Advances in Cognitive Neuroscience Methods

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SCHEDULE

Wednesday, July 10

2:15 **Rainer Goebel** *Modeling causality*
3:15 **Jarrod Lewis-Peacock** *Multi-voxel pattern analysis of fMRI data*

4:00 ---------------------*Break* -------------------------
4:15 **Brian Wandell** *The human connectome: Diffusion imaging and tractography*

Thursday, July 11

9:00 **Yaniv Assaf** *Advanced Imaging Techniques*
10:00 **Daniel Yoshor** *Studies of Perception in Human Subjects with Semi-Chronically Implanted Intracranial Electrodes*

11:00 ---------------------*Break* -------------------------
11:15 **Tilman Kispersky** *Variability in nervous systems as a guiding principle in constructing computational models*

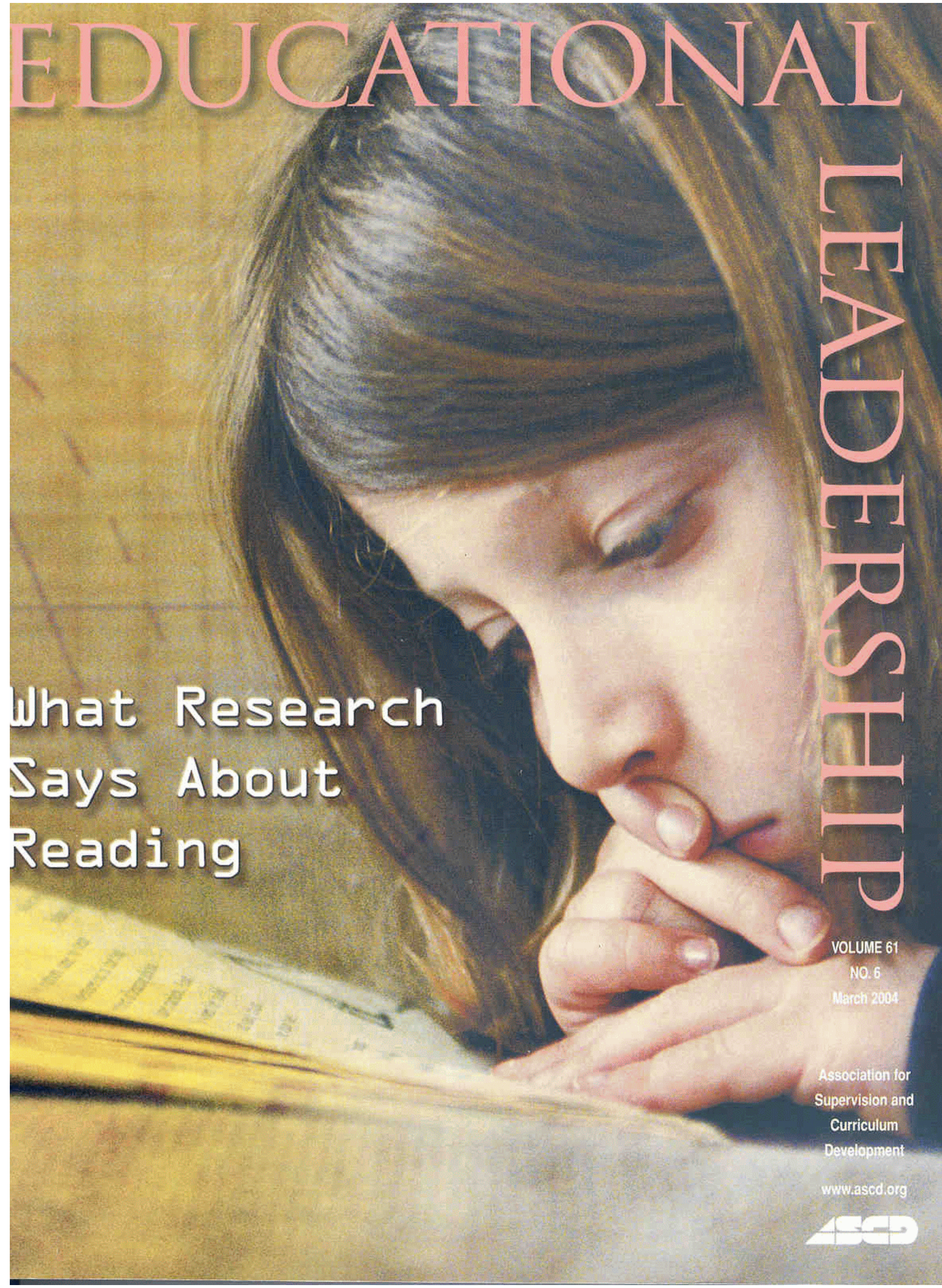
12:30 pm ---------------------*Break* ------------------------
2:00 **Karl Deisseroth** *Optogenetics*
3:00 **Dan Marcus** *Neuroimaging Informatics*

Diffusion imaging (and reading)

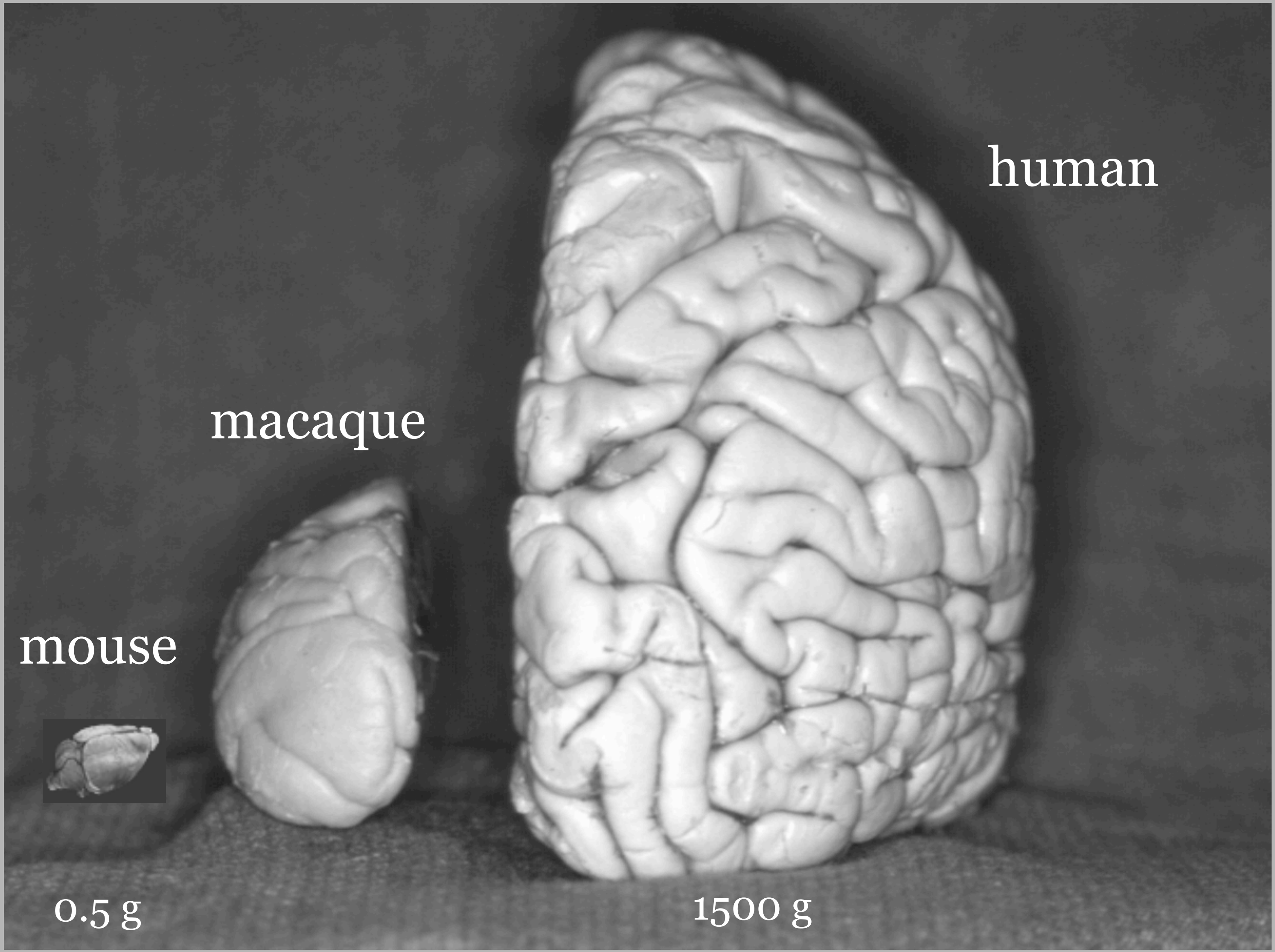
- What I would like to understand
- Why the white matter tracts (fascicles) matter
- How we measure fascicles with diffusion imaging
- What we learned about reading

Brain systems that must develop for a child to learn to read

- Most children in the US learn to read. But not all. Why?
- A safe neighborhood, supportive family, and a decent breakfast would often be the biggest help
- After accounting for these factors, some people still don't read (CS)
- Why?



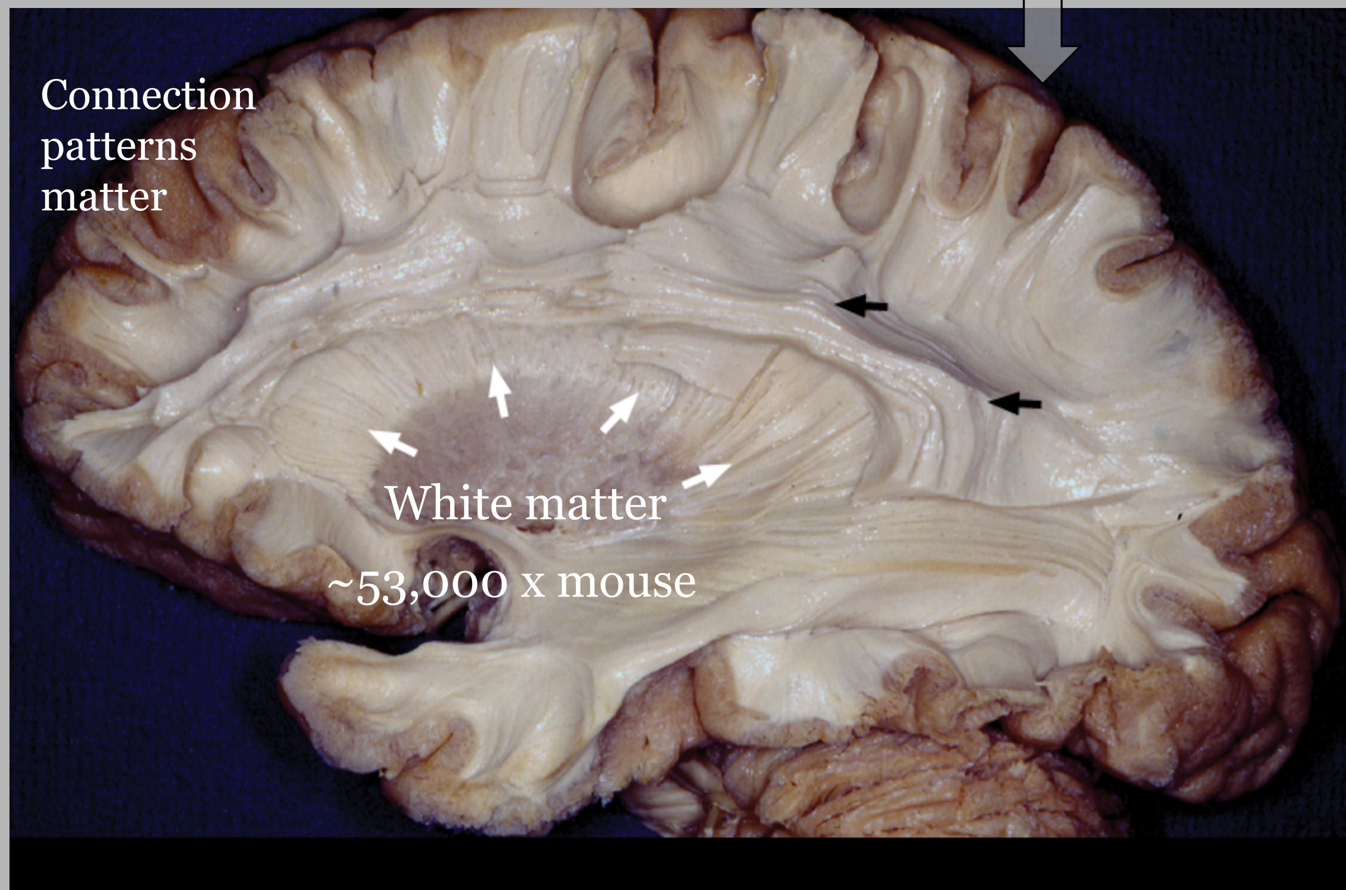
The human brain
(image adapted from J. Horton)



Human brain characteristics

- Neuron cell bodies in cortex
- Many long-range neuronal axons in white matter
- Glia everywhere
- A system with active wires
- Reading evokes neuronal signals in many locations
- Reading skill correlates with white matter tissue properties

Cortex ~7500 x mouse

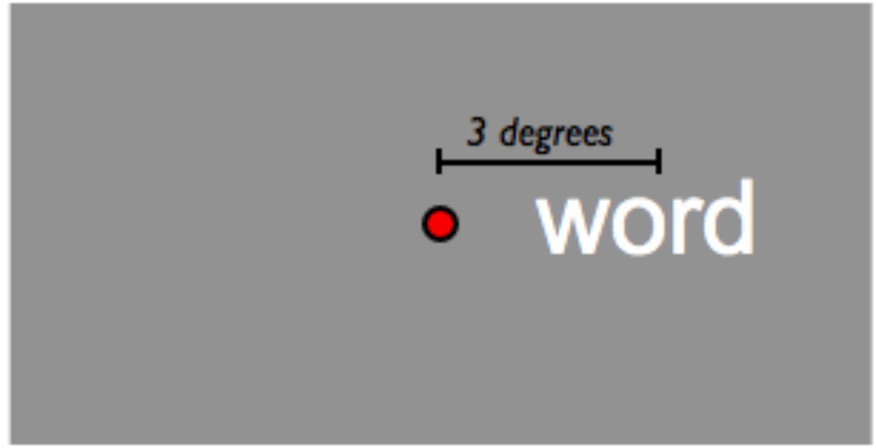


Courtesy Professor Ugur Ture

Functional MRI (fMRI)

Measuring reading activity in human cortex

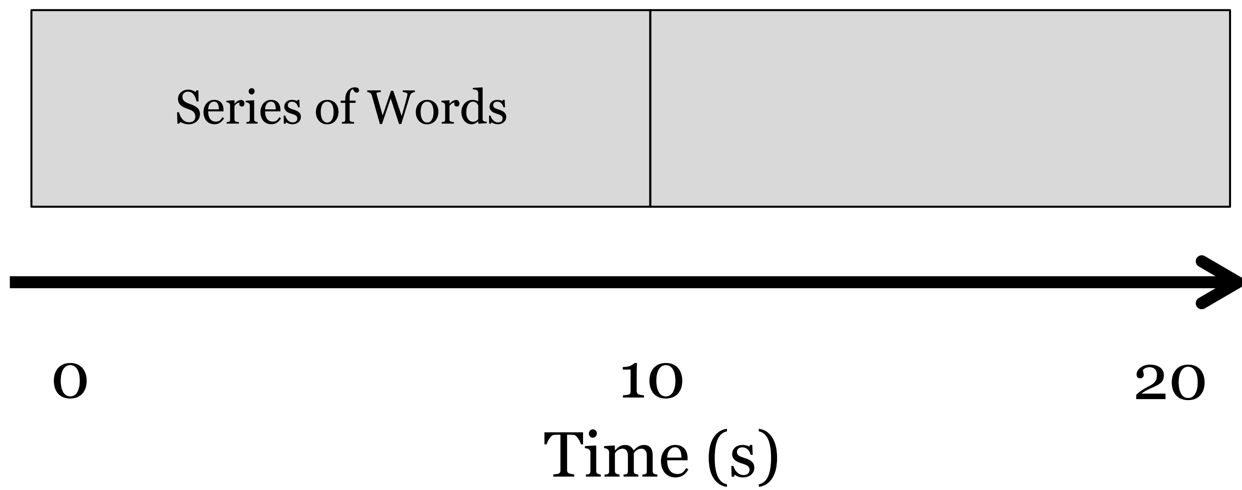
Reading single words



Subject is in an MRI scanner

S/he makes judgments about the words

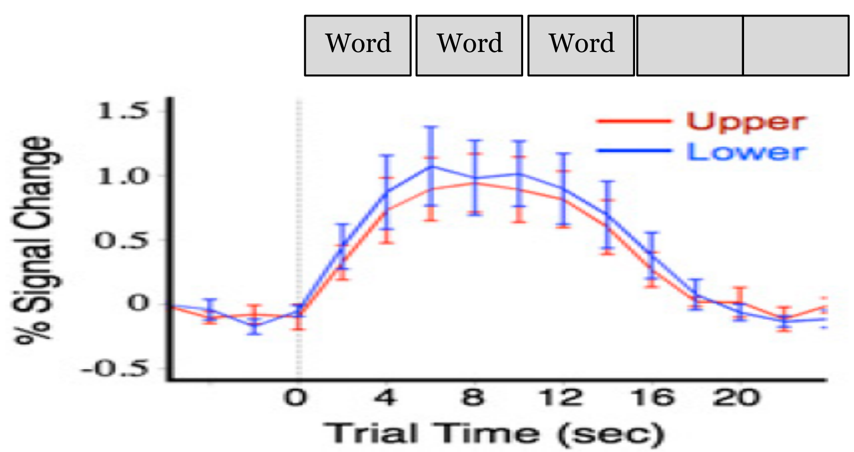
The scanner records activity corresponding to the subject's thoughts



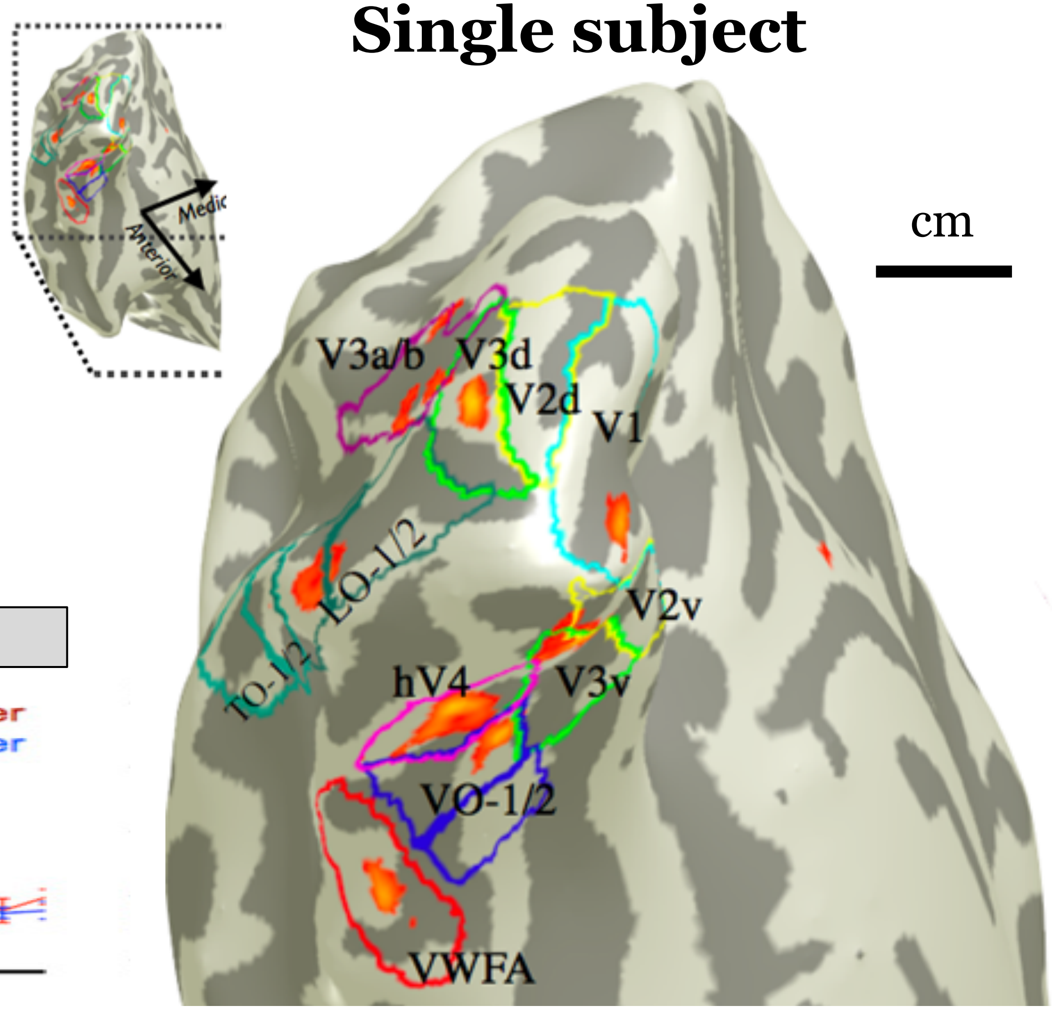
MRI has high spatial resolution

- Many locations respond – which we measure in the fMRI time series
- Some regions are general, others specific to reading

VWFA time series

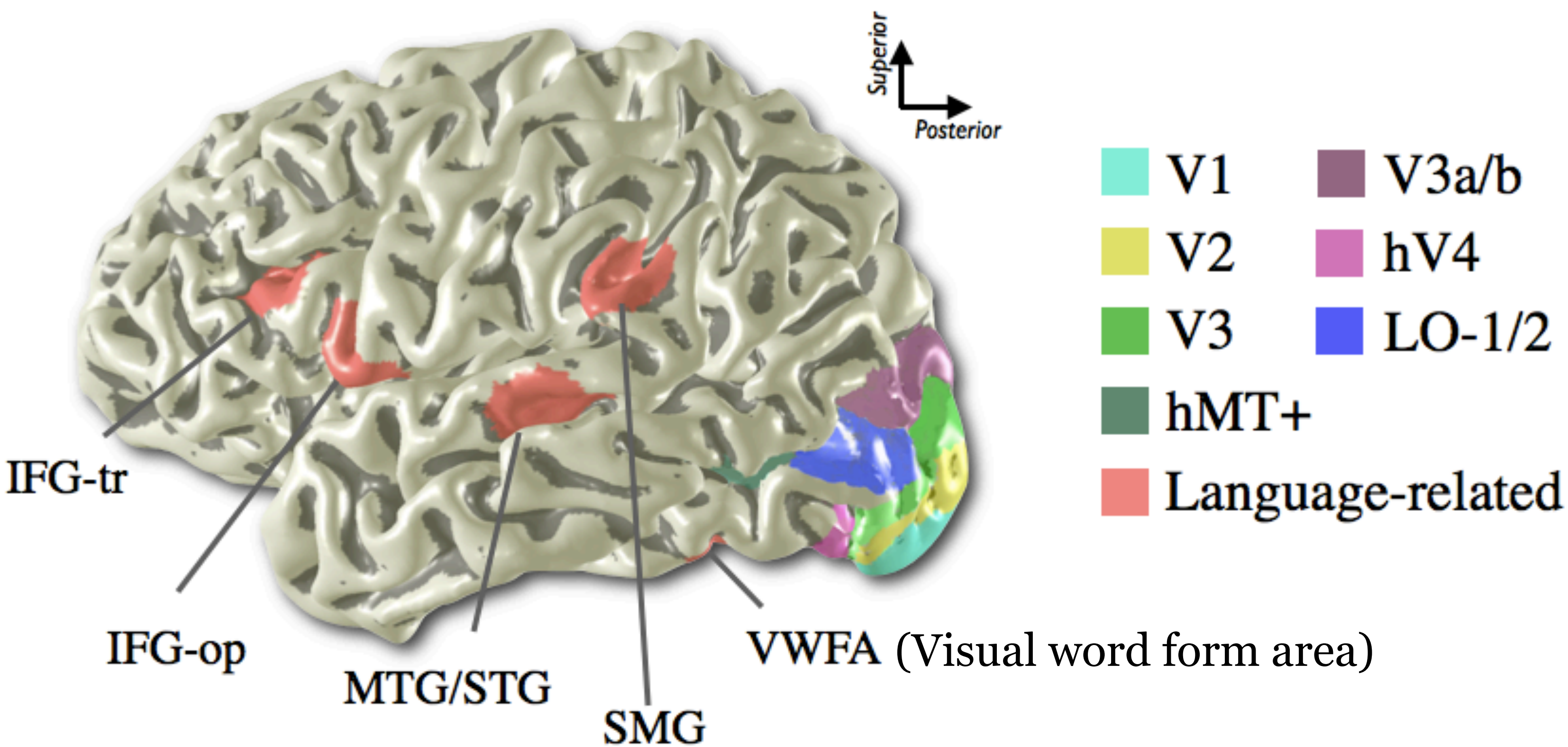


Single subject



MRI measures has a large field of view

The method can be used to find global circuitry

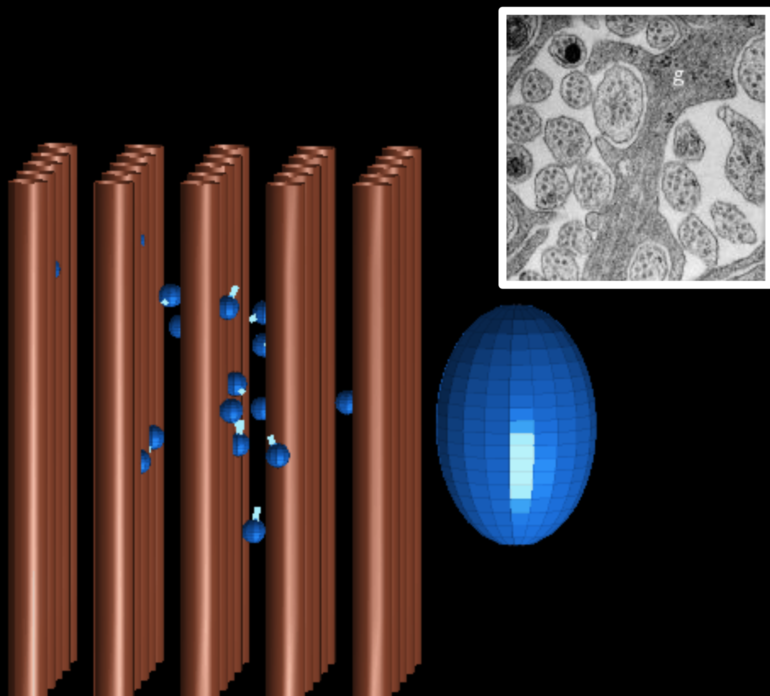


Diffusion MRI and quantitative MRI

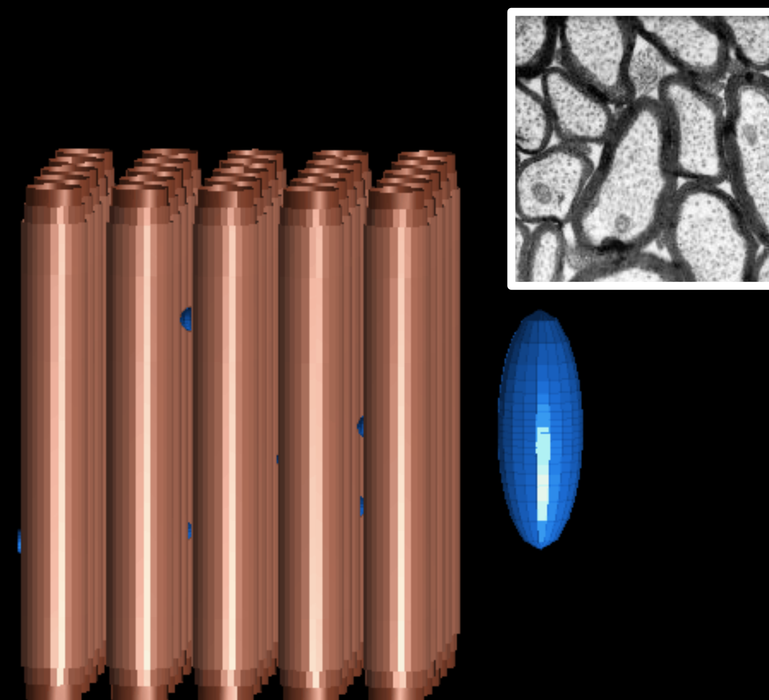
Measuring tissue properties

Inferring tissue biology from diffusion

- Diffusion is very sensitive to tissue changes and can generate hypotheses about potential biological processes

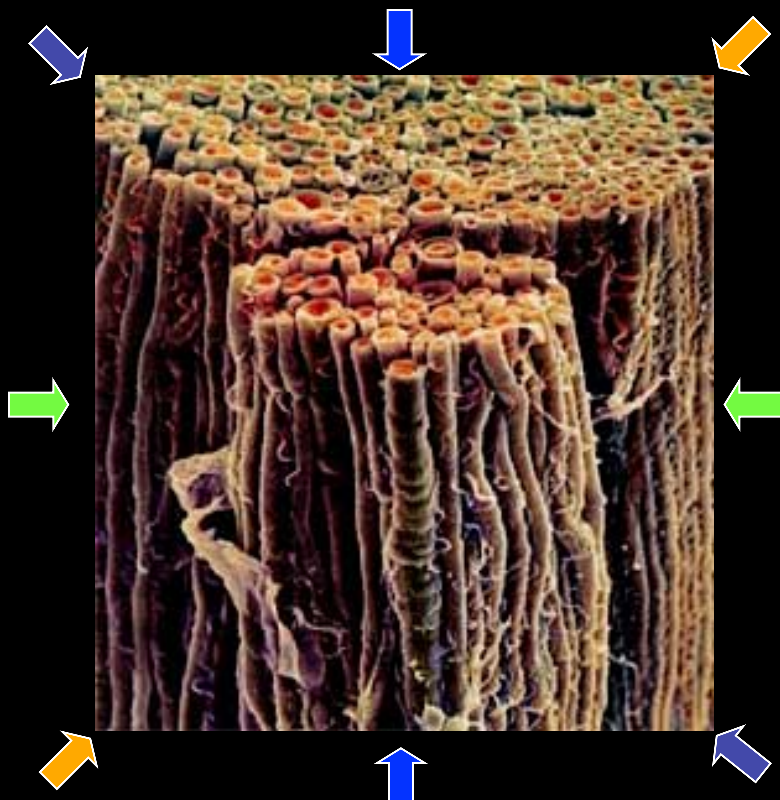


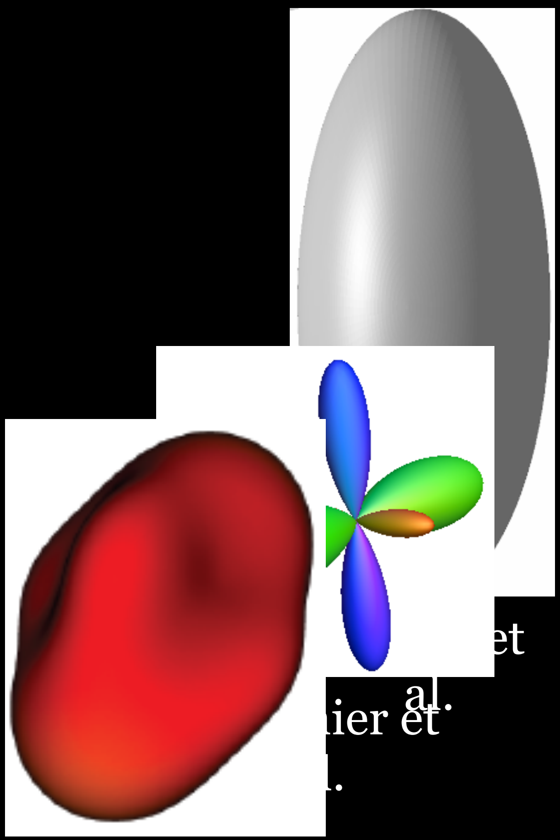
Low Fraction Anisotropy (FA)
High Apparent Diffusion Coefficient (ADC)



High Fraction Anisotropy (FA)
Low Apparent Diffusion Coefficient (ADC)

Summaries of diffusion





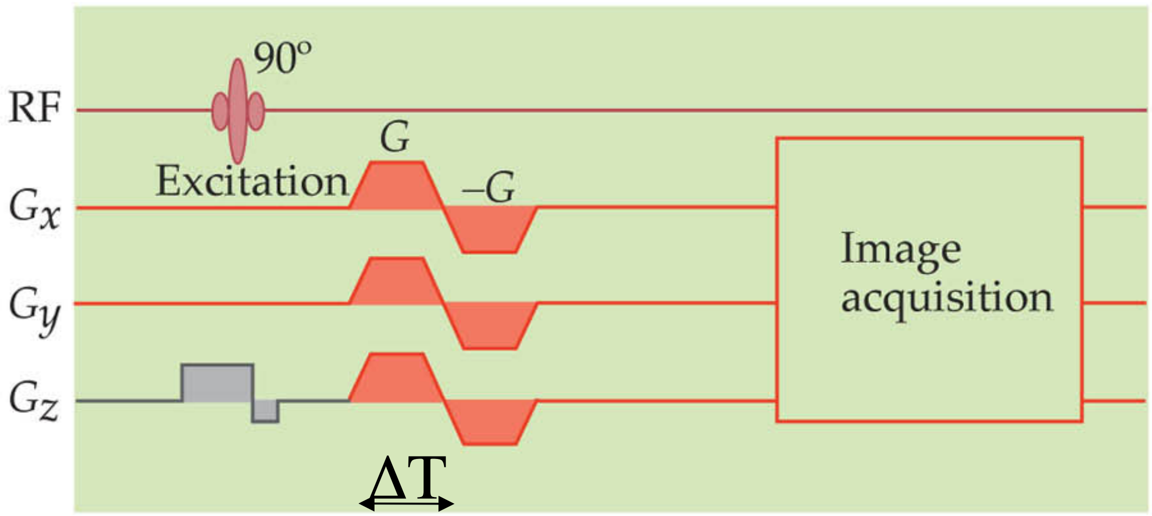
Rokem et al.

Basser (1995). *NMR Biomed; Feldman, Yeatman et al. (2010). J. Dev. Behav. Pediatr.*

Diffusion weighted MRI measurement

Diffusion-weighted gradient echo sequence
(Stejskal-Tanner)

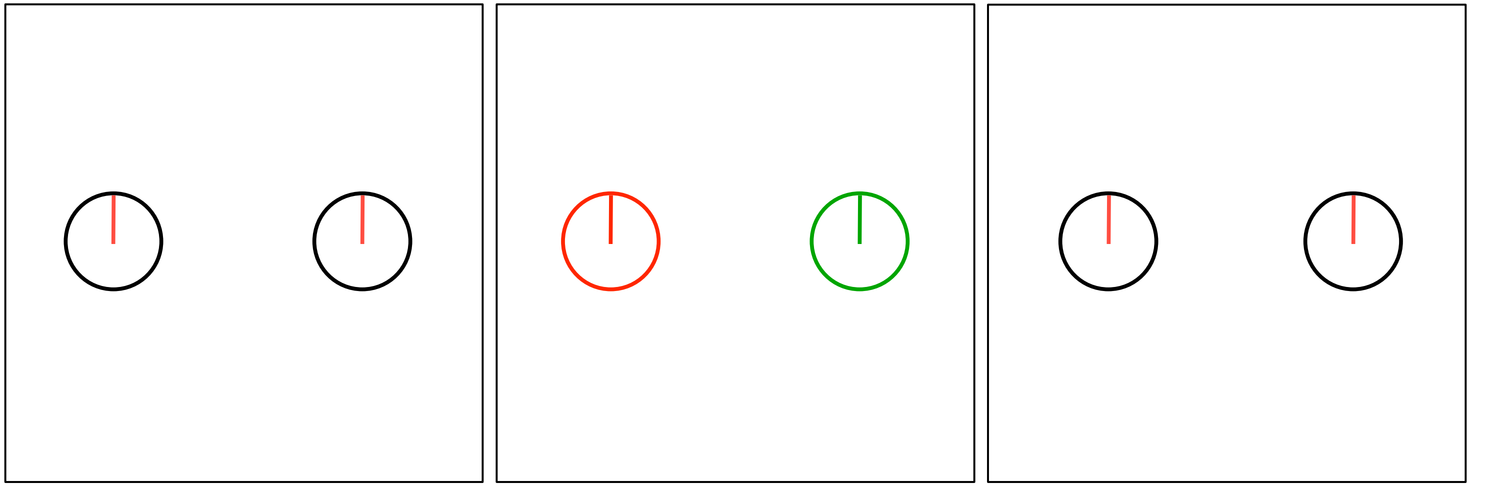
- Gradient pair (G,-G) has no net effect on stationary spin
- Moving spins are not re-phased by second pulse
- Phase-dispersion causes a signal decay that depends on the distance moved during time DT (diffusion time)



Functional Magnetic Resonance Imaging (2004). Huettel et al., Fig 5.19B

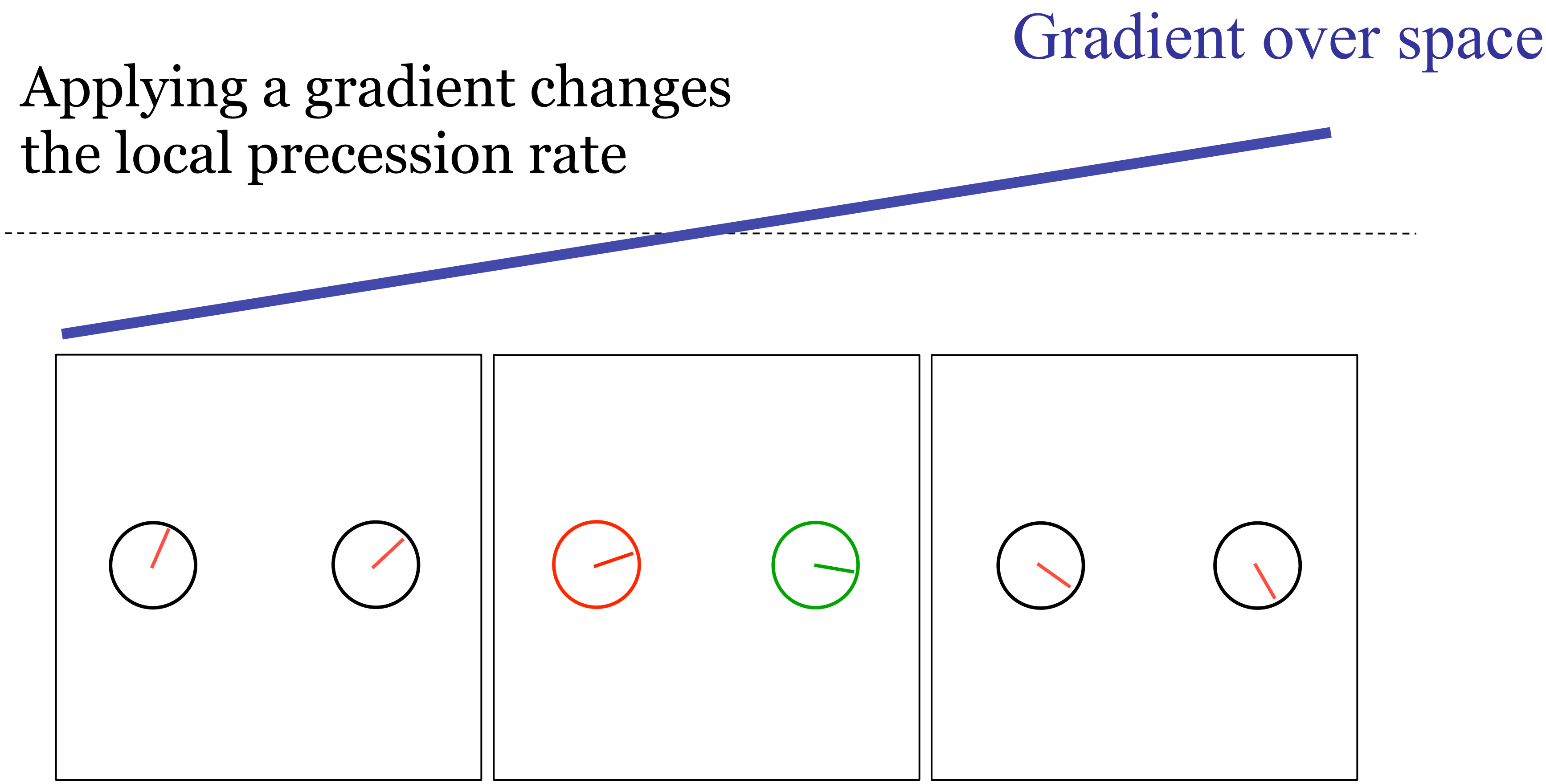
Protons precessing

In a steady-state magnetic field after an RF pulse, the protons precess in phase



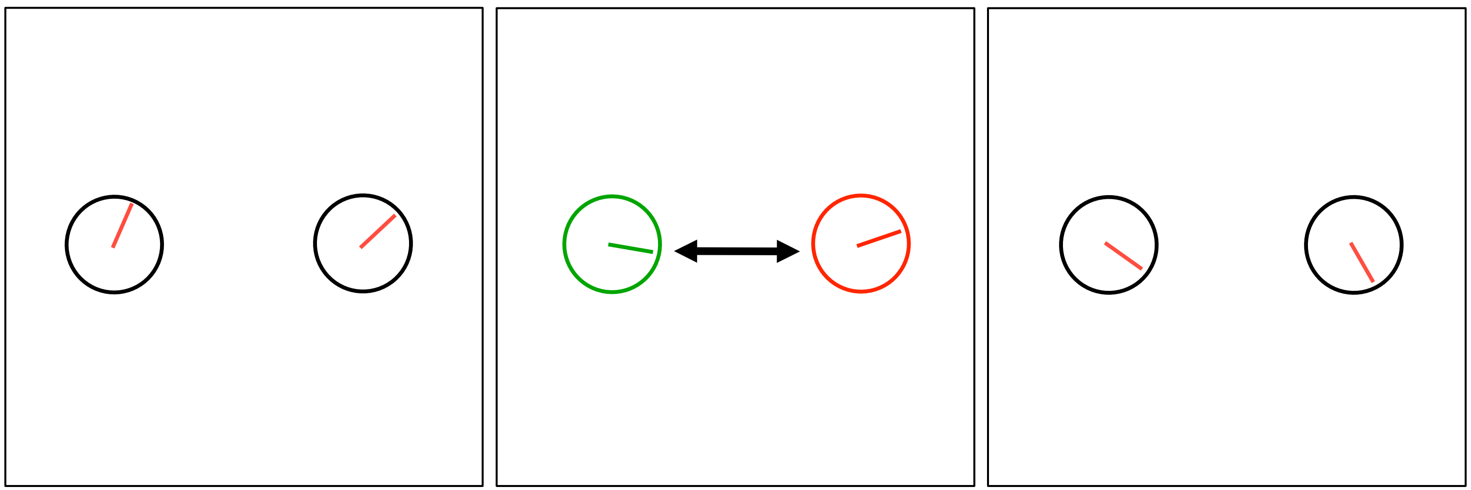
Diffusion weighting: First gradient

Applying a gradient changes the local precession rate



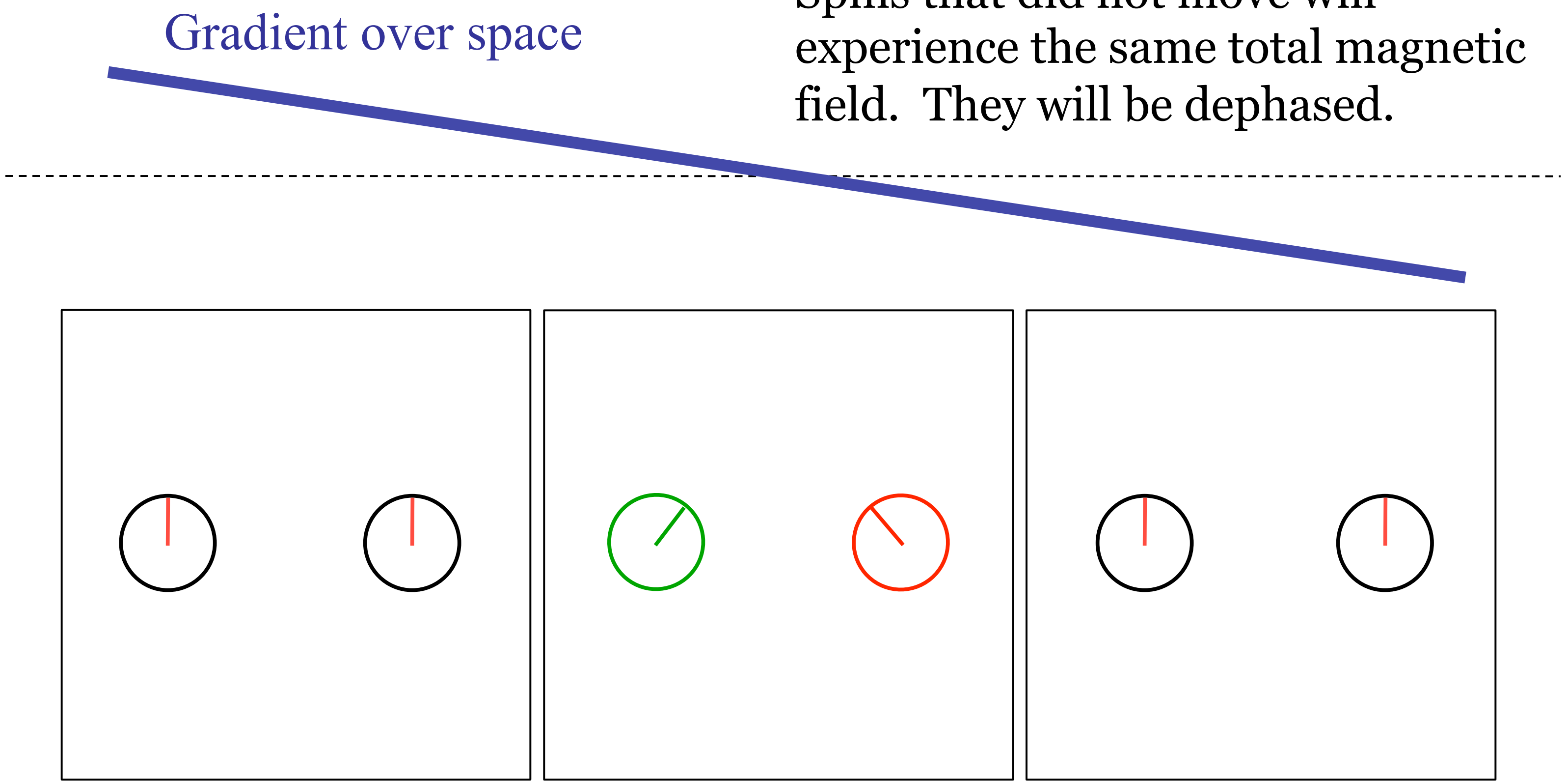
Time to diffuse

In 1 ms, a water molecule at body temperature will be, on average, 1um from its starting point; some more and some less because of hindered paths



Diffusion Weighting: Second gradient

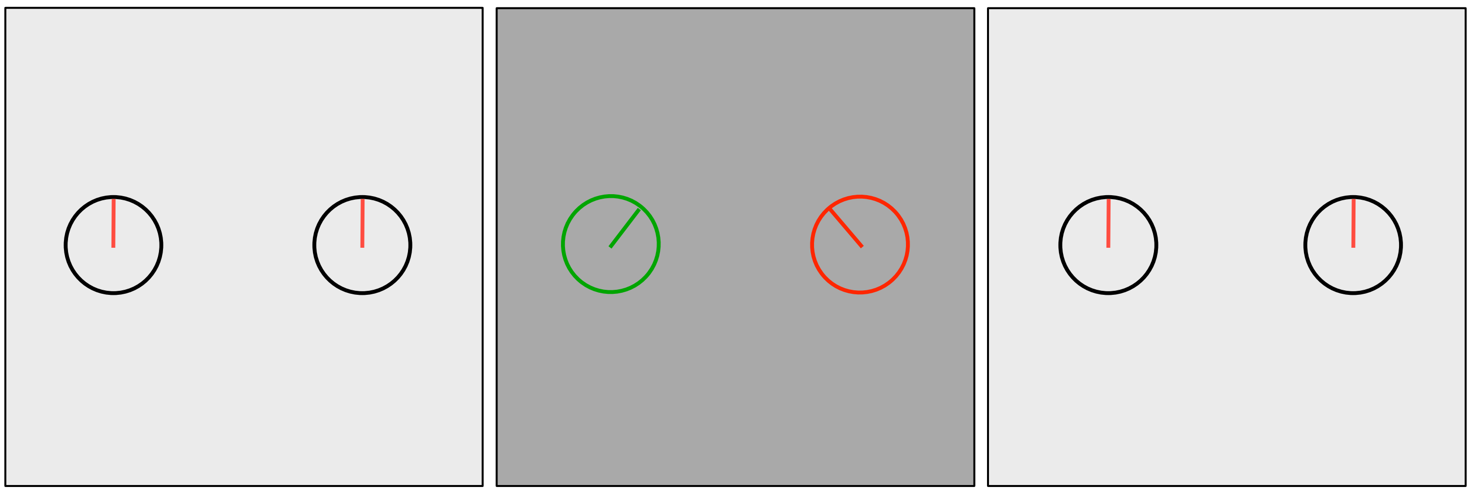
Spins that did not move will experience the same total magnetic field. They will be dephased.



Larger displacement reduces signal because of spin dephasing

Signal attenuation = exp(-b * ADC)

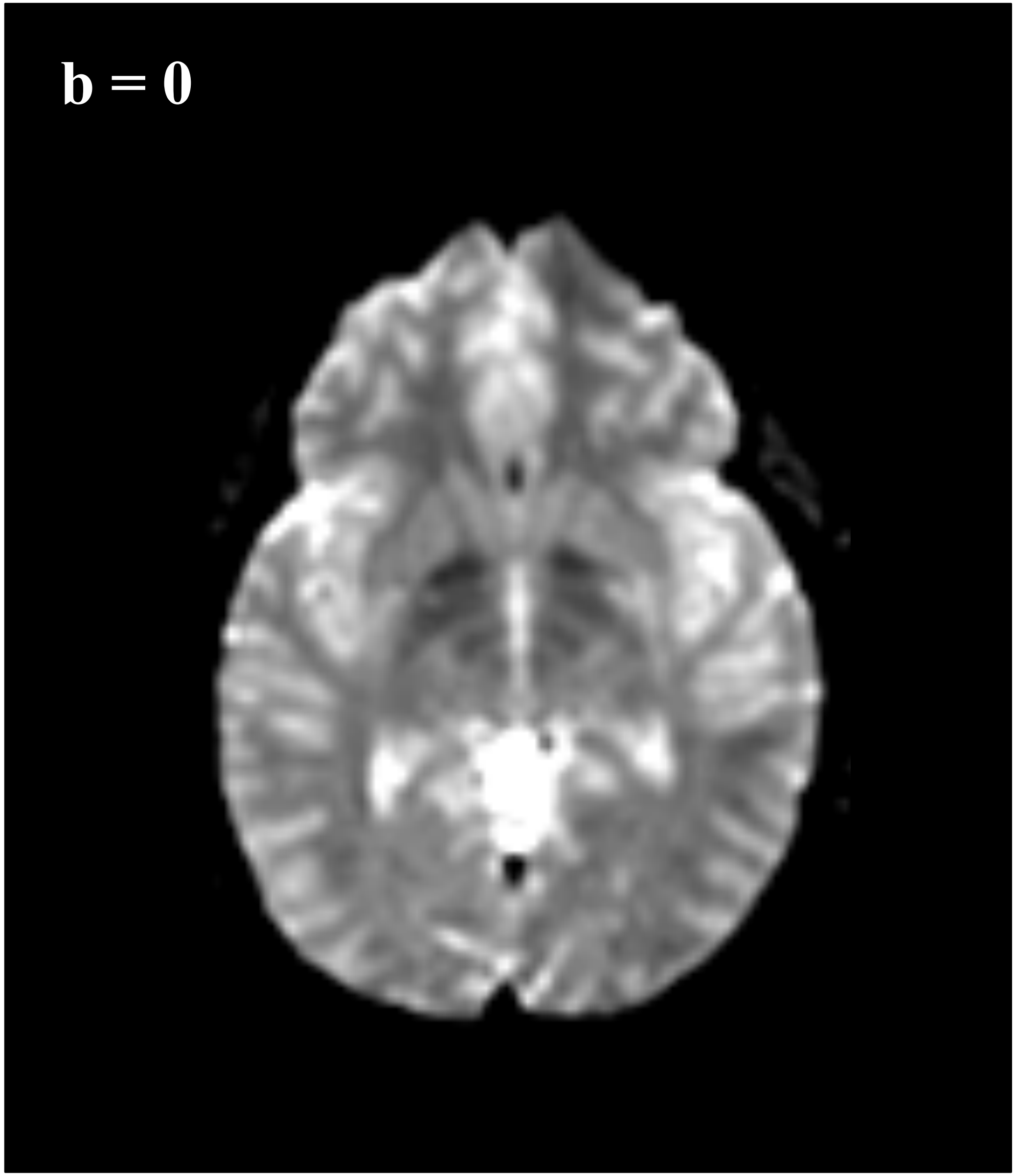
The b-value depends on the slope of the gradient, its duration and a few physical constants



Stejskal-Tanner equation:

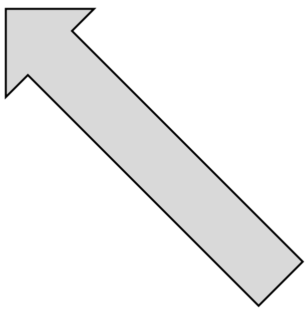
Non-diffusion MR image

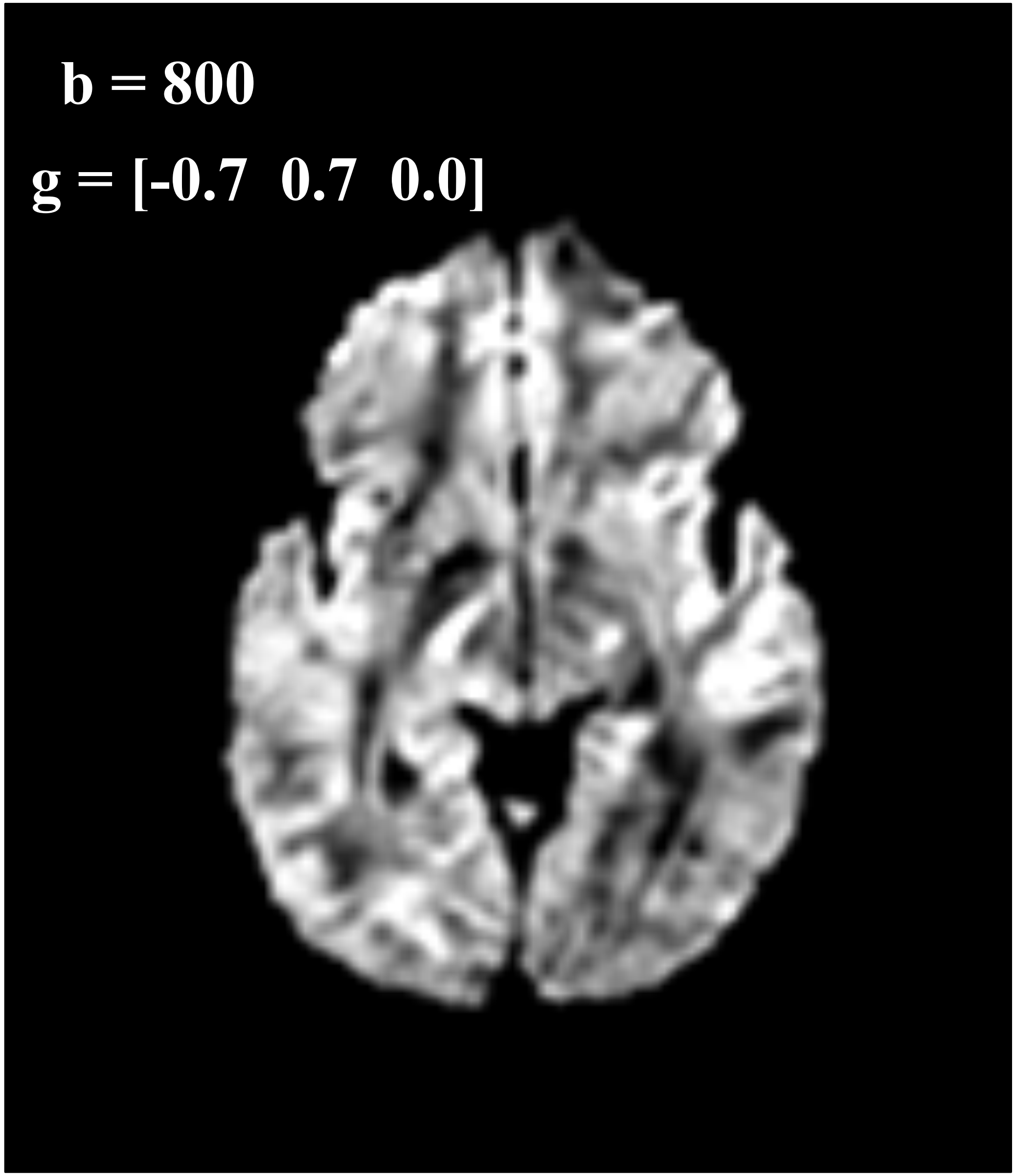
Dark means large
signal attenuation
High ADC



Diffusion weighted images

Dark means large signal attenuation
High ADC





Diffusion weighted images

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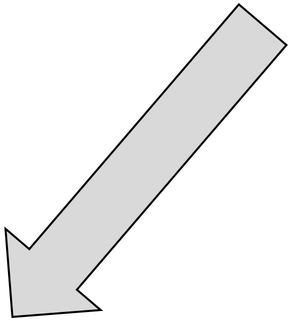
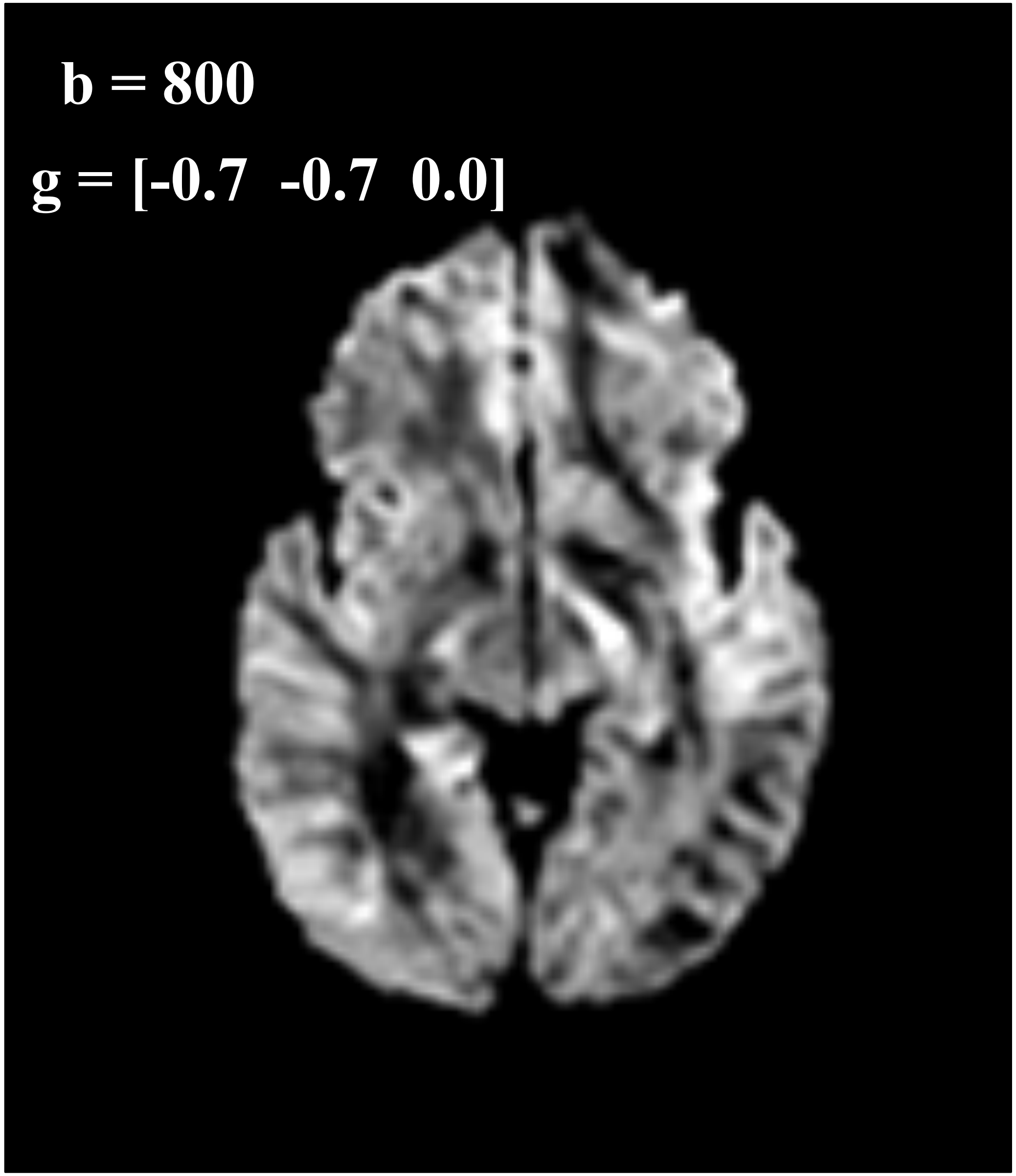
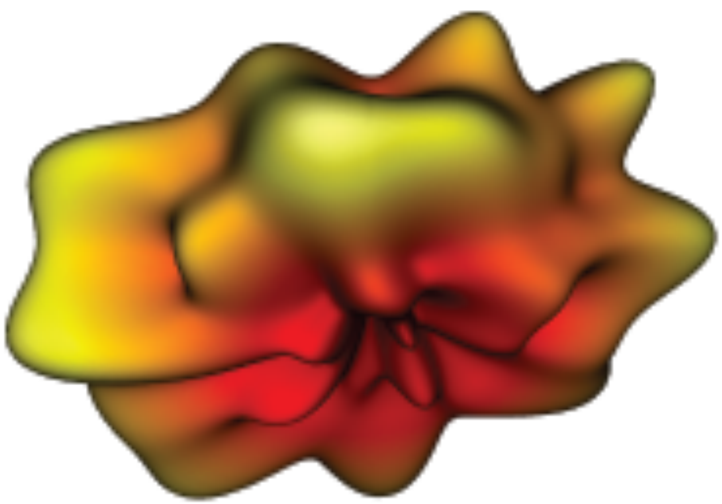




Diffusion data analysis

High angular resolution diffusion imaging (HARDI)

MRI diffusion signal



$$S(\theta) = S_0 \, e^{-bA(\theta)}$$

The measured diffusion signal in a direction, θ, is related to the apparent diffusion coefficient in that direction, A(θ), by this exponential formula

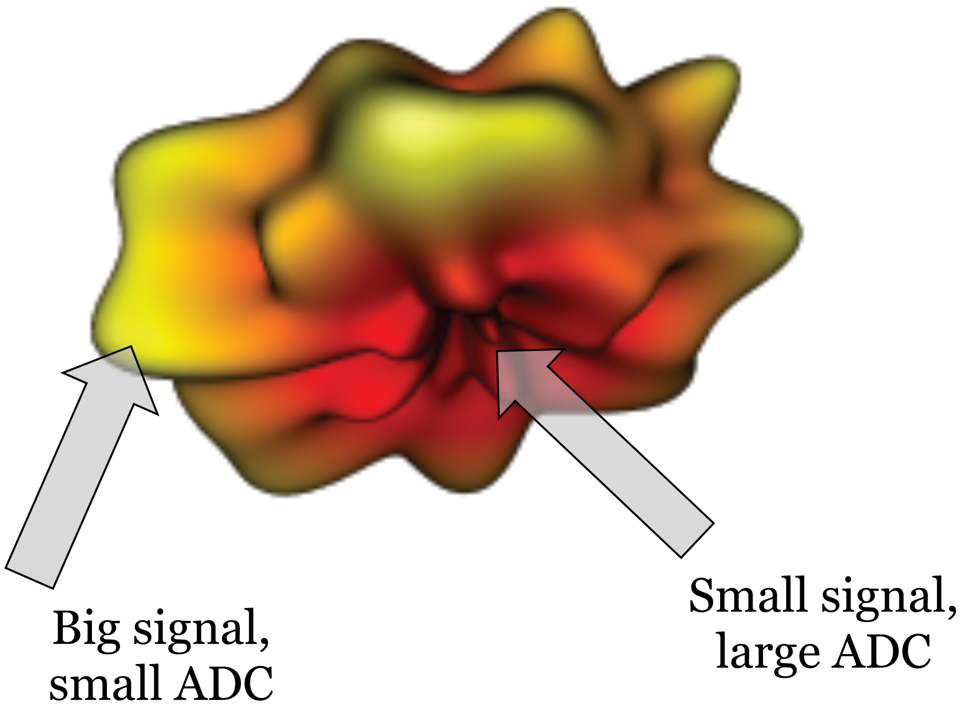
Thanks to Ariel Rokem

Diffusion data analysis

High angular resolution diffusion imaging (HARDI)

MRI diffusion signal

$$S(\theta) = S_0 \, e^{-bA(\theta)}$$



The measured diffusion signal in a direction, θ, is related to the apparent diffusion coefficient in that direction, A(θ), by this exponential formula

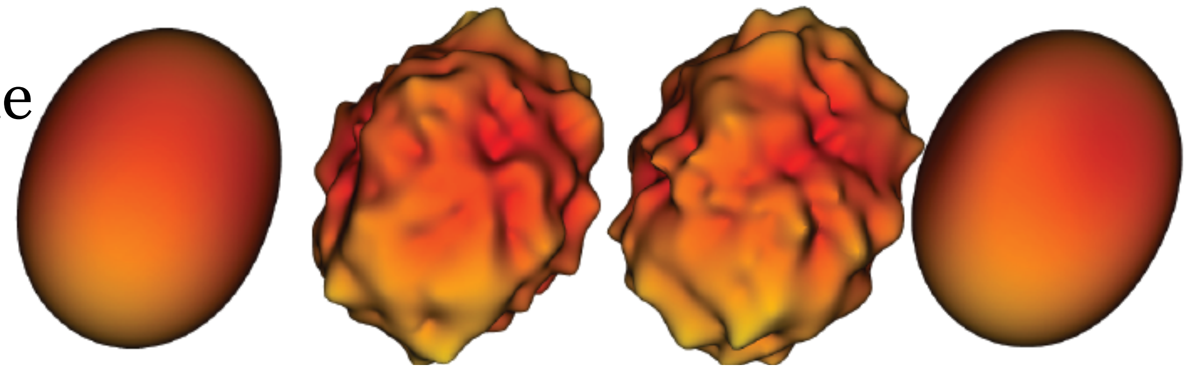
Thanks to Ariel Rokem

Models and data replication

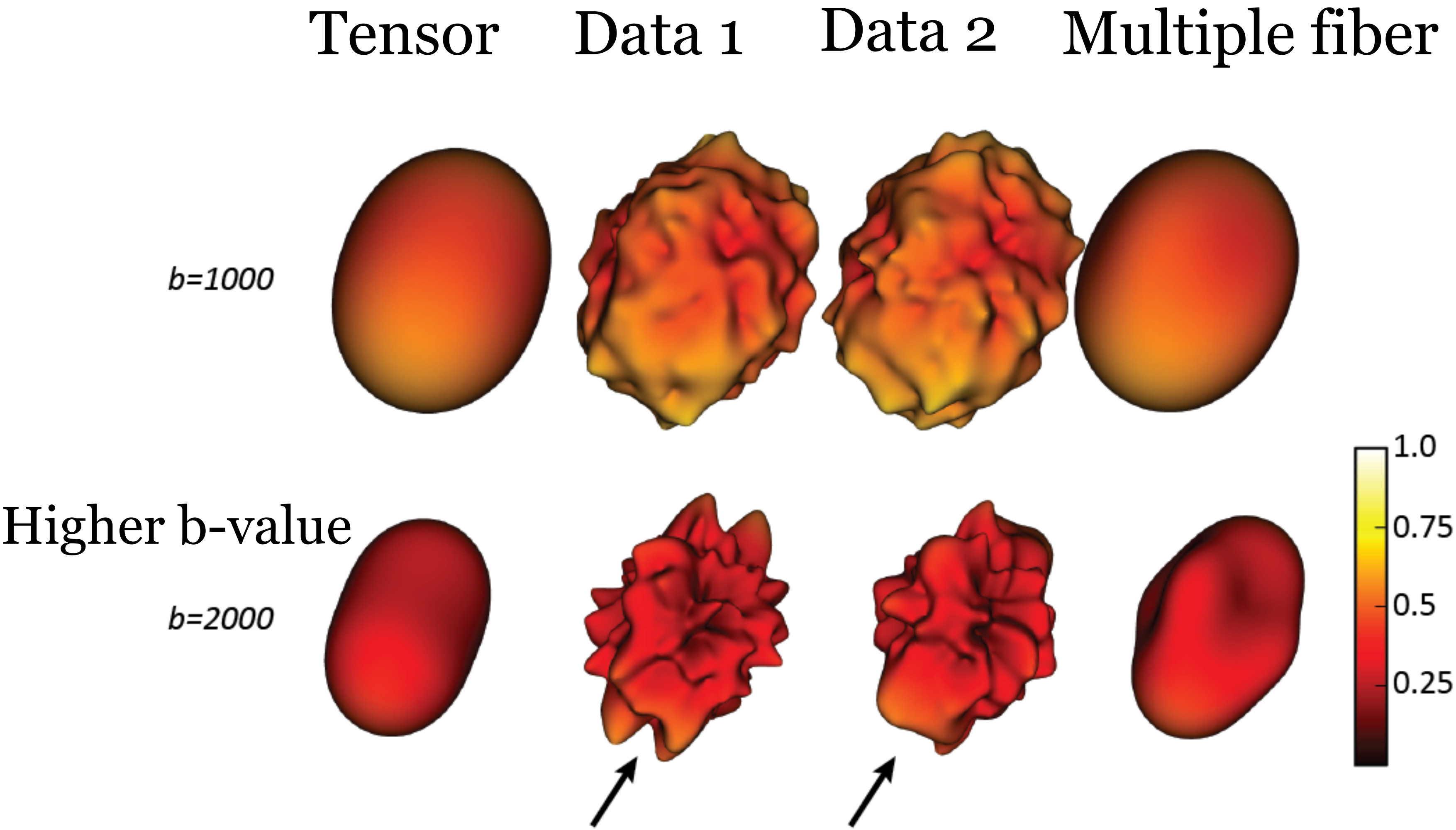
Tensor Data 1 Data 2 Multiple fiber

Low b-value

b=1000

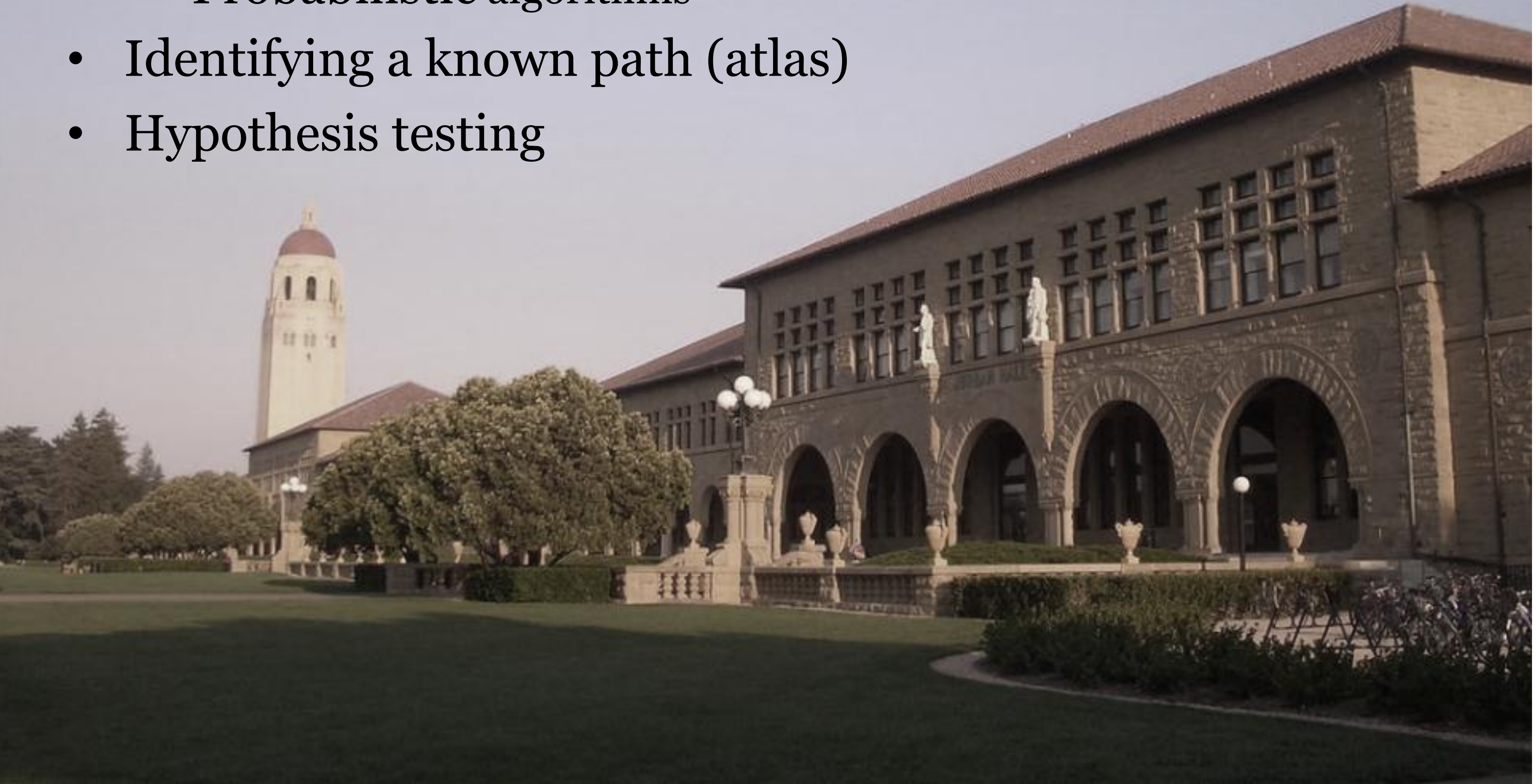


Models and data replication



Tractography

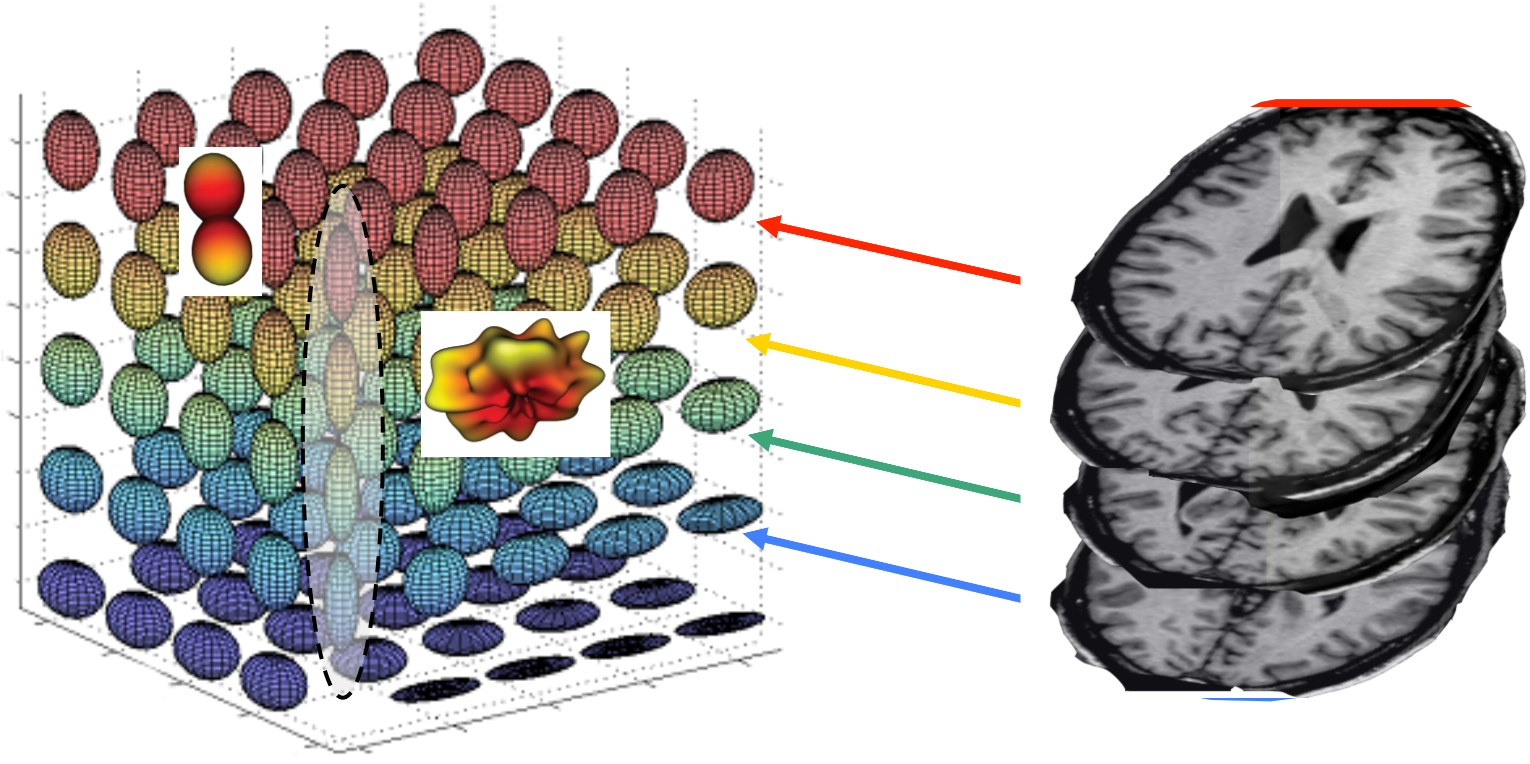
- Path discovery
  - Deterministic algorithms
  - Probabilistic algorithms
- Identifying a known path (atlas)
- Hypothesis testing



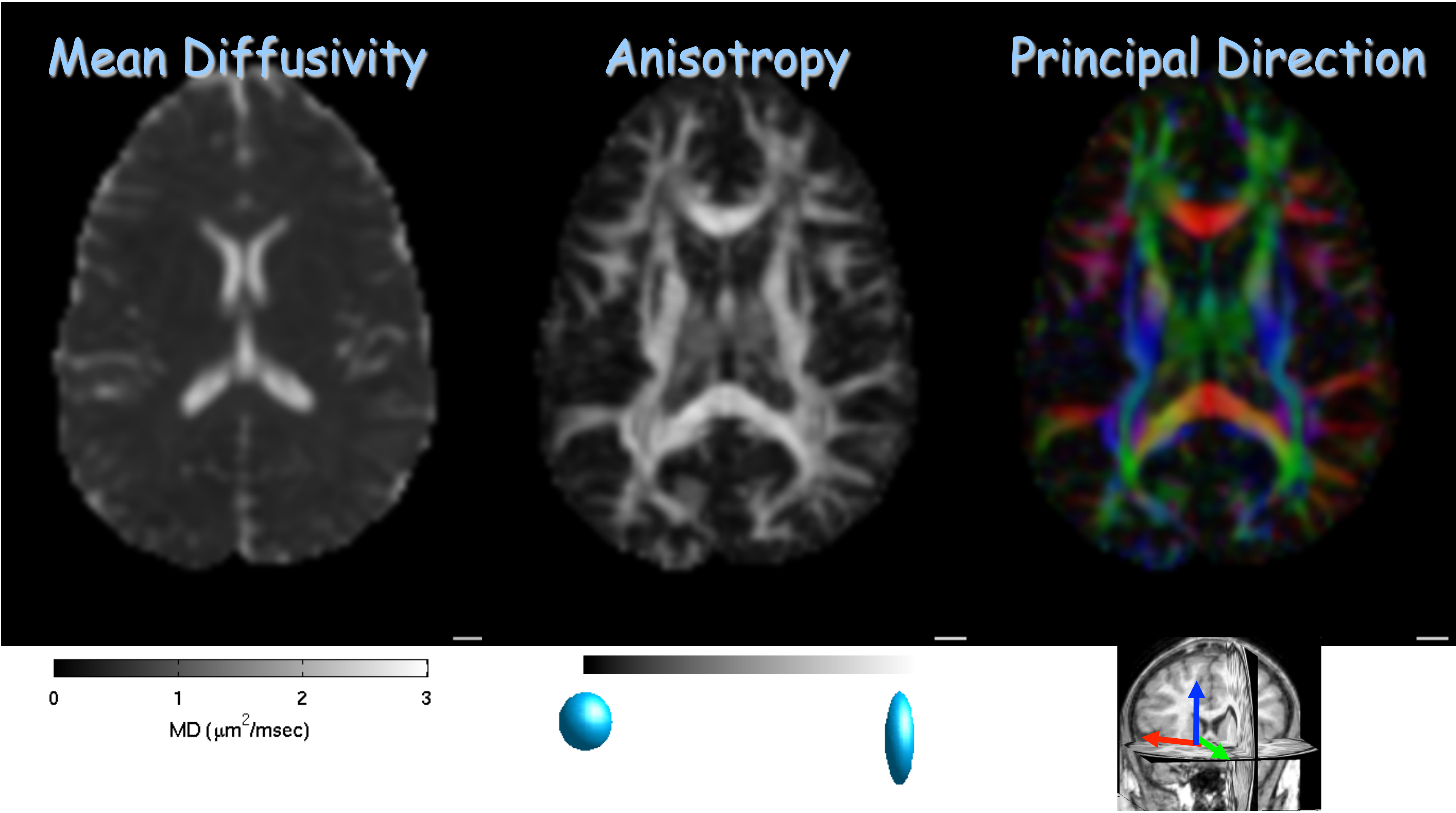
Tractography

Use the local (voxel) diffusion measurements to estimate white matter tracts

Diffusion data are surfaces



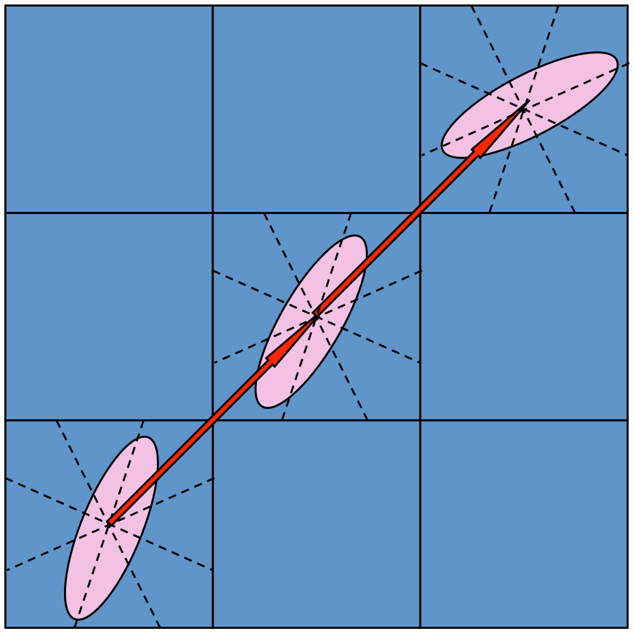
DTI Reveals White Matter Structure



Connect-the-Voxels

(Conturo et al., 1999; PNAS)

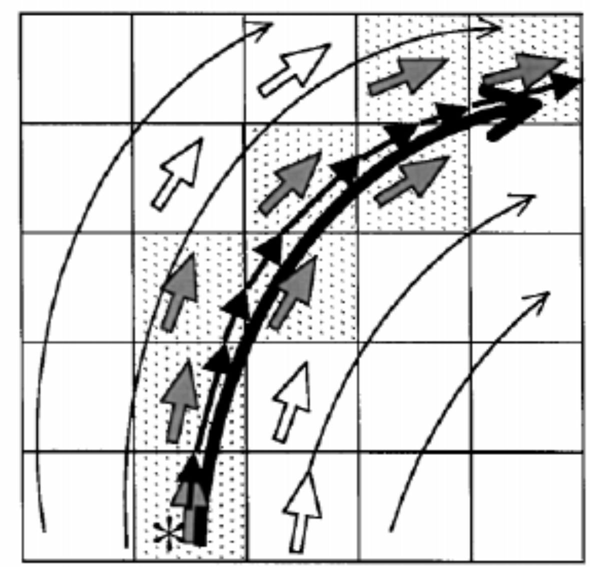
- Super-samples the tensor field (e.g., resample from 2 mm to 0.5mm)
- Bi-directionally follow voxels in PDD direction (on the grid)
- Stopping rule: Tensor anisotropy becomes small.



Fiber Assignment by Continuous Tracking
(FACT; Mori et al., 1999)

- Starting in a seed voxel, step in PDD until voxel edge
- Use tensor from the next voxel
- Continue in PDD until the next edge
- Paths fall between data samples; separates tensor sampling resolution and path resolution

Modified algorithm



• Mori et al. (1999). *Three-Dimensional Tracking of Axonal Projections in the Brain by Magnetic Resonance Imaging.* Annals of Neurology.

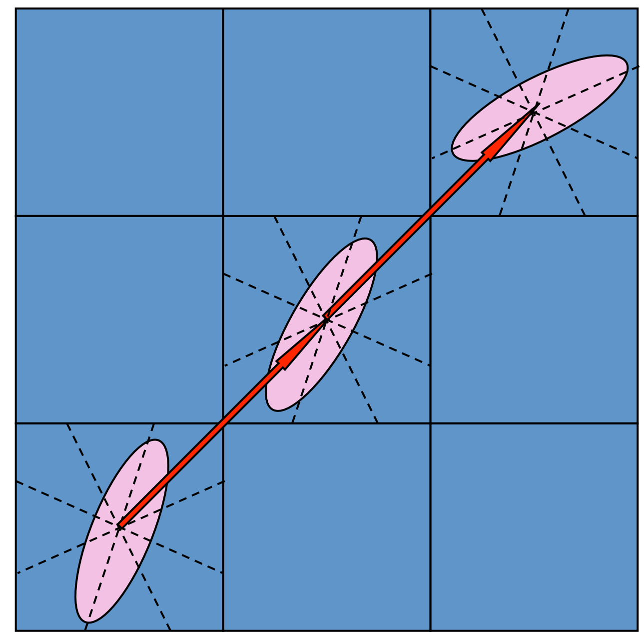
• Xue et al. (1999) *In Vivo Three-Dimensional Reconstruction of Rat Brain Axonal Projections by Diffusion Tensor Imaging.* MRM.

Probabilistic tractography

(Behrens et al.,2003; Danny Alexander's group)

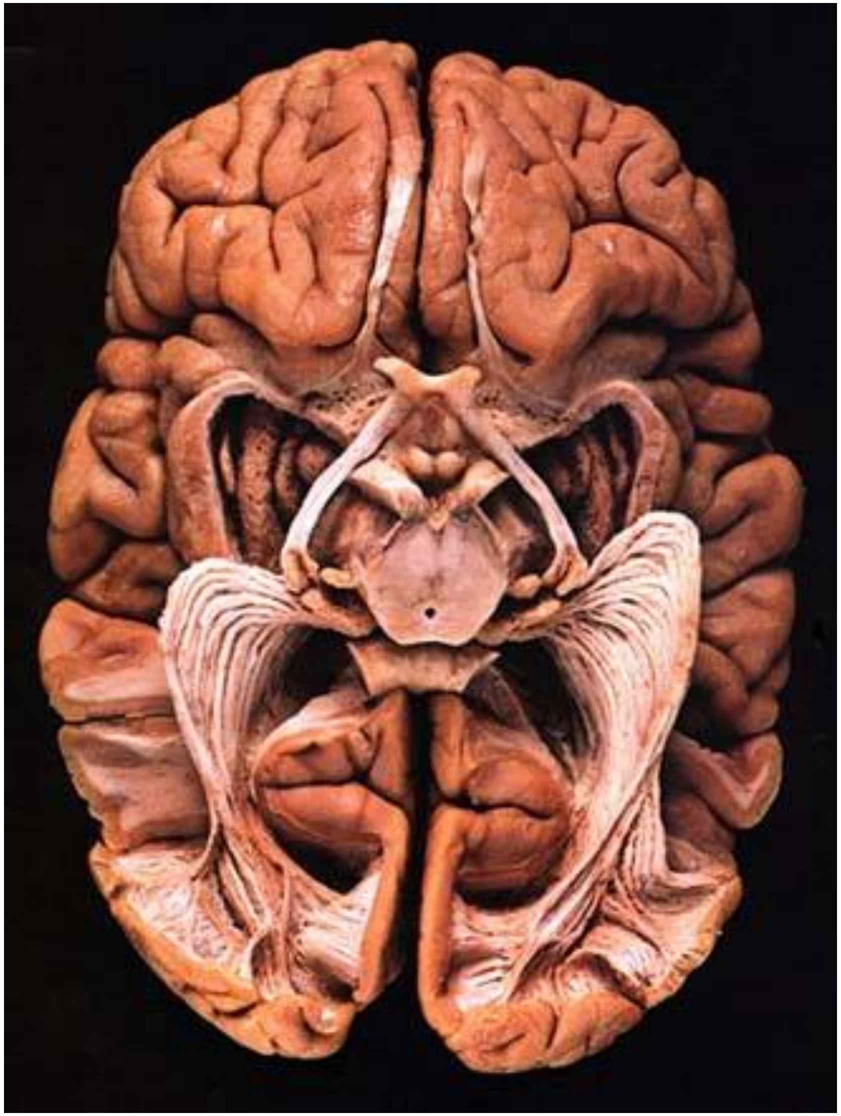
- Super-sample the field and allow non-tensor shapes
- Bi-directionally follow voxels in PDD direction (on the grid)
- Repeatedly trace a path, but choose directions at each step from a probability distribution of angles determined by local diffusion shape
- Stopping rule: No strong direction in local data
- Connection probability

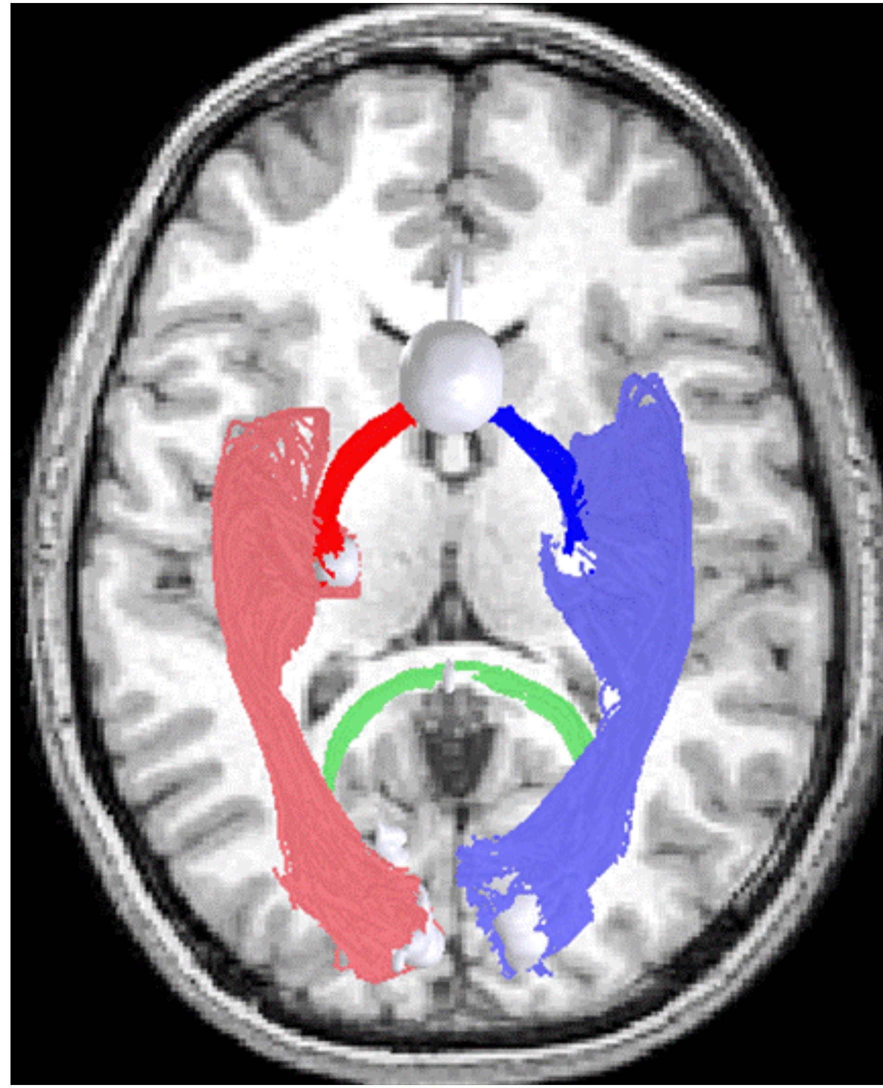
0.5 mm super-sampled data



Estimating pathways of known tracts (Contrack)

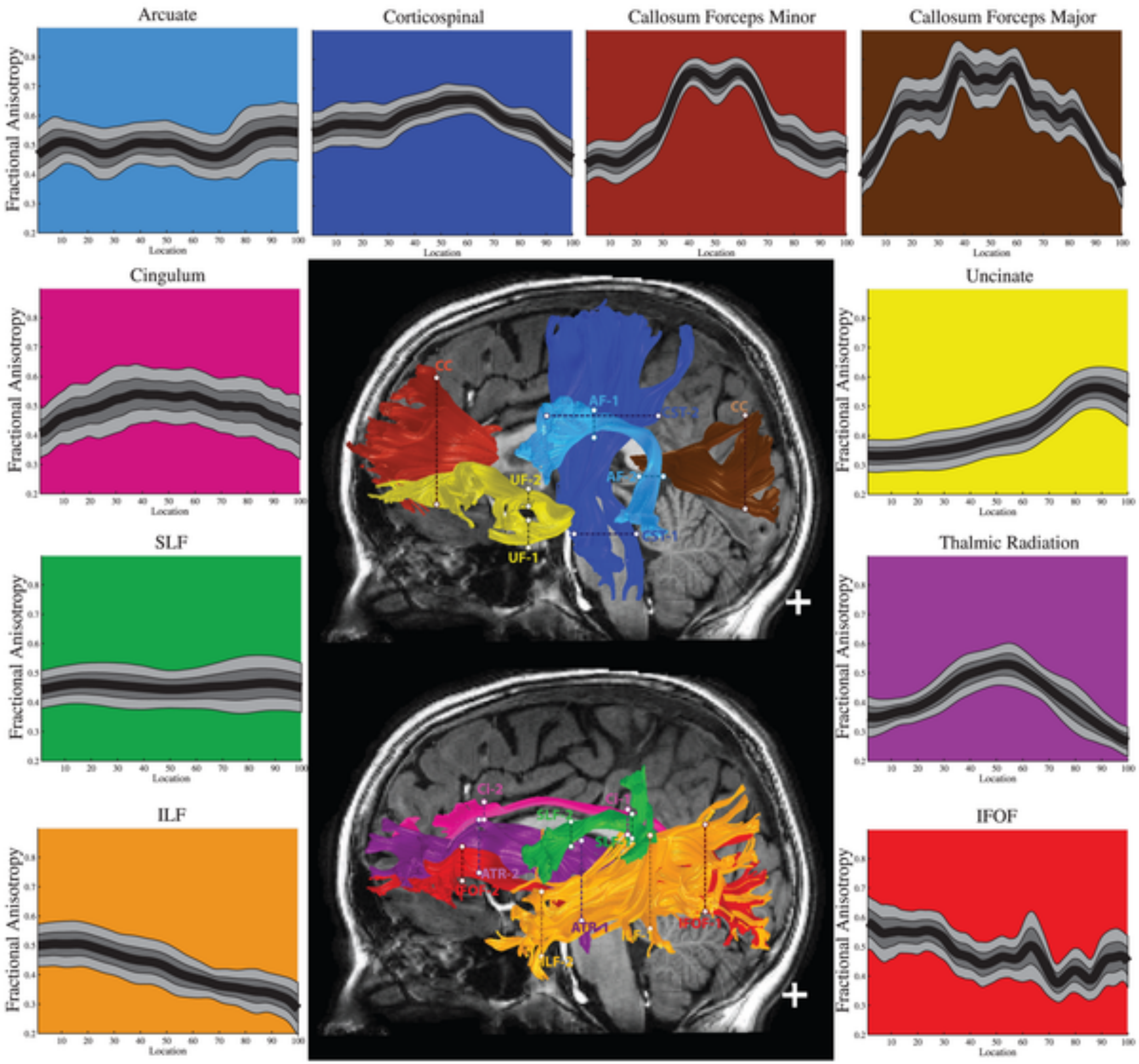
(Sherbondy et al., 2008;





Automated Fiber Quantification (AFQ)

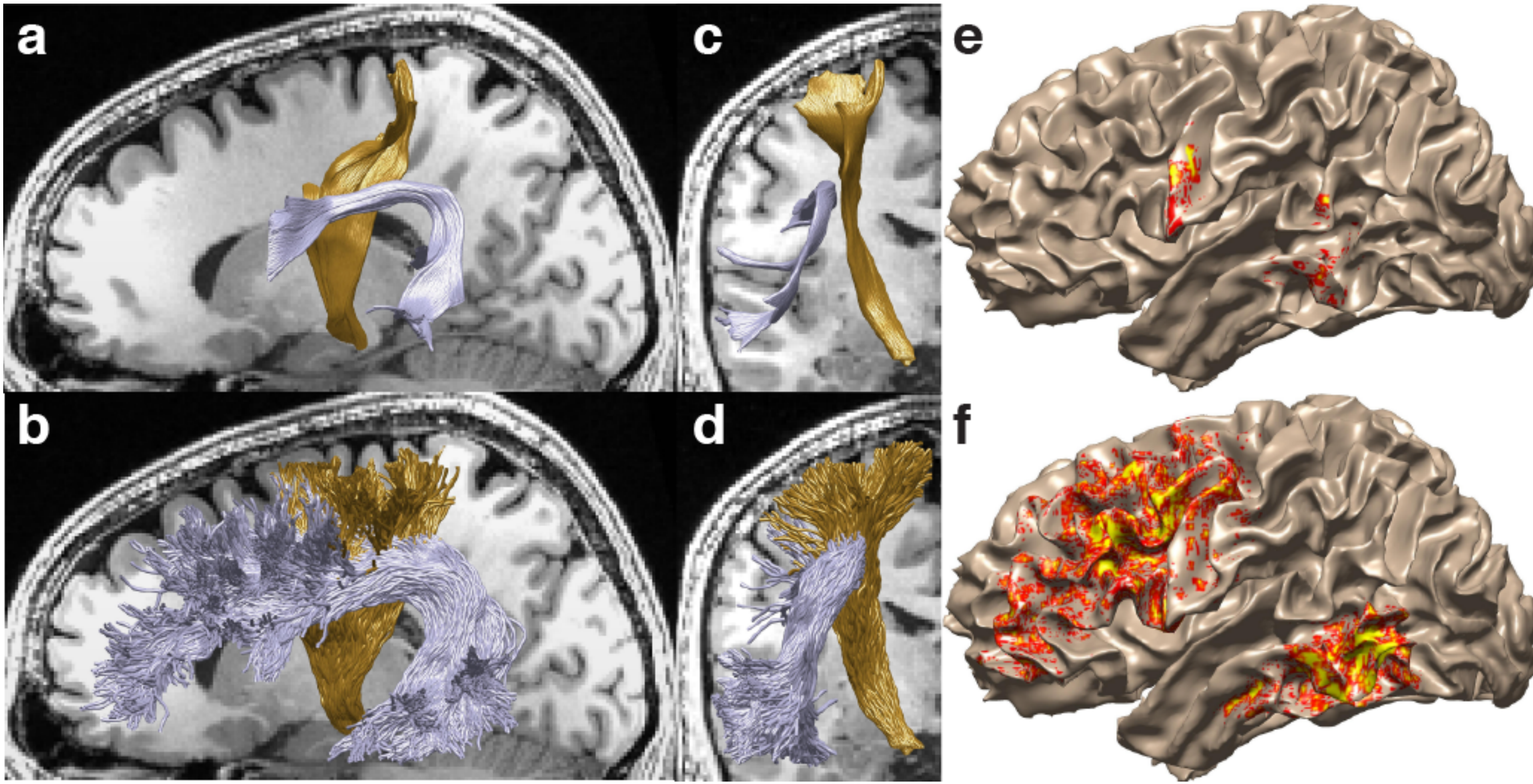
Yeatman et al., 2012



Statistical inference on white matter connections in the living human brain

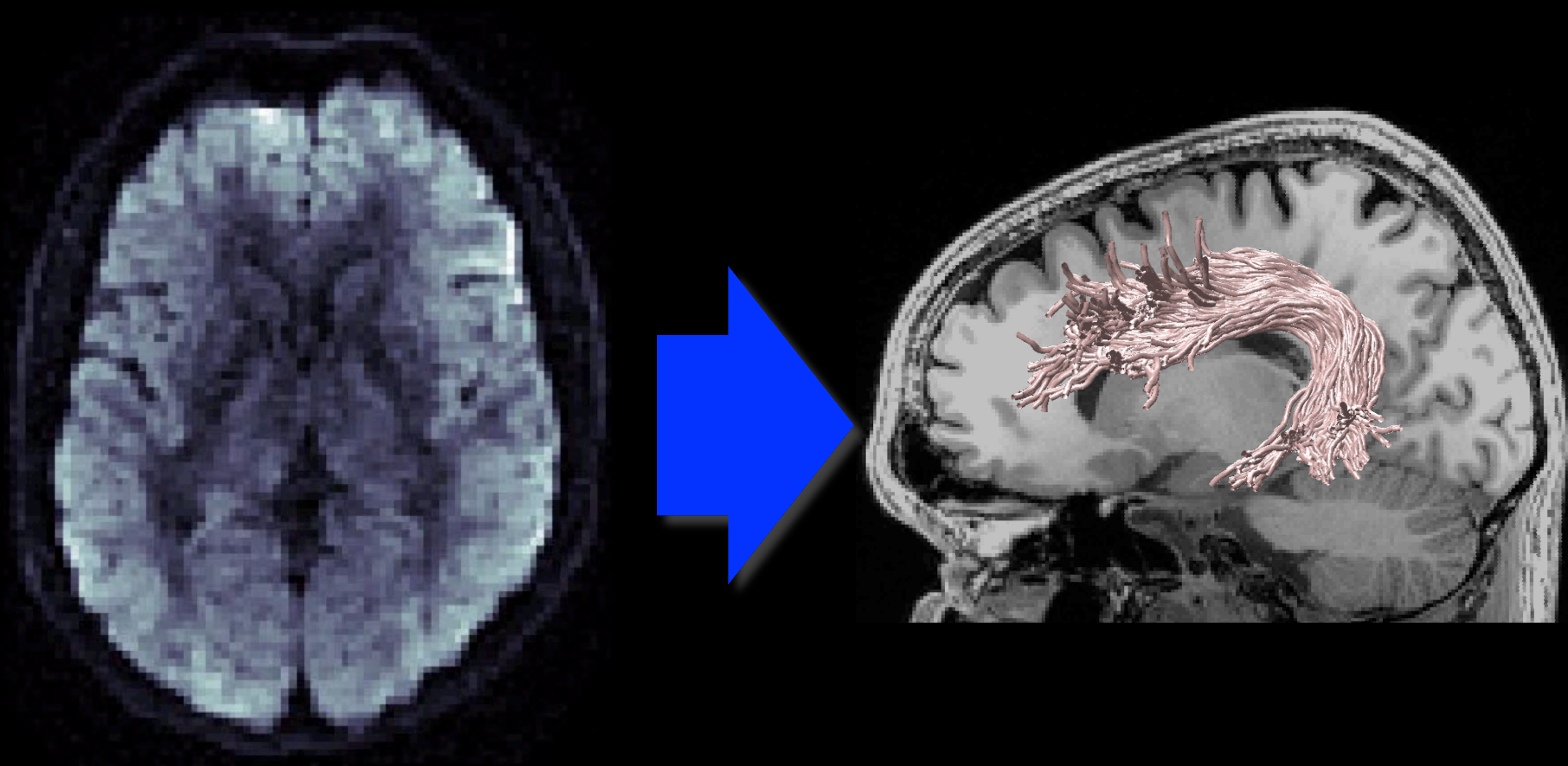
Franco Pestilli and me

The tractography problem



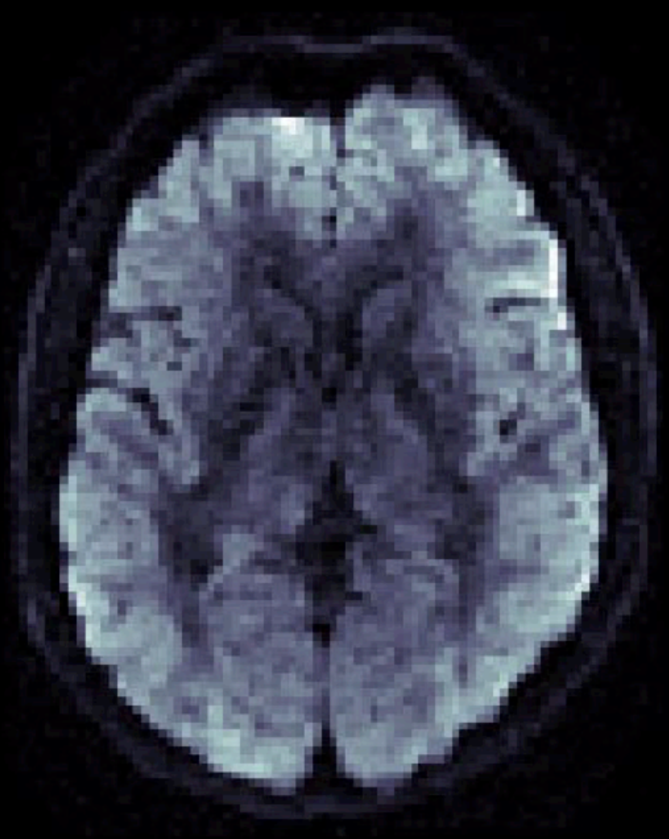
Standard tractography

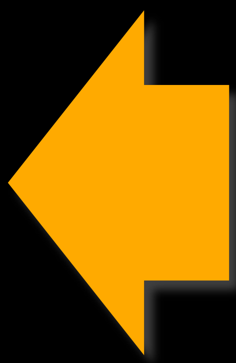
Estimate fascicles from diffusion data

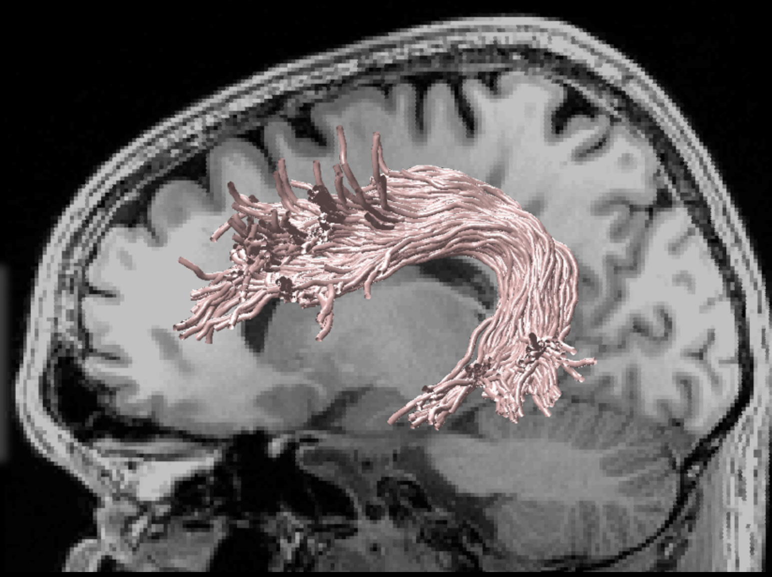


Linear iterative fascicle evaluation (LIFE)

Predict diffusion data from fascicles



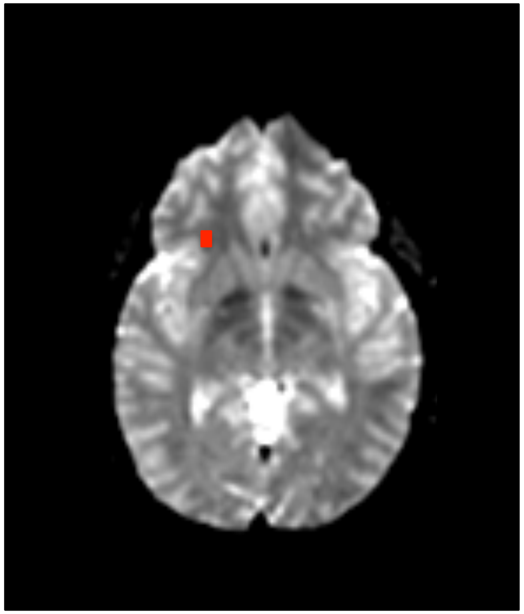




Diffusion in a single voxel

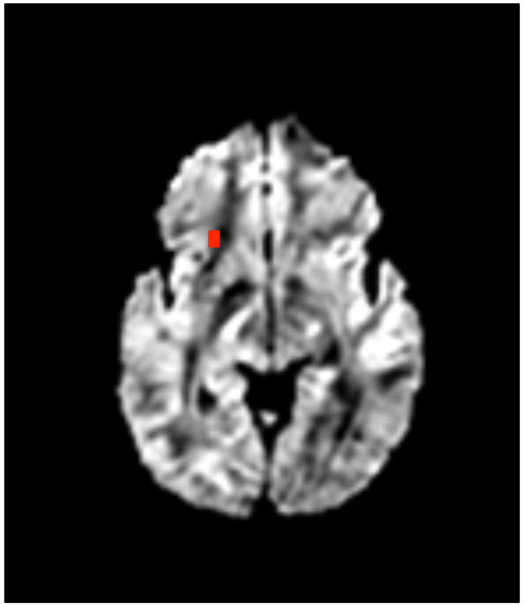
Non-diffusion weighted signal

$$S_0$$

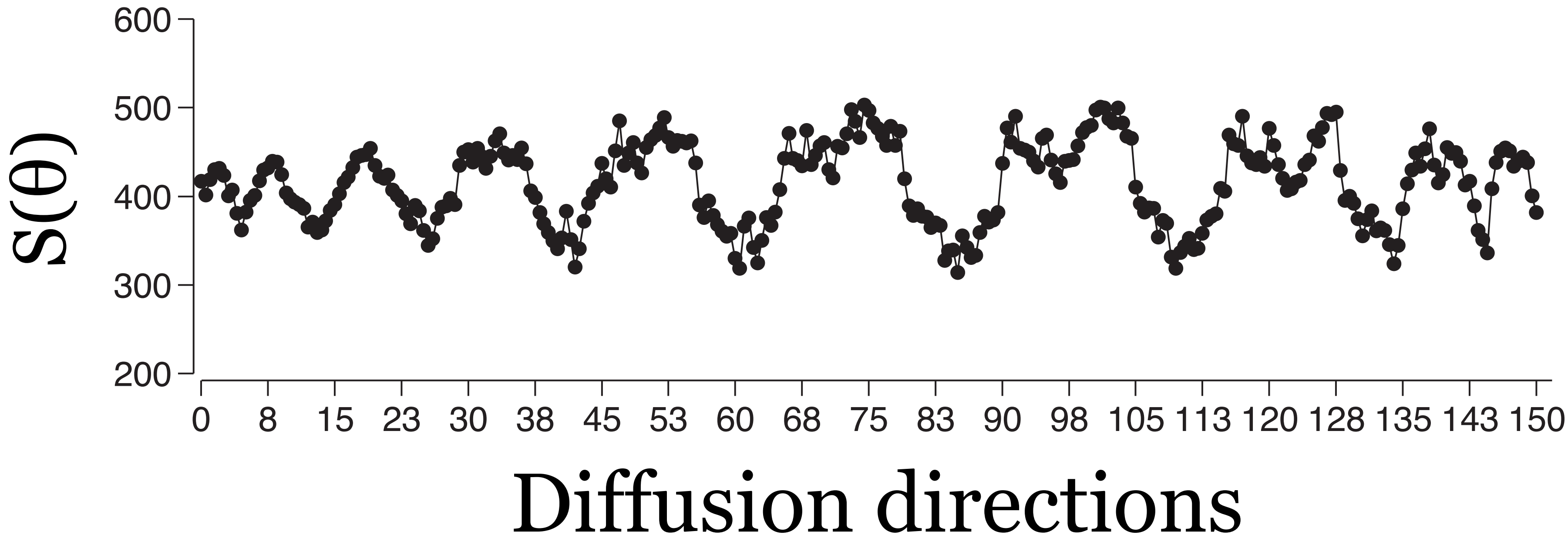


Diffusion weighted signal

$$S_b(\theta) = S_0\,\mathrm{e}^{-bA(\theta)}$$

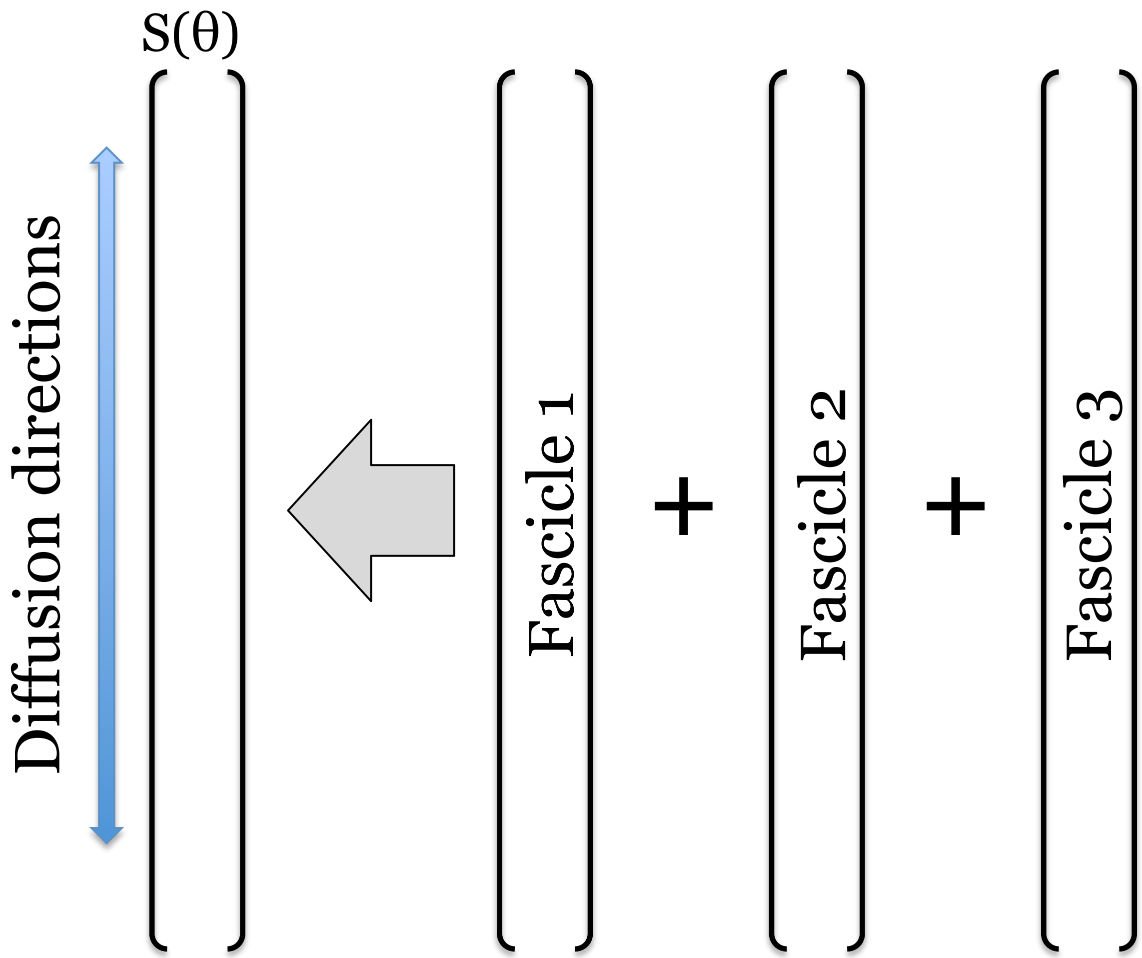


The signal measured in a voxel



Fascicle contributions

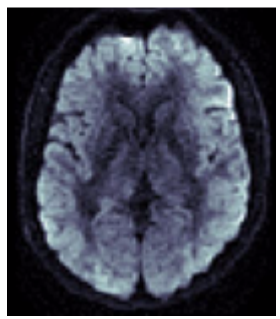
- Each fascicle makes a contribution to the diffusion signal for each voxel it passes through
- The contribution depends on the fascicle orientation



Weighting the fascicle contributions

- Each fascicle makes a contribution to the diffusion signal for each voxel it passes through
- The contribution depends on the fascicle orientation
- The fascicles can contribute somewhat different amounts (weighted)

Diffusion signal, S(θ)

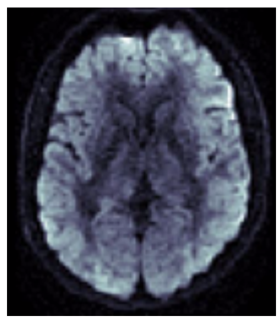


S(θ) = Each column is the set of fascicle predictions for this voxel × Weight for each fascicle

Whole brain connectome

- Each fascicle makes a contribution to the diffusion signal for each voxel it passes through
- The contribution depends on the fascicle orientation
- The fascicles can contribute somewhat different amounts (weighted)
- 100 directions
  100,000 voxels
  1,000,000 fascicles

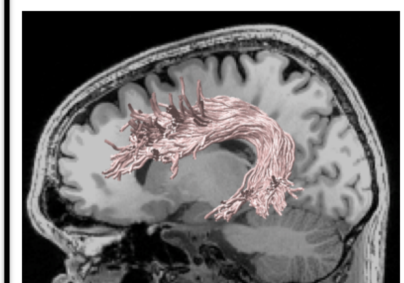
Diffusion signal, S(θ)



θ

=

Each column is the set of fascicle predictions in each voxel



Weight for each fascicle

Whole brain connectome

- Each fascicle makes a contribution to the diffusion signal for each voxel it passes through
- The contribution depends on the fascicle orientation
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- 100 directions
  100,000 voxels
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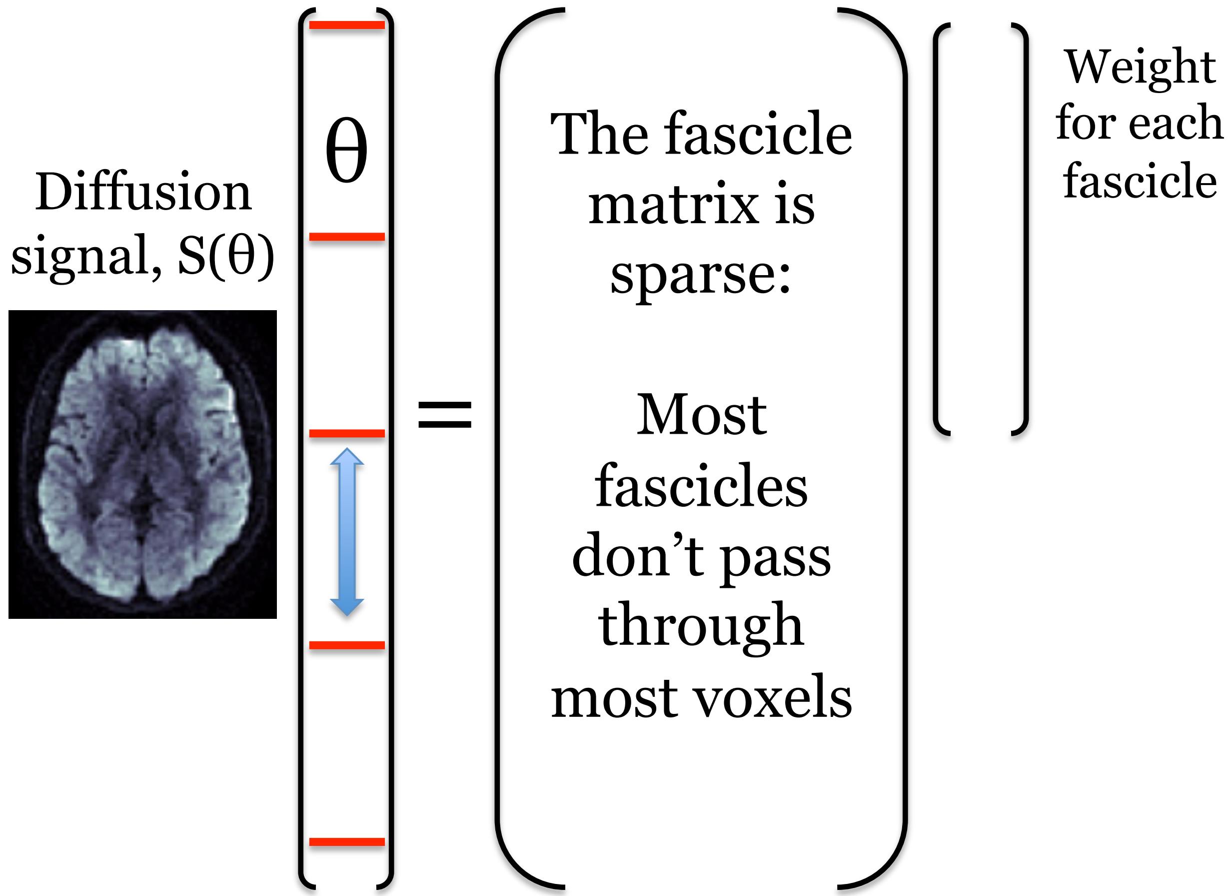
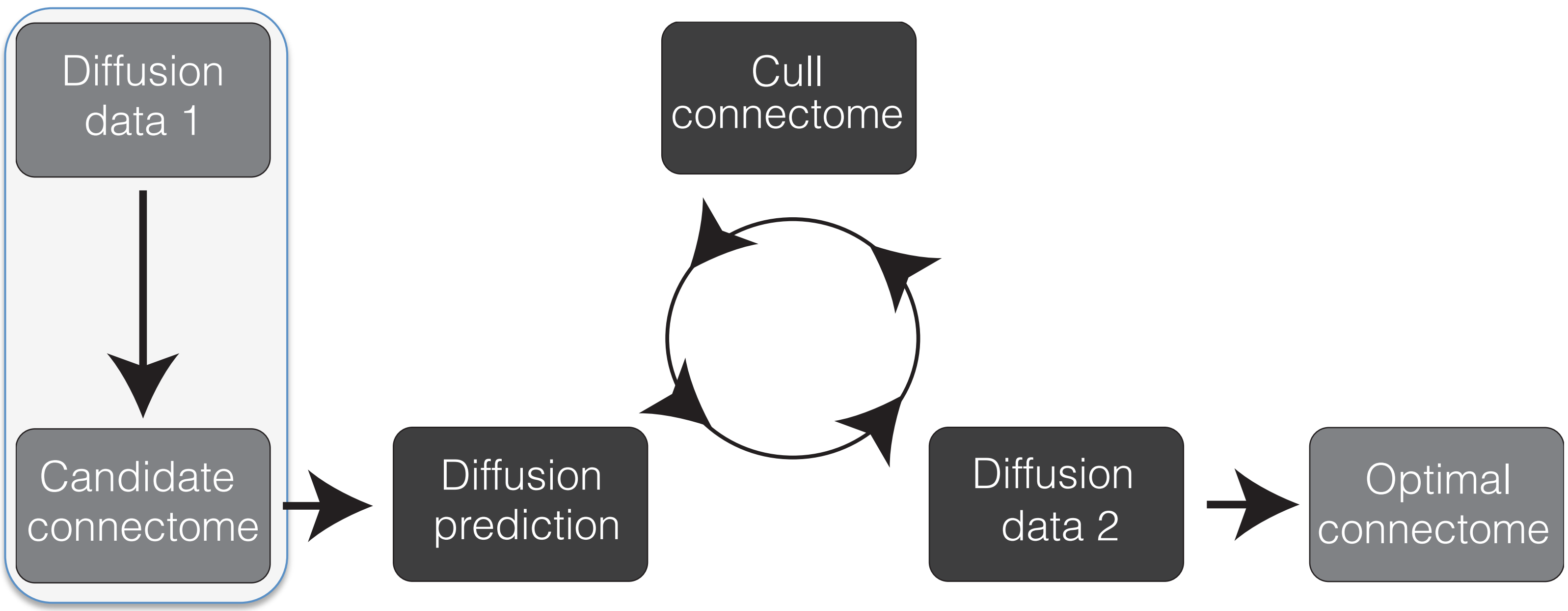
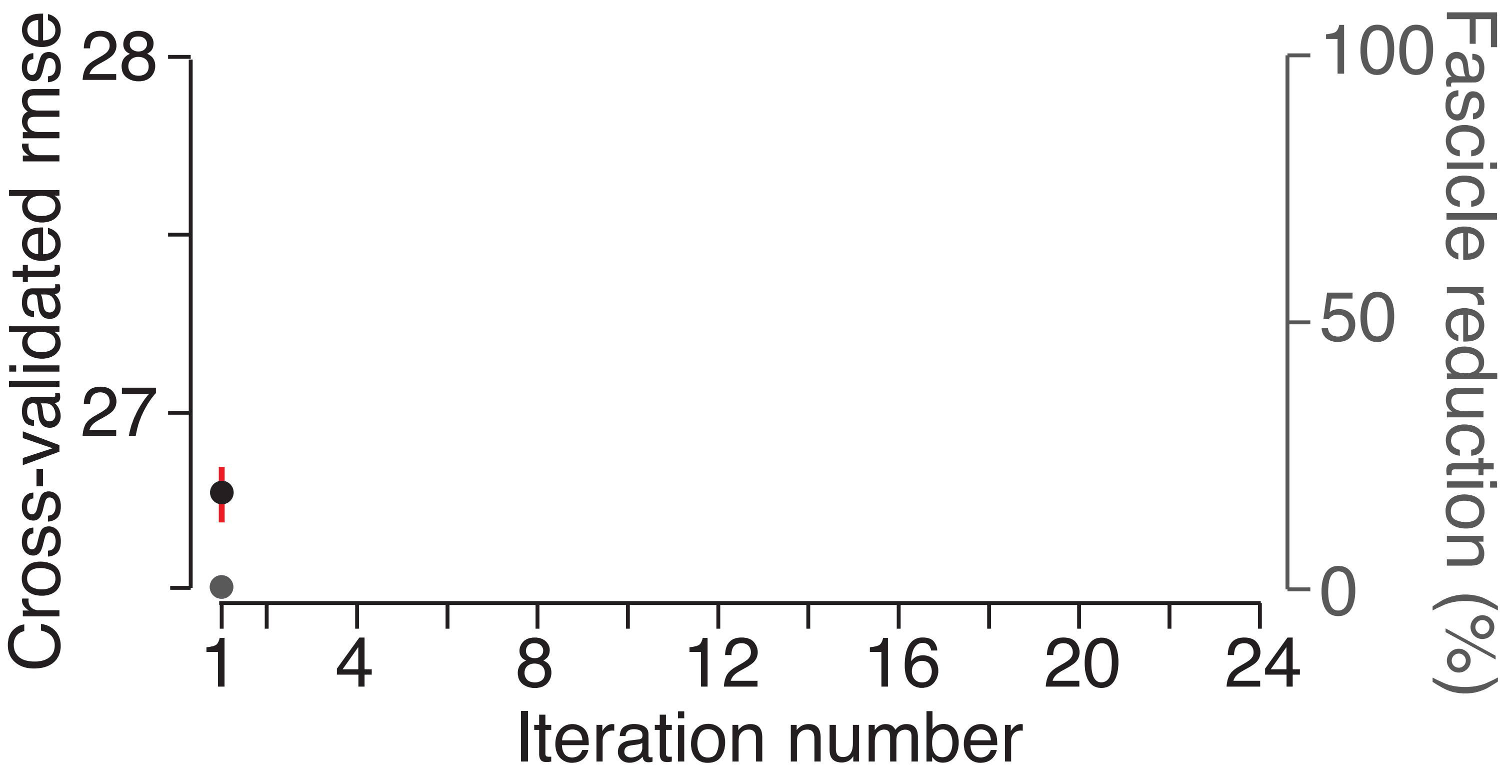


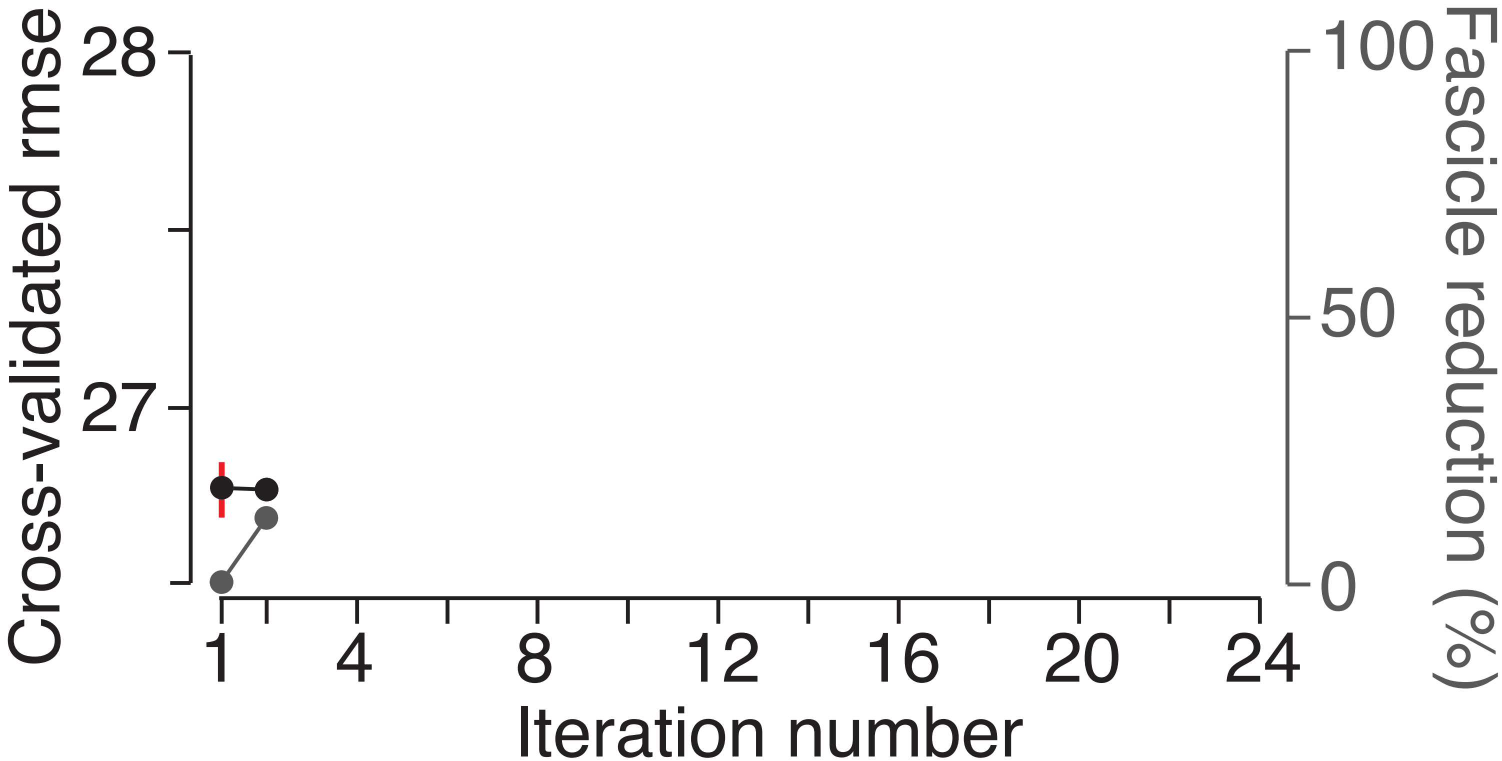
Linear Iterative Fascicle Evaluation (LIFE)



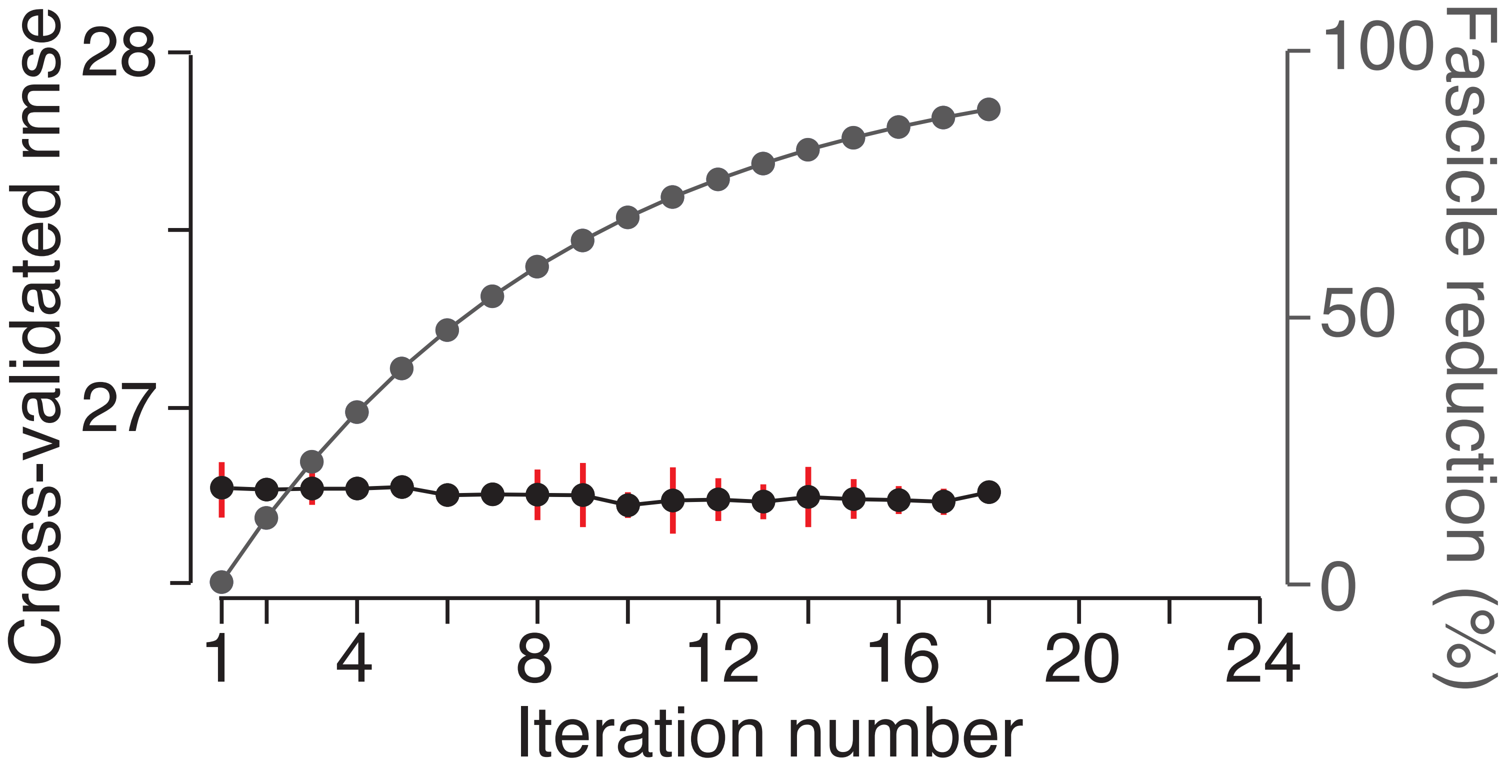
The cycle of LIFE



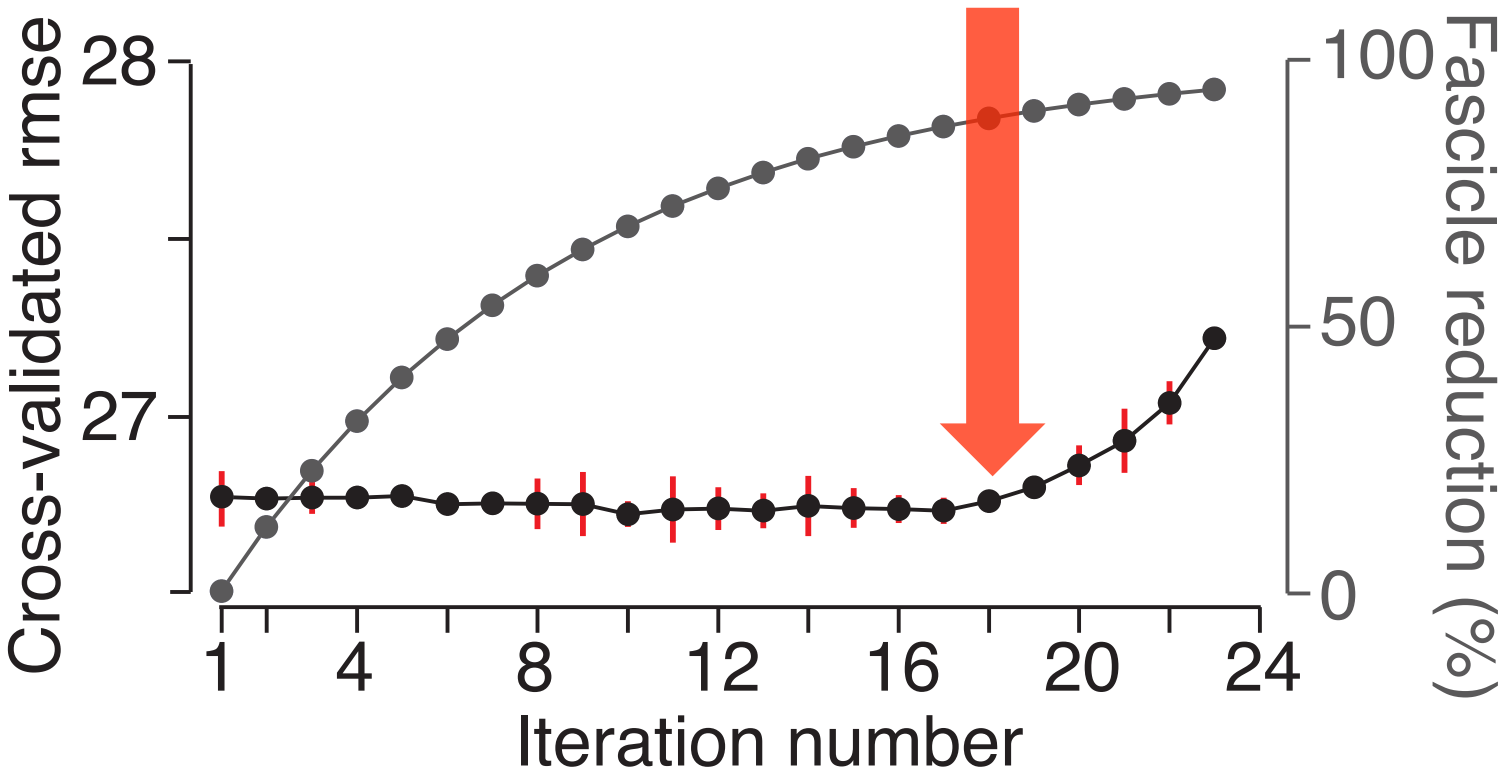
The cycle of LIFE



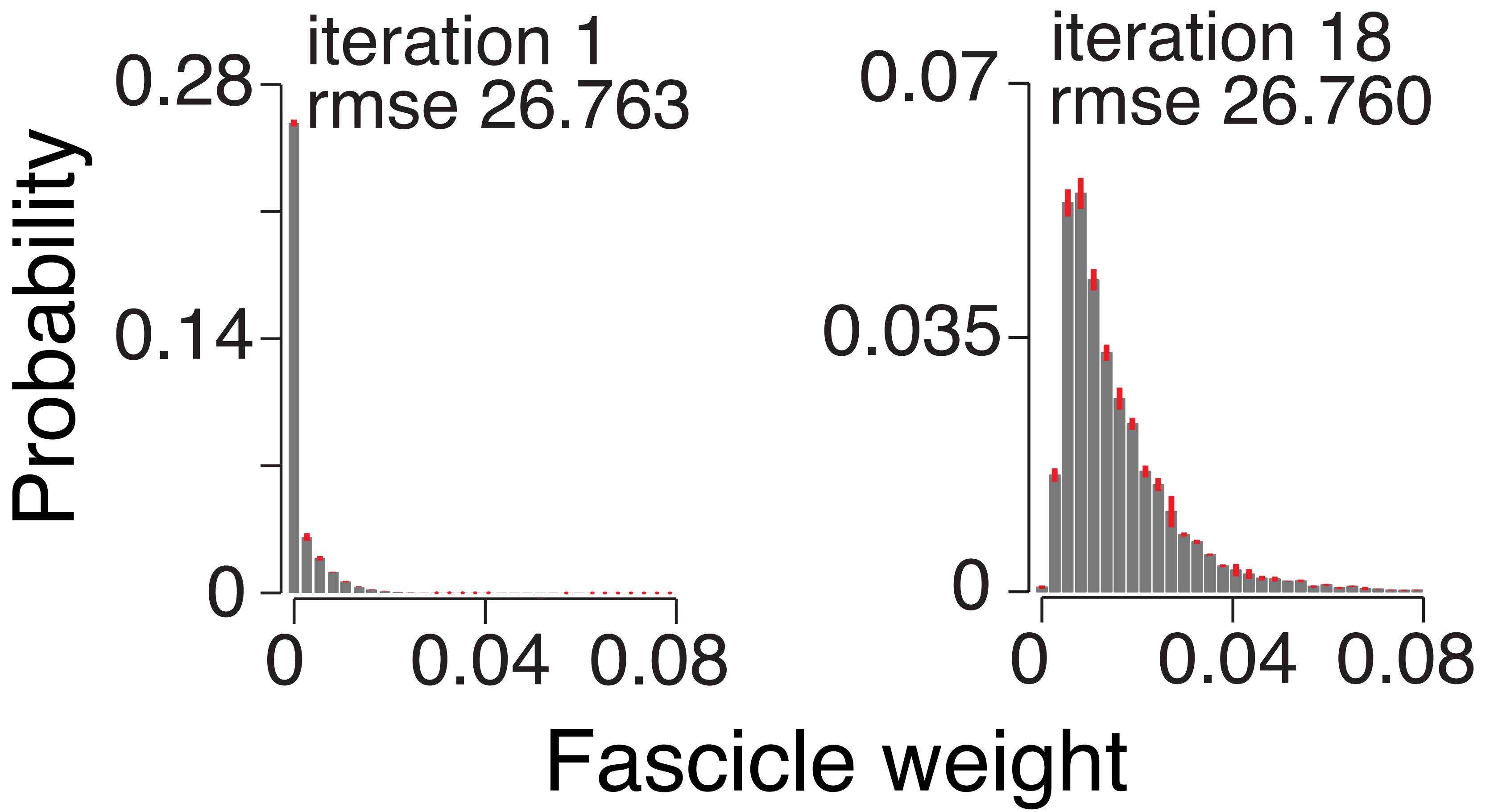
The cycle of LIFE



The optimal connectome



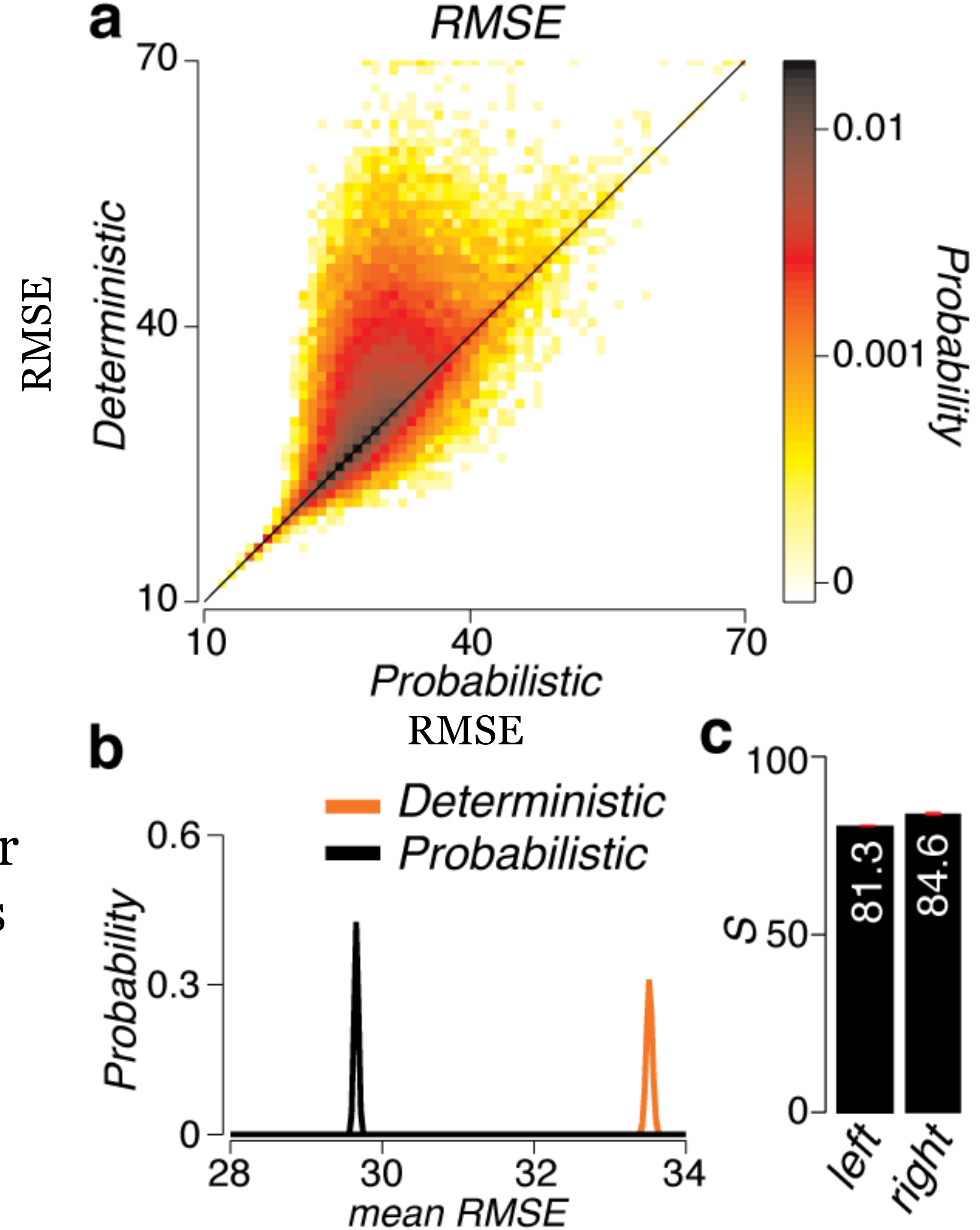
The optimal fascicles are not redundant



Method evaluation

Bootstrapping tests compare

- The quality of different connectomes fits
- The increase in error for removing specific tracts



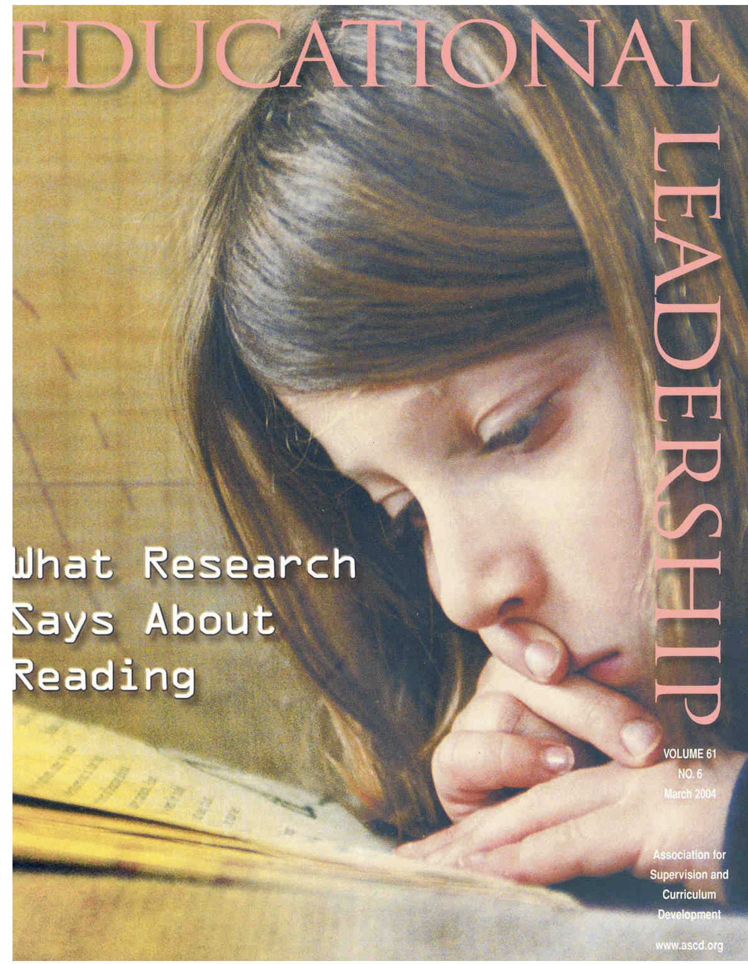
Neuroscience for Society

- Application of these methods to reading development (neuroprognosis)

Neuroscience for Society

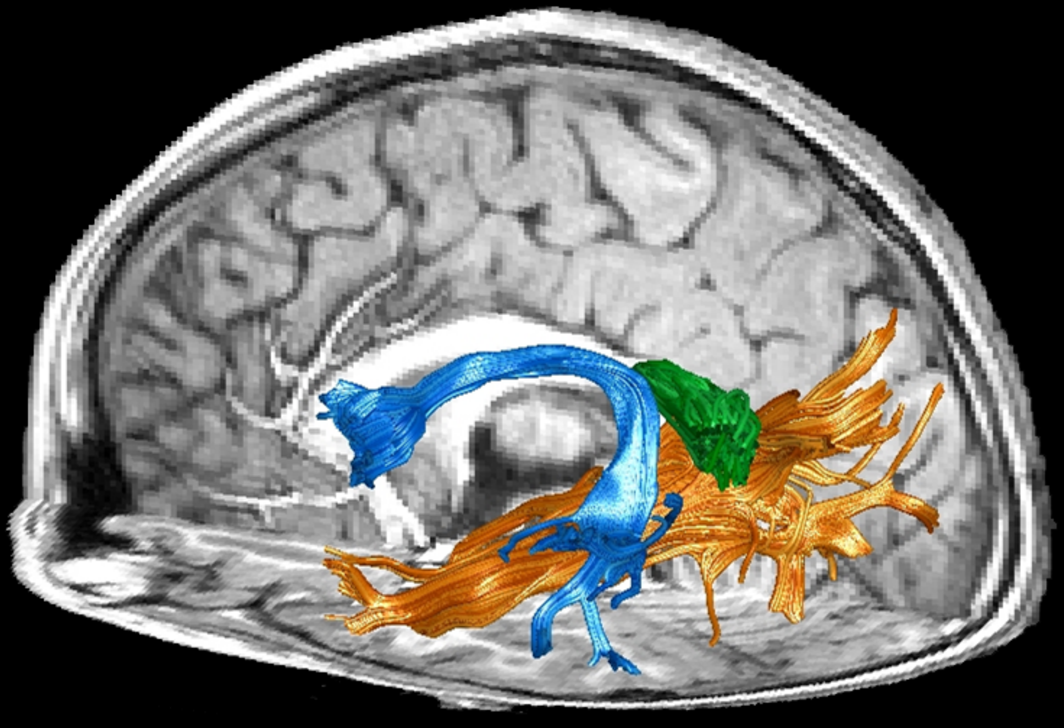
- Certain brain pathways become trained for rapidly recognizing words and reading

- Can we identify markers to understand when children are ready to learn to read and that guide how to help children who are having difficulty learning?



White matter reading tracts

(Wandell and Yeatman, Annual Review, 2013)

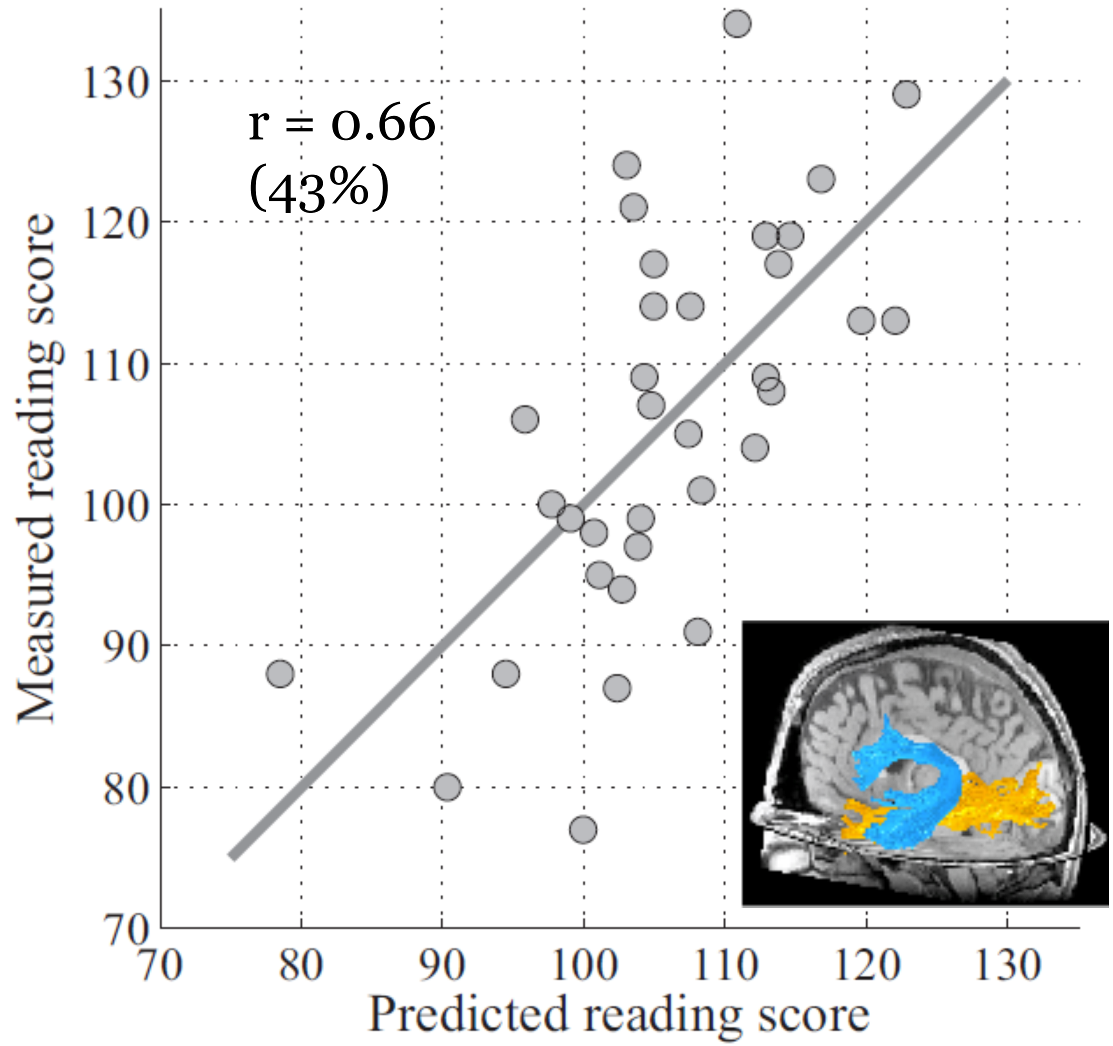


Predicting reading scores from white matter maturity

(Yeatman et al., PNAS, 2012)

- With very simple models based on diffusion data, we predict reading skill

- The predictions are statistically significant, but not yet useful



Thank you!

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