Introduction to:

DWI + DTI

AFNI Bootcamp (SSCC, NIMH, NIH)
Outline

+ DWI and DTI
  - Concepts behind diffusion imaging
  - Diffusion imaging basics in brief
  - Connecting DTI parameters and geometry
  - Role of noise+distortion →DTI parameter uncertainty
What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)
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**Diffusion**: random motion of particles, tending to spread out
→ here, hydrogen atoms in aqueous brain tissue

- particle
- motion
- random path/walk
What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)

**Diffusion:** random motion of particles, tending to spread out

→ here, hydrogen atoms in aqueous brain tissue

**Tensor:** a mathematical object (a matrix) to store information

→ here, quantifying particle spread in all directions

\[
D = \begin{pmatrix}
D_{11} & D_{12} & D_{13} \\
D_{21} & D_{22} & D_{23} \\
D_{31} & D_{32} & D_{33}
\end{pmatrix}
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What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)

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  → here, hydrogen atoms in aqueous brain tissue

Tensor: a mathematical object (a matrix) to store information
  → here, quantifying particle spread in all directions

Imaging: quantifying brain properties
  → here, esp. for white matter
The DTI model:
Assumptions and relation to WM properties
Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles $\rightarrow$ mixing or spreading

Ex: unstirred, steeping tea (in a large cup):
**Diffusion as environmental marker**

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**Ex: unstirred, steeping tea (in a large cup):**

*Empty cup, no structure:*
Atoms have equal probability of movement any direction
$\rightarrow$ spherical spread of concentration
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But in the presence of structures:
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But in the presence of structures:
Unequal probabilities of moving in different directions
→ non-spherical spread
Diffusion as environmental marker

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But in the presence of structures:
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$\rightarrow$ nonspherical spread

$\rightarrow$ Diffusion shape tells of structure presence and spatial orientation
Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures
Local Structure via Diffusion MRI

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2) Statistical motion measured using diffusion weighted MRI
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3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:

   + one direction:
     DTI (Diffusion Tensor Imaging)
Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures

2) Statistical motion measured using diffusion weighted MRI

3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:
   + one direction:
     DTI (Diffusion Tensor Imaging)
   + >=1 direction:
     HARDI (High Angular Resolution Diffusion Imaging)
     Qball, DSI, ODFs, ball-and-stick, multi-tensor, CSD, ...
Diffusion in MRI

Mathematical properties of the matrix/tensor:

\[
D = \begin{pmatrix}
D_{11} & D_{12} & D_{13} \\
D_{21} & D_{22} & D_{23} \\
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\end{pmatrix}
\]

Having: 3 eigenvectors: \( e_i \)
3 eigenvalues: \( \lambda_i \)

- Real-valued
- Positive definite (\( r^T Dr > 0 \))
  \[
  D e_i = \lambda \lambda_i e_i, \quad \lambda_i > 0
  \]
- Symmetric (\( D_{12} = D_{21} \), etc)
  6 independent values
Diffusion in MRI

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Having: 3 eigenvectors: \(e_i\)

3 eigenvalues: \(\lambda_i\)

- Real-valued
- Positive definite \((r^T Dr > 0)\)
- Symmetric \((D_{12} = D_{21}, \text{ etc})\)

6 independent values

Geometrically, this describes an ellipsoid surface:

\[
C = D_{11}x^2 + D_{22}y^2 + D_{33}z^2 + 2(D_{12}xy + D_{13}xz + D_{23}yz)
\]

**isotropic case**

\(\lambda_1 = \lambda_2 = \lambda_3\)

**anisotropic case**

\(\lambda_1 > \lambda_2 > \lambda_3\)

\(De_i = \lambda_i \lambda_i e_i, \quad \lambda_i > 0\)
DTI: ellipsoids

Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:
  tensor $D \rightarrow$ ellipsoid surface
  eigenvectors $e_i \rightarrow$ orientation in space
  eigenvalues $\lambda_i \rightarrow$ 'pointiness' + 'size'
DTI: ellipsoids

Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:
  tensor $D \rightarrow \text{ellipsoid surface}$
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+ Determine the minimum number of
  DWIs measures needed (6 + baseline)
DTI: ellipsoids

Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:
  \[ \text{tensor } D \rightarrow \text{ellipsoid surface} \]
  \[ \text{eigenvectors } \mathbf{e}_i \rightarrow \text{orientation in space} \]
  \[ \text{eigenvalues } \lambda_i \rightarrow \text{'pointiness' + 'size'} \]

+ Determine the minimum number of DWIs measures needed (6 + baseline)

+ Determine much of the processing and noise minimization steps
“Big 5” DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

first eigenvalue, $L_1$

($= \lambda_1$, parallel/axial diffusivity, AD)

$L_{1_1} < L_{1_2}$
“Big 5” DTI ellipsoid parameters

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first eigenvector, $e_1$
(DT orientation in space)
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\( (\text{DT orientation in space}) \)

$\text{L}_1_1 < \text{L}_1_2$

Fractional anisotropy, $FA$
\( (\text{stdev of eigenvalues}) \)

$FA \approx 0$

$FA \approx 1$
“Big 5” DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

**First eigenvalue, \( L_1 \)**
\((= \lambda_1, \text{parallel/axial diffusivity, AD})\)

**First eigenvector, \( e_1 \)**
(DT orientation in space)

\[ L_{1_1} < L_{1_2} \]

**Fractional anisotropy, \( FA \)**
(stdev of eigenvalues)

\[ FA \approx 0 \quad \text{FA} \approx 1 \]

**Mean diffusivity, \( MD \)**
(mean of eigenvalues)

\[ MD_{1_1} > MD_{1_2} \]
“Big 5” DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

<table>
<thead>
<tr>
<th>First eigenvalue, $L_1$</th>
<th>First eigenvector, $e_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$= \lambda_1$, parallel/axial diffusivity, $AD$</td>
<td>(DT orientation in space)</td>
</tr>
</tbody>
</table>

| $L_{1_1}$ $<$ $L_{1_2}$ | $e_1$ $<$ $e_2$ |

<table>
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<tr>
<th>Fractional anisotropy, $FA$</th>
<th>Mean diffusivity, $MD$</th>
<th>Radial diffusivity, $RD$</th>
</tr>
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<tr>
<td>(stdev of eigenvalues)</td>
<td>(mean of eigenvalues)</td>
<td>($= (\lambda_2 + \lambda_3)/2$)</td>
</tr>
</tbody>
</table>

| $FA \approx 0$ | $FA \approx 1$ | $MD_1$ $>$ $MD_2$ | $RD_1$ $>$ $RD_2$ |
Cartoon examples: white matter ↔ FA

GM vs WM
Cartoon examples: white matter ↔ FA
Cartoon examples: white matter ↔ FA

GM vs WM

WM bundle organization

FA ↑
Cartoon examples: white matter ↔ FA

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Cartoon examples: white matter ↔ FA

WM bundle density

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Cartoon examples: white matter ↔ FA

GM vs WM

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WM bundle organization

WM maturation (myelination)

FA ↑
Interpreting DTI parameters

**General literature:**

**FA:** measure of fiber bundle coherence and myelination
- in adults, FA > 0.2 is proxy for WM

**MD, L1, RD:** local density of structure

\( e_1 \): orientation of major bundles
Interpreting DTI parameters

**General literature:**

- **FA**: measure of fiber bundle coherence and myelination
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- **MD, L1, RD**: local density of structure
- **$e_1$**: orientation of major bundles

**Cautionary notes:**

- Degeneracies of structural interpretations
- Changes in myelination may have small effects on FA
- WM bundle diameter << voxel size
  - don't know location/multiplicity of underlying structures
- More to diffusion than structure-- e.g., fluid properties
- Noise, distortions, etc. in measures
Acquiring DTI data: diffusion weighted gradients in MRI
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

$D_W$ gradient
$g_i = (g_x, g_y, g_z)$
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

**DW gradient**

\[ g_i = (g_x, g_y, g_z) \]
Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

\[ S_i = S_0 e^{-b g_i^T D g_i} \]

→ ellipsoid equation of diffusion surface:
\[ C = r^T D^{-1} r. \]
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

Diffusion weighted imaging

DW gradient
\[ g_i = (g_x, g_y, g_z) \]

diffusion motion
ellipsoid:
\[ C_2 = r^T D^{-1} r. \]
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

Diffusion weighted imaging (DW gradient)

\[ g_i = (g_x, g_y, g_z) \]

Diffusion motion ellipsoid:

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For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

Diffusion weighted imaging

DW gradient $g_i = (g_x, g_y, g_z)$

diffusion motion ellipsoid:

$C_2 = r^T D^{-1} r.$
Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

Individual points → Fit ellipsoid surface
Individual signals → Solve for $D$

$g_i = (g_x, g_y, g_z)$

Ellipsoid:

$$C_2 = r^T D^{-1} r.$$
Sidenote: what DWIs look like

Unweighted reference
b=0 s/mm$^2$

Diffusion weighted images
(example: b=1000 s/mm$^2$)
Sidenote: what DWIs look like

Unweighted reference
\( b=0 \text{ s/mm}^2 \)

Diffusion weighted images
(example: \( b=1000 \text{ s/mm}^2 \))

(Each DWI has a different brightness pattern: viewing structures from different angles.)
Noise in DW signals

MRI signals have additive noise

\[ S_i = S_0 \ e^{-b g_i^T D g_i} + \epsilon, \]

where \( \epsilon \) is (Rician) noise.
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→ Leads to errors in surface fit, equivalent to rotations and rescalings of ellipsoids:

'Un-noisy' vs perturbed/noisy fit
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'Un-noisy' vs perturbed/noisy fit

Leads to standard:
+ 30 DWs (~12 clinical)
+ repetitions of \( b=0 \)
+ DW \( b \) chosen by:
  \[ \text{MD} \times b \approx 0.84 \]
+ nonlinear tensor fitting
Distortions in DWI volumes

There are also **serious** sources of distortion when acquiring DWIs:

+ **Subject motion**
  due to movement during/between volume acq. -> signal loss/overlap

+ **Eddy current distortion**
  due to rapid switching of gradients -> nonlinear/geometric distortions

+ **EPI distortion**
  due to B0 inhomogeneity -> geometric distortions along phase encoding dir, signal pileup or attenuation

--->
And effects combine! Need careful acquisition (sometimes perhaps even reacquisitions) and post-processing.
Distortions in DWI volumes

From subj motion: interleaved brightness distortions
Distortions in DWI volumes

From eddy and EPI distortions:
+ geometric/nonlinear warping
+ signal pileup and attenuation
SUMMARY

+ Diffusion-based MRI uses application of magnetic field gradients to probe the relative diffusivity of molecules along different directions.
+ DTI combines that information into a simple shape family, spheroids, to summarize the diffusivity.
+ From the DT, several useful properties are described in terms of scalar (e.g., FA, MD, L1) and vector (e.g., V1) parameters.
+ Many “standard” interpretations of DTI parameters exist (i.e., higher FA = “better” WM), but we must be cautious.
+ Distortions and noise affect all DTI estimates, and we must consider the consequences of these in all analyses.