Diffusion MRI Tractography: Limitations and advanced solutions

- Introduction
- Considerations for optimal tractography
- Applications of advanced diffusion processing
Diffusion MRI measures Brownian motion of water molecules

Path of diffusing water molecule

Water displacement distribution
Tissue structures determine which directions of motion are most probable

White matter fibre bundle: oriented structure

Water molecules prefer to travel parallel to fibre direction
Diffusion tensor imaging (DTI)

diffusion tensor measurement: model the displacement distribution as 3D Gaussian, which can be described by the diffusion tensor, $D$.

$$P(r_2 \mid r_1, \Delta) = \frac{1}{\sqrt{|D(\Delta)| (4\pi \tau)^3}} \cdot \exp \left( \frac{(r - r_0)^T D^{-1} (r - r_0)}{4\tau_d} \right)$$
Fibre tracking using diffusion MRI data

Diffusion MRI data
Water displacement profile
Fibre directions
Fibre tracts
Tractography

Streamline integration methods:
- “fibre assignment using continuous tracking” (FACT)
- Euler
- RK4

S. Mori et al, AN 45:265-269, 1999
Tractography

What does tractography tell us?
- is A connected to B?
- how are A and B connected?
- how confident are we in this connection?

Applications of tractography:
- visualization: localization, education
- segmentation (both white matter and grey matter)
- investigating clinically differences between pathways in different populations
- neuroanatomical questions
Tractography

Lateral connections?
Considerations for optimal tractography

- angular resolution
- choice of processing/modeling
- spatial resolution
- quantification of uncertainty
Considerations for optimal tractography

- angular resolution
- choice of processing/modeling
- spatial resolution
- quantification of uncertainty
Diffusion weighted images
Diffusion weighted signal intensity: high value in directions perpendicular to fibres
Probability of water displacement

orientation distribution function (ODF)

Diffusion tensor model
High Angular Resolution Diffusion Imaging (HARDI)

q-ball imaging
High Angular Resolution Diffusion Imaging (HARDI)
Why use high angular resolution diffusion MRI?

- Reduce false positive and false negative tractography results due to crossings.
- In voxels where fibres cross, single fibre approaches can yield:
  - ambiguous fibre direction
  - incorrect fibre direction
  - only one fibre direction (that of fascicle with largest volume fraction)
- Examples of such regions:
  - basis pontis, subcortical white matter, superior longitudinal fasciculus, acoustic radiations, projection from subgenual white matter to amygdala, optic chiasm, caudate nucleus, corpus callosum, cortical spinal tract, cingulate bundle.
DTI vs. HARDI:
Tractography in phantom

single fibre

multi-fibre

Campbell et al. ISBI 2006.
DTI vs. HARDI: tractography *in vivo*


single fibre tractography

multi fibre tractography
Considerations for optimal tractography

- angular resolution
- choice of processing/modeling
- spatial resolution
- quantification of uncertainty
Crossing fibre reconstruction approaches

- multi-tensor approaches (Alexander et al., Parker et al., others)
- multi ball and stick (Behrens et al.)
- Composite hindered and restricted model of diffusion (CHARMED) (Assaf et al.)
- diffusion spectrum imaging (DSI) (Wedeen et al.)
- q-ball imaging (QBI) (Tuch et al.)
- spherical deconvolution (Tournier et al., Anderson, others)
- other variants
Multi-tensor model
Behrens’ ball and stick model
Composite hindered and restricted model of diffusion (CHARMED)

hindered

restricted
Diffusion Spectrum Imaging (DSI)

3D diffusion pdf

2D diffusion ODF
q-ball Imaging (QBI)
Crossing fibre detection: QBI vs. Deconvolution

Diffusion ODF

Deconvolved ODF
Crossing fibre reconstruction approaches

- multi-tensor approaches (Alexander et al., Parker et al., others)
- multi ball and stick (Behrens et al.)
- Composite hindered and restricted model of diffusion (CHARMED) (Assaf et al.)
- diffusion spectrum imaging (DSI) (Wedeen et al.)
- q-ball imaging (QBI) (Tuch et al.)
- spherical deconvolution (Tournier et al., Anderson, others)
- other variants
Inferring higher angular resolution from limited datasets

Curve Inference using neighbourhood information
Beyond crossing: other complex subvoxel geometries

Curve Inference to distinguish fanning from bending fibres

Beyond crossing: other complex subvoxel geometries

subvoxel fanning of fibres
Beyond crossing: other complex subvoxel geometries

tracking without fanning

tracking with fanning
Considerations for optimal tractography

- angular resolution
- choice of processing/modeling
- spatial resolution
- quantification of uncertainty
Effects of limited spatial resolution

Jumping from tract system to tract system
Effects of limited spatial resolution

Jumping from tract system to tract system
Interpreting results:
using priors in tractography

Mori 2001
Missing information: small volume fractions
Missing information: small volume fractions
Missing information: small volume fractions

user-assisted tractography using priors
Considerations for optimal tractography

• angular resolution
• choice of processing/modeling
• spatial resolution
• quantification of uncertainty
Fibre directions and uncertainty

residual bootstrap statistical technique to estimate uncertainty in fibre directions
Fibre directions and uncertainty
Tractography incorporating uncertainty
Uncertainty and fanning fibres

[Diagrams showing comparisons between 'no fanning' and 'fanning']
Tractography

Lateral connections?
Tractography

different algorithmic approaches to the problem:

“are A and B connected, and what is our confidence in this connection?”

vs.

“A and B are connected. What is our confidence in this connection?”
Summary

Diffusion MRI tractography results include many false positives and false negatives: priors are essential.

- Tractography is good for segmentation of parts of pathways, but segmenting the entire pathway can be challenging.
- Characterizing unknown new anatomy is much more difficult than studying known anatomy.
- Tractography does not distinguish between afferent and efferent pathways, or between mono- and multisynaptic connection.
- Diffusion MRI has relatively course resolution: jumping from pathway to pathway is common.
- Tractography gives us a nice way to visualize fibre directionality in 3D.
Applications:

studies using crossing fibre approaches

- basic neuroanatomy
- nonhuman primates
- structure and function
- understanding disease
- understanding therapies
Dissociating the Human Language Pathways with High Angular Resolution Diffusion Fiber Tractography

Stephen Frey, Jennifer S. W. Campbell, G. Bruce Pike, and Michael Petrides

1Cognitive Neuroscience Unit and 2McConnell Brain Imaging Centre, Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada H3A 2B4
Applications: tractography in regions of crossing fibres

fibre crossings in regions of partial volume averaging of pathways, e.g., SLF - CC - CST
Applications: tractography in regions of crossing fibres
Applications: basic neuroanatomy

Applications – nonhuman primates

Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography

Jeremy D. Schmahmann,1 Deepak N. Pandya,3 Ruopeng Wang,2 Guangping Dai,2 Helen E. D'Arceuil,2 Alex J. de Crespigny2 and Van J. Wedeen2

1Department of Neurology, 2Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School and 3Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, USA
Applications – nonhuman primates

Applications: structure and function

Hemispheric asymmetries in language-related pathways:
A combined functional MRI and tractography study

H.W. Robert Powell, a,g Geoff J.M. Parker, b Daniel C. Alexander, c Mark R. Symms, a,g Philip A. Boulby, a,g Claudia A.M. Wheeler-Kingshott, d Gareth J. Barker, e Uta Noppeney, f Matthias J. Koepp, a,g and John S. Duncan a,g,*

a Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, Queen Square, London, WC1N 3BG, UK
b Imaging Science and Biomedical Engineering, University of Manchester, Oxford Road, Manchester, England
c Department of Computer Science, University College London, Gower Street, London, UK
d NMR Research Unit, Institute of Neurology, University College London, London, UK
e King’s College London, Institute of Psychiatry, Department of Neurology, Centre for Neuroimaging Sciences, London, UK
f Wellcome Department of Imaging Neuroscience, University College London, London, UK
g MRI Unit, National Society for Epilepsy, Chalfont St. Peter, Buckinghamshire, UK

NeuroImage

www.elsevier.com/locate/ynimng
Applications: structure and function

Individual Differences in White-Matter Microstructure Reflect Variation in Functional Connectivity during Choice

Erie Dell Boorman,¹,²,³,* Jacinta O’Shea,¹,²,³
Catherine Sebastian,² Matthew F.S. Rushworth,¹,²
and Heidi Johansen-Berg¹
¹ Centre for Functional MRI of the Brain
University of Oxford
Oxford OX3 9DU
United Kingdom
² Dept of Experimental Psychology
University of Oxford
Oxford OX1 3UD
United Kingdom

magnetic stimulation (TMS) [8, 12, 13] evidence has implicated interactions between the dorsal premotor cortex (PMd) and the primary motor cortex (M1) in the process of externally cued action selection, we focused our investigation on these two regions. We first assessed functional connectivity between the PMd and M1 during a particular cognitive state—action selection. We then tested for an association between this measure of functional connectivity and fractional anisotropy (FA) values calculated within a white-matter network.
Applications: structure and function

- paired pulse transcranial magnetic stimulation
- correlate modulation of motor evoked potentials (MEPs) with fractional anisotropy (FA)
- seed tractography in correlated regions

Applications: clinical research

Tractography of the parahippocampal gyrus and material specific memory impairment in unilateral temporal lobe epilepsy


Department of Clinical and Experimental Epilepsy, Institute of Neurology, UCL and National Society for Epilepsy, UK
Imaging Science and Biomedical Engineering, University of Manchester, UK
Department of Computer Science, UCL, UK
Department of Neuroinflammation, Institute of Neurology, UCL, UK
Department of Clinical Neuroscience, Centre for Neuroimaging Sciences, King's College London, Institute of Psychiatry, UK

Received 4 September 2007; revised 7 December 2007; accepted 20 December 2007
Available online 10 January 2008
Applications: clinical research

Findings:

- increased left intratract FA in L TLE
- 22% reduction in left tract volume in L TLE

Applications: understanding therapies

A Tractography Analysis of Two Deep Brain Stimulation White Matter Targets for Depression

David A. Gutman, Paul E. Holtzheimer, Timothy E. J. Behrens, Heidi Johansen-Berg, and Helen S. Mayberg
Applications: understanding therapies

- tractography seeded at sites used for deep brain stimulation
- overlap in tractography maps corresponds to areas involved in depression
- furthers our understanding of why this therapy is effective

Acknowledgements

G. Bruce Pike  Ives Levesque
Kaleem Siddiqi  Jean Chen
Ilana Leppert  Mike Ferreira
Peter Savadjiev  Christine Tardif
Parya Mamayyez Siahkal  Clarisse Mark
Steve Frey  Ileana Jelescu
Vladimir Rymar