Diffusion (Tensor) Imaging
A survey/primer

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Outline
- Why?
- Physics of diffusion
- Diffusion weighted imaging
- Diffusion tensors
- Imaging methodology
- Examples
- Advanced techniques, breaking the shackles of tensors

Anatomic Imaging

\[ T_2 \quad T_1 \quad FLAIR \]
The eigen values of a 3D rotation with respect to the laboratory frame of reference are known as the eigen vectors. The objectivity of the results of diffusion imaging is based on the assumption that the contrast of diffusion-weighted images is the result of tissue microstructure, and that the displacement from the origin to a point on the ellipsoid surface along the direction of the diffusion-orientation to the basis pedunculi, the fibers are fanning out to extension very narrow, especially the splenium and genu of the corpus callosum show typical arches. The upper surface of the median portion of the corpus callosum is connected by a thin barrier to water diffusion. Therefore, in DT-MRI imaging it is assumed that the displacement front of a diffusing substance can be modeled as an ellipsoid. Hence, each diffusion-weighted measurement represents a point on the ellipsoid surface to define its size, shape, and orientation to within the limits of sampling error. The mathematical construct used to characterize anisotropy and orientation is a second-order diffusion tensor. Acquiring MR data by using sensitizing gradient can show from above.

Fig. 1. Brain dissection showing the structure of white matter (Williams et al.) using the preserved sections of cerebral cortex. Corpus callosum, its radiation, and indusium griseum are visible. The commissural fibers traversing the splenium and genu of the corpus callosum show typical arches. The upper surface of the median part of the corpus callosum is connected by a thin barrier to water diffusion. Therefore, in DT-MRI imaging it is assumed that the displacement front of a diffusing substance can be modeled as an ellipsoid. The objectivity of the results of diffusion imaging is based on the assumption that the contrast of diffusion-weighted images is the result of tissue microstructure, and that the displacement from the origin to a point on the ellipsoid surface along the direction of the diffusion-orientation to the basis pedunculi, the fibers are fanning out to extension very narrow, especially the splenium and genu of the corpus callosum show typical arches. The upper surface of the median part of the corpus callosum is connected by a thin barrier to water diffusion. Therefore, in DT-MRI imaging it is assumed that the displacement front of a diffusing substance can be modeled as an ellipsoid.

Connectivity of white-matter

- Activation gives temporally correlated regions of grey matter

Unfortunately we can't put tracers in humans.
Physics of Diffusion (Brownian Motion)

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

Described by Brown and Einstein


Stokes-Einstein Equation gives diffusion coefficient $D$

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

(water versus honey)

What determines the properties of this random motion?

— Mass
— Size (a.k.a. radius)
— Energy (temperature $\rightarrow$ velocity)
Facts about diffusion:
no net displacement of particles but do have mean squared 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.
Coherent Phase | Incoherent Phase

\[ \sum \uparrow = \uparrow \quad \sum \uparrow = 0 \]

\[ \omega = \gamma B_0 \]

\[ B(x) = B_0 + Gx \]

\[ \omega(x) = \gamma(B_0 + Gx) \]

\[ \phi(x) = \omega(x)\delta, \quad \delta = \text{time} \]

Phase coherence sidebar

\[ \text{Spin } 1, \text{ Rotation } \theta \]
\[ S(b) = S_0 e^{-bD} \]

\[ b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3) \]

\[ D = -b \ln(S(b)/S_0) \]

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

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

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No diffusion and no changing phase

No diffusion, BUT changing phase

Diffusion but NO changing phase
Diffusion (Dx huge, Dy small) AND changing phase

Diffusion (??) AND changing phase

Diffusion Tensor

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

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

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

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.
What do these mean?

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

Eigenvectors inform you of the principal directions.
How can we summarize these highly complex data?

Fractional Anisotropy

\[ FA = \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}} \]

FA=0, isotropic
FA=1, fully anisotropic

Try:
\[ \lambda_1 = \lambda_2 = \lambda_3 = 0 \Rightarrow FA = 0 \]

Fractional Anisotropy
Additionally, the b-matrix was corrected for the rotational information between images using FSL-FLIRT software. Ear affine registration by maximizing normalized mutual were also motion and eddy current corrected using a linear kernel of FWHM 6 mm. Normalized FA and MD maps were smoothed with a Gaussian weighted anatomical images. Finally, the spatially normalizing the nonlinear transformation determined on the T1-...
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

Two EPI distortion correction implementations

FSL/topup and FSL/applytopup
http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TOPUP

Anima
https://github.com/Inria-Visages/Anima-Public/wiki
Echo Planar Imaging and negative going $k_y$

DWI Corrected via distortion correction schemes

Phase Encode Polarity

Corrected  Uncorrected
We can also encode the 1st eigenvector (associated with the largest eigenvalue) with:

- red = L/R
- green = anterior/posterior
- blue = inferior/superior

Advanced Topics

- Tractography
- Non-tensor imaging (q-space, Q-ball, diffusion spectrum, high angular resolution)
- Outstanding issues

Outstanding issues

Advanced Topics (assuming $r_0$ is on a putative fiber), calculating the direction of the maximum diffusion ($v_1$), and following that direction for a short distance just as described in the previous paragraph. This is known as Euler's method and is easy to implement but can suffer from large accumulated errors. It is therefore preferable to use other well-known numerical integration methods, such as the fourth-order Runge-Kutta or Adams' method [14,22] (Fig. 5). These techniques are superior to Euler's method particularly when large step sizes are chosen.

3.1.1. Continuous representation of the vector/tensor field

Due to the MR acquisition process, the diffusion tensor information is only available at discrete points. However, for the aforementioned methods and for the methods which will be discussed below, a continuous representation of the eigen vector/tensor field is required. In other words, $v_1(r)$ and $D(r)$ need to be known everywhere in a continuous 3D domain $\mathbb{R}^3$. This can be accomplished by (linear) interpolation of the vector field or by Lagrange polynomials [20] or by interpolating the tensor field by using B-spline functions [19,23,24]. Pajevic et al. [23] also proposed to use a continuous tensor field expressed in terms of B-spline functions that approximates the measured tensor field in a least-squares sense. They termed the former as B-spline interpolation and the latter as B-spline approximation [23,24]. While interpolation is more sensitive to noise, B-spline approximation is more robust but suffers from slightly diminished spatial resolution (Pajevic, Fig. 3. (a) Vector field: visualization of the orientation of the principal eigenvector $v_1$ on a per pixel basis (projection into the axial plane) in the splenium of the corpus callosum. For better visual perception, the orientation of $v_1$ is additionally used to index an RGB color model ($v_1x$/red, $v_1y$/green, and $v_1z$/blue). Furthermore, the vector field is superimposed on a diffusion anisotropy map (fractional anisotropy) for better orientation. To avoid display of randomly oriented vectors, only those are plotted which have a fractional anisotropy above a certain threshold. From a seed point, the vector field is used as data support for fiber tracking (red trajectory). (b) Space curve representation of a white matter fiber: the local tangent vector, $t(s)$, on the space curve, $r(s)$, is assumed to be equivalent with the eigenvector, $v_1(r(s))$, of the largest eigenvalue of the diffusion tensor $D(r(s))$ at this particular location. Fig. 4. Principles of tractography: (a) schematics for tracking on a discrete grid. The trajectory follows the indicated direction to the next closest voxel (shaded). The trajectory is limited to branching only to the adjacent eight neighbors and due to the limited angular continuity a strong deviation from the true trajectory is very likely; (b) continuous tracking using the fiber assignment by continuous tracking (FACT) algorithm. The continuous approach follows the fiber tract much more accurately (modified from Mori et al. [17]); (c) flow chart of the fiber tracking algorithm.
Equation \[3\] can be written in a simpler form by recalling the Hankel transform
\[f(r,z)\]
\[f(r,z)J_0(2kr)dr\]
and the X-ray transform (also known as the planar Radon transform)
\[X[f(r,z)]\]
\[f(r,z)dz\].
We then have
\[u\]
\[qE^2q/2\]
\[X^Pdq\].
The above relation states that the FRT of the diffusion signal is proportional to the Hankel transform of the X-ray transform of the diffusion function. Note that the X-ray transform evaluated at the origin is equivalent to the radial projection described by Eq. \[1\]. (It is important to note that the \[2\] term in Eq. \[3\] arises from the circle integral and so is equal to unity if the great circle sampling density is independent of the sampling wavevector \[q\]).

To understand Eq. \[4\] it is helpful to consider the integral in parts. The X-ray transform projects the diffusion function onto \(r\)-plane, which is the tangent plane to the direction of interest \(z\). Evaluating the X-ray transform at the origin \(r=0\) would give the radial projection exactly. Instead, the X-ray projection is multiplied by \(J_0\) through the Hankel transform. The integral over the plane \(dr\) and

![Cross fibers](image)
\[ I_1 = I_0 e^{-bD} \]

\[ \frac{I_1}{I_0} = e^{-bD} \]

\[ \ln \frac{I_1}{I_0} = -bD \]

\[ D \sim \ln \frac{I_0}{I_1} \]
Investigating the prevalence of complex fiber configurations in white matter tissue with diffusion magnetic resonance imaging. Hum Brain Mapp. 2012 May 19;34(11):2747–66.

Δ = 25 ms, δ = 17 ms, g = 50 mT/m

Δ = 65 ms, δ = 9.5 ms, g = 50 mT/m

Δ = 65 ms, δ = 1.6 ms, g = 300 mT/m

$b = 1000 \text{s/mm}^2$
Conclusion

- Exploitation of water diffusion leads to mapping of white matter
- DMRI 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.
Various diffusion packages

- http://www.mrtrix.org
- http://brainsuite.org
- http://surfer.nmr.mgh.harvard.edu/fswiki/Tracula
- http://cmrm.med.jhmi.edu
- http://exploredti.com
- http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT/UserGuide
- http://camino.cs.ucl.ac.uk

Various useful references.


Thanks

Come back to Luis’ talk in 15 minutes