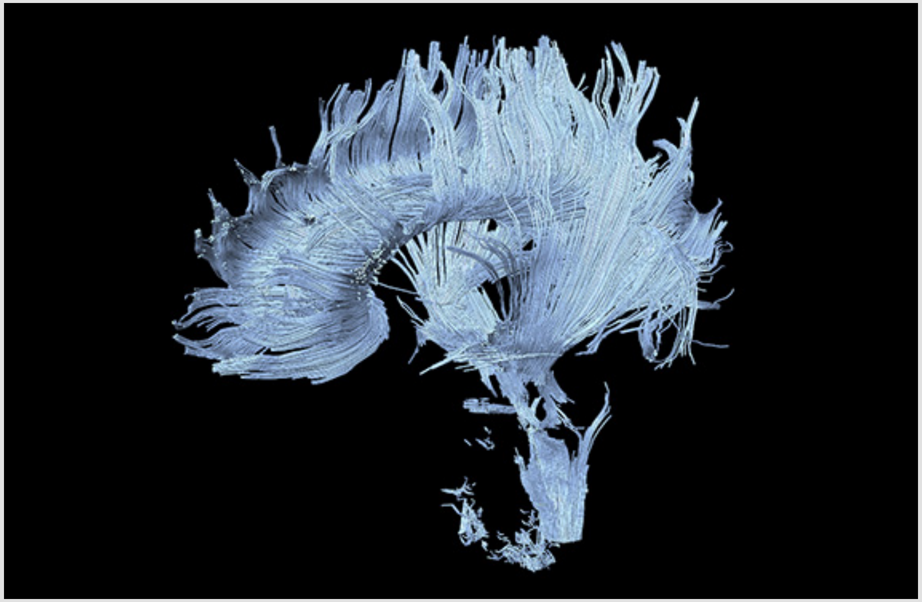

Diffusion Tensor Imaging: Concepts & Applications

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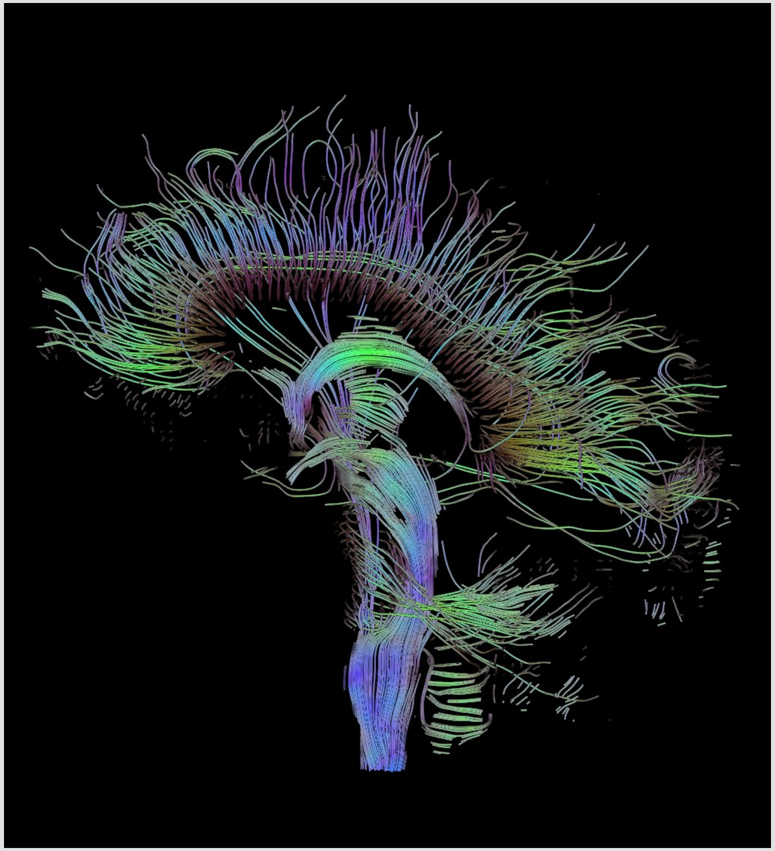
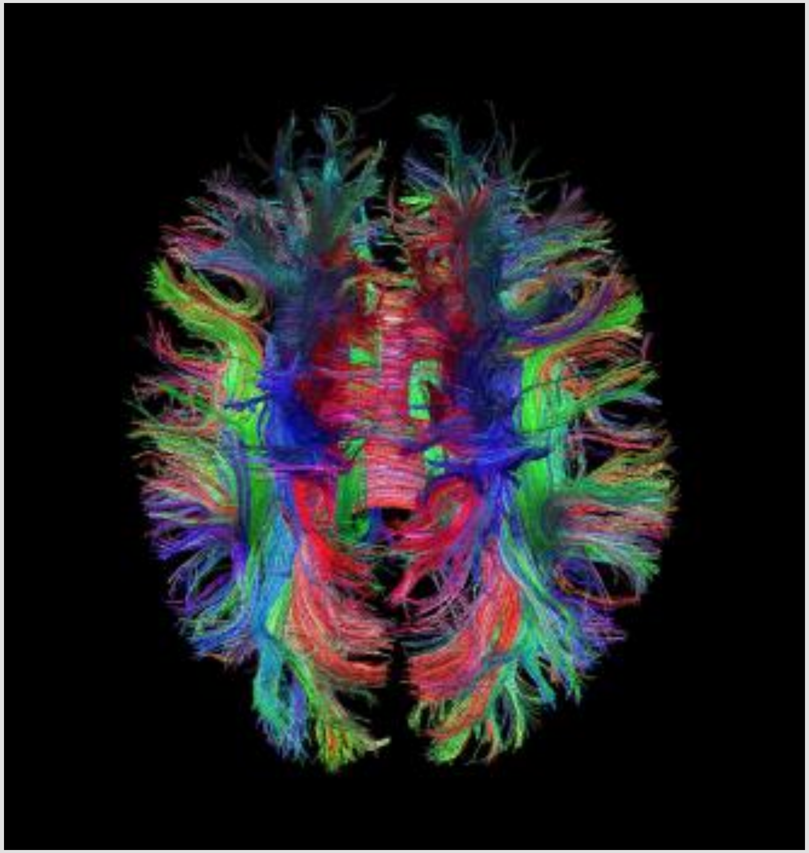
What is Diffusion Tensor Imaging (DTI)?

- Uses bipolar magnetic field gradient pulses to measures molecular diffusion within a voxel.
- Only diffusion in the direction of the gradient are detectable, requiring us use gradients in several directions.
- In myelinated axonal fibers, diffusion has been shown to be faster along the direction of the fibers than in the direction perpendicular to them.
  - DTI images can be used to estimate orientation of fiber tracks, and fiber track integrity.

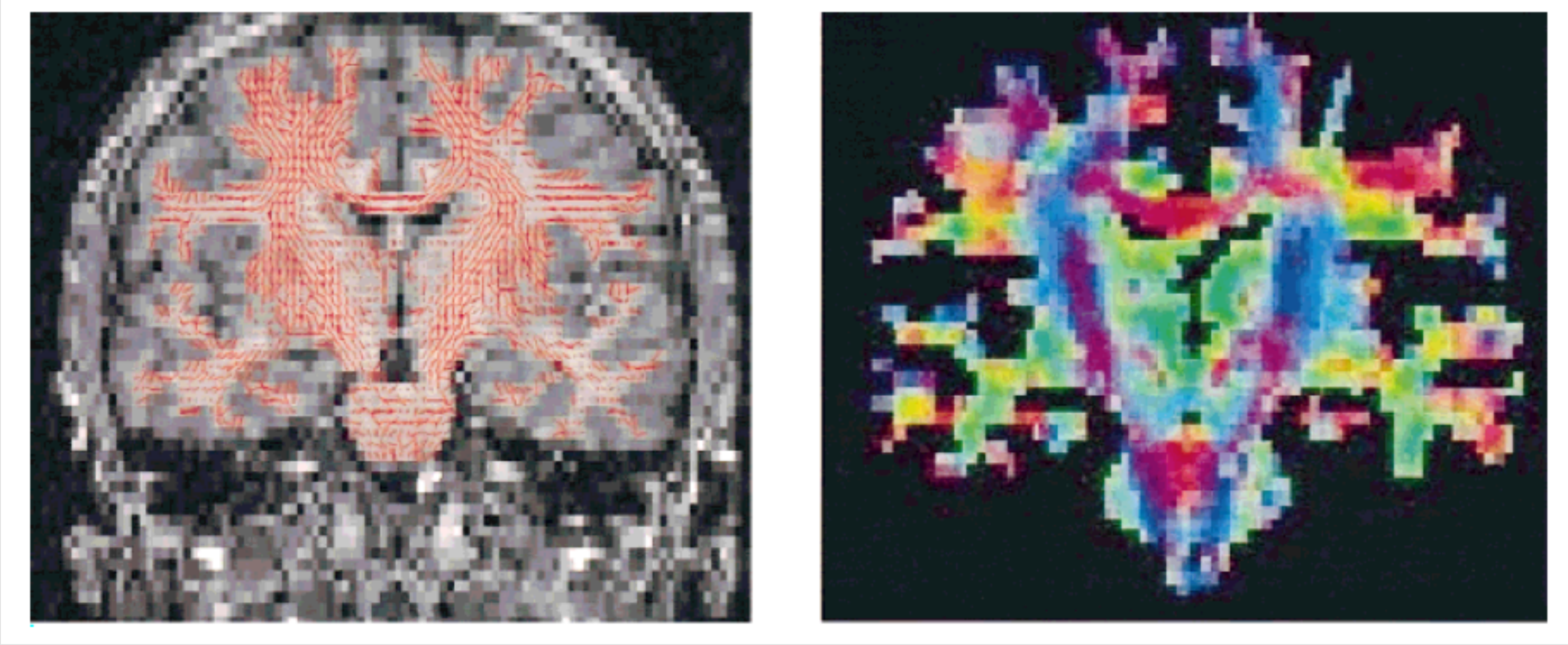
Who's the fairest modality of them all?





Link1, link2

Two ways to plot DTI



Diffusion tensor – data acquisition

- **Isotropic ("plain") diffusion**: Diffusion can be fully described by a coefficient *D.* This can be determined, using the equation:

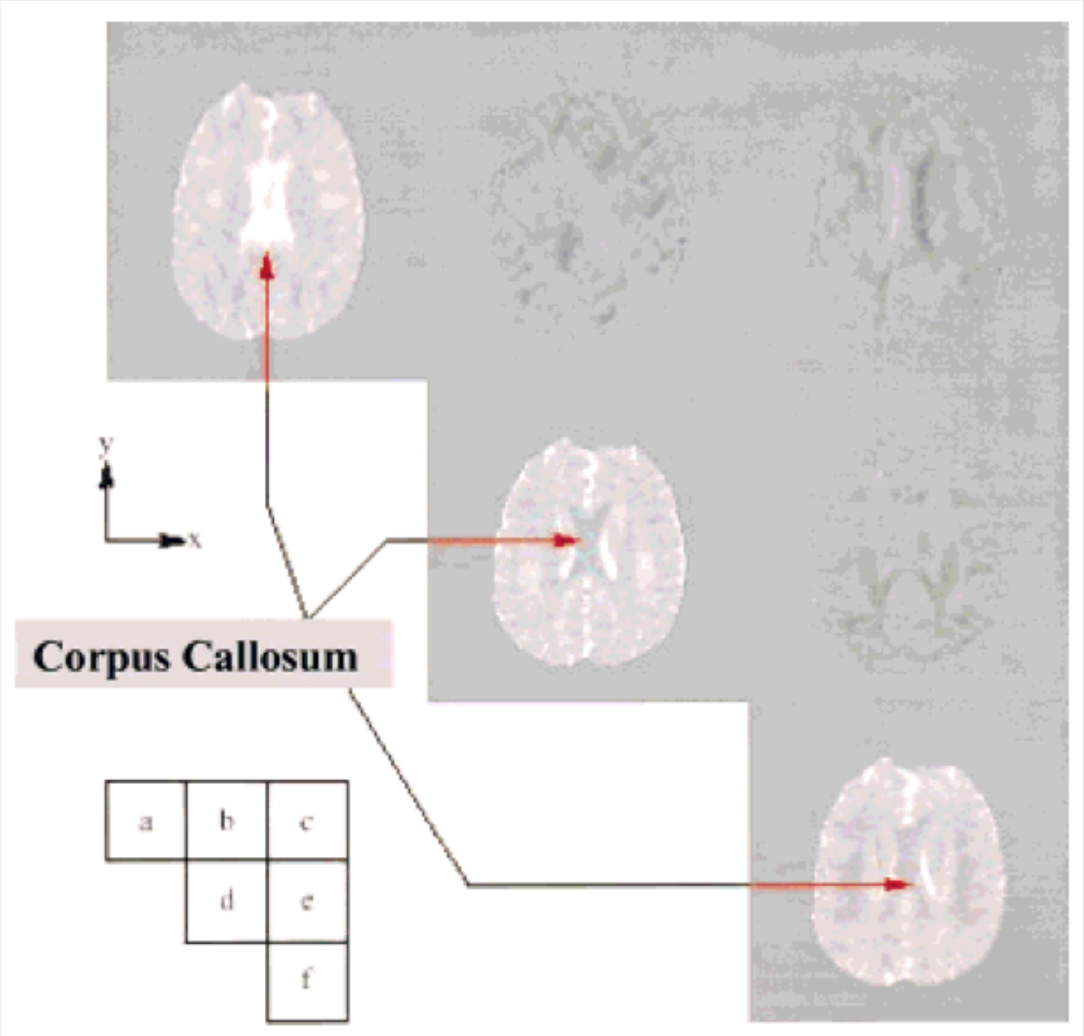
  $A = \exp(-bD)$

  where *A* represents spin echo signal attenuation, and *b* characterizes the gradient pulses used.

- ***Anisotropic diffusion***: Diffusion is characterized now by mobility in the x, y and z, dimensions, along with their correlations. We represent all of these directions with the tensor **D**.

$$\underline{\mathbf{D}} = \begin{matrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{matrix} . \qquad (2)$$

3D Tensor



Diffusion tensor – data acquisition

- Aquiring **D** in anisotropic case: *b* is also replaced by a 3 x 3 matrix ***b***, and signal attenuation is now:

$$A = \exp\left(-\sum_{i=x,y,z}\sum_{j=x,y,z} \underline{\mathbf{b}}_{\mathbf{ij}}\underline{\mathbf{D}}_{\mathbf{ij}}\right) \tag{4}$$

or

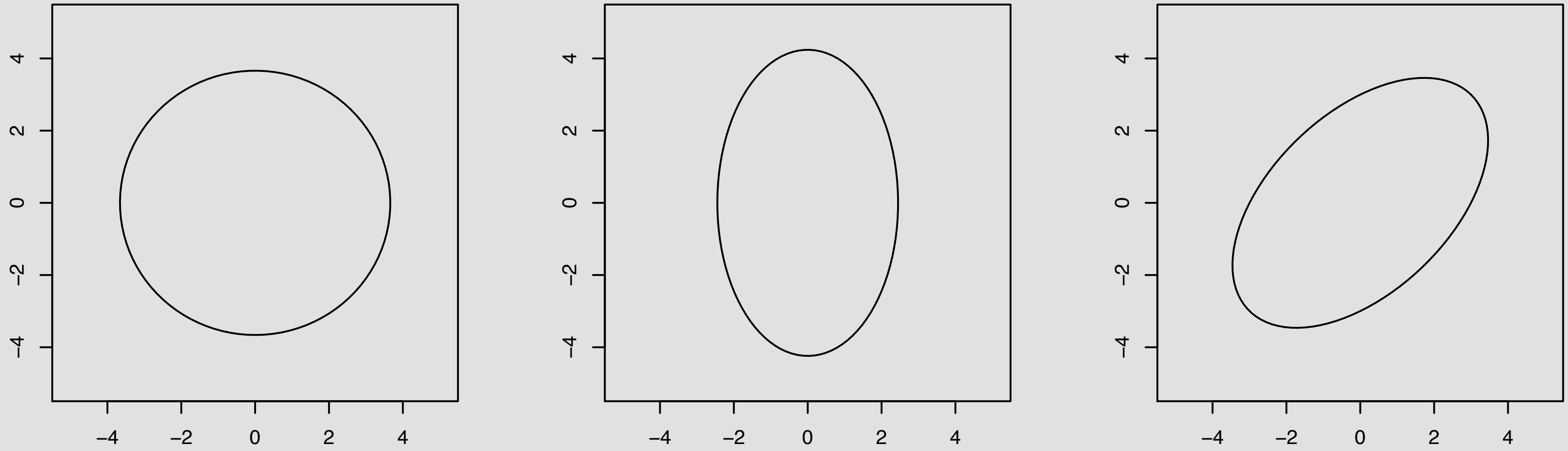
$$A = \exp(-b_{xx}D_{xx} - b_{yy}D_{yy} - b_{zz}D_{zz} - 2b_{xy}D_{xy} - 2b_{xz}D_{xz} - 2b_{yz}D_{yz}). \tag{5}$$

- **D** can be estimated using a regression based on the above equation.

Nondiagonal Diffusion Tensors – 2D illustrations

Ellipse: $\{x : x' D^{-1} x = c\}$

$$D_0 := \begin{bmatrix} \sqrt{5} & 0 \\ 0 & \sqrt{5} \end{bmatrix} \qquad D_1 := \begin{bmatrix} 1 & 0 \\ 0 & 3 \end{bmatrix} \qquad D_2 := \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$



Finding a reference frame

- Among other things, we want to know the primary directions of diffusivity, and the amount of diffusivity in each of these directions.

- A reference frame of orthogonal vectors [x’,y’,z’] is the basis in which **D** can be represented as a diagonal matrix.
  - These reference vectors x’, y’ and z’ will also correspond to the primary directions of diffusivity.

- This can be solved with by taking the singular value decomposition (SVD) of **D**.

Singular value decomposition of the diffusion tensor (in 3D)

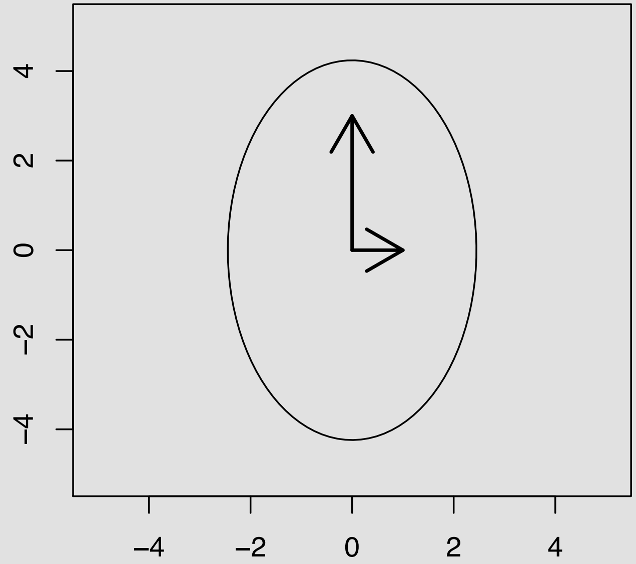
- Let **UΛU'** be the singular value decomposition (SVD) of **D**, where **U** is a 3x3 matrix, and **Λ** is a 3x3 diagonal matrix with diagonal elements denoted by λ_1, λ_2, and λ_3.

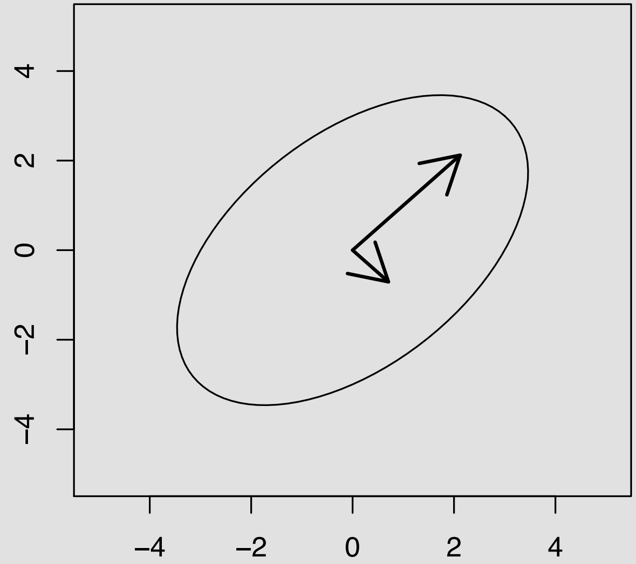
- **UΛU'= D**
- The three columns of **U** form an orthonormal basis corresponding to the primary directions of diffusion.
- λ_1, λ_2, and λ_3 represent the diffusion in each of these directions.

Finding a reference frame – 2D Illustration

Ellipse: $\{x : x' D^{-1} x = c\}$

$$D_1 := \begin{bmatrix} 1 & 0 \\ 0 & 3 \end{bmatrix} \qquad D_2 := \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$





$$SVD(D_1) =: U_1 \Lambda_1 U_1'$$

$$diag(\Lambda_1) = \begin{bmatrix} 1 & 3 \end{bmatrix}$$

$$U_1 = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

$$SVD(D_2) =: U_2 \Lambda_2 U_2'$$

$$diag(\Lambda_2) = \begin{bmatrix} 1 & 3 \end{bmatrix}$$

$$U_2 = \begin{bmatrix} \frac{1}{\sqrt{2}} & -\frac{1}{\sqrt{2}} \\ \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} \end{bmatrix}$$

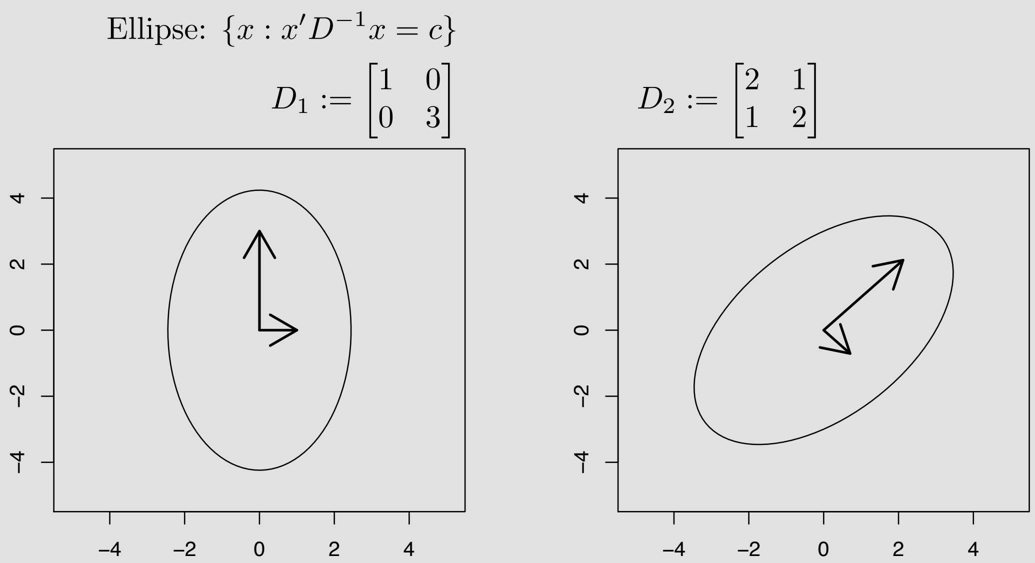
DTI Metrics

- Primary direction of diffusivity
  - Attainable from SVD(**D**)
- Mean diffusivity: characterizes the overall mean-squared displacement of molecules.
  - Independent of primary direction of diffusivity.
- Degree of anisotropy: the directedness of diffusion.

- All of these are measuring actual biological things. The unit's aren't just relative, they're meaningful.

Mean Diffusivity

- We want this quantity to be <u>invariant</u> to the orientation of the reference frame [x',y',z'], or U in our notation here.
- Mean Diffusivity := Trace(**D**)/3
  - Where Trace(**D**) = *D[x,x]* + *D[y,y]* + *D[z,z]*
  - Note, this is equal to $(\lambda_1+\lambda_2+\lambda_3)/3$, but this doesn't matter.



Diffusion Anisotropy Indices

$$\bar{\lambda} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Relative Anisotropy (RA): standardized squared deviations. (Range: 0-√2, √2 is anisotropic).

$$RA = \sqrt{\frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{3\bar{\lambda}}}$$

Fractional Anisotropy (FA): Magnitude of diffusion tensor explained by anisotropic diffusion. (Range: 0-1, 1 is anisotropic).

$$FA = \sqrt{\left(\frac{3}{2}\right) \frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

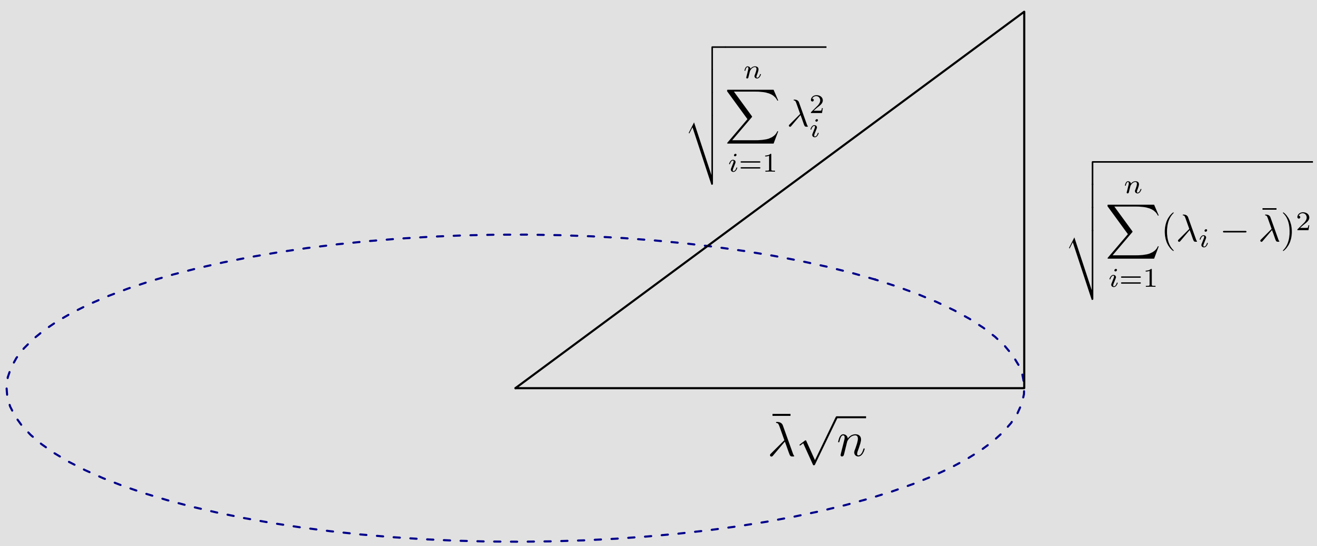
Volume Ratio (VR): Ratio of volume of the ellipse to the volume of the sphere with radius mean(λ). (Range: 0-1, but 1 is isotropic).

$$VR = \frac{\lambda_1 \lambda_2 \lambda_3}{\bar{\lambda}^3}$$

Visualizing Fractional Anisotropy

$$\sum_{i=1}^{n}(\lambda_i - \bar{\lambda})^2 + n\bar{\lambda}^2 = \sum_{i=1}^{n}\lambda_i^2$$

$$FA = \sqrt{\left(\frac{3}{2}\right)\frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$



Complications – Apparent Diffusion Coefficient (ADC)

- Voxels contain both intracellular and extracellular compartments. Low (b values?) gradients used are more sensitive to to fast diffusion compartments, (possibly?) corresponding more to the extracellular diffusion.

- Changes in ADC should be interpreted in terms of diffusion changes in the extracellular space, and in terms of changes in the relative volume of extracellular v. intracellular space.
  - This volume ratio relevant to detection of brain ischemia and other problems.

Interpreting ADC

- Generally it's been shown that anisotropy is high in myelinated white matter, and even before fibers become myelinated.

- This was once explained by myelin sheaths restricting the flow of intracellular water.

- It's now thought that since studies with low b-values are more sensitive to extracellular diffusion, this anisotropy is actually mostly due to the structures that impede the flow of extracellular molecules.
  - In a compact bundle of parallel fibers, movement perpendicular to fibers is more impeded than parallel movement.

Applications

- In general, mean diffusivity characterizes overall water content and anisotropy indices reflect myelin fiber integrity.

- Brain Ischemia – restriction in blood supply that corresponds with a drop in water diffusion, possibly due to shrinkage of the extracellular space.
  - DTI useful for detection, as the diffusion change precedes cell damage detectable on conventional MRI.

Applications – Diseases

- DTI shown useful in studying:
  - Brain maturation in children
  - multiple sclerosis
  - Leukoencephalopathy
  - Wallerian degeneration
  - Alzheimer's disease
  - Schizophrenia
  - Dyslexia
  - Brain Tumors
  - AIDS
  - Trauma
  - hypertensive hydrocephalus
  - Leukoaraiosis
  - Cerebral Auto- somal Dominant Arteriopathy with Subcortical Infarcts and Leucoenuphalopathy (CADASIL)
  - Migraine
  - Spinal cord studies
  - AIDS
  - Eclampsia

Thanks very much!

Paper:

Le Bihan, D., Mangin, J. F., Poupon, C., Clark, C. A., Pappata, S., Molko, N., & Chabriat, H. (2001). Diffusion tensor imaging: concepts and applications. *Journal of magnetic resonance imaging*, 13(4), 534-546.

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