Diffusion Tensor Imaging

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Outline
- Problem to be solved (attacked)
- Physics of diffusion
- Diffusion weighted imaging
- Diffusion Tensors
- Imaging methodology
- Examples
- Advanced techniques

Problem
- Anatomic imaging (TI, T2, FLAIR, MT, etc)
- MRS (spectroscopic imaging)
- Activation imaging (BOLD, ASL)
Problem
- Dynamics of white-matter
- Activation gives temporally correlated regions of grey matter

Unfortunately we can't put tracers in humans.
The use of diffusion-weighted imaging in clinical practice is expanding due to the need for non-invasive imaging of brain structures, such as white matter tracts. Diffusion-weighted imaging (DWI) has been used to study various brain regions and their relationships with diseases, development, and aging. Here, we present a brief overview of the techniques and applications of diffusion-weighted imaging.

**Fig. 1.** Brain structure showing the structure of white matter (Williams et al.) using the preservative method of Klüver from the brain of a 26-month-old child. Labels and arrows indicate (top left) the middle cyst, (top right) the corpus callosum, (bottom left) the splenium, (bottom right) the genu, and (bottom center) the indusium griseum. The image is representative of the extensive use of diffusion-weighted imaging in neuroimaging.

**Fig. 2.** Histograms showing the distribution of eigenvalues for different regions of the brain. The histograms are color-coded to represent different structures, such as the corpus callosum and the cerebellum. The x-axis represents the number of eigenvalues, and the y-axis represents the frequency of occurrence. The histograms demonstrate the variability in the eigenvalue distribution across different brain regions.

**Fig. 3.** Graph showing the relationship between diffusion coefficient and the number of fibers. The diffusion coefficient is plotted as a function of the number of fibers, revealing a linear relationship. The graph is used to illustrate the correlation between the diffusion properties and the structural integrity of the brain.

**Fig. 4.** Diagram showing the diffusion tensor estimation from DWI data. The tensor is represented as a ellipsoid, with the axes indicating the direction of diffusion. The figure highlights the anisotropic nature of white matter fibers, which is crucial for understanding the connectivity and functional organization of the brain.

**Fig. 5.** Graph showing the diffusion coefficient across different anatomical regions. The graph displays the variation in diffusion coefficient across various brain regions, including the thalamus, corpus callosum, and cerebellum. This information is essential for assessing the integrity of white matter tracts and identifying potential abnormalities.

**Fig. 6.** Diagram showing the diffusion tensor orientation and its relation to the fiber direction. The tensor orientation is depicted as a vector, indicating the direction of diffusion. The figure illustrates the importance of understanding the orientation of white matter fibers for accurately interpreting diffusion-weighted imaging data.

**Fig. 7.** Histograms showing the distribution of diffusion coefficients across different brain regions. The histograms are color-coded to represent different regions, such as the corpus callosum, thalamus, and cerebellum. The graphs demonstrate the variability in diffusion coefficients across different brain regions, highlighting the importance of regional specificity in diffusion-weighted imaging.

**Fig. 8.** Graph showing the diffusion coefficient as a function of age. The diffusion coefficient decreases with age, indicating a decrease in the integrity of white matter tracts. This information is crucial for understanding the effects of aging on brain structure and function.

**Fig. 9.** Histograms showing the distribution of diffusion coefficients in different age groups. The histograms are color-coded to represent different age groups, such as neonates, children, and adults. The graphs demonstrate the variability in diffusion coefficients across different age groups, highlighting the importance of age-related differences in diffusion-weighted imaging.

**Fig. 10.** Diagram showing the diffusion tensor orientation and its relation to the fiber direction in different age groups. The tensor orientation is depicted as a vector, indicating the direction of diffusion. The figure illustrates the importance of understanding the orientation of white matter fibers in different age groups for accurately interpreting diffusion-weighted imaging data.
Physics of Diffusion (Brownian Motion)

Particles (dust, molecules, atom) in liquid/gaseous state randomly move about.

Described by Brown and Einstein


Einstein A. About the movement of suspended particles in liquids at rest as required by the molecular kinetic theory of heat. [Uber die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen]. Ann Phys 1905;322:549–560. (Ger)

What determines the properties of this random motion?
What determines the properties of this random motion?

- Mass
- Size (a.k.a. radius)
- Energy (temperature → velocity)
Stokes-Einstein Equation gives diffusion coefficient $D$

$$D = \frac{kT}{6\pi \eta r}$$

(water versus honey)

Facts about diffusion:

- no net displacement of particles
- but do have root mean square displacement

$$R^2 = 2D\Delta$$

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Facts about diffusion:

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- But do have root mean square displacement

\[ R^2 = 2D\Delta \]

Diffusion Weighted Imaging (DWI)

We need to be able to detect random motion and to image this random motion. However, this random motion is on a microscopic scale compared to imaging resolution.
Concept of Phase

Coherent Phase

Incoherent Phase

\[ \sum = 1 \]

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\[ \sum_i = 1 \quad \sum_i = 0 \]

\[ \omega = \gamma B_0 \]
\[ B(x) = B_0 + Gx \]
\[ \omega(x) = \gamma(B_0 + Gx) \]
\[ \phi(x) = \omega(x)\delta, \delta = \text{time} \]
Simple Diffusion Weighted Imaging

\[ S(b) = S_0 e^{-bD} \]
\[ b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3) \]
\[ D = -b \ln(S(b)/S_0) \]

- \( b \) = diffusion weighting
- \( D \) = diffusion coefficient

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Phase accrual due to magnetic field gradient, with no diffusion.

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Phase accrual due to magnetic field gradient, with **no diffusion**.
Phase accrual due to magnetic field gradient, with no diffusion.

Time

Space (x)
Phase accrual due to magnetic field gradient, with **no diffusion**.

Time

Space (x)

Phase accrual due to magnetic field gradient, with **no diffusion**.

Time

Space (x)

Phase accrual due to magnetic field gradient, **with diffusion**.

Time

Space (x)

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Phase accrual due to magnetic field gradient, **with diffusion.**

**Time**

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**Space (x)**

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Phase accrual due to magnetic field gradient, with diffusion.

Time

Space (x)

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Phase accrual due to magnetic field gradient, with diffusion.

Space (x)

Time

Phase accrual due to magnetic field gradient, with diffusion.

Space (x)

Time

No diffusion and no changing phase

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No diffusion and BUT changing phase

Diffusion but NO changing phase

Diffusion AND changing phase
Diffusion (2x) AND changing phase

Diffusion (3x) AND changing phase

Diffusion (3x, 2x mixing) AND changing phase
No diffusion and BUT changing phase

Diffusion but NO changing phase

Diffusion but NO changing phase
Diffusion but NO changing phase

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Diffusion but NO changing phase

3

36

Diffusion but NO changing phase

3

36

Diffusion but NO changing phase

3

36

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Diffusion but NO changing phase
Final phase of spins

- $D_x, D_y = 0, G_x = 0$
- $D_x, D_y = 0, G_x > 0$
- $D_x, D_y > 0, G_x = 0$
- $D_x, D_y > 0, G_x = 0$

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Artifacts

- Unlike high resolution imaging, very susceptible to shot-to-shot (excitation) error
- VERY susceptible to bulk motion, cardiac pulsatility
- SPIRAL or EPI, but then low-resolution
- Parallel imaging (SENSE), or multi-shot with phase correction

Simple Diffusion Weighted Imaging

<table>
<thead>
<tr>
<th>$S_0$</th>
<th>$S(b)$</th>
<th>ADC</th>
</tr>
</thead>
</table>

$b = 800 \text{ s/mm}^2$
...but what if there is something that impedes free diffusion?

...or even impedes in one direction but not another?

We must be able to then describe diffusion according to directions.

Simplest is allowing three directions to be independent of each other.
Thus the diffusion tensor (matrix)

\[ D \rightarrow \hat{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \]

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\[ S(b) = S_0 e^{-b D} \rightarrow S(\hat{b}) = S_0 e^{-\hat{b} \hat{D}} \]
Imaging

- Must now take diffusion weighted images with magnetic gradients along different directions.
- 7 Unknowns...must make at least 7 measurements.
- Operationally like a time series, but each volume has "diffusion weighting". Very, very sensitive to movement.

33 direction dataset and 1 b=0 image

\[
\begin{align*}
S(b_1) &= S_0 e^{-b_1 \hat{D}} \\
S(b_2) &= S_0 e^{-b_2 \hat{D}} \\
S(b_3) &= S_0 e^{-b_3 \hat{D}} \\
&\quad \vdots \\
S(b_n) &= S_0 e^{-b_n \hat{D}}
\end{align*}
\]
Application of linear algebra

\[ \hat{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} \]

Application of linear algebra

\[ \hat{\lambda} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \]

Application of linear algebra

\[ \hat{\lambda} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \]

Eigenvalues \[ \lambda_1, \lambda_2, \lambda_3 \]

Eigenvectors \[ \epsilon_1, \epsilon_2, \epsilon_3 \]
What do these mean?

Eigenvalues give you indication of how freely or bounded the diffusion is.

Eigenvectors informs you of the principle directions.
How can we summarize this highly complex data?

Fractional Anisotropy

$$FA = \sqrt{\frac{\lambda_1 - \lambda_2}{\lambda_1 + \lambda_2 + \lambda_3}}$$

Fractional Anisotropy

FA=0, isotropic
FA=1, fully anisotropic

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Examples

- Calculate FA
- Co-Register $T_1/T_2$
- Normalize to MNI
Examples

Calculate FA → Co-Register T₁/T₂
Normalize to MNI

Examples

Calculate FA → Co-Register T₁/T₂
Normalize to MNI
† Tests
Additionally, the b-matrix was corrected for the rotational information between images using FSL-FLIRT software. EAR affine registration by maximizing normalized mutual information were also motion and eddy current corrected using a linear kernel of FWHM 6 mm. The spatially normalized FA and MD maps were smoothed with a Gaussian kernel of FWHM 6 mm.

For the new VBA and TBSS analysis, the DW images can be referred [Sage et al., 2007]. In short, after motion correction for the original and the new VBA and for the TBSS analysis is shown in Figure 1.

An overview of the different steps of the data processing for the original analysis, our previous publication is shown in Figure 1.

For an extensive description of the preprocessing steps applied in the original analysis, our previous publication [Sage et al., 2007]. This coregistration consists of a combination of an affine and a nonrigid transformation: the affine coregistration corrects for residual local morphological differences. Different information can be used to drive the coregistration process. For the affine method, FA was used to drive the coregistration, whereas for the non-rigid approach, we used the DT components in this respect. After coregistration, TR based on the preservation of principal direction (PPD) technique is performed to realign the tensors with the underlying microstructure of the brain.

Alternative normalization technique: FSL/TBSS

Induced FA change

Keller and Just, Neuron 2009

FSL Standard Skeleton, FSL 4.0.1

Sage et al 2009

Other examples

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We can also encode the 1st eigenvector (associated w/ largest eigenvalue) with color.

- red = L/R
- green = anterior/posterior
We can also encode the 1st eigenvector (associated with the largest eigenvalue) with color.

- **Red** = L/R
- **Green** = anterior/posterior
- **Blue** = inferior/superior

![Brain Image with Color Coding](image-url)
Issues

- Crossing fibers - Single DTI lacks description
- Noise - effect on eigenvalues
- Gold standard, quantifying connectivity, number of directions, diffusion time, etc.

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Conclusion

- Exploitation of water diffusion leads to mapping of white matter.
- DTI along with variety of mathematical techniques becoming very accessible.
- Leads to a better understanding of underlying neuroanatomy.
- Application to fundamental neuroscience as well as clinical science/practice.

Thanks