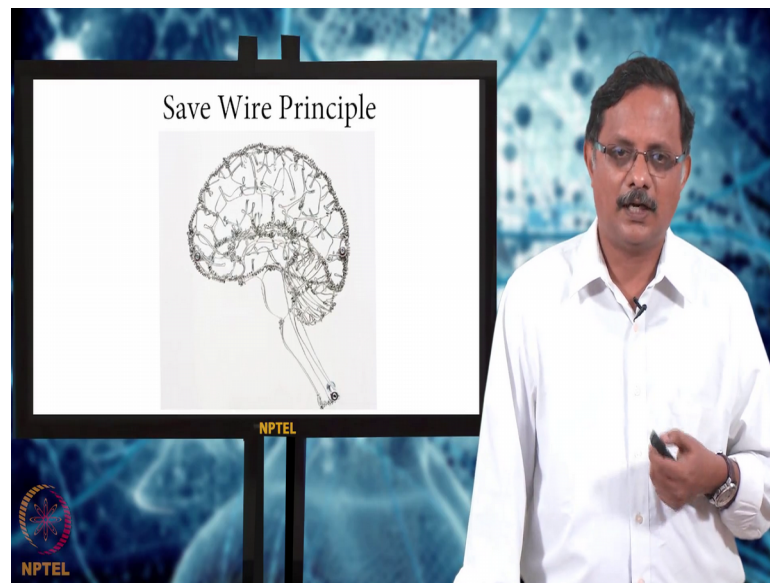
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So, this lecture has 3 segments, we already discussed the first segment on brain size intelligence. We look at some simple metrics that relate brain size intelligence, we started with brains weight and that did not work very well we looked at brain weight and body weight ratio, that also had its issues then we looked at this new interesting quantity called encephalization, quotient that seemed to work well, but still it was not too convincing because it does not give much insight into what aspects of brain structure a correlates with intelligence.

So, now let us look at the go deeper into this kind of investigation into properties of brain shape, structural properties and arrive at a principle called save wire principle.

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So, we will argue that and also show evidence that brain tries to minimize the total wire length alright. And we see that that kind of an attempt to minimize wire length is also very commonly seen in engineering domains. So, let us go deeper into this save wire principle.

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“Cyto-Census”

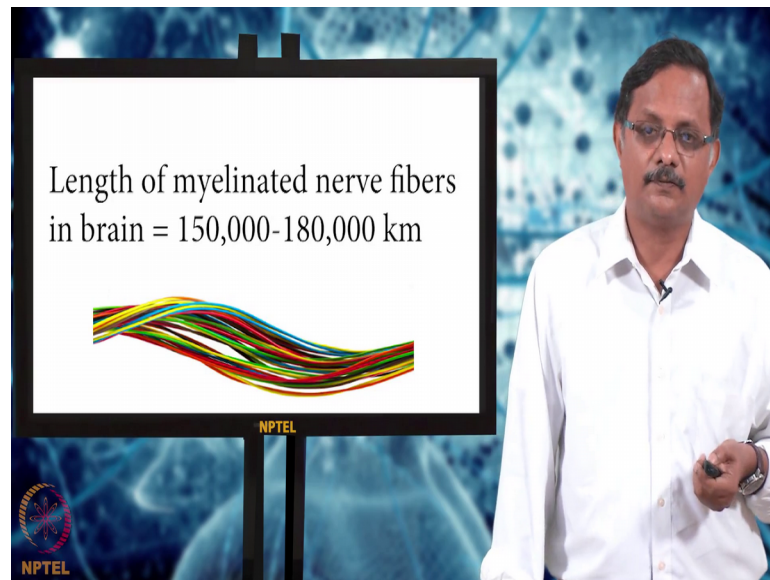
Species	# Neurons
Humans	100 billion
Octopus	300 million
Aplysia	18k – 20 k
C. Elegans	302

NPTEL

So, before we get into that let us look at some data related to number of neurons and number of wires and you know various brains etcetera, if you look at the number of cells, so in various brains.

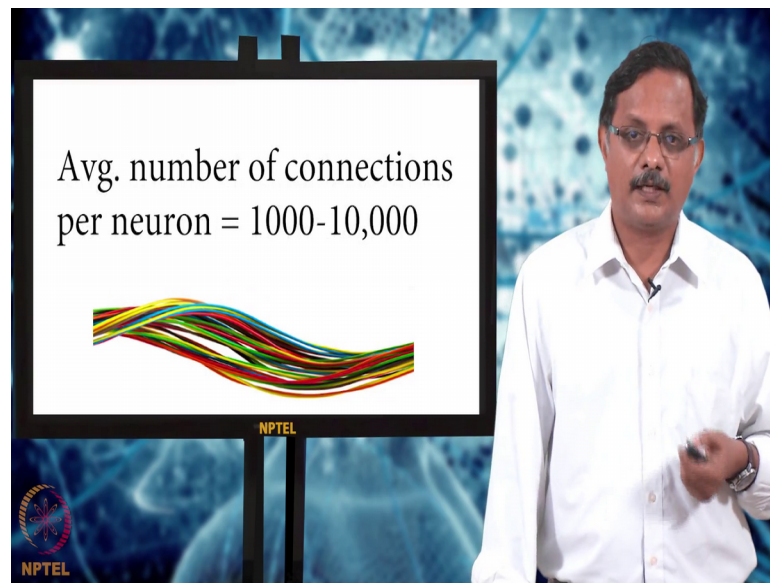
So, in humans it is about 100 billion in adult human brain in octopus it is about 300 million, in aplysia it is a very small water creature it is about 18000 to 20000 in a small worm called C Elegans or nematode they are exactly 300 and 2 neurons So, the number of neurons shows a lot of variation. So, shows many orders of magnitude variation.

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Now, if you look at the wiring, right the brains are full of wire and wire is a very important aspect of brains, because the connections evolution right as we have seen in the first lecture. As recognized that the wire is an important part of brain structure. So, if we look at human brain the total length of myelinated fibers is equal is about 150 thousand, kilometers to 180 thousand kilometers.

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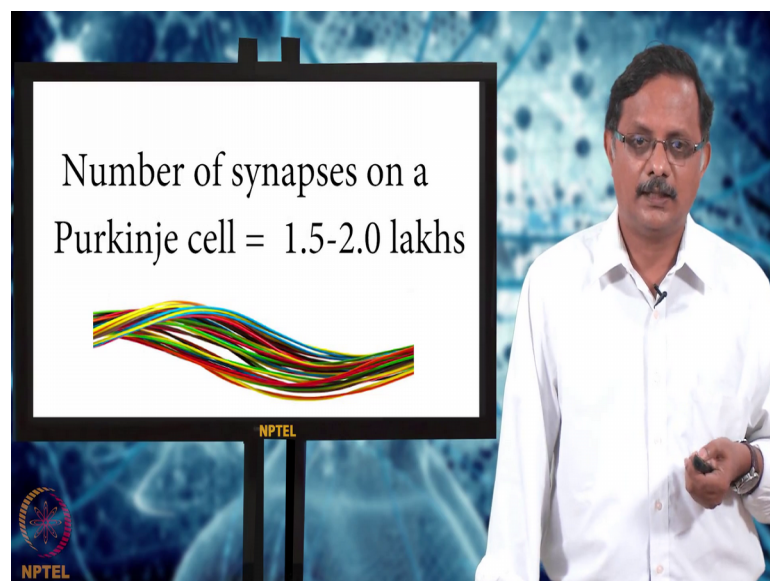


Avg. number of connections
per neuron = 1000-10,000

The presentation board features a diagram of multiple colored lines (red, yellow, green, blue) representing neural connections. The NPTEL logo is visible in the bottom left corner of the board.

And the average number of connections per neuron is about 1000 to 10000.

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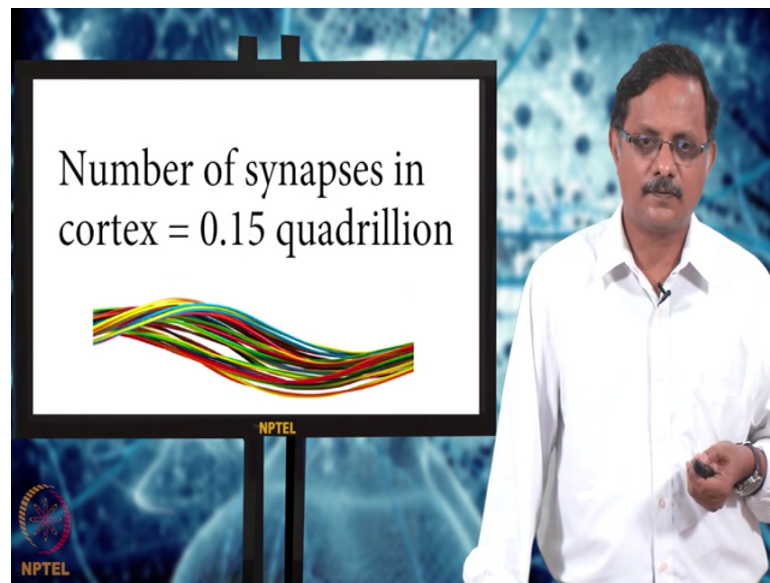


Number of synapses on a
Purkinje cell = 1.5-2.0 lakhs

The presentation board features a diagram of multiple colored lines (red, yellow, green, blue) representing neural connections. The NPTEL logo is visible in the bottom left corner of the board.

And the number of synapses on a very large cell, cell which has a large, large number of connections is about 1.5 to 2 lakh or 200 1000 connections.

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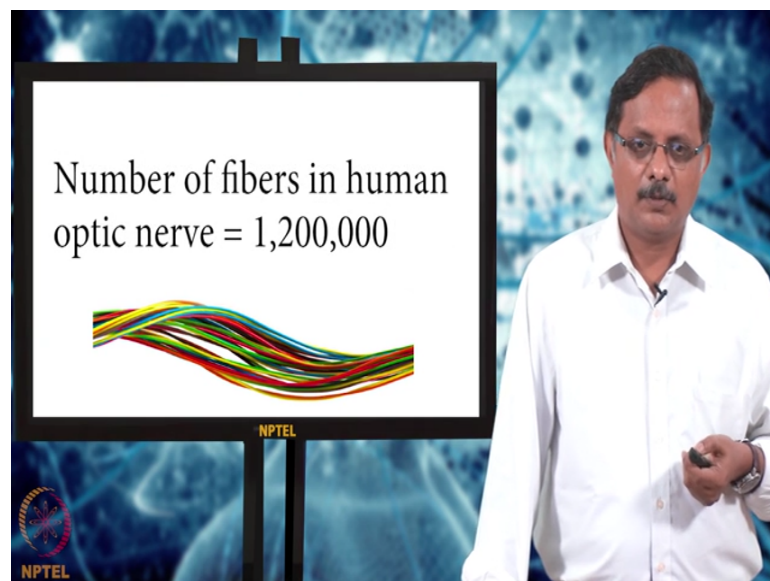


Number of synapses in
cortex = 0.15 quadrillion

NPTEL

And number of synapses in the cortex in total entire cortex, he is about 0.15 quadrillion.

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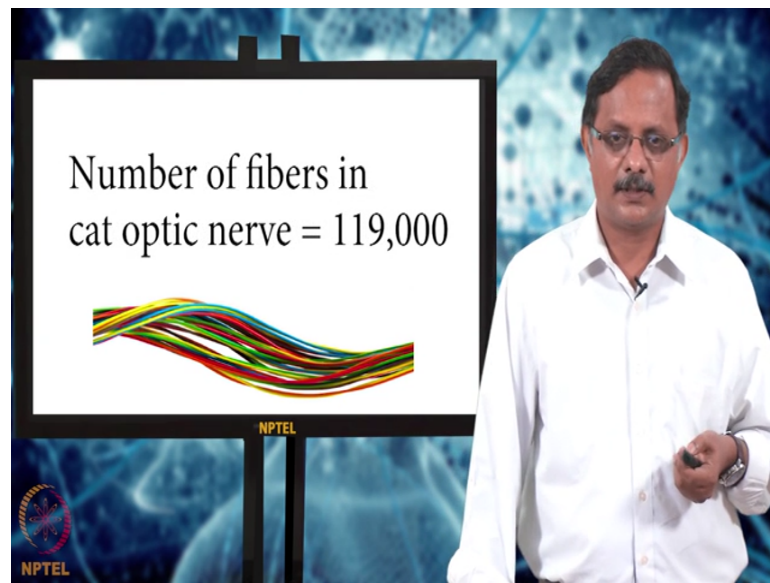


Number of fibers in human
optic nerve = 1,200,000

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Now, number of fibers in human optic nerve is 1.2 million of number of fibers.

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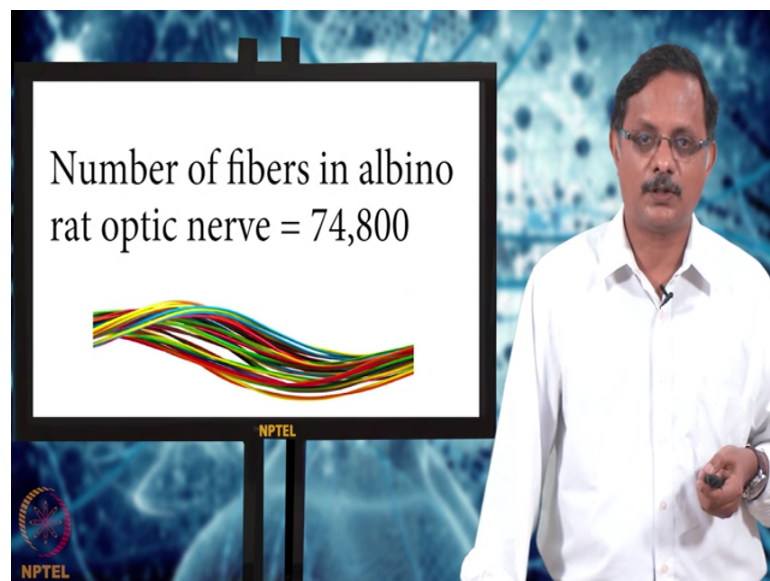
Number of fibers in
cat optic nerve = 119,000



The slide features a white rectangular box with a black border. Inside the box, the text "Number of fibers in cat optic nerve = 119,000" is displayed in a black serif font. Below the text is a graphic of a bundle of multi-colored fibers (red, yellow, green, blue, and purple) that are slightly curved. The slide is presented on a black stand with the NPTEL logo at the bottom. A man in a white shirt and glasses stands to the right of the stand. The background is a blue, abstract, textured pattern.

In cat optic nerve is 119000.

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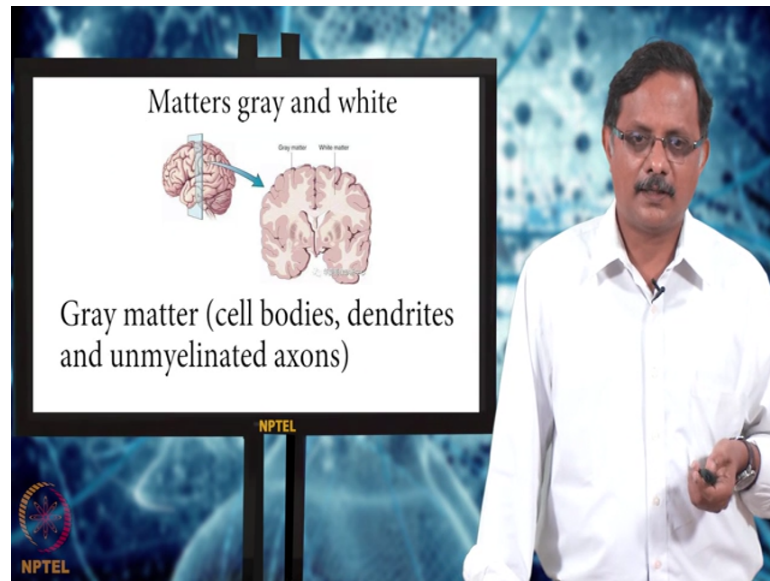
Number of fibers in albino
rat optic nerve = 74,800



The slide features a white rectangular box with a black border. Inside the box, the text "Number of fibers in albino rat optic nerve = 74,800" is displayed in a black serif font. Below the text is a graphic of a bundle of multi-colored fibers (red, yellow, green, blue, and purple) that are slightly curved. The slide is presented on a black stand with the NPTEL logo at the bottom. A man in a white shirt and glasses stands to the right of the stand. The background is a blue, abstract, textured pattern.

And number of fibers in albino rat optic nerve is about 74000. So, numbers that you are looking at are very large when it comes to the wiring let us look at these numbers slightly differently.

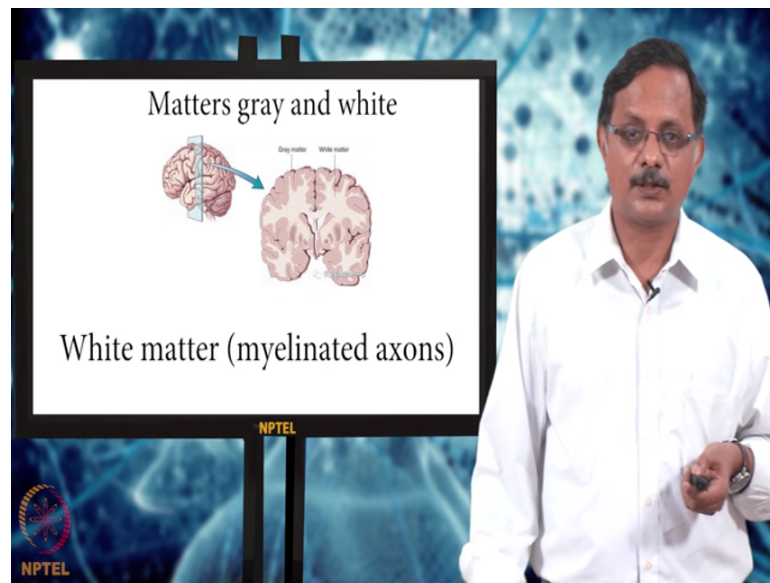
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For that we need to define, what is a gray matter, and what is white matter in common parlance we use the term gray matter as if it you know denotes the brains of a person or intelligence of a person, but basically gray matter refers to a part of the brain. So, if you look at this in this slide it shows a slice of a brain and, this slice shows kind of a brownish outline and creamy white colored interior.

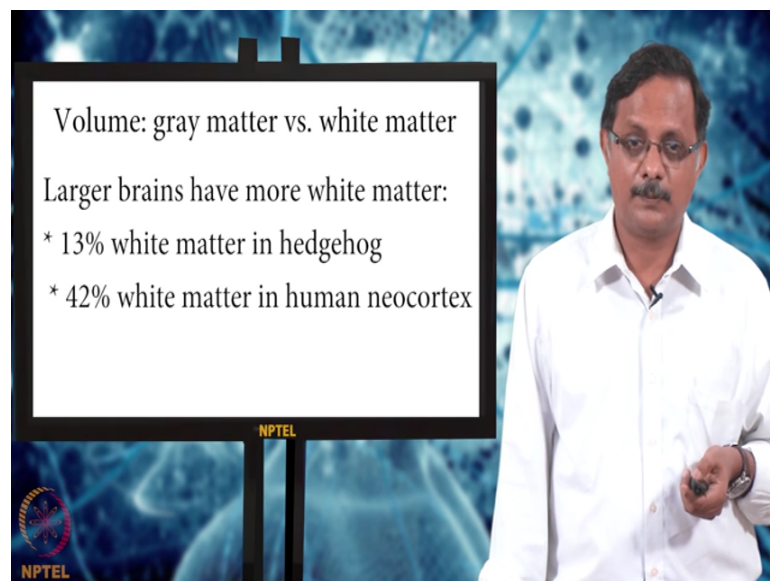
So, this brownish outline is actually what is called gray matter because that is where you have a lot of cell body. So, that is the cortex and the creamy white interior is the wiring, now this is white because these wires have a kind of coating called myelin sheath and myelin is white in color. So, the gray matter consists of cell bodies dendrites and unmyelinated axons.

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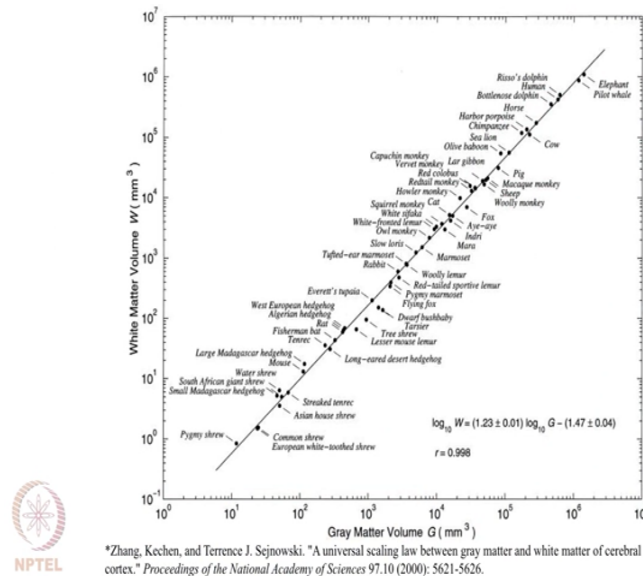
Whereas white matter consists of this myelinated axons.

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Now, it turns out that the amount of white matter grows as a brain size grows. So, for example, in a hedgehog the volume of white matter right is only 13 percent whereas, in human your cortex at the volume of white matter is 42 percent so; that means, as the brain size grows the volume of the white matter keeps growing that is a wire part keeps growing.

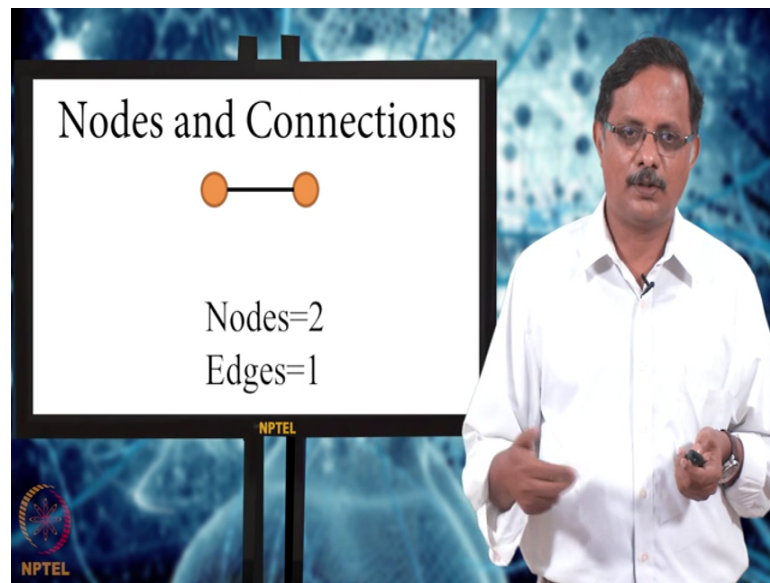
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Right and in this graph it shows the white matter to gray matter relationship right for a large number of species. So, in the x axis you see gray matter volume and the y axis you see white matter volume, now these numbers are represented in log scale. So, that is why it looks linear.

But that does not mean they are proportional actually there is a power law here and the power is 1.23 so; that means, the white matter volume is proportional to the gray matter volume to the power of 1.23 so; that means, the white matter volume increases faster than linear, right with respect to gray matter volume.

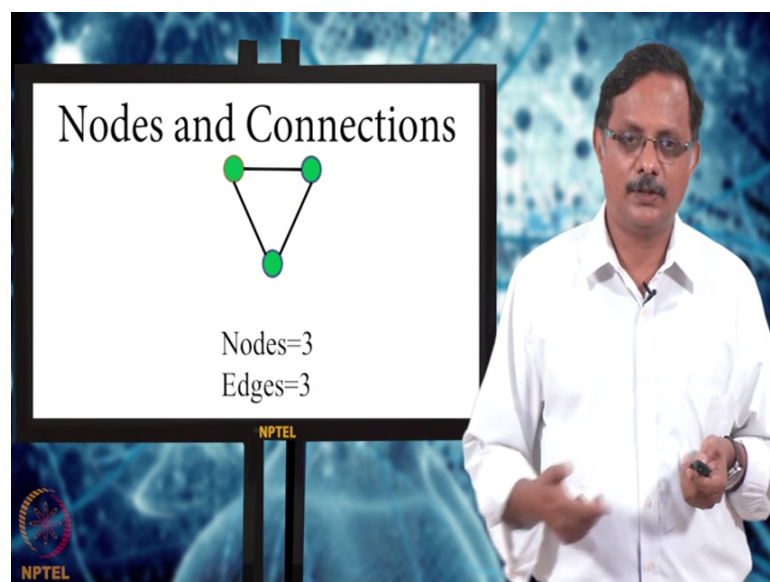
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The slide is titled "Nodes and Connections". It features a diagram of a graph with two orange circular nodes connected by a single horizontal black line representing an edge. Below the diagram, the text reads "Nodes=2" and "Edges=1". The slide is part of an NPTEL presentation, as indicated by the logo in the bottom left corner. A presenter is visible on the right side of the frame.

But that is not very surprising because if you think about it, if you think of brain as a network right of nodes and then 3 nodes are connected by edges you will look at a small graph which has only 2 nodes, as they can be connected only in 1 way giving you 1 edge.

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The slide is titled "Nodes and Connections". It features a diagram of a graph with three green circular nodes arranged in a triangle, connected by three black lines representing edges. Below the diagram, the text reads "Nodes=3" and "Edges=3". The slide is part of an NPTEL presentation, as indicated by the logo in the bottom left corner. A presenter is visible on the right side of the frame.

If it takes graph of 3 nodes you can have totally 3 edges.

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Nodes and Connections

Nodes=4
Edges=6

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If you take a graph of 4 nodes you can have totally 6 edges and so on

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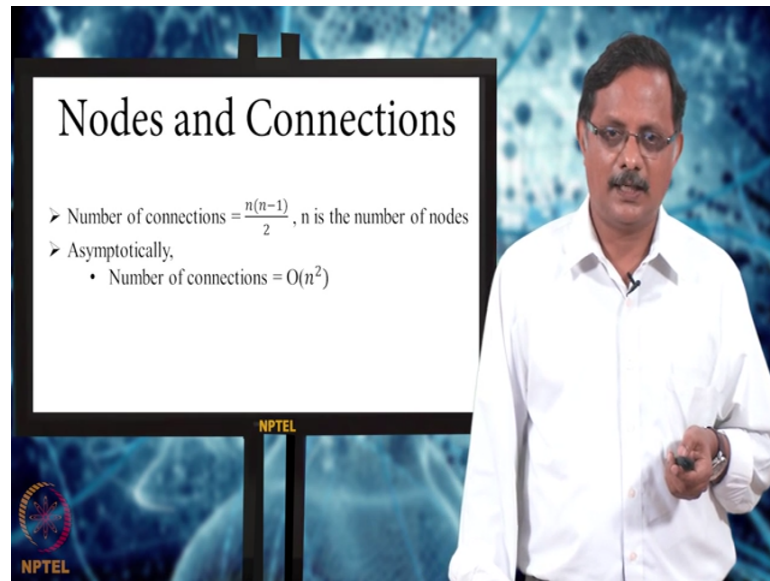
Nodes and Connections

Nodes=6
Edges=15

NPTEL

So, if you take a graph with 10 nodes.

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A man with glasses and a mustache, wearing a white button-down shirt, stands to the right of a presentation slide. The slide has a blue background with a network of nodes and connections. The title 'Nodes and Connections' is at the top. Below it, there are two bullet points: '➤ Number of connections = $\frac{n(n-1)}{2}$, n is the number of nodes' and '➤ Asymptotically, • Number of connections = $O(n^2)$ '. The NPTEL logo is visible in the bottom left corner of the slide.

Nodes and Connections

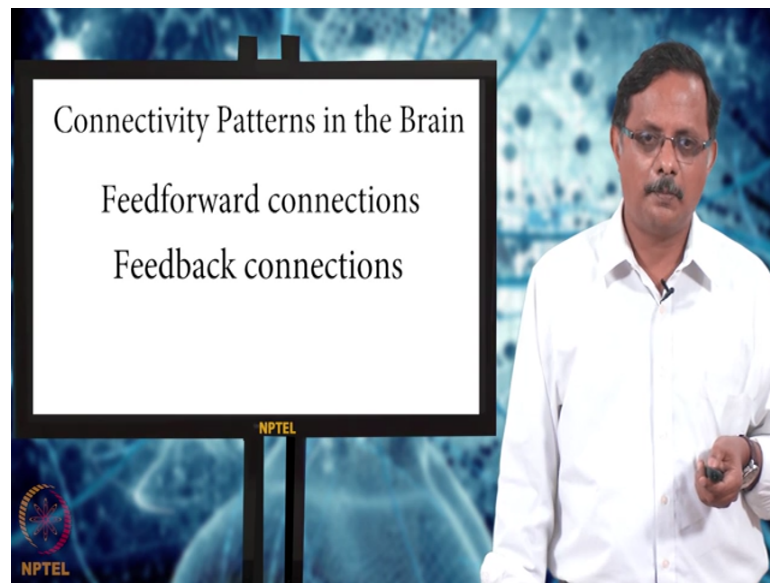
- Number of connections = $\frac{n(n-1)}{2}$, n is the number of nodes
- Asymptotically,
 - Number of connections = $O(n^2)$

NPTEL

You can have totally n into n minus 1 by 2 connection. So, that is about order n squared connections. So, basically if we take a graph in which every node is connected to every other node the number of connections increases n squared where n is the number of nodes.

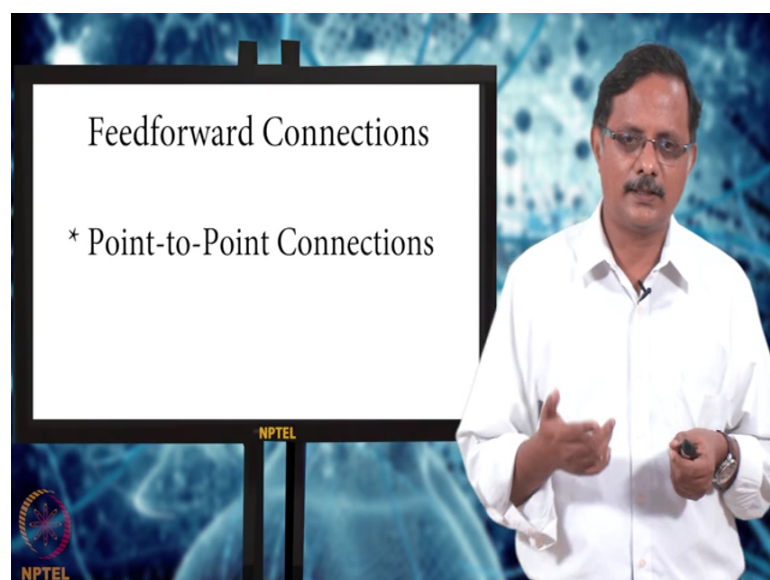
So, in case of real brains every neuron is not connected to every other neuron, but it is right. So, the power is not two, but it is not 1 either it is something between 2 that is it is 1 point 2 three. So, therefore, you can understand why the wiring volume increases right rapidly as the brain size grows.

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Now, let us go deeper into the connectivity patterns in the brain. So, broadly there are two kinds of connected to patterns there are feed forward connection where a region a simply sends projections to region b, and then there are feedback connections very region B sends projections region a connection sends projections to region B and also receives connections back from region b.

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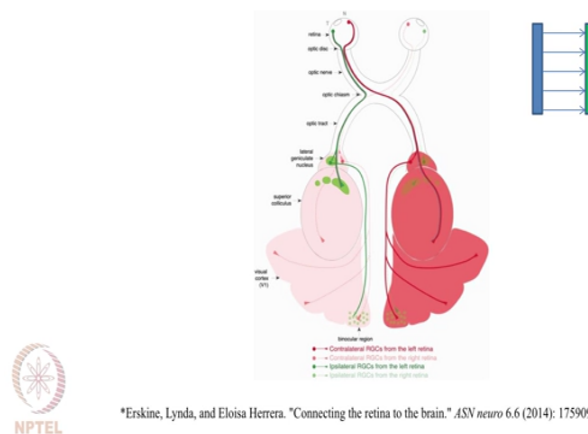


So, let us look at some examples of feed forward connections. So, there are point to point connections where 1 region sends projections to other region B and these present projections are kind of parallel, what does that mean let us look at this example.

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Feedforward Connections

- Point-to-Point Connections

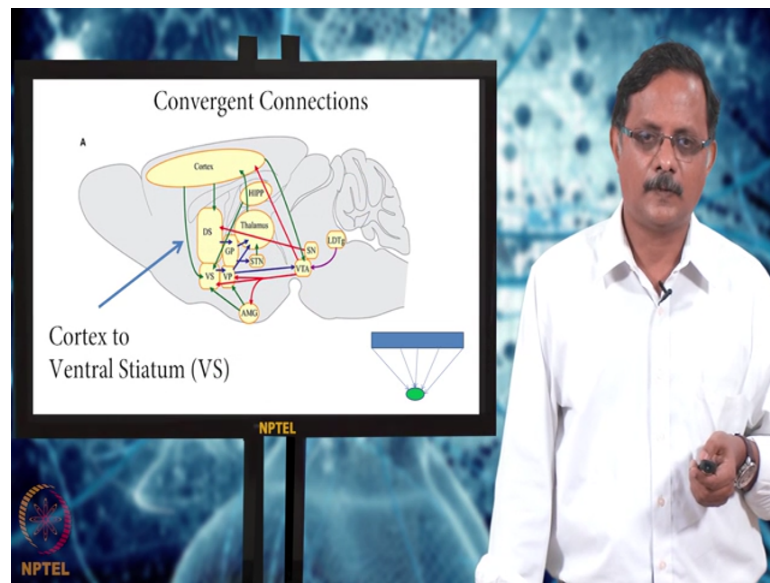


So, what you see on the slide is a wiring very approximate wiring pattern of the wires that take you from the retina, which is inside the eyes right. Where the image this received and captured and surrenders the back of the brain where you have the primary visual cortex.

So, the green line that you see in this image, which takes you from the left eye to the left brain all right, goes through a point on the retina back to a point in the brain, it is only the red line versus 1 point on the retina under the left eye and goes to the back of the brain in the right brain.

So, thing is if you. So, if you flash a dot of light on the retina right that little spot of light activates a very specific small local set of neurons in your primary visual cortex. So, if you move your that dot of light around on the retina that that will activate a series of very specific local set of neurons, right in the primary visual cortex. So, that is what we mean by point to point connections a point on in 1 region of the brain right, will activate a specific point in another region.

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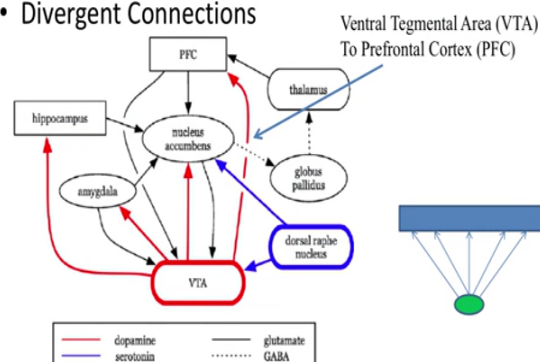
So, then there are converging connections where a large brain area sends projections to a very tiny brain area right. So, that is what is shown in the schematic at the right bottom part of this slide, and one example of that is cortex sending projections to a part of the brain called ventral striatum.

So, cortex is a large area and this item is much smaller it is deep inside the brain. So, these projections are examples of convergent connections.

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Feedforward Connections

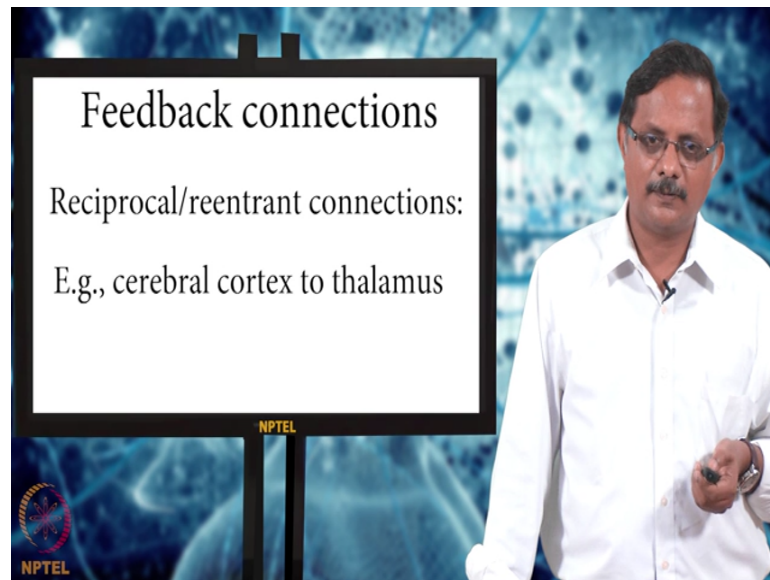
- Divergent Connections



Davey, Christopher G., Murat Yücel, and Nicholas B. Allen. "The emergence of depression in adolescence: Development of the prefrontal cortex and the representation of reward." *Neuroscience & Biobehavioral Reviews* 32.1 (2008): 1-19.

So, then there are divergent connection which are like opposite of convergent connections, where a small brain areas and projections to a large target area. So, an example of that is the ventral tegmental area VTA, setting projections to prefrontal cortex or PFC you sees that red arrow climbing from VTA all the way up to a box named PFC.

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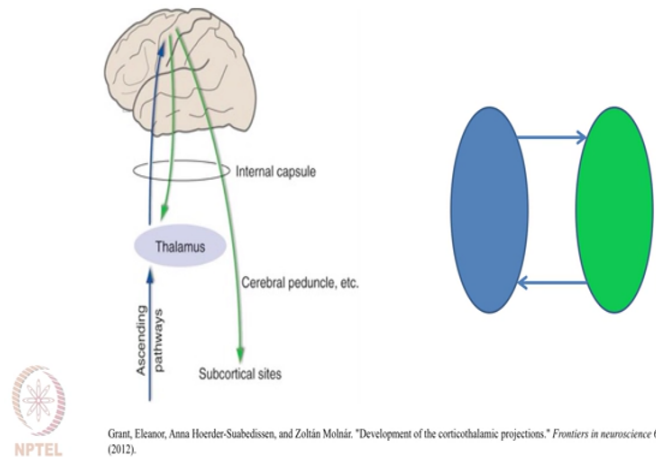


Then if you go to feedback connections that again two categories, there are what are called reciprocal reentrant connections. So, these connections simply go from 1 area a to another area B and go back from area B to area A.

So, it is a simple projection to a destination and written have written fibers back to the source. It is a good example of that kind of connectivity is the connections from cortex to thalamus.

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Reciprocal/reentrant connections

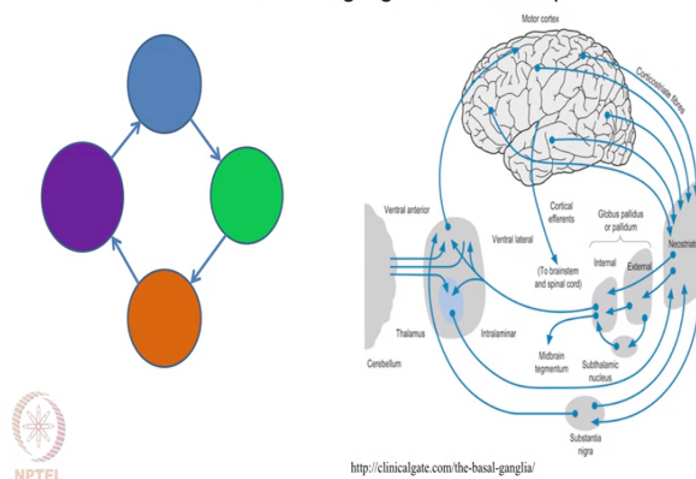


So, thalamus sends free powered projections to cortex and cortex sends feedback to the thalamus then there are more complicated types of you know feedback connections. Where region a sends projections to region b, B sends projections to c, C sends to d, and d sends projections back to the starting point which is the a.

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Loops:

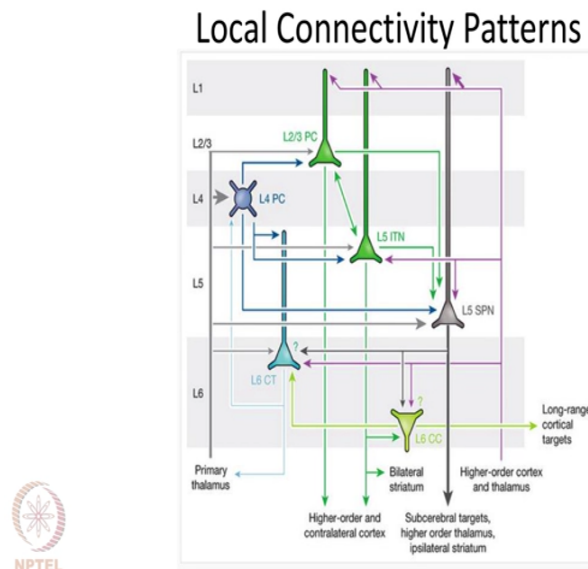
Cortico-basal ganglia-thalamic loop



An example of these kinds of connections is cortex sending projections to a region called newest stratum, which is in the middle to the right part of the image of the slide. And the aside and projects to the Globus pallidus external, or GPE and GPE projects to Globus

pallidus in turn or GPI, and then GPI then projects to the thalamus right and thalamus projects back to the cortex. So, that is a very long loop going over many stages.

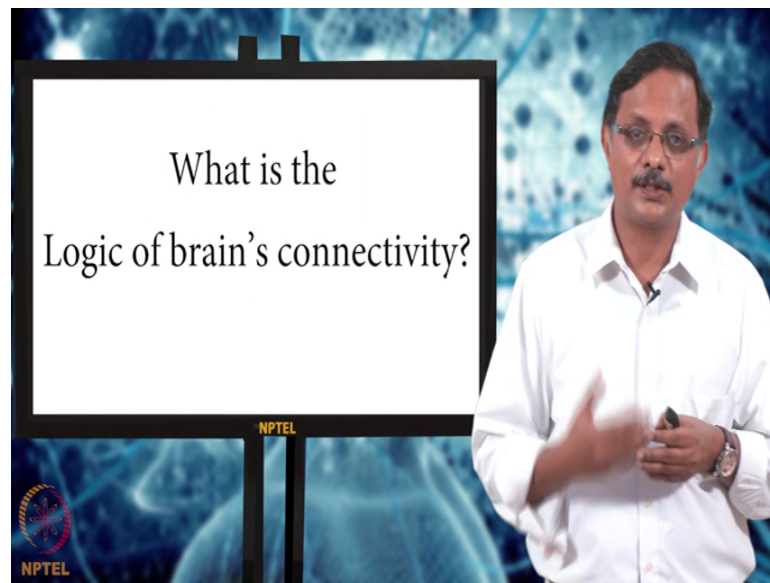
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Then, so the all the connections we have seen, so far are like slightly long range connections right. Whereas, there are also very intricate connectivity pattern at the local level for example, if we look at the cortex, which is a like I said before 2 to 5 millimeter thick sheet of neurons and within the cortex there are 6 layers and.

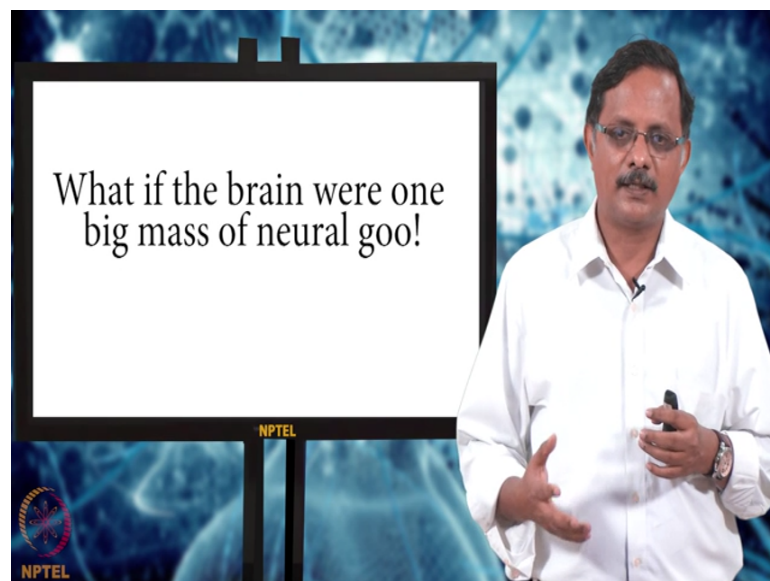
So, as the named as L 1, L 2 and L 6 up to 1 6 and there are neurons in each of these layers and these neurons send projections to neurons in the, neurons in a given layer send projections neurons in the other layers above it or layers below it, and also to neighboring neurons in the same rate. So, these kinds of circuits are called local circuits, so you can see that brain has a lot of interesting connectivity patterns, but the question is why is there this kind of intricate connectivity pattern.

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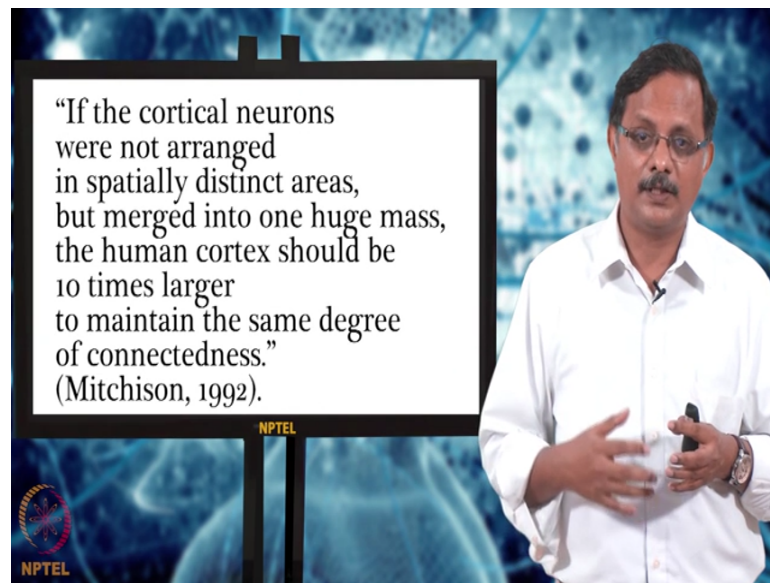
What is the underlying logic of brains connectivity?

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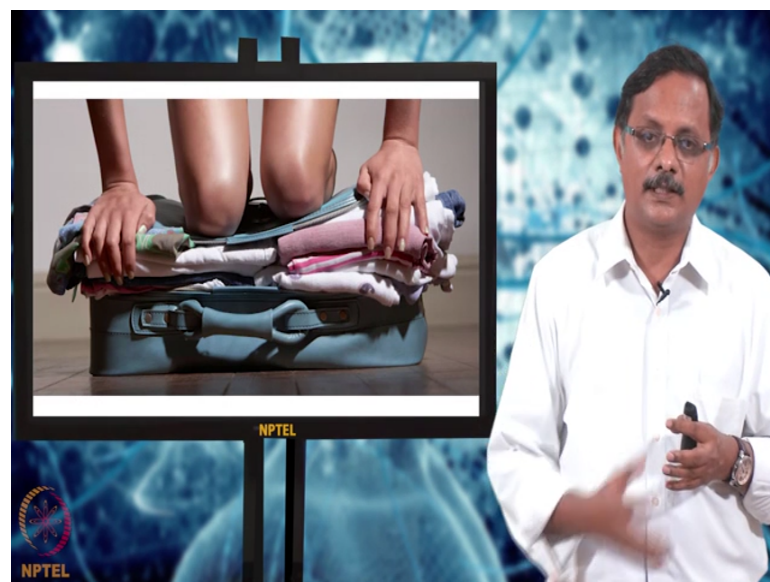
What happens if the brain were just 1 big mass of neural go. So, it turns out that people have done calculations.

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And found that if the cortical neurons were not arranged, in spatially distinct areas I and merged into 1 big huge mass right, the human cortex would be 10 times larger to maintain the same degree of connectedness.

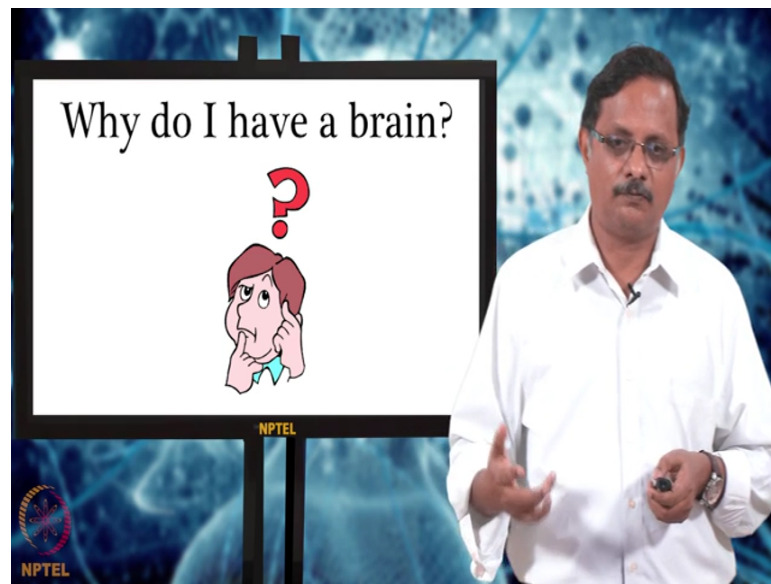
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This is something that you experience even when you pack your bags, when you go on a (Refer Time: 10:59) travel, but you have a bunch of things that you need to pack in a box. If you just put them in some kind of a random order right they start spilling out of the box. So, you need to pack them very judiciously optimally.

So, that everything and going to the box and apparently the even courses that which teach you how to packs you know packed boxes. So, that you can pack a lot of stuff in the same volume, so brain seems we are doing something like that and evolution seems you are pushing brain to pack the contents of the brain more optimally more efficiently within the volume of the cranium. So, to understand the logic of this kind of packing we need to ask first of all.

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What is a brain? What is the purpose of the brain? Why do we have a brain? Right to understand that let me take a small example.

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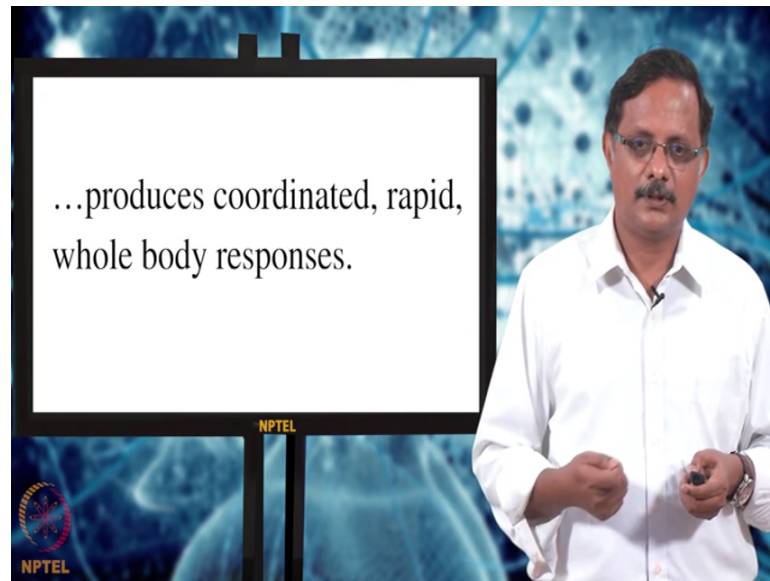


So, let us say you are walking and you know accidentally you step on a pin, right it hurts and then you withdraw your leg let us say it is left foot from the pin. Now when you do that if you just withdrew your left foot, and if you did not do anything else right then you would not have a fall because.

So, until then your body weight is was being supported by both the legs, and if you suddenly do your left foot right then your right foot may not be ready to take all the weight and you are going to have them fall. So, in order to for this withdrawal of the leg to work right you need to make sure that the left leg can immediately take all the weight of the body. And for that to happen the left leg muscles have to tighten, the antigravity muscles of the right leg will have to tighten. So, that the leg now can take the entire bodyweight.

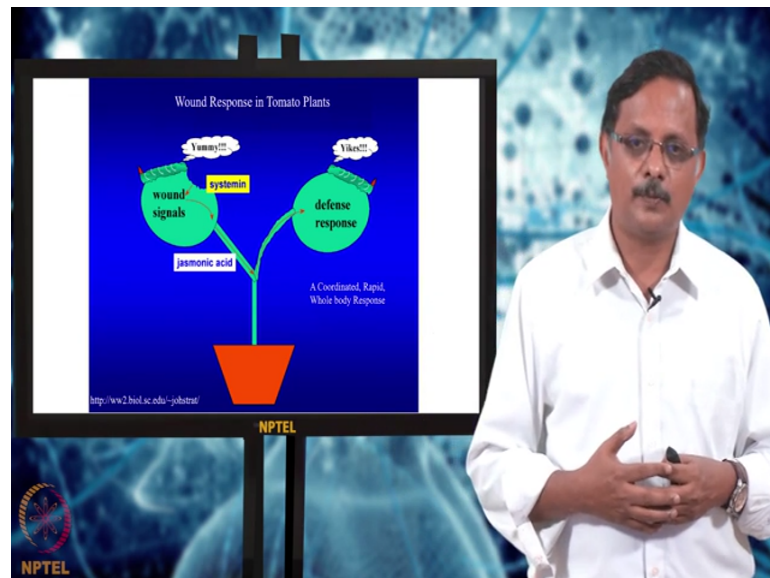
And that is not enough you need to also shift the body weight to your right side. So, that all the weight goes through the legs through the right leg and sometimes you may even have to stretch your arm. So, that you balance yourself and you would not lose balance you might even have to tilt your head. So, if you think about it a very tiny microscopic stimulus like the pin right.

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Is producing a whole body response, right integrating your entire body that is possible only because of your brain the brain is doing all this coordination. So, as you are stepping on the pin seems to produce a coordinated rapid whole body response. Let us take another example.

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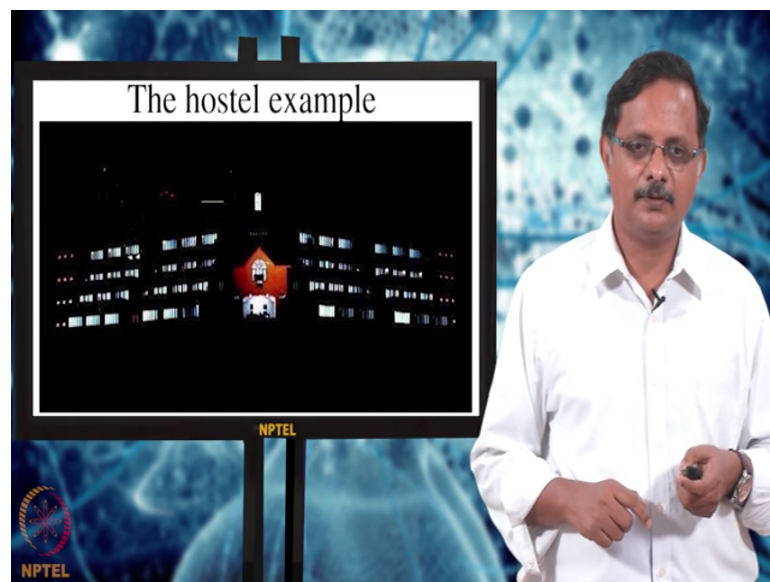


So, it is not just humans animals, but even plants seem to be capable of producing such you know large scale coordinated responses. So, take the example of a tomato plant in

this picture you can see a worm eating a certain leaf on the tomato plant. So, when that happens the plant launches a defense mechanism.

So, the leaf where which is being wounded releases a chemical which is harmful to the worm that is eating it. And this release chemical not only is at least locally within the that leaf, which is wounded the substance spreads all the way to the or the entire body of the plant. So, that at a distant location later on if another worm starts attacking the plant, right the newly released toxin will be harmful to the bug and the prevented from wounding the plant further. So, even a plant is able to produce a coordinated rapid either a time scale of the plant I suppose, but a coordinated extensive whole body response.

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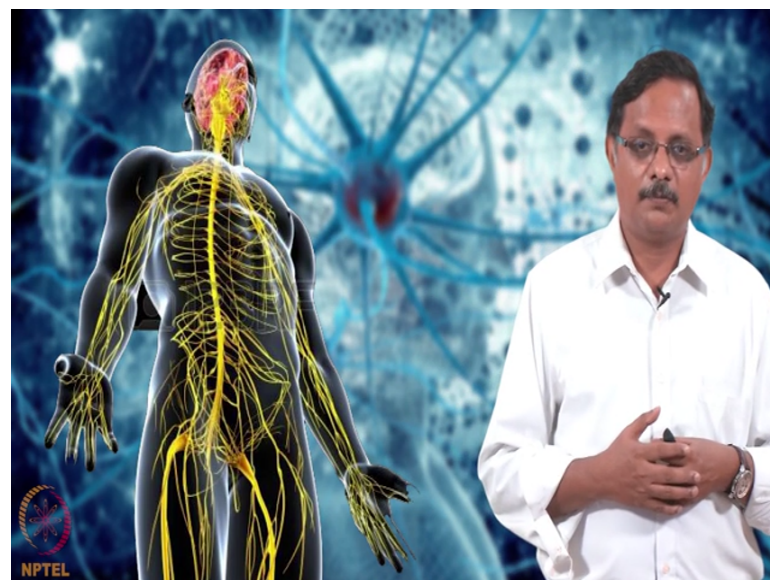
Let me take 1 more, example something that is more probably related to the experience of lot of students here. I am sure a lot of you live in hostels and let me just consider a situation which is not uncommon in hostels. Right imagine 1 fine night and you are all sitting along with your friends in the hostel wing and having a good time doing something that maybe you're not supposed to do at that time of the night.

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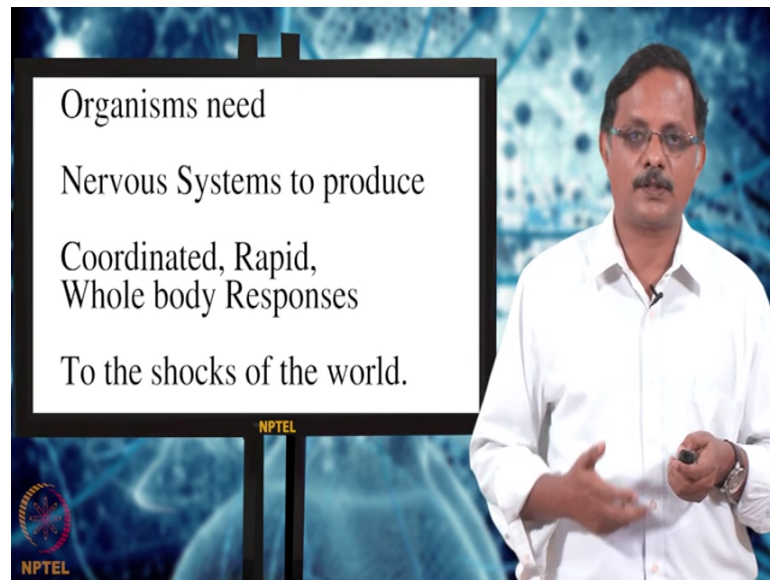
Then then suddenly the warden walks into the hostel, right and somebody in the ground floor sees the warden coming in and then (Refer Time: 14:43) sends a text right to some of his friends right. Who lives in the same hostel, and the guys who receive this message then further send this messages to few more friends and quickly the news that the hostel warden has just entered has come for inspection all right spreads all over the hostel. So, in this example you can see the hostel has produced a coordinated rapid whole hostile response ok.

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Now, that is what you need for a brain to do for the body right, for the body to survive right in a very hostile environment. It needs to have some kind of a communication network, which is spreaded all over the body and which can help enable communication rapidly to take place from 1 part of the body to another.

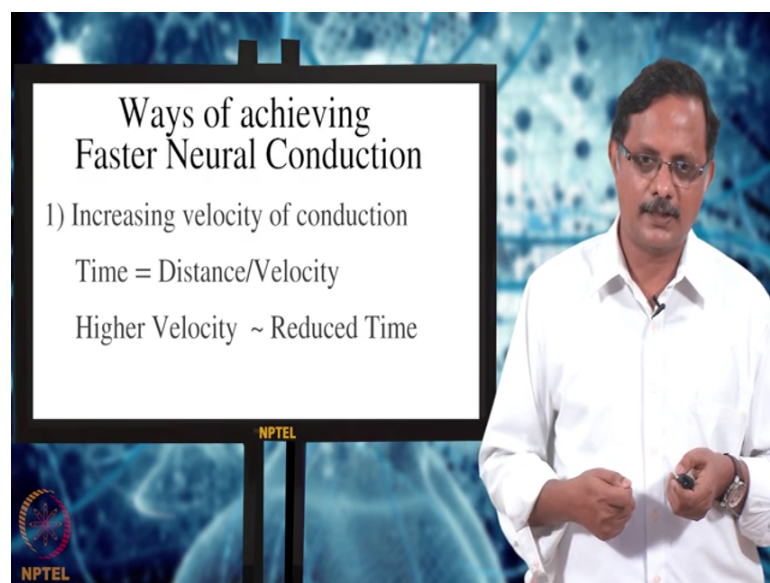
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Organisms need
Nervous Systems to produce
Coordinated, Rapid,
Whole body Responses
To the shocks of the world.

So, organisms need you know systems to produce coordinated rapid whole body responses right to the shocks of the world.

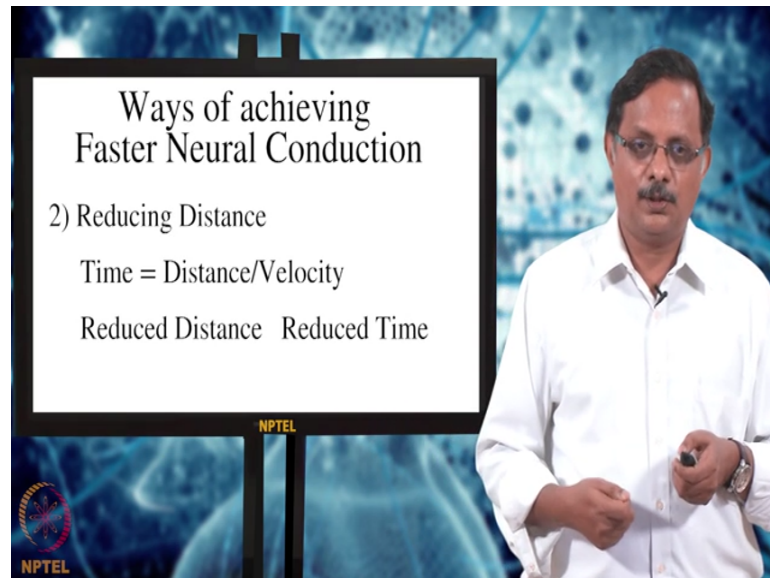
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Ways of achieving
Faster Neural Conduction
1) Increasing velocity of conduction
 $\text{Time} = \text{Distance} / \text{Velocity}$
Higher Velocity ~ Reduced Time

Now, how does a body produce you know produce this kind of responses, what how does a nerve system give the body these kinds of rapid responses. So, there is two ways of doing it right. So, if you want faster response basically time is distance by velocity. So, there are two ways to reduce time, 1 ways to increase velocity. So, that will reduce the time.

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**Ways of achieving
Faster Neural Conduction**

2) Reducing Distance

$\text{Time} = \text{Distance} / \text{Velocity}$

Reduced Distance Reduced Time

The other way is reduced distance, what does that mean and how do you achieve it let us look at that. Let's look at the first solution increasing the velocity of neural conduction.

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Increasing Velocity of Neural Conduction

Increasing fiber diameter → increases conduction velocity

Type	Schematic	Diameter (μm)	Velocity (m/s)
Thick Myelinated (Type A)		6-12	35-75
Thin Myelinated (Type B)		3	3-15
Thin Unmyelinated (Type C)		0.2-1.5	1-2



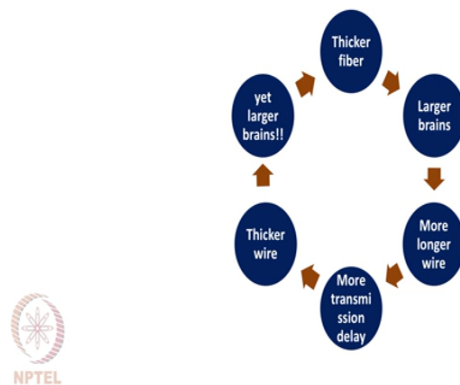
Now, it turns out that if we want to increase the velocity or conduction if the biophysics of nerve fibers tells you that, if you increase the fiber diameter that will increase conduction velocity. So, there are different kinds of nerve fibers there are these thick myelinated nerve fibers called type A, and then thin myelinated nerve fibers are type B fibers, and thin unmyelinated nerve fibers nerve fibers or type C fibers.

So, type A fibers have a diameter of you know 6 to 12 microns and velocity is about 35 to 75 meters per second, and type B thin or thinner, and the 3 microns diameter and velocity is 3 to 15 meters per second and the type C or even thinner and even slower. So, basically as you increase our diameter you got higher conduction velocities.

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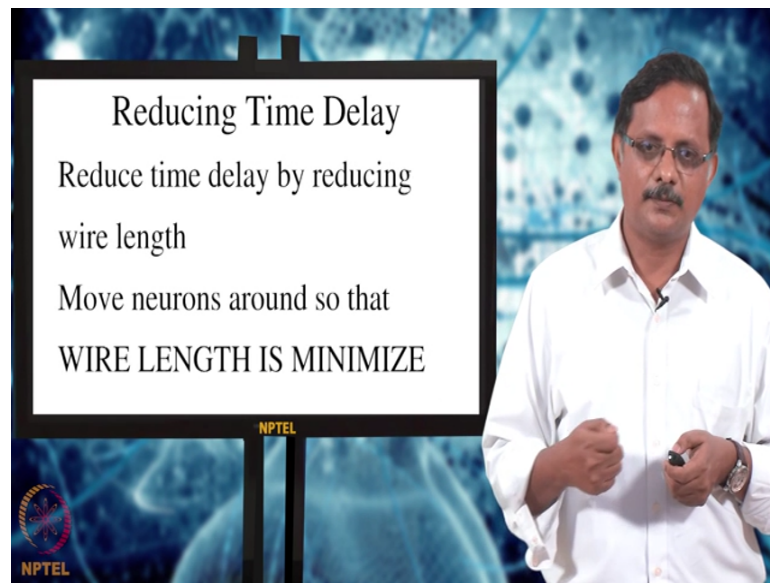
Issue with the approach of Increasing Velocity of Neural Conduction

Increasing fiber diameter → increases conduction velocity



But there is a problem with this approach to achieving faster communication, because if you use thicker fibers to achieve a higher conduction velocity and that will make the brains larger. And that will require more wire to connect these right various points in these larger brains. So, that will create no longer transmission delay and to compensate for that you use even thicker fiber and then you get even larger brains and so on, so forth.

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Reducing Time Delay

Reduce time delay by reducing wire length

Move neurons around so that

WIRE LENGTH IS MINIMIZE

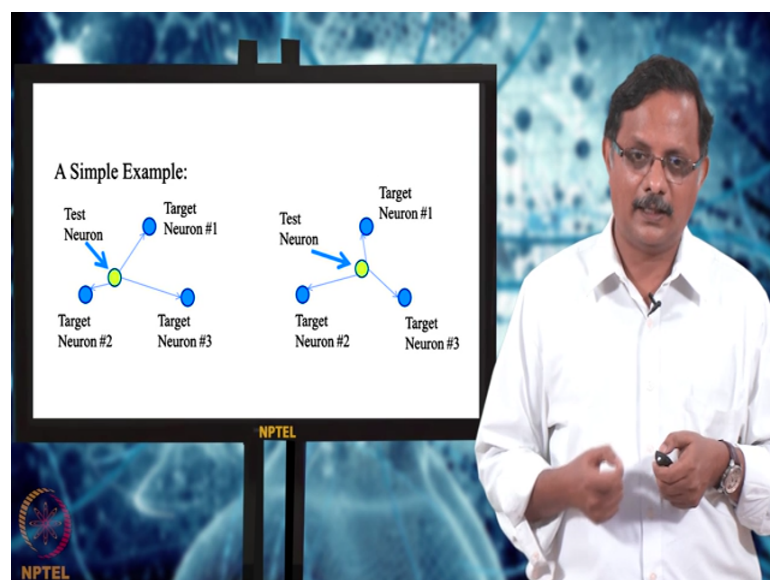
NPTEL

The slide features a speaker on the right and a whiteboard on the left. The whiteboard contains the text 'Reducing Time Delay', 'Reduce time delay by reducing wire length', 'Move neurons around so that', and 'WIRE LENGTH IS MINIMIZE'. The NPTEL logo is visible at the bottom left of the whiteboard.

So, you have a kind of a catch (Refer Time: 17:17) situation, where this approach does not seem to be very efficient way of reducing time delays.

The other way of reducing time delay is to reduce wire length, what does that mean I look at this simple example shown in the lower part of the slide.

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A Simple Example:

Test Neuron

Target Neuron #1

Target Neuron #2

Target Neuron #3

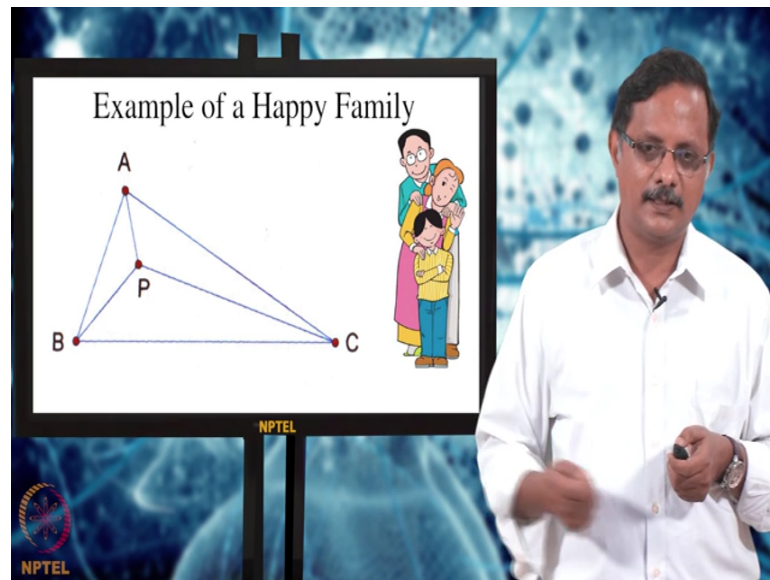
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The slide features a speaker on the right and a whiteboard on the left. The whiteboard contains the title 'A Simple Example:' and two diagrams. Each diagram shows a green 'Test Neuron' connected to three blue 'Target Neuron' nodes (labeled #1, #2, and #3). The left diagram shows the test neuron in a central position, while the right diagram shows it moved closer to Target Neuron #1 to minimize total wire length. The NPTEL logo is visible at the bottom left of the whiteboard.

So, you have 3 target neurons, target neuron 1, target neuron 2, and 3, and then there is a test neuron which is a green neuron. Now you are free to put wherever you want this test neuron, but you would like to place it. So, that it is the total wire length connecting the

test neuron to the their target neurons is minimum. So, if you do that the total transmission delay for connecting all these 3 you know the test neurons to the other 3 neurons, will be minimized now something like this you can relate to real world experience also.

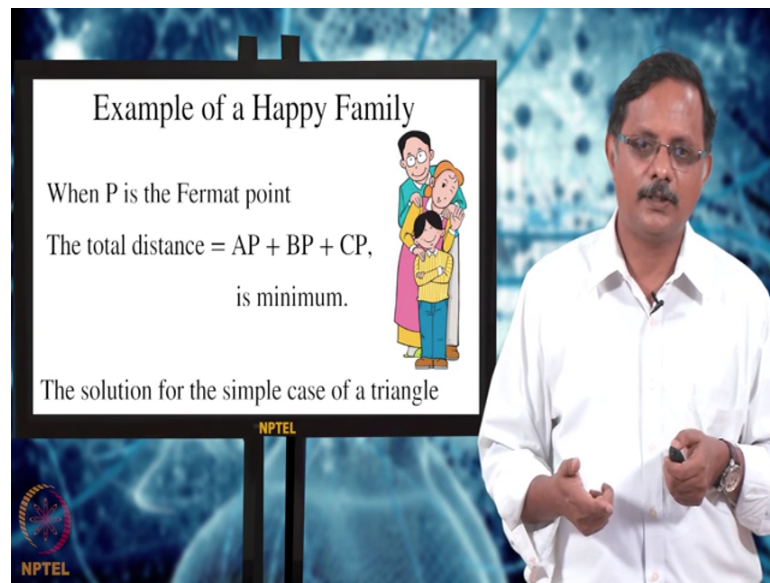
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Consider the problem of this happy family that that lives in a city and. So, there is a mom there is a dad and then there is a kid now they want to decide where to pick and choose their home, so that they all can go to their respective workplaces right.

So, the mother works at workplaces at A, and kids school is at B, and father's workplaces at C. Now P is where they want to live now where will you put the P in this, but the place the point P in this triangle.

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Example of a Happy Family

When P is the Fermat point
The total distance = $AP + BP + CP$,
is minimum.

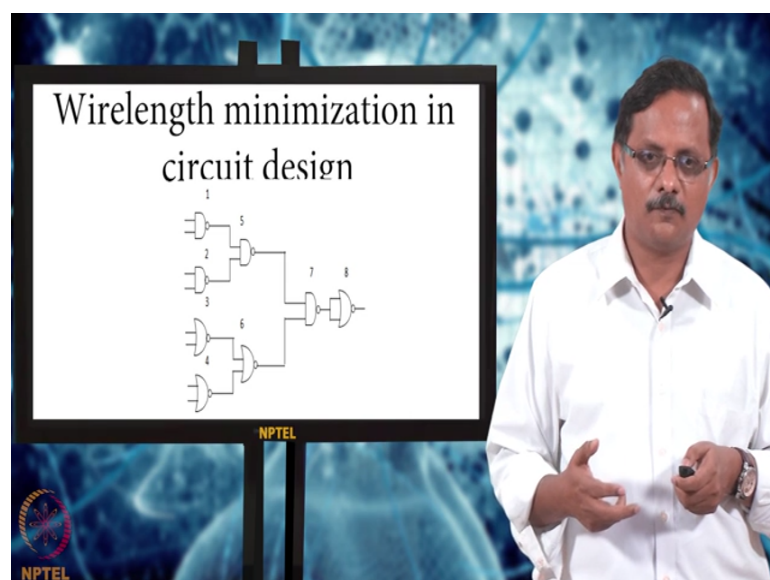
The solution for the simple case of a triangle

NPTEL

The slide features a cartoon illustration of a family (father, mother, and child) on the right side. The background is a blue abstract pattern. The NPTEL logo is visible in the bottom left corner.

But; obviously, will place it. So, that the total distance AP plus BP plus, you know CP is minimum, because assuming that the travel costs are the same which are you travel right this is what you would like to do. Now this problem has been solved in geometry a long ago and this is the scalar point is called a Fermat point of a triangle right, and there are ways of constructing the location of the point P these kinds of.

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Wirelength minimization in circuit design

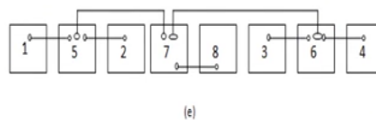
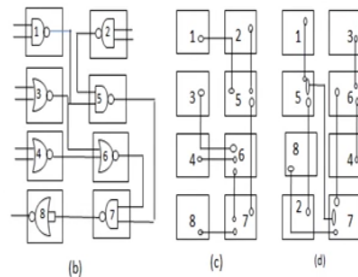
The slide displays a logic circuit diagram with 8 numbered inputs (1-8) and 2 outputs (7, 8). The circuit consists of several logic gates (AND, OR, NOT) connected in a way that minimizes wirelength. The background is a blue abstract pattern. The NPTEL logo is visible in the bottom left corner.

Problems where you try to minimize the total wire length are often encountered by electrical engineers; when they design their you know logical circuits on chips.

So, let us look at the figure a in this slide and where you are you are looking at a logic circuit, right you see all these logic gates and you know they are numbered from 1 to 8.

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Wirelength minimization in circuit design

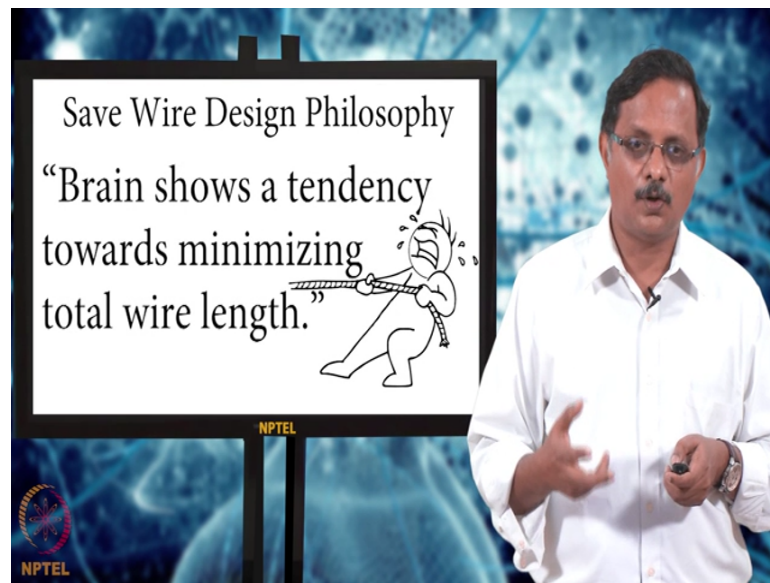


Wire length for (c) or (d) = 10; wire length for e = 12.
(c) or (d) are preferred over (e).

So, b is actually just a logical placement of the gates of figure a, in various boxes c shows 1 particular configuration right, by which these logic gates are dissipated in the boxes and if you look at the total wire length in c right it adds up to 10.

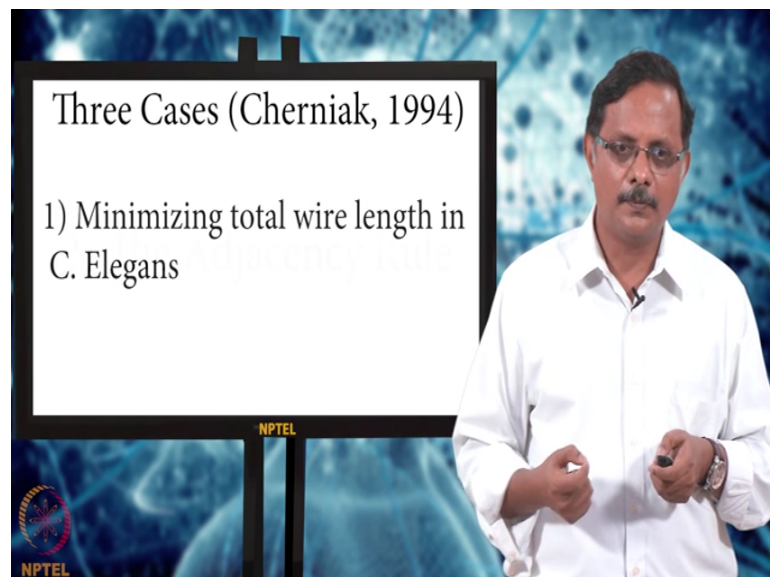
So, similarly even in d, the total wire length adds up adds up to 10, but instead of organizing the gates in 2 columns, if in organize them as this has 1 big long row right, as shown in figure e, the total wire length that you get happens to be 12. So, if you want to minimize the wire length right c or d are preferred over the configuration e.

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So, these ideas are relevant to even understanding brain structure you know how wiring is organized or is being is organization brain structure, because it turns out that brain shows a tendency towards minimizing total wire length this is this called save wire principle of brains organization.

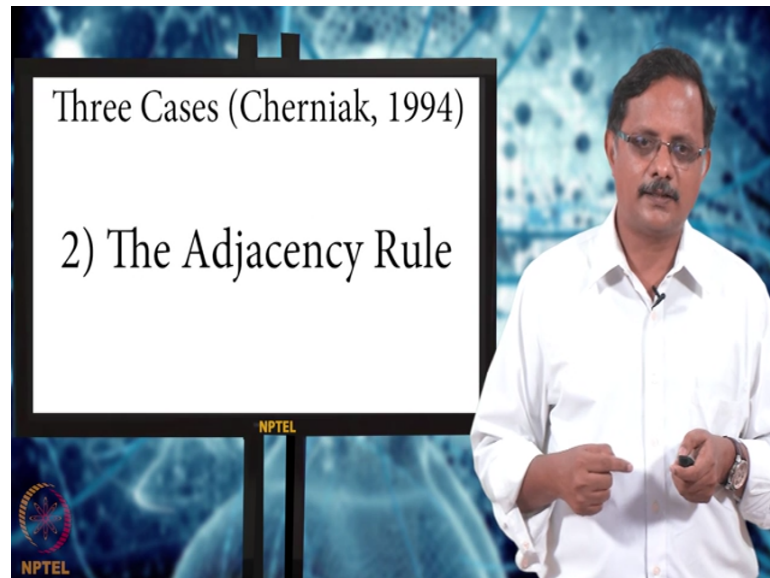
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Now, there is a lot of evidence to support this kind this principle and I will just look at 3 examples, taken from this paper by the study by cherniak, a paper is published in 1994.

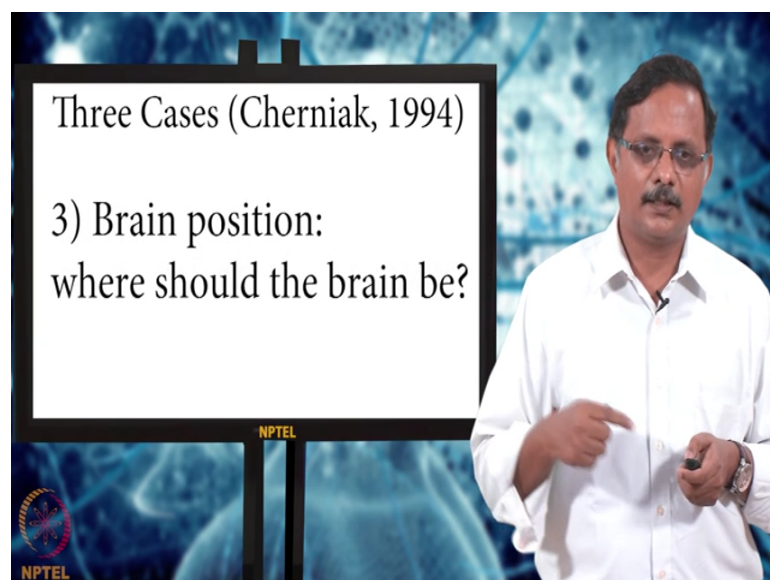
So, in the first of the examples we show we take a small worm called C Elegans, and show that the total wire length is minimized in a nerve system of this worm.

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In the second example we show that the adjacency rule which has is consistent with the save wire principle I is respected in (Refer Time: 20:55) animal brains.

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And the third principle, we argue about the placement of brain position we ask the question why is the brain positions in post position in the head and what is its implication to the question of save wire principle.

(Refer Slide Time: 21:12)

1) Minimizing total wire length in C. Elegans



Common name: Nematode
Length: 1 mm
Diameter: 80 microns
Nervous system has 302 neurons
Connectivity completely mapped out
Excellent model organism for
Neuroscience research

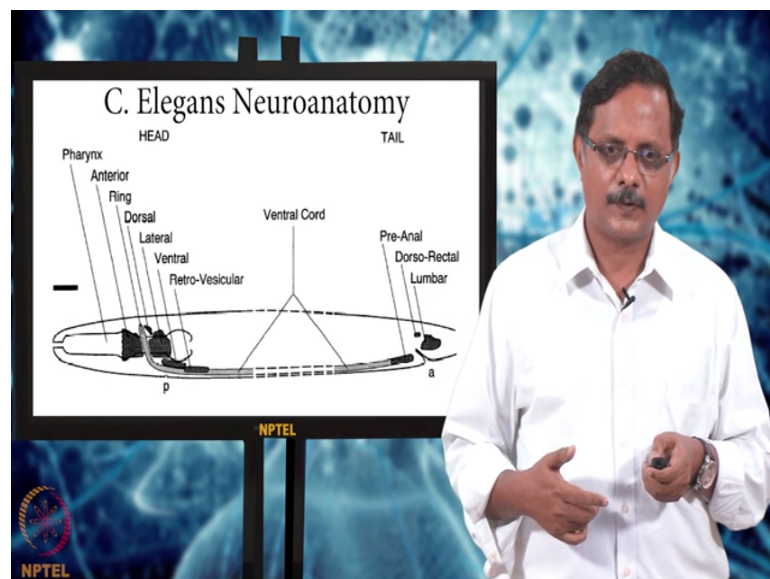


https://en.wikipedia.org/wiki/Caenorhabditis_elegans

So, in this animation you see the C Elegans, nerve it is a small worm its common name is nematode it looks kind of creepy, but actually it is a very small worm its length is only 1 millimeter it is only 80 microns thick. So, it is, so small that you need a microscope to look at it in a culture or in a dish.

So, it has a very small nervous system it has exactly 302 neurons, and the connectivity pattern of all these neurons has completely worked out. So, it is an excellent organism for studying nerve systems and connectivity patterns in neuroscience.

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Here is a simple cartoon picture of various ganglia that are located inside this in nerve system. So, their various names given to the ganglia are going to get into that.

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Table 4. Connectivity matrix for 10 ganglia of *C. elegans*

	To:	Head (187 n)								Tail (39 n)					
	Head sens.	PH 20	AN 36	RNG 0	DO 6	LA 64	VN 32	RV 20	V VC 58	PA 12	DR 3	LU 24	Tail sens.	Totals	
Pharynx		mc: 11													
PH	(13)	18.5												31.5	
Anterior				mc: 12											
AN	32	2		36										70	
Dorsal															
DO	4			6					mc: 1	1			1	12	
Lateral			mc: 10			ps: 4									
LA	28		64			12	2	12	8	5	4	10.5		145.5	
Ventral			mc: 12						cp: 15						
VN	2		32	3		2.5		1.5		2	2	3		48	
Retrovesicular															
RV				8		12	5	16	12	2	1	2.5	1	59.5	
Ventral C									mc: 58						
VC							2	13	53.5	11	2	2		83.5	
Prenatal									mc: 1	mc: 9					
PA				2		2	2		8.5	11	2	4.5		32	
Dorsorectal											mc: 1				
DR				3		1	3	2	1	3	1	1		15	
Lumbar									mc: 2						
LU				11		17	6	10	5	12	10	19.5	14	104.5	
Totals	79	20.5		162	3	46.5	20	54.5	88	47	22	43	16	601.5	

Each cell gives number of fibers (not synapses) from ganglion in designated row to site in designated column. m, muscle connections; ps, posterior sublateral processes; cp, cord processes. Fiducial points: p, excretory pore; v, vulva; a, anus. Symmetrical gap junctions count as 0.5 synapse for each participating ganglion. See Results for nonreciprocal connections.

And this table tells you which ganglia is connected to which other ganglia and how many fibers connect a pair of ganglia.

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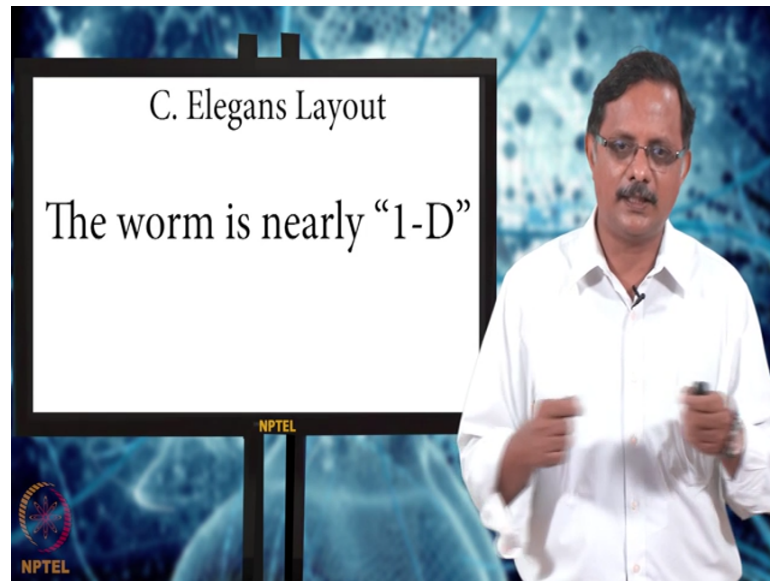
C. Elegans Layout

A network of 11 (10 + 1) ganglia



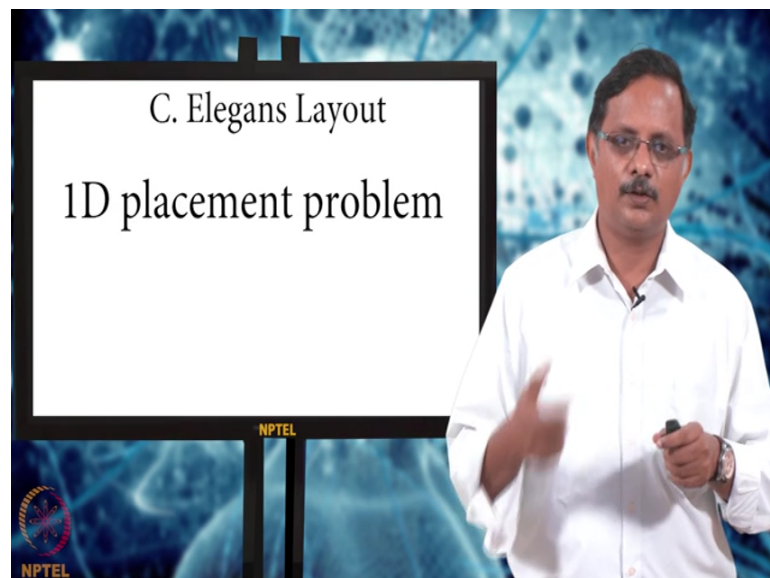
They are totally 1 plus 10 or 11 ganglia, there's a head ganglion and then all the other ganglia.

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So, now if you think of the body of the worm has 1 dimension because it is very thin compared to its length. So, the ganglia are placed along the length of the body of this worm right. So, now you can so imagine that given the connectivity pattern of all this ganglia, you can move around the ganglia anywhere inside the body right and calculate the wire length of the internal system, so the connectivity is fixed.

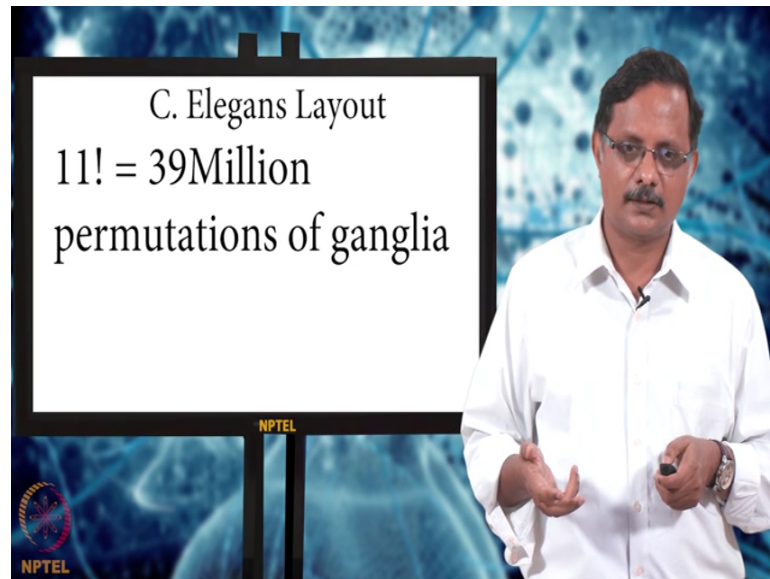
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But the placement is it can be varied and for every configuration of the ganglia you can look at the total wire length.

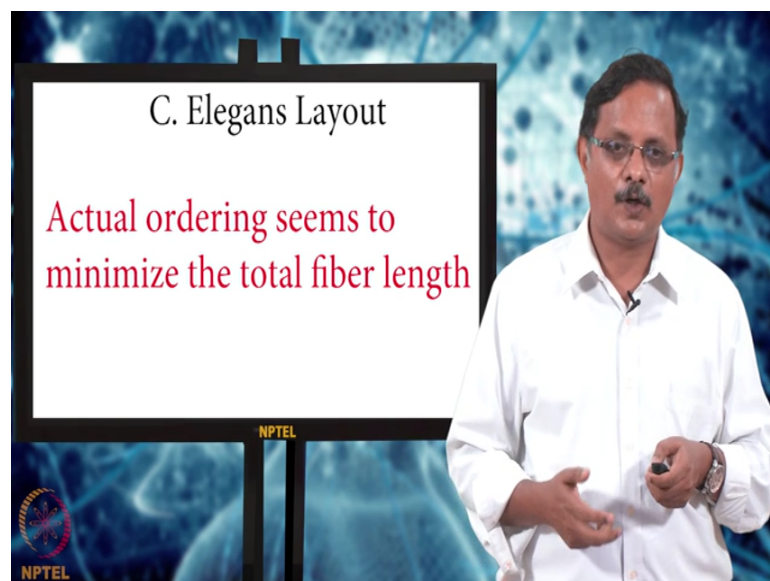
So, assuming that the ganglia positions are fixed only the relative ordering is can be varied right.

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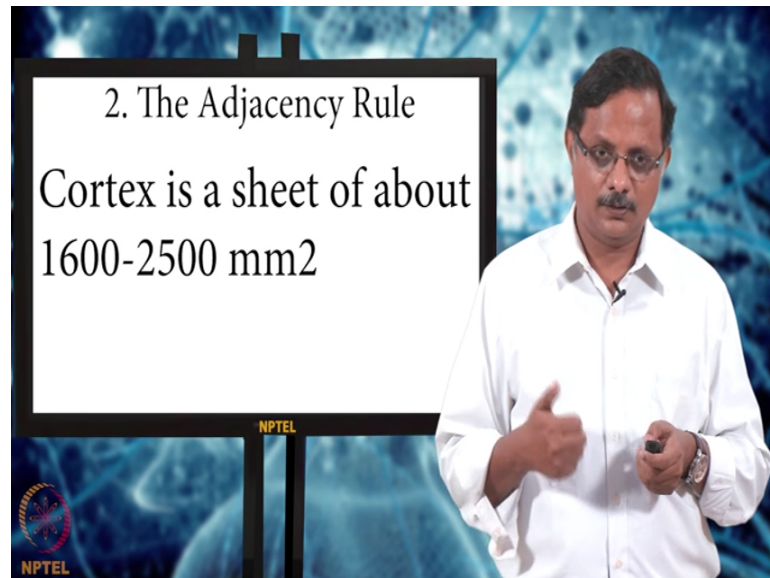
So, these 11 ganglia can be permuted, along these 11 possible positions, in 11 factorial ways, that suppose a team in million permutations it turns out that.

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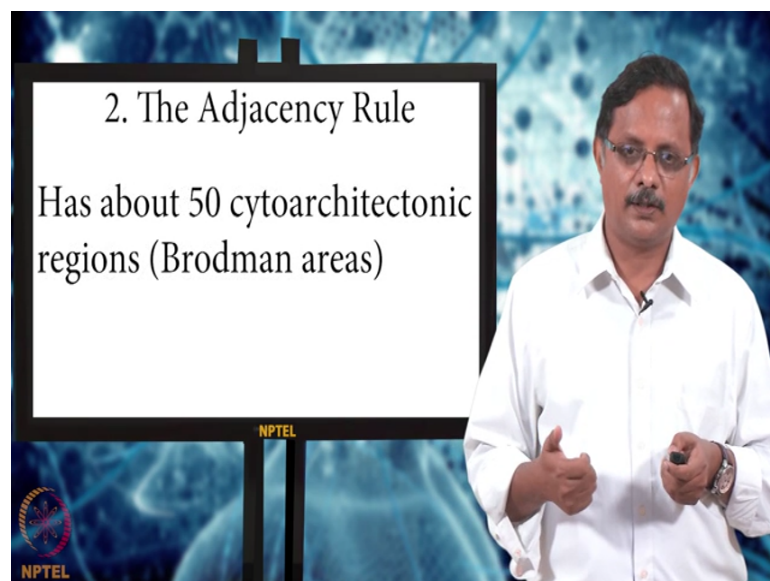
The actual configuration of the C Elegans, right has a minimal wire length. So, which is a pretty interesting it is almost as if an engineer has designed nerve system of C Elegans.

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Then let us look at the adjacency rule right to explain this rule or to define this rule we need to understand the organization of the cortex. So, cortex in human brain is about 1600 to 2500 millimeter square in a total area.

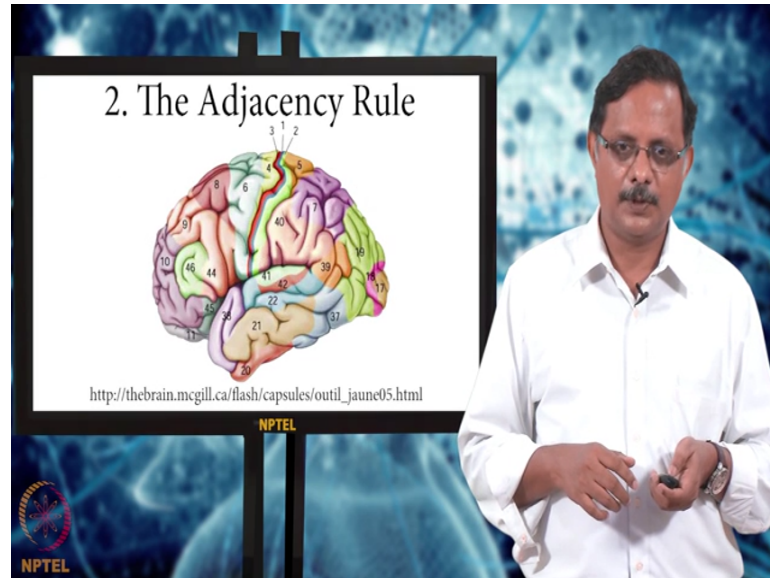
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It is about 50 cytoarchitectonic areas, these are called brodman areas. So, cytoarchitectonic sounds kind of pretty fancy, but basically it is like a cellular geographic

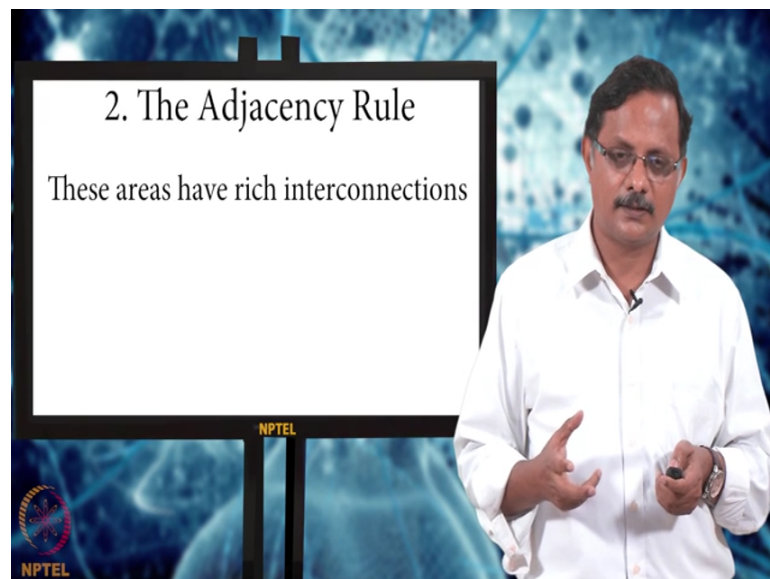
region. So, these are certain regions and thus in the surface of the cortex which can be seen in this picture.

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So, this classification of brain regions is based on the analysis of the cell types or neuron types formed in a given in different parts of the brain surface all right. So, they are numbered from 1 to 50.

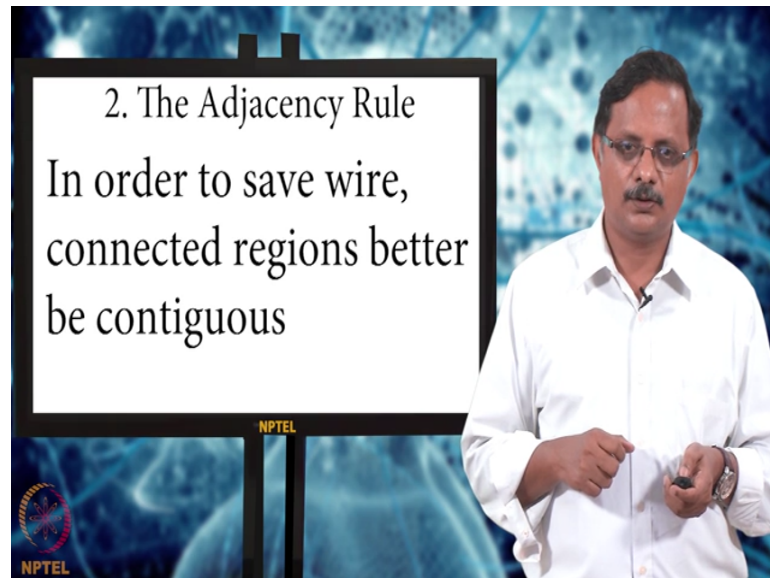
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They are easily connected; now thing is if you assume if you want to prove that the connectivity of the cortex of the cortical regions satisfies some kind of a bad

minimization principle, like it makes sense to make sure that the current nearby regions are connected.

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That is connected regions better be contiguous then you can minimize wires. So, let us look at the data from cats visual cortex.

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Cat visual cortex areas (18)			
Contiguous pairs			
	Yes	No	Total
Connected pairs			
Yes	70	108	178
No	0	128	128
Total	70	236	306
Significance of effect	$p < 0.0001$		
Magnitude of effect	$r_s = 0.46$		

(Cherniak 1994)

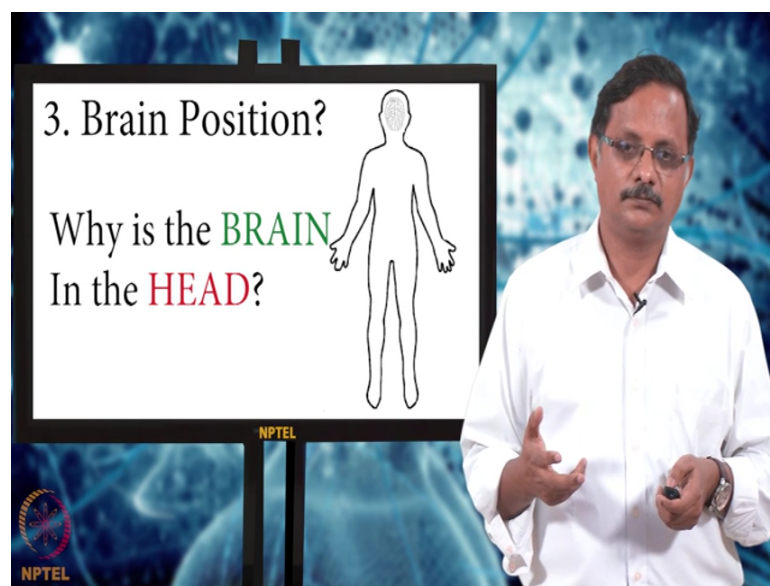
Contiguous cortical areas are more likely to be connected!

So, and on the rows you can see the connected pairs number of, so they are totally eighteen regions which are considered in this study and in the rows you see there whether the connected in the pairs of regions are connected or not connected, in the

columns you see whether they are contiguous or not contiguous. So, there are totally 70 contiguous pairs which are also connected.

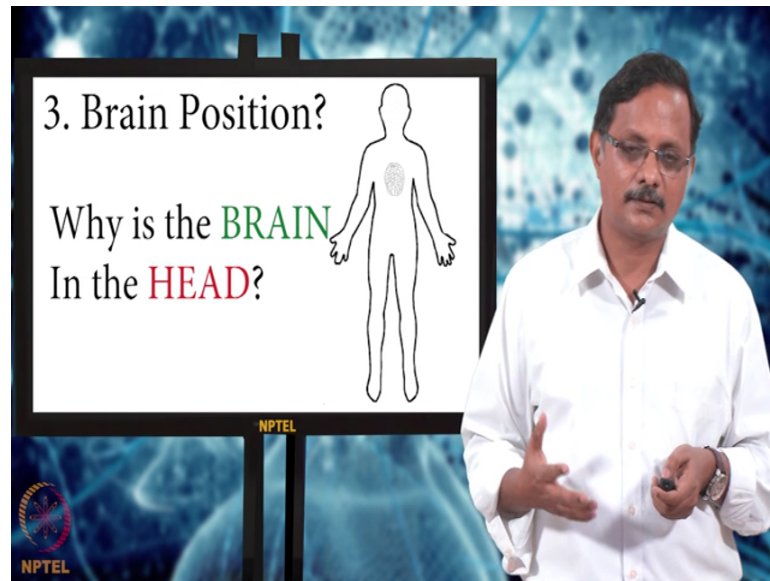
All right and 100 and 8, non-contiguous pairs which are connected, and there are no contiguous pairs which are non-connected not connected and then there are number of cases where the pairs are not contiguous and not connected also very big 128. So, basically it shows that if cells are contiguous they are completely they are always connected. So, that is consistent with the save wire principle.

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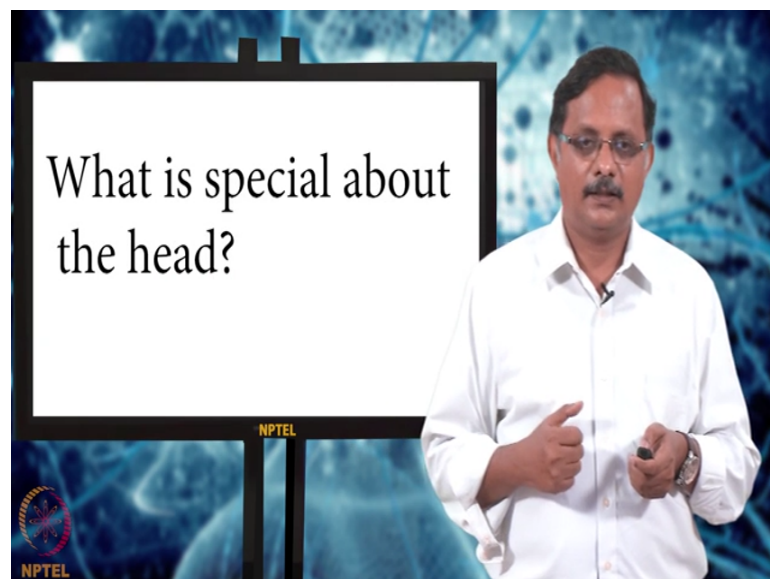
Now, let us look at the third question the question of brains position. Now, what is the question? What is the problem with brains position; well 1 interesting question you can ask is why is the brain inside the head alright why cannot it be somewhere else inside the body for example.

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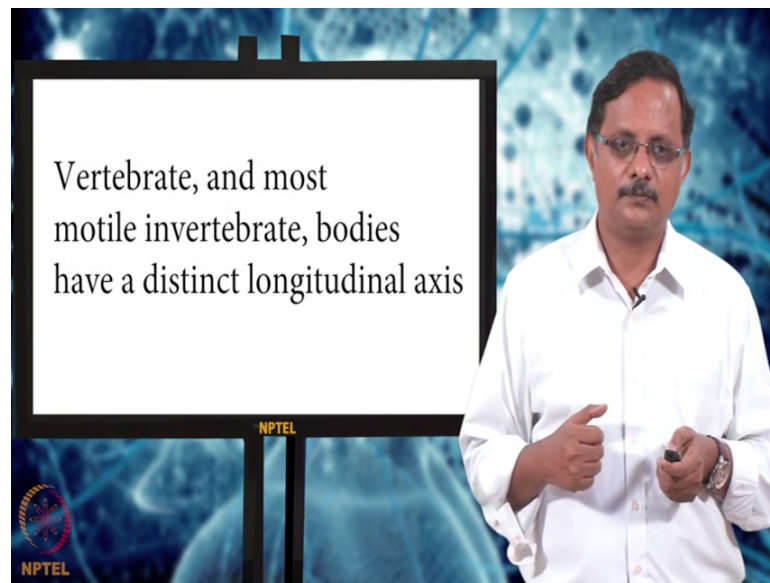
Inside the chest, because if you argue that brain is better a better place inside the head because it is better by the skull which is hard you know this bony casing of the brain, but that argument is not quite valid because the head is vulnerable because of the neck and neck is vulnerable. So, you are probably better off placing the brain inside the chest right, but why is the brains at the head to us answer this question we need to first ask.

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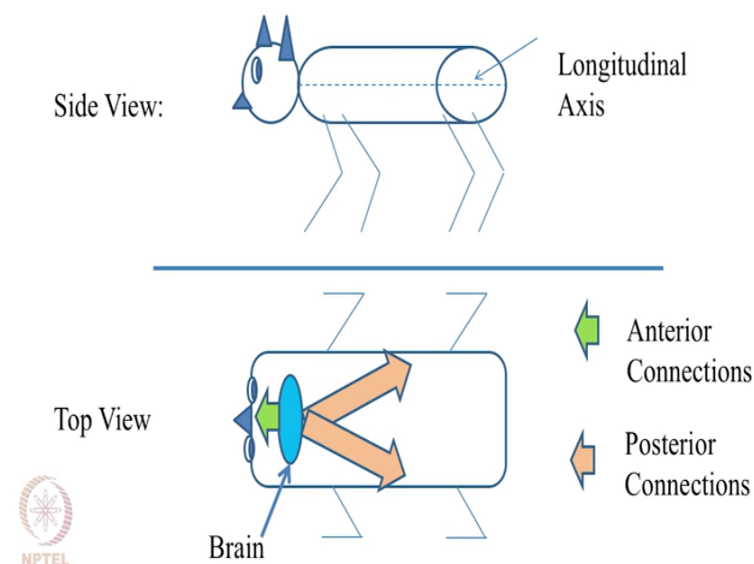
What is the head what is what does a head mean what is special about the head right. So, we know that.

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Both vertebrate and most invertebrate bodies have a distinct longitudinal axis that that kind of like a tube right and the head is usually the place where right. So, it is a frontal most part of this kind of a tube like body.

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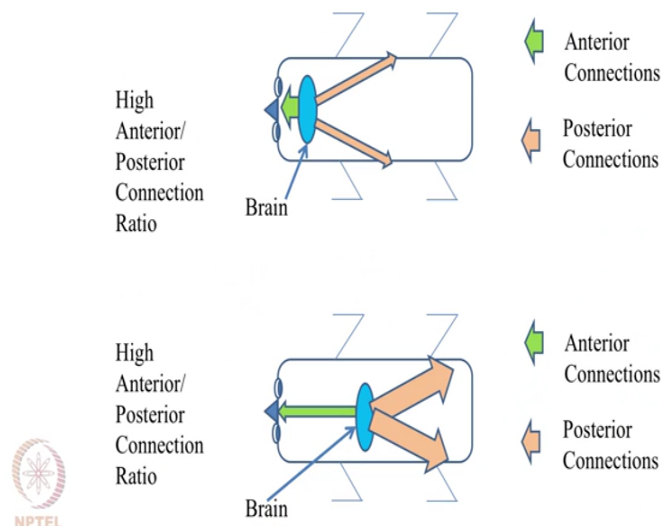
Right, let us look at a simple schematic, so on the top of this slide you see kind of a cartoon like animal, who's just a tube like body and then you can see the longitudinal axis right and the body is parallel to the red to the horizontal. So, now, once you have a body which is like a tube, right and this body is moving through the world and because

what is moving then it may moves through the world. as a body moves through the world right suppose it was the body it keeps making measurements on the surrounding world. Right wants to see what is the head of it right, it will smell what is a head or what is around it will try to process the sounds as I coming around it now imagine a body of an organism which can only afford.

So, many eyes are, so many photoreceptors are now. So, many years or has, so, many the olfactory receptors inside the nose and, so on. Now if it has freedom to put them wherever it wants around its body right, where will it put them it is logical to put all these sensors right in the front of the body, because the front of the body is a part which comes into contact with the world has this tube like body moves through the world? So, you can see that most there is a high density of sensors like eyes and ears and nostrils and whiskers, right all these things and I you see packed very close tightly or in the front of the animals bodies, which is the face or the head.

Right if that is the case then you have brain somewhere inside now let us look at the question of where should the brain be placed inside a body let.

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Say we are looking at 2 situations, in the top figure you can see the brain plays slightly closer to the front, or to the head right in the bottom figure you see brain plays far away from the head deeper inside the body. If the brains are trying to minimize wire length

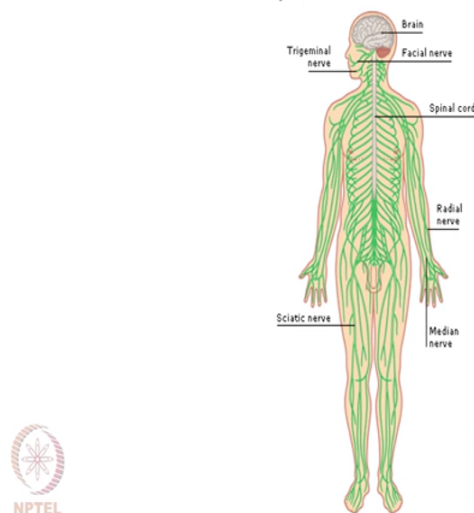
right and if you look at, if you find out that this lot of wire go running from the brain to the head.

Then you are better off putting the placing the brain closer to the head because that way you can minimize the wire length, but if you find that the brains have lot of wire going not to the head, but remaining parts of the body then you are better off placing the brain somewhere in the middle of the body because that way you can save wire length right.

So, which is the correct thing, so what is really happening in real brains let us look at that. So, if we look at human nerve system right if you would look at human wiring patterns.

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The Peripheral Nervous System



So, this is a peripheral system, a peripheral system is there is a consists of a bunch of nerve fibers called the wires, these come out of the central nervous system which is, so basically the variant spinal cord and. So, there are 2 sets of wires the cranial nerves which are 12 in number and which basically run from the brain proper to the 2 parts, 2 points on the head. Then the spinal nerves which run from the spinal cord to the rest of the body there are 31 in number, there are 31 pairs of them right and going to the both sides of the body.

Now, what we need to see here is, what is the ratio of anterior to posterior connections right. So, the in this figure the green arrow is anterior connections and the orange arrow

is the posterior connections right. If the anterior connections are much higher than posterior connections the brain has to be in the head and whereas, if it is other way around brain will be somewhere far from there.

So, if you look at the data from human's right in this table. So, you see the cranial nerves and they all added up to about 12 million fibers 4.5 million fibers these form your anterior connections.

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Table 1. Anteroposterior connection ratio for the human brain

	Fibers (both sides)
Cranial nerves	
Olfactory	~10,000,000
Optic	2,000,000
Oculomotor	60,000
Trochlear	6,000
Trigeminal	300,000
Abducens	14,000
Facial	20,000
Cochlear	60,000
Vestibular	40,000
Glossopharyngeal	7,000
Vagus	70,000
Accessory	7,000
Hypoglossal	15,000
Total	12,599,000
Spinal cord	
Dorsal	2,000,000
Ventral	400,000
Total	2,400,000

Anterior connections exceed posterior ones (ratio anterior:posterior connections = 5.25). Compiled from Blinkov and Glezer (1968) and Shepherd (1979).



And the fibers of the spinal nerves right the spinal the dorsal ventral nerves that all add up to about 2.4 million fibers. So, the anterior posterior ratio is about 5.25. So, so when you have a high anterior to posterior fiber ratio how your head your brain has to be inside the head and; obviously, this what happens in case of humans, but if we take a worm like the C Elegans, and do a similar calculation.

(Refer Slide Time: 30:18)



Table 2. Anteroposterior connection ratio for "brain" of *C. elegans*

Fibers	
Anterior connections	
Labial processes (6)	44
Amphid sensilla, etc.	34
Deirid sensilla, etc.	4
Pharynx ganglion connections	24 (sensory + motor)
Head/neck motor connections	38 (via ring)
Total	146
Posterior connections	
Dorsal ganglion	2
Lateral ganglion	16
Ventral ganglion	15
Retrovessel ganglion	12
Ventral cord	14
Prenal ganglion	2
Dorsorectal ganglion	3
Lumbar ganglion	23
Nonganglionic	9
Total	96

"Brain": pharynx, anterior, dorsal, lateral, ventral, retrovesicular ganglia (+nonganglionic head neurons) = 189 neurons. Anterior connections exceed posterior ones (ratio anterior:posterior connections = 1.52). Compiled from White et al. (1986) and Wood (1988).

You will find that the anterior posterior fiber ratio is only 1.5, I guess therefore, it does not its forehead is further down it actually does not have like a brain puppet it just has kind of a diffused nervous system unlike in humans, where we have a compact brain in the spinal cord right and then you have all these fibers going out of the brain spinal cord, but in case of C Elegans, it has a more diffuse nerve system consists of consisting of a bunch of ganglia distributed all over the body.

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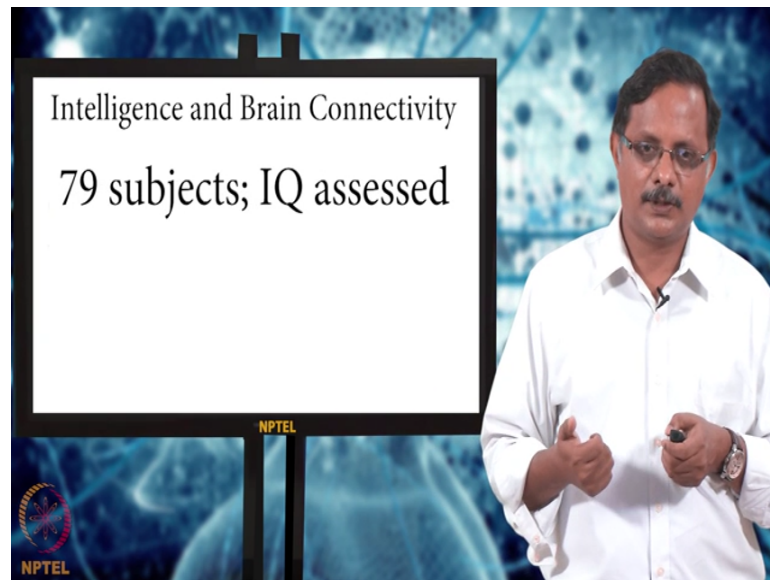
Intelligence and Brain Connectivity

Study on linking wiring patterns and IQ
(Li et al, PLoS Comp Bio, 2009)

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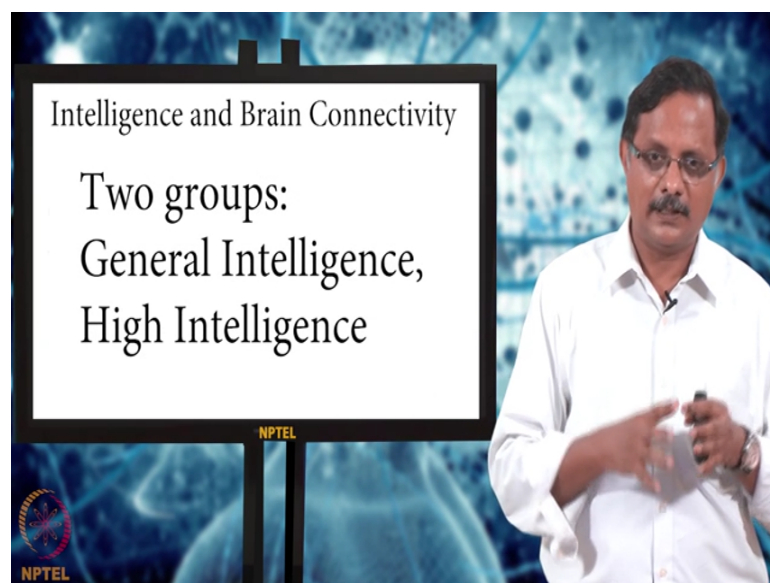
Finally I want to present this interesting study right is there any connection between intelligence and brains connectivity. So, it turns out that I know there is an interesting connection. So, the study by li et al they have looked at the connection between the wiring patterns of the brain and IQ or intelligence quotient of individuals.

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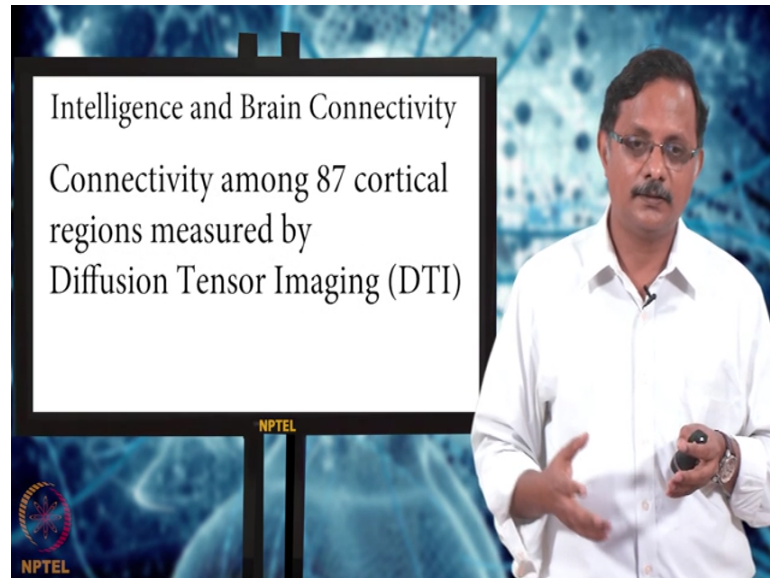
In this study they have taken seventy eight subjects their assess their IQ, and the group them in 2 categories.

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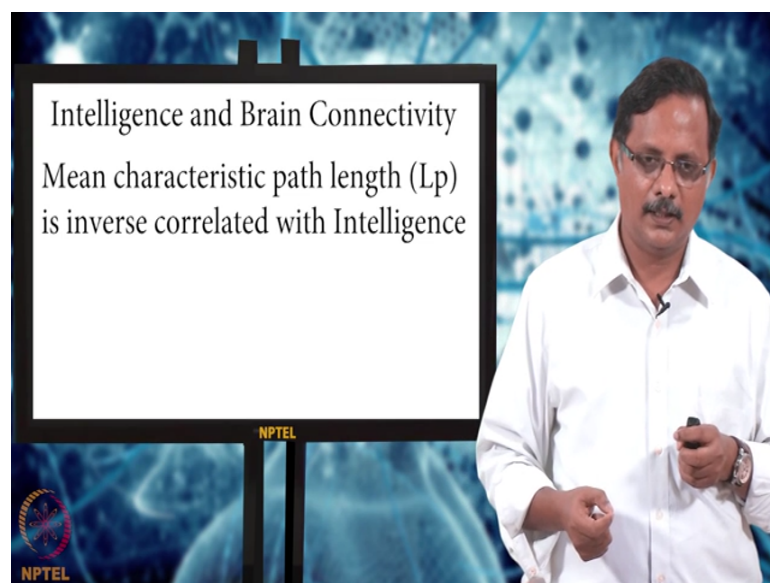
People with general intelligence and people with high intelligence or high IQ, so then they have scanned the brains of these individuals using special new imaging technique called.

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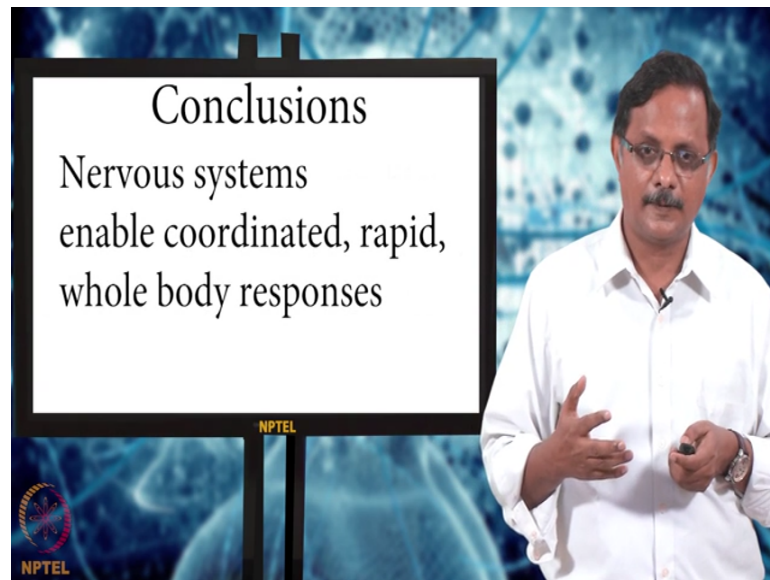
A diffusion tensor imaging or DTI, and they looked at the connectivity patterns among 87 cortical areas and they measured a certain quantity called mean characteristic path length.

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Which basically tells you what is the mean path length of any given pair of cortical regions, among these 87 cortical regions, it turns out that mean characteristic path length is inversely correlated with intelligence; that means, part of smarter people have more efficient packing of brain areas inside this brain volume.

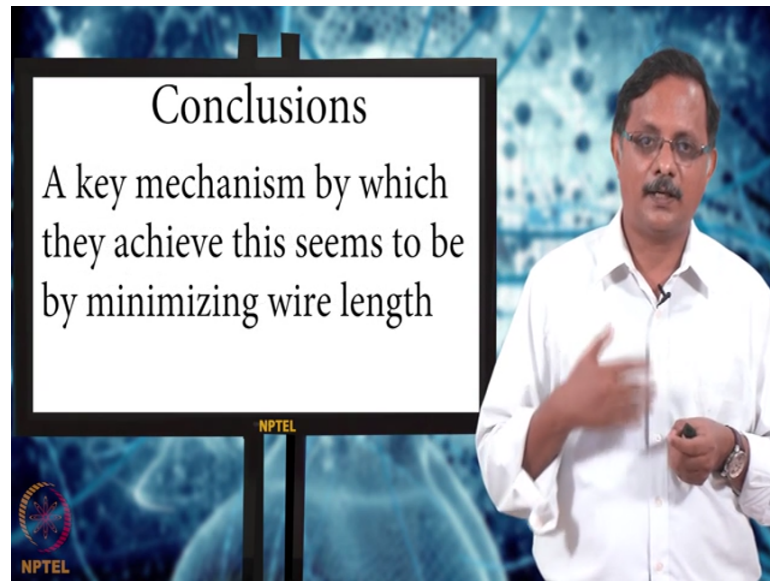
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So, in conclusion we set off with the question of trying to link brain structure with intelligence and efficiency and things like that.

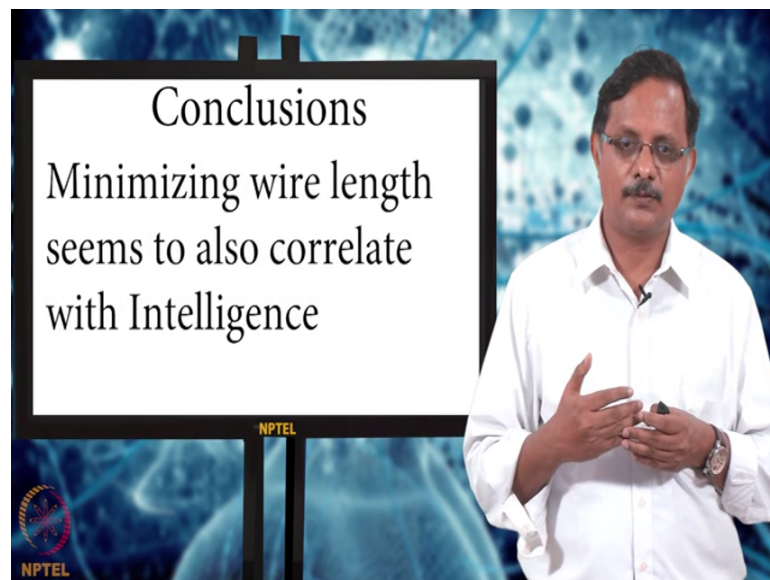
So, we have kind of concluded that there are certain structural correlates relevant, anatomical correlates to intelligence right and we are basically observed they required to produce coordinated rapid whole body responses.

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And a key mechanism by which they achieve this seems to be by minimizing wire length and.

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Minimizing wire length seems or also correlates with intelligence. So, in the next part of this talk will apply these principles to account for the brain's evolution right. Now as we have this kind of a nerve system in which there is a brain and a spinal cord and the peripheral nerve system, right in mammals and you know higher animals, but in very primitive creatures you do not have a brain and spinal cord.

So, there is a look we have covered a long evolutionary trajectory from a small a creature like say hydra right to humans now what is the logic of this evolution. So, so we will try to apply the same minimum wire principles to account for this kind of an evolution.

Thank you.