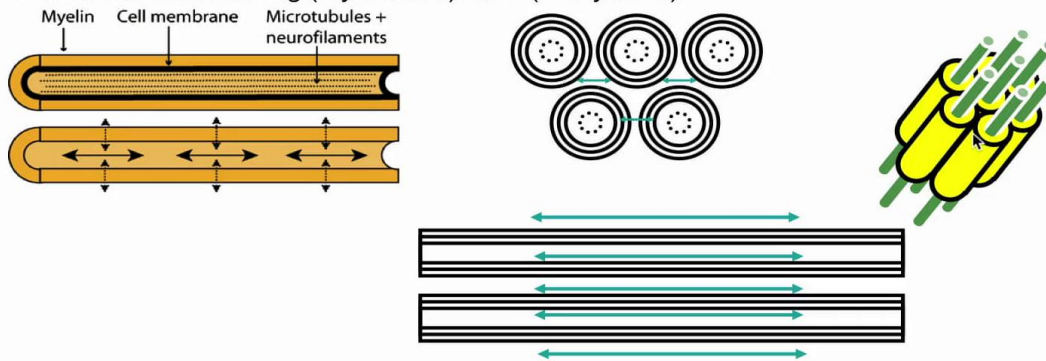


13-3. How is Anisotropic Water Diffusion described ?

Consider structure along (myelinated) axon (or myofibril)



13-7

So, for the situation of a liquid sample, a fluid that's stationary, the situation is fairly simple. Now, in reality, in living tissue, we're confronted with a more complex situation, and that is we have cells, we have membranes, and so the water molecules cannot diffuse at their free will in all directions as they wish as they would in a beaker. So we're considering here two cases: one is an axon, so that's the nerve fiber that connects neurons in the brain; or muscle cells, muscle is myofibrils. These are one-dimensional structures. Here's the example of myelin, so the axon is in here with the microtubules and neurofilaments, we have cell membrane, and then the myelin sheath encasing the axon. So it's a one-dimensional structure, you can think of it as a tube, and we'll consider the membranes-- this is simplification-- but we'll consider them for the sake of the argument-- that they are impermeable to the water molecules. In three-dimensions this is what a bundle of nerves, or muscle cells, would look like. They're one-dimensional, for the nerve cells in the axons, here is the myelin sheath, they are lined up like this. And now what we are going to consider is the motion in the cells.

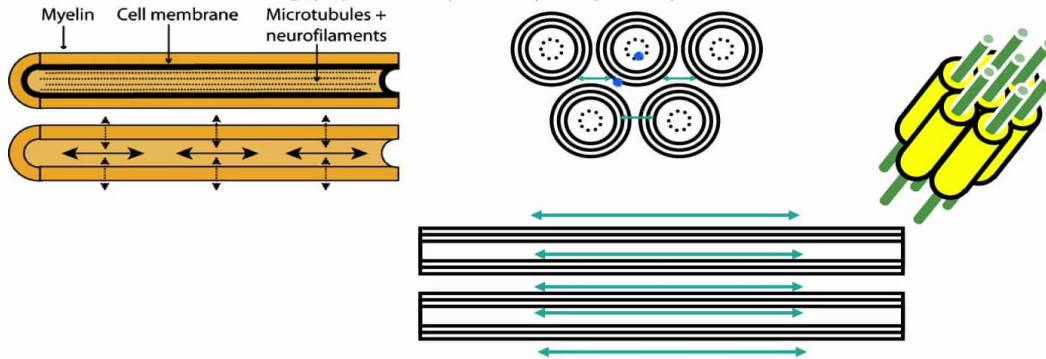
Notes

Summary



13-3. How is Anisotropic Water Diffusion described ?

Consider structure along (myelinated) axon (or myofibril)



13-7

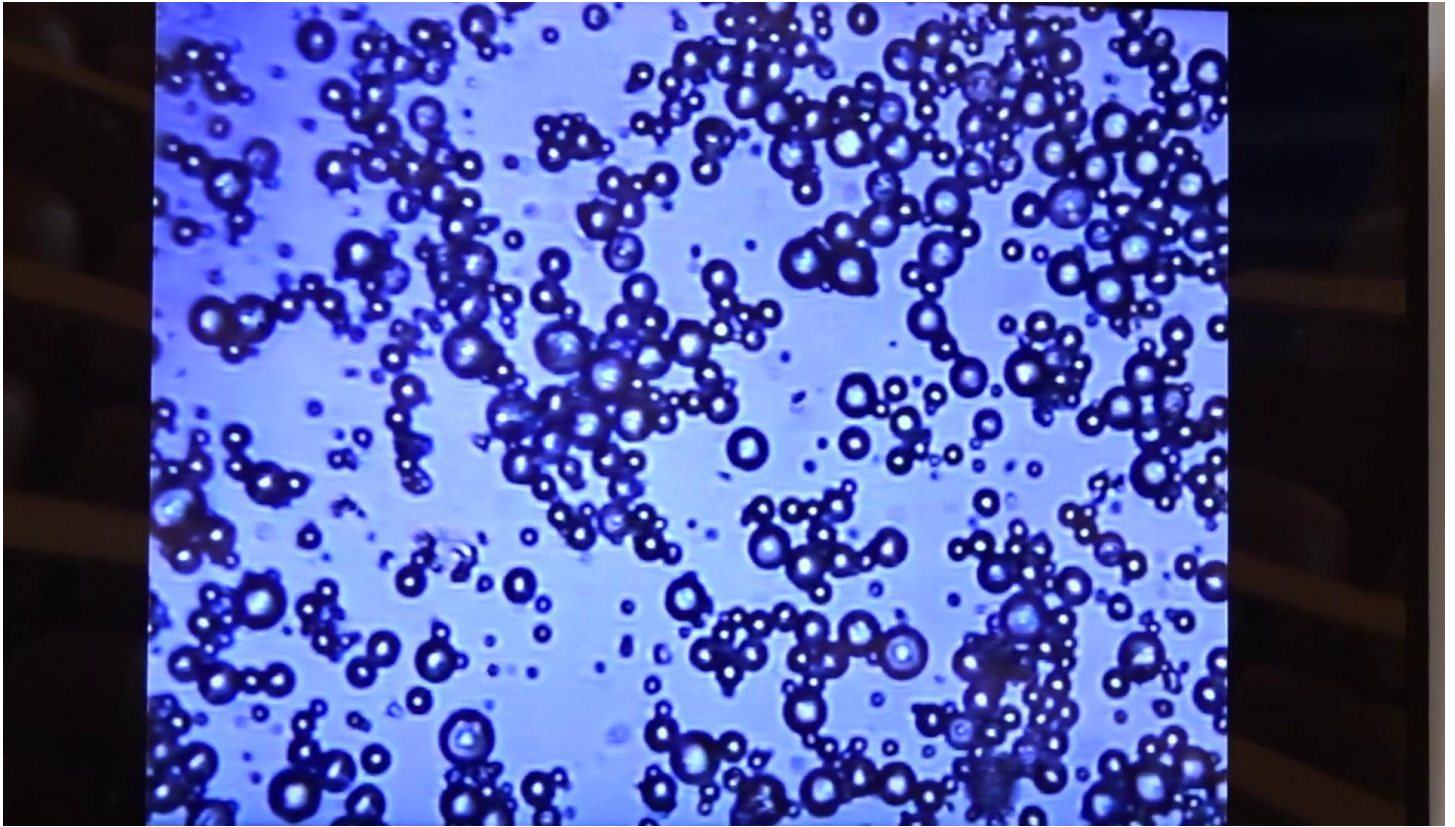
And so we have inside the cell, we have the molecule that is confined to the cell, and between the cells the molecule can move a little bit further. So a molecule that is between the cells, it can essentially move in the extracellular space from my right here, to my left here. If it's inside the cell, it's stuck to the volume of the cell. And the following experiment visually demonstrates this with a colloid, the motion of particles, and you'll see that some particles can move more freely than others.

Notes

Summary



1m 30s



So what we see here is there's some particles that are fixed by the glass in the microscope. They're colloids, but you see the smaller objects that are moving between them, the smaller particles, and this is similar to the water molecules that we have in the tissue. They're diffusing around in the free space, but you can also see that there are some molecules, or some of the smaller particles, they bump into the bigger ones and they can't pass them. This is akin to the situation that we have in living tissue where the water molecules bump into cell membranes, and they have to go around the membranes, or they're stuck within the cells.

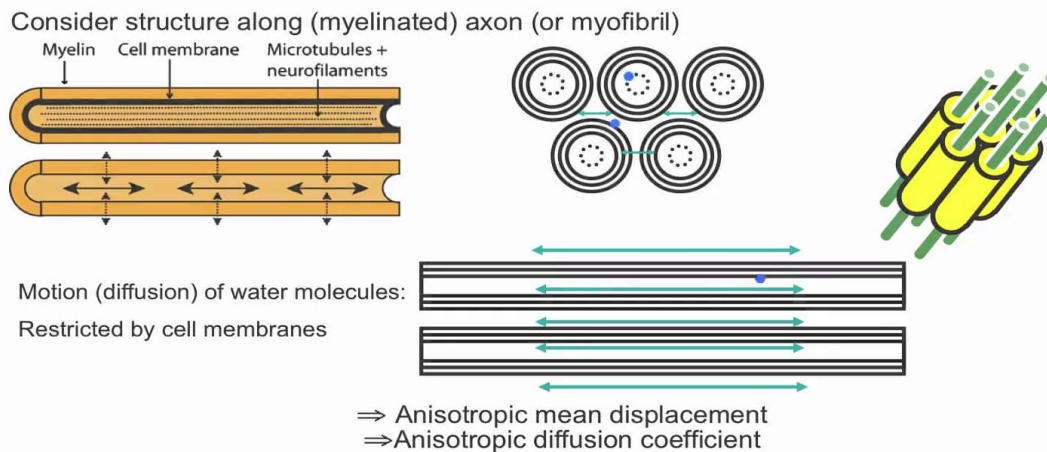
Notes

Summary



2m 06s

13-3. How is Anisotropic Water Diffusion described ?



13-7

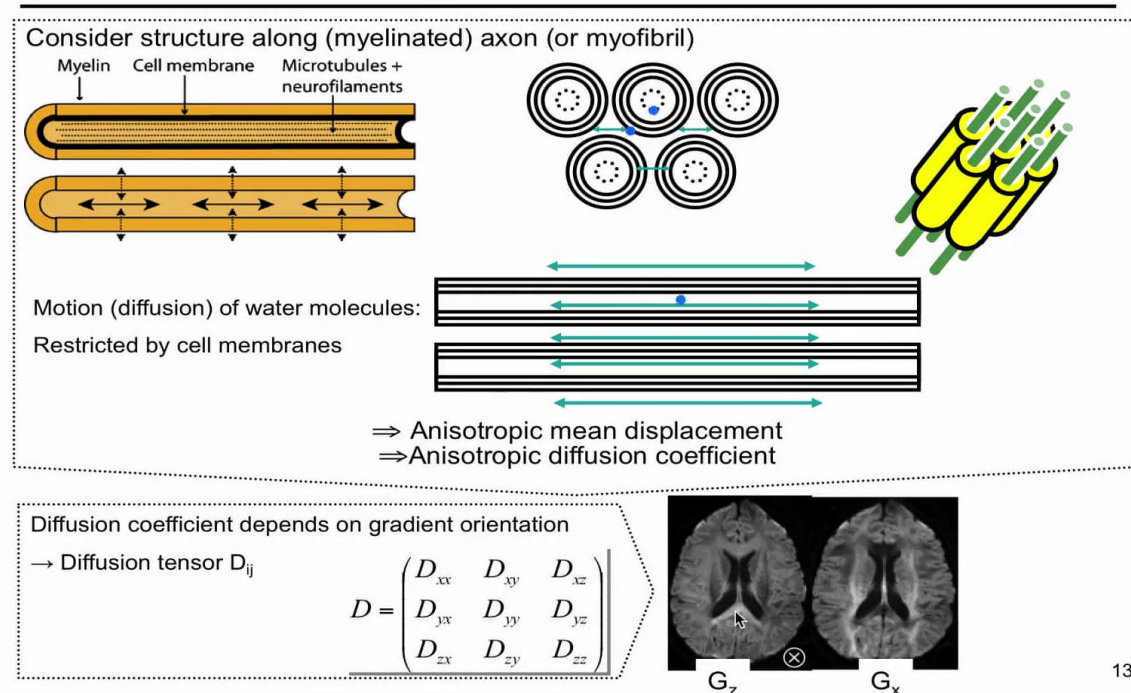
So consequence is, if you look here, in this is a cut perpendicular to the cells, the molecule here is inside the cell, is stuck to the dimensions of the cell-- this is typically a micron-- extracellularly it can diffuse further, although it has to diffuse around the cells. If you now look at a cut along the axon, here along the cell structure, now the distance is pretty much much longer, and pretty much unrestricted. So consider the motion here, and the motion here. Here the mean displacement can be much bigger than the mean displacement is here. So with a restricted motion by cell membranes in one-dimensional structures like we see often in nature-- in the brain and in the muscle-- the motion is restricted by membranes, and the membrane structure is not isotropic, the cell structure is not isotropic. So what does this mean? We are getting, clearly here, this distance is much smaller than this distance, we're getting an anisotropic mean displacement, and from Einstein's equation, we're getting an anisotropic diffusion coefficient.

Notes

Summary



13-3. How is Anisotropic Water Diffusion described ?



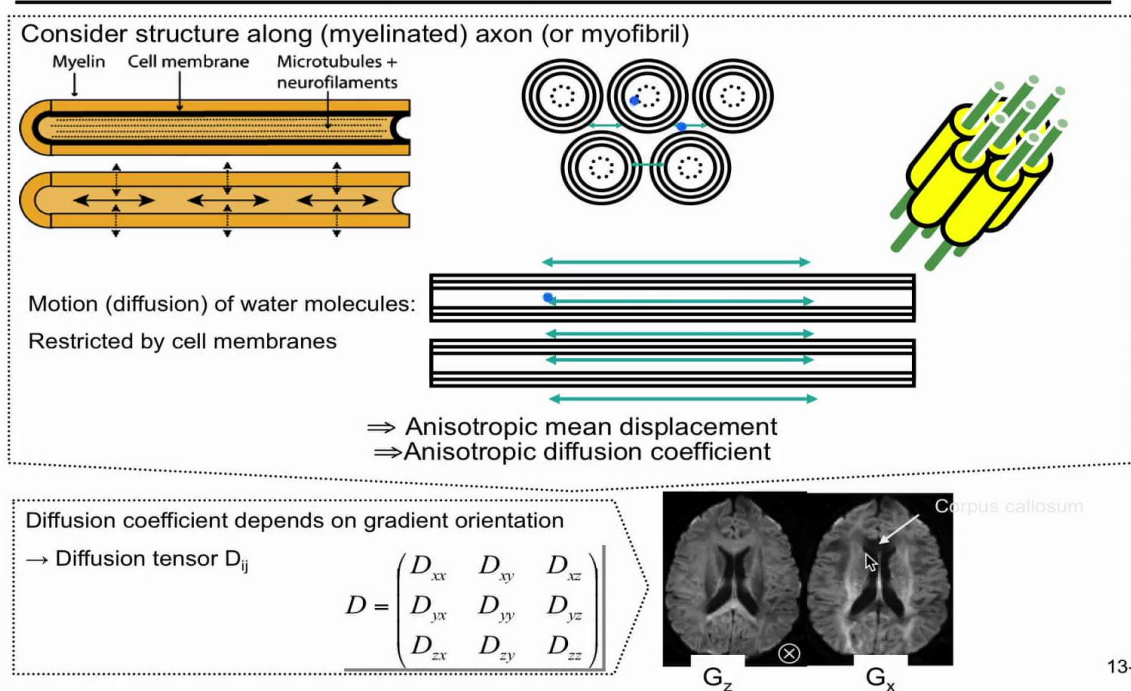
So what does this mean? This means that depending whether I measure in the direction of the axon, or perpendicular, that is if I apply the gradient perpendicular-- I mentioned the motion perpendicular to the axon-- here the motion is restricted to a small distance. If my gradient is along the direction of the axon in this direction, the mean displacement is larger, and so depending what type of gradient I apply, I get a different apparent diffusion coefficient, and this is spatially anisotropic. So consequently, the diffusion coefficient that one measures, the apparent diffusion coefficient, depends on the gradient orientation. This is mathematically-- a good approach is to describe this mathematically by a diffusion tensor D_{ij} . What is this mathematically? Well, basically, it's a 3 x 3 matrix, and here it is. So this is what describes the diffusion process. Now let's look at some examples to convince ourselves that this is real. So here's a diffusion-weighted image, so we're looking at *just* the diffusion weighting, the gradient is applied along z. So this means it is going perpendicular to the plane. Bright means very little diffusion, dark means a lot of diffusion.

Notes

Summary



13-3. How is Anisotropic Water Diffusion described ?



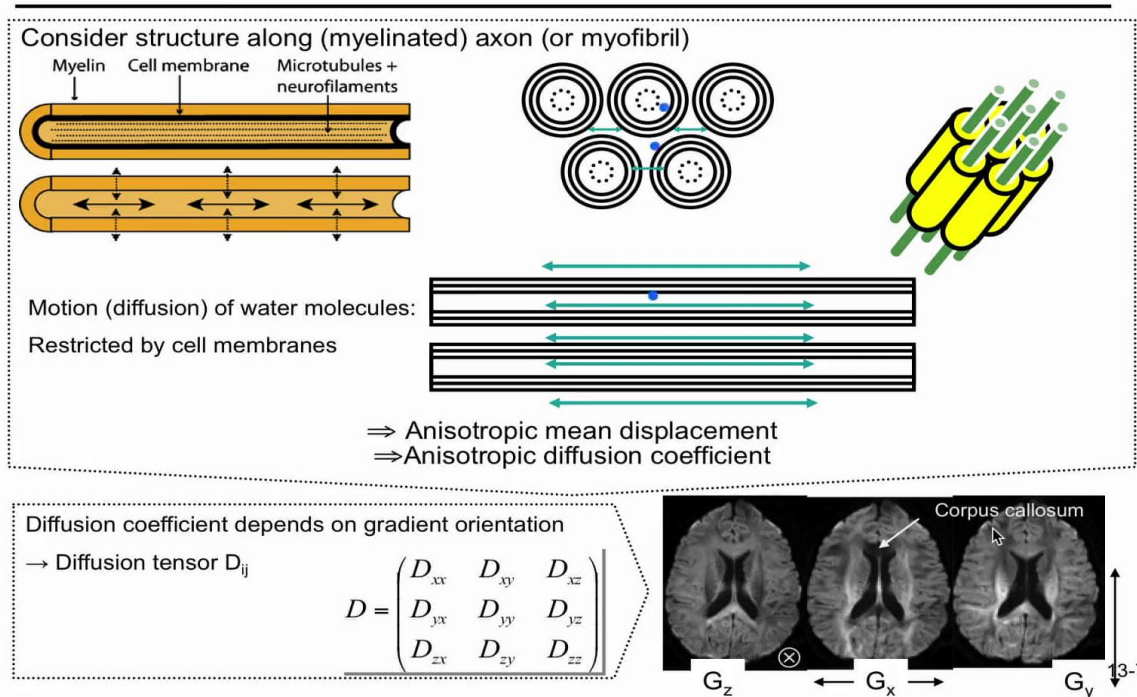
So here we have a lot of diffusion, here we have very little, and here, in this area, we have *substantial* diffusion, the signal is strongly attenuated. So bright is less attenuation, dark is a lot of attenuation. Now, the next image is the diffusion in the x direction, so this is horizontal. And now, notice this area here. I'll go back. Here, it's the same image, here we had not so much diffusion, and here it gets essentially dark, so there's a lot of diffusion. And this is the area of the corpus callosum.

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Summary



13-3. How is Anisotropic Water Diffusion described ?



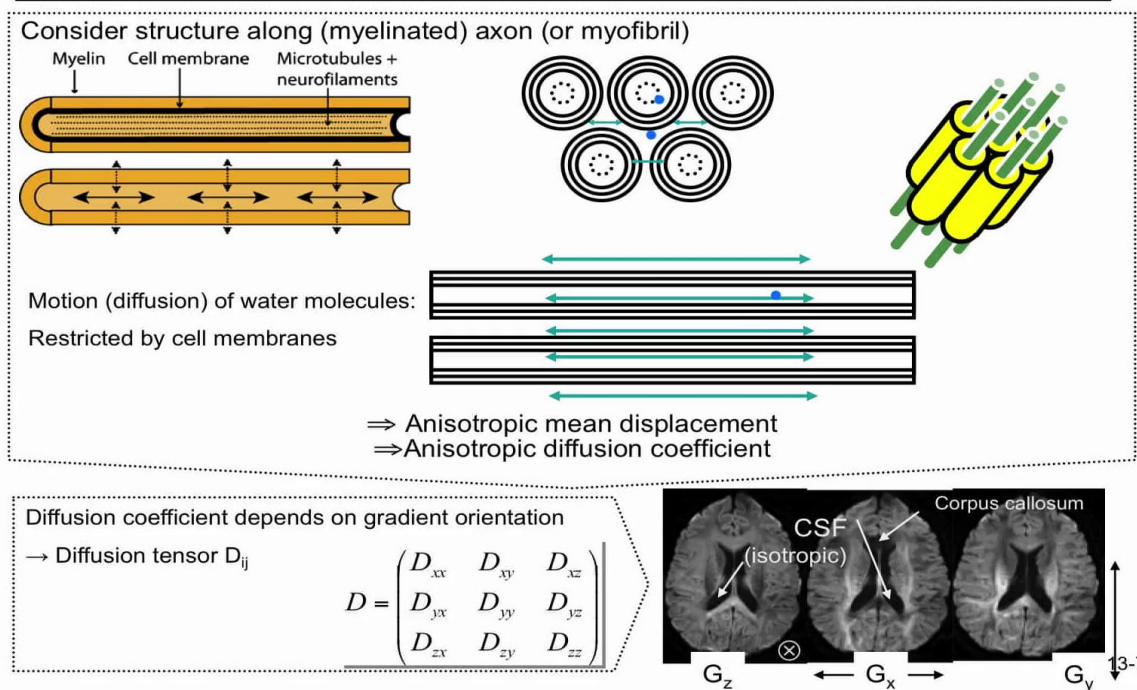
The corpus callosum, if you think of it, that's the bus, that's the ribbon cable that connects the nerve fibers from the right hemisphere and the left hemisphere. It's like a ribbon bus. In this direction are the orientation of all the axons, and they're very colinear aligned, so we have a lot of diffusion, right-left in this direction. And that's why, if we apply the gradient in right-left orientation, this signal is strongly attenuated. Here also, as you can see, it's very much not attenuated, so it's bright, and here it gets dark, the same area. So also here we have right-left orientation of the diffusion process. And, finally, we're looking at the diffusion process from front to back, so from here to here, and now we can see, again, corpus callosum is regaining its intensity here, here again. And now we have these areas that are losing intensity, here and here. Can you guess what we're looking at there? So this is the back of the head, here, is the back of the head, the eyes are in the front. Now, what we are looking at here is the optic nerve, the connection from the eyeballs to the back of the head, the primary visual cortex where the primary processing of visual information occurs.

Notes

Summary



13-3. How is Anisotropic Water Diffusion described ?



So we're seeing that directionality here. Notice that in all three images this area is always dark. That's the ventricles, it's filled with cerebrospinal fluid, so it behaves like free water. It's isotropic, and since there's no membrane restriction for water in that space, it will have a much higher diffusion coefficient in that area. And that's why it is seen dark and isotropic in all three cases. So this is isotropic diffusion for the cerebrospinal fluid, or CSF.

Notes

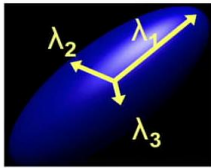
Summary



Diffusion tensor imaging (DTI)

imaging anisotropic diffusion

Diffusion tensor symmetric: $D_{ij} = D_{ji}$



$$DT = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

3 orthogonal **Eigenvectors**

→ **Eigenvalues** λ_i



Now, we have seen the diffusion tensor, and there's one property that this diffusion tensor has: it's a symmetric tensor. Now, here we have to make use of some things that you might remember from your linear algebra course-- or then you have to accept it here-- if you have a 3 x 3 matrix that is symmetric, and so real numbers, then we can characterize it with three orthogonal eigenvectors. And if we choose to describe this diffusion tensor in a basis system where x corresponds to one eigenvector, y to another one, and z to another one, then the mathematical description of the diffusion is given by the eigenvalues. So here, we have one eigenvector in this direction, usually λ_1 is the biggest one, and λ_2 and λ_3 are the two other eigenvectors. And if we choose that as our coordinate system for describing the coordinates, then in this coordinate system our diffusion tensor now becomes a diagonal matrix with these three diffusion processes describing the diffusion along the first eigenvector, second eigenvector, and third eigenvector. And so this is the experiment that one can do, one can actually obtain this diffusion tensor.

Notes

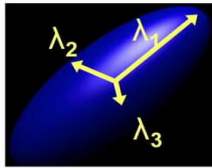
Summary



Diffusion tensor imaging (DTI)

imaging anisotropic diffusion

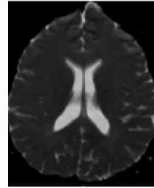
Diffusion tensor symmetric: $D_{ij} = D_{ji}$



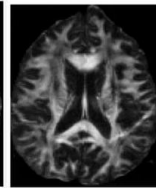
$$DT = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

3 orthogonal **Eigenvectors**

→ **Eigenvalues** λ_i



Mean
diffusivity
(trace D_{ij})



Fractional
Anisotropy
($\lambda_1 - \lambda_3$)

13-8

One can obtain the mean diffusivity. This is the trace of the tensor, and that overall is actually a not very interesting information. We can see the cerebrospinal fluid, but the rest of the image, as you notice here, is pretty much gray, so there is not a huge difference in mean diffusivity across the brain. Take now here, an example. This is the fractional anisotropy-- that's another parameter which one can characterize-- and typically we have the situation for one-dimensional structures, that λ_2 and λ_3 are small, they are corresponding to a small displacement, λ_1 along the direction of the axon is the big displacement. So if we look at the difference of this to the other two, this gives us the fractional anisotropy-- the two formulae are different, but I don't want to go into the details here, I want to stick with the principal-- what this measures is the difference between the biggest eigenvector and the other two, the fractional anisotropy. And now we can see there's a lot of spatial information here. So it basically measures, how much is this ellipsoid, described by the three eigenvalues, how much this is cigar-shaped, or it is round.

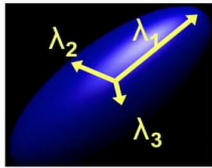
Notes

Summary



Diffusion tensor imaging (DTI) imaging anisotropic diffusion

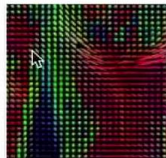
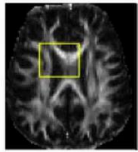
Diffusion tensor symmetric: $D_{ij} = D_{ji}$



$$DT = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

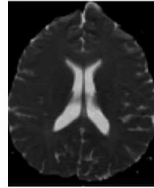
For each voxel determine direction of principal eigenvector (largest λ):

Pseudocolor directionality

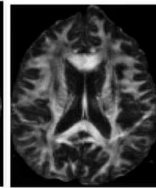


3 orthogonal **Eigenvectors**

→ **Eigenvalues** λ_i



Mean
diffusivity
(trace D_{ij})



Fractional
Anisotropy
($\lambda_1 - \lambda_3$)

13-8

So fractional anisotropy that is zero means isotropic diffusion. So zero is here, so we have isotropic diffusion. We have also, largely in the gray matter, isotropic diffusion. This is, however, a reflection of the fact that we no longer have an oriented structure in the gray matter. But now we can see corpus callosum, like I mentioned, this is the bus, very ordered structure, the fractional anisotropy is very high. Optic nerve here, we've seen that example also. It's essentially the white matter structures where we have the fractional anisotropy, and this is where the axons, the cabling between the brain cells, occurs. Now, finally, therefore, in each voxel we can determine the diffusion tensor. Once we've determined the diffusion tensor, we can determine in each voxel the direction of the major eigenvector, so that is the direction of the largest eigenvalue, and then color the image with pseudocolor intensity. So this gives us pseudocolor directionality. Here's the image, we're going to now look at a box cutout here. And if you look now in this box here, we can see for each of the voxels an ellipsoid describing the orientation of the diffusion tensor is drawn.

Notes

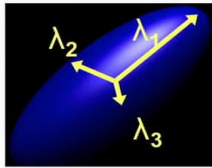
Summary



Diffusion tensor imaging (DTI)

imaging anisotropic diffusion

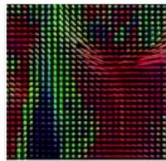
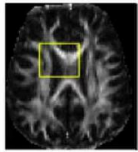
Diffusion tensor symmetric: $D_{ij} = D_{ji}$



$$DT = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

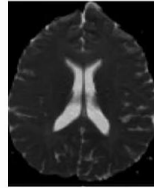
For each voxel determine direction of principal eigenvector (largest λ):

Pseudocolor directionality

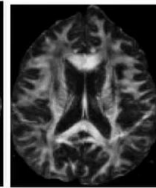


3 orthogonal **Eigenvectors**

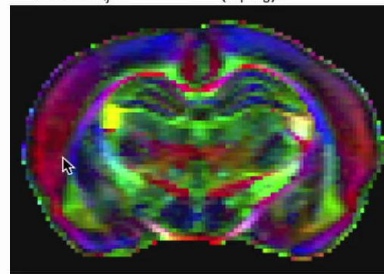
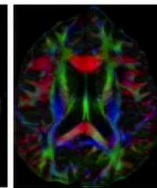
→ **Eigenvalues** λ_i



Mean
diffusivity
(trace D_{ij})



Fractional
Anisotropy
($\lambda_1 - \lambda_3$)



13-8

We have in red, left-right, we have in green, top-bottom, and blue, front to back. Actually, I'm sorry, this is the other way around. In blue is top-bottom, and in green is front to back. Red is right to left, and this is a generally accepted norm, how this is pseudocolored. So if one now takes this image here-- so this diffusion tensor image of a brain-- and color codes onto directionality of the principal eigenvector, we have here, of course, right-left, we have here, top-bottom, as we've seen on the previous image, here is right-left again, and green is front to back in this case. Actually, here it's different, the blue is out of the screen. This is an example of a rat brain, so, again, color-coded. And we have here, now, the rat brain has very little white matter. The white matter is essentially this structure here, and the rest is gray matter, yet we can see directionality. Let's look at this, so red means right to left, here, and here we have top to bottom, but this is gray matter, this structure here, that's cortex. So what does this mean? In here it goes between red and blue, the color changes. This basically means that the diffusion process is perpendicular to the surface.

Notes

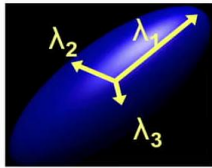
Summary



Diffusion tensor imaging (DTI)

imaging anisotropic diffusion

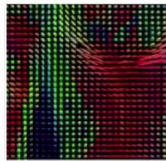
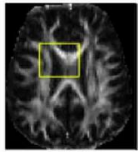
Diffusion tensor symmetric: $D_{ij} = D_{ji}$



$$DT = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

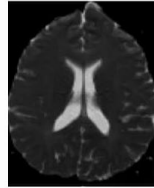
For each voxel determine direction of principal eigenvector (largest λ):

Pseudocolor directionality

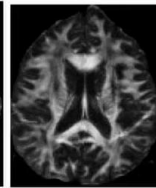


3 orthogonal **Eigenvectors**

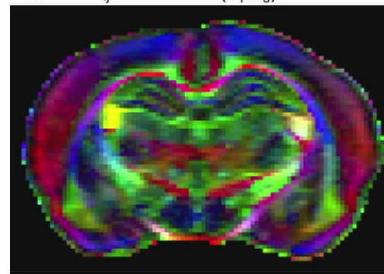
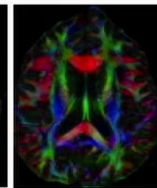
→ **Eigenvalues** λ_i



Mean
diffusivity
(trace D_{ij})



Fractional
Anisotropy
($\lambda_1 - \lambda_3$)



13-8

There's a directionality of the diffusion process of the water diffusion in the cortex in the gray matter of the rat that is perpendicular to the surface. And this reflects some of the neuronal structures which are very laminar-columnar in organization, so the cells are perpendicular to the surface, protruding through the cortical layers. And this directionality can be picked up with diffusion imaging, and displayed as such.

Notes

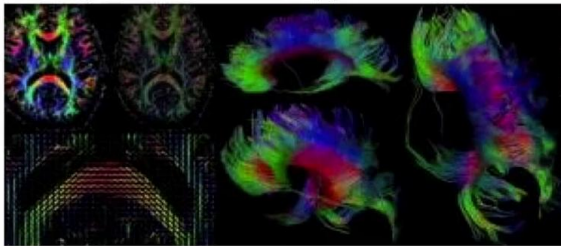
Summary



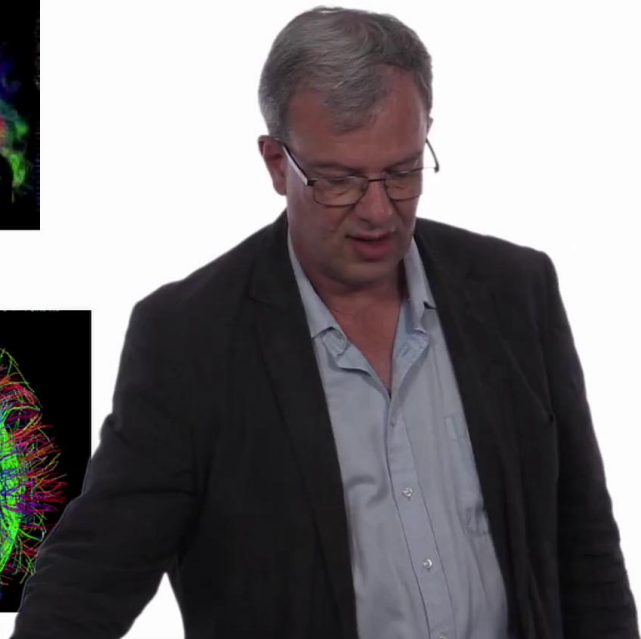
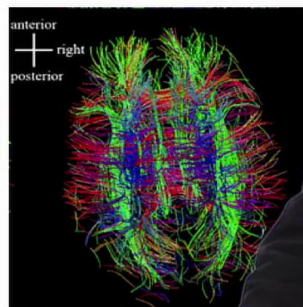
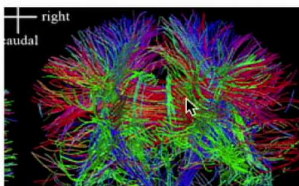
Application: Fiber Tracking using Diffusion MRI

from diffusion anisotropy to connectivity

1. Image of diffusion anisotropy



2. Directionality of water diffusion connects adjacent voxels (spaghettis)



So I want to give you some examples of what has the neuroscience community very much excited, and that is the ability to quantify this anisotropy. So, if one does an image of the diffusion anisotropy, we have the ellipsoids in each voxel here-- that's a cutout-- the color-coded maps of the diffusivity, the direction anisotropy. And now what is being done is determining each voxel the principal direction of diffusion. Then we do it for the next voxel, which may be like this, and then the next voxel. And we'll suppose that this diffusion is provided by a bundle of nerves, of axons, that go along the direction of the principal eigenvector, the vector with the biggest eigenvalue. So in this case, we would get a connection of the voxels in this direction. And this is then done to connect the adjacent voxels, and one obtains with that, spaghetti-like images. So here is a cut from the brain, so we're looking on the top of the brain, this is the left side, this is the right side. And here we can see the corpus callosum, the connection between right and left, and these are all the projections of white matter into gray matter.

Notes

Summary

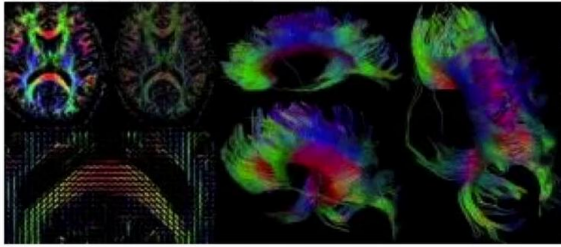


13m 48s

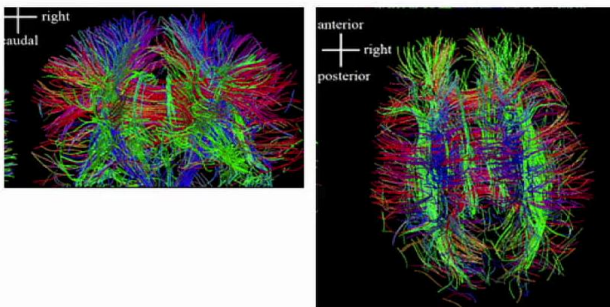
Application: Fiber Tracking using Diffusion MRI

from diffusion anisotropy to connectivity

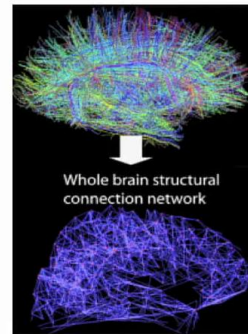
1. Image of diffusion anisotropy



2. Directionality of water diffusion connects adjacent voxels (spaghettis)



3. Establish fiber tracks



13-9

And this is now a view from the top, again, we have the optic nerve going here, we have the corpus callosum being connected, and we have some other connections perpendicular. So this gives us a spaghetti-like representation of the connections. One can establish with that the fiber tracks, and, finally, one can ask the question, "Which part of the brain is connected to which part?" This provides information on probability that if we take a brain region here and another brain region here, what is the probability that there indeed exists a connection, in terms of cabling, between these brain regions. Thus leads to a whole brain structural connection network, or also known as a *connectome*. So these are applications that have neuroscience very excited. One gets inside in the individual subject on which parts of the brain are connected somehow, how they are connected, and, in some diseases, how much these connectivities are perturbed by the disease in question.

Notes

Summary



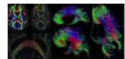
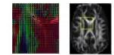
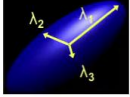
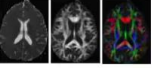
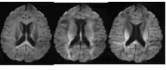
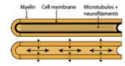


Fig. 4 from Patric Hagmann et al. Radiographics 2006; 26: S1

Creative commons pictures,
DIFFUSION TENSOR IMAGING Marija Cauchi and Kenji Yamamoto.

“Diffusion Modeling in BrainSuite”, Justin P. Haldar
http://brainsuite.org/data/training-092813/Diffusion_jhaldar.pdf

Fig. 2 from Ming-Chang Chiang et al., J. Neurosci 2009; 29:2212

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http://www.med.lu.se/klinvetlund/mr_physics/research/molecular_motion

Brain structural connection network
Public domain
<http://alfa-img.com/show/brain-network.html>

“Diffúziós jelenségeken alapuló képalkotás”, Dr. Jakab Andras, Dr. Berényi Ervin.
<http://www.slideshare.net/jakaba/1-diffzis-jelensgeken-alapul-kpalkots>

Notes

Summary

