Lecture 16

Geometric Optics guided by Entropy Spectrum Pathway

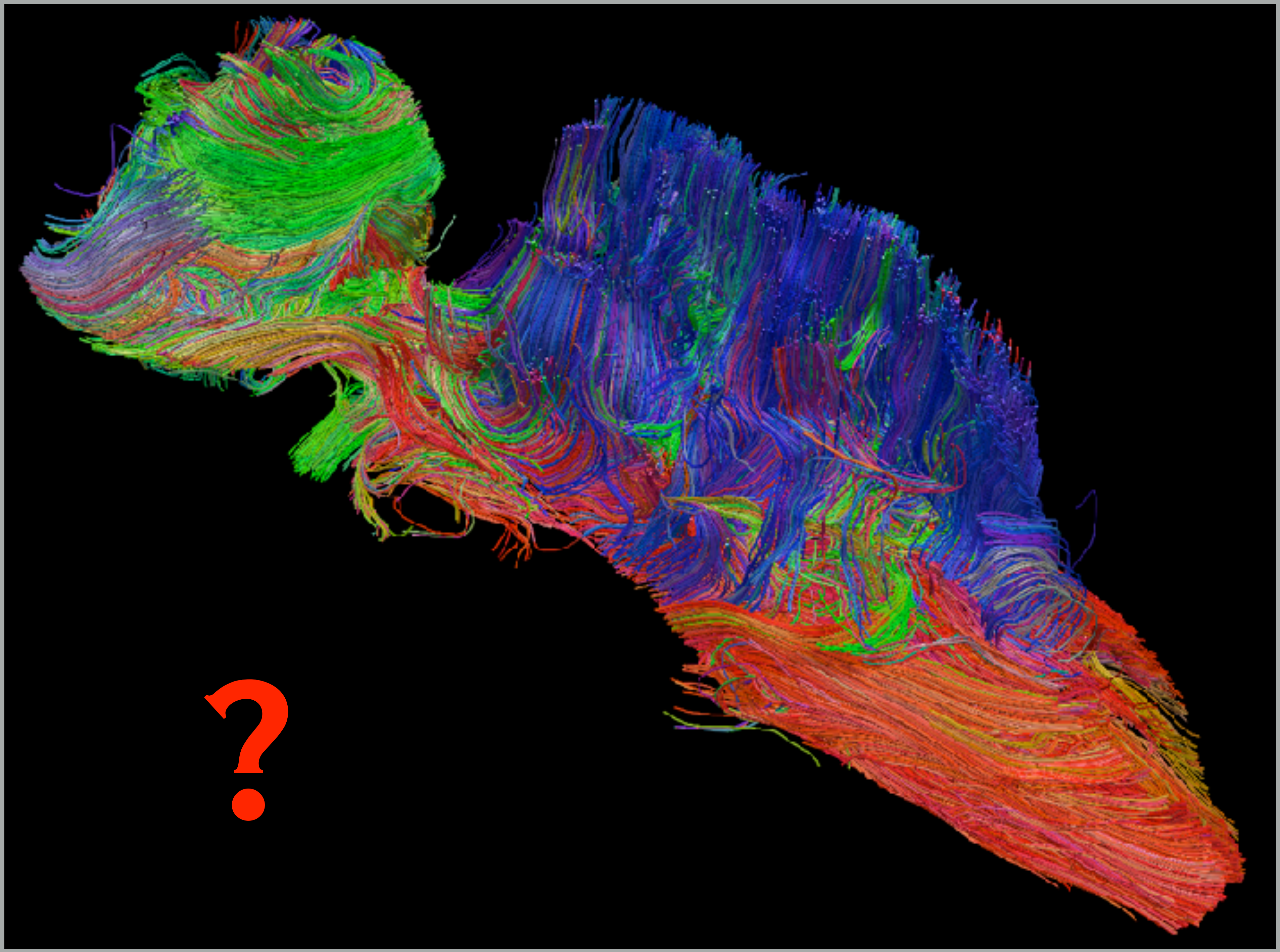
GO-ESP

High Resolution MRI of Elasmobranchs

Elasmobranchs have an elaborate sensory system

Brown Smoothhound *Mustelus henlei* (Data courtesy JM Tyszka)

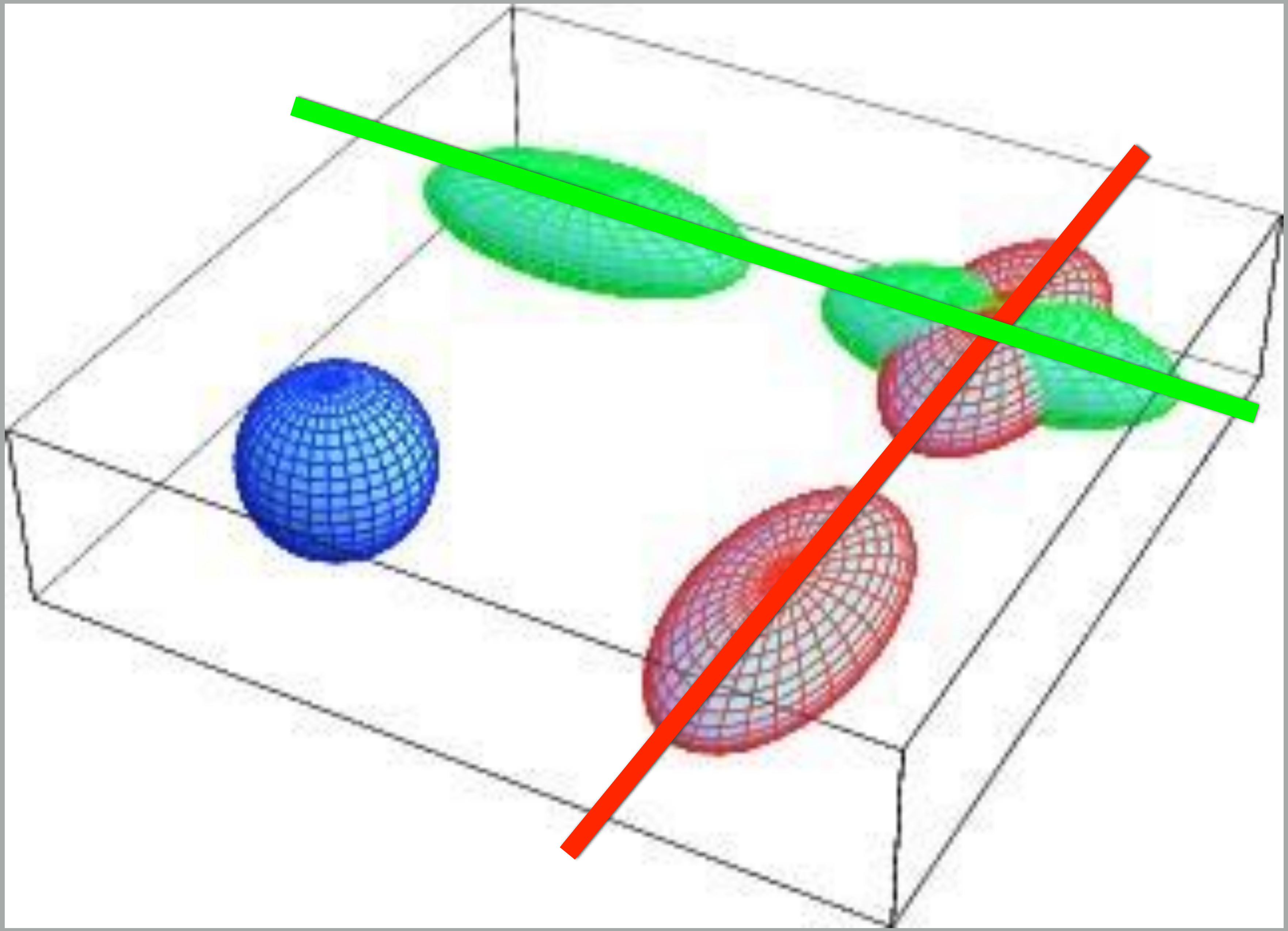
Connectivity



DTI in *Mustelus henlei* @ 9.4T

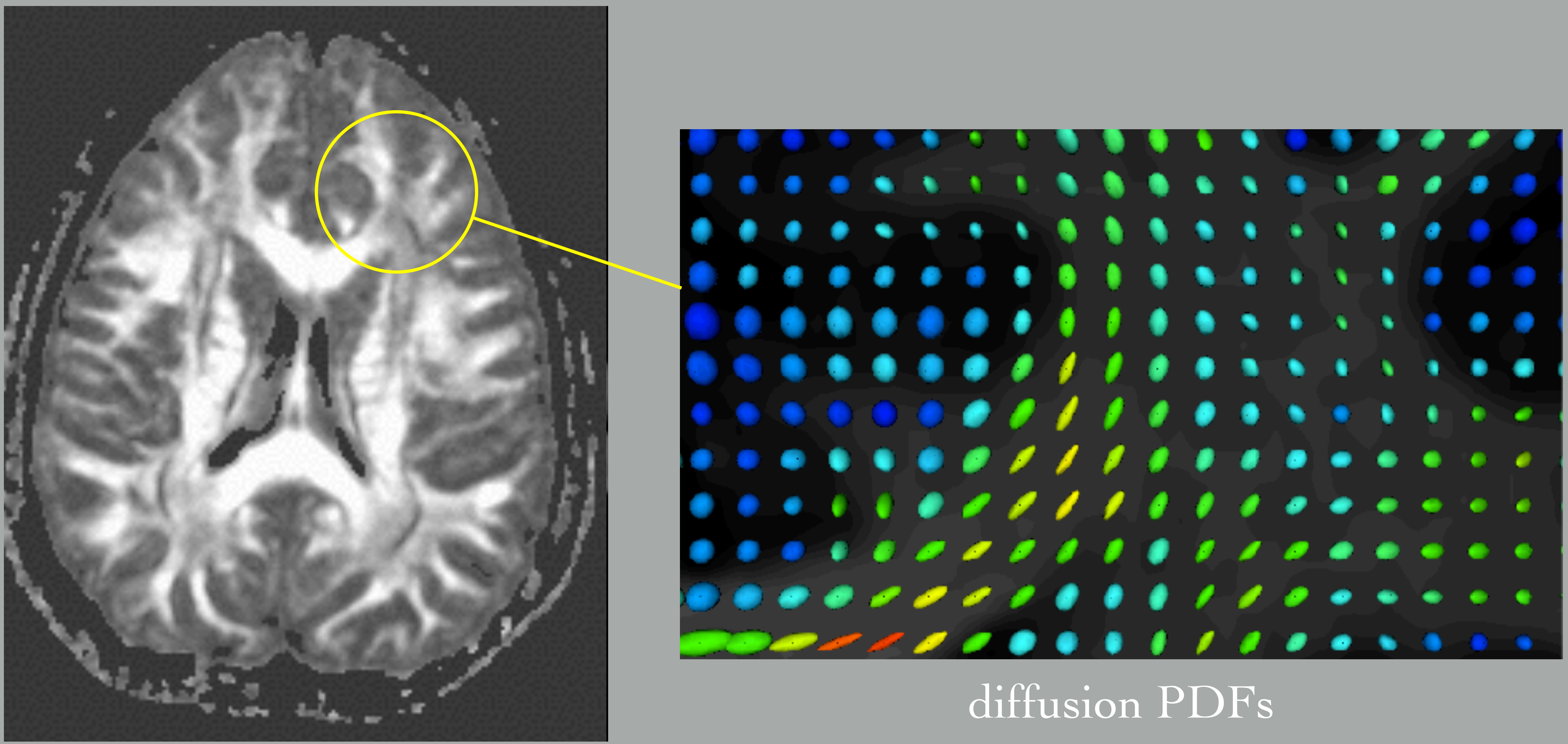
Data: M. Tyszka, CalTech

Ambiguity of the diffusion tensor



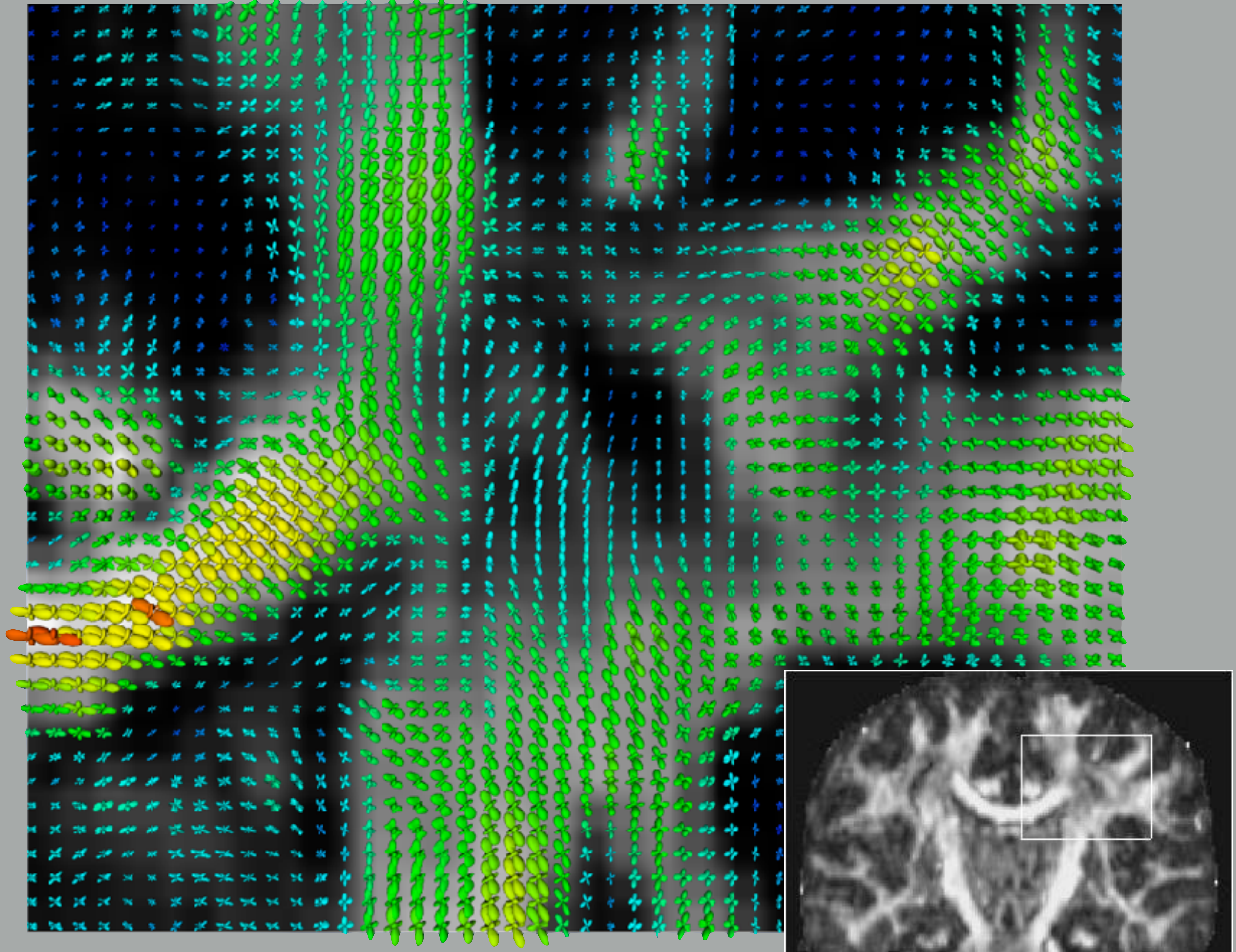
crossing fibers

The Crossing Fiber Problem

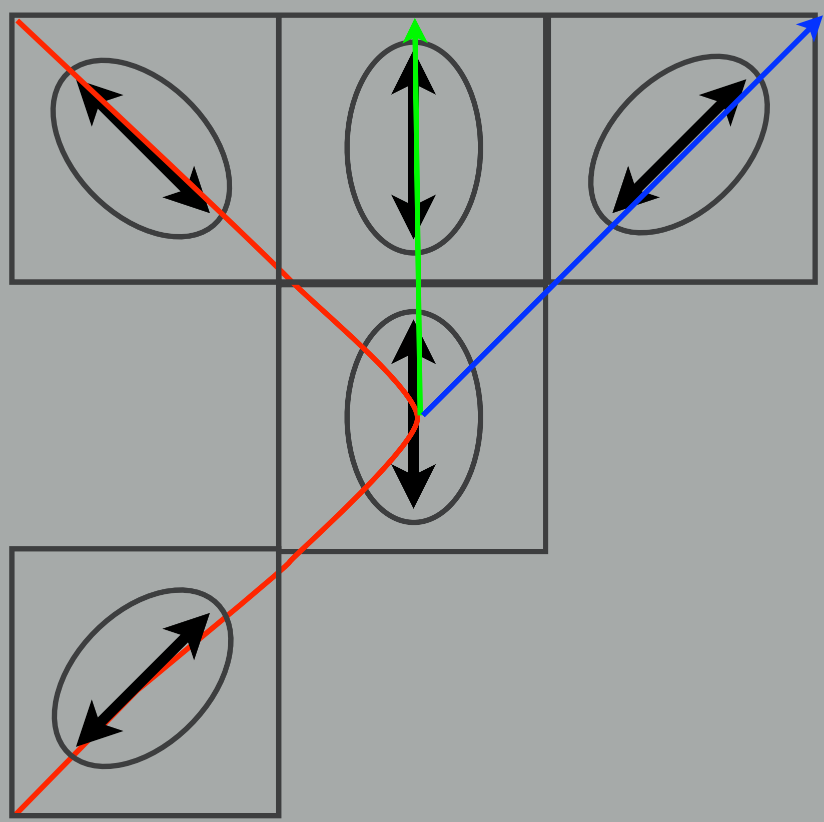


diffusion PDFs

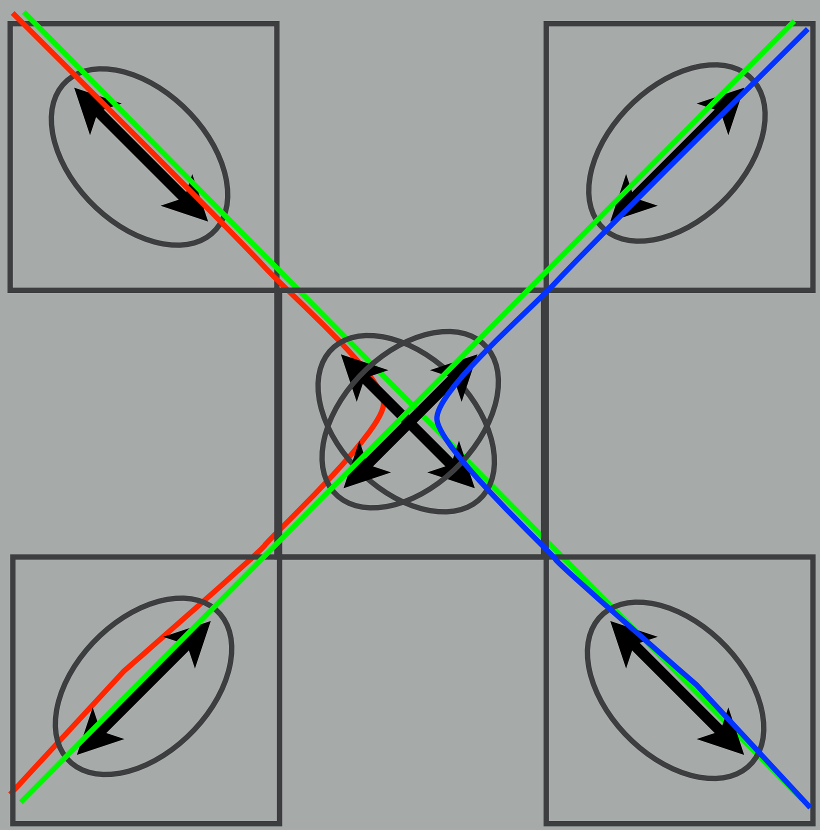
Reducing Tracking ambiguity using higher order tensors



Tracking ambiguity



single fibers



crossing/kissing fibers

The Logical Fallacy of most tractography methods

Algorithm

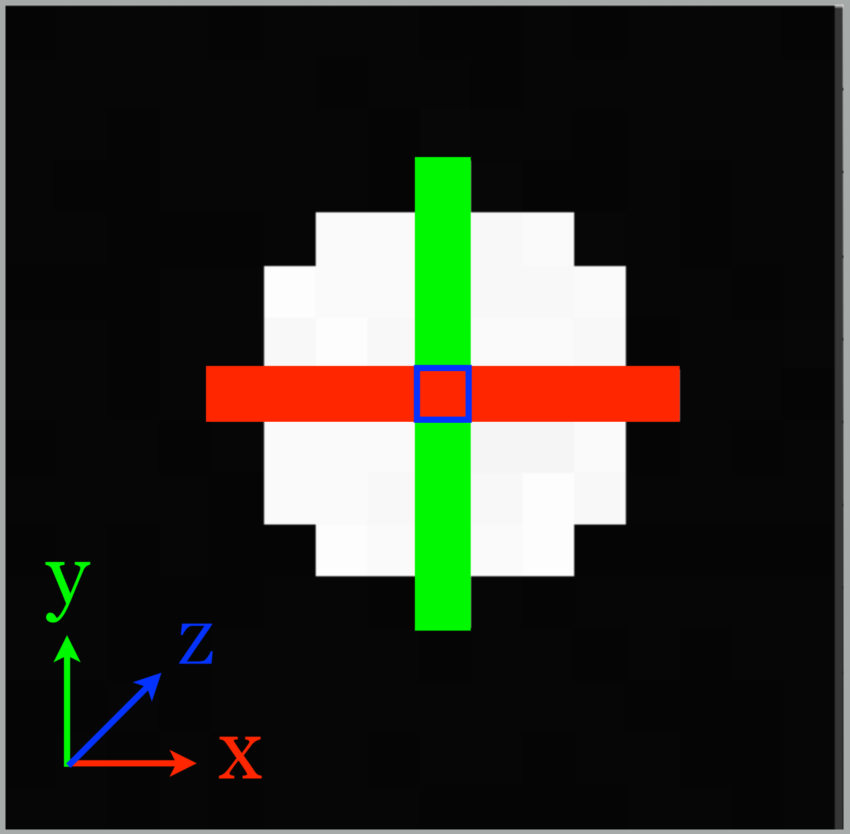
1. Estimate diffusion in each voxel independently
(Assumes voxels are *independent* of one another)

2. Create tracts from these estimates
(Assumes voxels are *dependent* on one another)

Can't both be correct!

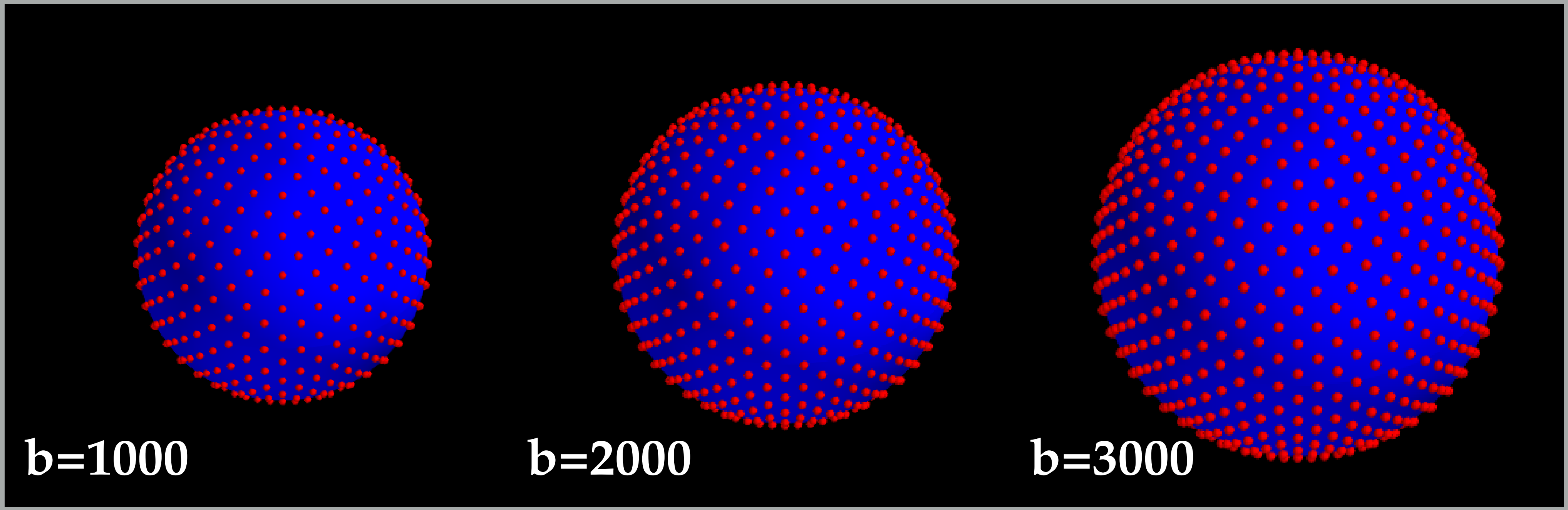
a single field model

Test Phantom



Spherical "head" with three orthogonal fibers (red, green, blue)

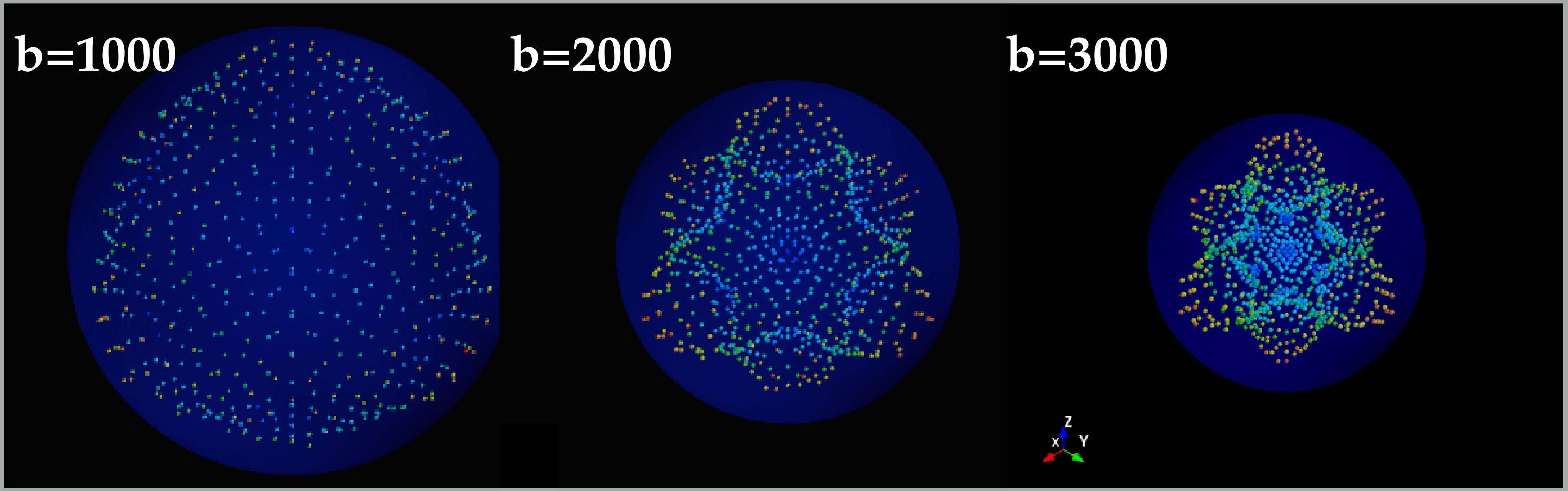
Data sampling



3 shells with Healpix

n=(588,768,972)

Signal at the center voxel



Actual data is combined signal from all three shells

DWI Signal in single voxel

$$W(\boldsymbol{r}, \boldsymbol{q}) = \int Q(\boldsymbol{r}, \boldsymbol{R}) e^{-i\boldsymbol{q}\cdot\boldsymbol{R}} d\boldsymbol{R}$$

$$Q(\boldsymbol{r}, \boldsymbol{R}) = \boxed{\rho(\boldsymbol{r})}\boxed{p_{\Delta}(\boldsymbol{r}, \boldsymbol{R})}$$

spin density

average propagator

$$\boldsymbol{R} = \boldsymbol{r}(t_0 + t) - \boldsymbol{r}(t_0)$$

$$\boldsymbol{q} = \gamma \boldsymbol{G} \delta / 2\pi$$

$$\boldsymbol{R} = R\hat{\boldsymbol{R}} \quad \text{where } R = \|\boldsymbol{R}\|$$

$$\boldsymbol{q} = q\hat{\boldsymbol{q}} \quad \text{where } q = \|\boldsymbol{q}\|$$

Signal in single voxel

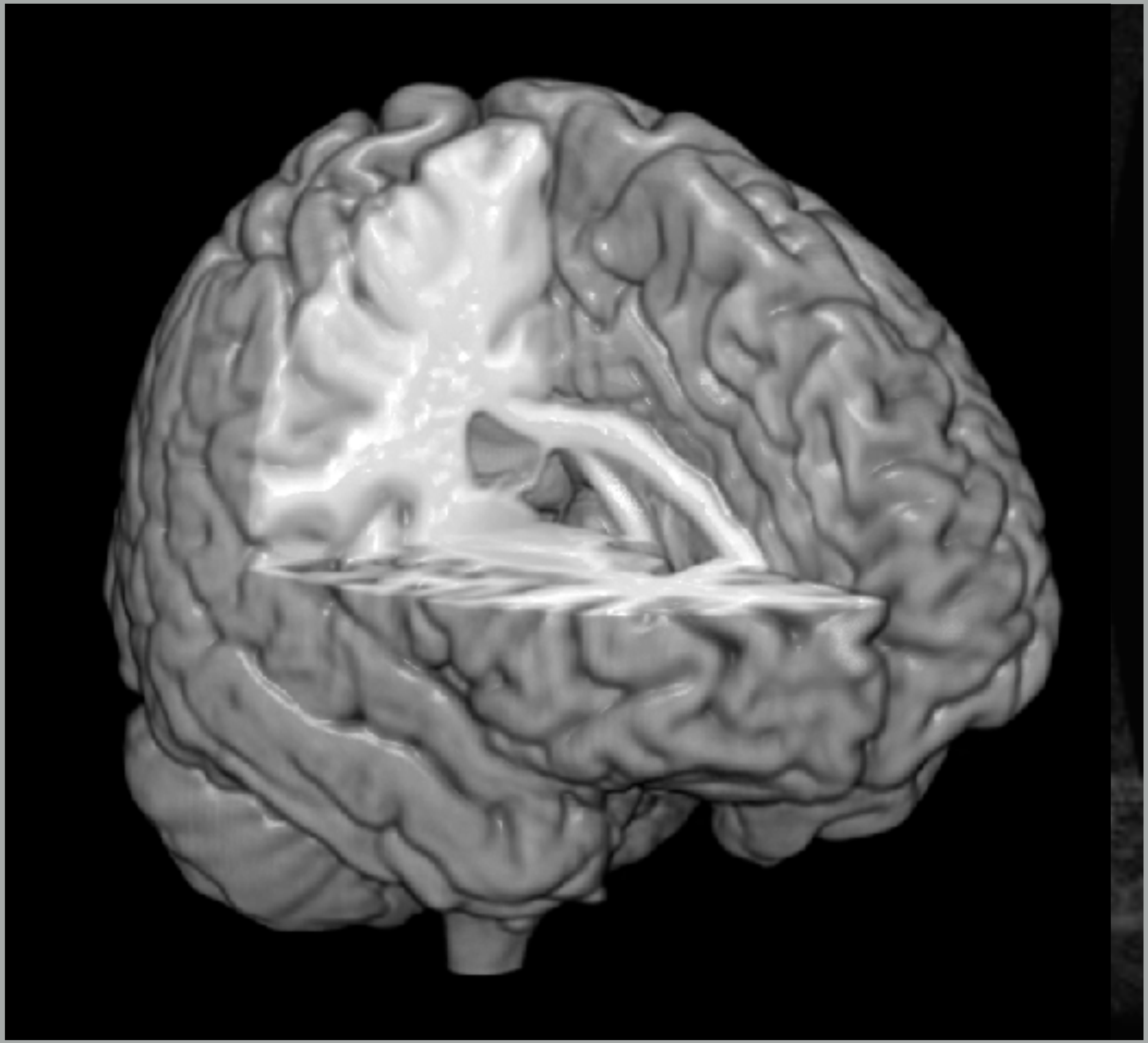
$$Q(\boldsymbol{r}, \boldsymbol{R}) = 4\pi \sum_{l=0}^{\infty} \sum_{m=-l}^{l} i^l Y_l^m(\hat{\boldsymbol{R}}) s_{lm}(\boldsymbol{r}, R),$$

$$s_{lm}(\boldsymbol{r}, R) = \int W(\boldsymbol{r}, \boldsymbol{q}) j_l(qR) Y_l^{m*}(\hat{\boldsymbol{q}}) d\boldsymbol{q}.$$

where $$Y_l^m(\hat{\boldsymbol{q}}) = Y_l^m(\Omega_{\hat{\boldsymbol{q}}}) = Y_l^m(\theta_q, \phi_q)$$

Spherical wave decomposition (SWD)

Automated Shape characterization of Volumetric Data



Galinsky and Frank, *NeuroImage* 2014

How do we incorporate microscopic phenomena and models into macroscopic prediction?

The Logical Inconsistency of DTI Tractography

Step 1: Estimate diffusion profile in each voxel

Implicit assumption

Voxels are all independent of one another

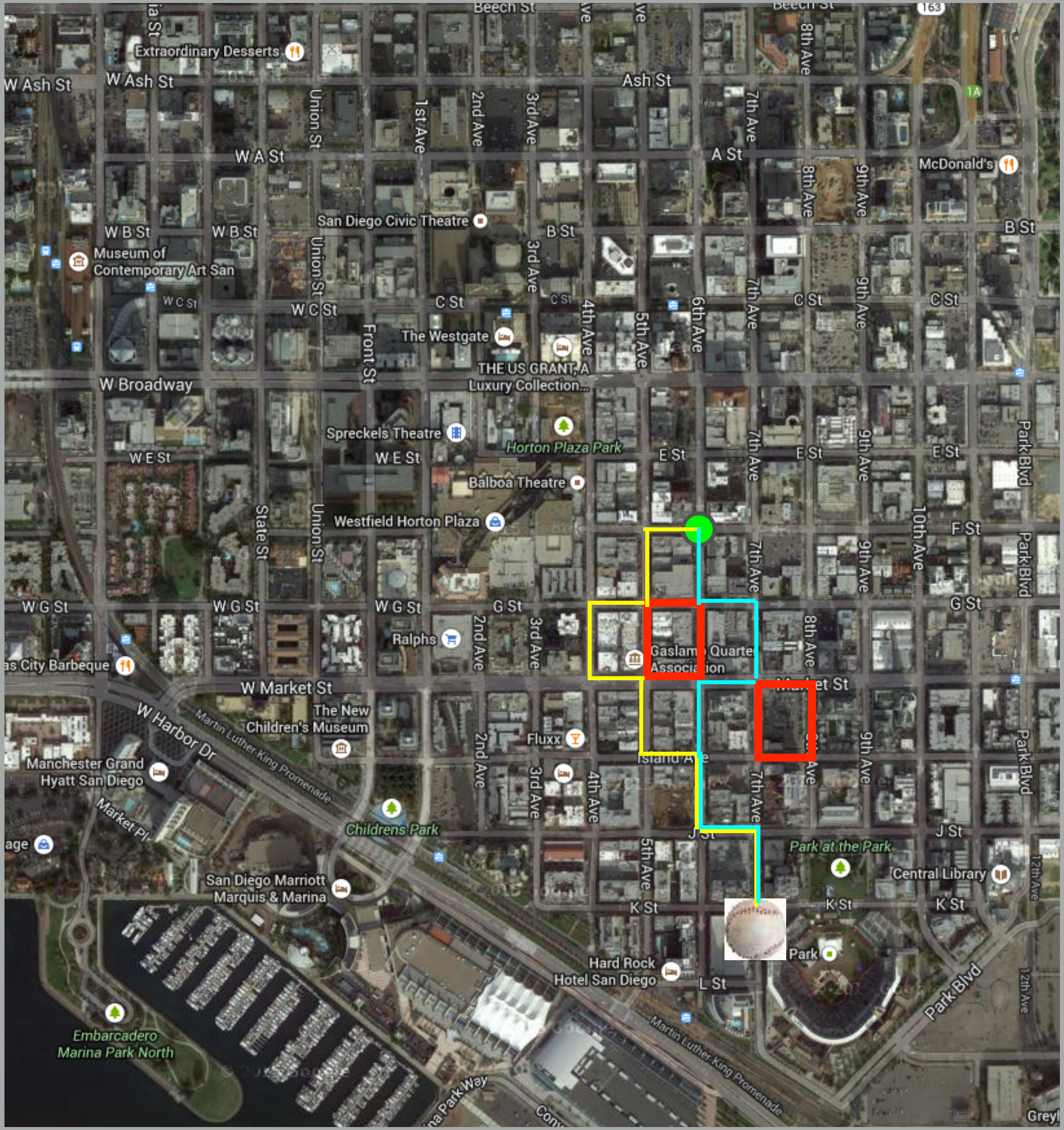
Step 2: Construct tract by connecting neighboring voxels

Implicit assumption

Voxels are dependent on one another

These can't both be true!

Incorporating local (voxel) and global (Tracts) information



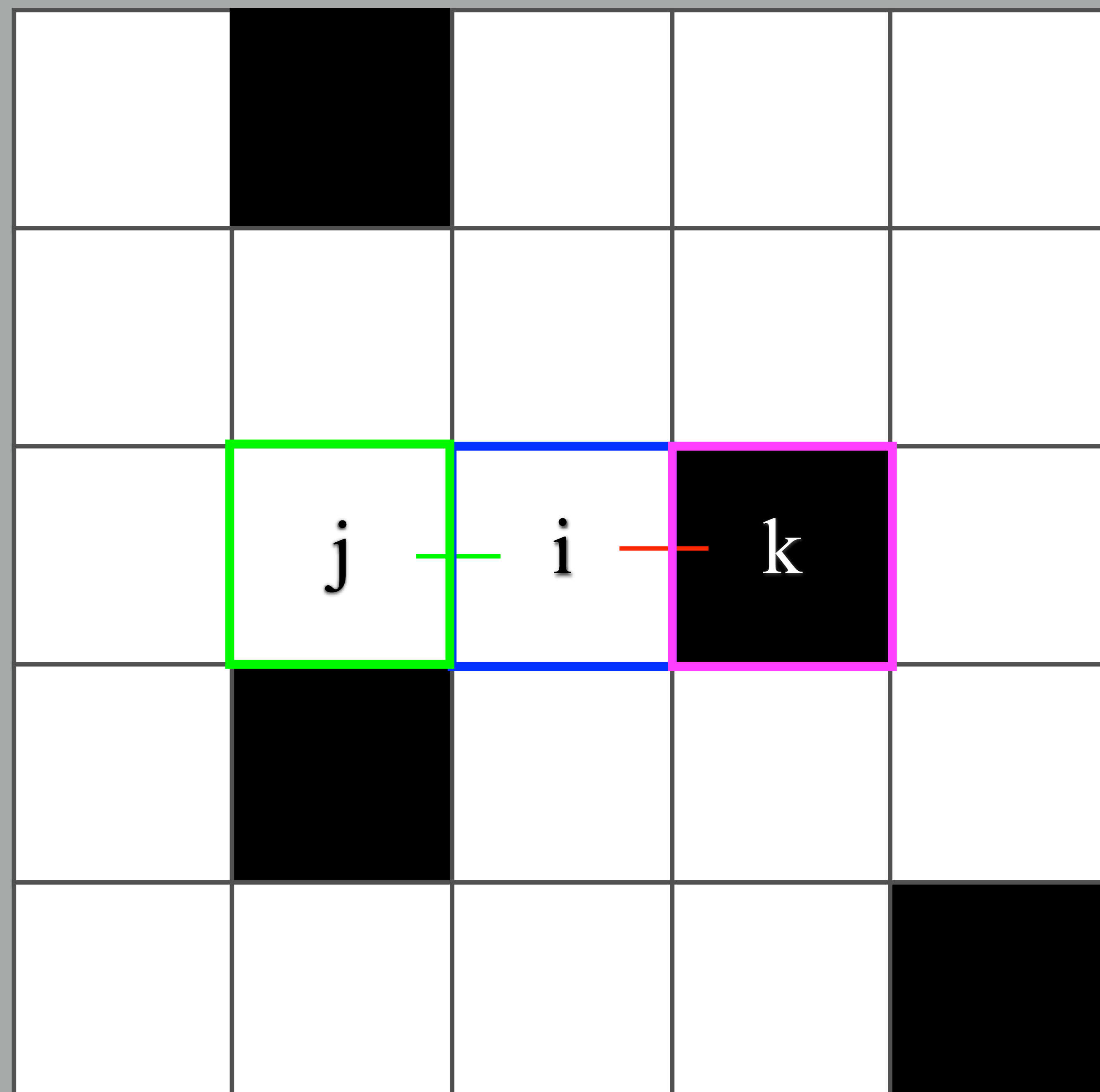
Entropy Spectrum Pathways (ESP)

Frank & Galinsky, *Phys Rev E* (2014)

Entropy Spectrum Pathways (ESP)

Q_{ij} is an element of the *coupling matrix* Q that describes the interaction of points x_i and x_j

$Q_{ij} = 1$



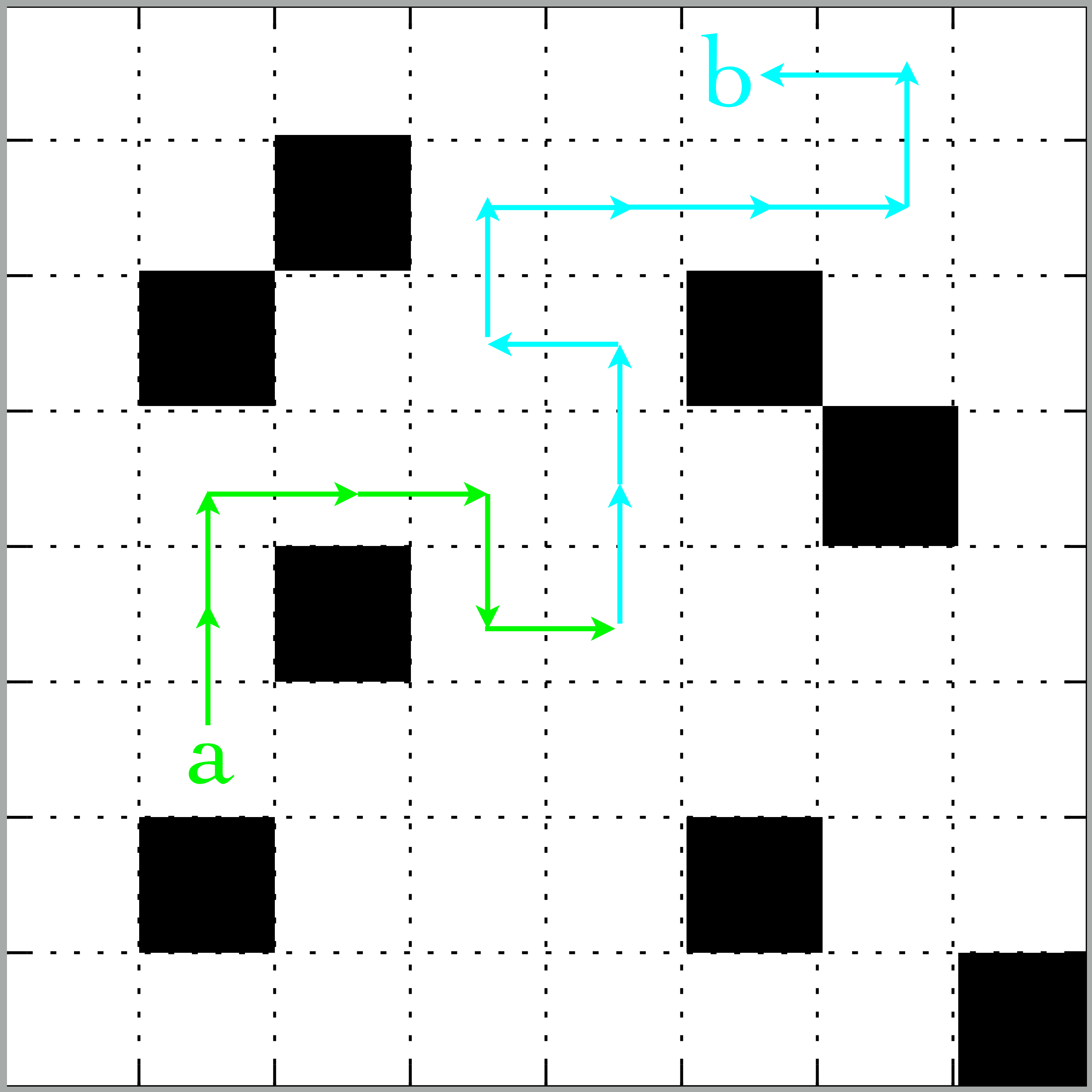
$Q_{ik} = 0$

Eigenvectors $\phi^{(l)}$ of Q tell us the most accessible regions of the parameter space

= inaccessible

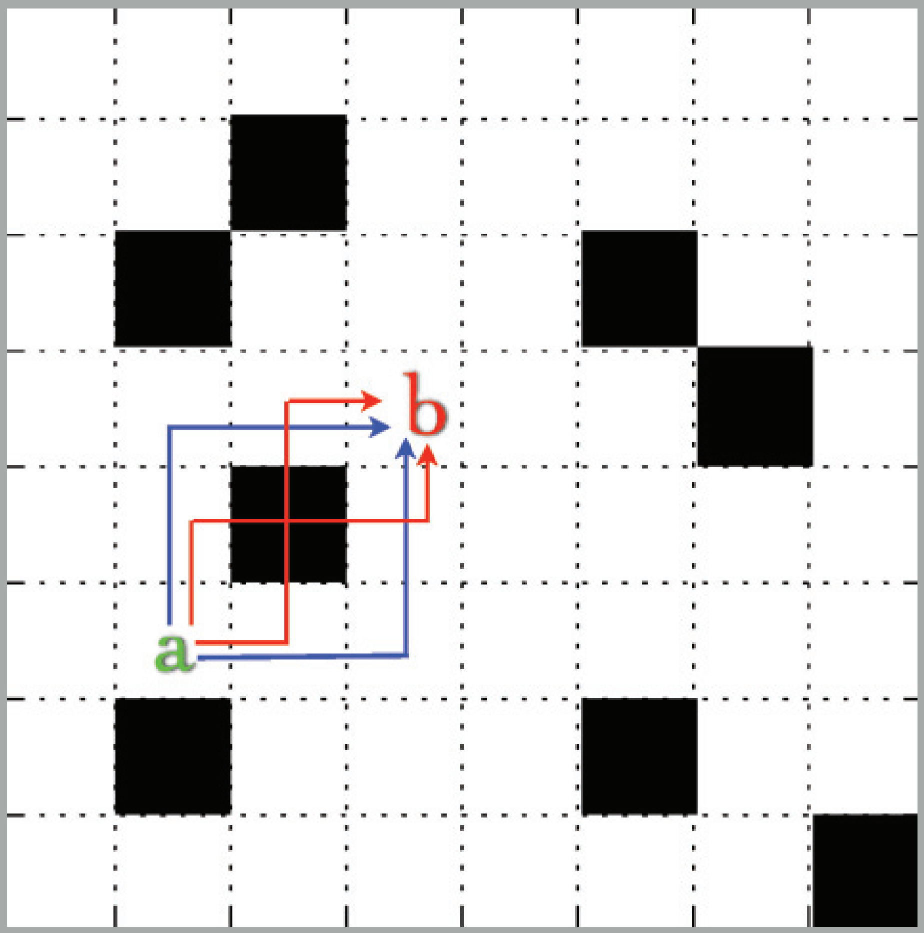
= accessible

Prior Information: Entropy Spectrum Pathways (ESP)

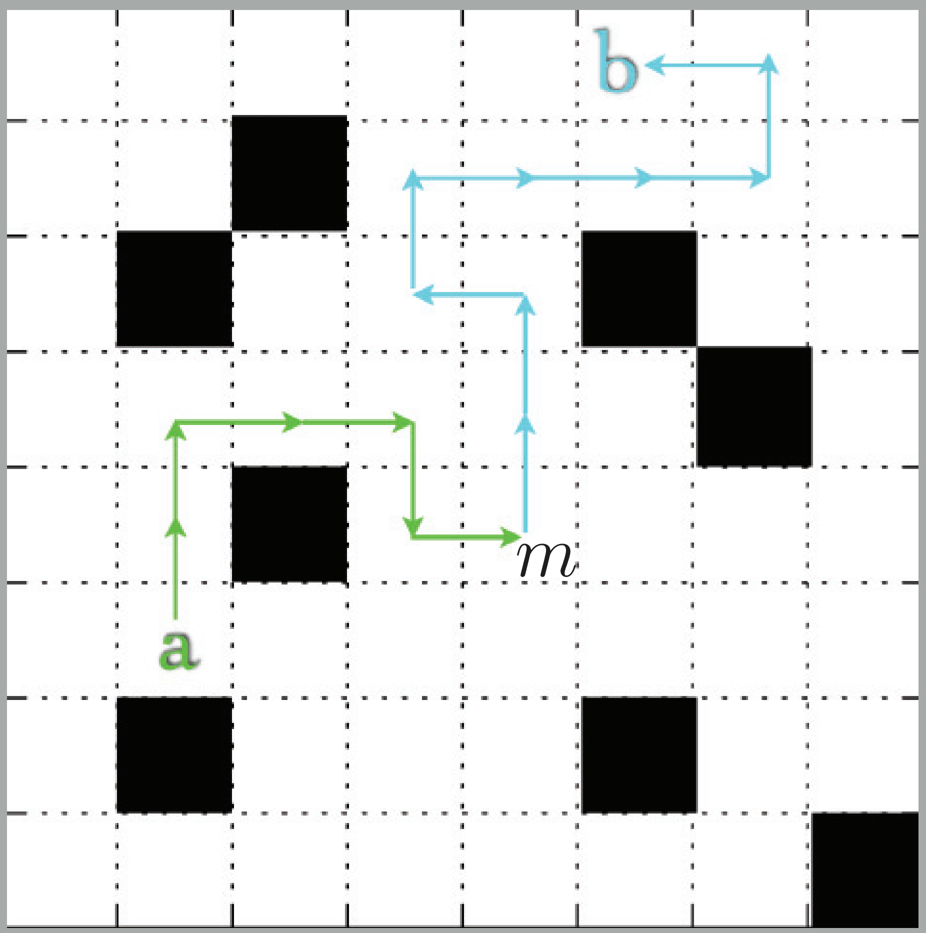


So How do we better incorporate prior information?

Entropy Spectrum Pathways (ESP)



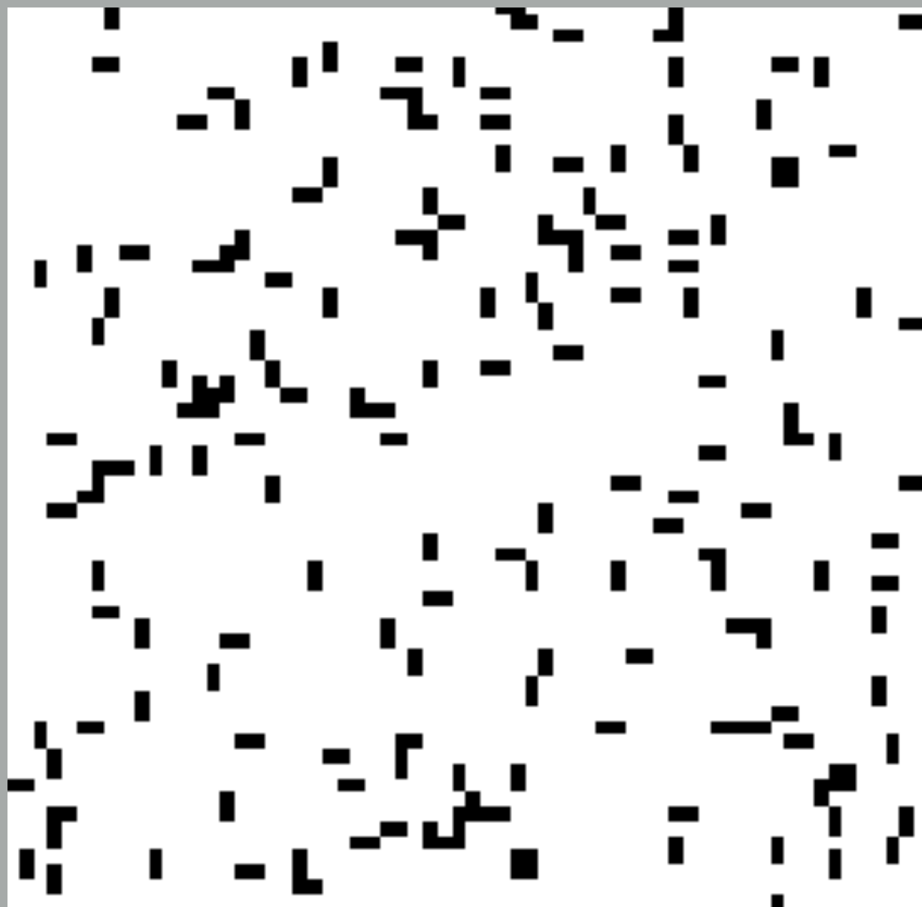
(a)



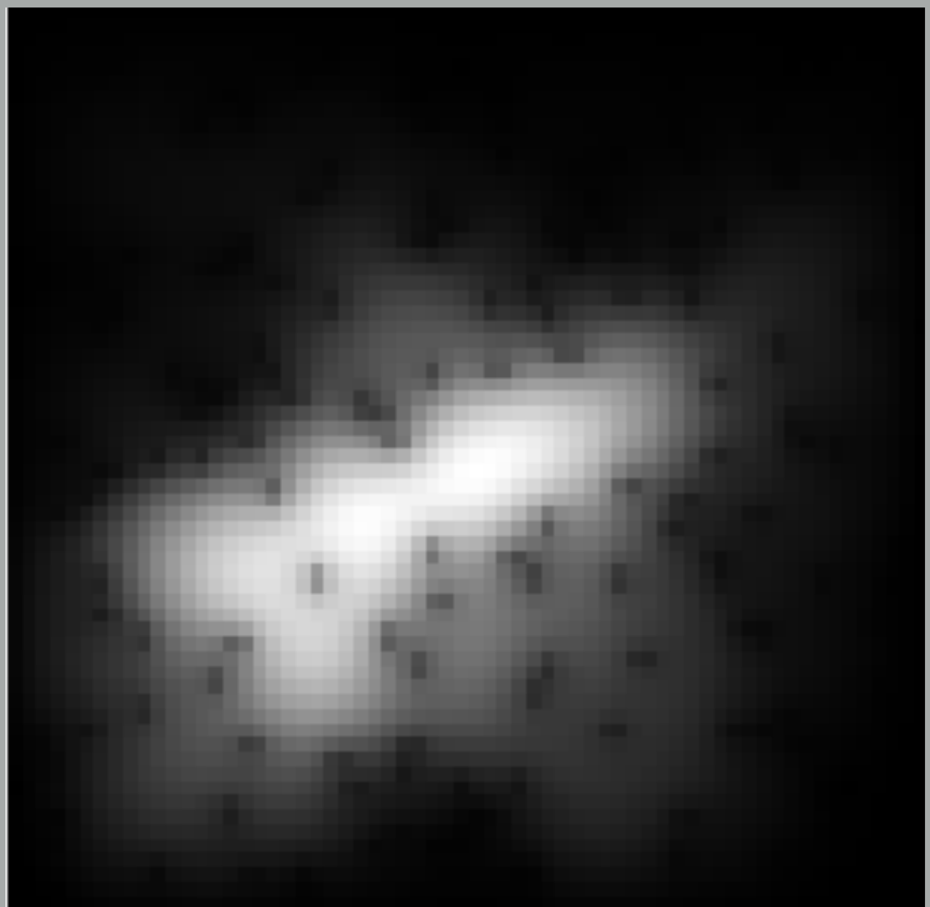
(b)

Frank & Galinsky,
Information pathways in a disordered lattice.
Phys Rev E, 89, 032142 (2014)

Local coupling informs global structure!



binary lattice with adjacency matrix **A**

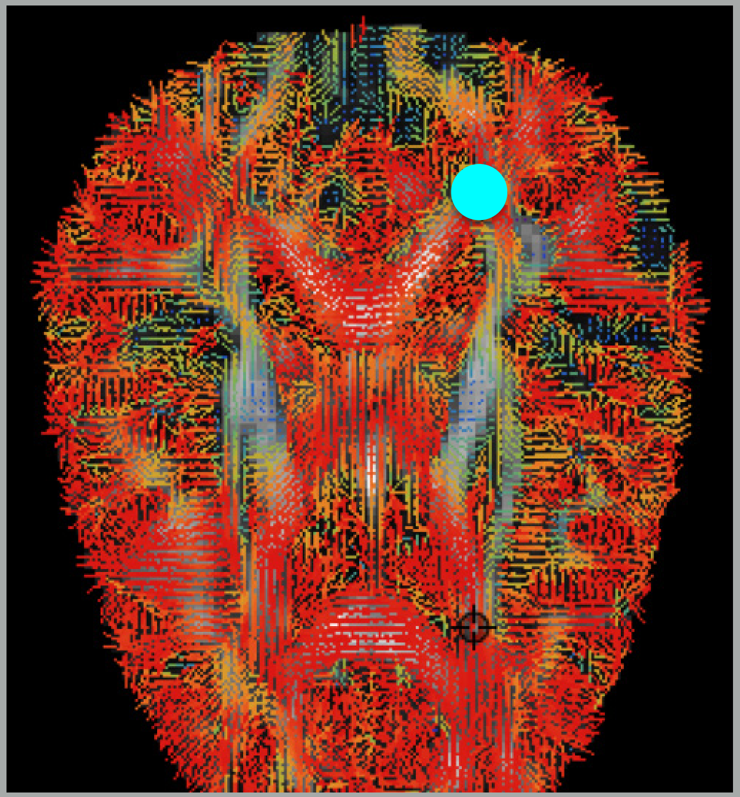


Equilibrium Probability (EP) ~(principal eigenvector of **A**)^2

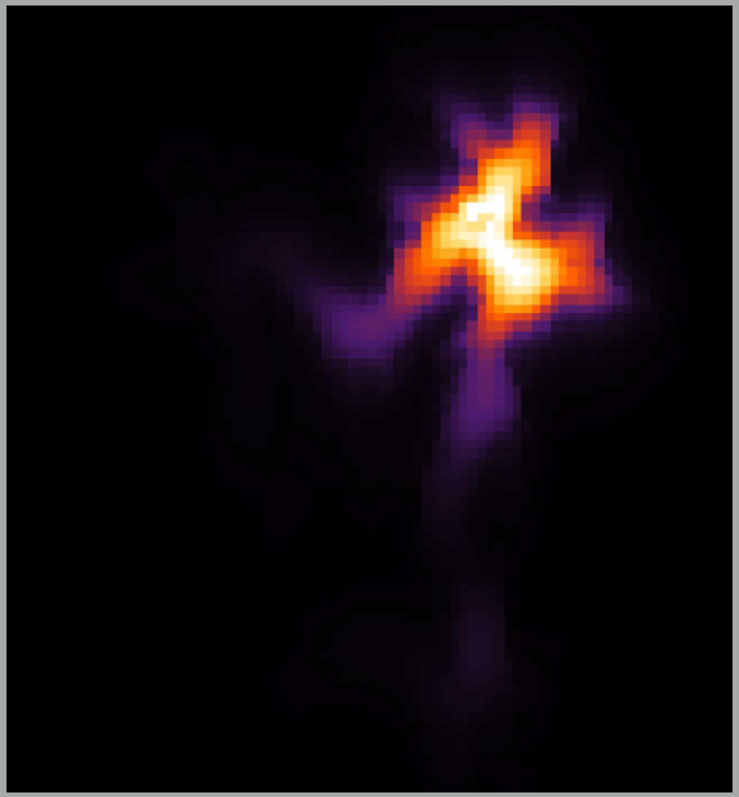
= inaccessible   = accessible

In ESP theory, **A** is *any* coupling matrix, and there are a spectrum of pathways ranked by their path entropy.

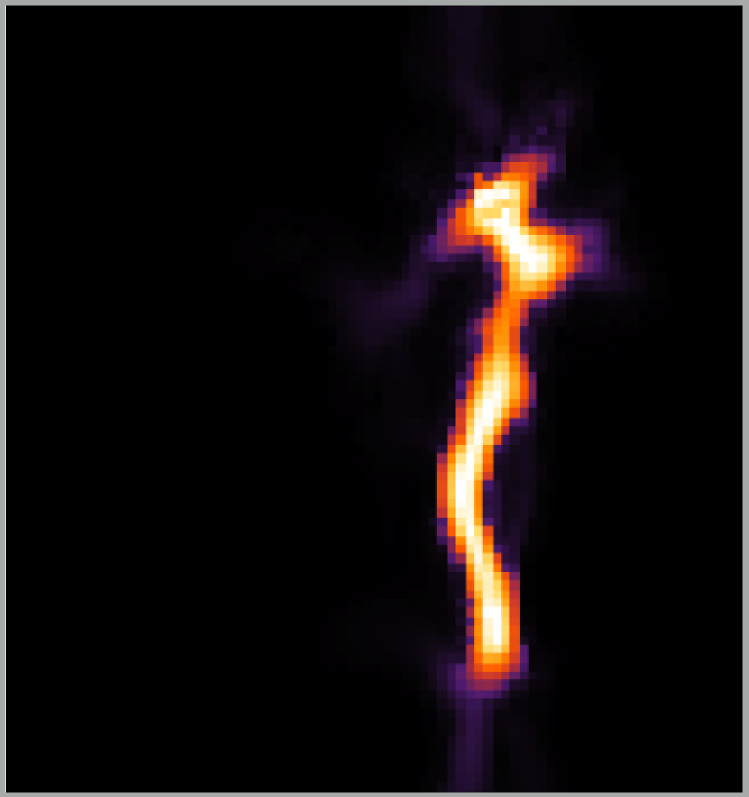
Dynamics - microscopic to macroscopic



DTI data



Random Walk

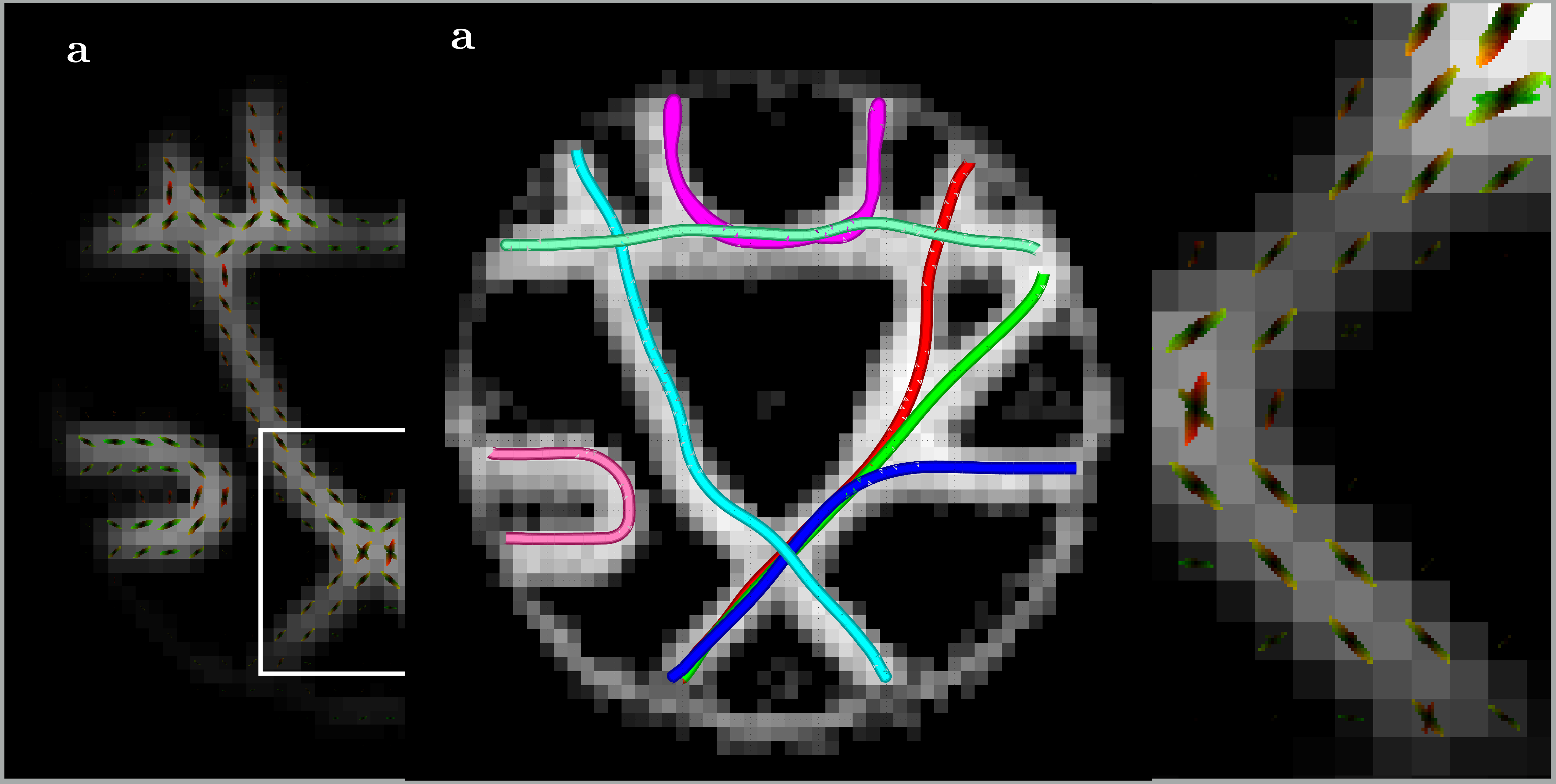


ESP

Local diffusion generates global paths
through nearest neighbor coupling

GO-ESP

Geometric Optics diffusion estimation and tractography using ESP



"Fiber Cup"

Galinsky & Frank *IEEE Trans Med. Imag.* 2015

Test datasets

1. Human Connectome Project MGH 1010 Single Subject
   - 140x140x96 with 1.5x1.5x1.5 voxel
   - 4 shells, b-values of b=(1000,2000,3000,4000,5000)
   - 64x64x128x256 q-vectors

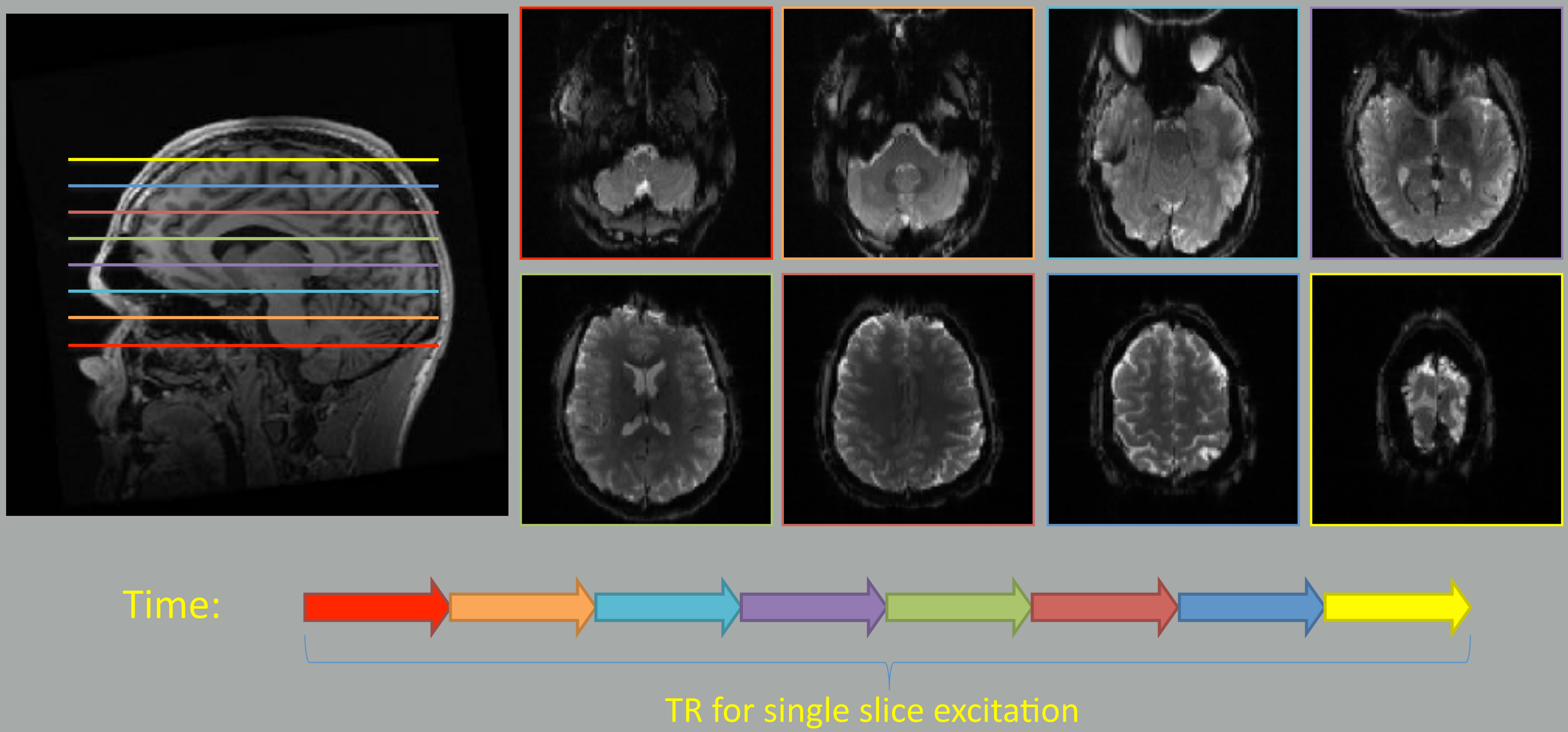
2. BCAIPI Single Subject UCSD CFMRI protocol
   - 100x100x62 with 2.2x2.2x2.2 voxel
   - 3 shells, b-values of b=(1000,2000,3000)
   - 30x45x60 q-vectors

Each scan is done twice, (TOPUP, TOPDOWN)

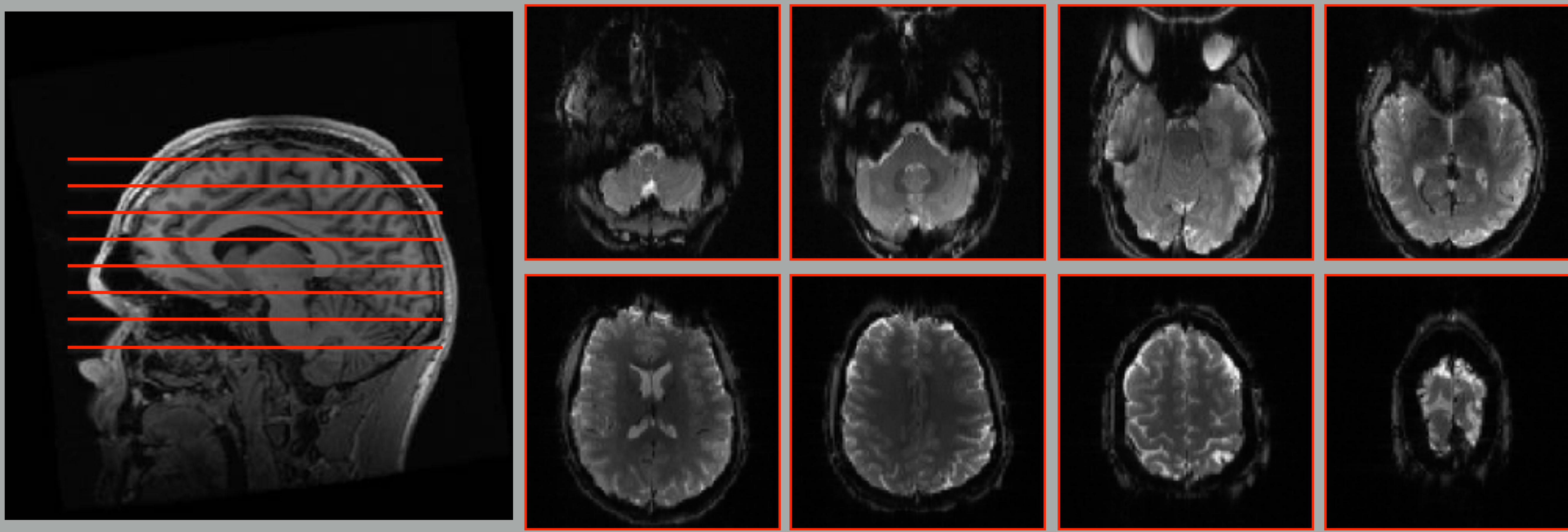
“Multi-shell” - just a simple and efficient method for sampling some of q-space

diffusion sensitivity space

Why Multiband?

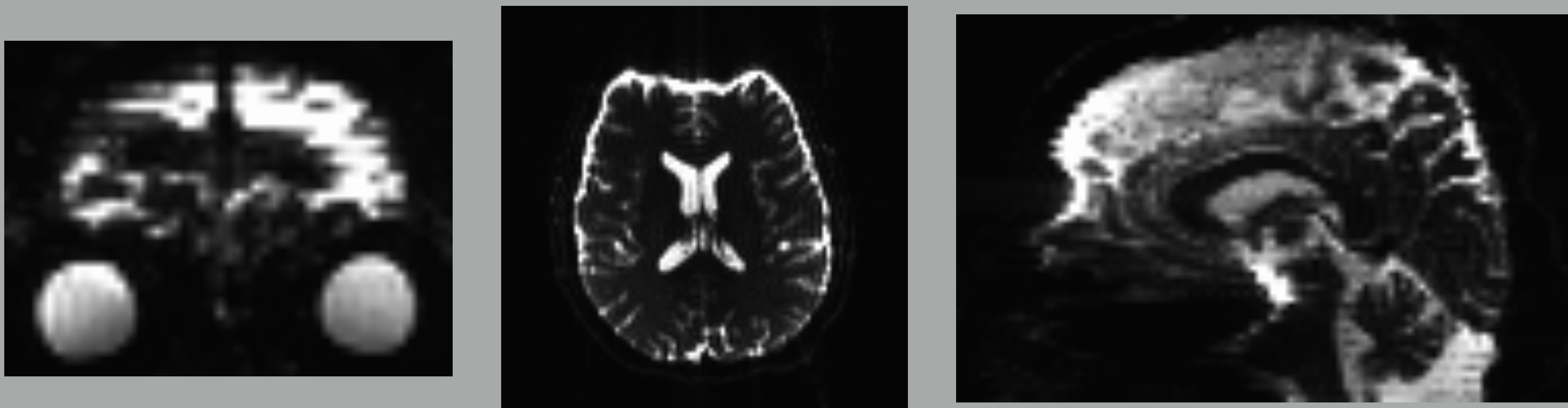


Why Multiband?

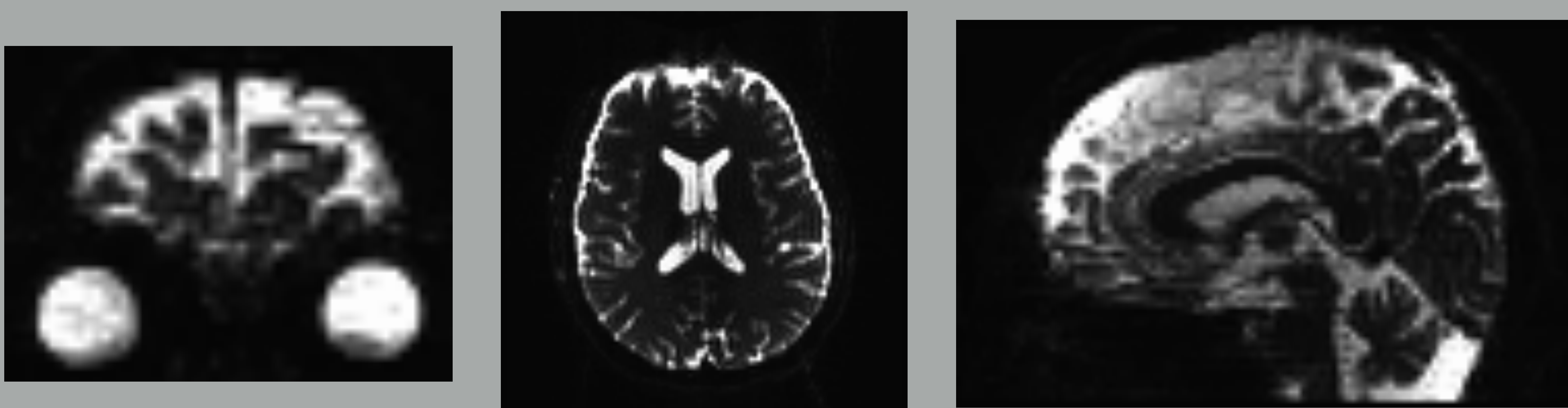


UCSD CFMRI
Distortion Correction (TOPUP)

Andersson, Skare, Ashburner, *NeuroImage* 20 (2003) 870

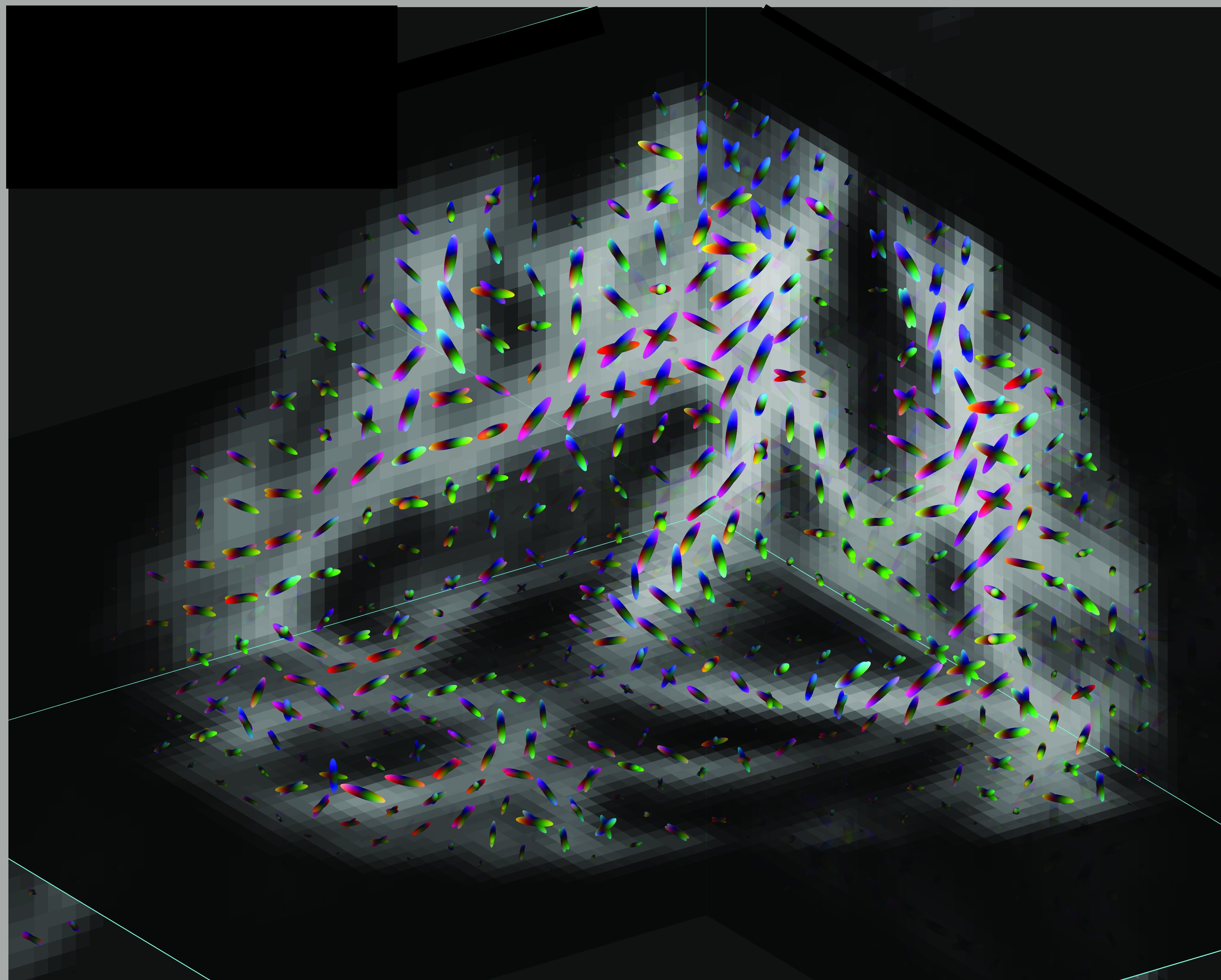


Original data (forward PE grad direction)



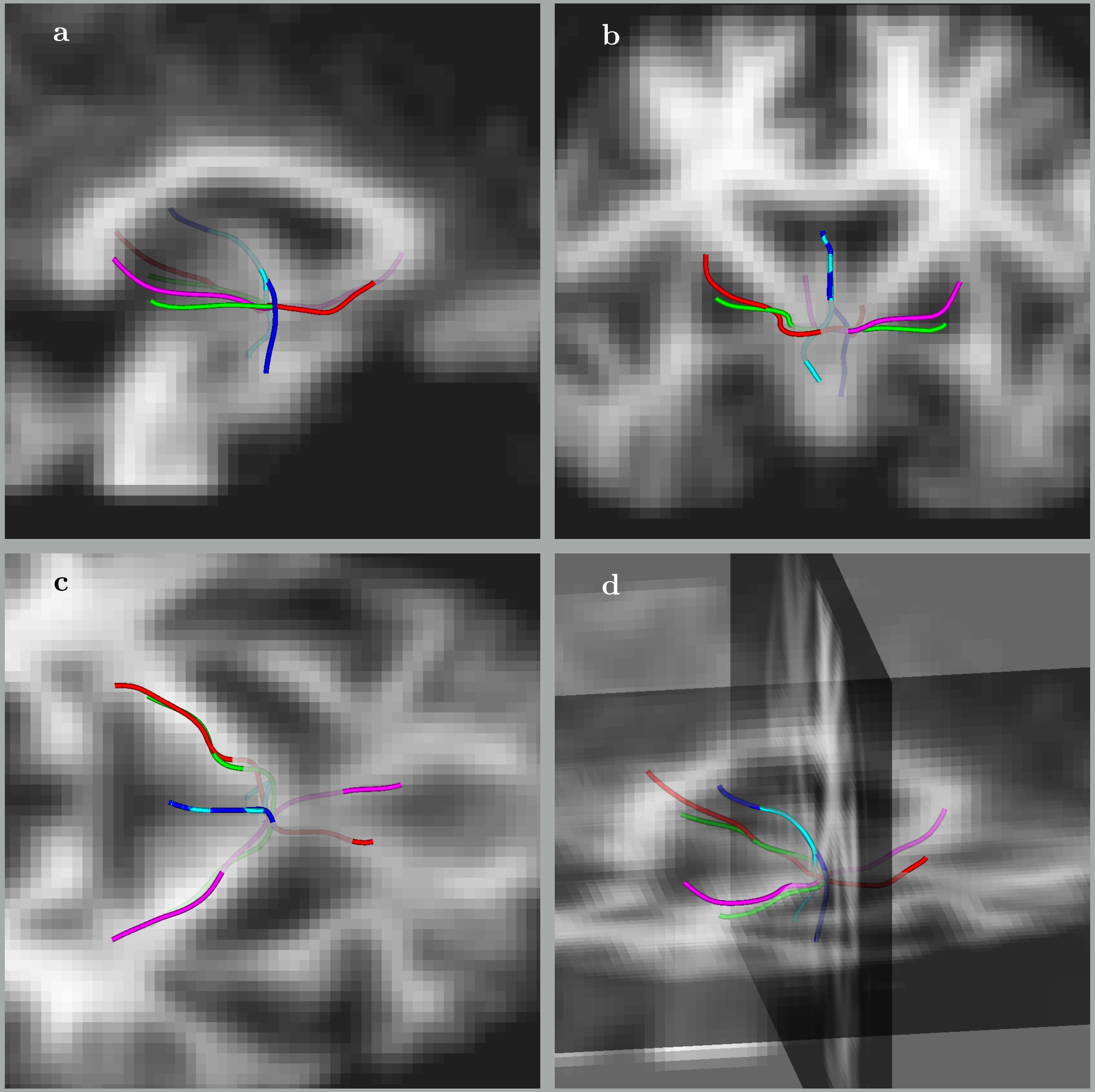
FSL TOPUP and eddy current corrected

GO-ESP



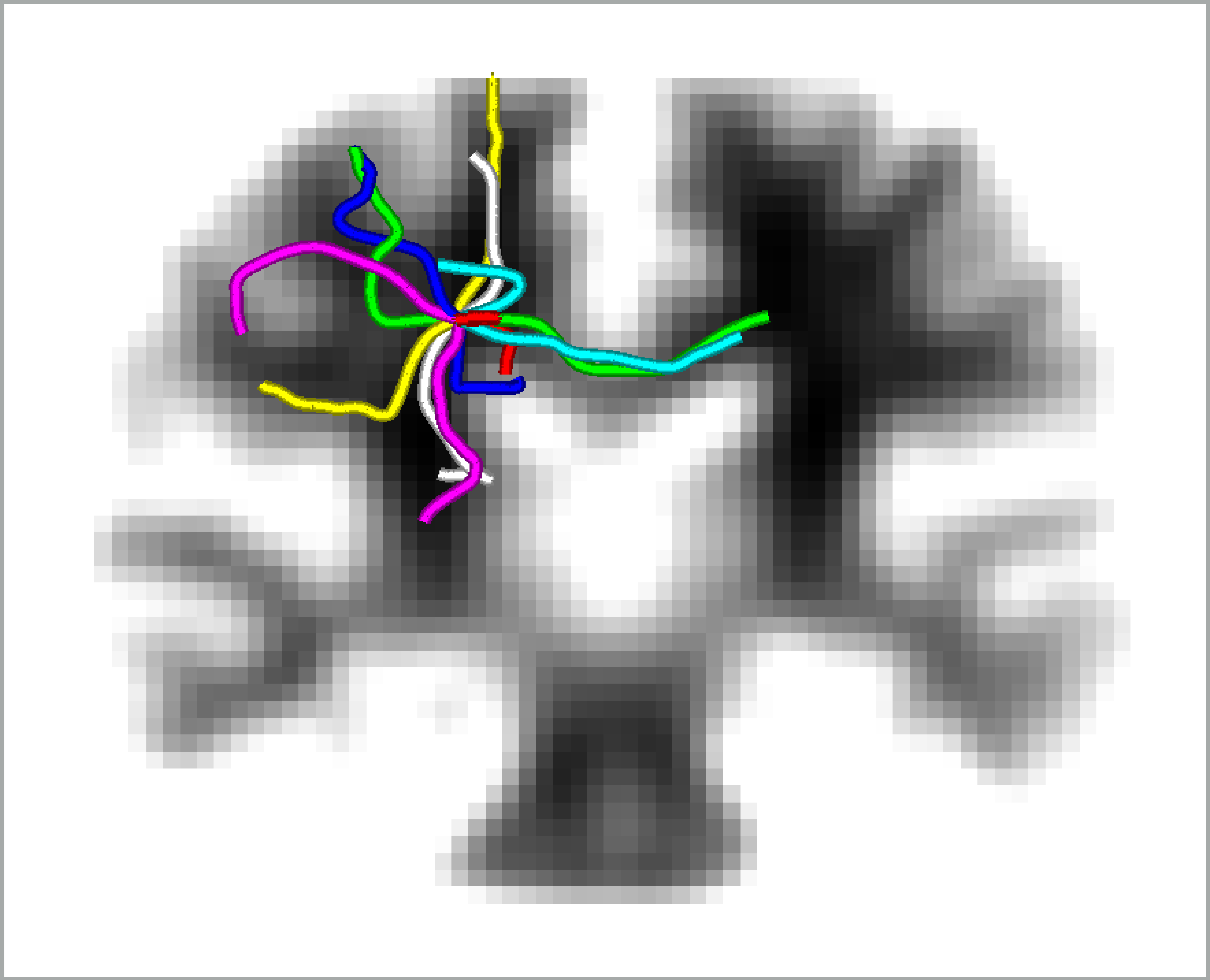
Transition probabilities NOT pdf's

GO-ESP



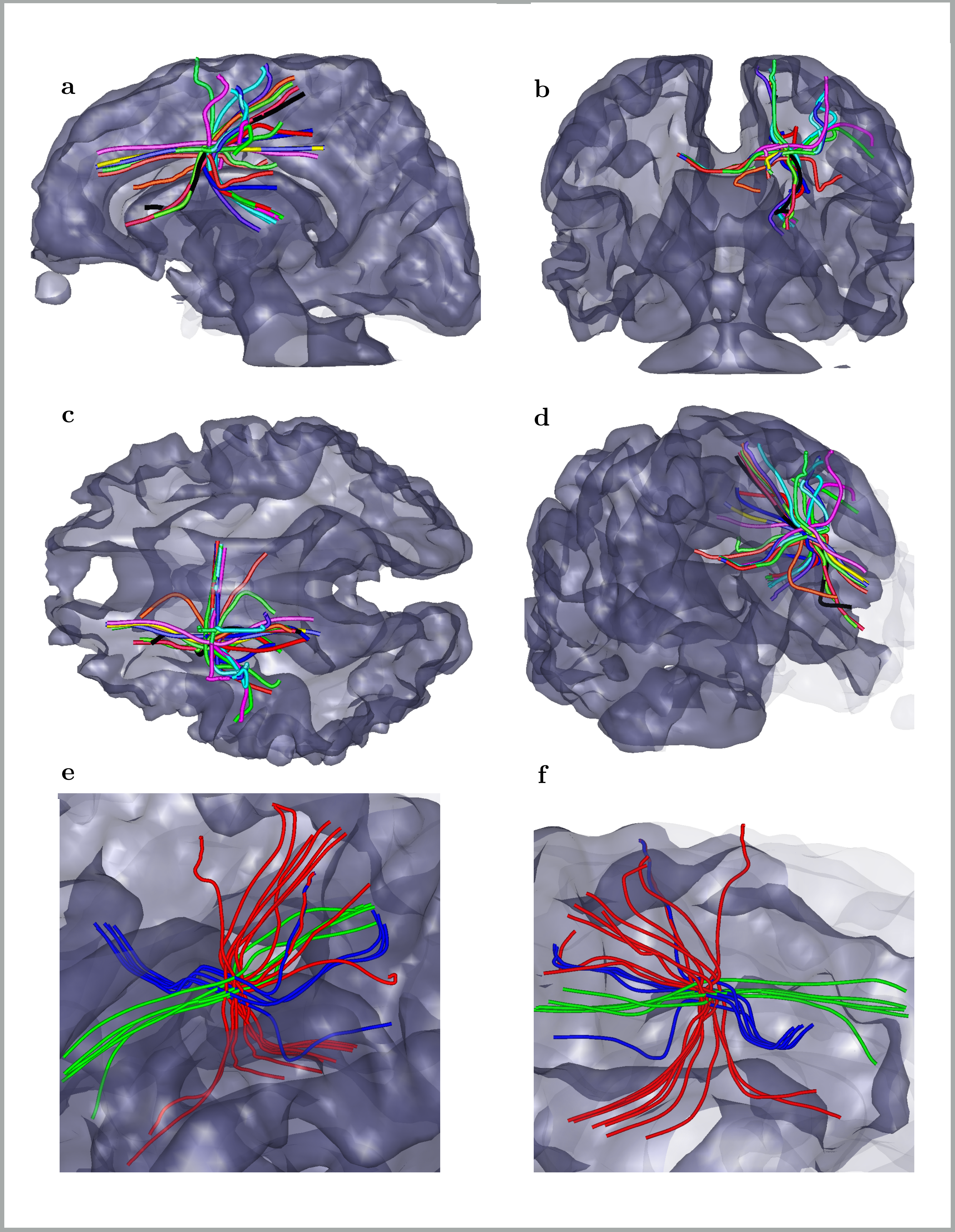
Five fiber tracts: different fiber orientations at different scales.

GO-ESP

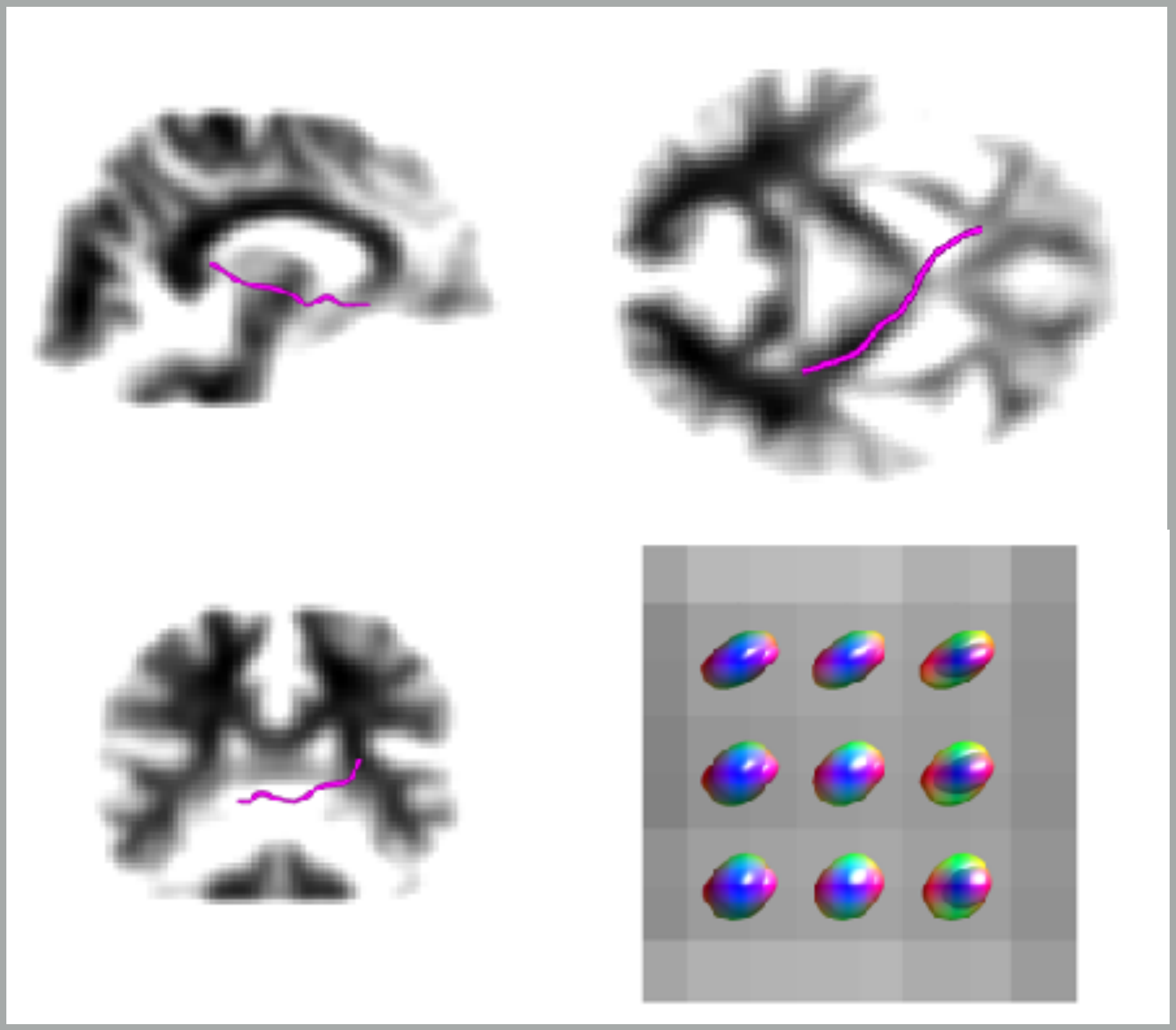


Seven tracts corticospinal tract crossing corpus callosum.

GO-ESP

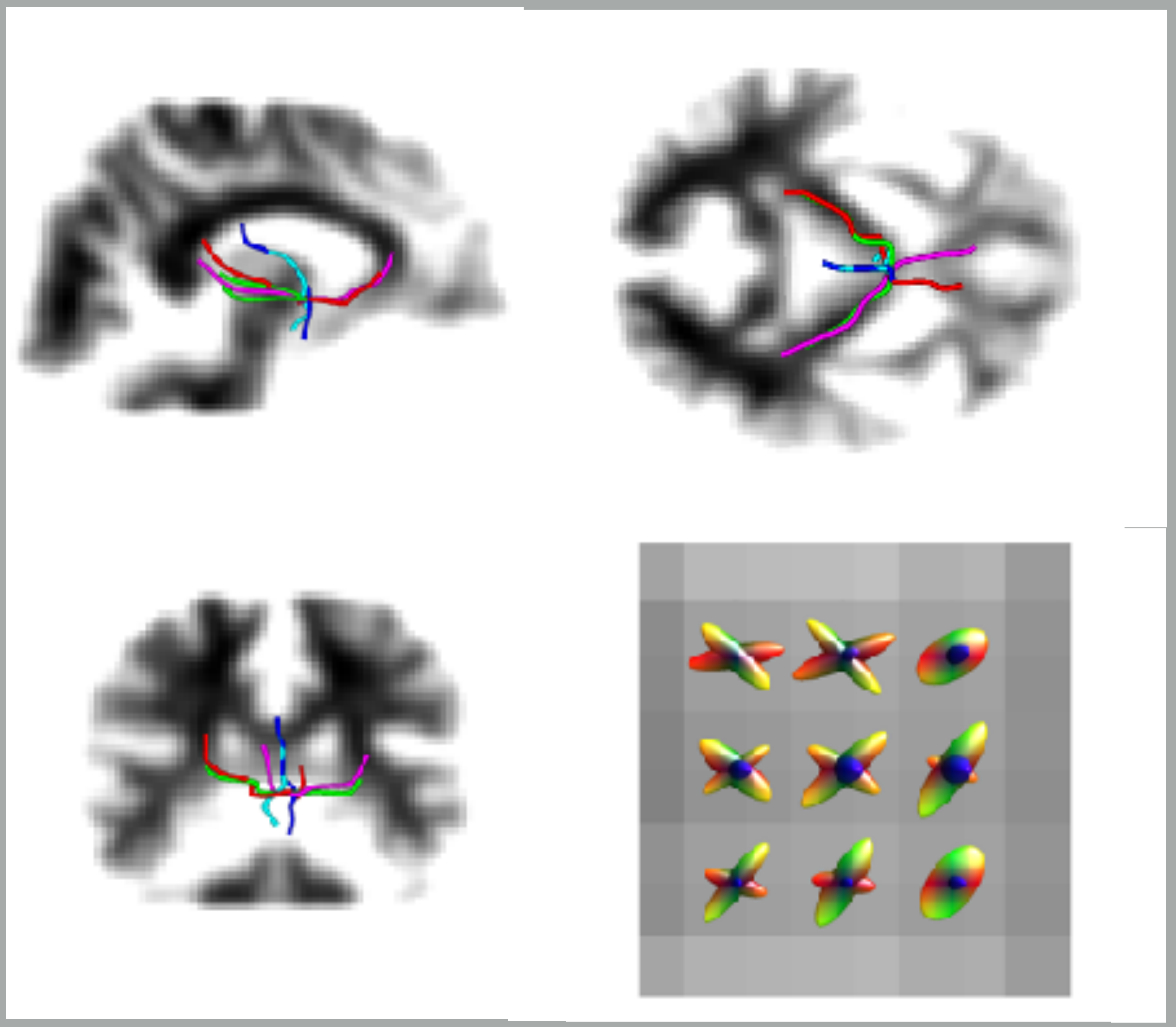


ESP vs Standard PDF methods



RSI

Produces incorrect reconstruction at multiple fibers crossing



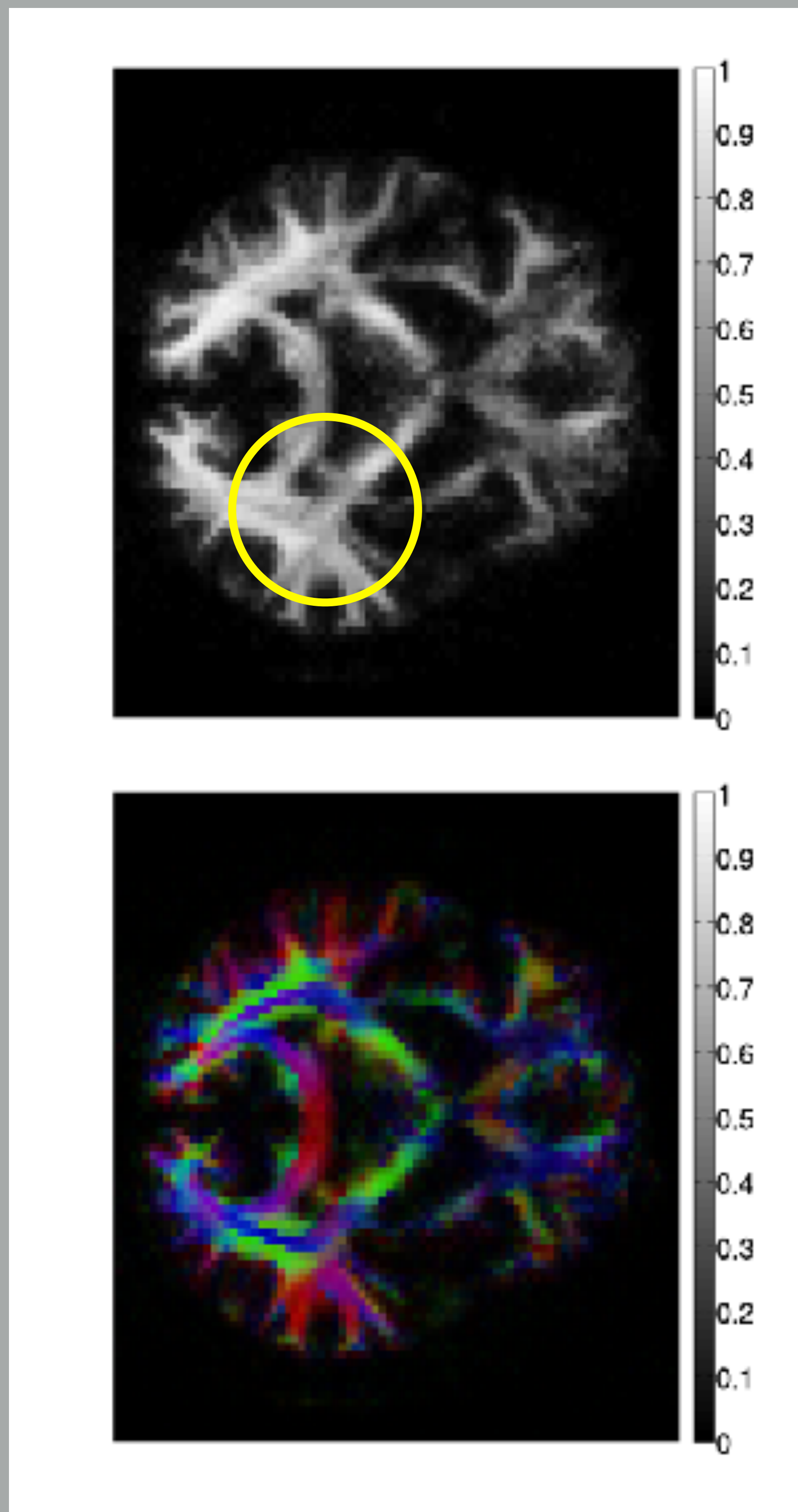
ESP

Correctly reconstructs fibers at multiple fibers crossing

GO-ESP vs RSI

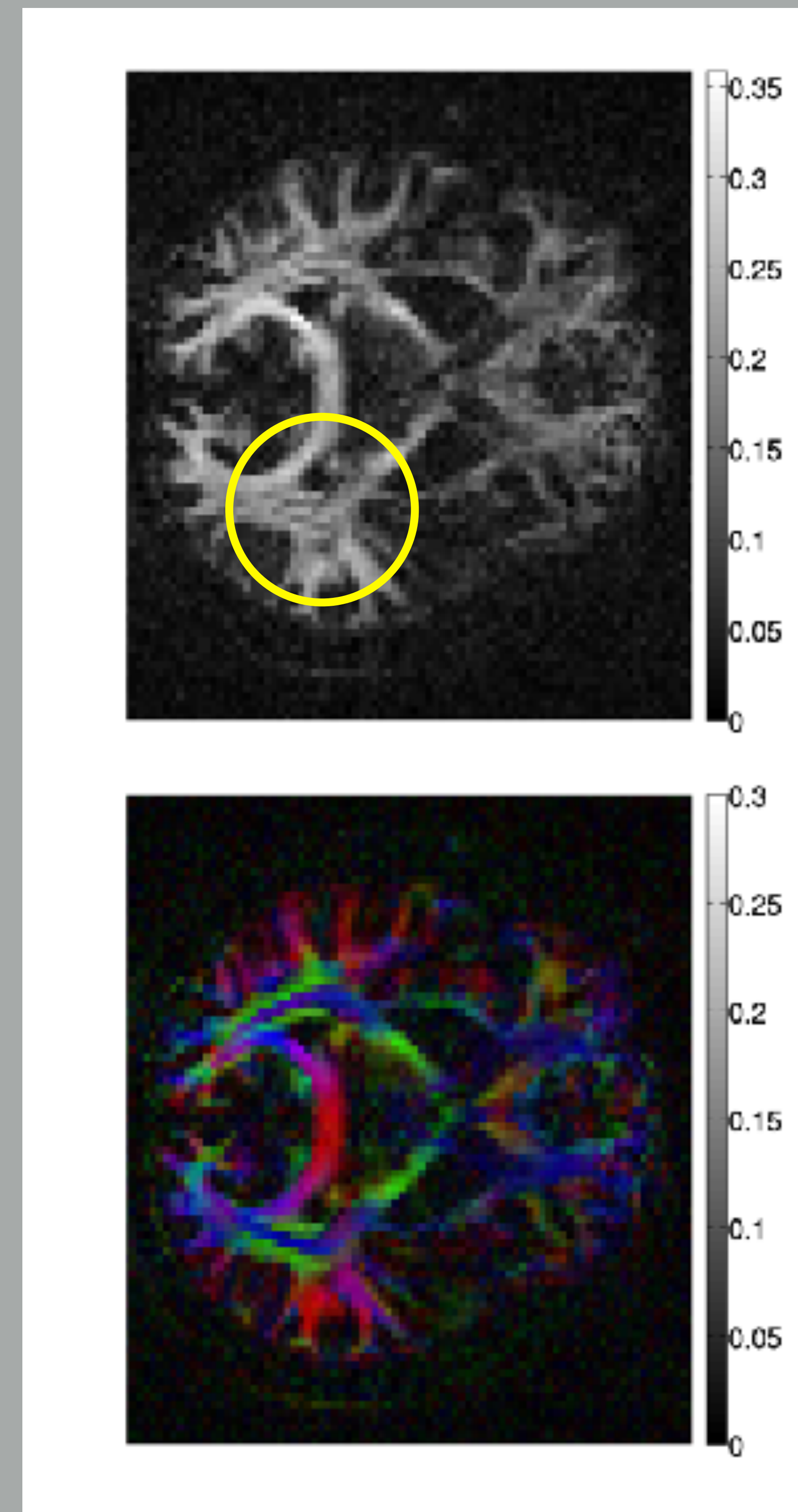
(rescaled RSI color scale)

(scaled RSI color scale)



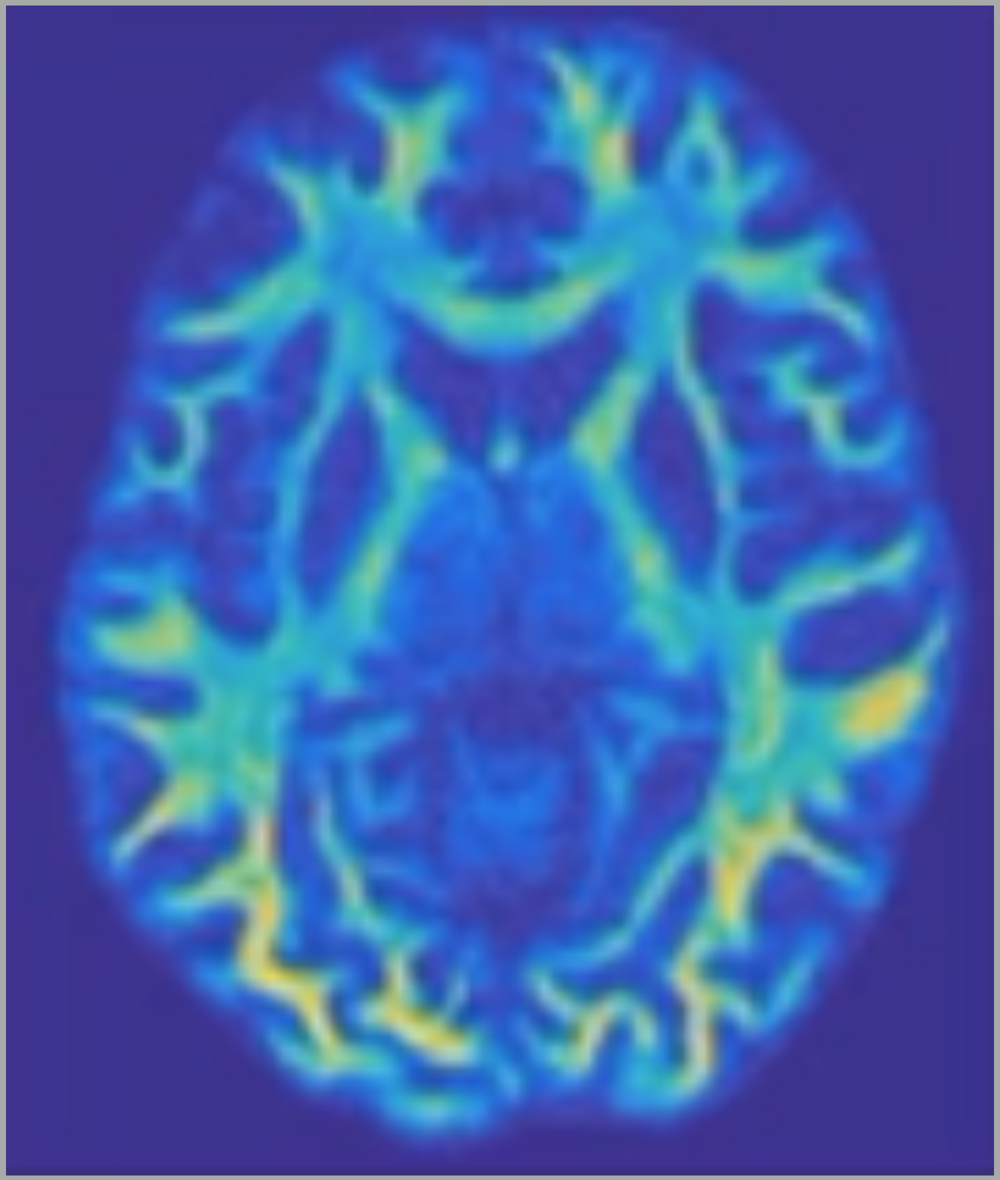
DWI-ESP

FA

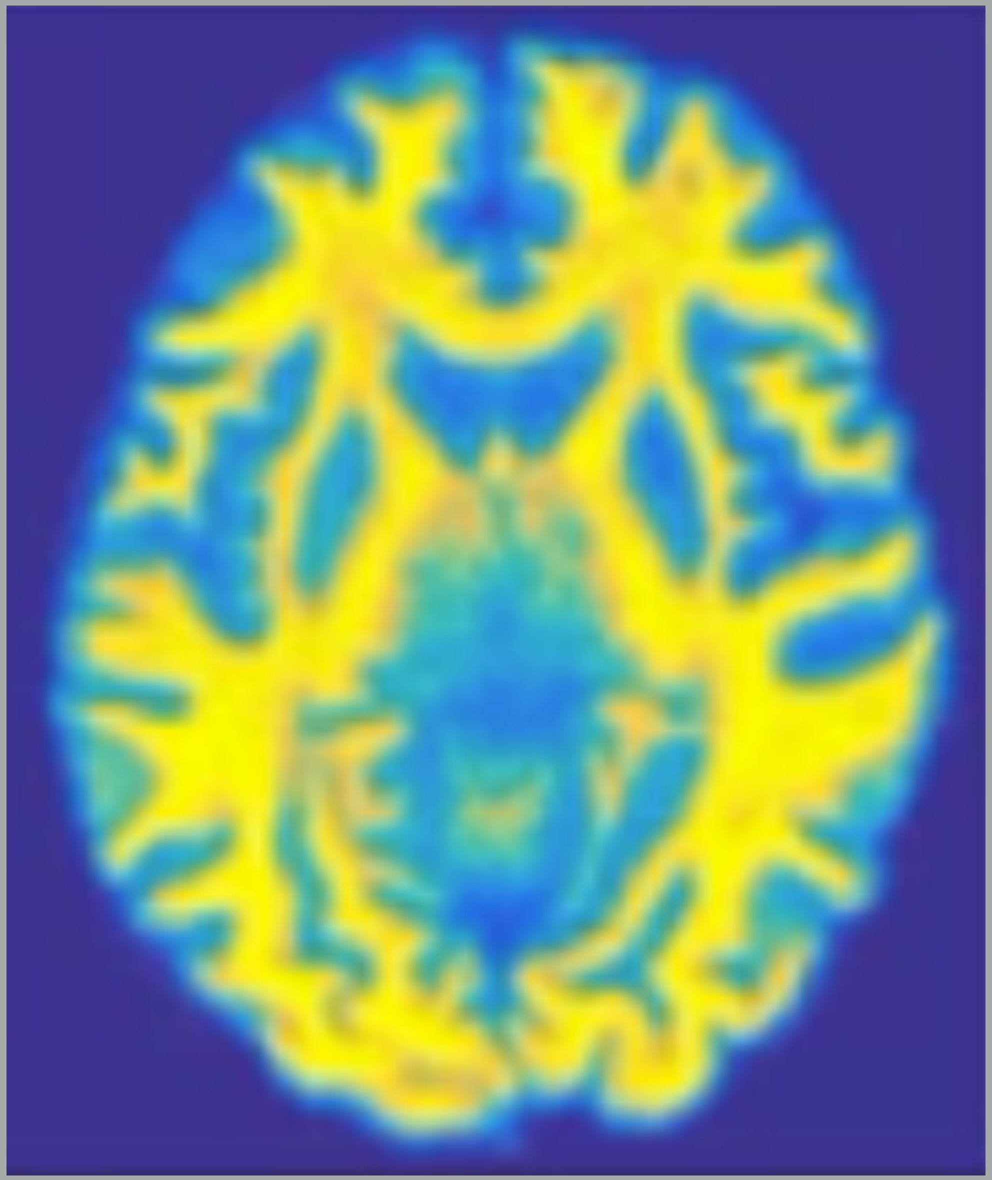


RSI

Anisotropy

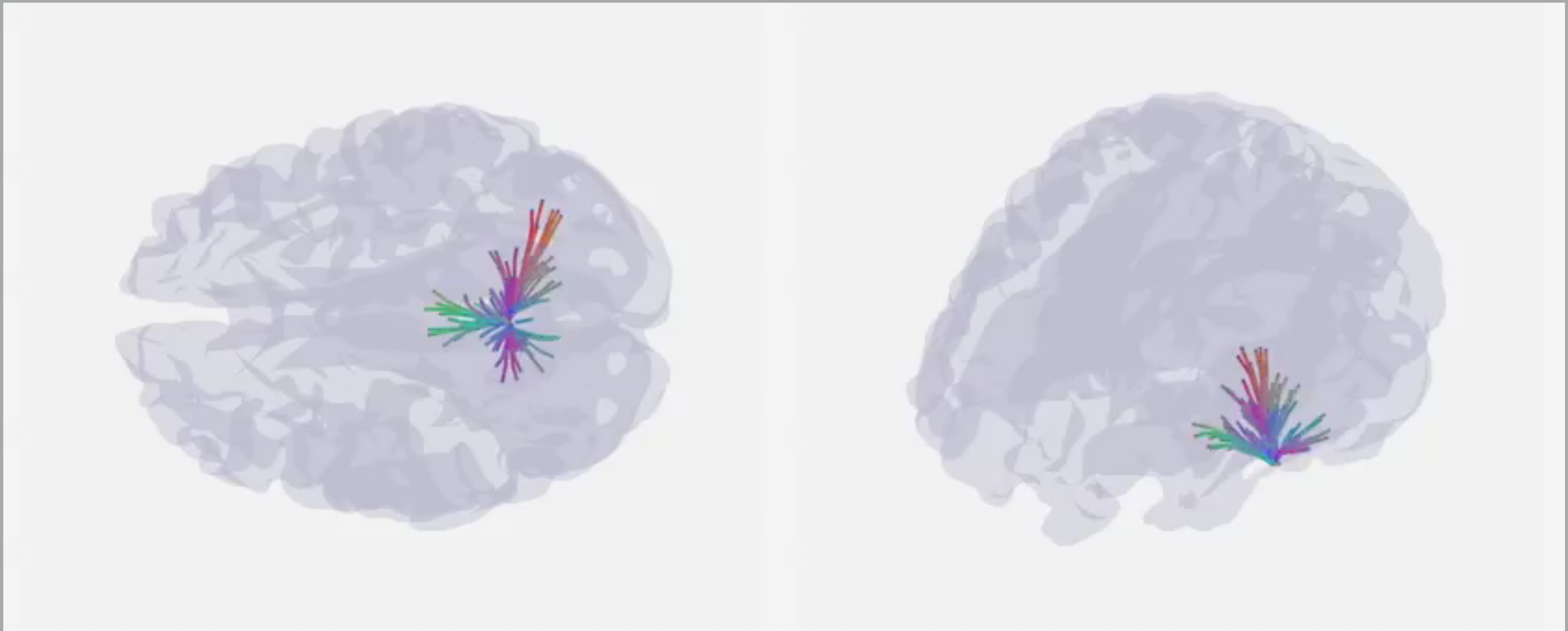


FA

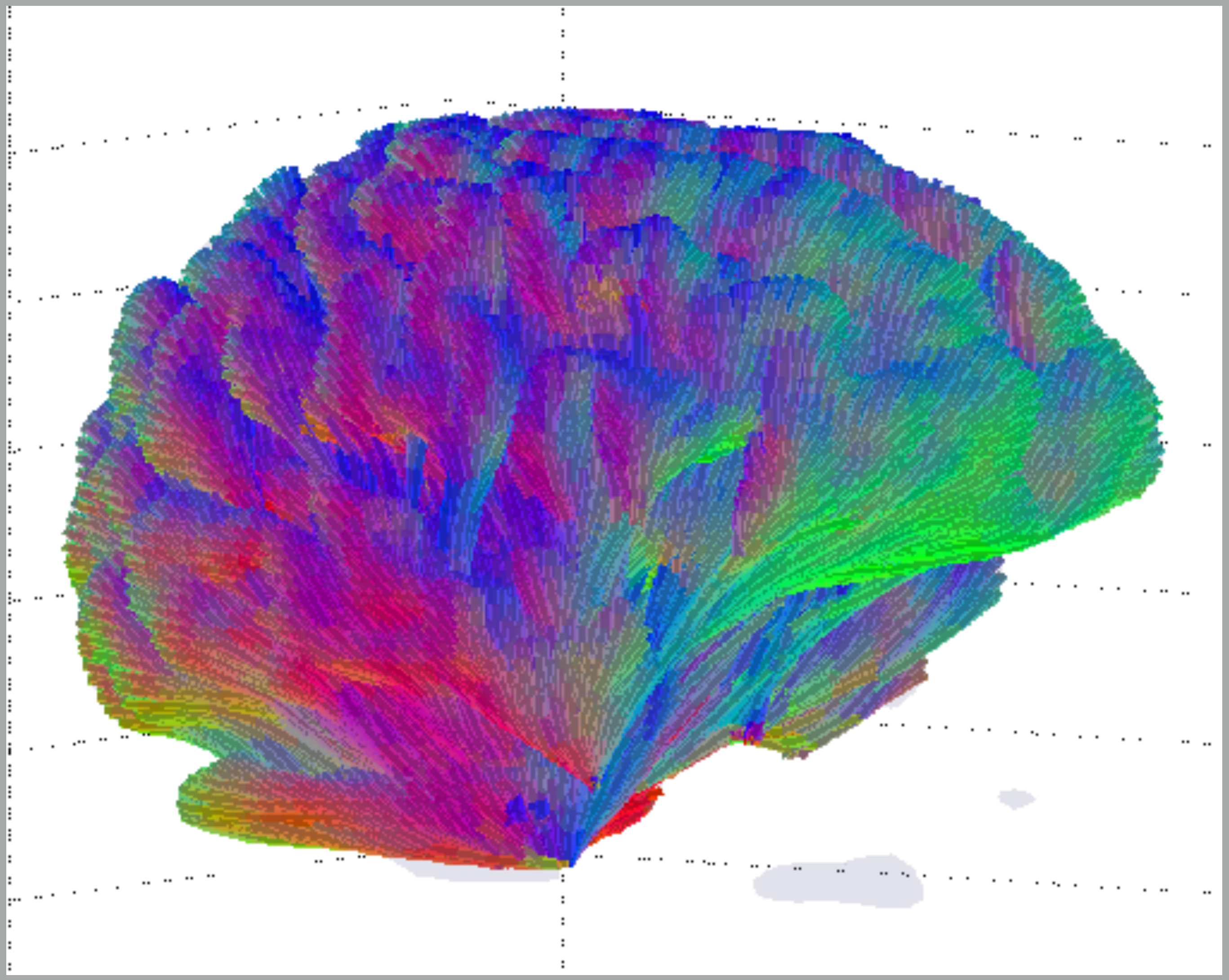


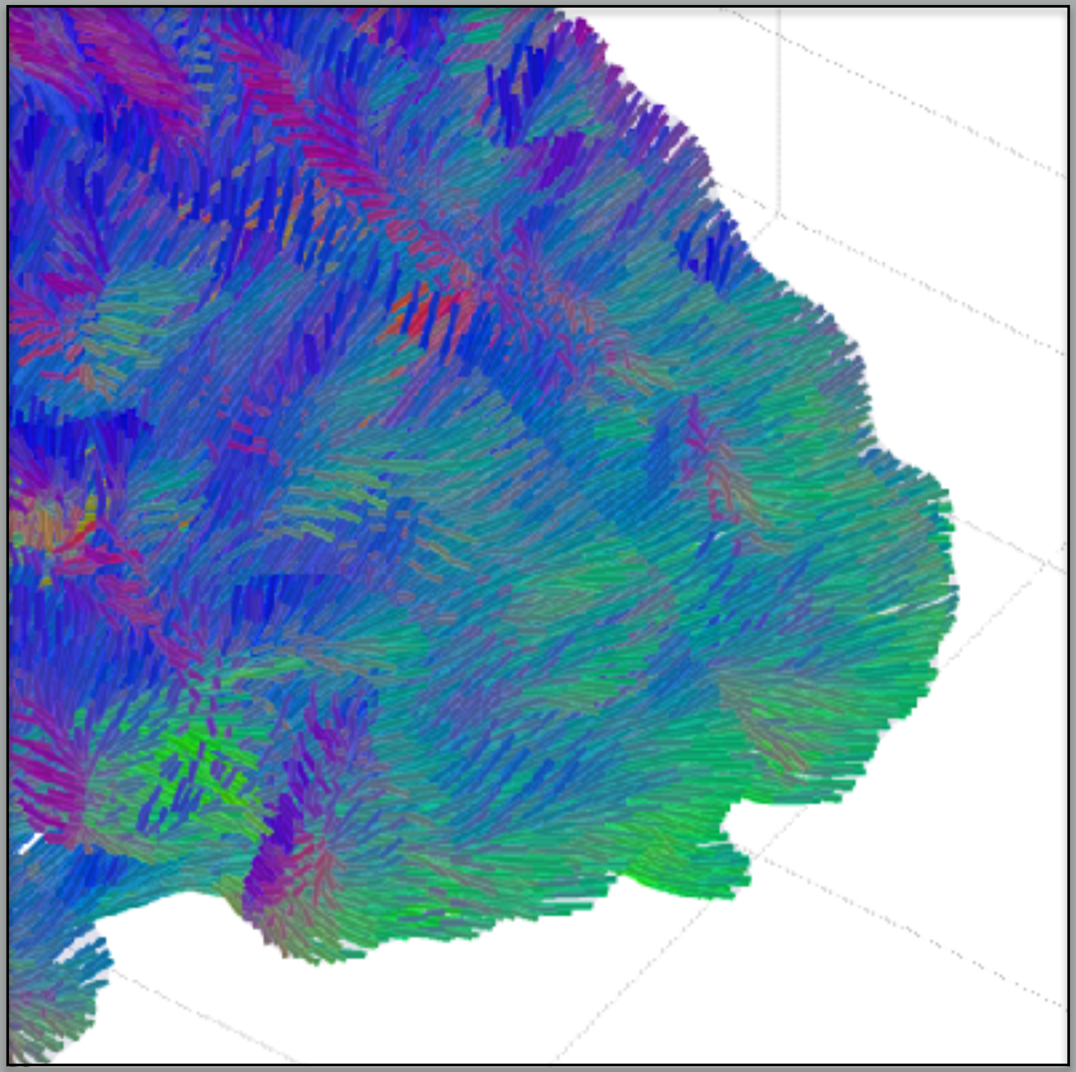
Equilibrium Probability

Whole brain GO-ESP



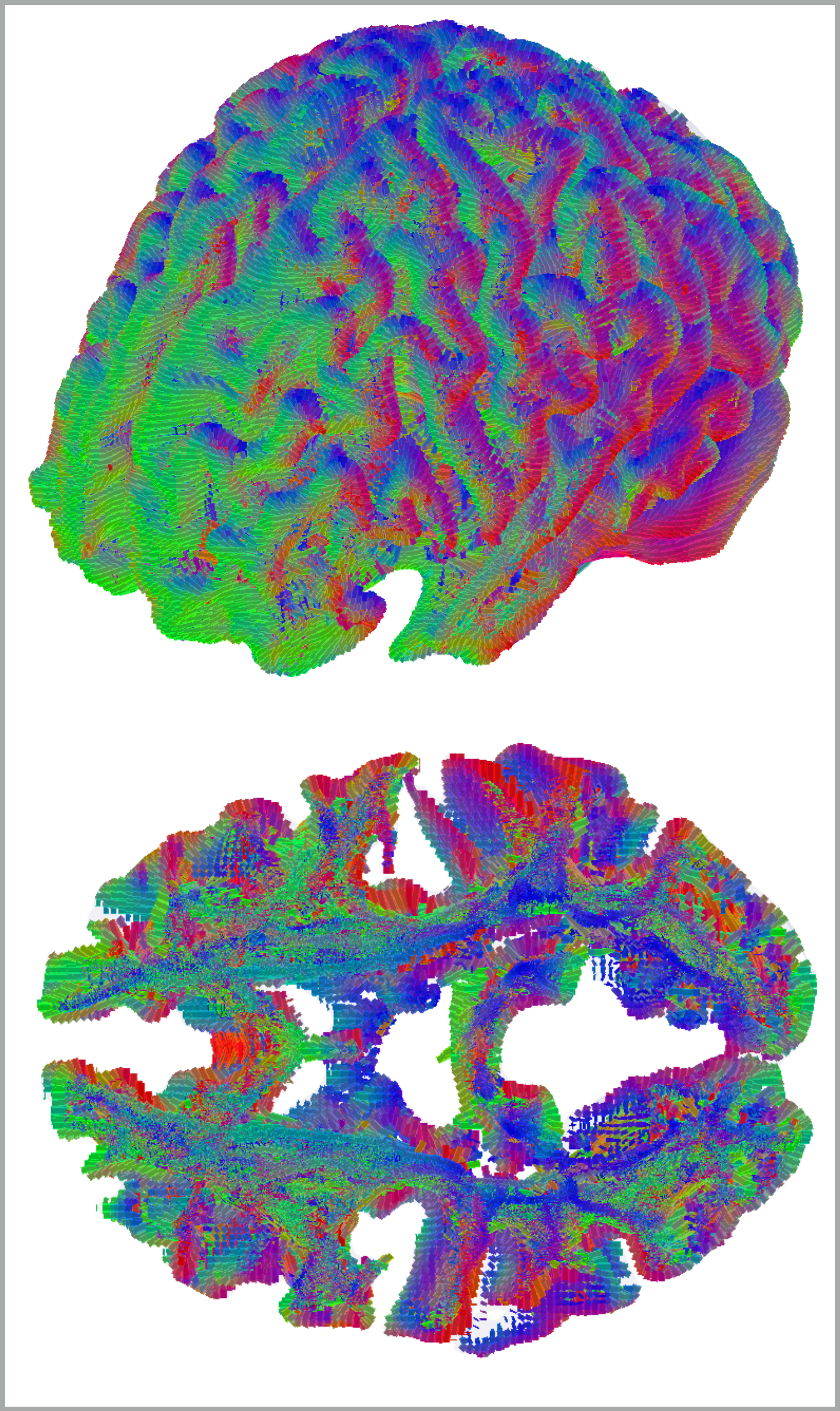
GO-ESP results from UCSD CFMRI protocol

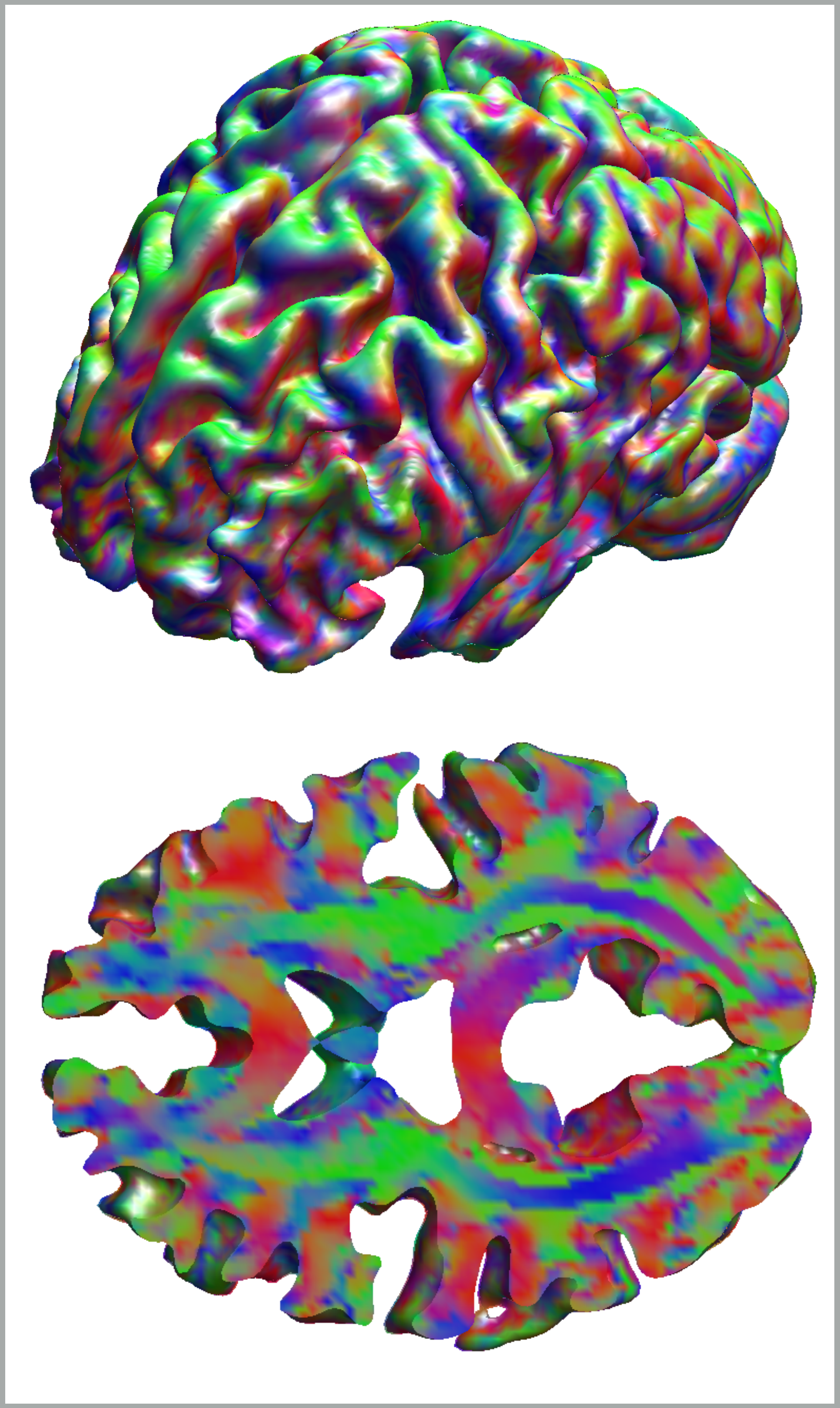




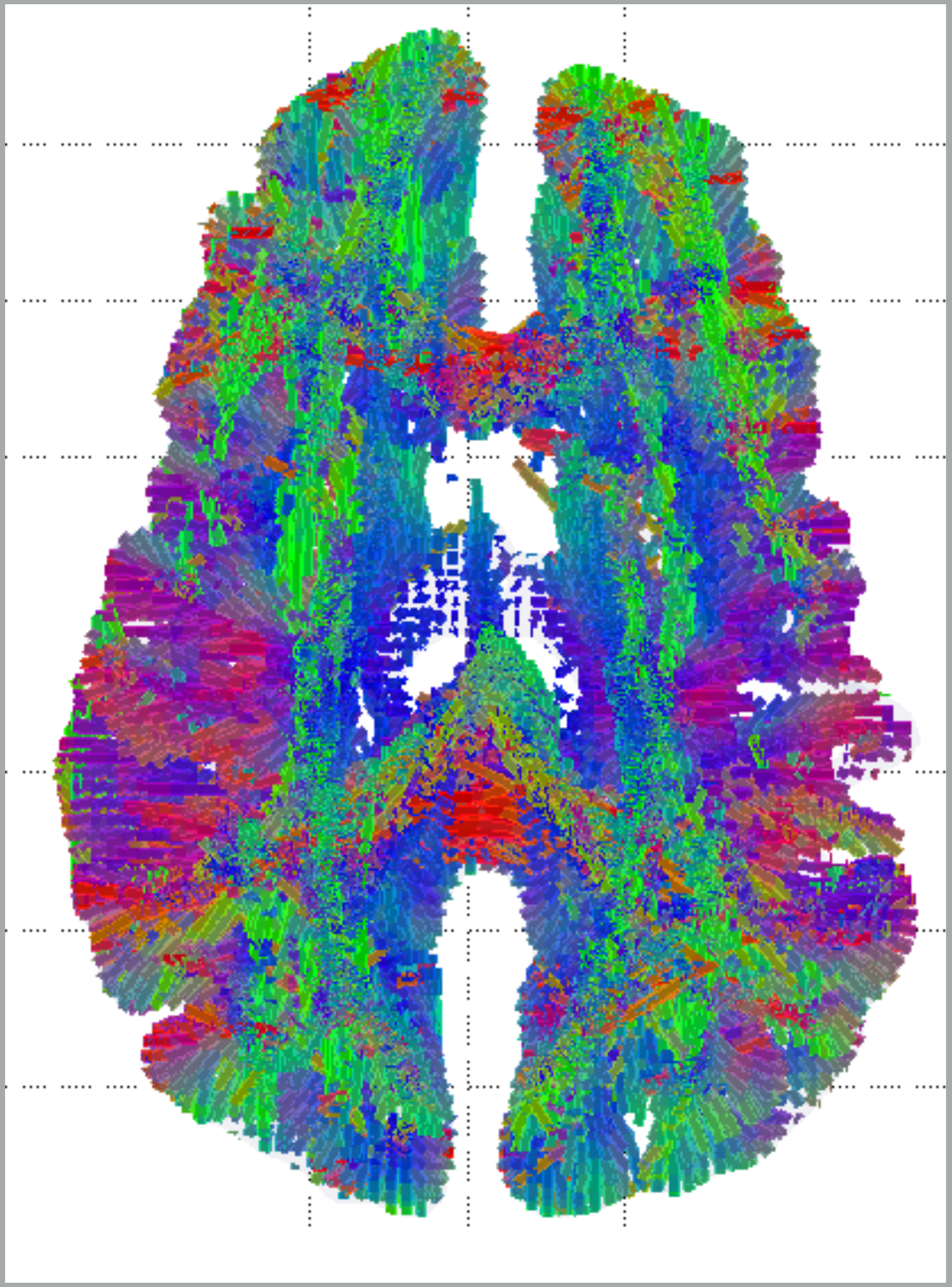
whole brain tractography

Whole brain GO-ESP



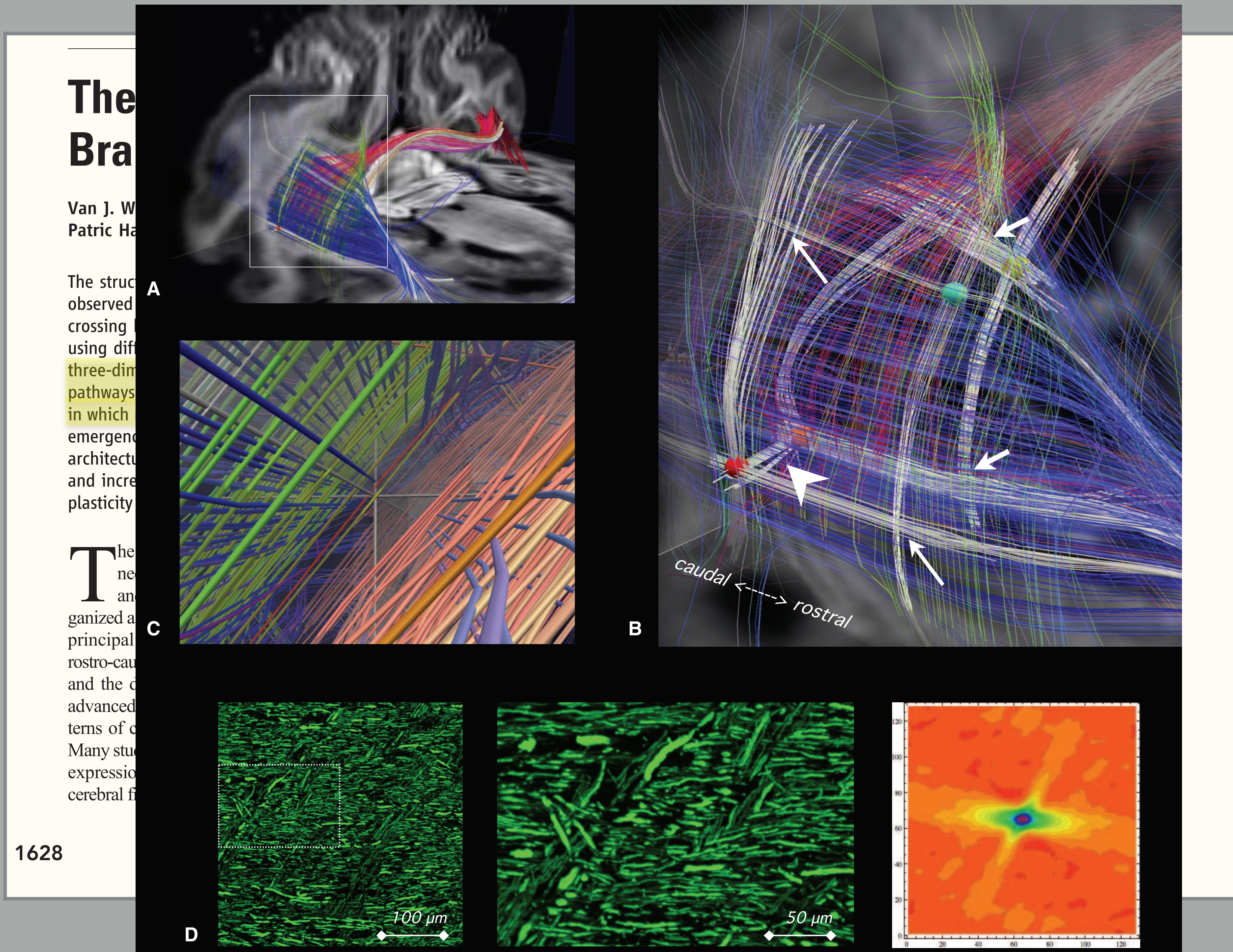


GO-ESP results from UCSD CFMRI protocol



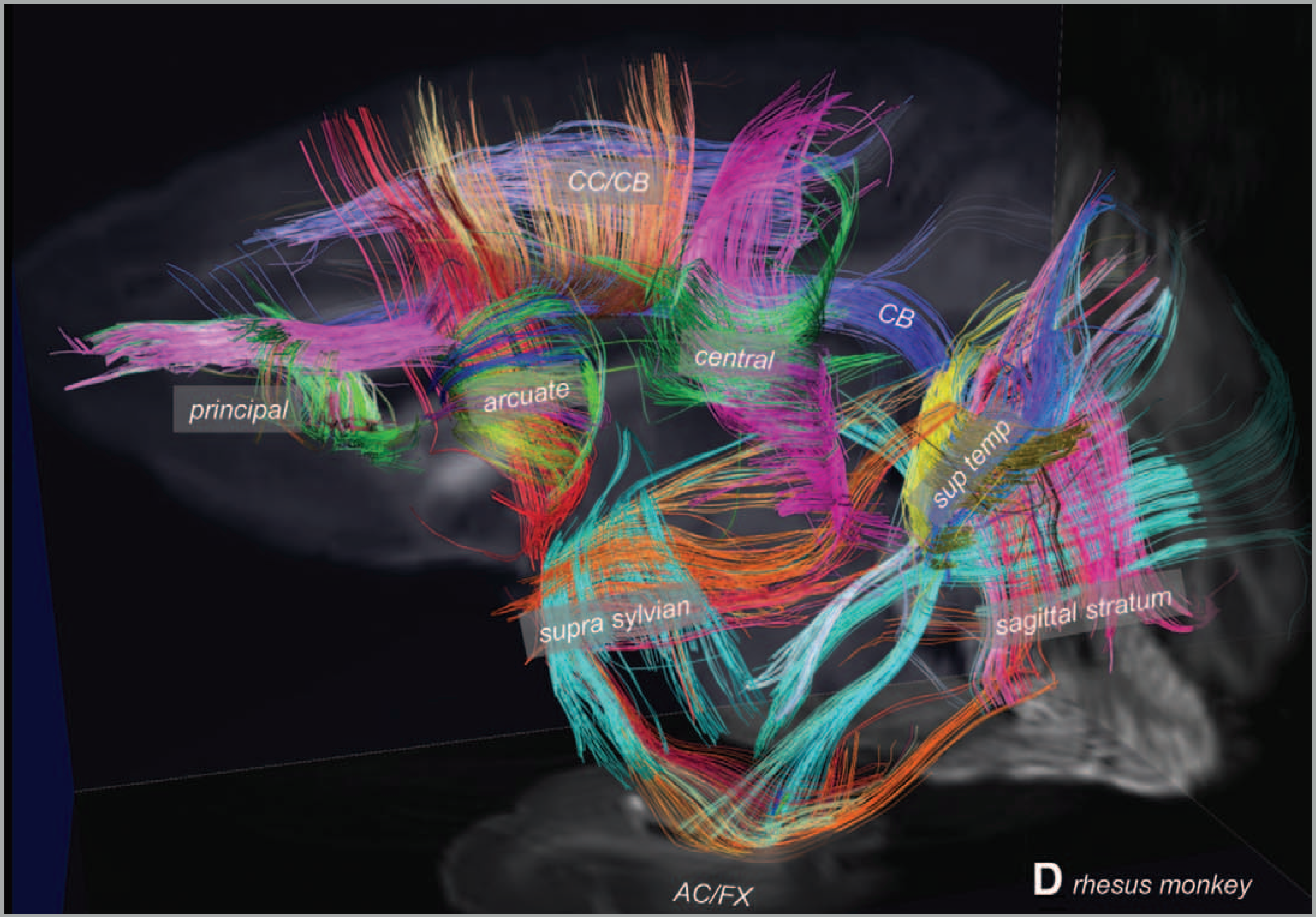
a slice of tractography

What is the Geometric Structure of Brain Fiber Pathways?



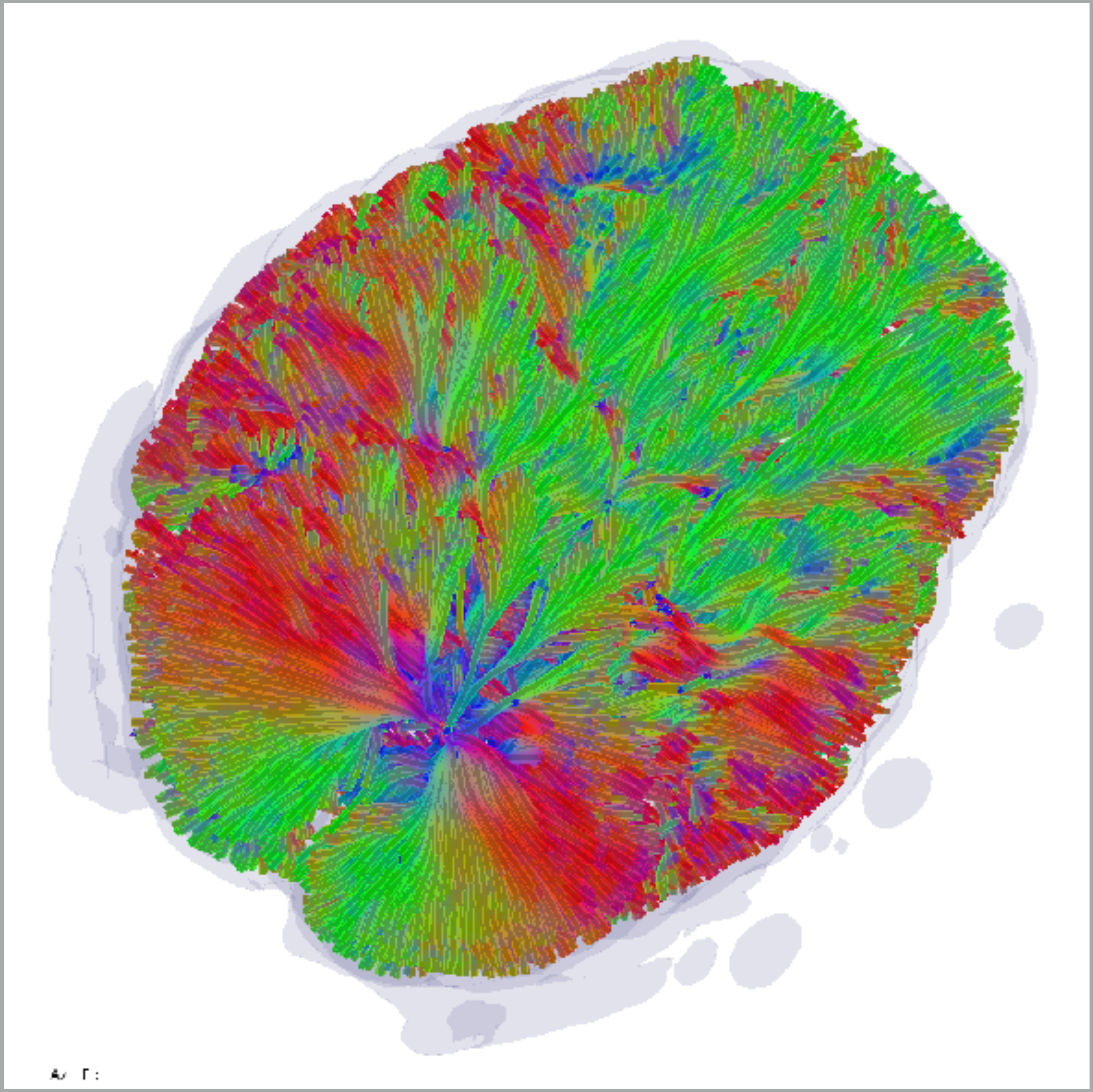
Wedeen, et.al. *Science 2012*

What is the Geometric Structure of Brain Fiber Pathways?



Wedeen, et.al. *Science 2012*

GO-ESP



whole brain tractography

What is the Geometric Structure of Brain Fiber Pathways?

"The cerebral fiber pathways formed a rectilinear three-dimensional grid continuous with the three principal axes of development".

"Cortico-cortical pathways formed parallel sheets of interwoven paths in the longitudinal and medio-lateral axes, in which major pathways were local condensations."

". . . the near orthogonal structure of pathways is not limited to a particular plane but exists throughout a 3D volume . . . "

Wedeen, et.al. *Science 2012*

The Catani Objection

Comment on "The Geometric Structure of the Brain Fiber Pathways"

Marco Catani *et al. Science* **337**, 1605 (2012)

Comment on “The Geometric Structure of the Brain Fiber Pathways”

Marco Catani,[1,2]* Istvan Bodi,[3] Flavio Dell’Acqua[1,4]

Wedeen *et al*. (Reports, 30 March 2012, p. 1628) proposed a geometrical grid pattern in the brain that could help the understanding of the brain’s organization and connectivity. We show that whole-brain fiber crossing quantification does not support their theory. Our results suggest that the grid pattern is most likely an artifact attributable to the limitations of their method.

The Catani Objection

Comment on "The Geometric Structure of the Brain Fiber Pathways"

Marco Catani *et al. Science* **337**, 1605 (2012)

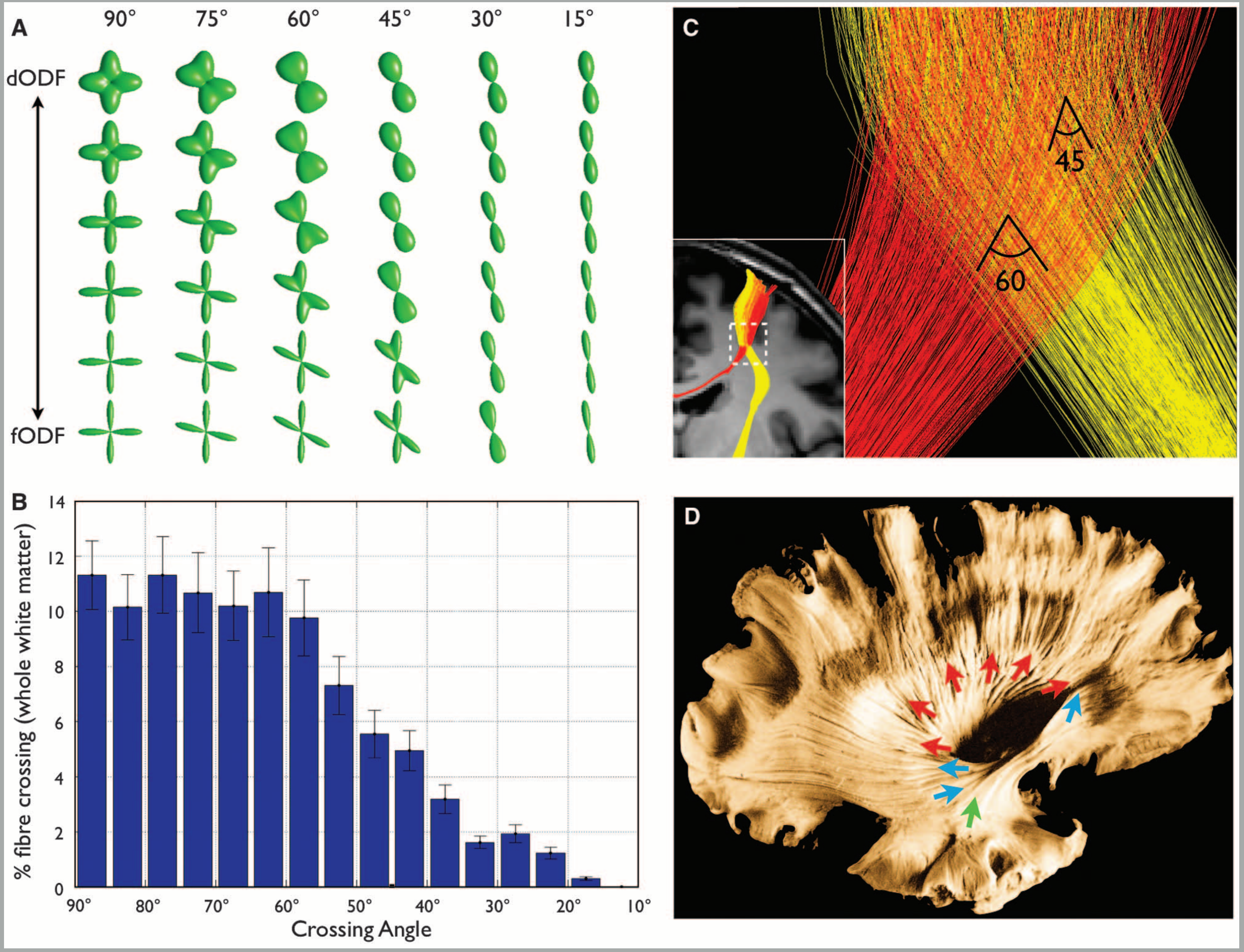
“Other methods are able to obtain sharper ODF profiles by extracting directly the underlying fiber orientation (i.e., fiber-ODF or fODF) using a specific diffusion model for white matter fibers. “

“Furthermore, the experimental results reported by Wedeen et al. (3) are mainly qualitative. In our view, the lack of a quantitative and comprehen- sive analysis of the entire brain across individuals limits their ability to extend their conclusions to the whole brain”

The Catani Objection

Comment on "The Geometric Structure of the Brain Fiber Pathways"

Marco Catani *et al. Science* **337**, 1605 (2012)



The Catani Objection

Comment on "The Geometric Structure of the Brain Fiber Pathways"

Marco Catani *et al. Science* **337**, 1605 (2012)

"To us, the architecture of the brain, seen through the lens of alternative diffusion methods, bears a closer resemblance to the intricate streets of Victorian London. . "

The Wedeen Response to the Catani Objection

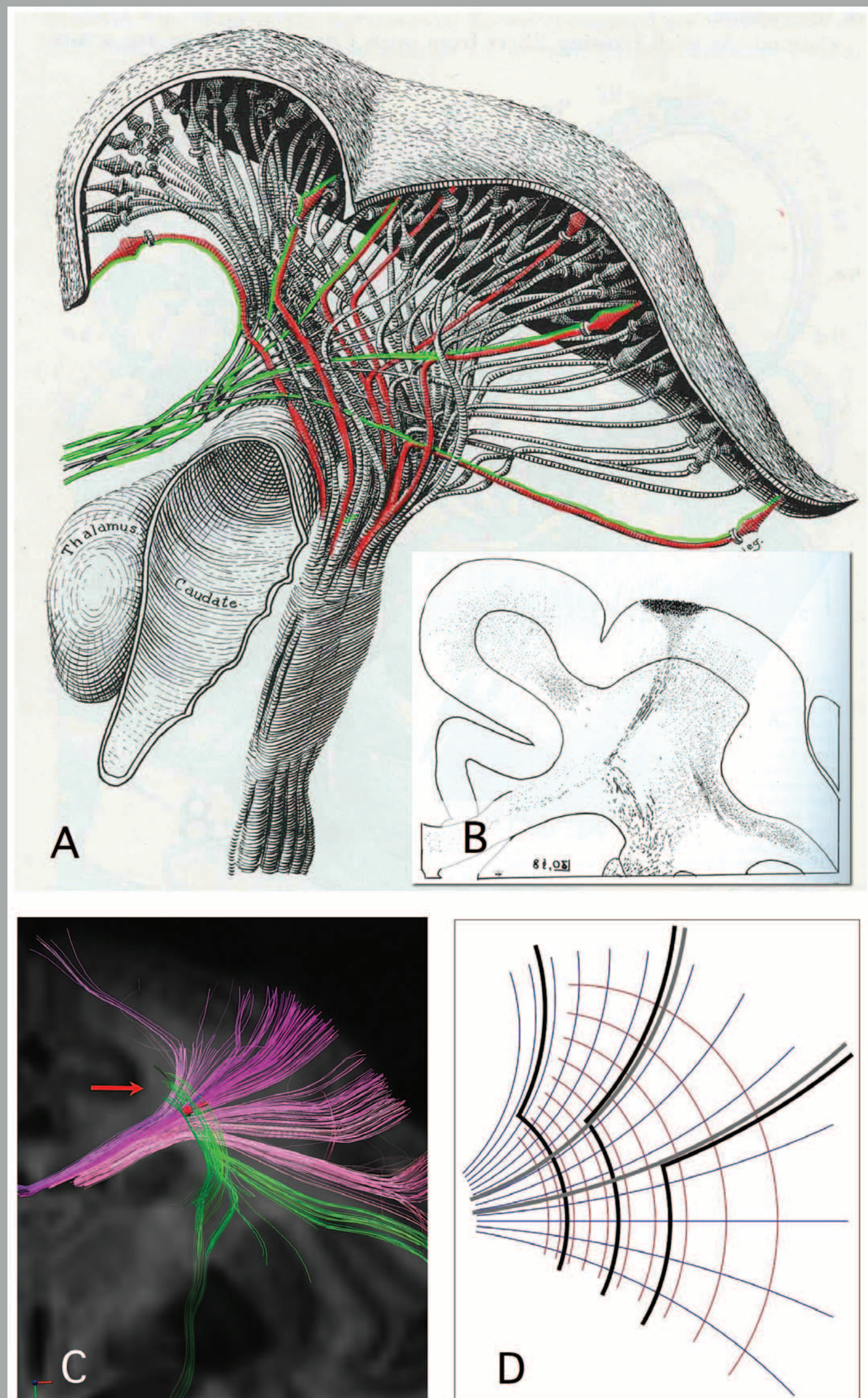
Response to Comment on
"The Geometric Structure of the Brain Fiber Pathways"
Van J. Wedeen *et al. Science* **337**, 1605 (2012);

Response to Comment on "The Geometric Structure of the Brain Fiber Pathways"

Van J. Wedeen,[1,2]* Douglas L. Rosene,[3] Ruopeng Wang,[1] Guangping Dai,[1] Farzad Mortazavi,[3] Patric Hagmann,[4] Jon H. Kaas,[5] Wen-Yih I. Tseng[6]

In response to Catani *et al.*, we show that corticospinal pathways adhere via sharp turns to two local grid orientations; that our studies have three times the diffusion resolution of those compared; and that the noted technical concerns, including crossing angles, do not challenge the evidence of mathematically specific geometric structure. Thus, the geometric thesis gives the best account of the available evidence.

The Wedeen Response to the Catani Objection



Corticospinal and callosal pathways of the rhesus monkey (A), corticospinal paths (red) leave the prefrontal cortex parallel to transverse callosal paths (green), then turn sharply by approximately 90° ("drop") to the caudal direction.

In DSI of rhesus monkey ex vivo (C), rostrocaudal segments of corticospinal paths (vertical) are nearly perpendicular locally to curved callosal paths (horizontal).

An illustrative model of the geometric thesis [the mapping $f(z) = 1/(z + -1) + 1/(z - -1)$ of the complex variable z] (D). The callosal paths (gray) adhere to a transverse coordinate (blue-gray), whereas corticospinal paths (black) adhere to both transverse and rostrocaludal (red) orientations via sharp 90° turns.

The Wedeen Response to the Catani Objection

Central to our thesis is the finding of sheet structure in cerebral fibers. We have shown that the pathways of the brain are equivalent to coordinate functions because they form in crossing parallel 2D sheets that fill 3D space like pages of a book.

As we emphasize, this is mathematically specific and highly atypical, entailing long-range correlations between paths that are as nonrandom as a lock and key (having prior probability ≈ 0).

This property does not depend on fiber orthogonally or the absence thereof—the concern of Catani et al.— but rather on a 3D relationship among crossing planes at different locations (the Frobenius integrability condition).

As we have shown, this can be represented as an angle between subsheets of fibers, which must be as close to zero as noise allows, or by the topology of the embedding of the reconstructed paths in 3D, which must be interwoven rather than mutually helical.

The Wedeen Response to the Catani Objection

“The thesis that brain pathways adhere to a simple geometric system best accounts for the available evidence—not like London, but Manhattan; not unfathomable, but unlimited. “

Tax's Sheet Structure Efforts

Towards Quantification of the Brain's Sheet Structure in Diffusion MRI Data

Chantal M.W. Tax[*,1], Tom C.J. Dela Haije[†,1], Andrea Fuster[†], Remco Duits[†], Max A. Viergever[*],
Evan Calabrese[‡], G. Allan Johnson[‡], Luc M.J. Florack[†], and Alexander Leemans[*]

[*] Image Sciences Institute, University Medical Center Utrecht, Utrecht, the Netherlands. [†] Imaging Science & Technology, Eindhoven University of Technology, Eindhoven, the Netherlands. [‡]Center for In Vivo Microscopy, Duke University Medical Center, Durham, North Carolina, USA

Tax's Sheet Structure Efforts

II. Theory and Methods

A. Lie bracket theory

The Lie bracket $[V,W]_p$ is a measure of the deviation from p when trying to move around in an infinitesimal loop along the integral curves of the fields V and W (Fig. 1). If and only if $[V,W]_p$ lies in the plane spanned by V_p and W_p, i.e., when the normal component of the Lie bracket [1] $[V,W]_p^{\perp} = [V,W]_p \cdot (V_p \times W_p)$ is equal to zero, the vector fields form a sheet at p [6]. The Lie bracket can be approximated by various difference vectors $r|_p$ [2] according to

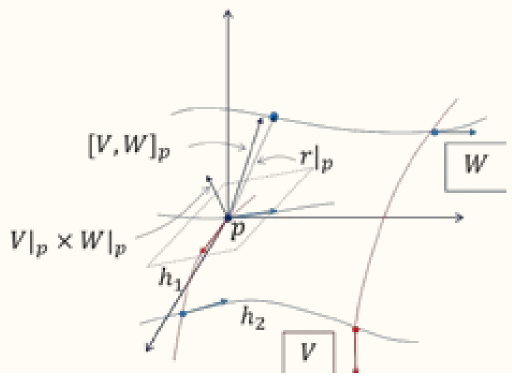


Fig. 1 Walking loop with $(\Phi_{-s}^{W} \circ \Phi_{-s}^{V} \circ \Phi_{s}^{W} \circ \Phi_{s}^{V})(p)$ [2] the end point. Difference vector $r|_p$ approximates $[V,W]_p$ [5].

$$r|_p(h_1,h_2) = h_1 h_2 [V,W]_p + \Delta(h_1,h_2)\ , \qquad (1)$$

Where h_1 and h_2 are walking distances and $\Delta(h_1,h_2)$ an error term that scales with h_1 and h_2. See references [5,7] for details.

B. Implementation and experiments

Starting from point p in the data, we assign two fiber orientation distribution function (fODF) peaks [4] as representative members of vector fields V and W.

METRIC AND TOPO-GEOMETRIC PROPERTIES OF URBAN STREET NETWORKS:
some convergences, divergences and new results

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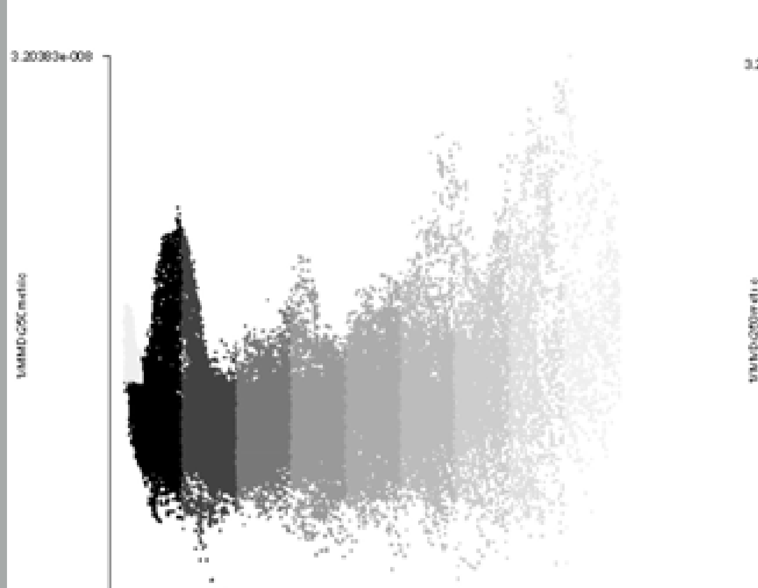
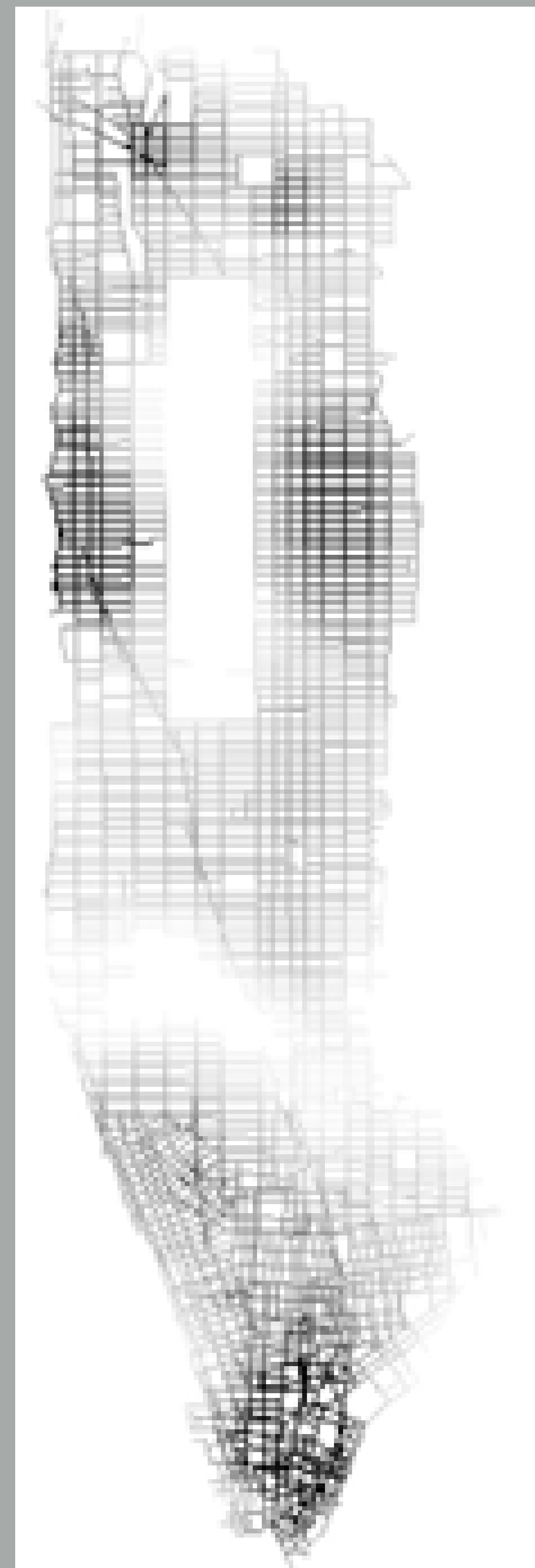
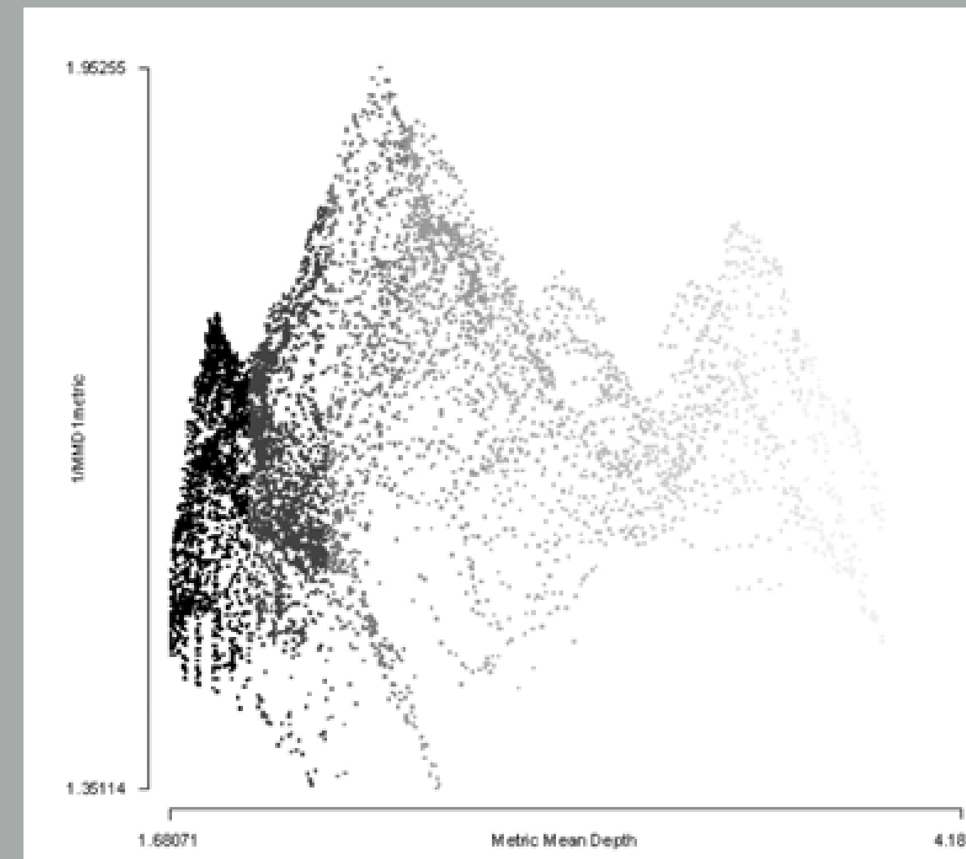
The Streets of Manhattan and London



London

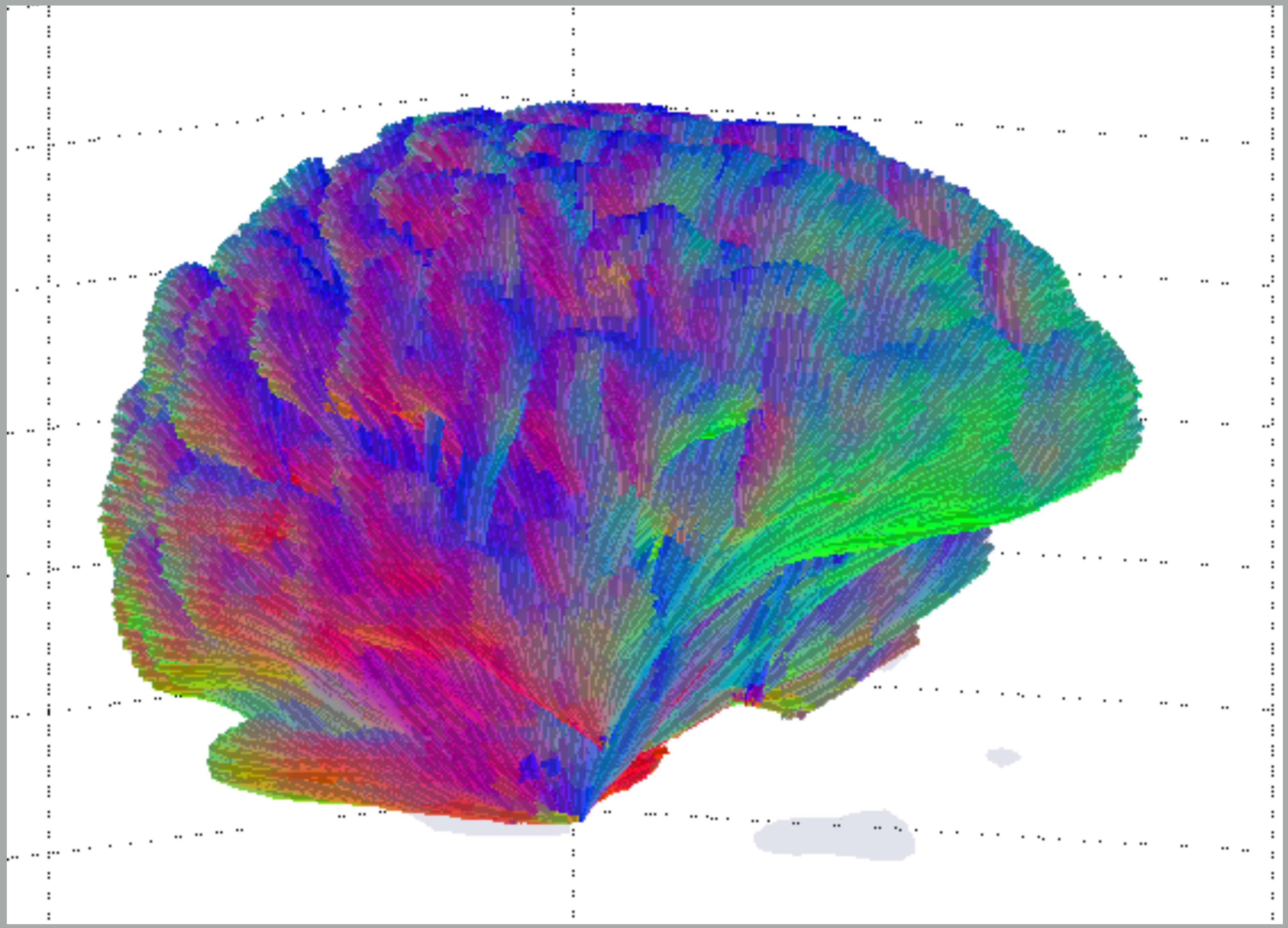


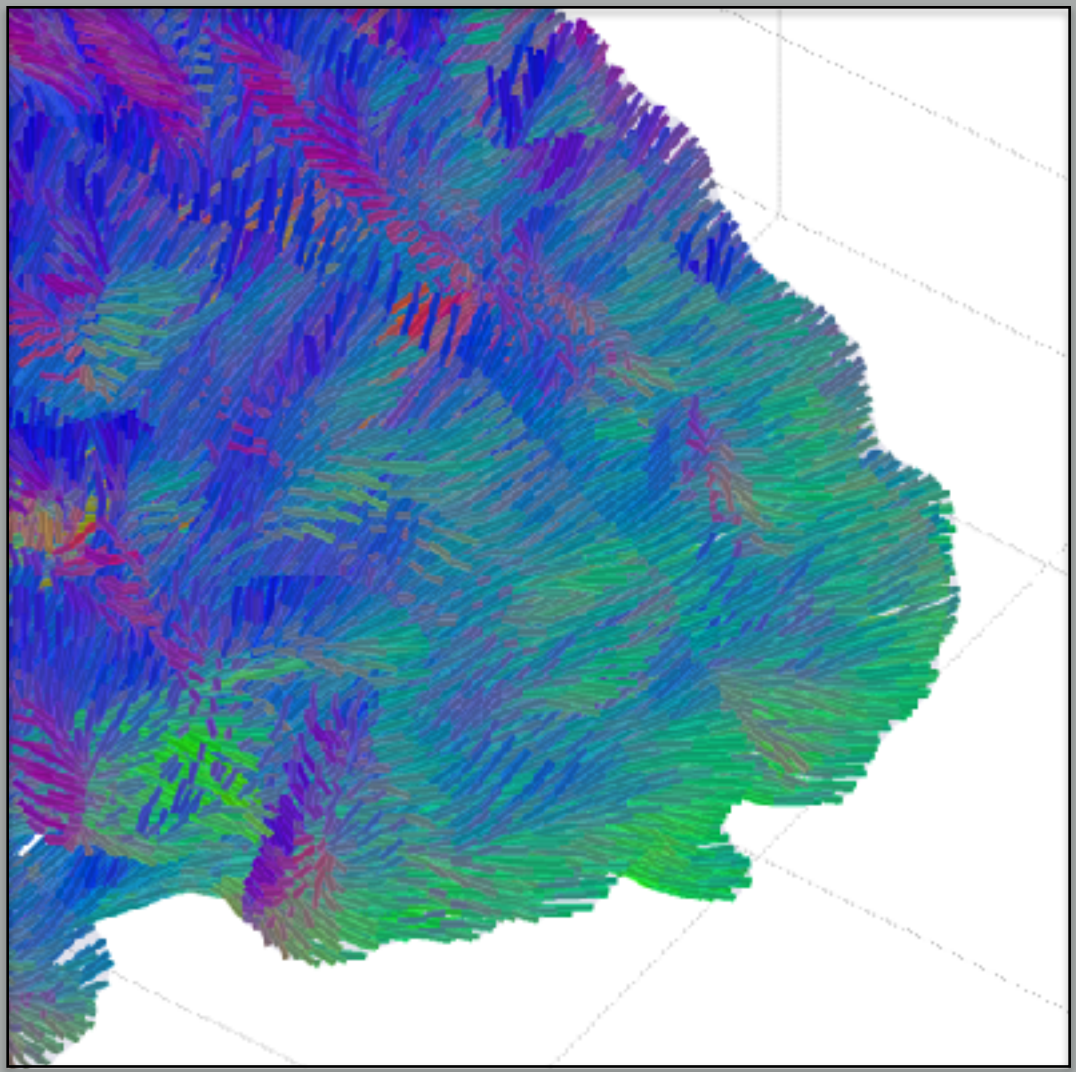


Manhattan

Hillier, et.al.

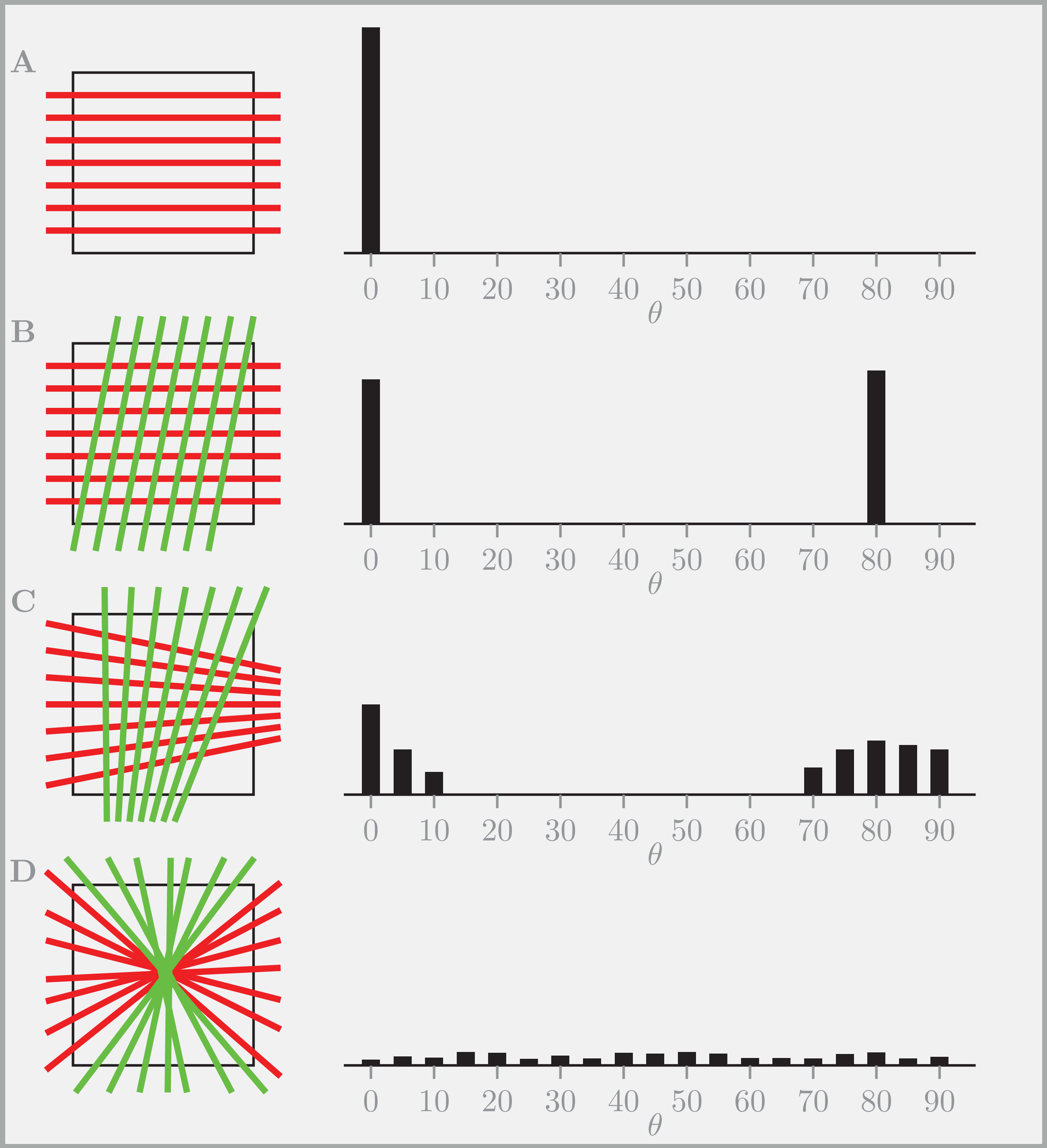
GO-ESP results from UCSD CFMRI protocol





whole brain tractography

A STATISTICAL ASSESSMENT USING GO-ESP



(A) a single family of parallel fibers

(B) two families of crossing parallel fibers

(C) two families of crossing diverging fibers

(D) A random fiber distribution

Pairwise crossing fiber distribution density

Galinsky and Frank, *Neural. Comp. 2016*

A statistical assessment using GO-ESP

Pairwise crossing fiber distribution density

$$f(\theta) = \frac{nN_\theta}{\Theta N_c} \qquad \int_0^\Theta f(\theta)\, d\theta = 1$$

$n = \text{number of bins}$

$N_\theta = \text{number of crossing in each bin } i$

$N_c = \text{total number of crossings}$

A statistical assessment using GO-ESP

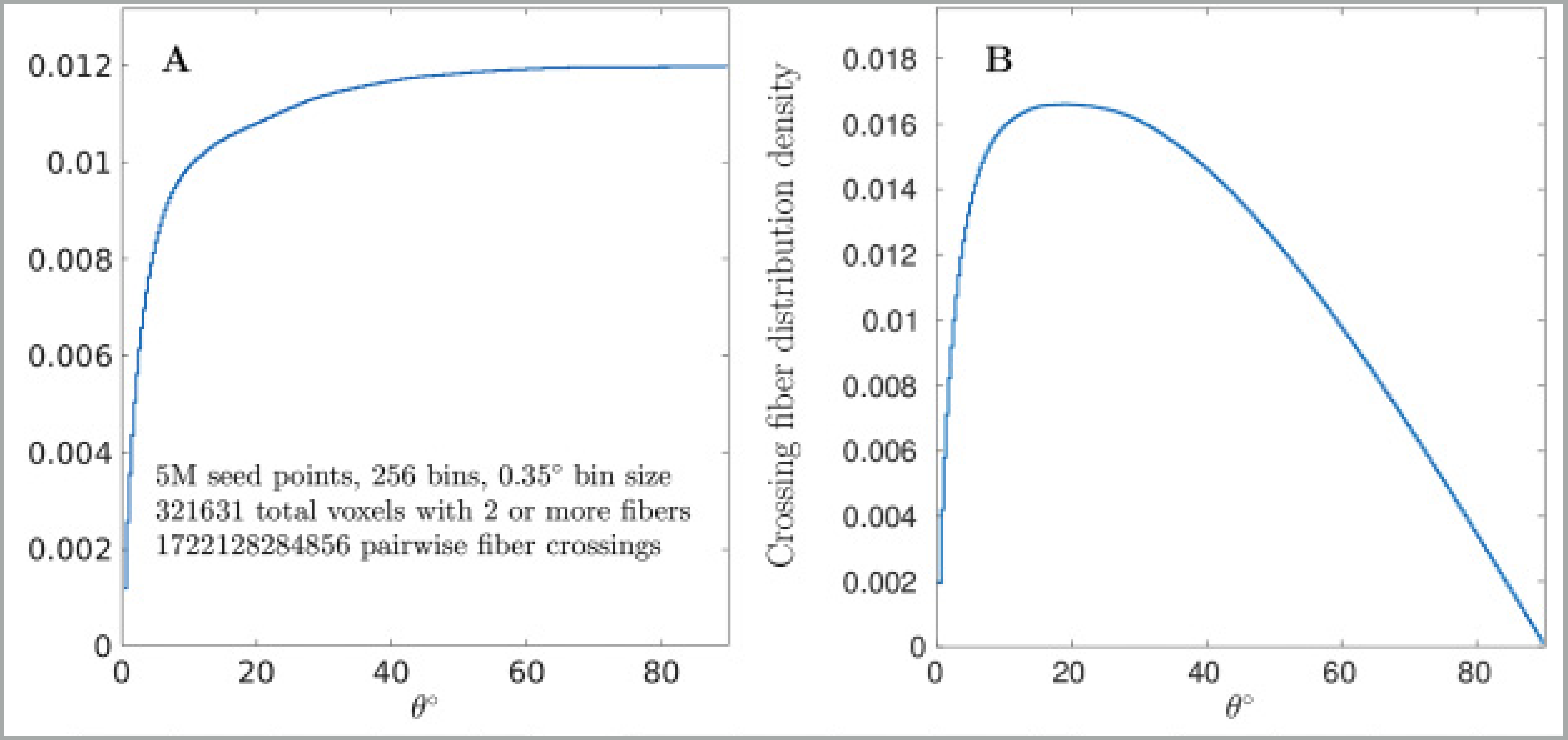
The main claim of Wedeen et al. is that the white matter has a grid-like organization formed by crossing of quasi-orthogonal sheets of fibers.

Though the crossing angles are not necessarily 90 degrees, they are nevertheless assumed to show some distinction between directions, which would translate into a pairwise crossing angle distribution containing peaks at both small and large angles.

A statistical assessment using GO-ESP

Pairwise crossing fiber angle distribution for whole human brain.

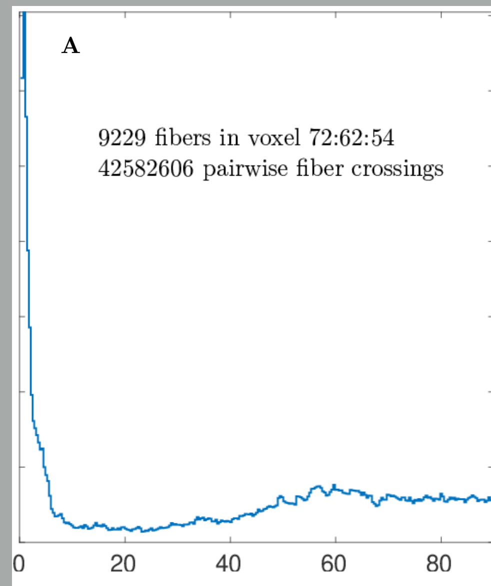
Angle distribution rescaled by cos θ , which takes into account the difference in solid angle measures of each bin.



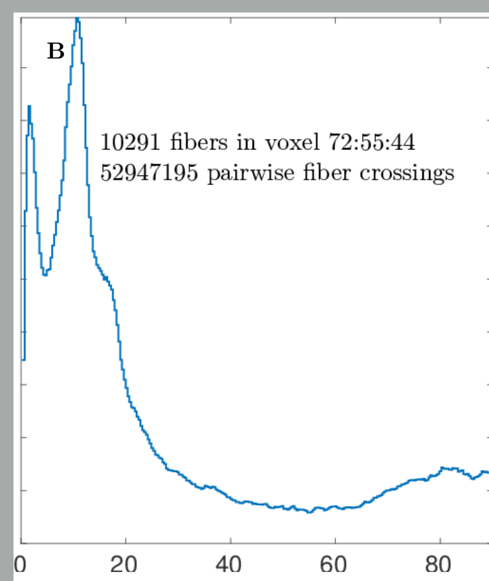
Our results do not find any quantitative statistical evidence that this is the case.

A statistical assessment using GO-ESP

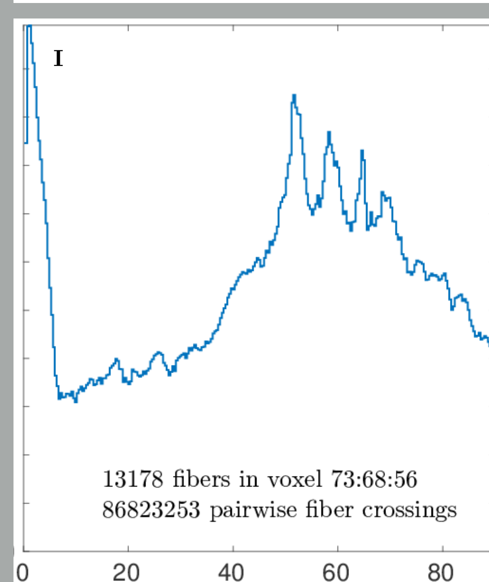
Pairwise crossing fiber angle distributions in several individual voxels



Single fiber

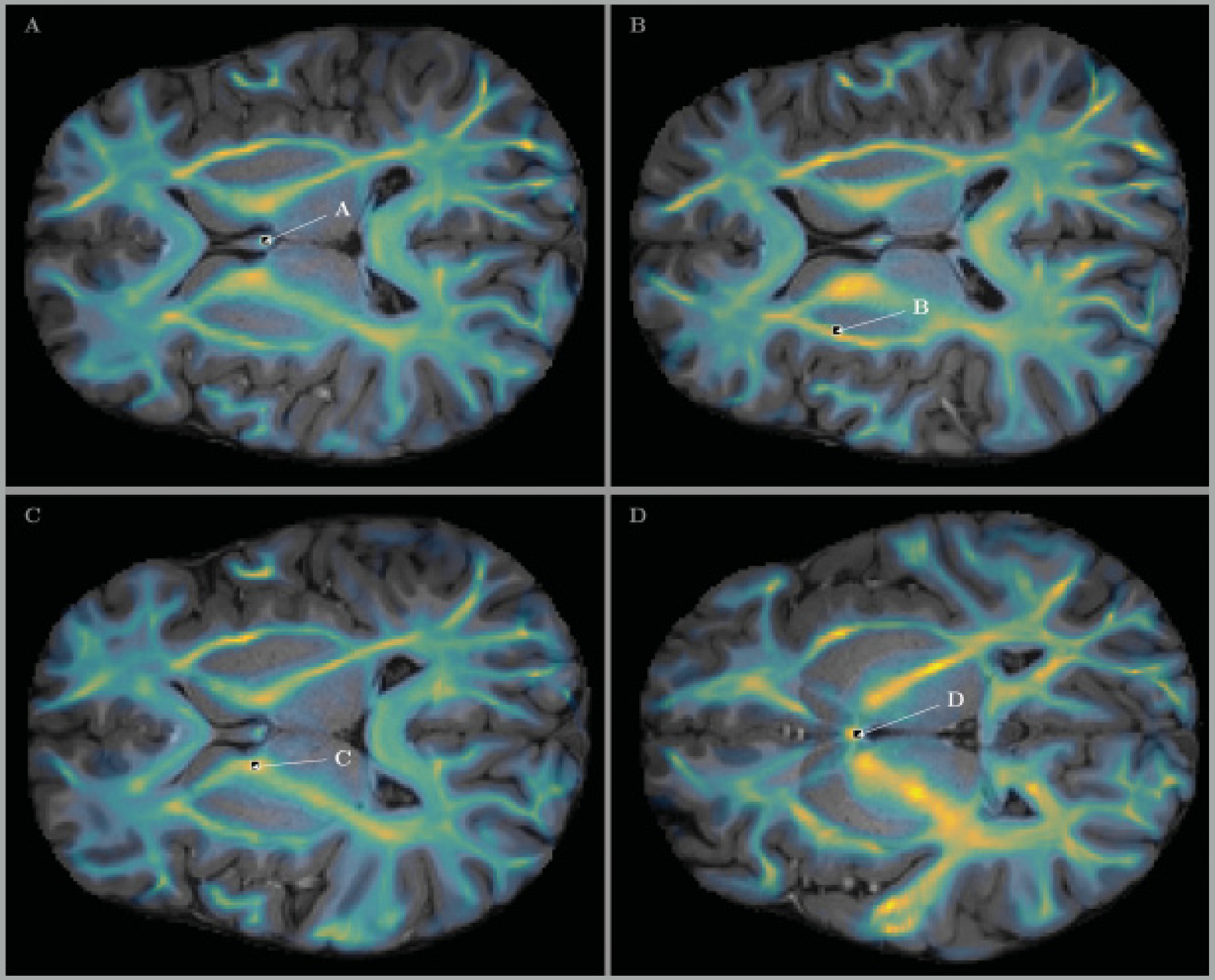


Approximate 10 degrees crossing of two fibers



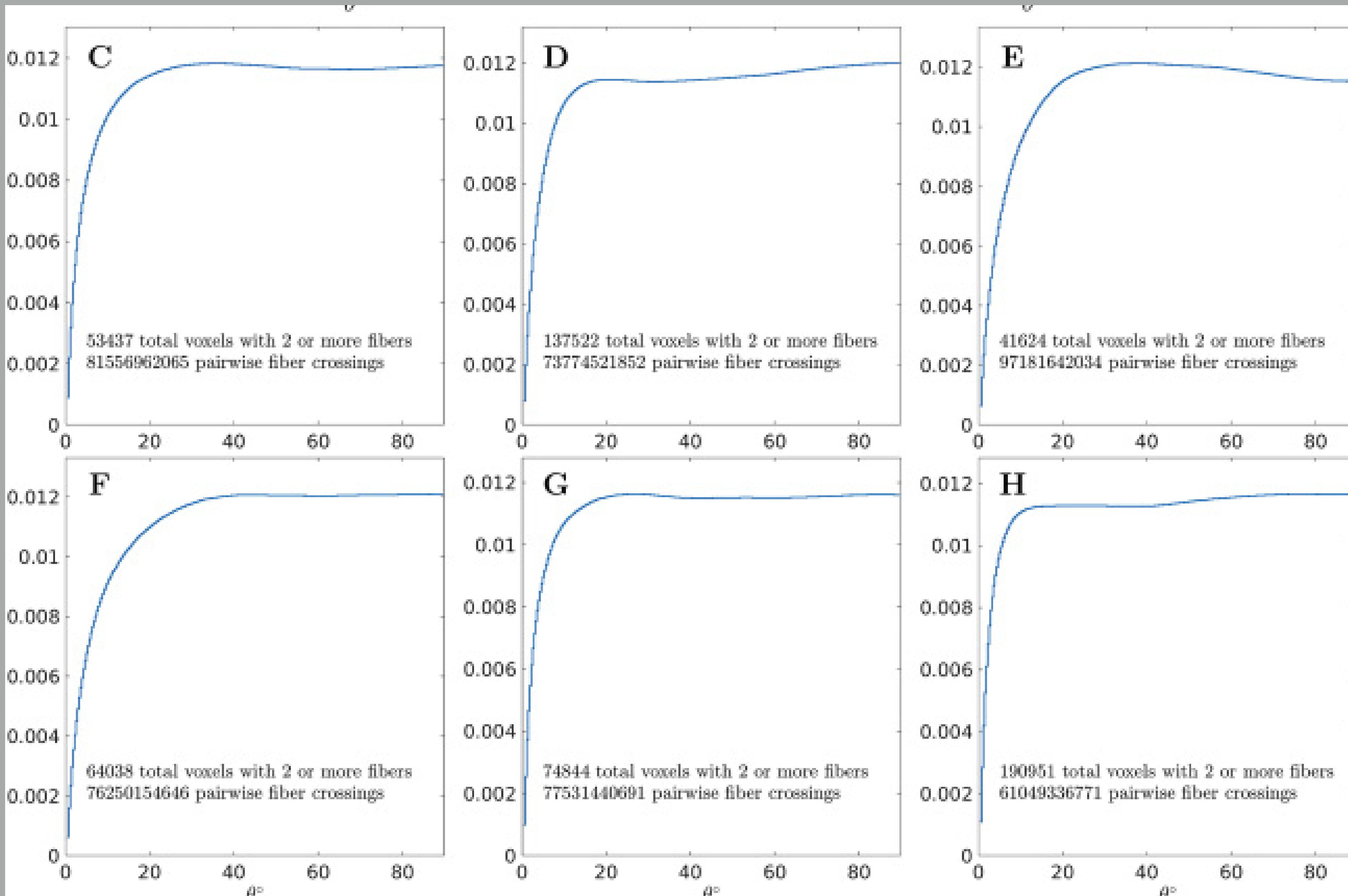
Crossing of multiple fibers.

A statistical assessment using GO-ESP



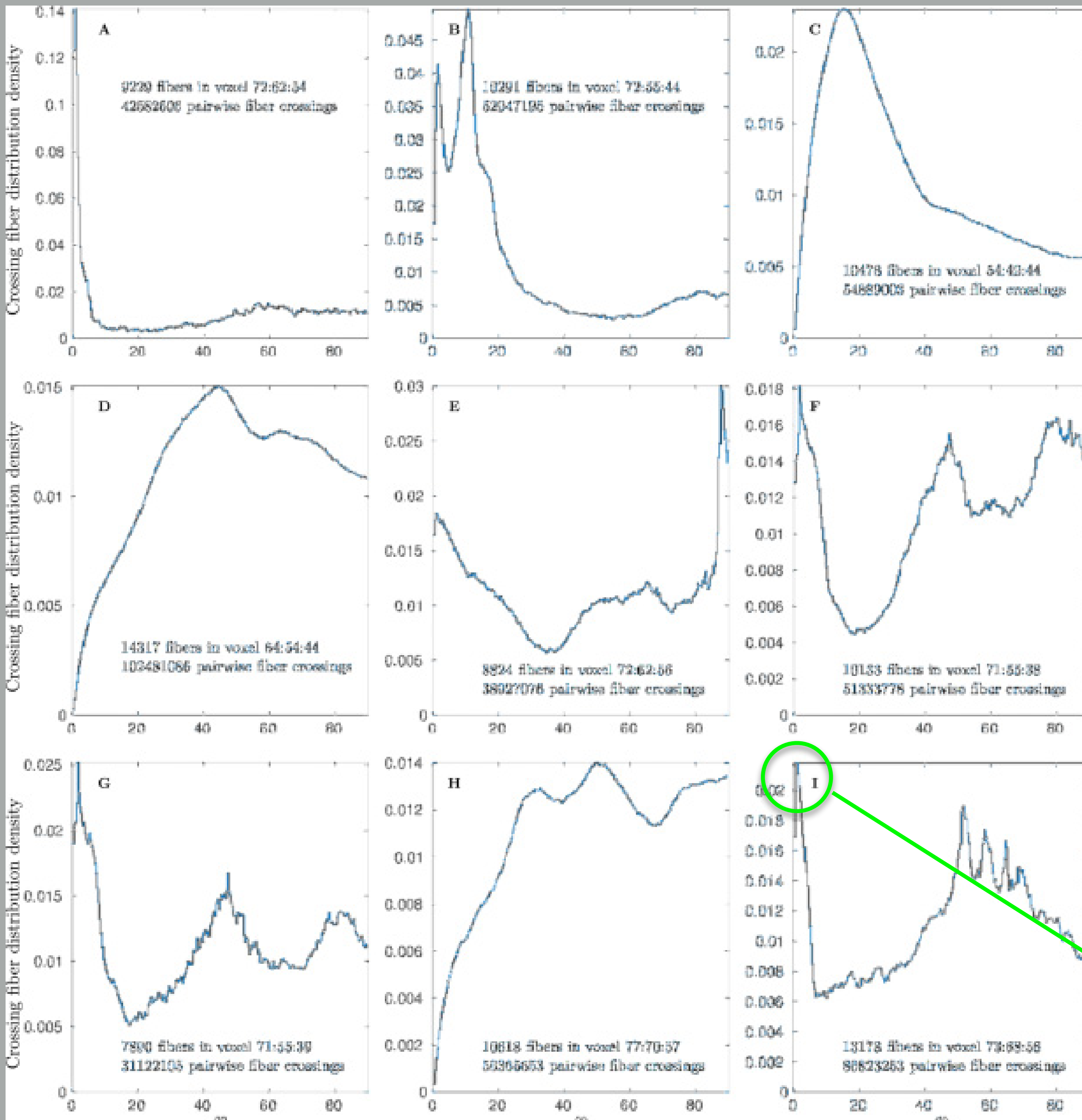
Galinsky and Frank, *Neural. Comp. 2016*

A statistical assessment using GO-ESP



6 subjects

A statistical assessment using GO-ESP



(A)
Single fiber

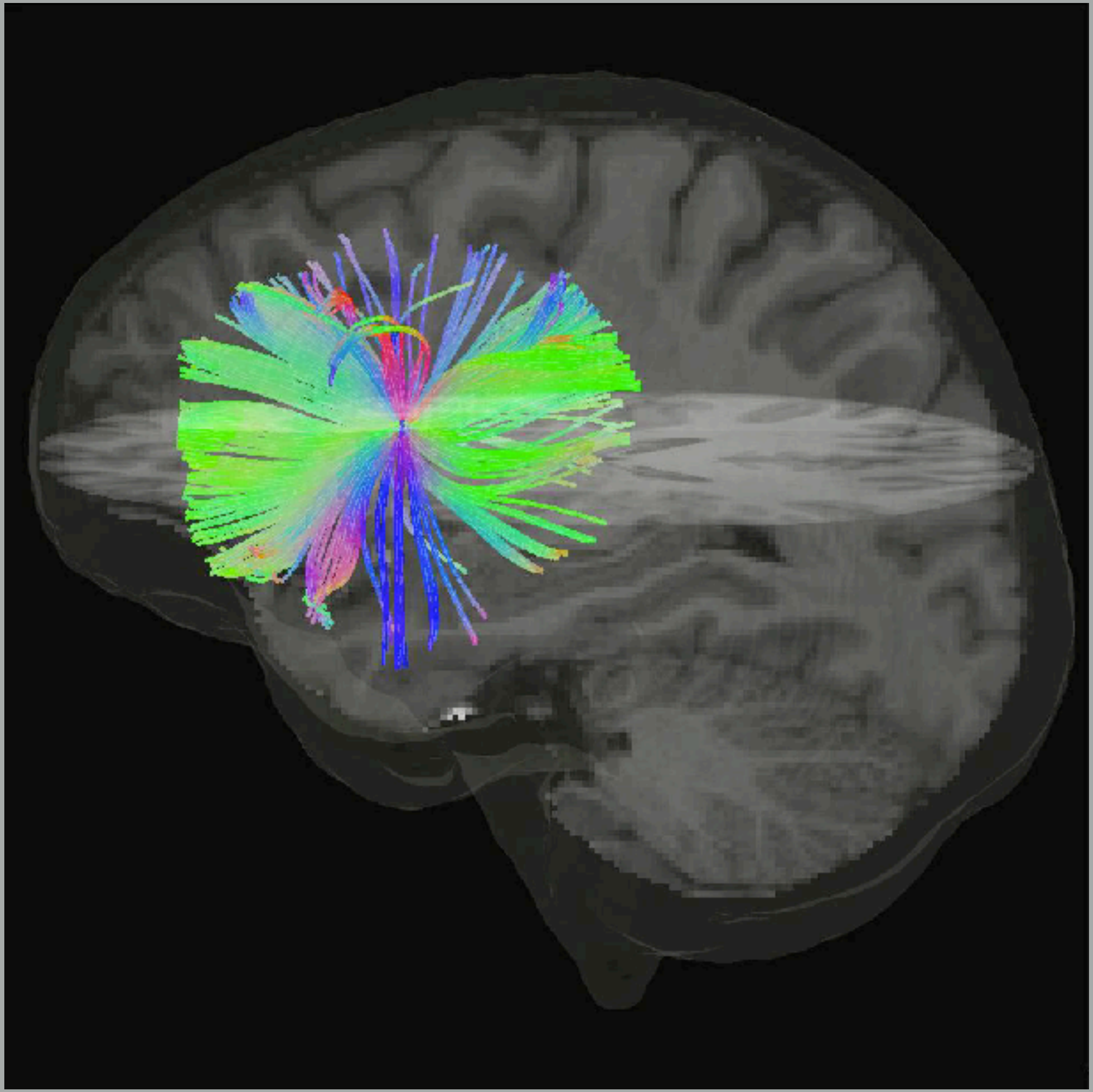
(B,C,D,E):
approximate 10, 20, 45, and 90 degrees crossing of two fibers

(F, G, H, I):
Crossing of multiple fibers.

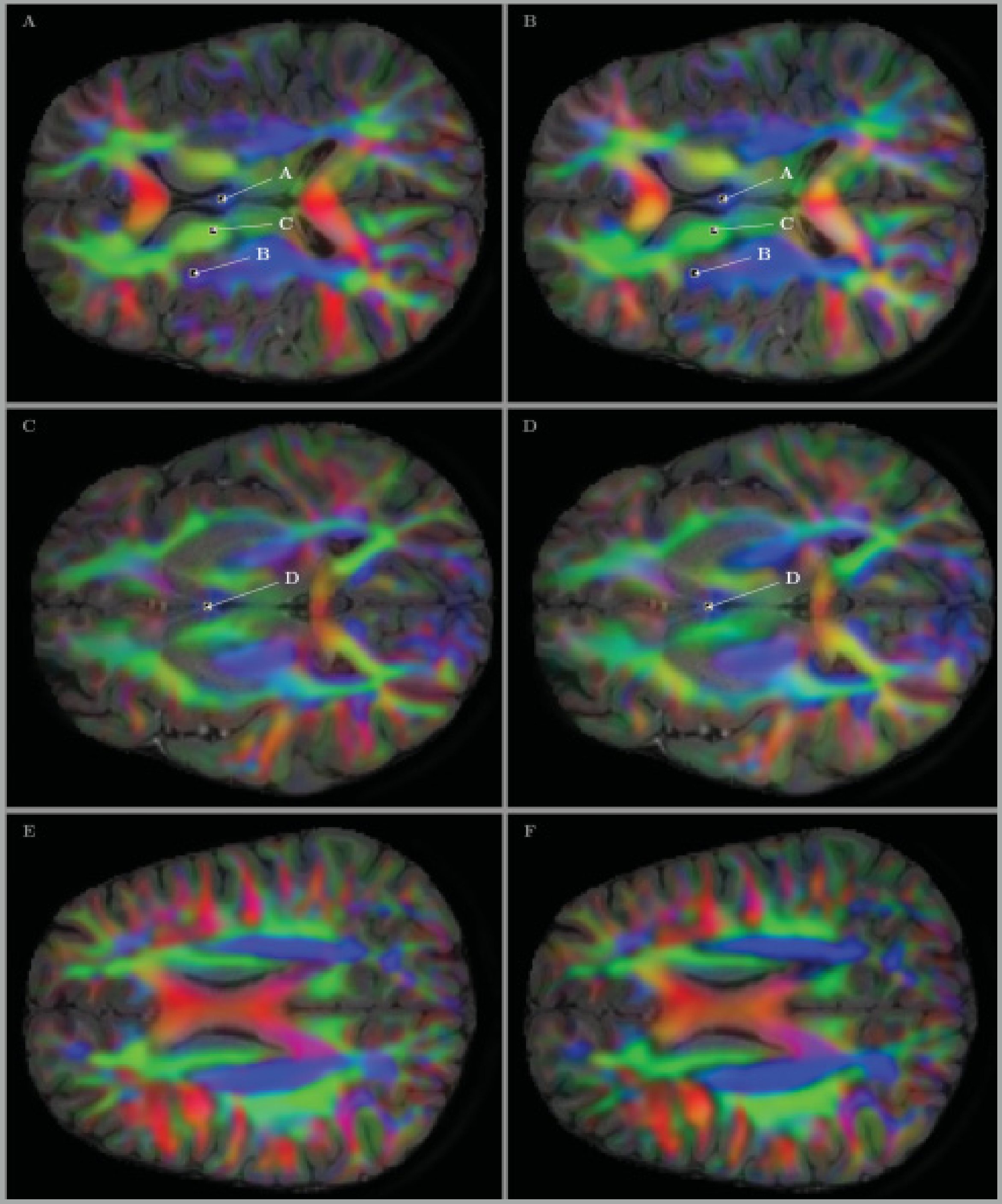
$\approx 8^\circ$ 600σ

Pairwise crossing fiber angle distributions in several individual voxels

So what is the structure of the Brain Fiber Pathways?

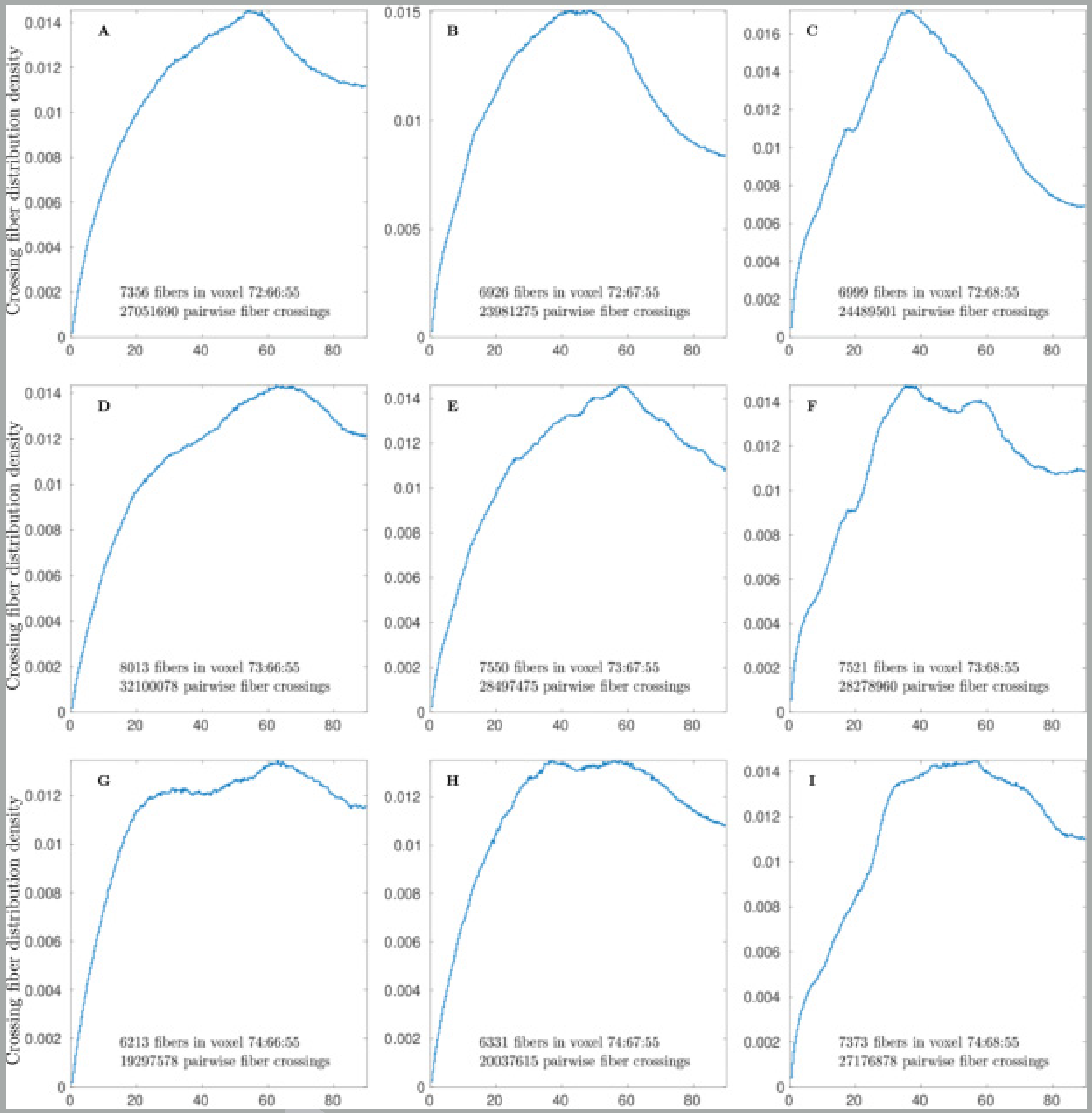


A statistical assessment using GO-ESP



Galinsky and Frank, *Neural. Comp. 2016*

A statistical assessment using GO-ESP



Pairwise crossing fiber angle distributions in a 3×3 block of adjacent voxels showing the continuity of distributions across voxel boundaries.
The fraction of fiber crossings in the voxel is shown on the ordinate axis.

A statistical assessment using GO-ESP

LETTER Communicated by Adam Anderson

The Lamellar Structure of the Brain Fiber Pathways

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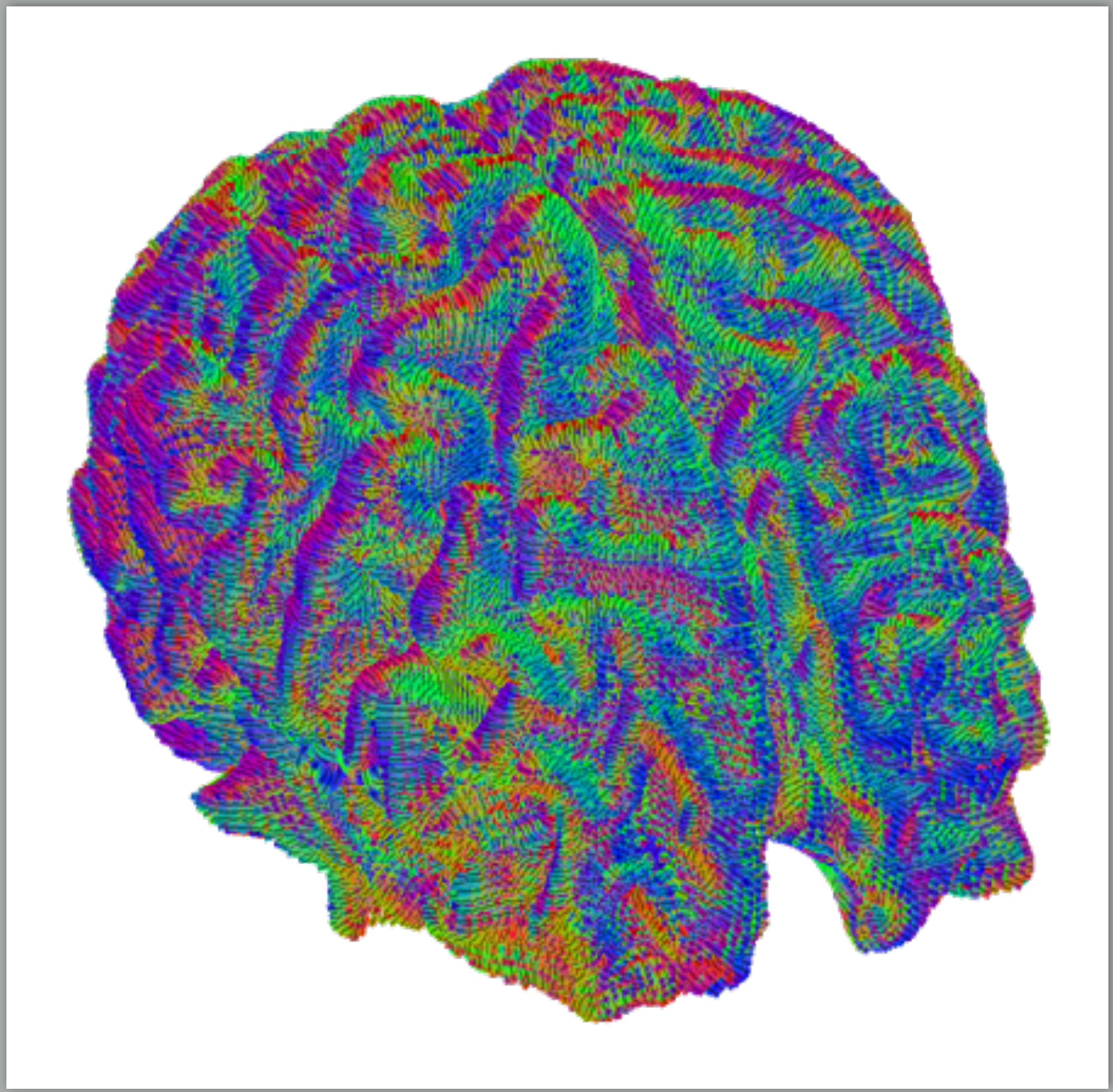
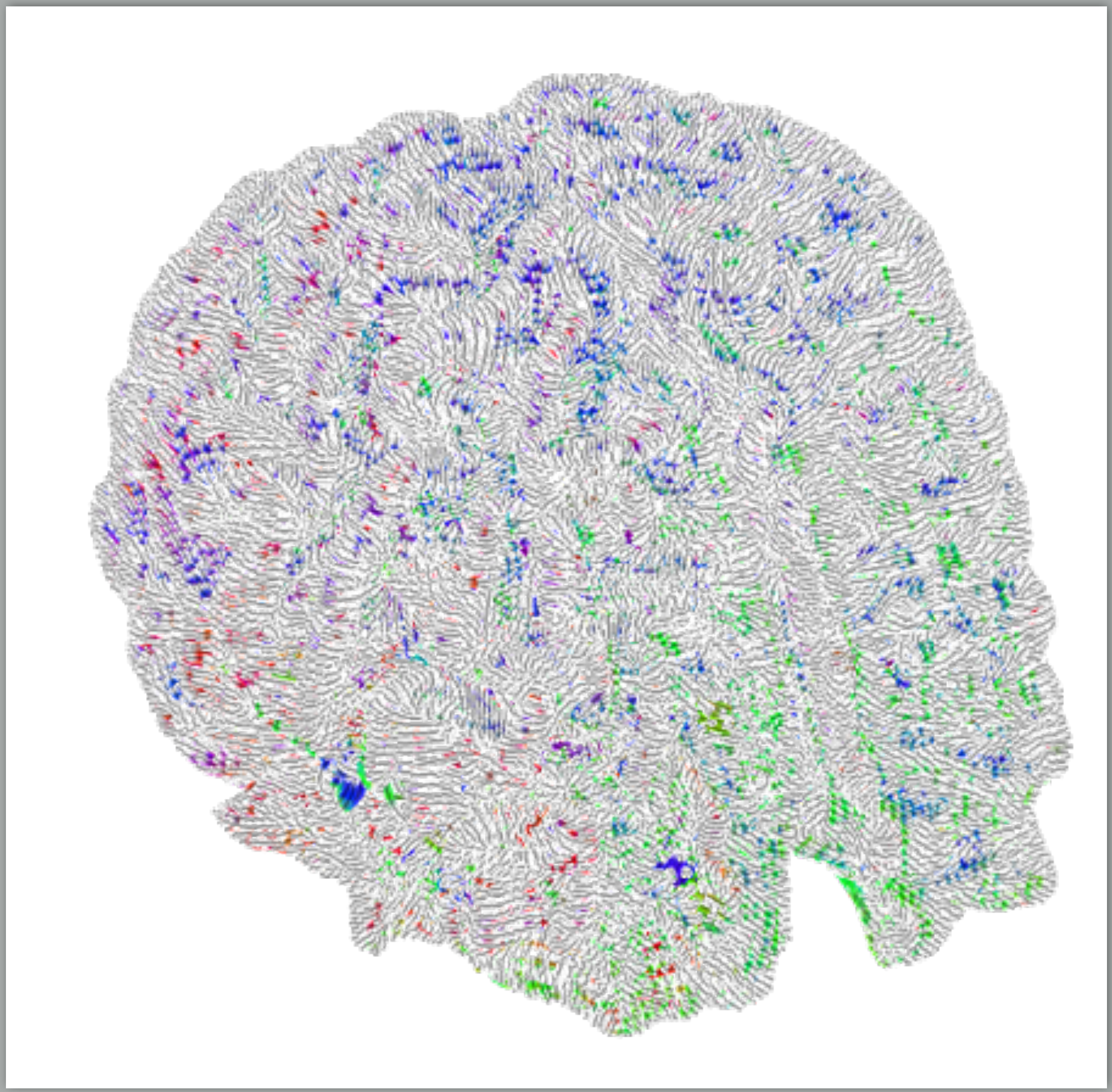
We present a quantitative statistical analysis of pairwise crossings for all fibers obtained from whole brain tractography that confirms with high confidence that the brain grid theory (Wedeen et al., 2012a) is not supported by the evidence. The overall fiber tracts structure appears to be more consistent with small angle treelike branching of tracts rather than with near-orthogonal gridlike crossing of fiber sheets. The analysis uses our new method for high-resolution whole brain tractography that is capable of resolving fibers crossing of less than 10 degrees and correctly following a continuous angular distribution of fibers even when the individual fiber directions are not resolved. This analysis also allows us to demonstrate that the whole brain fiber pathway system is very well approximated by a lamellar vector field, providing a concise and quantitative mathematical characterization of the structural connectivity of the human brain.

"…. confirms with high confidence that the brain grid theory (Wedeen et al., 2012a) is not supported by the evidence."

So what is the Geometric Structure of Brain Fiber Pathways?

The Lamellar Structure of the Brain Fiber Pathways





lamellar

$$v \cdot \nabla \times v = 0$$

helical

$$v \times \nabla \times v = 0$$

Galinsky and Frank, *Neural. Comp. 2016*

Science: Rejected

Referee 1: "The science is sound and I believe that it provides an important contribution to the current debate around the advantages and pitfalls of using neuroimaging to study connectivity."

Referee 2: "…the authors provide unreasonable claims about the potential of their tractography methodology … this leads them to provide charts accounting for millions of crossing in one single voxel that are just beyond reach using diffusion imaging, because of the ill-posedness mentioned by the authors."

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The "most frequent" crossing angle of 18 degrees observed in Fig 1 could just be related to the fan structure of most of the bundles rather than to crossing.

"…the authors discard too rapidly the theory of Van Wedeen that may have some links with this lamellar structure. Focusing on 90 degree crossing is misleading.."

NeuroImage: Rejected

Referee 1:
"much of the results seem anecdotal and the figures don't convey the main findings"

Referee 2:
"…in my opinion, still fails to correctly address the merits and pitfalls of that [Wedeen] work."

Referee 3:
"… the current manuscript does not seem to address "the main finding of their study: the existence of sheet structure. This structure does not depend on fiber orthogonality or the absence thereof" (Wedeen et al. (2012a)). The orthogonal angle hypothesis of Wedeen et al. (2012b) can be seen as a rather separate one, and was already addressed by Catani et al. (2012)."