Diffusion Tensor Imaging (DTI)

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Introduction

Diffusion weighted imaging (DWI)
- Spins in motion
- Attenuation of the signal
- Creation of image that represent Diffusity

Diffusion tensor imaging (DTI)
- Diffusion tensor
- Representation of the tensor
- Visualisation in 2-dimensional image

Fibre tracking

Limitations of DTI
Reconstruct the diffusion of water molecules, mainly used for searching diseases in the human brain.

**Application:**
- Faster diagnosis of a stroke (important for treatment)
- Brain surgery (prevent damage to nerve tracks)
- Diagnose other diseases
  (inflammatory: MS, degenerative: Creutzfeld-Jakob, ....)
Assumption for the MRI: spins are stationary in the time-scale of the imaging process

Reality: spins are in motion

- Physiological processes in the body
  - blood flow
  - respiration
  - cardial motion

- Diffusion
  - atoms with temperature above 0 K perform a random motion, called Brownian motion

→ Motion leads to artifacts in the image (signal loss, ghosting, miss-registration of pixels), normally unintended
Brownian motion

Idea: Use the motion to create the contrast in the MRI image

Brownian motion (random walk):

\[ \frac{\sqrt{6Dt}}{r} \]
→ Add a pair of diffusion-sentizing gradients to a T2-weighted spin-echo sequence (before and after $180^\circ$ RF-Pulse)
Stejskal-Tanner-sequence:

What is the impact on the spins?
Exitation by the $90^\circ$ RF-Pulse leads to the alignment of the spins in the xy-plane
The first diffusion gradient adds a net phase change to the regular phase change induced by the transverse relaxation.
The 180° RF-Pulse refocuses the spins and reverses the phase change that sets in after the 90° RF-Pulse.
The second diffusion gradient induces a negative phase shift that reverses the phase change that occurred in the first gradient, and further refocuses the spins and forms an echo.
Reduced Echo

Without diffusion:

- Perfect refocusing
  → higher signal

With diffusion:

- No perfect refocusing
  → lower (reduced) signal

Only valid for diffusion movement in the direction where the gradient is applied!
Attenuation of the signal:

\[ S(b) = S(0)e^{-\gamma^2 G^2 \delta^2 \Delta D} = S(0)e^{-bD} \]

- \( \gamma \) = proton gyromagnetic ratio
- \( G \) = diffusion gradient strength
- \( \delta \) = how long the diffusion gradient is on
- \( \Delta \) = time between the diffusion gradients
- \( D \) = diffusion coefficient

\( b \) = weighting factor in the image

→ Higher b-value means a higher diffusion weighting
To measure the diffusion coefficient (diffusivity) $D$ and generate a map of mean diffusivity two images with different b-values are needed:

unweighted: \[ S_1 = S(0)e^{-b_1D} \quad \text{with} \quad b_1 = 0 \text{ s mm}^{-1} \]
weighted: \[ S_2 = S(0)e^{-b_2D} \quad \text{with} \quad b_2 = 1000 \text{ s mm}^{-1} \]

\[ \rightarrow \quad \text{diffusion coefficient:} \quad D = -\frac{\ln \left( \frac{S_2}{S_1} \right)}{b_2 - b_1} \]

No free (isotopic) diffusion, restricted movement due to biological tissue like cellular membranes and other biological barriers

Model not accurate \[ \rightarrow \quad \text{Apparent diffusion coefficient (ADC)} \]
Pictures of a patient with a stroke 3-4 hours earlier:

- Stroke not visible with the conventional MRI
- Bright region in the weighted picture has low ADC → indicates the infarcted region
Direction dependence

Problem: ADC depends strongly on the direction of the diffusion encoding gradient

High diffusion in the left-right direction
(nerve tracks connecting the cerebral hemispheres)

Solution: Diffusion tensor modell
Anisotropic diffusion

Isotropic diffusion
- Equal in all directions
- Probability distribution has the shape of a sphere

Anisotropic diffusion
- One dominant direction
- Probability distribution has the shape of an ellipsoid

Strong anisotropic diffusion in regions with white matter (due to the longitudinal structure of the axons, that collectively form the nerve fibers)
Anisotropic diffusion

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The ellipsoid can be characterized by three eigenvalues $[\lambda_1, \lambda_2, \lambda_3]$ and three eigenvectors $[e_1, e_2, e_3]$ defining length and orientation of the principal axes
Signal attenuation:

\[ A = \frac{S(b)}{S(0)} = \exp(-b \mathbf{D}) \quad \text{with} \quad \mathbf{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \]

In a reference frame \([x', y', z']\) that coincides with the principal directions of diffusivity, the off-diagonal terms do not exist, and the tensor is reduced only to its diagonal terms

\[ A = \exp \left( -b_{x'x'} D_{x'x'} - b_{y'y'} D_{y'y'} - b_{z'z'} D_{z'z'} \right) \quad \text{with} \quad D_{i'i'} = \lambda_i \]
Signal attenuation:

\[ A = \frac{S(b)}{S(0)} = \exp(-bD) \quad \text{with} \quad D = \begin{pmatrix}
D_{xx} & D_{xy} & D_{xz} \\
D_{yx} & D_{yy} & D_{yz} \\
D_{zx} & D_{zy} & D_{zz}
\end{pmatrix} \]

Measurements are made in the reference frame \([x, y, z]\) of the MRI scanner gradients \(\rightarrow\) consider coupling of the nondiagonal elements

\[ A = \exp(-b_{xx}D_{xx} - b_{yy}D_{yy} - b_{zz}D_{zz} - 2b_{xy}D_{xy} - 2b_{xz}D_{xz} - 2b_{yz}D_{yz}) \]

Tensor is symmetric, therefore \(D_{ij} = D_{ji}\) with \(i, j = x, y, z\)

We need to measure diffusion in 6 directions + one non diffusion weighted image
What to do with the tensor?

- Determining the reference frame \([x', y', z']\) where the off-diagonal terms of \(\mathbf{D}\) are zero

- Diagonalization of the diffusion tensor leads to the eigenvectors \(e_i\) and eigenvalues \(\lambda_i\)

\[
\Lambda = \begin{bmatrix}
\lambda_1 & 0 & 0 \\
0 & \lambda_2 & 0 \\
0 & 0 & \lambda_3
\end{bmatrix} = \mathbf{R} \cdot \mathbf{D} \cdot \mathbf{R}^T
\]
Main axis of the ellipsoid gives the main diffusion direction in the voxel (coinciding with the fiber direction) and provides information about the degree of **axial anisotropy** ($\lambda_1$).

Other axis define the form of the ellipsoid and provides information about the degree of **radial anisotropy** ($\lambda_2 + \lambda_3/2$).
Visualisation in a 2-dimensional image:

- **Problem:** In an ellipsoid-map we would see only the shape of the ellipsoid, not the orientation.

- **Solution:** Missing information about the direction of the principal eigenvalue can be complemented by adding color.
Ellipsoid map

Colour orientation:

- **red** = medial - lateral (left - right)
- **green** = anterior - posterior (up - down)
- **blue** = superior - inferior (forward - backward)
In an overall evaluation of the diffusion in a region, anisotropic diffusion effects are avoided. A quantity independent of the orientation of the reference frame is needed:

\[
\text{Mean Diffusity: } \text{MD} = \frac{\text{Tr}(D)}{3} = \frac{D_{xx} + D_{yy} + D_{zz}}{3}
\]

On the other hand, indices for diffusion anisotropy without dependence from the respective orientation of the gradients

Most common:
- Fractional Anisotropy (FA)
- Volume Ratio (VR)
FA is a normalized standard deviation that represents the ratio of the anisotropic part in $D$ to its isotropic part:

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

with $\langle \lambda \rangle = (\lambda_1 + \lambda_2 + \lambda_3) / 3$

Provides information about the degree of directionality in a voxel (Sphere: $FA = 0$, Ellipsoid: $0 < FA < 1$)
Fractional Anisotropy

Fractional anisotropy map + Orientation-color conversion → Color-coded FA map
VR represents the ratio of the ellipsoid volume to the volume of a sphere of radius:

\[ VR = \frac{\lambda_1 \lambda_2 \lambda_3}{\langle \lambda \rangle^3} \]

Similar range to the FA, but inverse behavior
(isotropic diffusion: \( VR = 1 \), anisotropic diffusion: \( VR < 1 \))

\[ \rightarrow \text{Sometimes } (1 - VR) \text{ is preferred} \]
The DWI-signal is noisy. The execution of the measurement with 6 directions for the diffusion encoding gradient is enough to solve the problem, but leads to poor image quality.

Solution: More directions for better statistical estimation of the diffusion tensor (usually $30 - 60$, but increases measurement time)
Represent diffusion with a vector field, vectors in the direction of $\lambda_1$ (main ellipsoid axis)

Two common types of methods for tractography of nerves:

- **Line propagation technique:**
  Draw a line from a starting point by following the local vector orientation

- **Energie minimization technique:**
  Draw a Line from a starting point to an arbitrary point on the energetically favorable path. This balances the stiffness of the line and the energy minimization process (the more the line aligns to the vector field, the lower the energy)
Line propagation technique

How to create a smooth line:

A: Starting Point is set in the discrete number field \([1,1]\)

B: Transfer to continuous field to follow the actual track

C: Define a small step size and calculate distance-average vector orientation for each move. In this case the average between the two closest pixels is used.
Line propagation technique

Termination criterion:

- FA-Threshold to avoid gray matter (typically 0.2)
- Threshold for angle change to avoid sharp turns

Limitation: Contributions from multiple white matter tracks in one voxel → No predominant direction of diffusion in the tensor model
Limitation of DTI

Tensor model assumes diffusion based on Gaussian probability distribution in each voxel, the Gaussian function has only a single directional maximum:

→ cannot describe diffusion functions with multiple maxima

Are there alternative models/algorithms available to recover more information about the fibre orientations?
Alternative Approaches

Model based approach:
- Multi tensor model (build of tensor compartments with the same shape, but variable volume fractions and orientations)

Approach without model:
- Q-Ball imaging (Reconstructing a orientation distribution function (ODF) for the diffusion by using Funk–Radon transformation (FRT))
Thank you for listening!
Live Eikenes, Lecture: Spins in motion, Institute for circulation and imagediagnostic, NTNU: Norwegian University of Science and Technologie


Susumu Mori and Peter C. M. van Zijl, Fiber tracking: principles and strategies - a technical review, Johns Hopkins University School of Medicine (2002)


MathWorks, Simulation for Brownian Motion

Bernard H. Lavenda, Nonequilibrium Statistical Thermodynamics (2011)