Magnetic Resonance Imaging

III, Diffusion, and Susceptibility

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August 25, 2010

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Outline for Today

In today's lecture we consider two other contrast mechanisms. The two contrast mechanisms are connected to diffusion and magnetic susceptibility. But first, let's use Jeremy Magland's simulator to see the effects we described in the last lecture.

Spoiled GRE T_1-weighted

$T_E = 10 \quad T_R = 50.$

Short T_E decreases effects of T_2 and short T_R enhances effects of T_1.

Greater grey/white matter contrast, grey matter has longer T_1.

Spin Echo T_2-weighted

$T_E = 50 \quad T_R = 6000.$

Long T_E increases effects of T_2 and long T_R decreases the effects of T_1. Using a spin echo means that we see T_2-decay, rather than T_2^*-decay.

Spin Echo Proton Density-weighted

$T_E = 10 \quad T_R = 6000.$
Short T_E decreases effects of T_2, and long T_R decreases the effects of T_1.

The Effects of Relaxation on Image Density

If the experiment has a flip angle θ, an echo time T_E and repeat time T_R, then, using a GRE protocol, the magnitude at the start of each acquisition will satisfy

$$\overline{\rho}_m(\boldsymbol{x}) = \overline{\rho}(\boldsymbol{x}) \sin\theta e^{-\frac{T_E}{T_2^*}} \frac{[1 - e^{-\frac{T_R}{T_1}}]}{1 - \cos\theta e^{-\frac{T_R}{T_1}}} \tag{1}$$

The parameters T_1 and T_2^* are spatially dependent.
This formula indicates how the choice of imaging protocol, flip angle, and timings effects the contrast in the image. If we refocus using a spin-echo, then T_2^* would be replaced by T_2.

The Steady State

MR-imaging experiments are usually repeated many times and hence are performed in a steady state, which does not pass through the equilibrium magnetization. At the start of the procedure, wherein we flip the spins and phase encode, then acquire, we do not usually start at the equilibrium, but instead at a steady state which reflects the relaxation effects in a spatially localized way:

$$\overline{\rho}_m(\boldsymbol{x}) = \overline{\rho}(\boldsymbol{x}) \sin\theta e^{-\frac{T_E}{T_2^*(x)}} \frac{[1 - e^{-\frac{T_R}{T_1(x)}}]}{1 - \cos\theta e^{-\frac{T_R}{T_1(x)}}} \tag{2}$$

After the acquisition the residual transverse magnetization is purposely dephased, so that it will not "contaminate" subsequent measurements. This is called *spoiling* and is usually performed with *crusher gradients*.

Diffusion Imaging

- At finite, non-zero temperatures, water molecules are in continual motion. The extent of these motions is a reflection of the local physical environment. The first phenomenon we consider is connected to the possibility of observing the effects of diffusion in an MR-image. This is very useful in medical imaging for a variety of reasons.
- In fact the rates of diffusion in fibrous structures are different in different directions, and MRI can be used to detect the presence of fiber tracts by measuring the diffusion tensor.

Susceptibility Imaging

- The second phenomenon we consider is connected with the interactions of materials and magnetic fields. We are all familiar with ferromagnetism, wherein iron becomes permanently magnetized by a magnetic field. Many materials respond to a static magnetic field, $\boldsymbol{B}$ by producing a small magnetic field, $\boldsymbol{M} = \chi \boldsymbol{B}$, called the magnetization. When the object is removed from the field the magnetization disappears.
- Here the constant of proportionality, χ, is called the magnetic susceptibility. It can be either positive (paramagnetic) or negative (diamagnetic). For materials of interest in MRI χ is on the order of 10^{-6}, which can have a noticable effect on an MR-image.
- The basis of functional MRI (fMRI) is the fact that oxygenated and deoxygenated hemoglobin have different magnetic susceptibility, with $\Delta\chi \approx .5 \times 10^{-6}$.

The Basic Physical Model for Diffusion

Recall that in MRI we image the distribution of protons in water molecules. At room temperature water is a liquid and this means that the water molecules themselves are constantly in motion. This motion is highly irregular and is usually descibed as Brownian motion. In an isotropic homogeneous medium this is characterized by a single scalar constant D, called the self diffusion constant. We let $P(\boldsymbol{x}, \boldsymbol{y}; t)$ denote the probability that a water molecule at spatial position $\boldsymbol{y}$ at time 0, will be at position $\boldsymbol{x}$ at time t. This conditional probability satisfies the PDE:

$$\partial_t P = \nabla \cdot D \nabla P \text{ with } P(\boldsymbol{x}, \boldsymbol{y}; t) = \delta(\boldsymbol{x} - \boldsymbol{y}). \tag{3}$$

The solution in n-dimensions is

$$P(\boldsymbol{x}, \boldsymbol{y}; t) = \frac{e^{-\frac{\|\boldsymbol{x}-\boldsymbol{y}\|^2}{4Dt}}}{(4\pi\, Dt)^{\frac{n}{2}}}.$$

A Simple Diffusion Experiment, I

Suppose that we place a sample of water with density $\rho(\boldsymbol{x})$, in a large homogeneous magnetic field long enough for the spins to be polarized. We then apply a 90° to the entire sample without any gradients turned on. Shortly after we turn on a a very strong gradient of the form $(\star, \star, \langle \boldsymbol{g}, \boldsymbol{x} \rangle)$ for a very short period of time δ. Spins located at $\boldsymbol{x}$ will acquire an additional phase equal to $\gamma\, \delta \boldsymbol{g} \cdot \boldsymbol{x}$. After a time τ we apply an inversion pulse, and then shortly later we again turn on the same gradient for the same very short period of time. A spin that was located at $\boldsymbol{x}$ for the first gradient pulse, but is now located at $\boldsymbol{y}$ after the second, will have a total accumulated phase of $\Delta\phi(\boldsymbol{x}, \boldsymbol{y}) = \gamma\, \delta \boldsymbol{g} \cdot (\boldsymbol{y} - \boldsymbol{x})$.
If the spins are stationary, then this is zero.

A Simple Diffusion Experiment, II

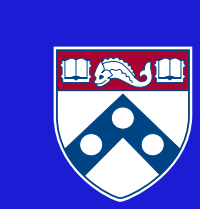
But the spins are not stationary. Suppose that the time between the first and second gradient pulses was Δ. If we measure the MR-signal, then, in the absence of any other relaxation effects, we would expect to find that

$$S_{\Delta,\boldsymbol{g}} = C \int_{\mathbb{R}^3} \int_{\mathbb{R}^3} \rho(\boldsymbol{x}) P(\boldsymbol{x}, \boldsymbol{y}; \Delta) \exp[i\gamma\, \delta \boldsymbol{g} \cdot (\boldsymbol{y} - \boldsymbol{x})] d\boldsymbol{y} d\boldsymbol{x}. \quad (4)$$

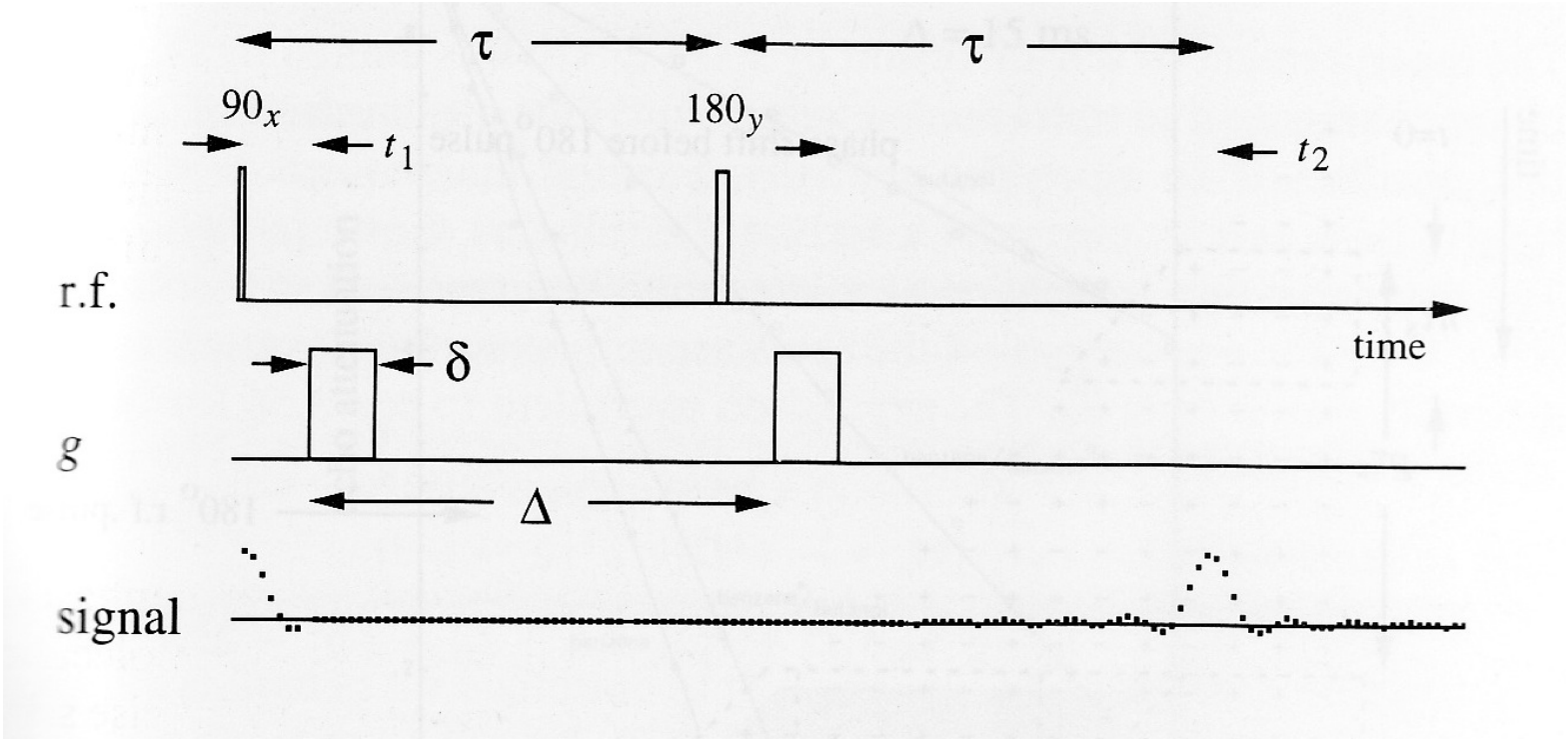
Note that with $\boldsymbol{g} = 0$ the signal would be

$$S_{\Delta,0} = C \int_{\mathbb{R}^3} \rho(\boldsymbol{x}) d\boldsymbol{x}. \quad (5)$$

This experiment is called the *pulsed gradient spin echo* (PSGE) experiment.



The PSGE Pulse-Sequence Diagram



A pulse sequence diagram for the PSGE experiment, which is used for measuring diffusion constants.

A Simple Diffusion Experiment, III

Ignoring boundary effects, we can use the formula above for $P(\boldsymbol{x}, \boldsymbol{y}; t)$ to obtain that:

$$\frac{S_{\Delta,g}}{S_{\Delta,0}} = e^{-\gamma^2\delta^2\|\boldsymbol{g}\|^2 D\Delta}. \tag{6}$$

This simple experiment allows us to determine the value of D, the self diffusion constant.
We took δ to be quite small and assumed that little diffusion takes place while the gradient fields are on. As we shall see a more accurate result is given by the Stejskal-Tanner Formula:

$$S_{\Delta,g}/S_{\Delta,0} = e^{-\gamma^2\delta^2\|\boldsymbol{g}\|^2 D(\Delta-\delta/3)}.$$

This simple idea can be combined with imaging protocols to obtain a method to image the spatial variation of the diffusion constant.

The Bloch Torrey Equation

To obtain the more precise result relating the diffusion coefficient to the signal attenuation in the PGSE experiment we need to use a model that combines diffusion with the Bloch equation. Such a model was introduced by Torrey, it is called the *Bloch-Torrey* equation:

$$\frac{d\boldsymbol{M}}{dt}(x;t) = \gamma\, \boldsymbol{M}(x;t) \times \boldsymbol{B}(x;t) - \frac{1}{T_2}\boldsymbol{M}^{\perp} - \frac{1}{T_1}(\boldsymbol{M}^{\parallel} - \boldsymbol{M}_0) + \nabla \cdot \boldsymbol{D}\nabla(\boldsymbol{M} - \boldsymbol{M}_0). \quad (7)$$

Here $\boldsymbol{D}$ is the diffusion tensor, which often reduces to a scalar multiple of the identity, $\boldsymbol{D} = D\,\mathrm{Id}$. Torrey derived this equation from first principles, its predictions are similar to those obtained above by heuristic arguments. We usually omit the term $\nabla \cdot \boldsymbol{D}\nabla\boldsymbol{M}_0$, as it is normally quite small.

Measuring the ADC, I

To better estimate the effect of diffusion on the size of the transverse magnetization, we solve the Bloch Torrey equation with a diffusion gradient field of the form $\boldsymbol{G}_{\text{dif}} = (\star, \star, \langle \boldsymbol{g}, \boldsymbol{x} \rangle)$. We first consider the case of an isotropic medium, where the rate of diffusion is equal in all directions. In this case we can choose a gradient pointing in any direction, for example, $\boldsymbol{g} = (0, 0, g)$. This is not a realistic model for many biological environments, which tend to be filled with fibrous tracts, or where the water is divided between intracellular water, trapped in cells and an extracellular component.

Measuring the ADC, II

If we write $m_x + i m_y = e^{-t/T_2}\varphi$, for the transverse component in the rotating frame, then we see that the B-T equation predicts that

$$\partial_t \varphi = -i\gamma\, g(t) z \varphi + \nabla \cdot D \nabla \varphi. \tag{8}$$

Assuming that $\varphi = M_0 e^{-i\gamma G(t) z} A(t)$, where

$$G(t) = \int_0^t g(s) ds \tag{9}$$

we see that $\partial_t A = -(D\gamma^2 (G(t))^2) A(t)$, and therefore, if $g(s) = g$, then $A(t) = \exp(-\frac{1}{3} D\gamma^2 g^2 t^3)$. This shows that diffusion in a gradient field, even for a short time, diminishes the magnetization. Performing this experiment allows the determination of D, called the *apparent diffusion constant*.

The Stejskal-Tanner Formula

To obtain the formula above

$$S_{\Delta,g}/S_{\Delta,0} = e^{-\gamma^2\delta^2\|\boldsymbol{g}\|^2 D(\Delta-\delta/3)},$$

we use the equation

$$\partial_t A = -D\gamma^2(G(t))^2 A(t) \Rightarrow A(t) = \exp\left(-D\gamma^2\int_0^t G(s)ds\right). \tag{10}$$

where now $g(t) = -g\chi_{[0,\delta]}(t) + g\chi_{[\Delta,\Delta+\delta]}(t)$. An elementary calculation shows that

$$A(t) = \exp[-D\gamma^2 g^2(\Delta - \frac{1}{3}\delta)], \text{ for } t > \Delta + \delta, \tag{11}$$

thus verifying the formula above.

Imaging the ADC

The procedure outlined above can be added to one of the basic imaging sequences, to obtain a method for obtaining spatially localized information about the ADC.

This is a basic example of what is called diffusion weighted imaging. It is usable in an isotropic medium.

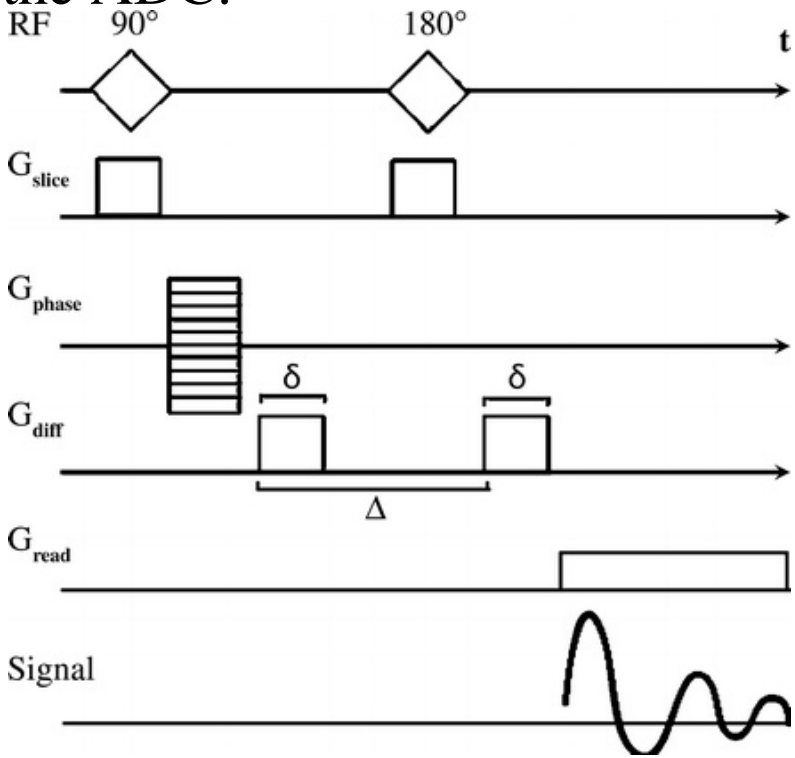
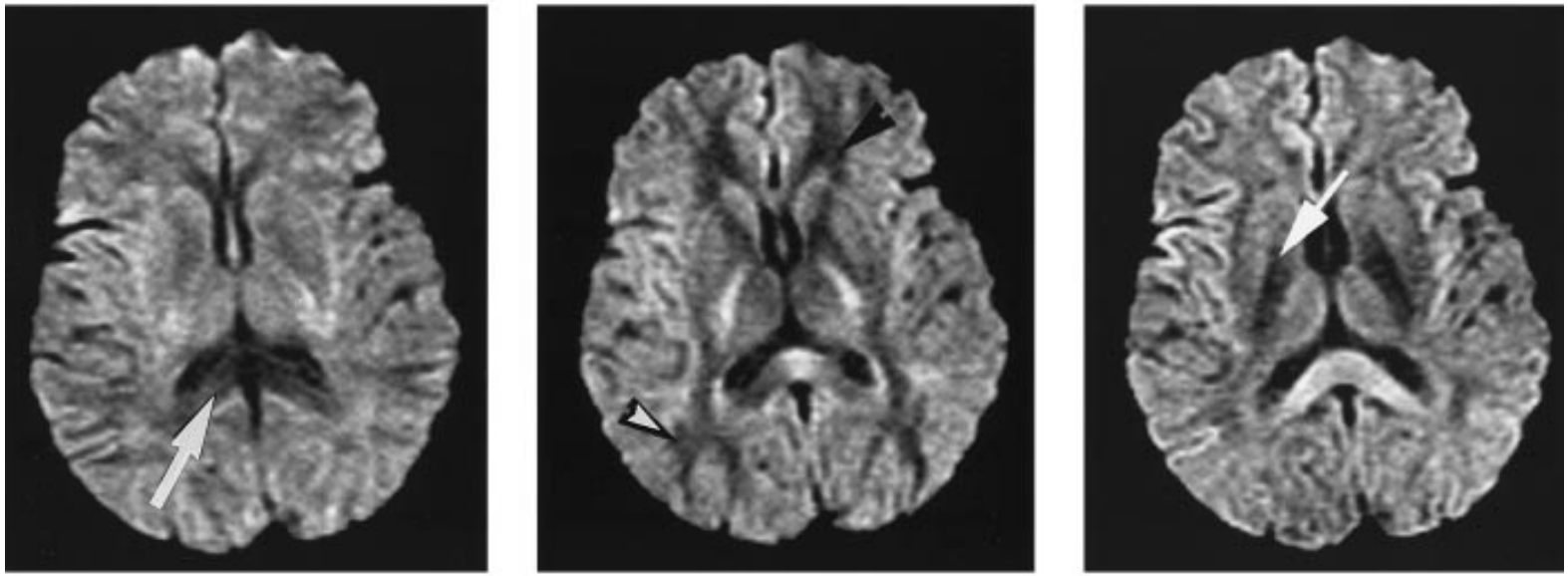


Image reference

Pulse seequence diagram from: *Understanding Diffusion MR Imaging Techniques: From Scalar Diffusion-weighted Imaging to Diffusion Tensor Imaging and Beyond*, by Patric Hagmann, Lisa Jonasson, Philippe Maeder, Jean-Philippe Thiran, Van J. Wedeen, Reto Meuli. In RadioGraphics 2006; 26:S205 S223; Published online 10.1148/rg.26si065510.

Diffusion Weighted Images



From: *Diffusion-weighted MR Imaging of the Brain*, by Pamela W. Schaefer, P. Ellen Grant, R. Gilberto Gonzalez. In: Radiology 2000; 217:331-345.

Diffusion Tensor Imaging

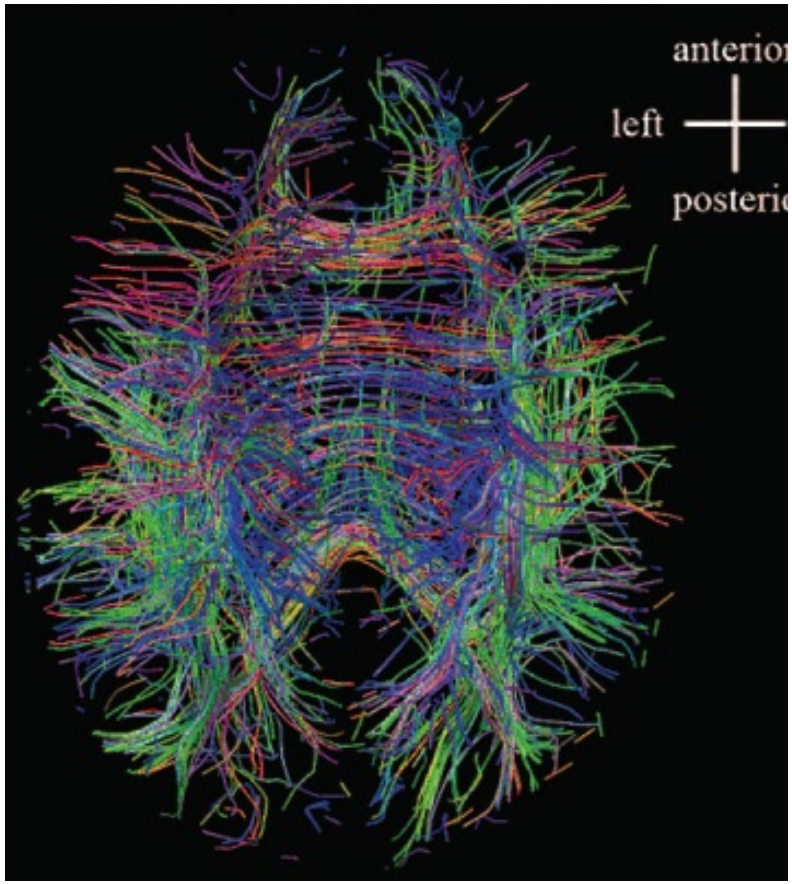
In most biological tissues, the diffusion is neither free nor isotropic. A more sophisticated model is to associate a diffusion tensor $D_{ij}(\boldsymbol{x})$ to each point. This tensor is symmetric and therefore has 6 independent components. To use MRI to measure it, we perform the experiment described above six times, with the diffusion gradient pointing in six sufficiently independent directions, e.g. $\{v_1, v_2, v_3, v_4, v_5, v_6\} = \{e_1, e_2, e_3, (e_1 + e_2)/\sqrt{2}, (e_1 + e_3)/\sqrt{2}, (e_2 + e_3)/\sqrt{2}\}$. We get six numbers $\{d_k(\boldsymbol{x}) : k = 1, \ldots, 6\}$ for each point. To find the diffusion tensor we need to solve

$$d_k(\boldsymbol{x}) = \langle D_{ij}(\boldsymbol{x}) v_k, v_k \rangle \text{ for } k = 1, \ldots, 6. \tag{12}$$

This is called *diffusion tensor imaging* or DTI.

Tractography

Once the diffusion tensor is found we can use its eigenvectors to define direction fields. Integrating these fields allows for the tracking of nerve fibers. This image is obtained by integrating the direction of fastest diffusion.



From: *Understanding Diffusion MR Imaging Techniques...* An even more sophisticated approach is called *diffusion spectrum imaging* (DSI), but we'll stop here.

Other Possibilities

The data derived in a DTI experiment can be used to shade an image in many different ways. One can use the trace of $\boldsymbol{D}(\boldsymbol{x})$ as a measure of average local diffusivity, one can also use the ratio of the largest and smallest eigenvalues as a measure of an-isotropy. These techniques for detecting random motion, can also be combined with techniques for measuring flow, which is accomplished by using flow compensating gradients.

A Little E and M

The next modality we consider involves utilizing small differences in the magnetic susceptibility as a contrast agent. Recall that if a material is paramagnetic or diamagnetic, then placing it in a magnetic field $\boldsymbol{B}$ results in a small induced magnetic field $\boldsymbol{M} = \chi \boldsymbol{B}$, called the magnetization. Here χ is called the magnetic susceptibility. For MR-applications χ takes values in the range $[-10^{-5}, 10^{-5}]$.

If the voxel is a composite of several materials with differing susceptibilities, then this will affect the size of the local T_2^*. This is the basis of the BOLD effect used in functional MRI.

Piecewise Constant Susceptibility, I

The induced magnetization changes the local field experienced by spins close to it. If the material has a fairly uniform local susceptibility, that jumps across interfaces, then this leads to non-localized field distortions, which can lead to serious artifacts in the reconstructed image. If the jumps are small, then they can be visualized in a *phase image*. Using this sort of data to construct a map of susceptibilities is a current field of research in MRI.

Piecewise Constant Susceptibility, II

The field produced by the interface propagates away from the interface and requires a detailed understanding of the geometry of the surface. A jump of $\Delta\chi$ across a surface S leads to an offset field of the form

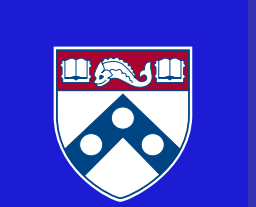
$$\Delta B = \Delta\chi \nabla_{\boldsymbol{x}} \int_S \frac{\boldsymbol{B}_0 \cdot \boldsymbol{n} dS(y)}{\|\boldsymbol{x} - \boldsymbol{y}\|}. \tag{13}$$

For example if we have an infinite cylinder of radius a making an angle θ with $\boldsymbol{B}_0$,

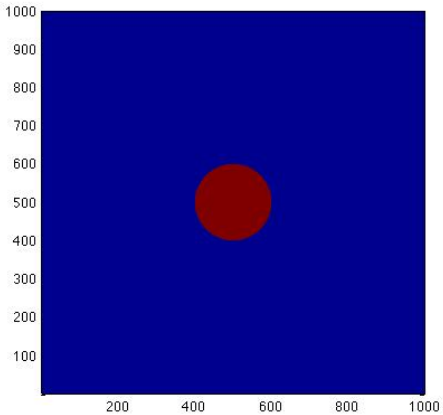
$$\Delta B_{\text{in}} = \Delta\chi b_0 (3\cos^2\theta - 1)/6, \tag{14}$$

$$\Delta B_{\text{out}} = \Delta\chi b_0 \sin^2\theta \cos(2\phi)\frac{a^2}{2r^2}. \tag{15}$$

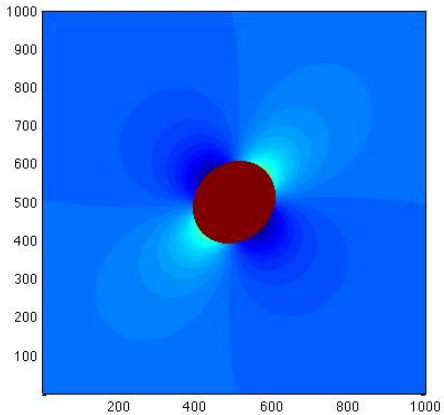
Here ϕ is the azimuthal angle and r the distance from $\boldsymbol{x}$ to the axis of the cylinder.



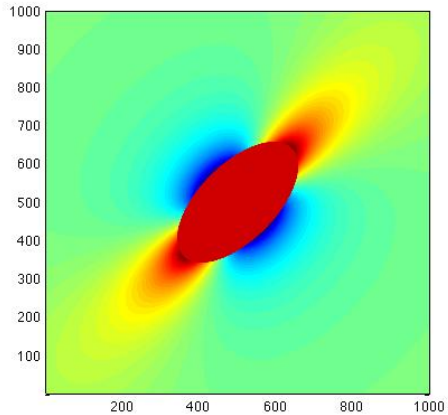
Cylindrical Objects



ΔB resulting from a cylinder parallel to $\boldsymbol{B}_0$.



ΔB resulting from a cylinder at a 30° angle to $\boldsymbol{B}_0$.



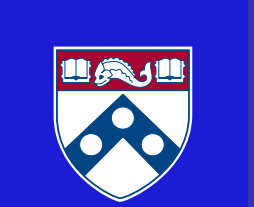
ΔB resulting from a cylinder at a 60° angle to $\boldsymbol{B}_0$.

Susceptibility Weighted Imaging

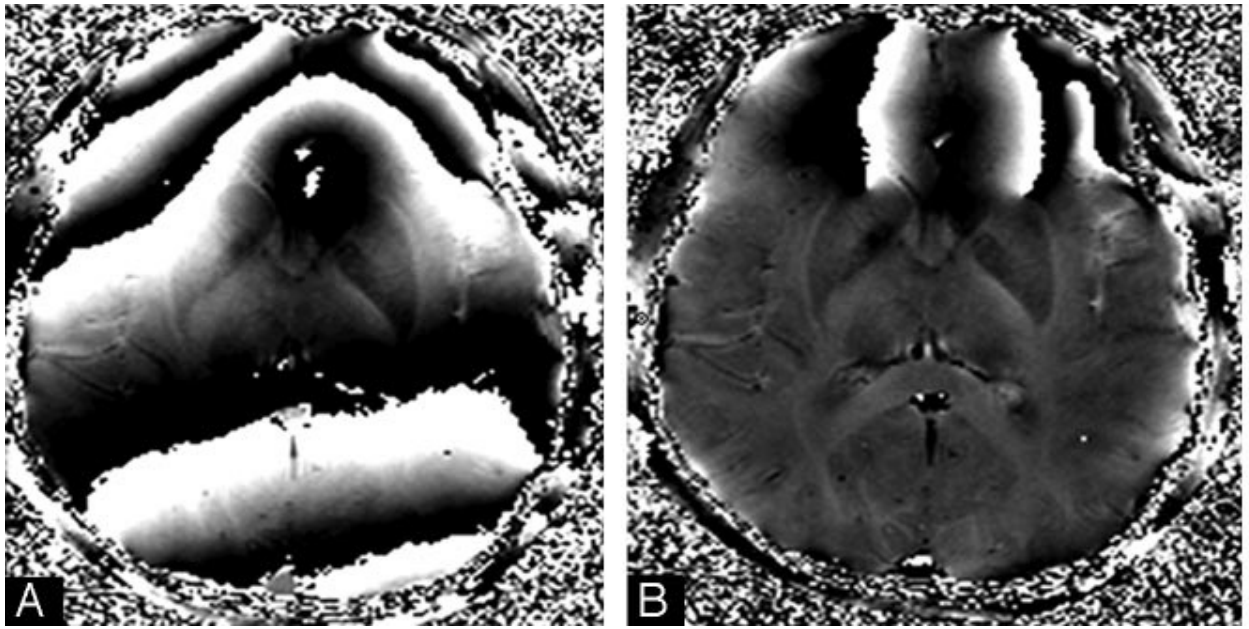
So long as the susceptibility differences are about a part-per-million the main effect of the varying suscpetibility is that the reconstructed image is not real but is of the form

$$\overline{\rho}(\boldsymbol{x})e^{-i\gamma g\Delta\chi(\boldsymbol{x})b_0T_E}. \tag{16}$$

Here g is called a geometric factor, which is related to the effects studied in the previous slide. The raw data in such a protocol is high-pass filtered to remove slow changes in phase resulting from $\boldsymbol{B}_0$-inhomogeneity and other large scale effects, leaving an image that reflects small scale variation in the susceptibility.

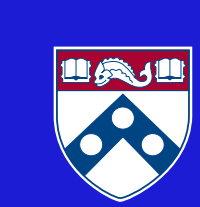


Phase Images, I

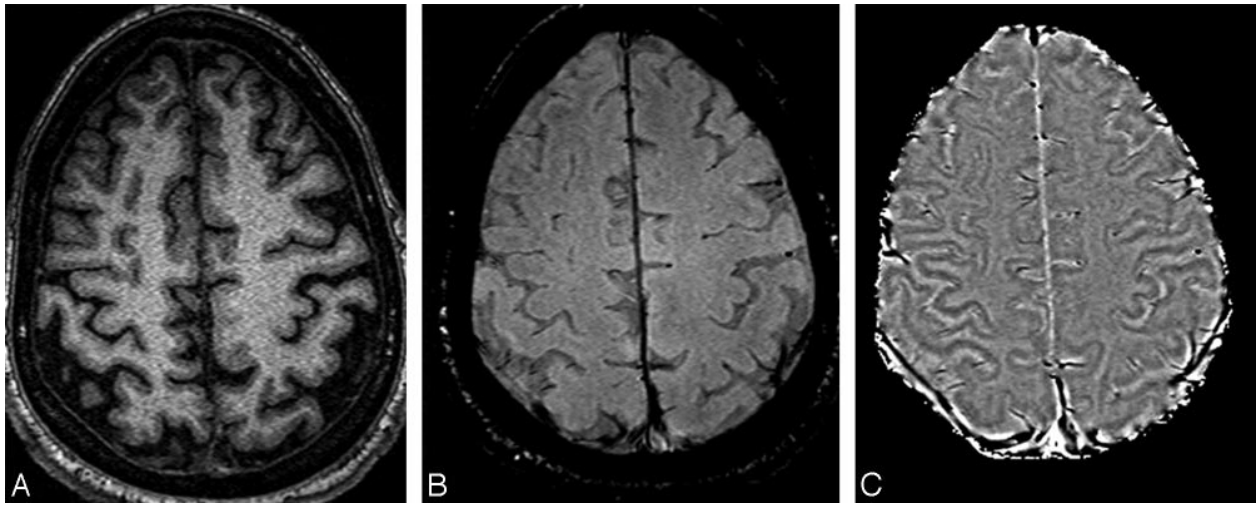


A raw phase image and the result of applying a high pass filter.

From: *Susceptibility-Weighted Imaging: Technical Aspects and Clinical Applications, Part 1*, by E.M. Haacke, S. Mittal, Z. Wu, J. Neelavalli, Y.-C.N. Cheng in Am J Neuroradiol, 30:19-30 Jan 2009.



Phase Images, II



The phase information can also be used to shade an otherwise-weighted image. Short-echo T1-weighted image (A), compared with the SWI long-echo gradient-echo processed magnitude (B) and HP-filtered phase data (C).
From E.M. Haacke et al.

The BOLD Effect, I

The final topic we consider, related to susceptibility imaging, concerns the Blood Oxygen Level Dependent (BOLD) imaging. This is the most commonly used technique employed for functional MRI (fMRI), which attempts to use MR-imaging to ascertain where cognitive processes are actually performed in the brain.

This is a complex technique whose theoretical foundations have not yet been firmly established. We give only a brief outline of the basic ideas.

The BOLD Effect, II

The observation underlying this method is the empirical fact that oxygenated and deoxygented hemoglobin (HbO HbD) have magnetic susceptibilities that differ by about 0.5 p.p.m. The energy required for increased neural activity exhausts the local supply of oxygenated homeglobin, and there is then a localized rapid influx of oxygenated hemoglobin.

In fact there is an overshoot and the local ratio between HbO/HdD changes, leading to a reduction in the rate of T_2^*-decay "near" to the increased neural activity.

There is considerable controversy as to exactly where the difference in magnitude derives from. Susceptibility calculations show that different sized vessels make different constributions.

The BOLD Effect, III

There is a 2-6 second delay between the neural activity and the increased blood flow.
This effect is used in fMRI by making two rapidly acquired T_2^*-weighted images, and comparing their magnitudes. Differing local magnitudes are then posited to be correlated to brain function. The change in magnitude is in the 2-6% range. This poses a serious challenge as the images must be acquired rapidly, leading to a decrease in SNR, but there must be enough accuracy in the reconstruction to detect changes of this size. Usually the images are low resolution, and this allows for some reduction in imaging time.

Thanks

I would like to thank you for your attention, I hope I've made MRI look like an interesting, and fundamentally understandable subject.
I would also like to thank Gunther for inviting me to participate in this very interesting meeting.
My research on this material has been supported by a variety of grants from the NSF, NIH and DARPA.
Some material connected to these questions can be found at my web-site:
http://www.math.upenn.edu/c̃le