Towards Validation of DTI Tractography

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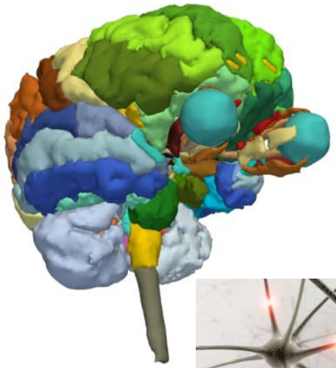
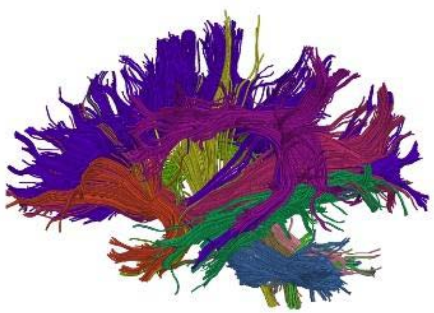
39th Annual Meeting of the Society for Neuroscience – Oct.17-21, 2009 Chicago, IL

Brain Connectivity

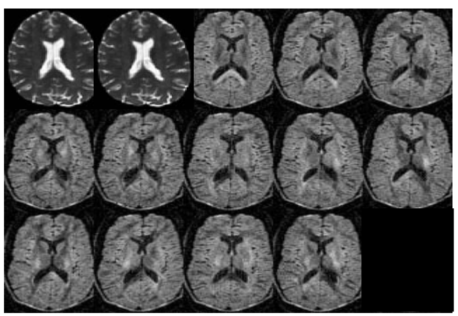


- 100 billions of neurons
- Complex neuronal networks

Brain Connectivity



Courtesy of L O'Donnell & CF Westin



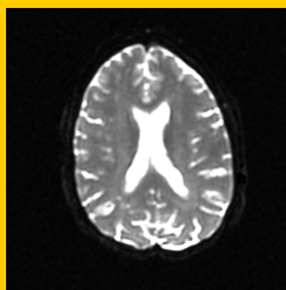
- 100 billions of neurons
- Complex neuronal networks
- Diffusion MRI is the first non-invasive window on the organization of the brain white matter pathways

DTI as a Neuroimaging marker

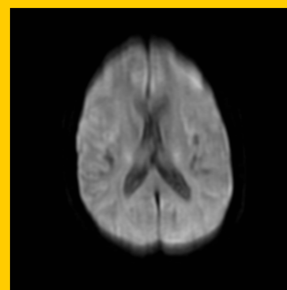
- Visualization of *in-vivo* normal and pathological anatomy

- Insights into white matter abnormalities which may include changes in direction, radial displacement or diameter of white matter fiber bundles

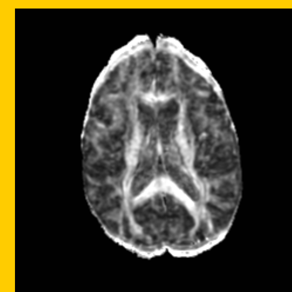
DTI Analysis Pipeline



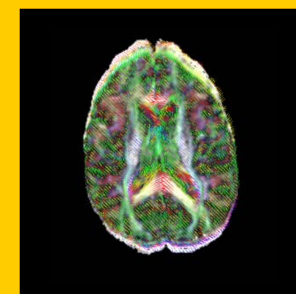
DWI
Acquisition



Tensor
Calculation



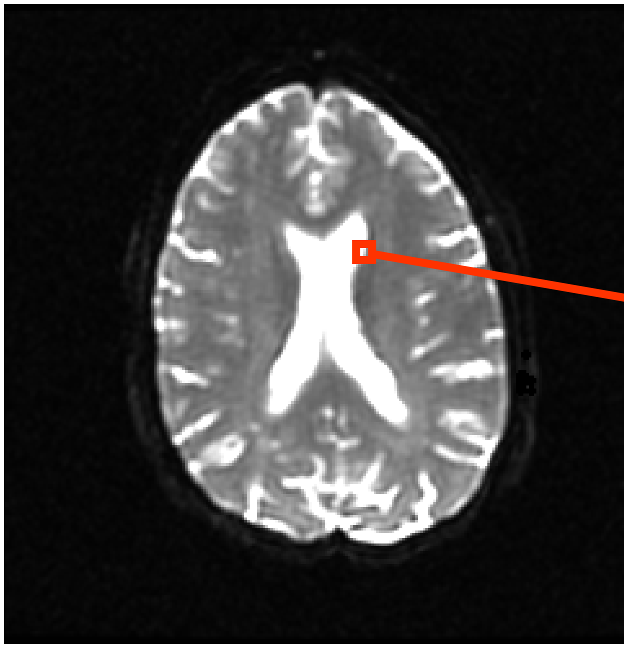
Scalar
Maps



3D
Visualization

Diffusion Tensor

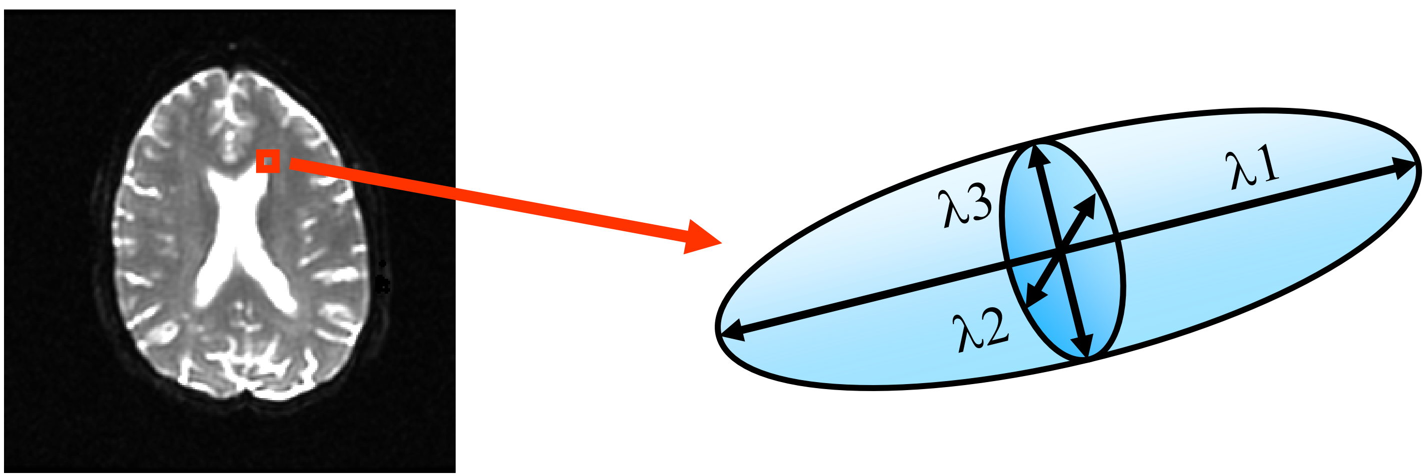
Stejskal-Tanner $S_i = S_0 e^{-b\hat{g}i^T \underline{D}\hat{g}_i}$



$$\underline{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

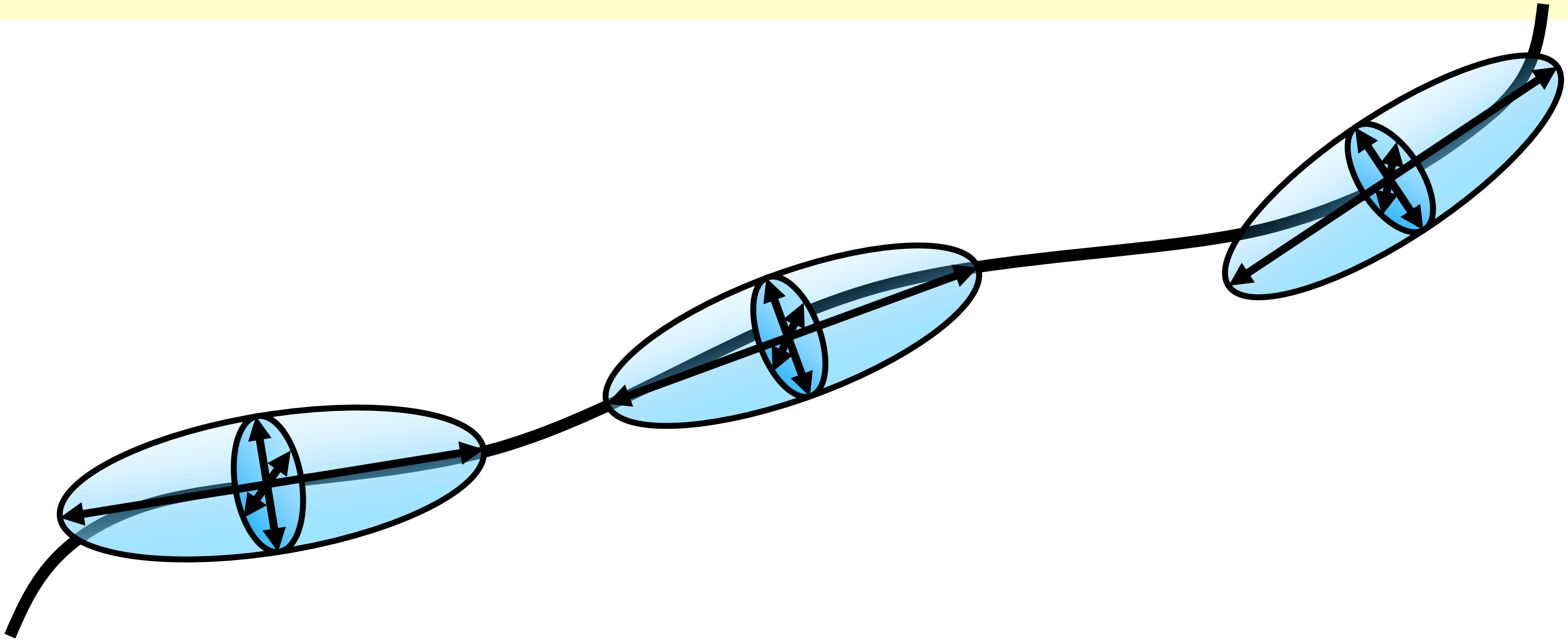
Physical Interpretation

The diffusion tensor D in the voxel (I,J,K) can be visualized as an ellipsoidal isoprobability surface in which the principal axes correspond to the eigenvectors.

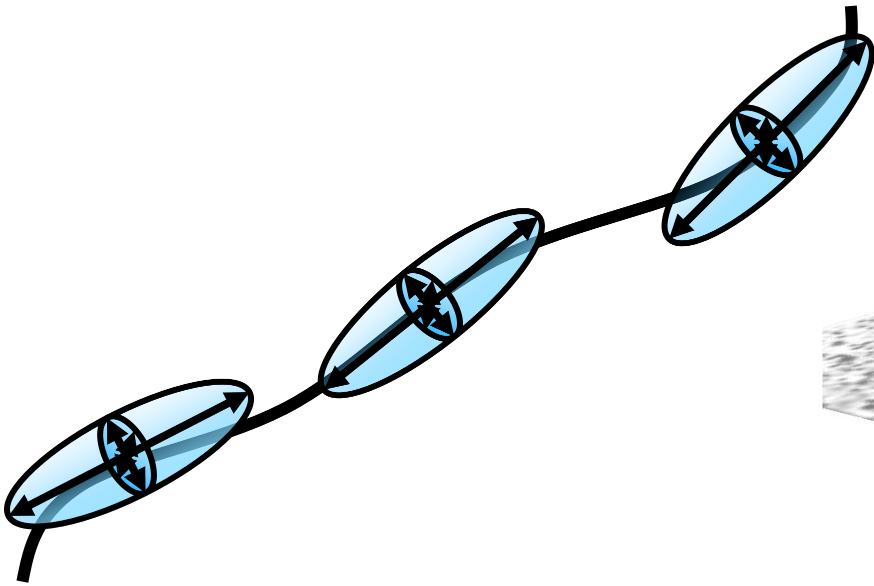


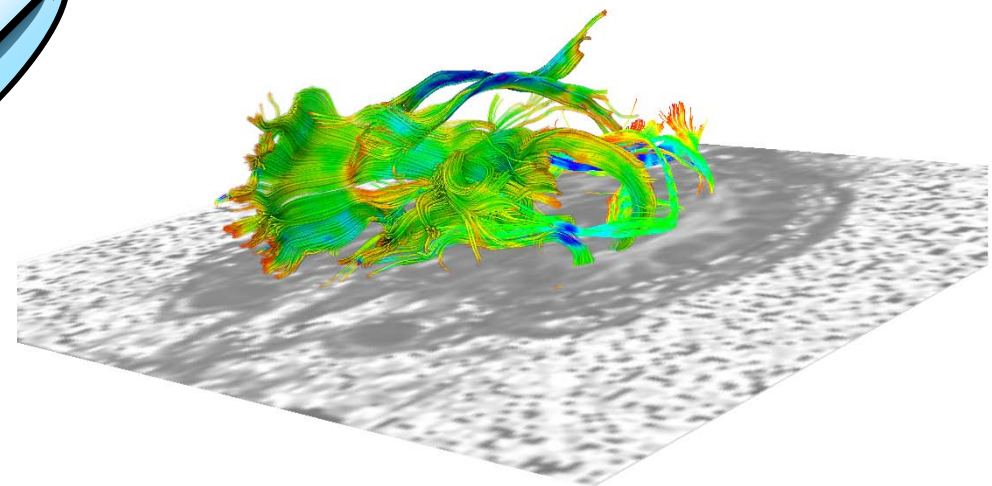
Streamline tractography

- Hypothesis: the direction of the fibers is collinear with the direction of the eigenvector associated with the largest eigenvalue.



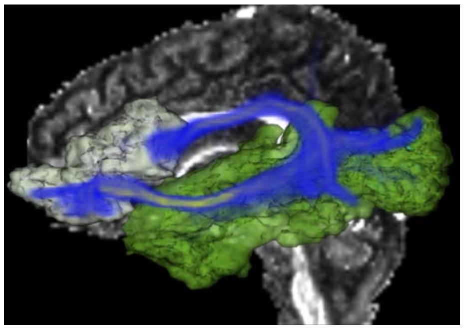
Tractography



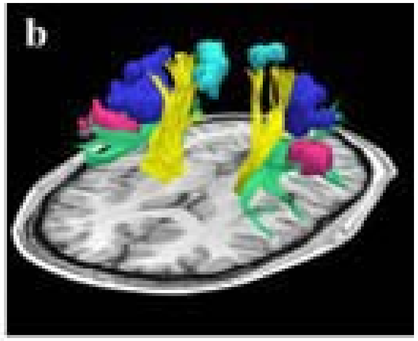


The goal of tractography is to determine white matter fibers' trajectory from a set of DTI voxels.

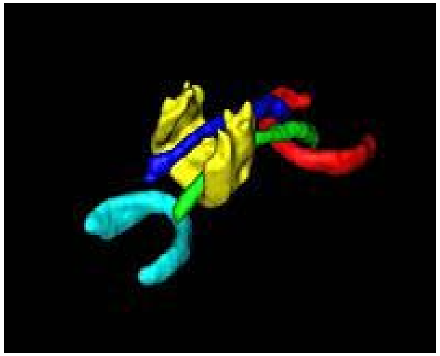
Tractography



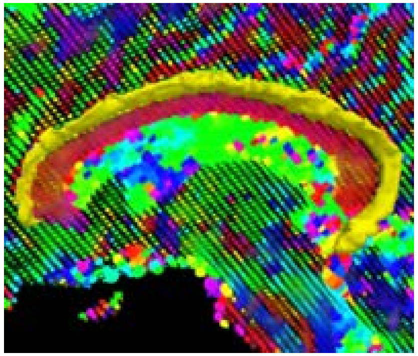
Courtesy of J De Siebenthal & CF Westin



Courtesy of A. Areza & CF Westin



Courtesy of T.Fletcher & R. Whitaker

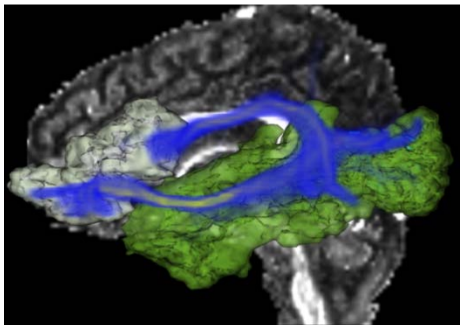


Courtesy of A. Tannenbaum

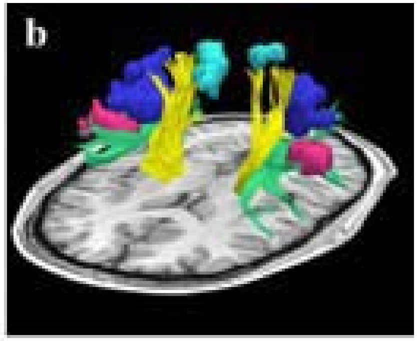
Current achievements include:

- 3D visualization of healthy & pathological anatomy
- Assessment of group differences (e.g Schizophrenia, Alzheimer's disease)

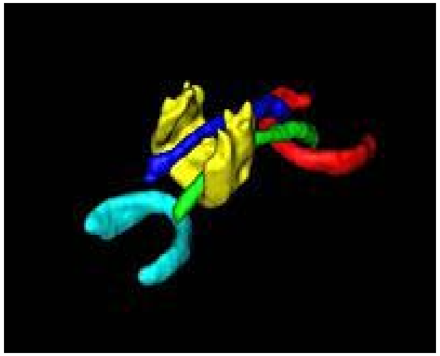
Tractography



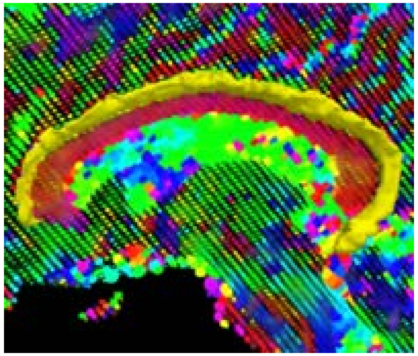
Courtesy of J De Siebenthal, CF Westin



Courtesy of A. Areza CF Westin



Courtesy of T.Fletcher & Ross Whitaker

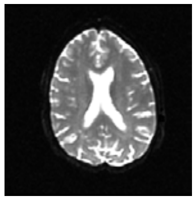


Courtesy of A. Tannenbaum

Current Challenge:

Characterization of different tractography approaches

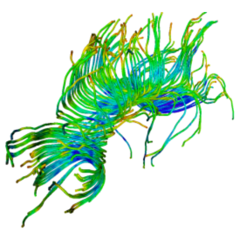
Sources of variability



patient

acquisition

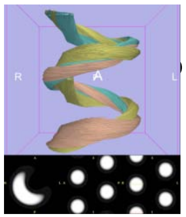
fascicle



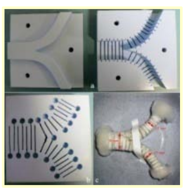
algorithm/models

$$\ln p(X \mid \pi, \mu, \Sigma) = \sum_{n=1}^{N} In \, \{\sum_{k=1}^{K} \pi_k N(x_n \mid \mu_k, \Sigma_k)\}$$

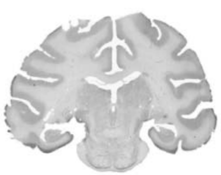
Validation Approaches



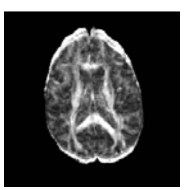
Mathematical Phantoms



Physical Phantoms

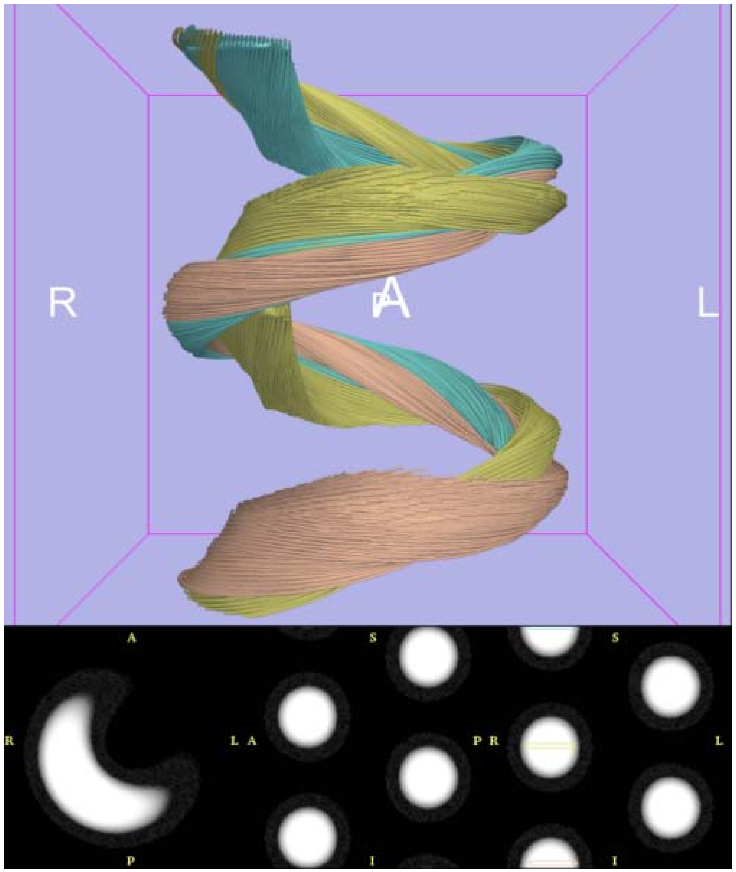


Histological Studies



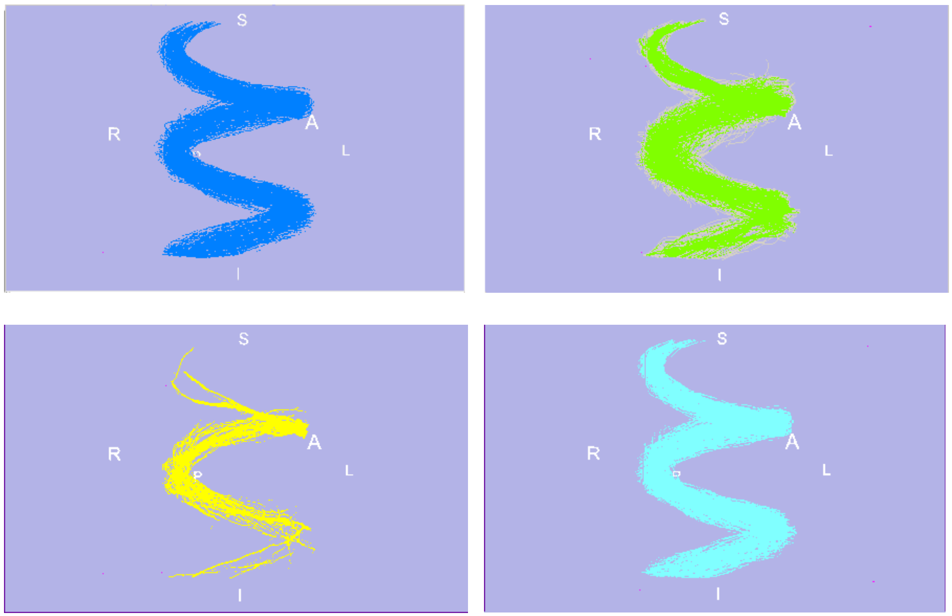
Real Subject Data

Mathematical Phantoms



- Known absolute ground truth
- Freedom of shape design

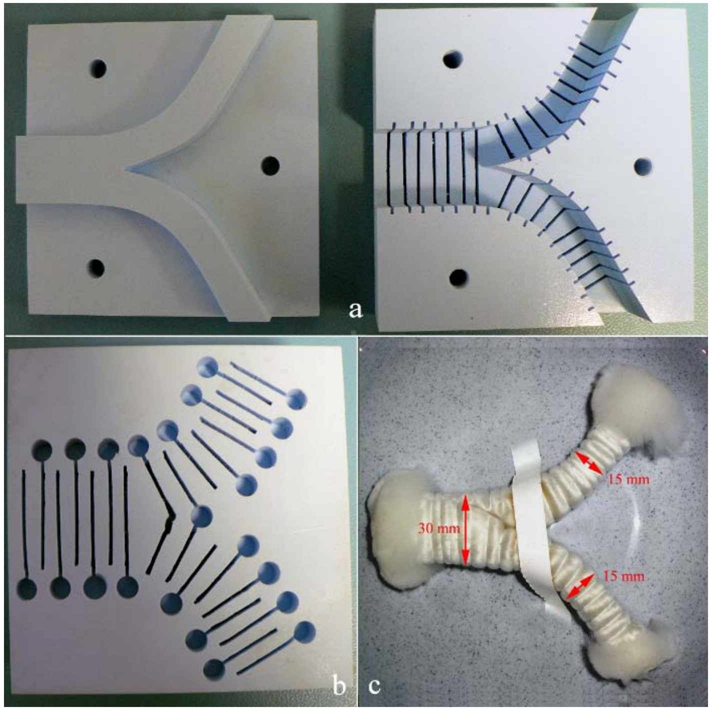
Mathematical Phantoms



- Known absolute ground truth
- Freedom of shape design
- Freedom of parameter selection

Performance evaluation

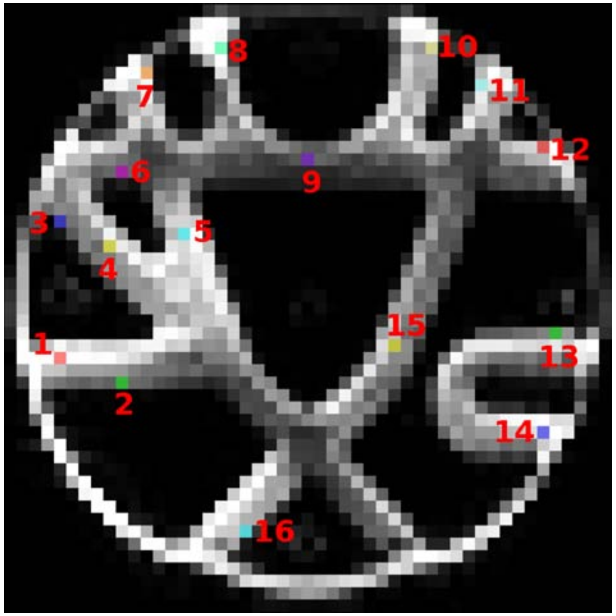
Physical Phantom



- Simple/complex tract configurations

Poupon et al. Magn Reson Med. 2008 Dec;60(6):1276-83.

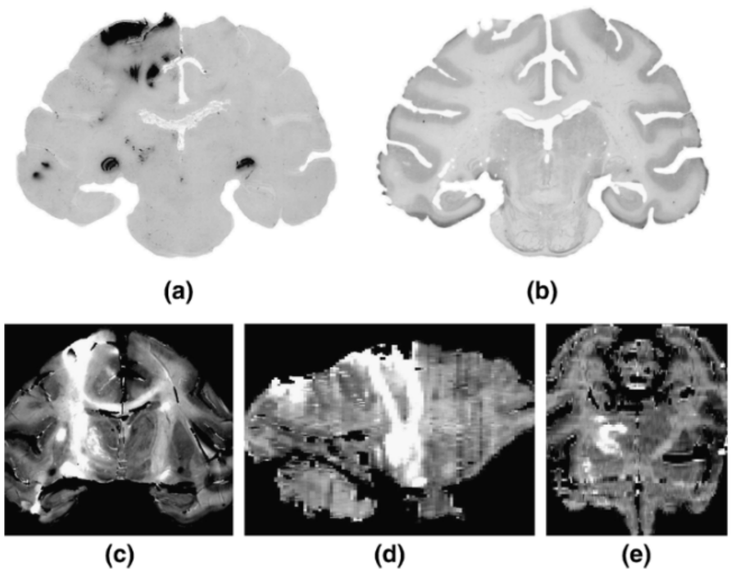
Physical Phantom



- Simple/complex tract configurations
- Real MR images
- Variations in voxel size, B-value and SNR

Courtesy of C.Poupon and P.Fillard, LNAO

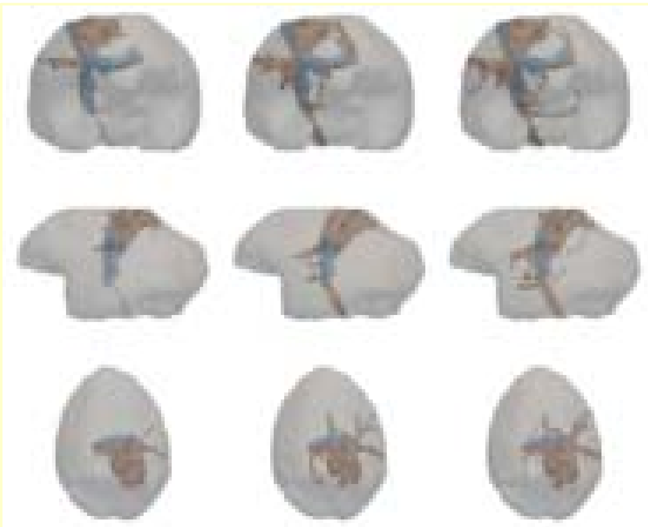
Histological studies



- Real anatomical structures

Dauguet et al, MICCAI 2006

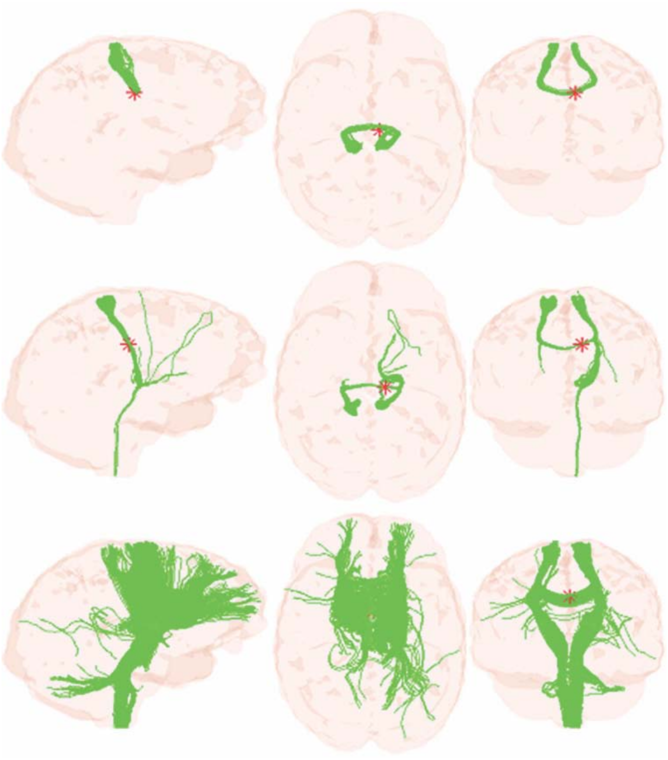
Histological studies



- Real anatomical structures
- Correlation with ground truth white matter anatomy

Dauguet et al, Neuroimage 2007

Boostrapping



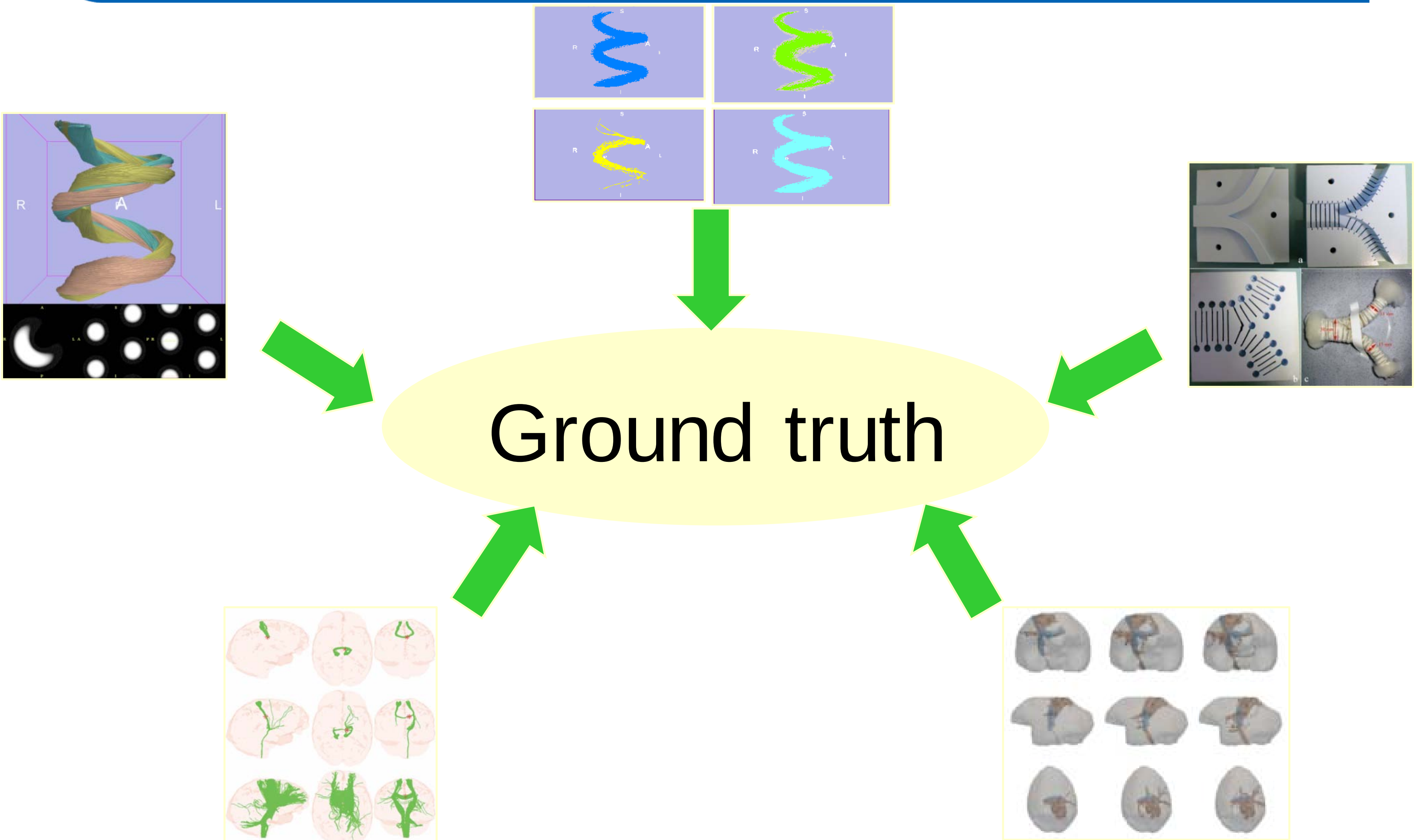
- Non parametric statistical approach
- Assessment of

the precision of

DTI tractography

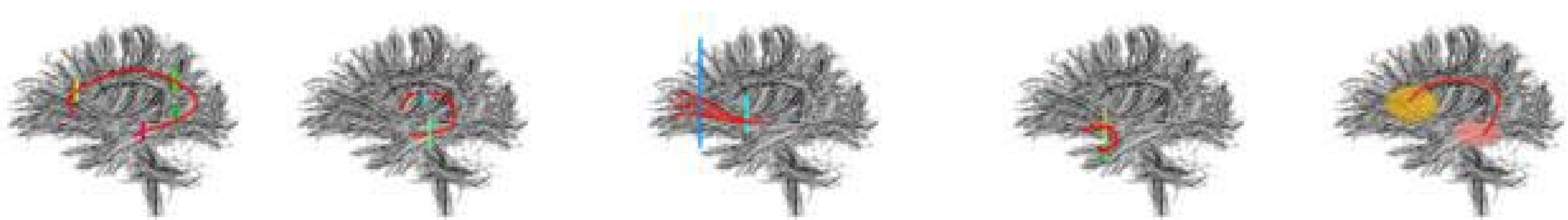
Jones and Pierpaoli, MRM 2007

Complementary approaches



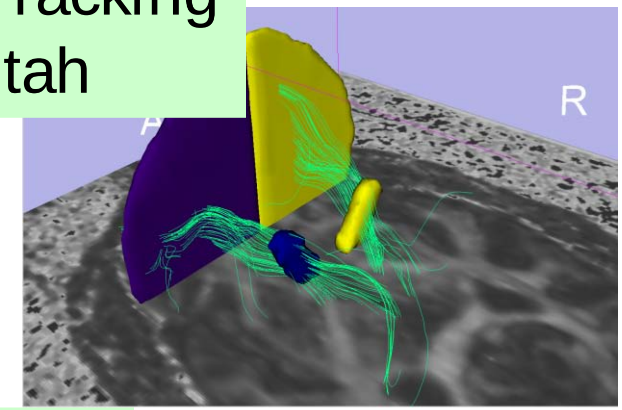
NA-MIC pilot initiative

- Exploratory work initiated by the National Alliance for Medical Image Computing
- 7 major research centers across the US
- Cross-comparison of tractography algorithms on five white matter fascicles

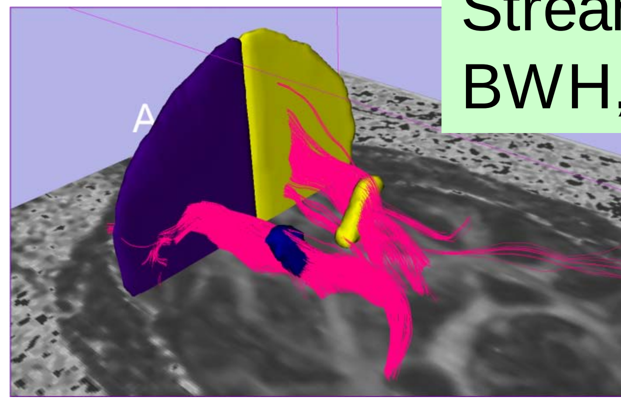


Implementation

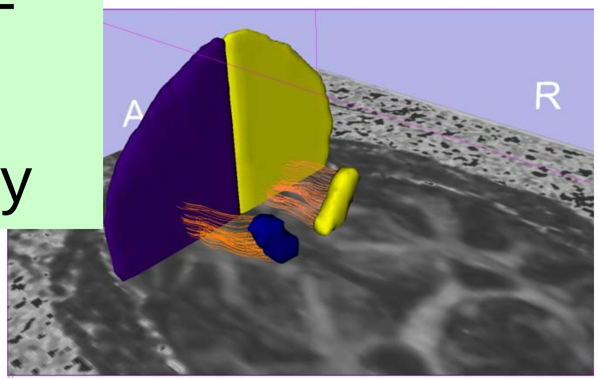
Fiber Tracking
SCI, Utah



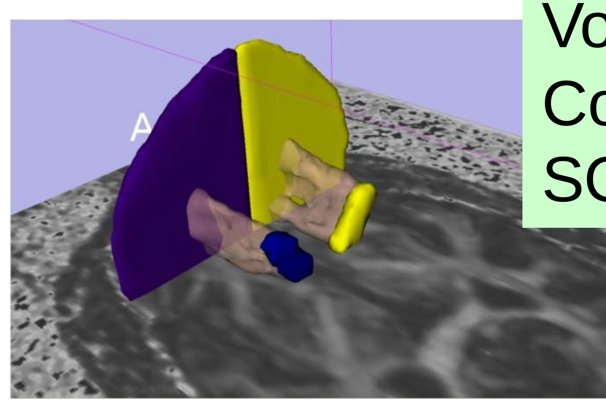
Streamline
BWH, Harvard



GTRACT
Iowa
University



Volumetric
Connectivity
SCI, Utah



Our approach

- Comparison of segmentation of structural images in the absence of ground truth: STAPLE

Warfield SK, Zou KH, Wells WM. STAPLE. Simultaneous Truth and Performance Level Estimation (STAPLE): An algorithm for the Validation of Image Segmentation. IEEE Trans Med Imaging. 23(7):903-21.

➡ Application to DTI Segmentation

Tractography evaluation

- The complete data (D,T) is composed of the detected tracts D (known), and true tracts T (unknown).
- The tractography algorithm decision at each voxel is regarded as being incomplete, and is regarded as an observable of the complete data.
- The models parameters $\theta = (p, q)$ are given by the sensitivity p and the specificity q.

STAPLE

(Simultaneous Truth and Performance Level Evaluation)

- Expectation-Maximization algorithm (EM) to maximize the incomplete data log likelihood function

$$In\ f(D \mid p, q)$$

*Warfield SK, Zou KH, **Wells WM.** STAPLE. Simultaneous Truth and Performance Level Estimation (STAPLE): An algorithm for the Validation of Image Segmentation.*
IEEE Trans Med Imaging. 23(7):903-21.

STAPLE

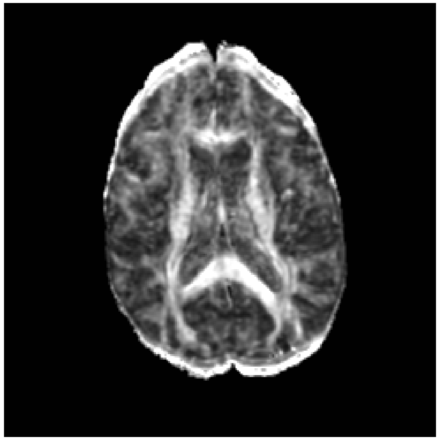
E-Step: Evaluate the posterior distribution $f(T, D \mid \theta^{(0)})$ and compute the Conditional Expectation of the complete data log likelihood

$$Q(\theta \mid \theta^{(0)}) = \sum_T f(T \mid D, \theta^{(0)}) Ln\, f(T, D \mid \theta)$$

M-Step: Maximization step

$$\theta^{(new)} = \arg_\theta \max Q(\theta, \theta^{(0)})$$

Computational Experiment: DWI Data



Acquisition:

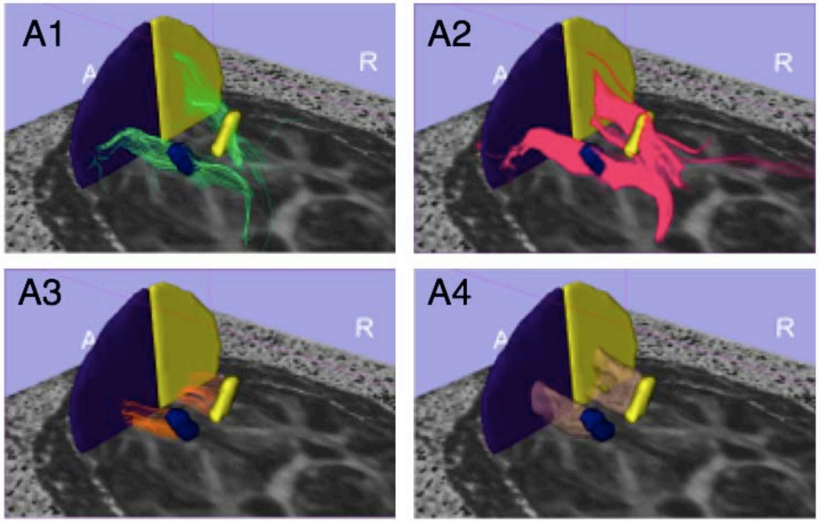
- 1.5 T Siemens scanner - 60 gradient & 10 baselines
- B = 700 s/mm²
- 2.0 mm voxel size

Pre-Processing:

- Eddy-current and EPI distortion correction
- Weighted least square tensor estimation

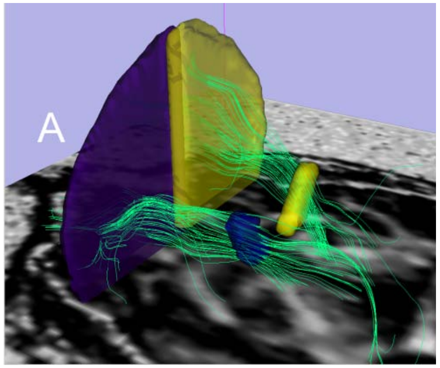
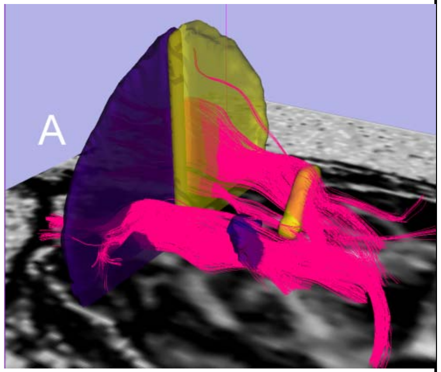
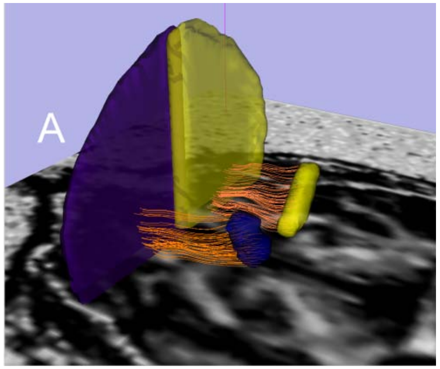
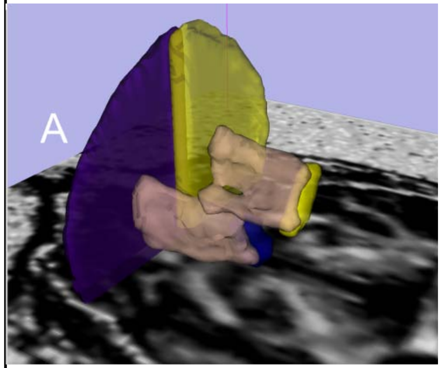
STAPLE analysis

- Preliminary results showed differences in sensitivity among algorithms



(Pujol et al, ISMRM 2009)

Internal Capsule

Fib.Tract	Slicer WB	Gtract	Vol Conn
			
Left - (0.52, 0.99) Right -(0.52, 0.99)	(0.80, 0.99) (0.81, 0.99)	(0.42, 0.99) (0.42, 0.99)	(0.74, 0.99) (0.75, 0.99)

STAPLE analysis

- Preliminary results showed differences in sensitivity between algorithms

→What is the statistical significance of the differences observed ?

Statistical Analysis: Tract of interest

Arcuate Fasciculus:

- connects the Broca's and Wernicke's area
- involved in language function

Statistical Analysis: Tractography Algorithms

A1: Fast Marching (FMT)

(Parker et al, TMI 2002)

A2: Guided Tracking (GTRACT)

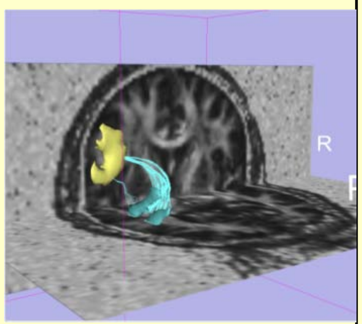
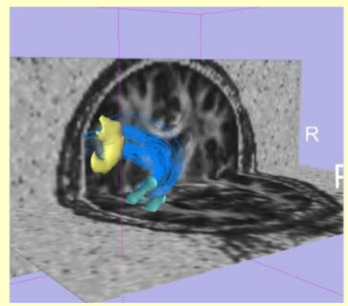
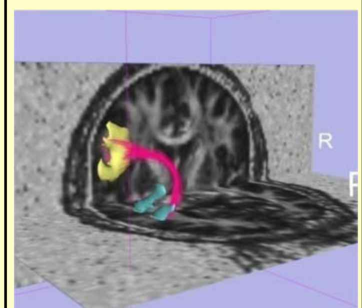
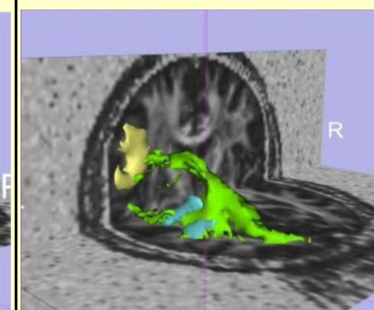
(Cheng et al, Neuroimage 2006)

A3: Streamline Tractography brute force approach (SLT) *(Basser et al, MRM 2000)*

A4: Stochastic Tractography

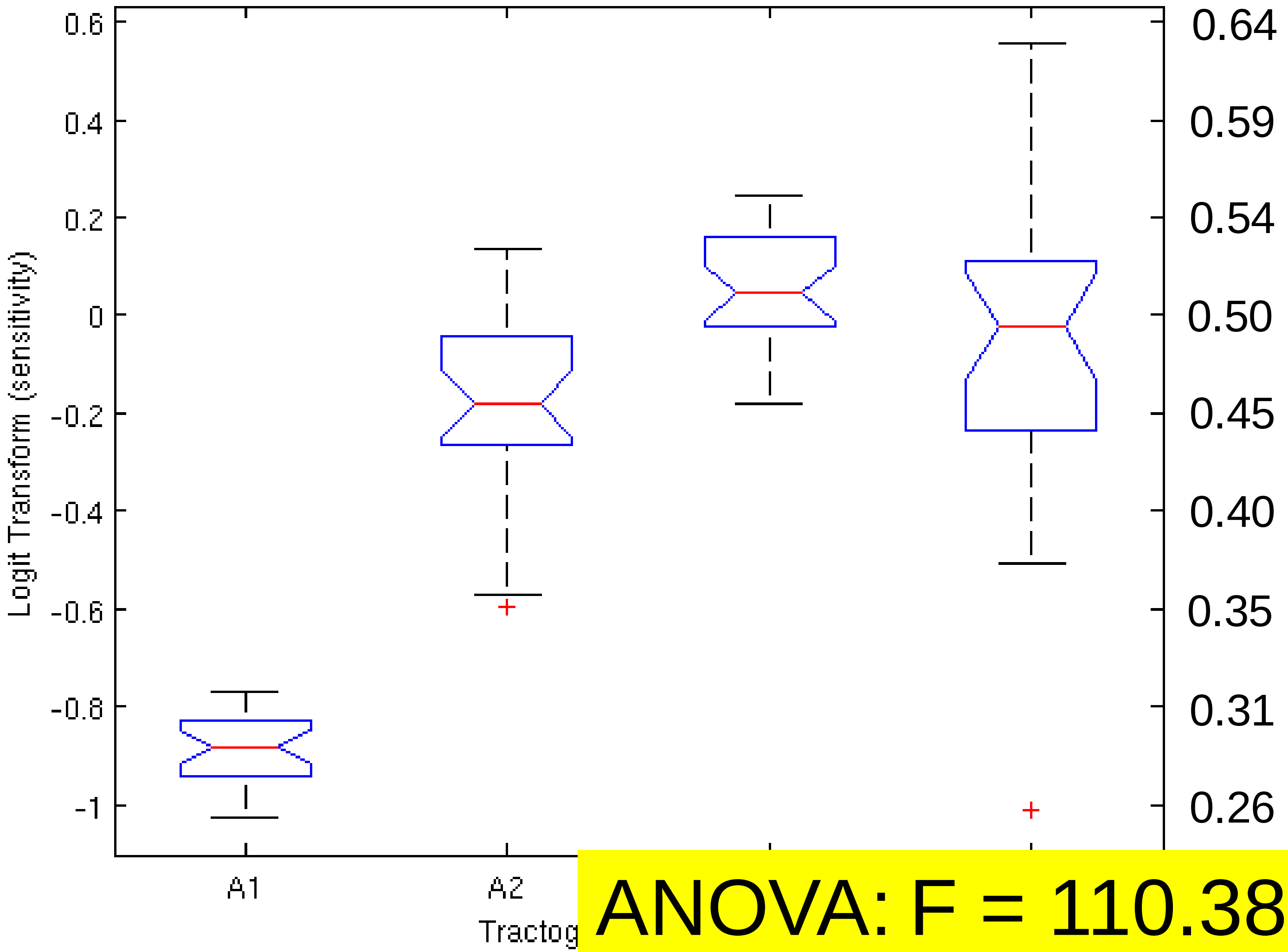
(Frieman et al, TMI 2006)

Results: Sensitivity

Tractography Algorithm	A1 (FM) 	A2 (GTRACT) 	A3 (SLT) 	A4 (Stochastic) 
μ	0.29	0.45	0.51	0.48
std	0.01	0.04	0.03	0.08

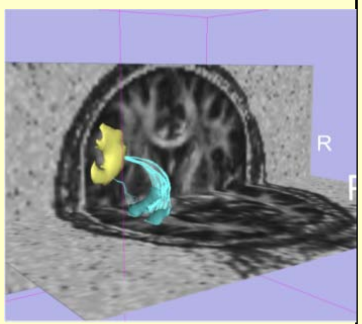
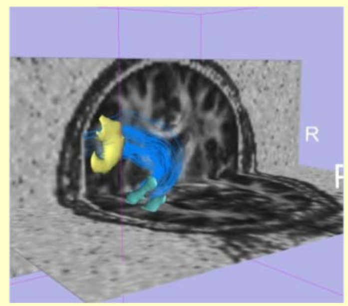
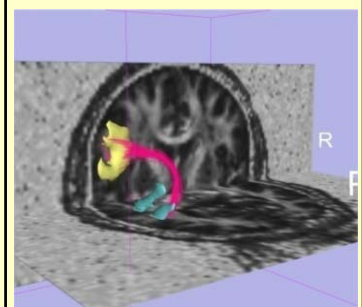
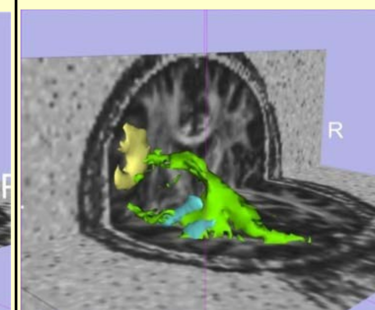
ANOVA and Tukey tests

Results: Sensitivity



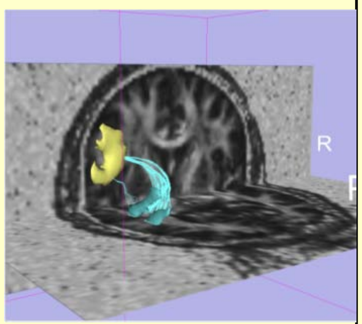
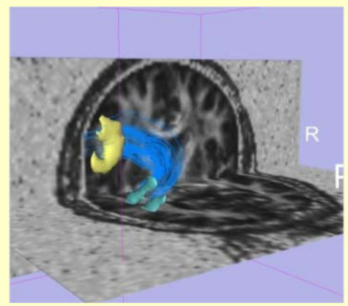
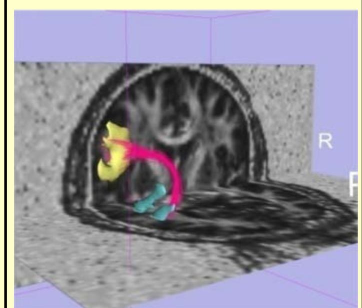
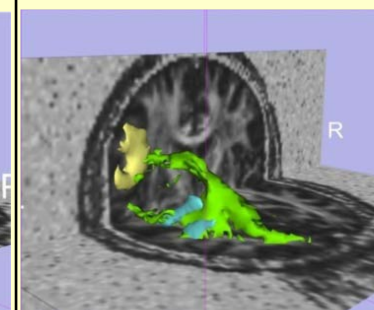
ANOVA: F = 110.38, p = 0

Results: Specificity

Tractography Algorithm	A1 (FM) 	A2 (GTRACT) 	A3 (SLT) 	A4 (Stochastic) 
μ	0.99	0.99	0.99	0.99
std	3.10^{-5}	3.10^{-4}	3.10^{-5}	7.10^{-5}

ANOVA: $F = 313.13$, $p = 0$

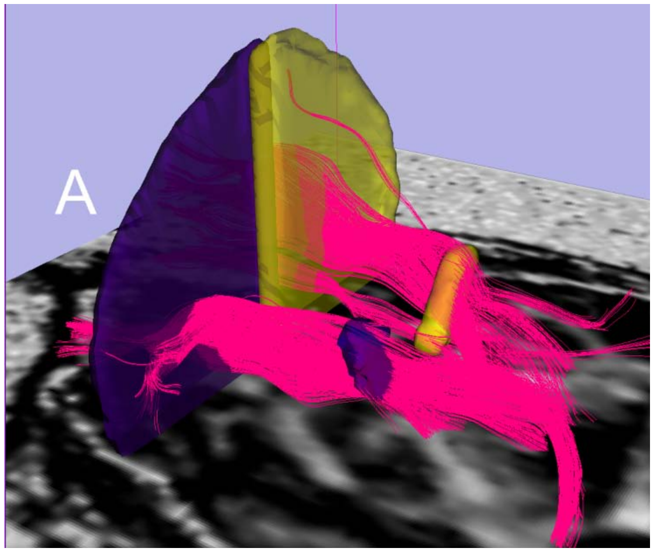
Results: Specificity

Tractography Algorithm	A1 (FM) 	A2 (GTRACT) 	A3 (SLT) 	A4 (Stochastic) 
μ	0.99	0.99	0.99	0.99
std	3.10^{-5}	3.10^{-4}	3.10^{-5}	7.10^{-5}

~~ANOVA: F = 313.13, p = 0~~

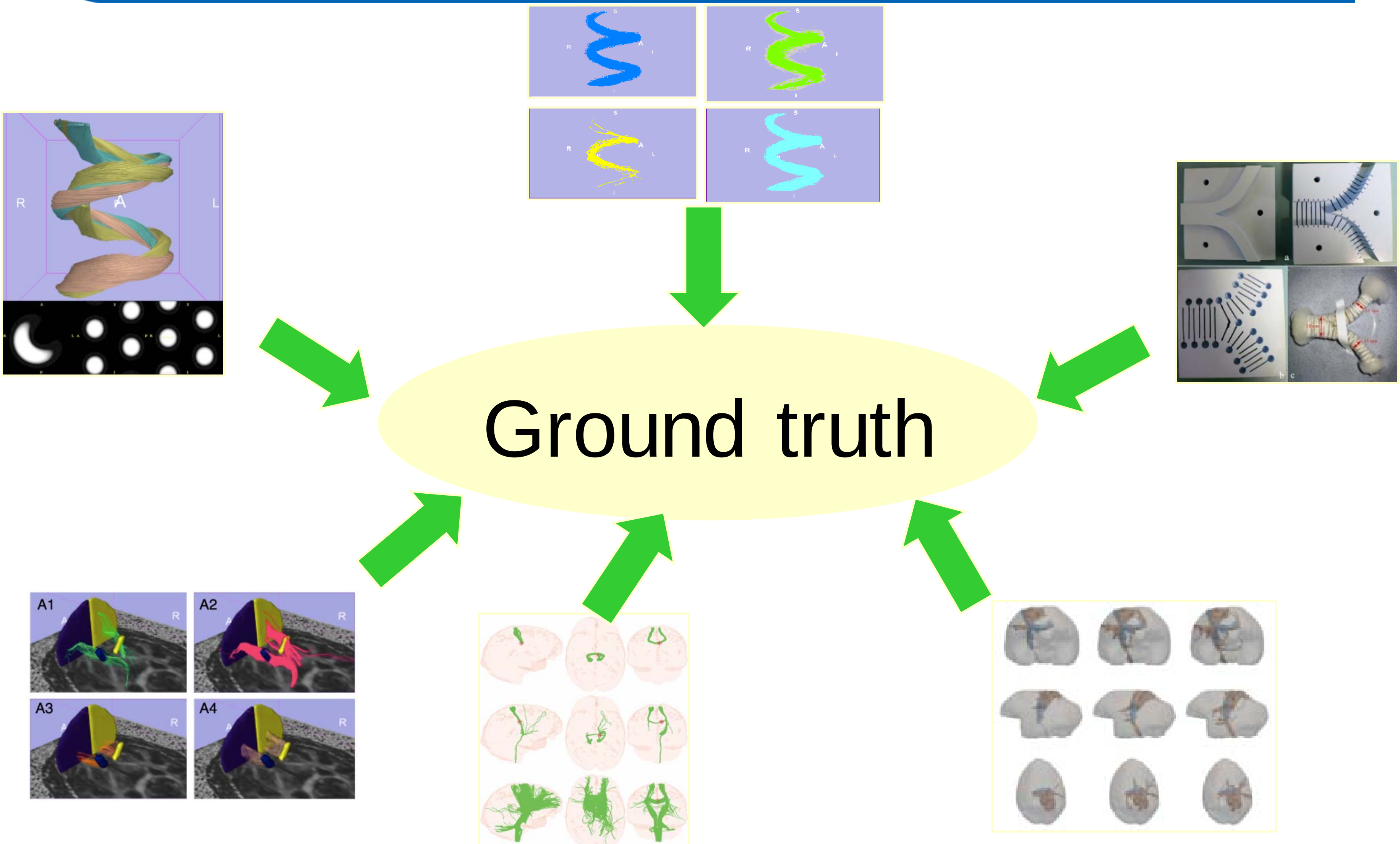
No practical significance

NA-MIC Pilot Study

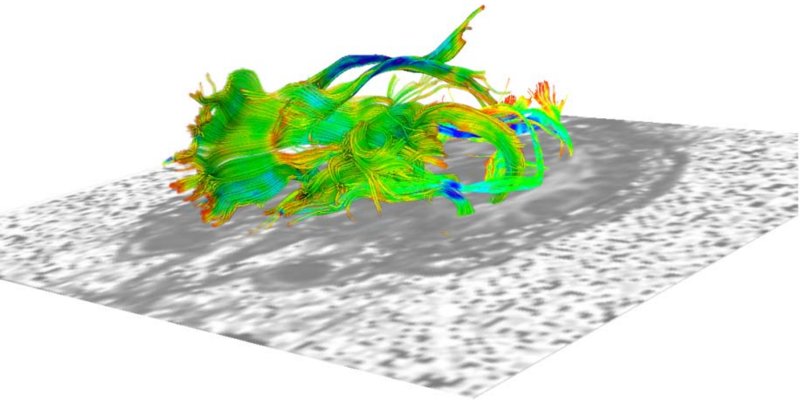


- Preliminary results on DTI tractography evaluation in the absence of ground truth
- Statistical analysis showed significant differences in sensitivity among algorithms

Complementary approaches



Conclusion



- Evaluation of various tractography approaches in the absence of ground truth
- Validation is key to the transfer from bench to bedside
- DTI tractography as an *in-vivo* neuroimaging marker

Acknowledgements

National Alliance for Medical Image Computing (NA-MIC)
(NIH Grant U54EB005149)

Neuroimage Analysis Center (NAC)
(NIH Grant P41 RR013218)