12.2 BOLD contrast

Fundamentals of Biomedical Imaging

Prof. Rolf Gruetter

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Video

EPFL

12-2. What is the Biophysical basis of T_2* changes ?

Blood Oxygenation Level Dependent (BOLD)

Magnetic susceptibility χ: magnetic field in object depends on object properties

$$B(\vec{r}) = (1 + \chi(\vec{r}) \cdot 10^{-6}) B_0$$

χ<0: diamagnetism (repelling force)

χ>0: paramagnetism (attracting force)

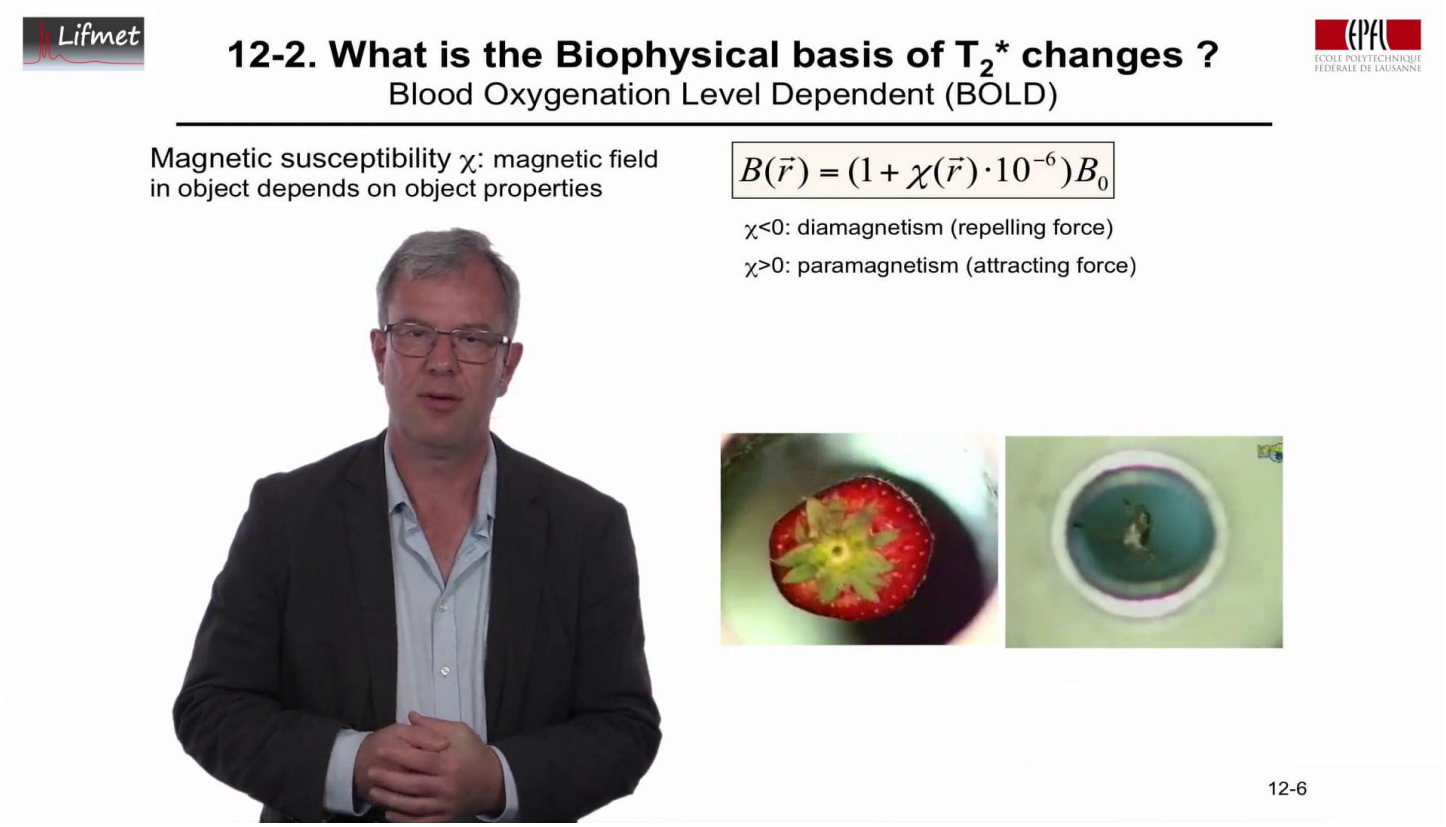
12-6

So, I've introduced *T_2 star* changes, I've introduced *T_2 star*, now the question is, how do these changes in *T_2 star* relate to something useful, to some biophysical mechanism? Now we'll start here with magnetic susceptibility. And we know from magnetism that the magnetic in an object depends on the object's properties. So we have the magnetic field and the magnetic field inside the object is linked to the externally applied magnetic field *B_0* through the susceptibility. You can see this is multiplied by *10^-6* so the susceptibility here is given in ppm so it is a relatively small effect. And the major effects that we're looking at is diamagnetism, that's a repelling force, and paramagnetism, which is an attracting force-- it has to do with interactions between the atoms and the external magnetic field. So here I want to illustrate an example. This is a levitating strawberry, it's placed on a strong magnet-- permanent magnet-- that is very inhomogeneous, and the strawberry is primarily water so it's diamagnetic and so it levitates in air here as you can see on this video from YouTube. Here's another example.

Notes

Summary

0m 04s

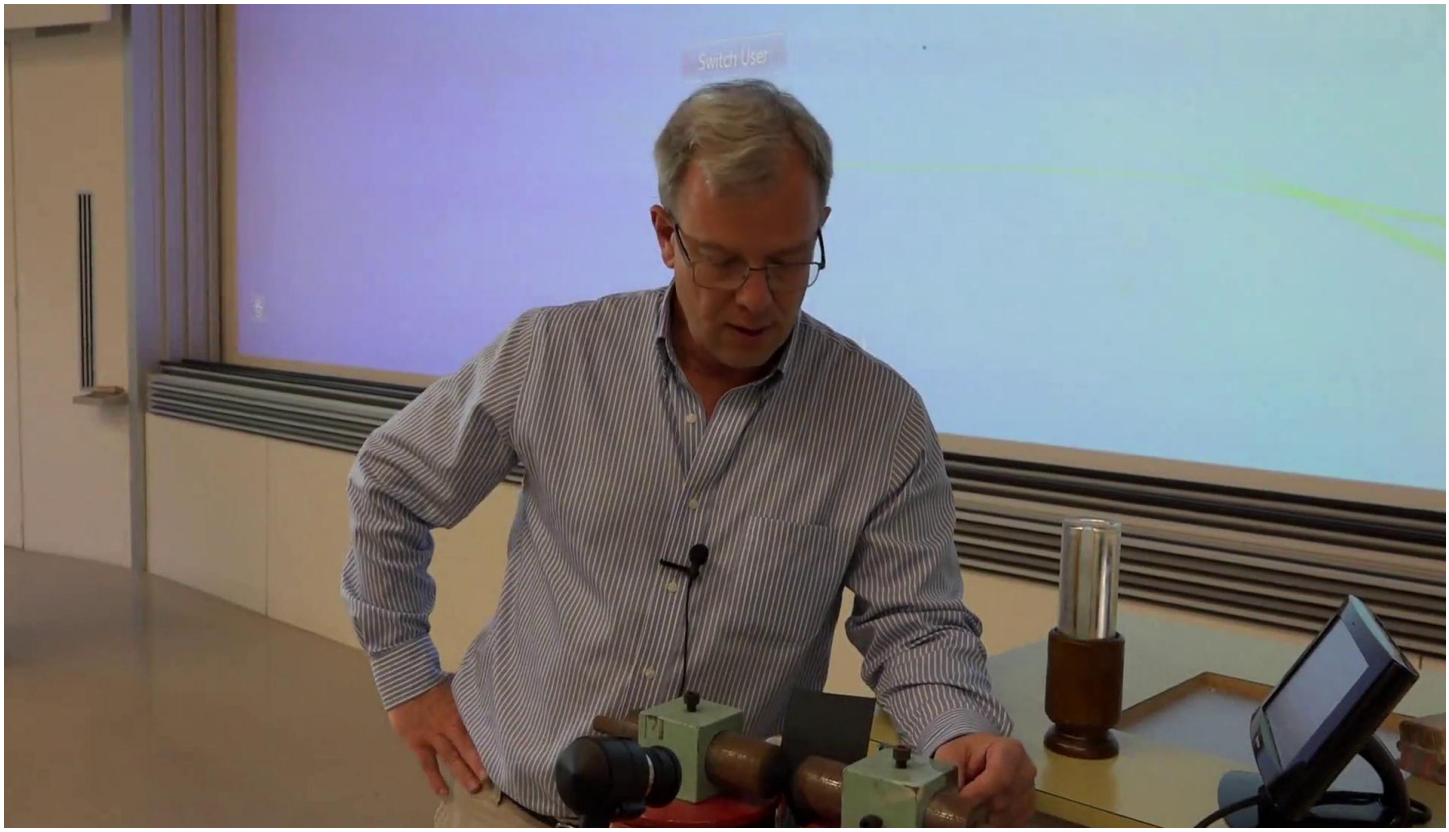


And that is a Canadian frog that is also placed on top of a strong magnet field, the frog is very light so it has the same repelling force as the strawberry, and about a comparable weight, so this animal is floating on top of the magnet. We could of course ask the question, at what point are we able to levitate humans, but this is more of an academic interest than of reality, what we want to do. So these are the effects on two living examples from life sciences. In the following experiments that I will be showing, I will be showing you the effect, the levitation effect, then we'll look at -- the effect on fluids in a magnet as it's turned on, and finally, what we're going to be seeing is the difference between molecular oxygen and nitrogen-- that molecular oxygen is paragmagnetic and nitrogen is diamagnetic just like water and we'll see these three experiments just now.

Notes

Summary

1m 31s

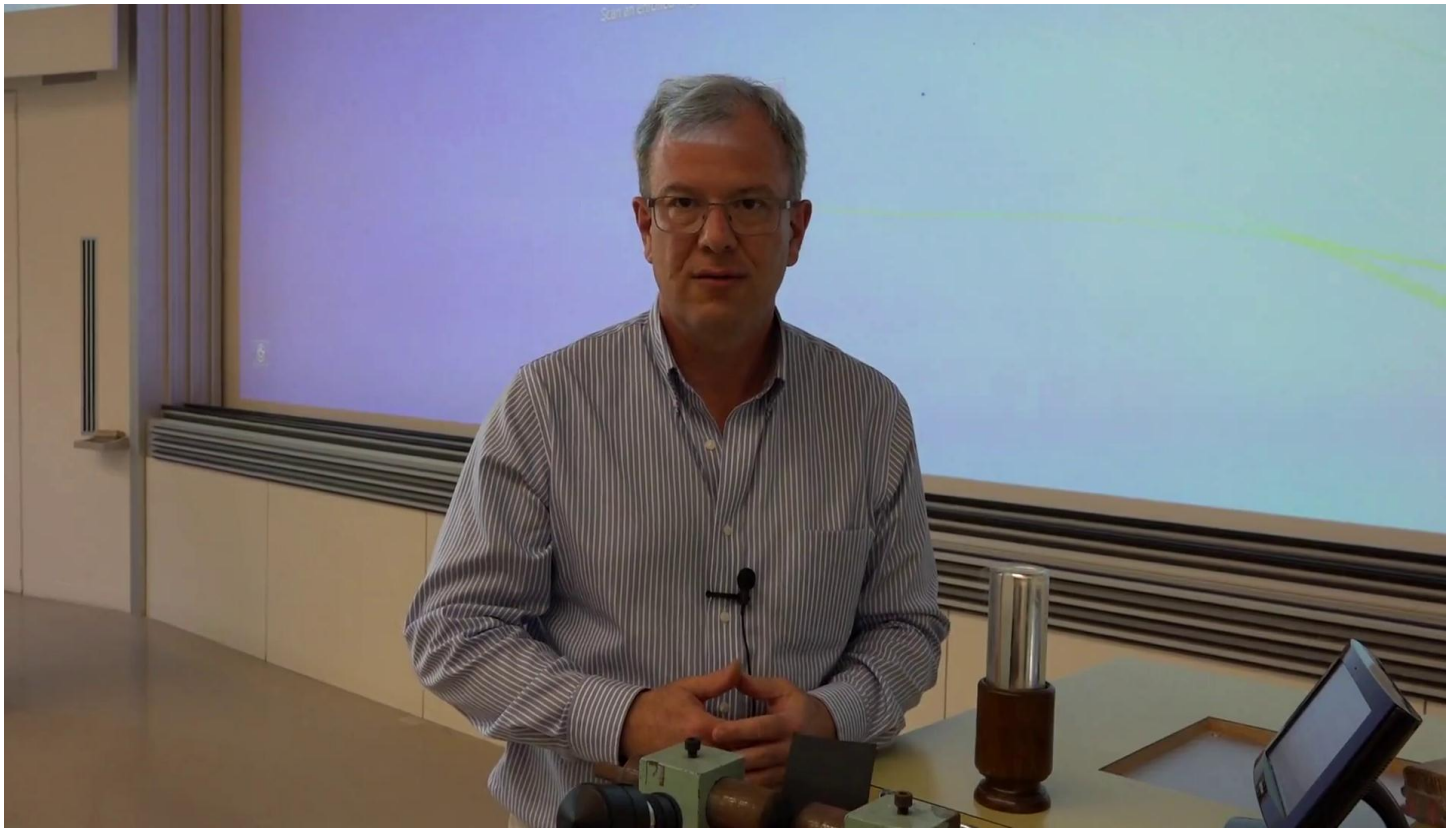


So in this experiment what we have here is a strong magnet, on top of it, a diamagnetic substance which is held down by another magnet. So I relieve it now and now you can see the repelling force of diamagnetism of the magnet on the object-- it is hovering in mid-air. So if I take here a piece of paper I can easily slide it underneath, and you can clearly see how it is hovering on top of the magnet-- there's no physical connection, there's a distance. That's the repelling force of diamagnetism. Okay, so in this experiment we have again an electromagnet with the poles. Between the two poles, where the magnetic field is established, we have two cuvettes; in those two cuvettes, on your right side, we have water, and on the left side, we have iron perchloride which is paramagnetic. Currently the magnet is off-- so you can see the level of the water which is on the same level-- and when I turn it on, the magnetic field, the paramagnetic substance is pulled upwards, much more so than the water is pushed downwards because it's being repelled by the magnetic field. Okay, so what we have here is a magnet which is on-- so it's a magnetic field created between these two poles-- and we'll first pour liquid nitrogen, in this experiment, on top of here.

Notes

Summary

2m 47s

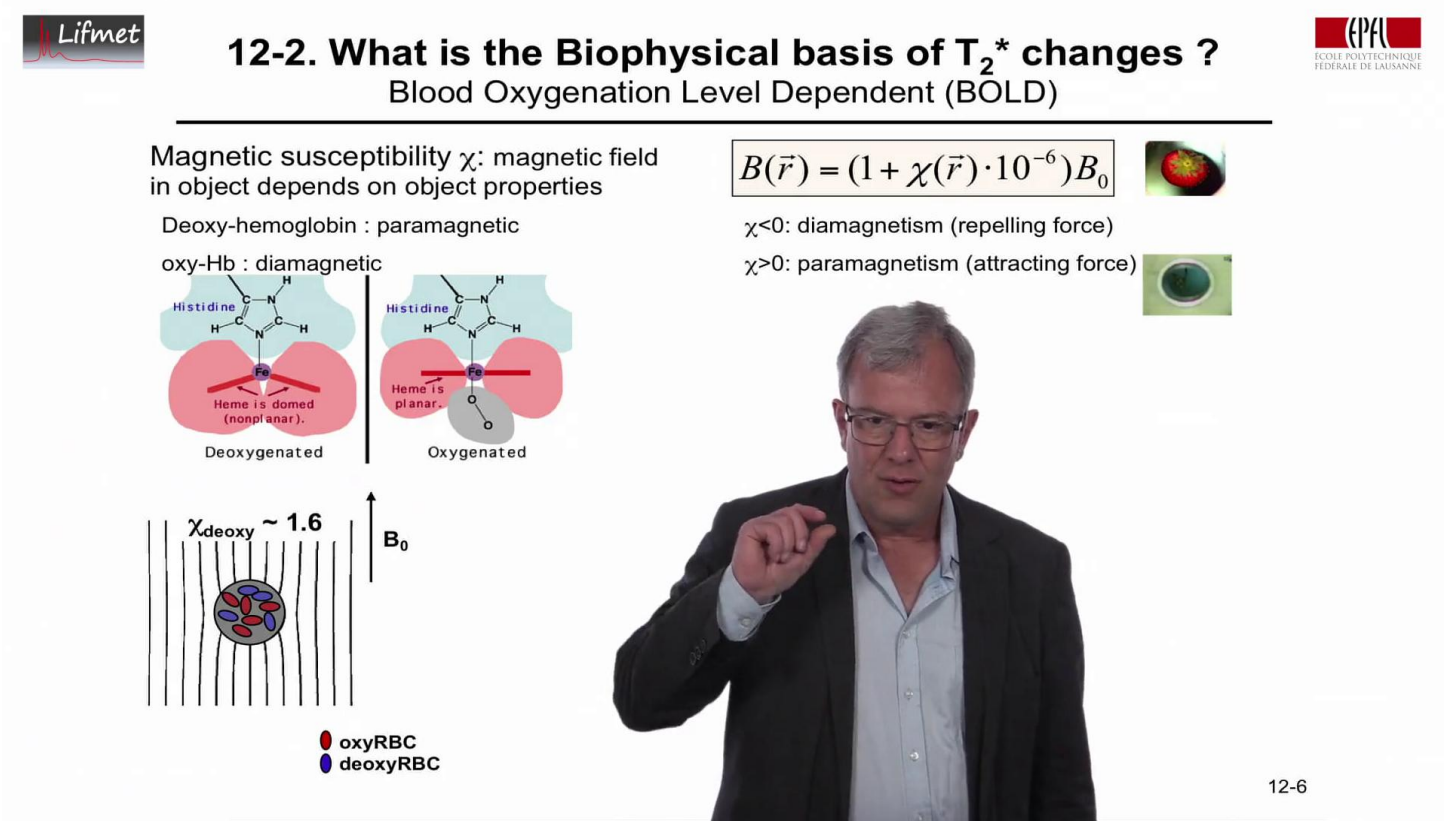


And what you'll see is that the liquid nitrogen will just fall through. So I'll take it now-- and you can see the liquid nitrogen just falls through. As we have seen in the course, liquid nitrogen is diamagnetic so there's no force on it. Now if on the other hand I take liquid oxygen-- I'll repeat the same experiment-- and now we can see how it is being retained between the two poles by the magnetic field-- that's the force of the magnetic field on the paramagnetic molecular oxygen.

Notes

Summary

4m 10s

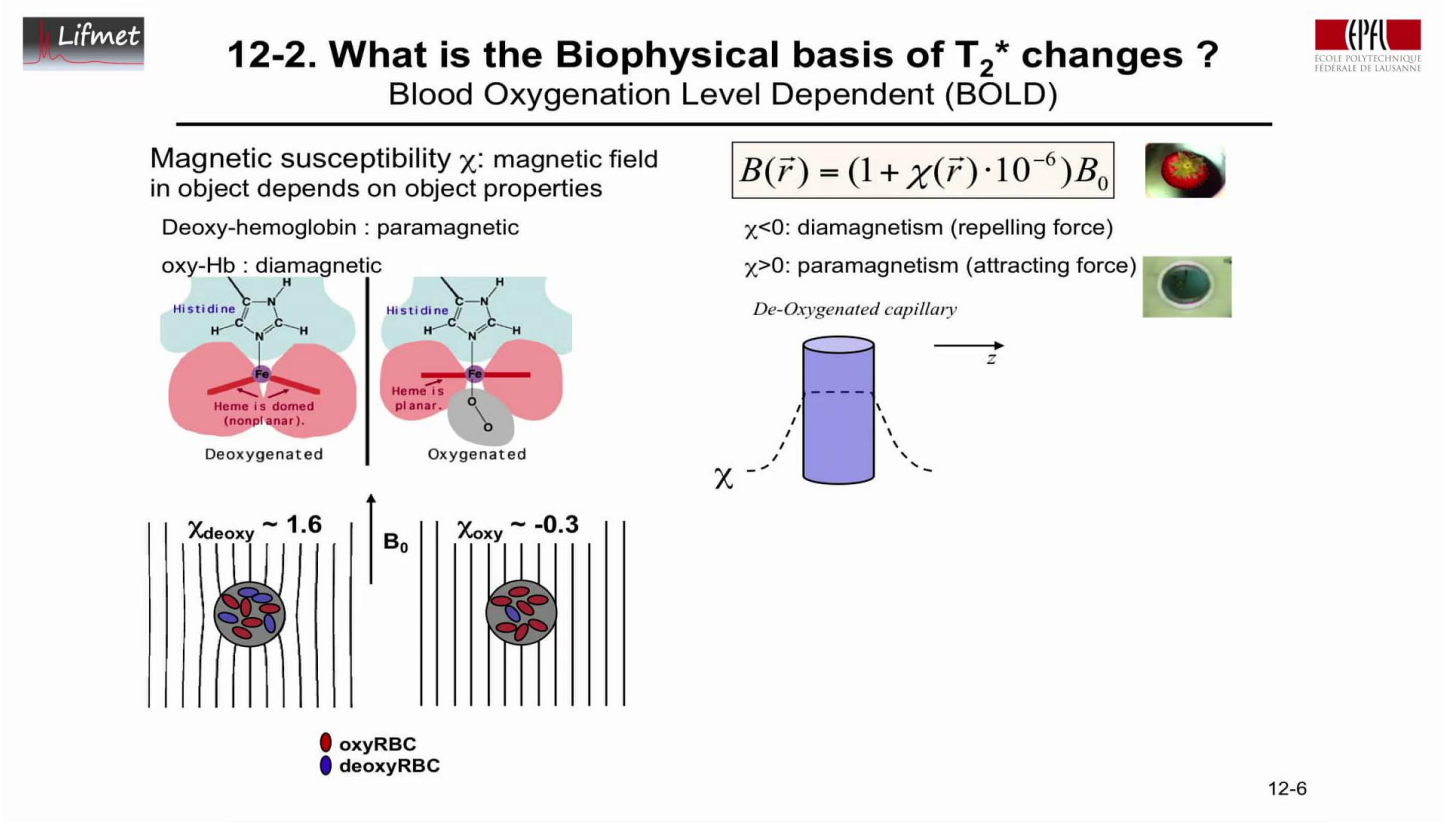


Okay. And a similar situation arises in tissue, that we have seen now with the demonstration with paramagnetic oxygen and diamagnetic nitrogen. We have in our tissue, in our blood actually, we have two types of hemoglobin: deoxy-hemoglobin, which is paramagnetic, and oxy-hemoglobin, which is diamagnetic. This has to do with the fact whether there's oxygen bound to the heme, iron, or not. This changes the configuration of the electrons and therefore changes whether they are para- or diamagnetic. So now what happens if we are looking at a blood vessel that's put into an external field *B_0* like this. And here we have the situation with a lot of deoxygenated red blood cells. So we have a number of red blood cells here that are deoxygenated-- they're in blue; in red are the oxygenated red blood cells. The paramagnetism, the effect, the paramagnetic deoxy-- the susceptibility of deoxyhemoglobin is 1.6. So now what happens is there is a distortion in magnetic field that is generated. We do know that this actually happens based on the orientation: if you take an infinitely long cylinder-- for those of you who are familiar with electromagnetics or remember the calculations-- if you put an infinitely long cylinder in a magnetic field, parallel to the magnetic field, we would not see a distortion of the magnetic field like this is seen here.

Notes

Summary

4m 41s

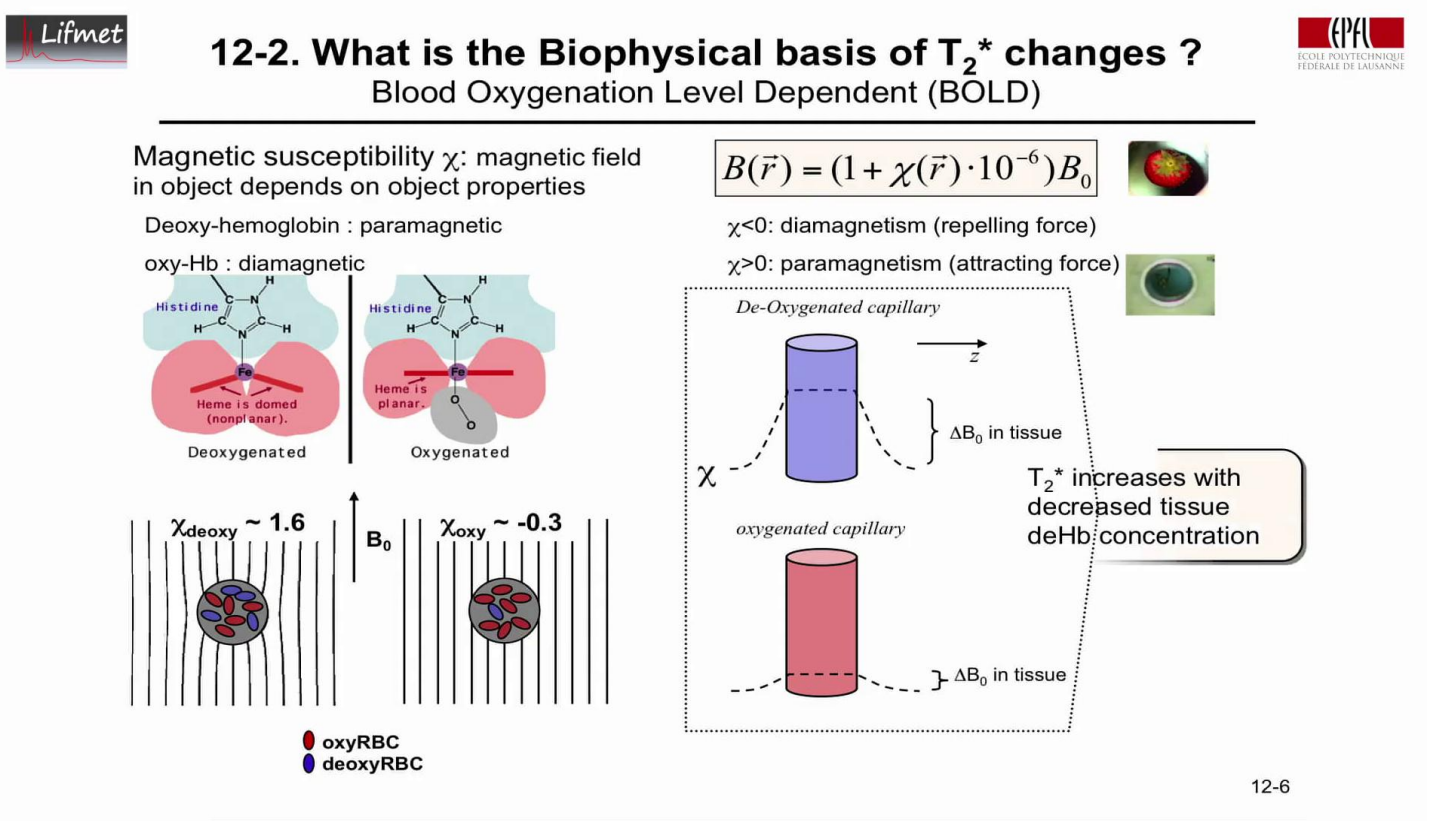


This one here is our perpendicular, and here the effects are quite substantial-- there's a distortion around the vessel of the magnetic field. If we take now an oxygenated vessel-- let's take an artery, here we have a vein-- we have much more oxygenated red blood cells and very few deoxygenated red blood cells, so the average susceptibility in the blood vessel is around -0.3. And here we have very little distortions of the magnetic field outside of the vessel. So, inside the vessel, we have a big susceptibility effect-- and here I'll take first the deoxygenated capillary, the magnetic field is along *z*, so it's to the right-- and I'll plot here the susceptibility as a function of position. It's a rough approximation; it's a sketch. We know that we have a deoxygenated capillary, deoxygenated blood, so the susceptibility, the magnetic field, inside is higher. We have the tissue, which is essentially just water, the susceptibility is lower. So we have a difference of susceptibility between inside the vessel and outside. What this means in terms of magnetic field is that we have a different magnetic field inside the vessel, and outside the vessel.

Notes

Summary

6m 11s



And somewhere there is a transition between the two magnetic fields. The transition is not immediate-- we don't have a discontinuous nature-- so it falls off gradually with an appreciable gradient. So, what this means is that actually, outside of the capillary, we have a change in magnetic field, a change in *delta B-0*, that's happening inside the tissue. If we look at the oxygenated capillary, I'll draw it in red here, the difference in magnetic field, the change that happens in the tissue, is much smaller because we have almost a nearly perfect diamagnetic situation in the blood here. Now, the consequence, if we have such a gradient of magnetic field surrounding the capillary, the image voxel is much bigger, so this means that we are going to have a *delta B* that is induced by physiology and that is *non-zero*. So there is a consequence here that the *T_2 star* increases with decreased deoxy-hemoglobin concentration in the tissue. So, that is in the blood, but that's the average deoxy-hemoglobin concentration changes-- if it decreases, then *T-2 star* will increase because we are reducing the *delt B_0* term here which we have seen previously influences the *T_2 star*.

Notes

Summary

7m 32s

12-2. What is the Biophysical basis of T_2* changes ?

Blood Oxygenation Level Dependent (BOLD)

Magnetic susceptibility χ: magnetic field in object depends on object properties

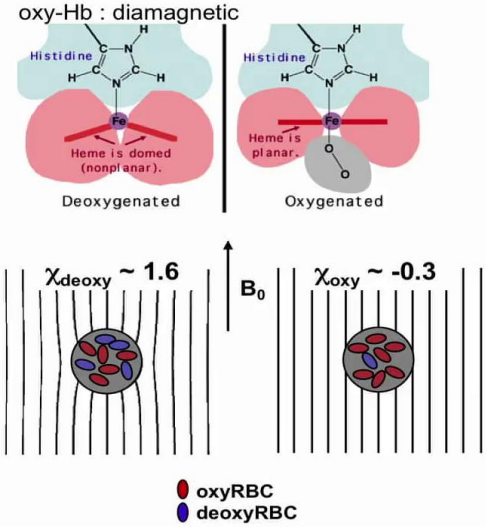
$$B(\vec{r}) = (1 + \chi(\vec{r}) \cdot 10^{-6}) B_0$$

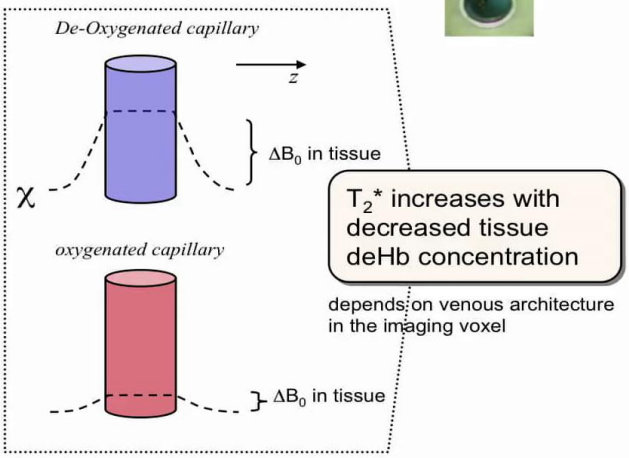
Deoxy-hemoglobin : paramagnetic

oxy-Hb : diamagnetic

χ<0: diamagnetism (repelling force)

χ>0: paramagnetism (attracting force)





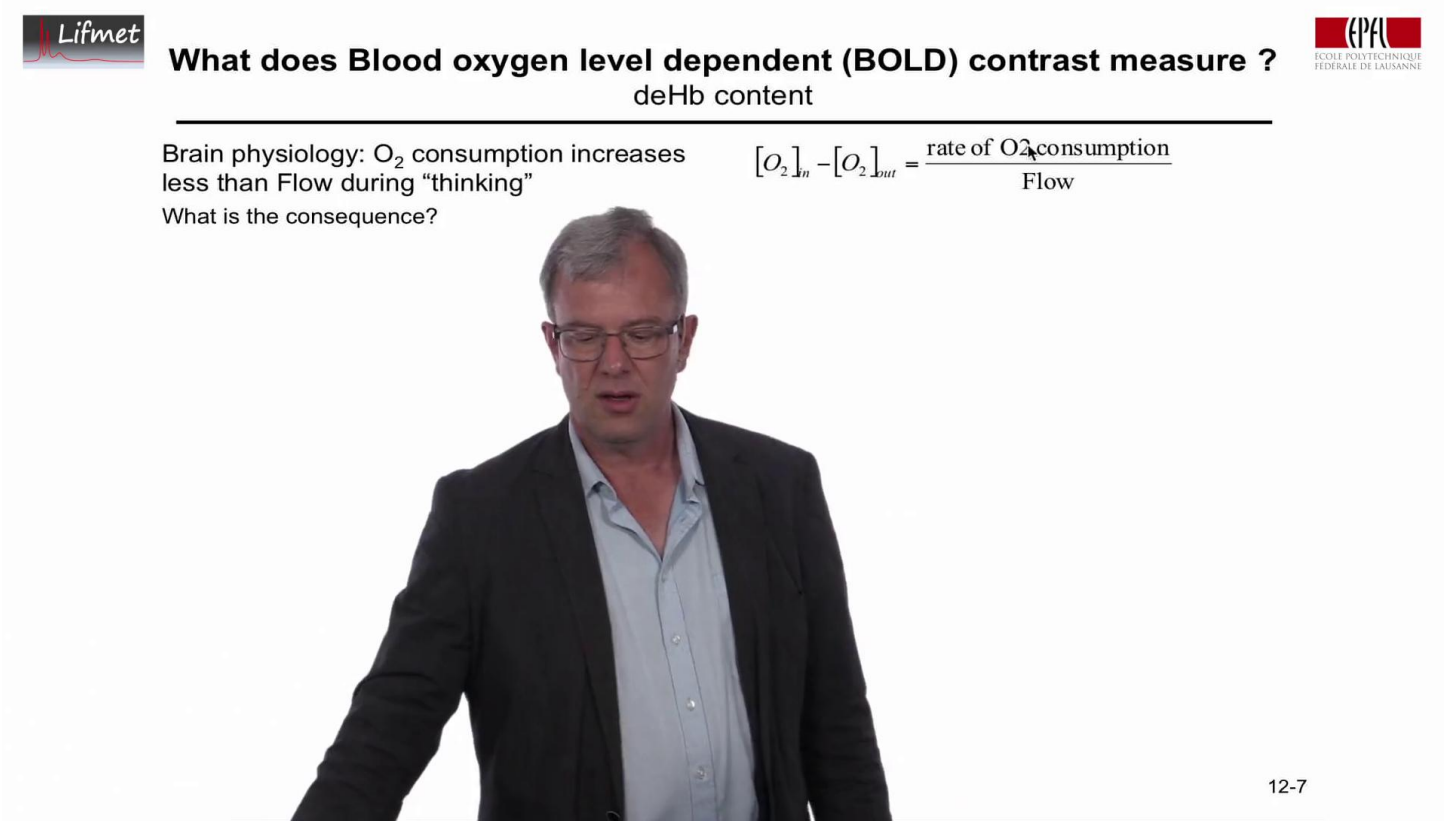
12-6

Of course, a little caveat, this depends on the venous architecture in the voxel depends on blood volume, it depends on the orientation of the blood vessels, but we'll assume here for the rest that this is fairly randomly ordered.

Notes

Summary

9m 03s



So now, how do we get from a change in *delta B_0* that's induced by susceptibility changes in the vessel, to a contrast that is dependent on the blood oxygen level? We know from brain physiology-- we discussed this in the first part of this course-- that the oxygen consumption increases much less than blood flow during a mental task. The mental task can be finger tapping, it can be really a mental task, it can be looking at an image, it can be listening to a sound, etc. So what is the consequence if oxygen consumption increases less, or doesn't increase, above blood flow increases? And this is also something that we've discussed in Course 7, is from mass balance, from fixed principle, the concentration of oxygen flowing in-- the arterial oxygen concentration-- minus the venous oxygen concentration, is equal to the rate of oxygen consumption divided by flow. So if we take the simplified assumption that a situation-- just for mentally thinking it-- that the oxygen consumption does not change, but blood flow increases, then this difference has to decrease and the only thing that we can change is the oxygen consumption in the veins and this one will increase.

Notes

Summary

9m 18s

What does Blood oxygen level dependent (BOLD) contrast measure ?

deHb content

Brain physiology: O_2 consumption increases less than Flow during "thinking"

What is the consequence?

steady-state hemodynamic response

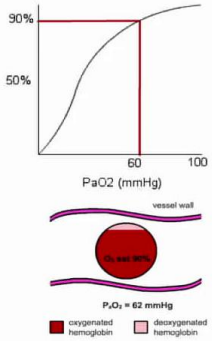
↑ cerebral blood flow (CBF) : ↓ dHb : ↑ BOLD

↑ cerebral blood volume (CBV) : ↑ dHb : ↓ BOLD

$$BOLD \propto \frac{\Delta CBF}{\Delta CBV \cdot \Delta CMRO_2}$$

$$[O_2]_{in} - [O_2]_{out} = \frac{\text{rate of O2 consumption}}{\text{Flow}}$$

Saturation=%oxy-Hb
(deHB=100%-saturation)



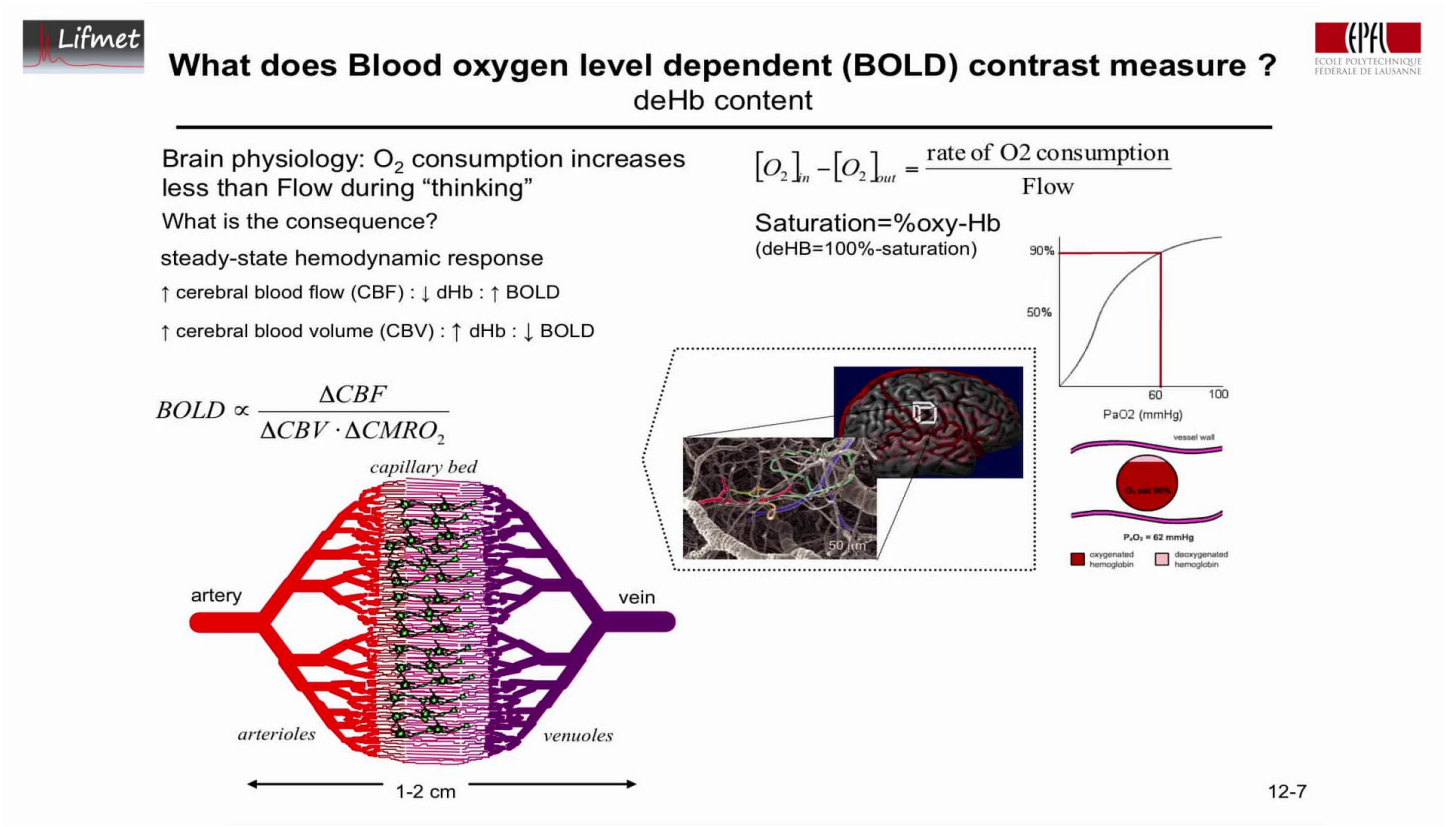
12-7

The oxygen consumption in the veins is linked to the partial pressure of oxygen in the blood and this, in turn, is linked to the percent saturation of the hemoglobin molecules. This is the saturation curve of hemoglobin here-- it's a monotonous curve-- and so the oxygen concentration in the blood will change the saturation of the deoxy-hemoglobin in the blood. Here we have typically around 90-95%-- most of the hemoglobin is saturated but this will change in the blood. We're now looking at the hemodynamic response, what one sees in physiology is that there's an increase in blood flow, so there's a decrease in deoxy-hemoglobin in the tissue, there's an increase in BOLD. There is, however, a counteracting effect that is also a typical increase in blood volume. This increases the number of red blood cells in the tissue, so the deoxy-hemoglobin increases and that decreases the BOLD effect. And I won't go into much of the details-- it's not the purpose of the course to be a course on fMRI-- but in general, the BOLD response, the BOLD signal, is positively correlated with changes in blood flow, inversely correlated with changes in blood volume and inversely correlated with changes in oxygen consumption rate.

Notes

Summary

10m 34s

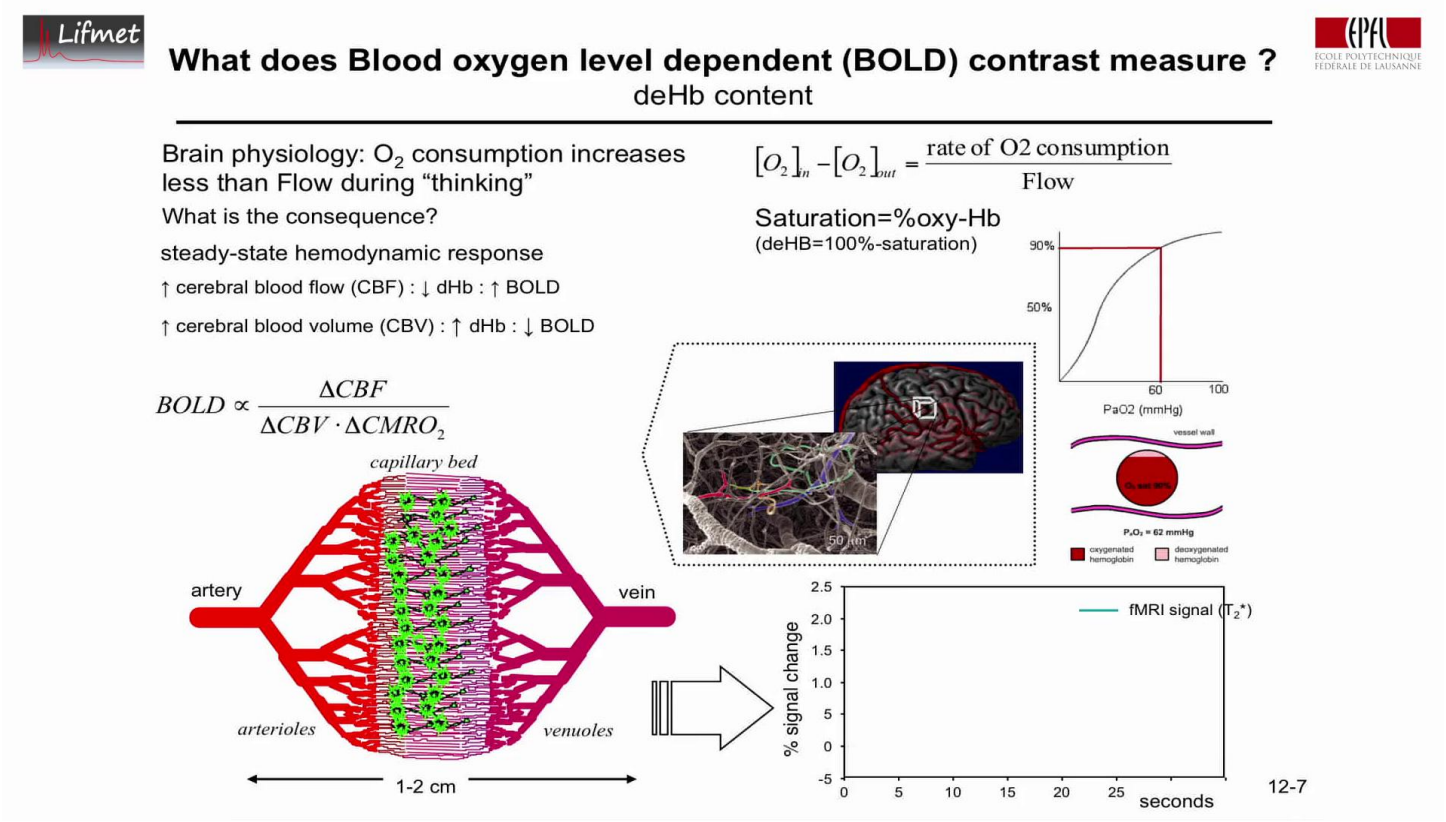


This is the cerebral rate of metabolic oxygen, cerebral blood volume, and cerebral blood flow. So if we look at the vessel architecture of the brain-- this is what we see in an MRI-- in red are the blood vessels typically. And now, if we zoom in to an imaging voxel-- that's our MRI voxel here-- then we see inside the voxel the fine architecture. So we'll see here the arterial input, and we see the venules and the capillary bed. So this is essentially what contributes the changes in *delta B_0*, we're looking at a voxel here, inside the voxel we have this architecture. And this changes now, depending on oxygenation here, of this vessel-- this will change the gradient in magnetic field surrounding the vessel. So if we look at the situation now cartoon-wise, we have the artery supplying oxygenated blood into the arterioles, then we come to the capillary bed, and in the capillary bed we have all our brain cells here-- we'll focus on the neurons-- then we have the venules, and finally the vein-- that's the venous effluent. The whole thing that I've drawn here corresponds to a length scale of roughly 1-2cm. So we have the feeding artery, the draining vein, and in between, at some point, we'll have the capillary bed.

Notes

Summary

11m 52s



Now what happens if we apply an external stimulus, the neurons fire. As they fire, afterwards we get the blood flow response, and the blood flow response is much stronger than the oxygen consumption. That response results in an increased blood flow in general. The increased blood flow decreases the deoxy-hemoglobin content and the venous blood becomes pink. You can actually verify that-- if you cut yourself in the foot, you're standing, then the blood that comes out is fairly dark. If you cut yourself in the foot, and the foot is high up, and you put some warm pads around your leg, so you arterialize the blood flow-- you increase the blood flow-- then the blood that comes out of the wound is more pink. So what is this in time? So this sequence of events-- we have neurons firing, we have a change in blood flow, we have an increase in oxy-hemoglobin in the veins, a decrease in deoxy-hemoglobin-- how does this look over time? We're going to look here at the fMRI signal-- *T_2 star*-weighted signal-- we have the stimulus, which was applied here, in the green bar, and a few seconds later, we have a change in the *T_2 star*-weighted signal.

Notes

Summary

13m 12s

What does Blood oxygen level dependent (BOLD) contrast measure ?

deHb content

Brain physiology: O_2 consumption increases less than Flow during "thinking"

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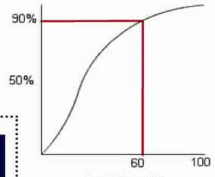
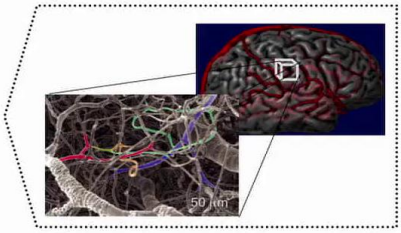
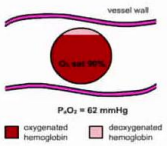
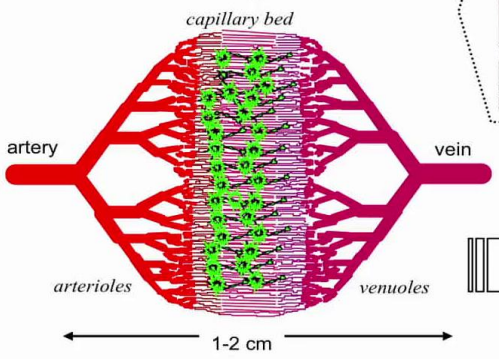
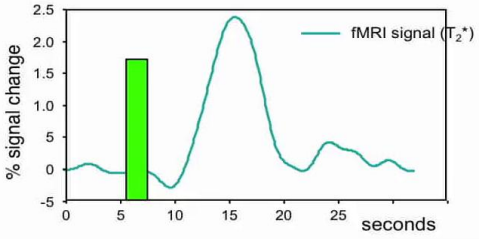


$$BOLD \propto \frac{\Delta CBF}{\Delta CBV \cdot \Delta CMRO_2}$$









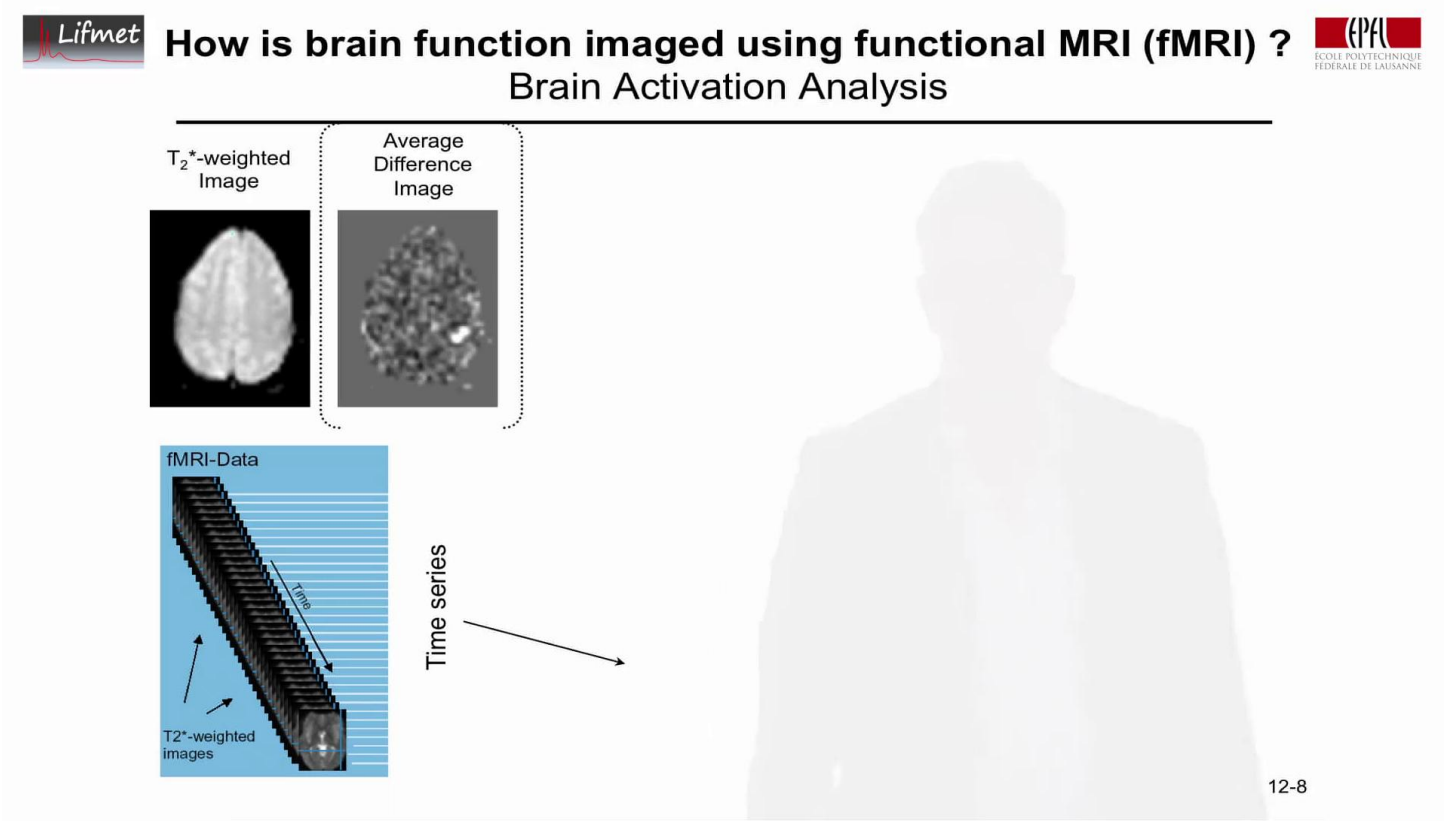
12-7

Notice here the scale: it's percent change, so it's only in the order of a few percent, the signal change. It's a big enough change to capture it with statistical means. It's not a big enough change to be able to look at an MRI and say what you're thinking. So MRI as a lie detector, may work-- people are trying it-- but in general you don't need to worry if you go into an MRI, one does not need to worry, if one goes into an MRI, that one is able to read from the MRI right away what you're thinking.

Notes

Summary

14m 28s

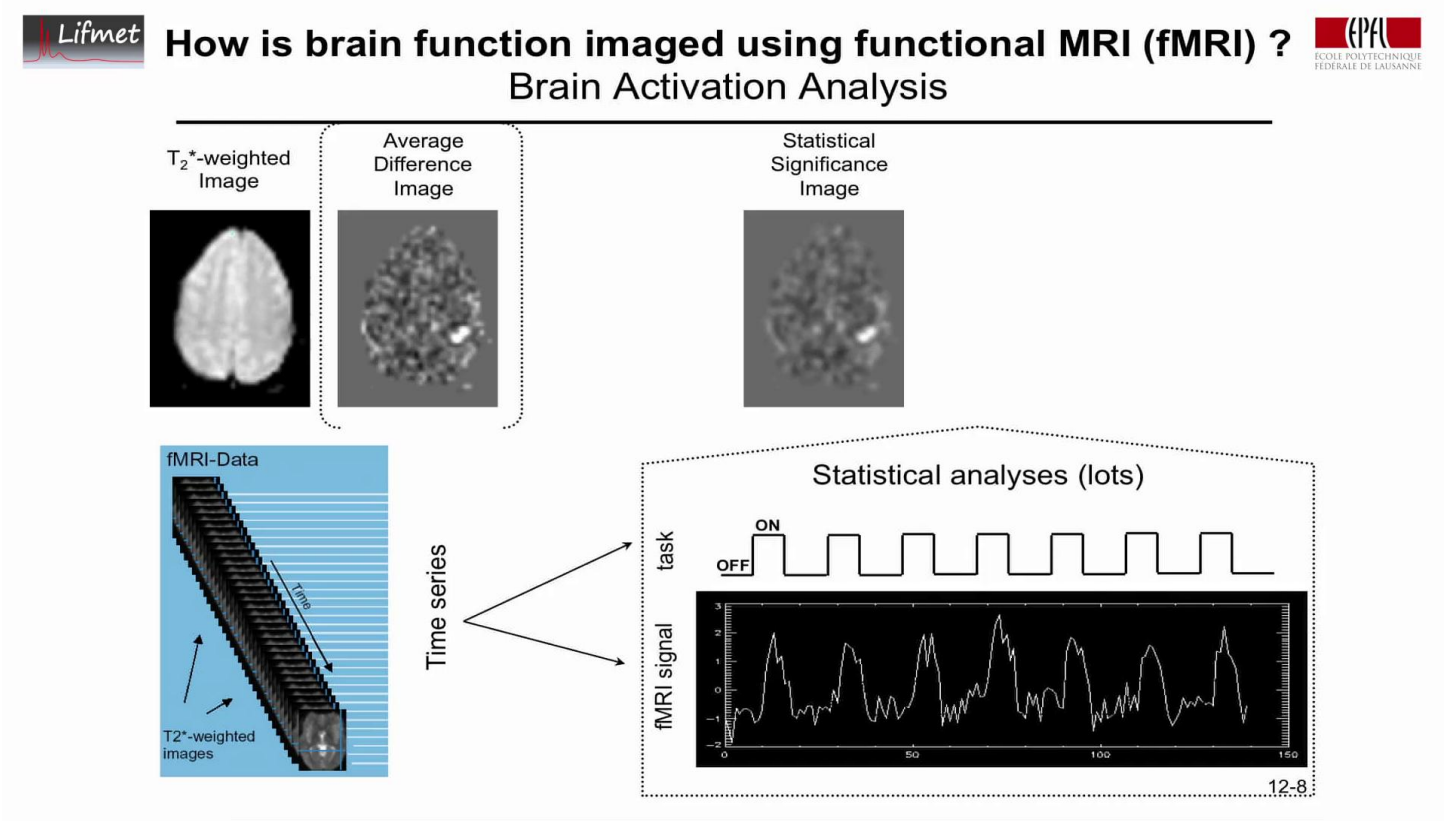


Okay, so we have now the BOLD response, we see a signal in *T_2 star*-weighted image, and the question is now, how is this used to image brain function? So here's a *T_2 star*-weighted image of the human brain and if one now takes a task condition, like looking at a light versus not looking at a light, takes the *T_2 star*-weighted images, and takes the difference between these two time periods, then one gets an image like this. Fairly noisy-- outside here is no noise because it's been zeroed-- and here we see an area that is fairly bright. This was in the early days how people looked at brain activation, to convince the critics that indeed one could see brain activation, but this is no longer the way this is being done. But I'm showing it here for curiosity reasons. What is actually done nowadays is that one collects an entire series, time series, of images over time, over and over again, with special techniques that allow us to acquire this much faster, and so this is a series of *T_2 star*-weighted images; a time series. This is recorded-- here's, for example, the time series of a single pixel in a brain activation task-- and you can see that the signal changes relatively periodically.

Notes

Summary

15m 00s

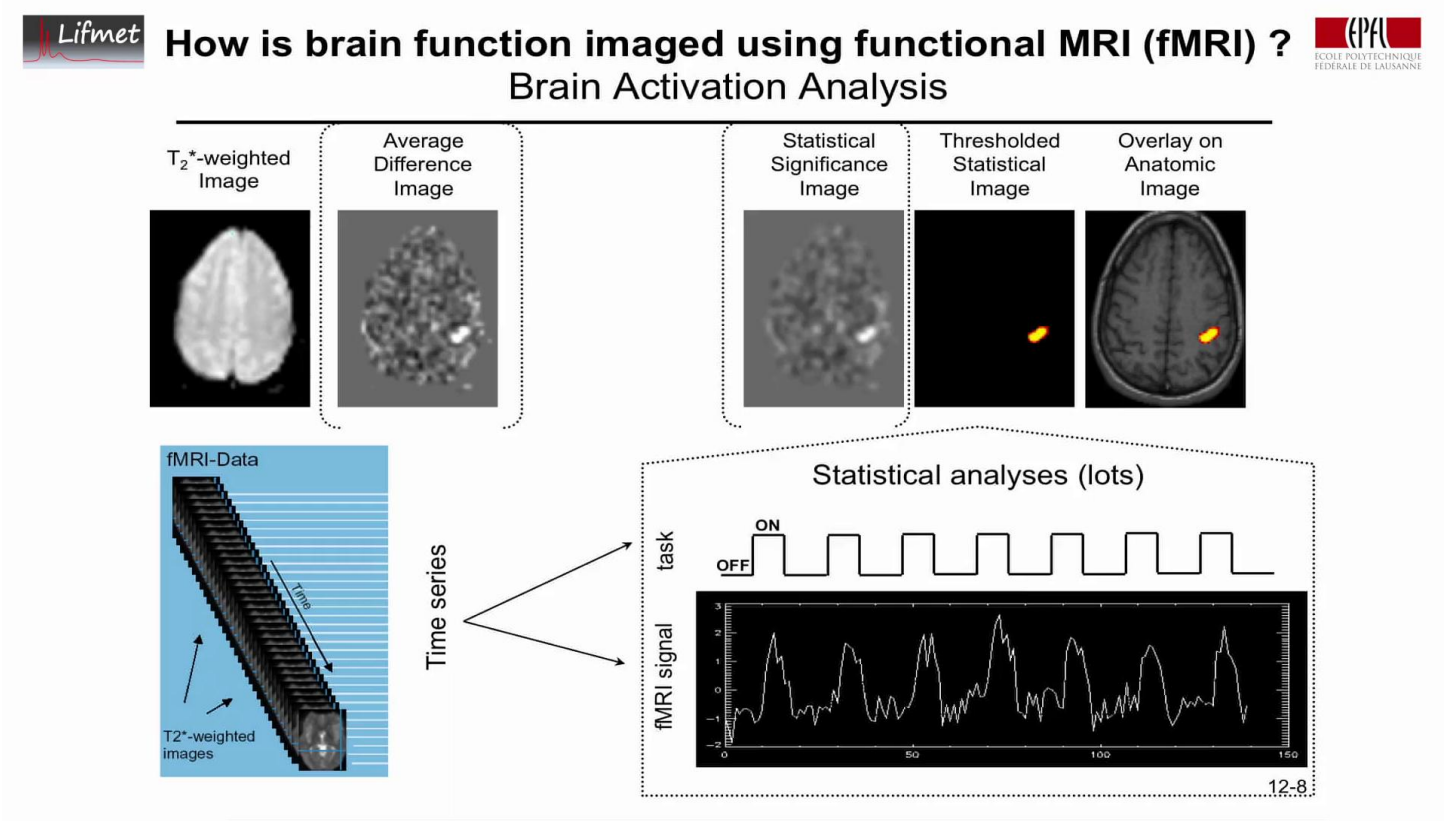


These activations are linked to the task-- in this particular case, there were 7 tasks, always the same task-- and the change in *T_2 star*-weighted image here, the BOLD change, corresponds to the application of this task, of the repetitive measure of this task. So now, since what we are looking for is a change in pixel intensity, to say this is corresponding to a change in *T_2 star*-- in outlying deoxy-hemoglobin changes-- what one does is, one takes this time series, compares it to the measured time series, the task, and then does a statistical analysis. So here, this means "on", and this means "off"-- actually, it's *state A* and *state B* is the more correct term-- so now comes the hard part and that's a lot of statistical analysis. We're not going to go into the details here-- one has to be very careful, very stringent how it's being done-- but what happens next. So what one gets then is a statistical significance image. That basically just says, "I'm looking at the statistical probability that a particular pixel here is indeed following the activation pattern given by the task." And here we can see a higher statistical significance.

Notes

Summary

16m 24s



This actually is not looked at directly-- what is looked at typically is the thresholded statistical image-- so after a certain *z-score*, statistical relevance score, one decides, yes, this pixel is indeed activated, it is responding to this particular task. And so one thresholds out the low statistical probability pixels and leaves only the high probability of statistical images. And of course, it's much more interesting to overlay this on anatomical imaging, too see exactly where the activation is, otherwise it appears just as a blob here-- we won't exactly know where that is. So this is far more intuitive to see where one exactly is. So this is -- in neuroscience, a very important imaging technique has become-- to study brain activation in systems neuroscience. It has, since the 90s, essentially replaced positron emission tomography as a means to look at brain activation.

Notes

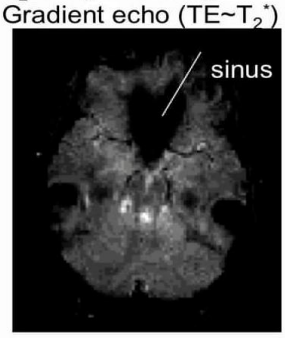
Summary

17m 43s

How do magnetic susceptibility differences affect T_2^* ?

(B_0 imperfections, e.g. air-tissue interface, implants)

T_2^*-weighted image
Gradient echo (TE~T_2^*)



Tissue: diamagnetic

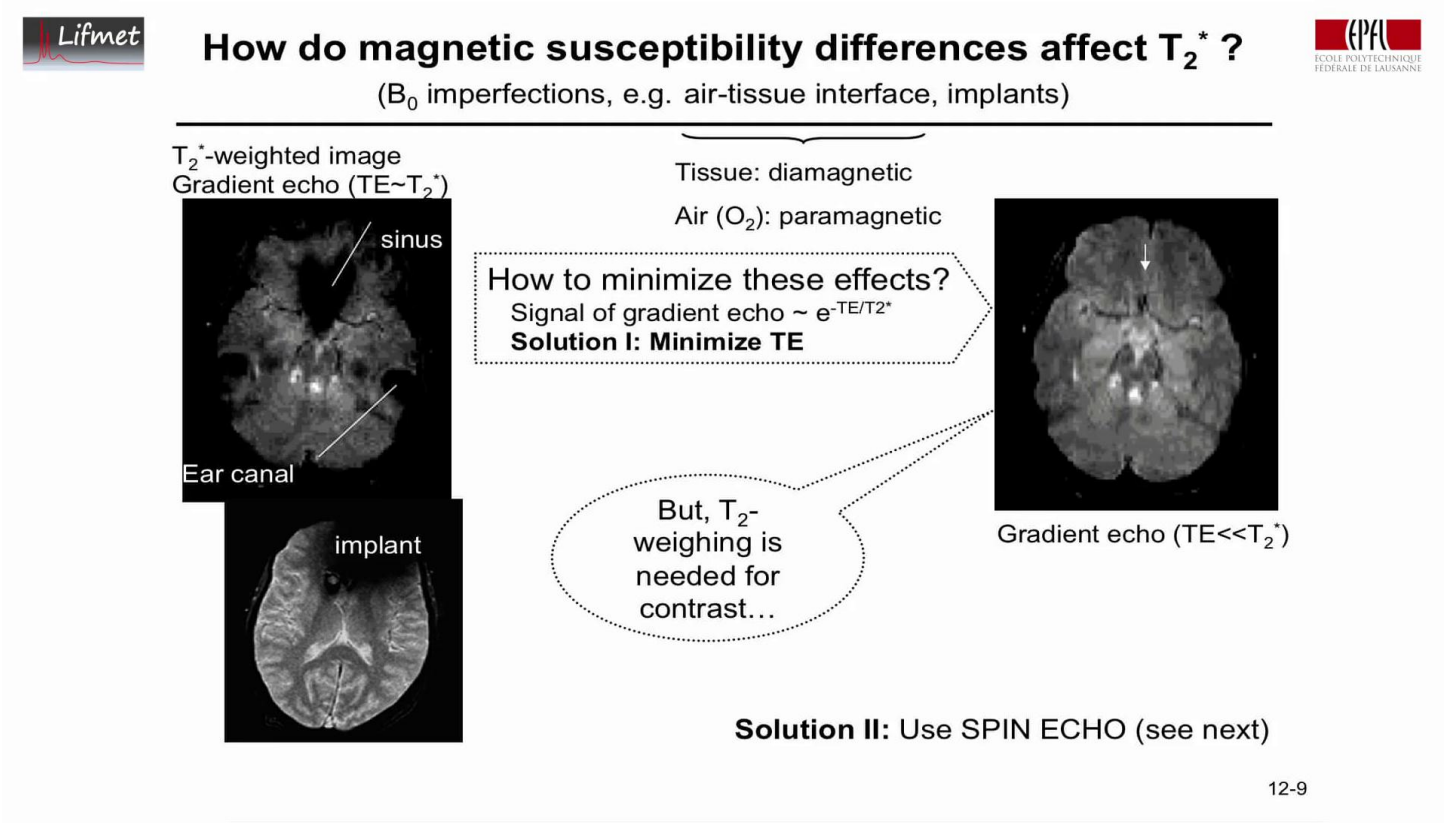
Air (O_2): paramagnetic

Now we've talked about susceptibility: the difference between diamagnetic oxy-hemoglobin and paradiamagnetic deoxy-hemoglobin. But we have also other susceptibility effects to contend with. And this is particularly at the air-tissue interface, because tissue is diamagnetic, just like oxy-hemoglobin, and the air-- molecular oxygen is paramagnetic. We have seen this: 20% oxygen in the air produces sufficient paramagnetism in the air, compared to our bodies which are essentially water and therefore diamagnetic. So we'll have the same kind of transition between the paramagnetic species, which is the air around us, and the diamagnetic surrounding-- well, that's our body-- that creates changes in *B_0* at *delta B_0*. And so here is a gradient echo image taken from the brain at a *TE* that's roughly *T_2 star*. And now we can see here different black areas. This is an image of the brain-- it's a cut like this, about here-- and can you guess what these black areas correspond to? Well, this area up here is the sinus-- we have here, behind the nose, we have the sinuses air-filled cavity, so it's filled with paramagnetic molecular oxygen.

Notes

Summary

18m 50s



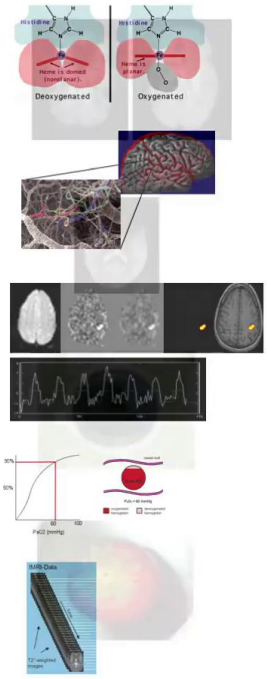
And here we have the ear canal that is also filled with paramagnetic oxygen. And this creates, on this type of image, it creates a fallout of the signal because there's dephasing of the magnetization due to the *delta B_0*. Here's another example of an implant. Implants, if their susceptibility doesn't match that of the tissue, they can produce the same effect. One example is, for example, the TWOS. So, how can we minimize these effects? Here we notice that the signal of the gradient echo is proportional to *e* to the minus *TE* over *T_2 star*. So we can minimize these effects by minimizing *TE*. And if we do this, then such a *T_2 star*-weighted image will look like this-- this is a gradient echo with a short *TE*. However, we actually want to have *T_2* weighting to obtain contrast-- one still wants to be able to see tissue contrast. So this solution is not applicable. And here comes the second solution that we will discuss now, and that is to use SPIN ECHO, which eliminates the effects of static field homogeneity. This is now coming up.

Notes

Summary

20m 14s

Credits (1/2)



Hemoglobin and the Heme Group: « Metal Complexes in the Blood for Oxygen Transport », Rachel Casiday and Regina Frey
http://www.chemistry.wustl.edu/~edudev/LabTutorials/CourseTutorials/LabTutorials/Hemoglobin/MetalComplexinBlood.html

Harrison et al. Cerebral Cortex (2002)
http://limpeter-mriblog.blogspot.ch/2011/12/arterial-spin-labeling-asl.html

« Physiologic Basis of fMRI SignalsFocus on Perfusion » MRI, John A. Detre, M.D.
http://www.slideserve.com/vevina/physiologic-basis-of-fmri-signals-focus-on-perfusion-mri

Creative commons pictures

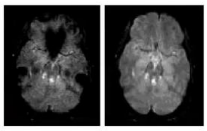
fMRI data (creative commons pictures)
http://megaslides.com/doc/4857340/biomedical-imaging-ii

Notes

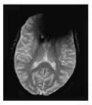
Summary

21m 34s

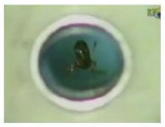
Credits (2/2)



Bold signal dropout (creatives commons pictures)
http://users.fmrib.ox.ac.uk/~peterj/lectures/fMRI_Exp_V/sld032.htm



'Do you see what I see?', Professor David Manning Public Inaugural Lecture, 5th December 2005
http://insight.cumbria.ac.uk/1019/1/Inaugural_Lecture.pdf



Levitating frog
https://youtu.be/A1vyB-O5i6E

Levitating Strawberry
https://youtu.be/uY8btfJZ9Z8

Notes

Summary

21m 40s