Stats 233 Statistical Methods for Biomedical Data

fMRI & DTI (Diffusion Tensor Imaging)

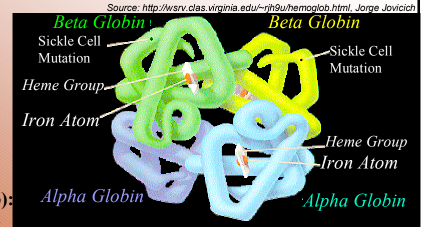
Ivo Dinov

dinov@stat.ucla.edu

http://www.stat.ucla.edu/~dinov

Hemoglobin – a molecule to breathe with

Source: http://wsrv.clas.virginia.edu/~rjh9u/hemoglob.html, Jorge Jovicich



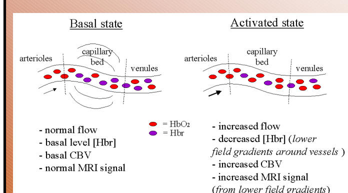
Hemoglobin (Hgb):

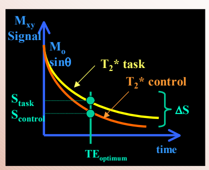
- four globin chains
- each globin chain contains a heme group
- at center of each heme group is an iron atom (Fe)
- to each heme group an oxygen atom (O_2) can attach
- oxy-Hgb (four O_2) is **diamagnetic** → **no** ΔB (net magnetization) effects
- deoxy-Hgb is **paramagnetic** → if [deoxy-Hgb] ↓ → local ΔB ↓. **like aluminum/platinum**, deoxy-Hgb, **has small positive magnetic susceptibility**

BOLD signal

Blood Oxygen Level Dependent signal

↑neural activity → ↑ blood flow → ↑ oxyhemoglobin → ↑ T2* → ↑ MR signal

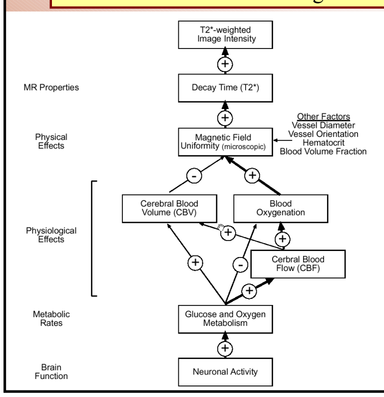




Source: fMRIB Brief Introduction to fMRI

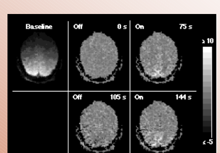
Source: Jorge Jovicich

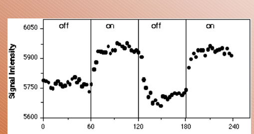
BOLD signal



Source: Doug Noll's primer

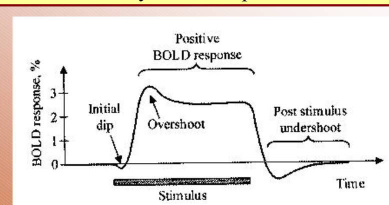
First Functional Images





Source: Kwong et al., 1992

Hemodynamic Response Function



% signal change
= (point – baseline)/baseline
usually 0.5-3%

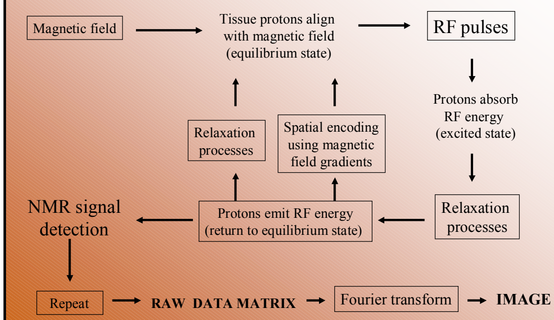
initial dip
-more focal and potentially a better measure
-somewhat elusive so far, not everyone can find it

time to rise
signal begins to rise soon after stimulus begins

time to peak
signal peaks 4-6 sec after stimulus begins

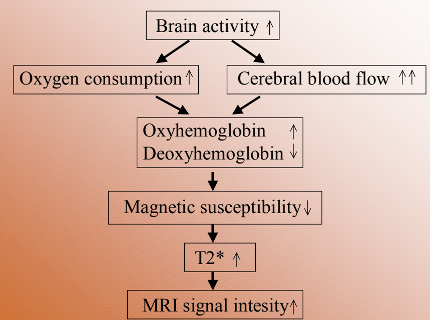
post stimulus undershoot
signal suppressed after stimulation ends

Review

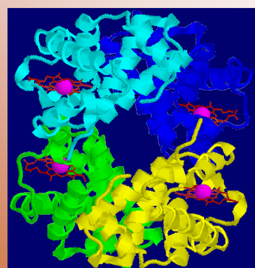


Source: Jorge Jovicich

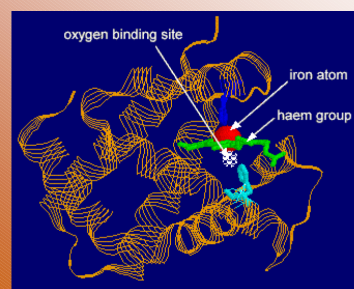
Mechanism of BOLD Functional MRI



Haemoglobin



Haemoglobin



Oxy-haemoglobin

Diamagnetic

substance that is repelled by a magnet

magnetization in the opposite direction to that of the applied magnetic field, *e.g.*, the susceptibility is negative away from the magnetic field

Deoxy-haemoglobin

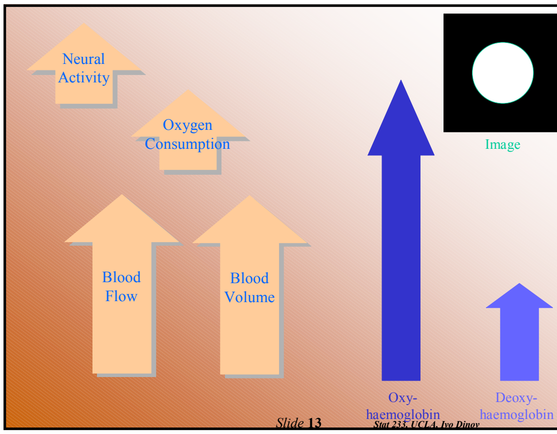
Paramagnetic

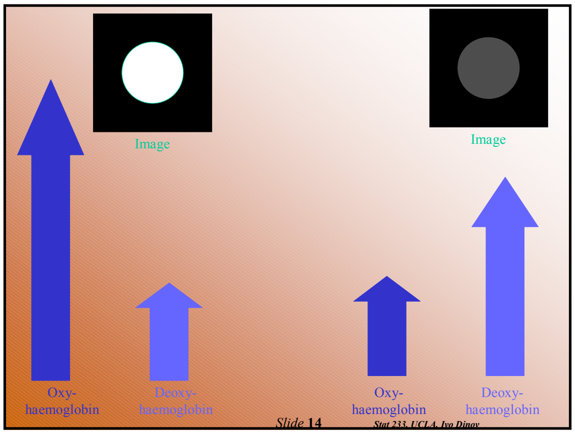
- alignment of a substance in the direction of the field

like aluminum/platinum has small positive magnetic suseptability

BOLD Contrast

- Haemoglobin acts as an endogenous intravascular contrast agent.
- As the level of oxygenation changes, so too does the contrast in the images.





Activation Imaging using BOLD

- Resting state verses active state
  - e.g. Finger tapping, remembering some numbers.
- Whole brain scanned in ~3 seconds using a high speed imaging technique (EPI).
- Perform analysis to detect regions which show a signal increase in response to the stimulus.

Problems with BOLD

- How local is the BOLD response to the site of neural activity?
  - Is the signal from draining veins rather than the tissue itself?
- How is signal change coupled to neural activity?
  - Do changes in timing of BOLD responses reliably tell us about changes in timing of neural activity?

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DTI (DWI)

- **What is Diffusion ?**
- **What is Diffusion MRI ?**
- **What is a Diffusion Tensor ?**
- **What are the principles of DTI ?**
- **How to process the MRI data and what is the required data ?**

WHAT IS DIFFUSION ?

- In a beaker of water, the molecules are able to move around freely-we call this phenomenon diffusion isotropy.
- In the Brain the surrounding structures prevent the water molecules from moving so freely and their motion is restricted
- The diffusion coefficient changes with direction
- Thus the size or magnitude of diffusion changes with direction – we call this phenomenon diffusion anisotropy
- We can use magnetic resonance imaging (MRI) to obtain pictures or maps of diffusion coefficients in the brain

Diffusion MRI

What is diffusion MRI

Diffusion imaging is a recently developed MRI technique that provides quantitative information about the integrity and orientation of white matter tracts in the brain. It is a unique method of assessing the important tract disruption in disease states.

What is Diffusion Tensor Imaging

Diffusion Tensor Imaging (DTI), is an application of diffusion imaging where several sets of diffusion-weighted images are acquired with the **diffusion gradients applied in different directions**. This technique enables the detection of diffusion anisotropy in various mediums such as brain white matter.

What is a Diffusion tensor

- The diffusive properties of an anisotropic medium can be described with a 3x3 symmetric tensor
- The eigenvalues of the diffusion tensor are the **diffusion coefficients** in the three **principal directions of diffusivity**, and the eigenvector corresponding to the largest eigenvalue is the main diffusivity direction in the medium

$$D = \begin{bmatrix} Dxx & Dxy & Dxz \\ Dyx & Dyy & Dyz \\ Dzx & Dzy & Dzz \end{bmatrix}$$

Principles of DTI

The diffusion signal attenuation (in I D) in a spin or gradient echo experiment at echo time ***t = TE*** is given by

$$A(TE) = \exp\left\{-\gamma^2 \int_0^{TE} \left[D_\xi \left(\int_0^t G_\xi(\tau) d\tau \right)^2 + D_\eta \left(\int_0^t G_\eta(\tau) d\tau \right)^2 + D_\zeta \left(\int_0^t G_\zeta(\tau) d\tau \right)^2 \right] dt \right\},$$

where subscripts **ξ , η**, and **ζ**, denote the principal axes of diffusion, *D* the diffusivity, *G* the time-varying magnetic field gradient, and **γ** the spin gyro magnetic constant. In x-y-z coordinate system the **signal attenuation** is given by

$$s = s_0 . e^{(-T2/TE)} . e^{(bxx.Dxx + byy.Dyy + bzz.Dzz + 2bxy.Dxy + 2bxz.Dxz + 2byx.Dyz)}$$

………

Observed Detectable Signal Desired Diffusion Tensor

How to solve for the Diffusion Tensor

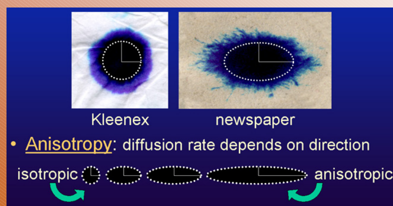
- Simultaneously solve a set of the following linear equations for the unknowns $D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}$:
- $a_{nx}^2 . D_{xx} + a_{ny}^2 . D_{yy} + a_{nz}^2 . D_{zz} + 2 . a_{nx} . a_{ny} . D_{xy} + \\ + 2 . a_{nx} . a_{nz} . D_{xz} + D_0 - \ln(S_{mn}) + 2 . a_{ny} . a_{nz} . D_{yz} = bm$
- Where n=1,2,3,…,N (total number directions) and m=1,2,3,…,M (the total number of b values)
- $a_{i,j}$ (encoding level) is the magnitude of the i^{th} vector in the j^{th} direction (diffusion vector)

  $\ln(S_{mn})$ is the natural logarithm of the **signal attenuation** corresponding to the m^{th} *b* value and n^{th} direction
- The total number of simultaneous linear equations are N x M

Required data

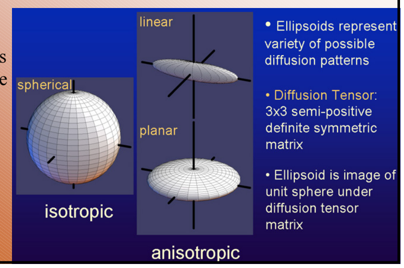
- The *minimum* DTI dataset would consist of 7 MRI acquisitions, including 1 unweighted image
- Image noise can adversely affect the accuracy of diffusion tensor measurements
- Consequently, practical DTI experiments often employ in excess of 6 encoding directions and multiple encoding levels in each direction.

Water molecules move through tissue, and within it, by a **process called diffusion**. Some materials have the interesting property that diffusion happens faster in some direction than in others. Here some scans of inkblots on two kinds of materials: *kleenex*, and *newspaper*. In *kleenex*-the ink spreads at same rate in all directions, but newspaper has a preferred direction where the ink moves faster. The name for this phenomenon is **anisotropy**. The wider the variation in diffusion rate as a function of direction, the more a anisotropic a material is.

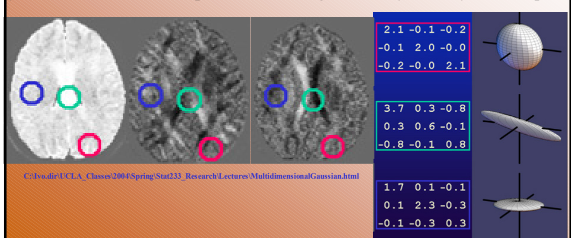


In 3D there are different kinds of anisotropy. If the material isn't isotropic the ink blot could take on this cigar shape or a pancake shape, depending on whether you have, as its called, "linear" or "planar" anisotropy, respectively. Mathematically, we represent the tensor with a 3x3 symmetric semi-positive definite matrix. The connection between the matrix and the ellipsoid is that the ellipsoid is the image of the unit sphere under the linear transform of the matrix.

Also, the eigenvectors of the ellipsoid are the axes of symmetry of the ellipsoid, and the eigenvalues are the scalings along those axes.



At the surface of the brain, there's the gray matter, which is isotropic. More inside the brain, there's the white matter, where the axons are organized into **white matter fiber tracts, which are anisotropic**. We can see those characteristics in actual measured MRI data such as this: Each image shows one component of the diffusion tensor across a full two-dimensional slice of the data. Here's the corresponding matrix, and you can see from the ellipsoid that the region is very linearly anisotropic.



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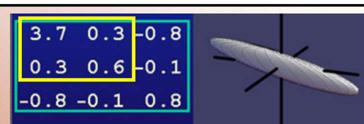


$$S^1=\left\{v=\begin{pmatrix}x\\y\end{pmatrix} \mid \text{s.t. } \|v\|^2=\left\|\begin{pmatrix}x\\y\end{pmatrix}\right\|^2=(x,y)\begin{pmatrix}x\\y\end{pmatrix}=x^2+y^2=1\right\}$$

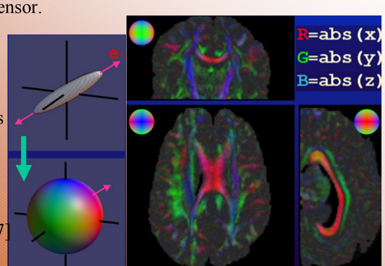
$$A=\begin{pmatrix}3.7 & 0.3\\0.3 & 0.6\end{pmatrix}: S^1 \longrightarrow E^1(Ellipse);\ A\begin{pmatrix}x\\y\end{pmatrix}=\begin{pmatrix}x'\\y'\end{pmatrix}=\begin{pmatrix}3.7x+0.3y\\0.3x+0.6y\end{pmatrix}$$

$$E^1=\left\{v=\begin{pmatrix}x\\y\end{pmatrix} \mid \text{s.t. } 1=\|v\|^2=(x,y)A\begin{pmatrix}x\\y\end{pmatrix}\right\}$$

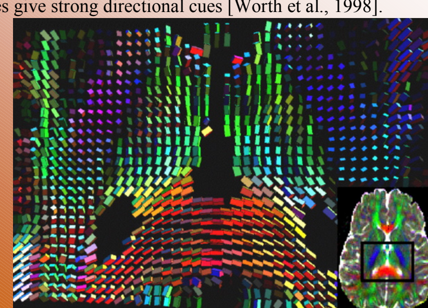
$$E^1=\left\{v=\begin{pmatrix}x\\y\end{pmatrix} \mid \text{s.t. } \frac{x^2}{\left(\sqrt{1/3.7}\right)^2}+\frac{y^2}{\left(\sqrt{1/0.6}\right)^2}+\frac{yx}{\left(\sqrt{1/0.6}\right)^2}=1\right\}$$

Slices of tensor data. One popular way of doing that is to simplify the whole tensor down to a single vector, the *tensor's principal eigenvector*. You use that direction as a lookup into some spherical (S^2) colormap which is fixed relative to the coordinate frame, such as this one. This assigns a color to the tensor.

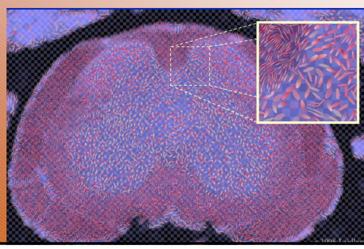
There's a second step, which is to darken or desaturate the color where the anisotropy is low. You can pretty clearly see the various structures inside the white matter. [Pierpaoli'97, Jones'97]

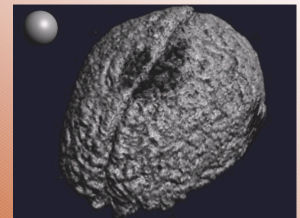


This is another idea along the same lines. This time, instead of using the image of the unit sphere under the tensor matrix, you use the image of the unit cube. And then this also colors it according to the direction of the major eigenvector. It makes a pretty picture, and the edge of the cubes give strong directional cues [Worth et al., 1998].



David Laidlaw uses lots of parameters in showing little ellipse-shaped brush strokes: their density, shape, frequency of striations along their length, the color of the under-coat, and so forth. So all of the tensor information is packed into this one rich image. In light of our goal, the problem with this technique, and with the boxes and ellipsoids is that its not clear how to create a picture which can show the three-dimensional structure within volume data. You have this problem of too much density of information, and visual cluttering.





Source: David Weinstein & Gordon Kinddlmann