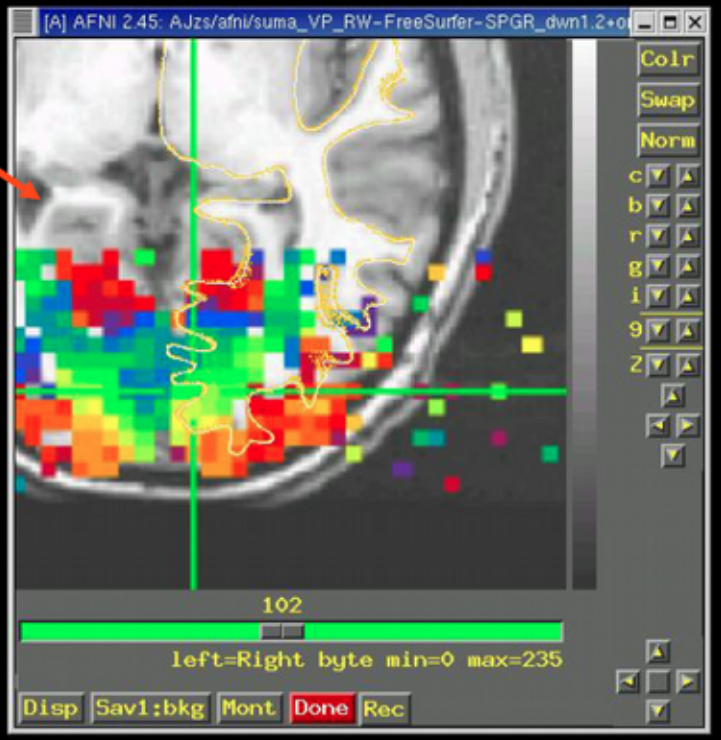
The AFNI-based Functional and Anatomical Connectivity Platform (including SUMA + FATCAT)

Paul A. Taylor
SSCC, NIMH, NIH


AFNI!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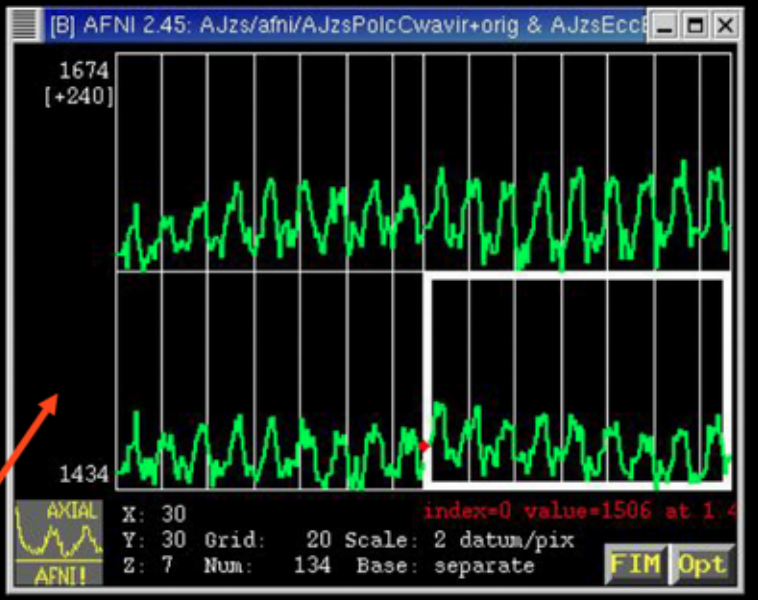
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AFNI!
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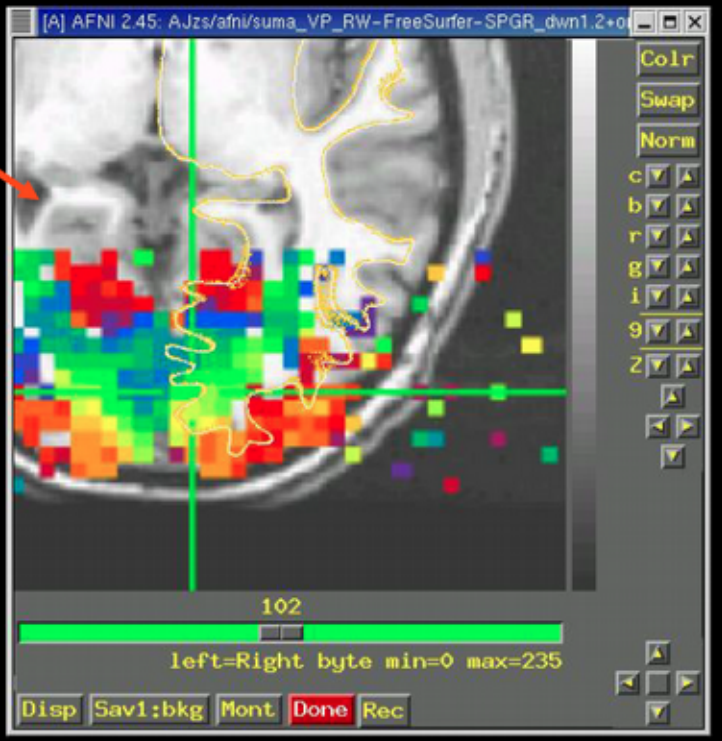
AFNI!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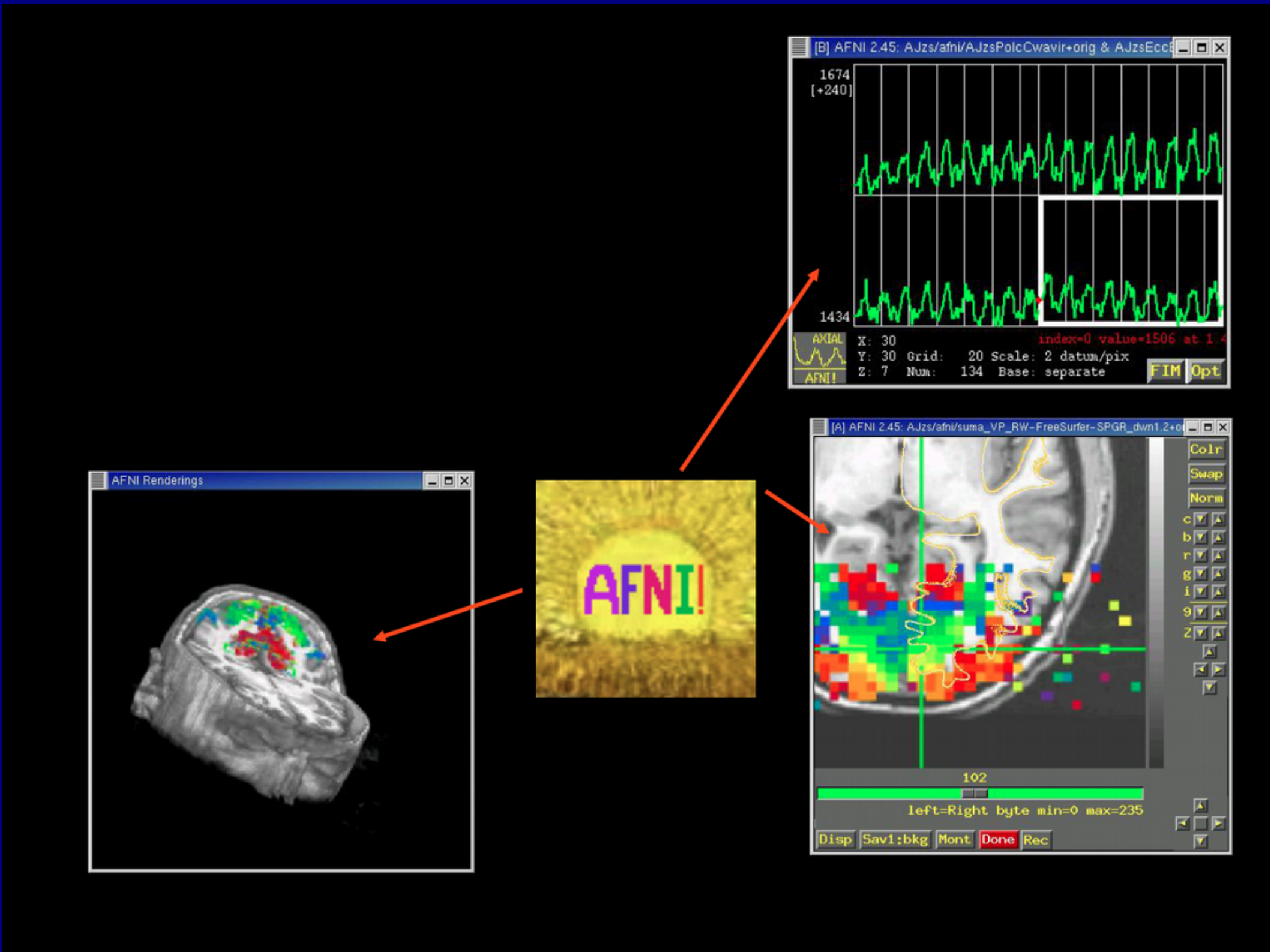
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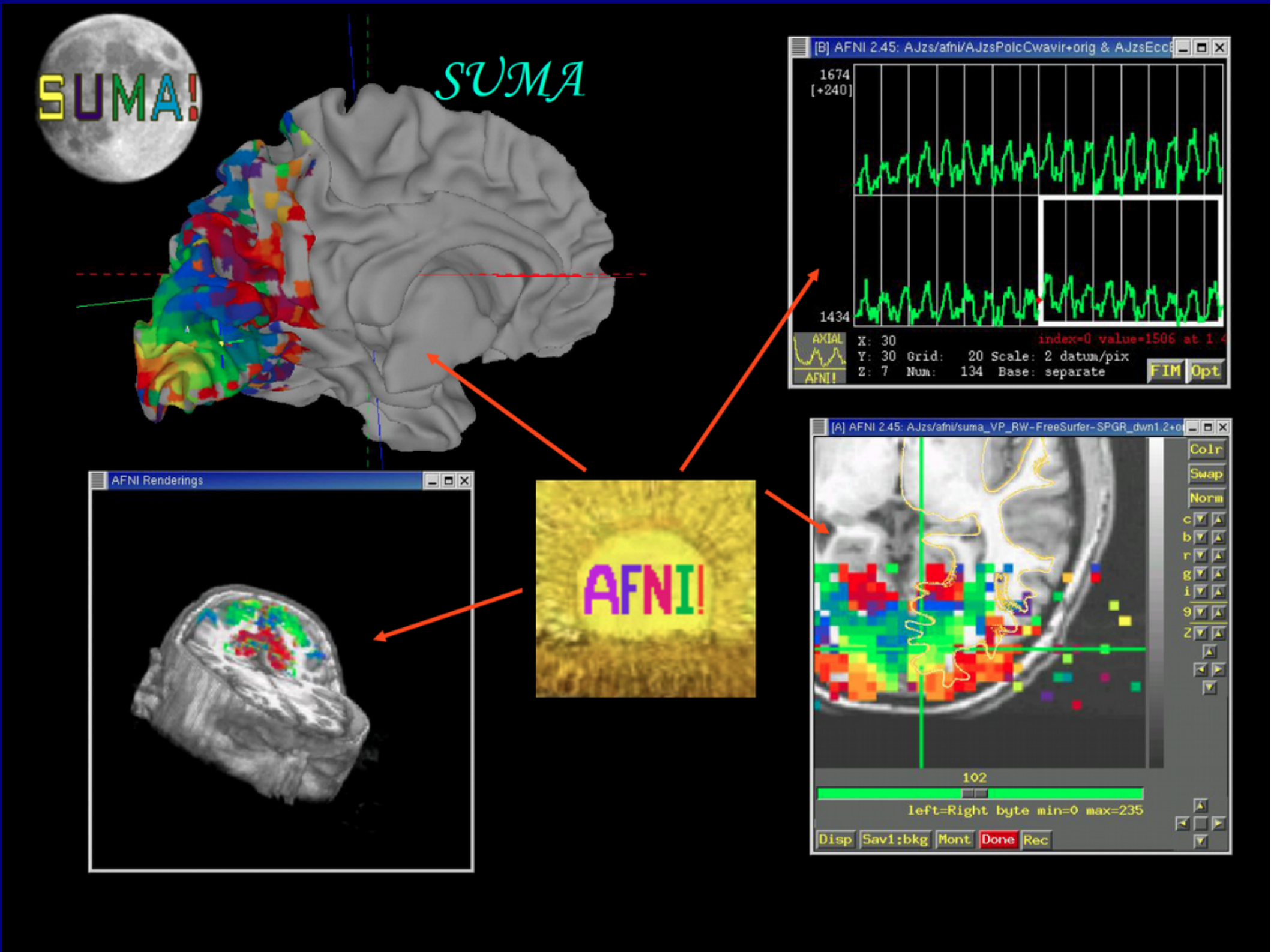
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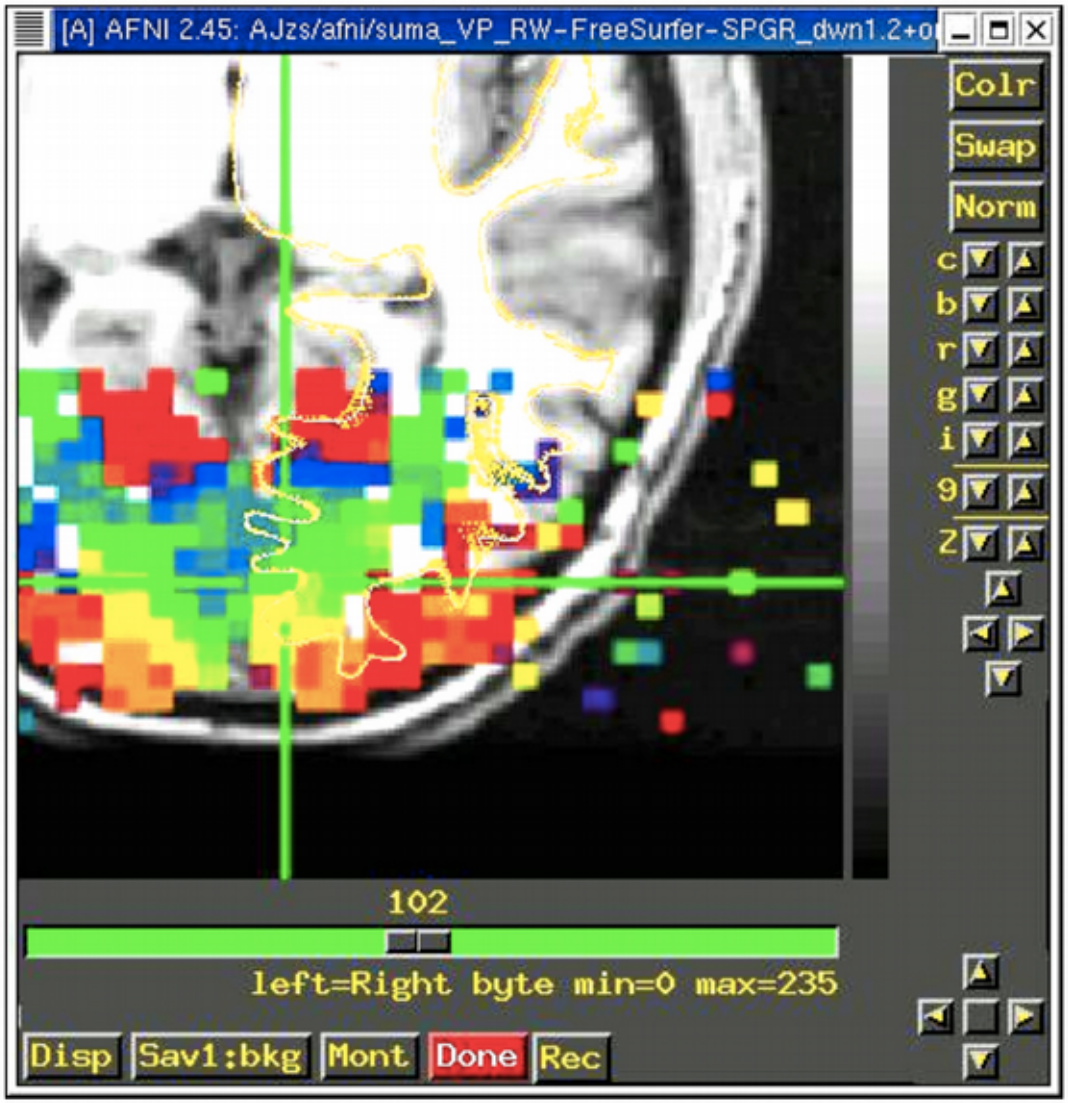
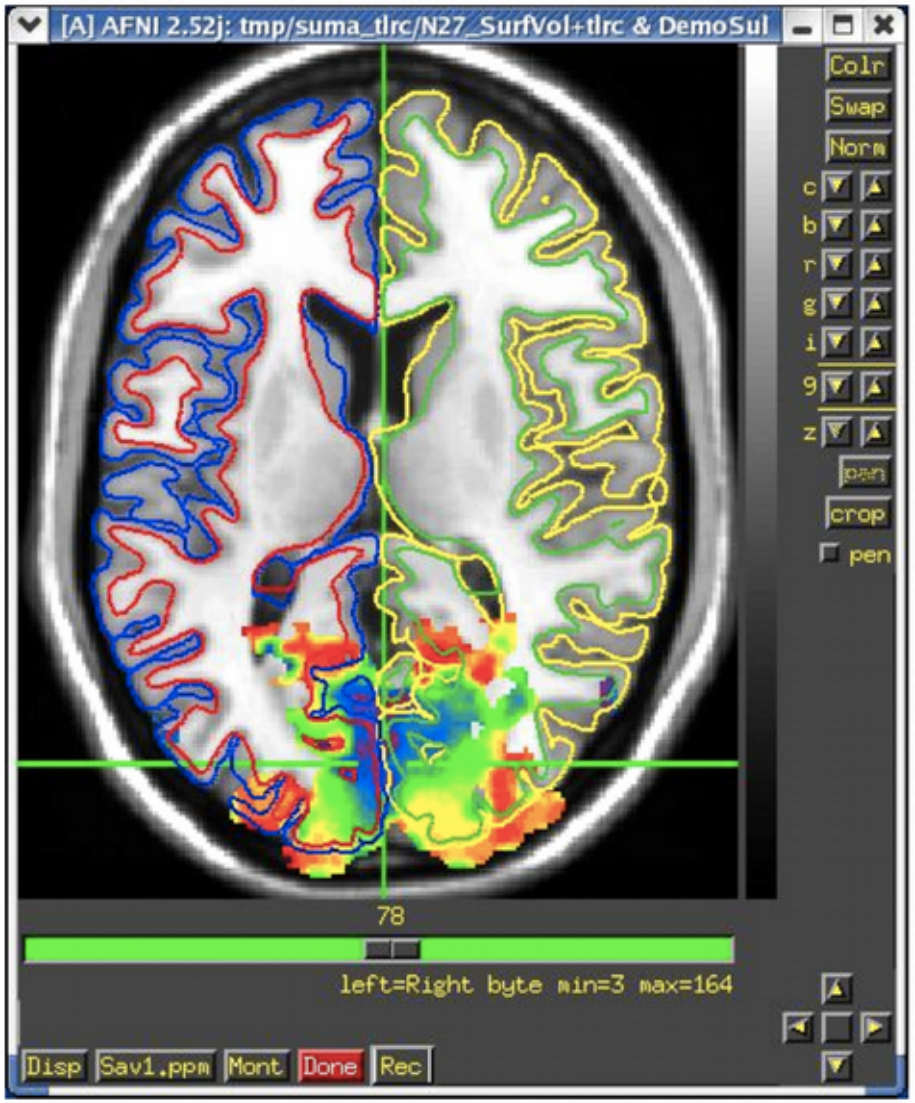
Ziad Saad

With SUMA: complement volume info.

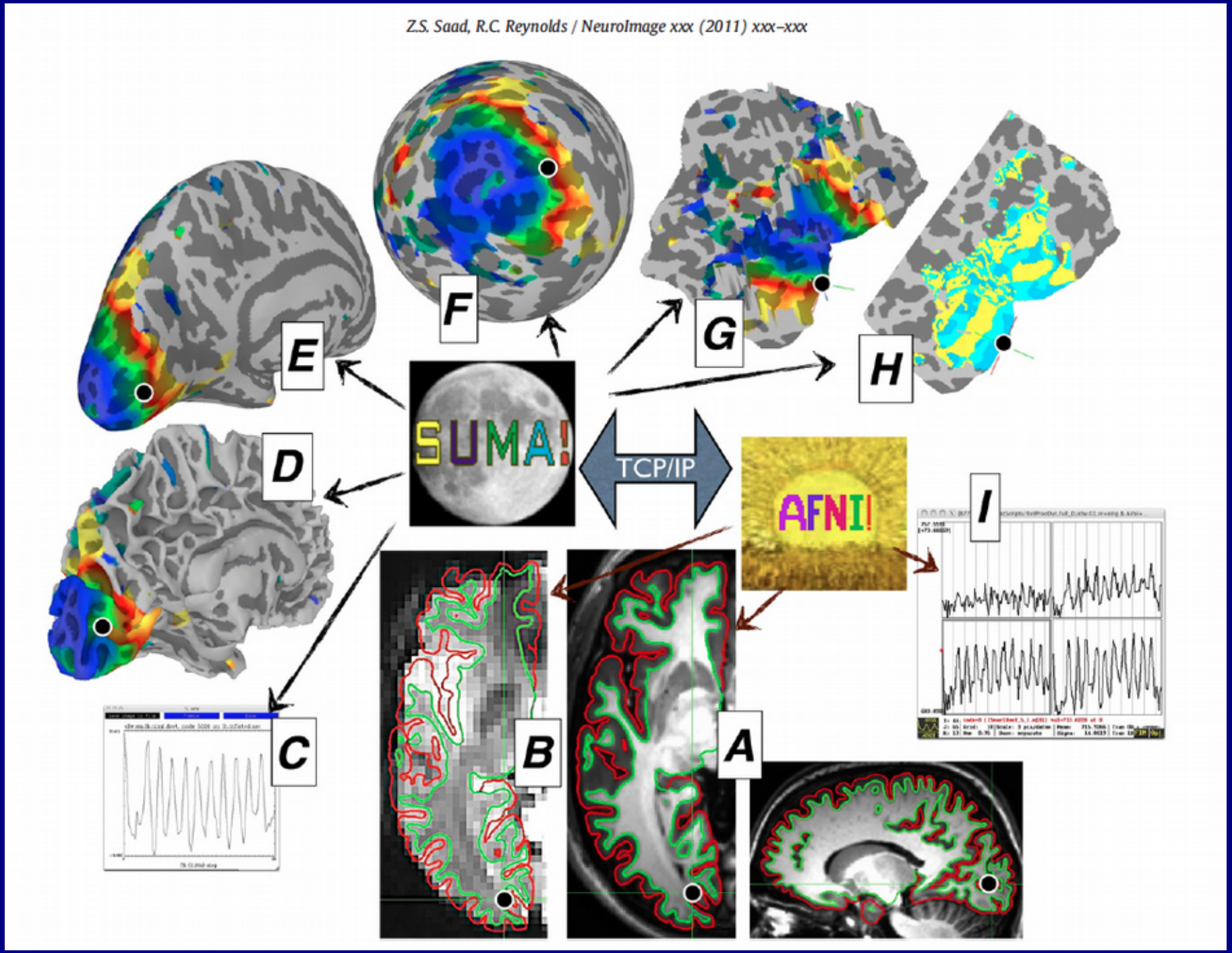
- Surface/volume Intersection



- Shell/volume Intersection



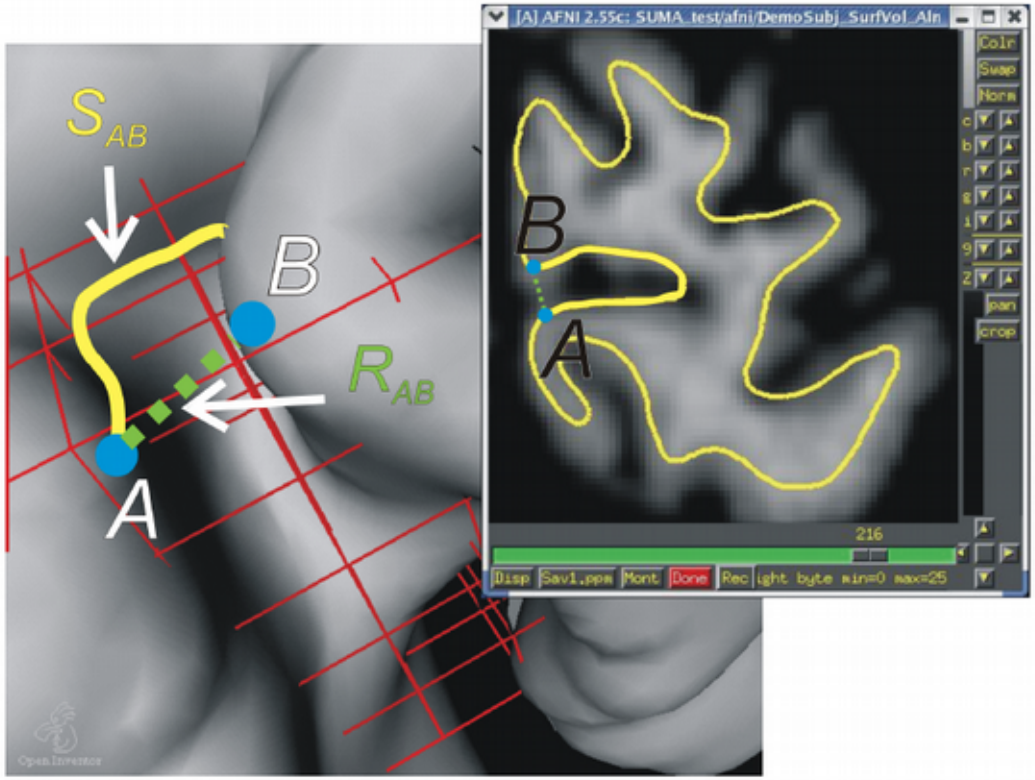
SUMA: ***Su***rface ***Ma***pping



SUMA: why use the surface?

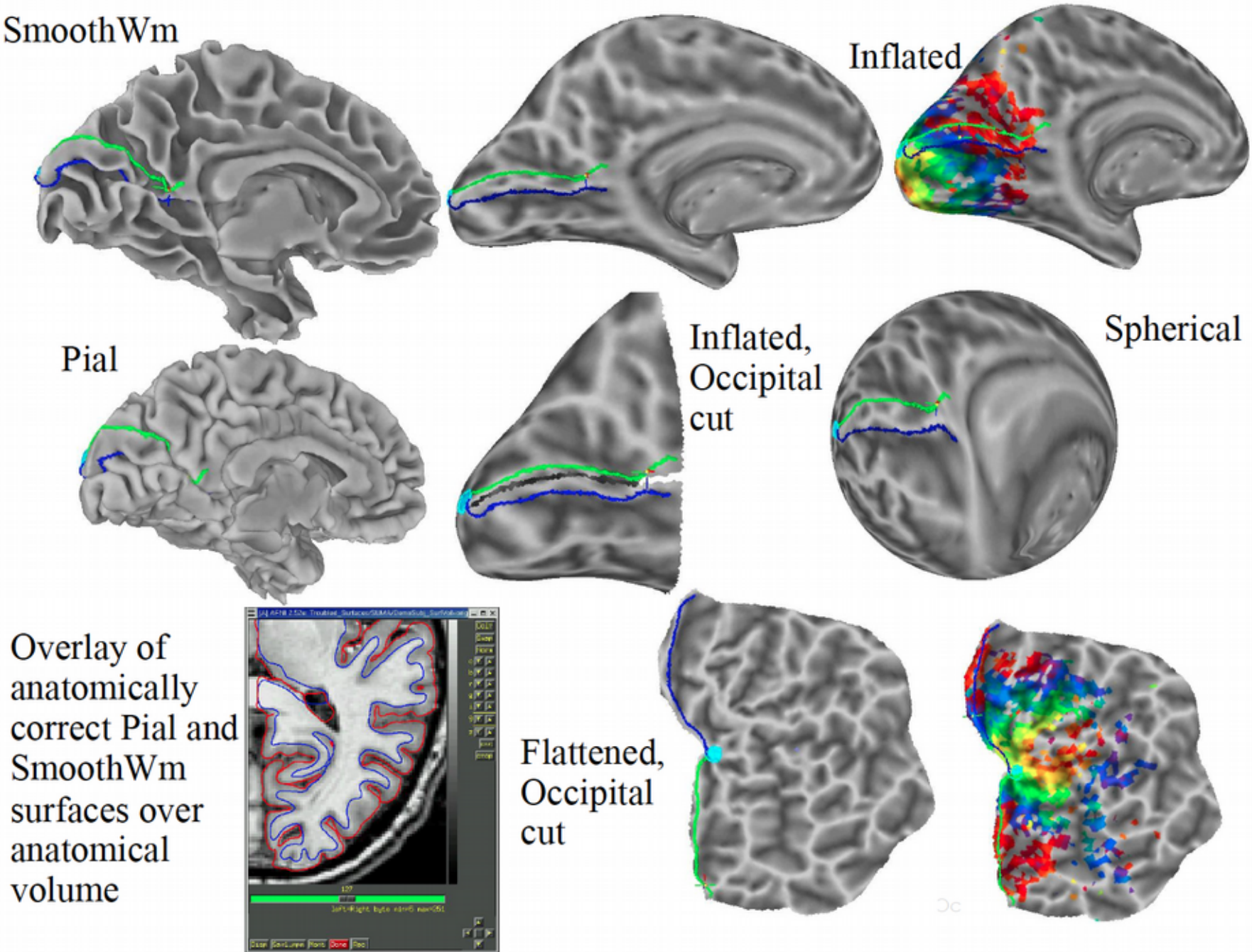
Geometry and Topology

- Geometry: Spatial location
  - ★ X,Y,Z coordinates of brain structures
- Topology: Spatial connectivity
  - ★ Relative positions of brain structures along the surface



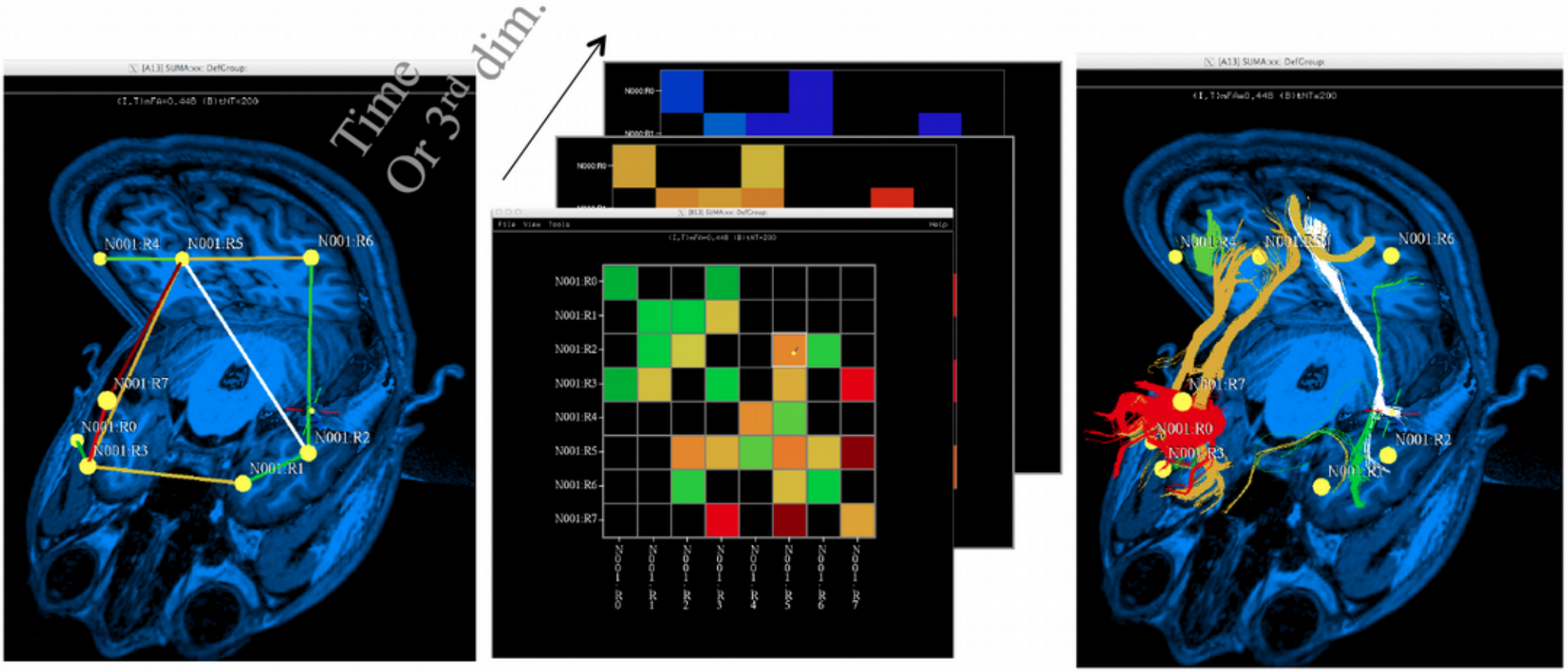
- Geometric proximity does not imply topological proximity
  - If you care about the topology of activation, you should transfer FMRI data onto the surface before spatial manipulations of the data

With SUMA: surface representations



With SUMA: graph + matrix + tract + anatomy ...

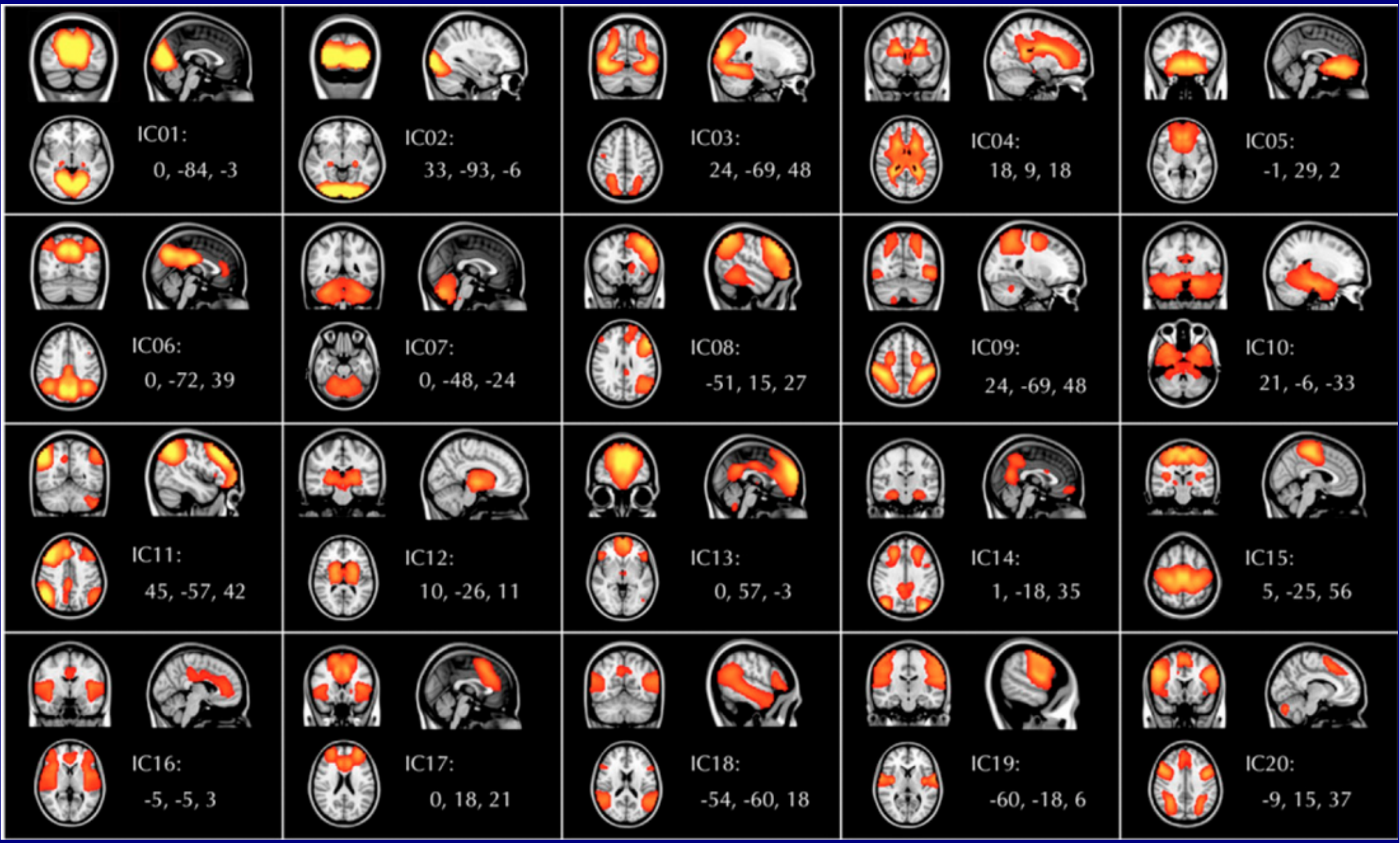
Simultaneous linked rendering in graph and matrix modes
3D matrices supported (e.g. time varying correlation matrix)



Outline

+ Why Function+Structure
+ DWI and DTI (→ local structures)
  - Brief diffusion imaging basics and parameters
  - Role of noise → DTI parameter uncertainty
+ Using tractography (→ estimate extended structures)
  - goals of tracking.
  - algorithms/properties
  - final thoughts on interpretation

FMRI: GM Networks



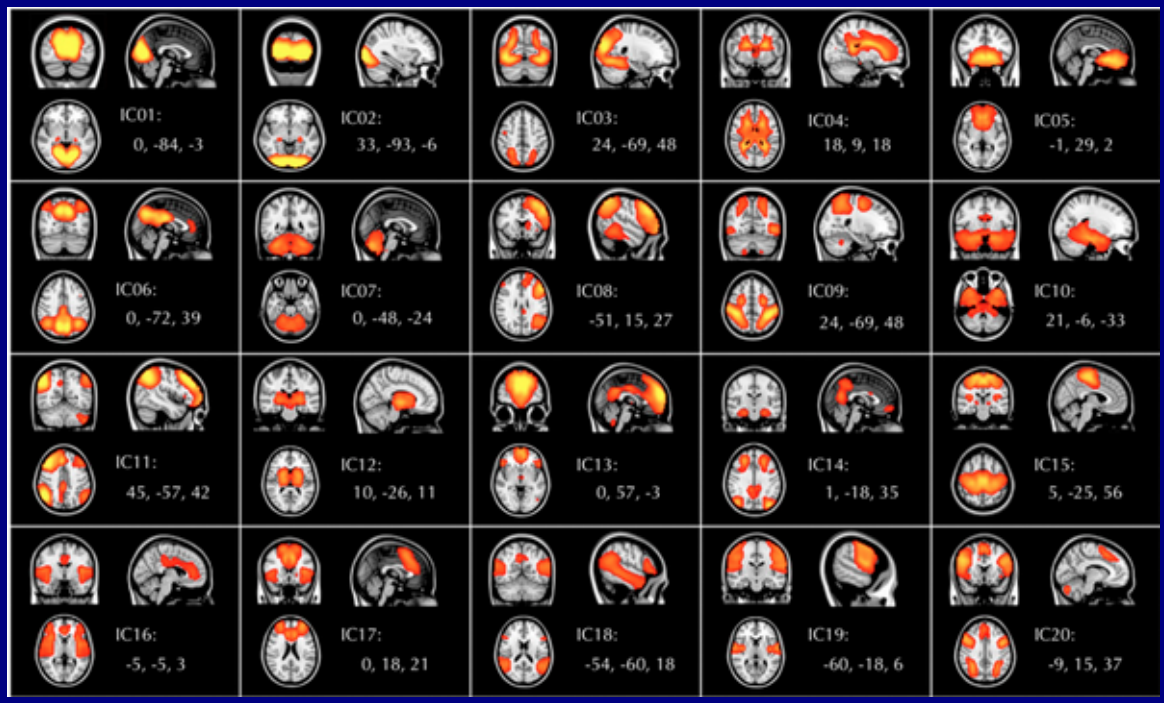
(Biswal et al., 2010 PNAS)

FMRI: GM Networks

Functional connectivity networks of distinct GM regions, from BOLD time series during task or rest/no task.

+ Quantify GM properties: ALFF, fALFF, RSFA, σ, ReHo, GMV, etc.

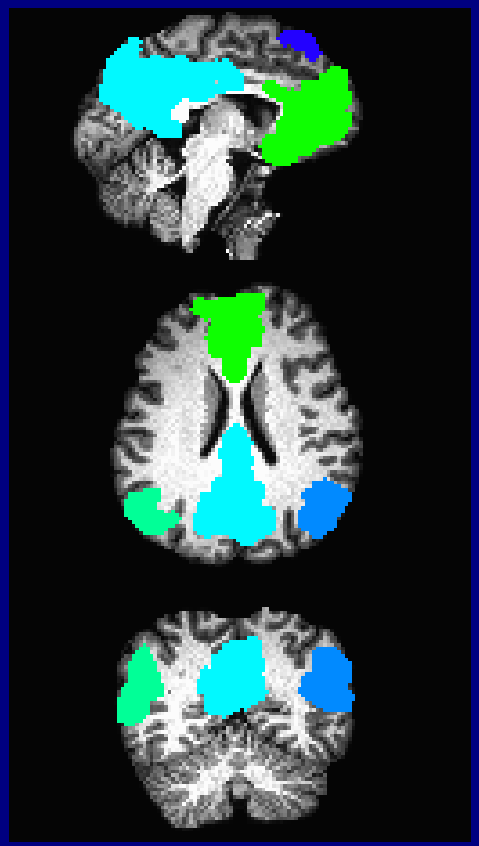
+ Quantify network props: seedbased correlation, ICA, graph theoretical measures, etc.

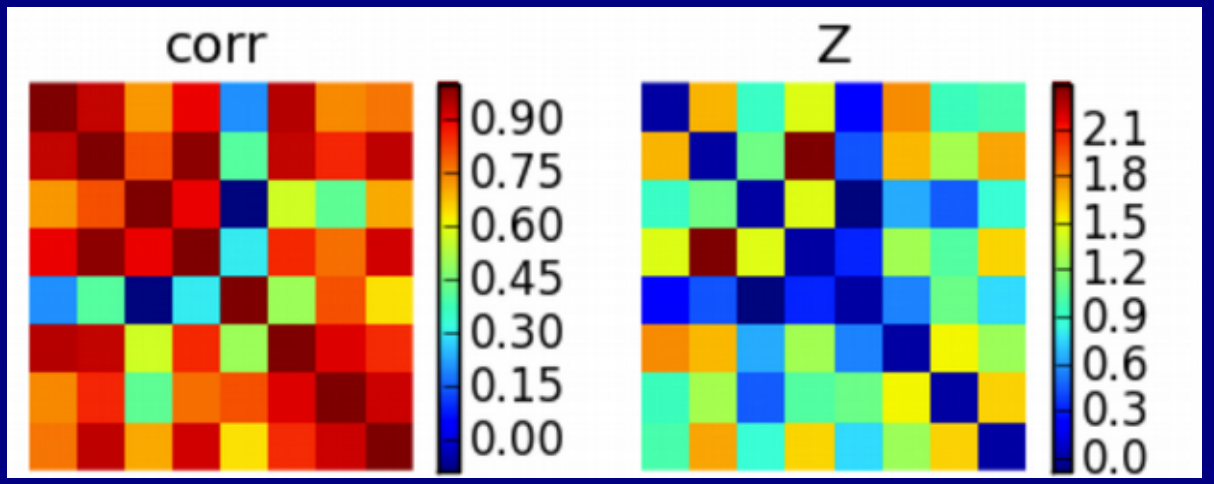


Functional connectivity: networks

For {RS- | TB-}FMRI: correlation matrices

+ 3dNetCorr: calculated post-processing, input time series data + network maps
  - can be multi-brick maps, 1 network per brick
  - calculate average time series per ROI, correlation among network ROIs
  - outputs correlation matrix/matrices, (can also do Fisher-Z transform output)





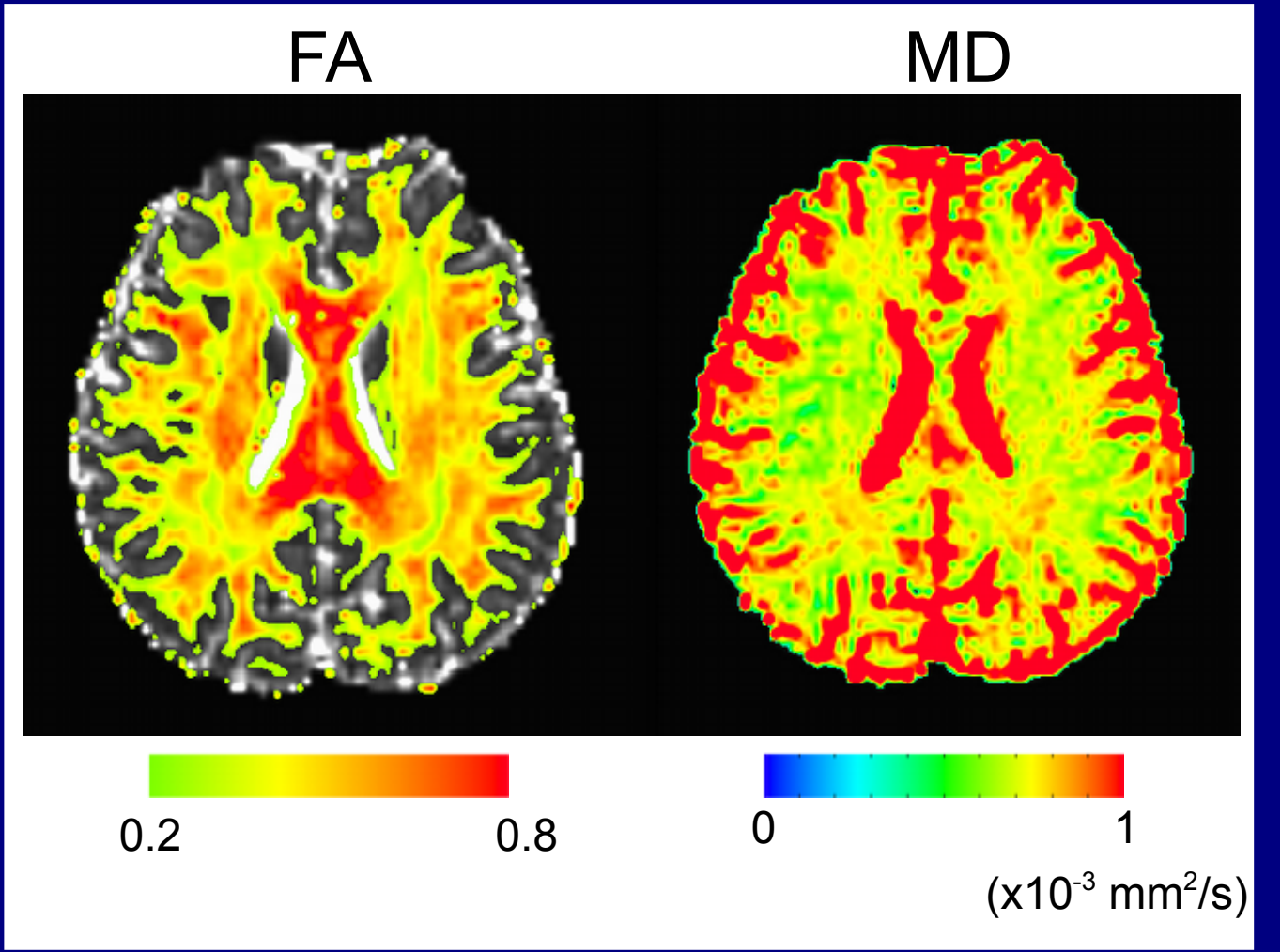
++ Can also calculate ReHo, ALFF, fALFF, etc. in FATCAT/AFNI.

DTI: WM structure

DTI-based parameters characterize some local structural properties and also show the presence of spatially-extended WM structures.

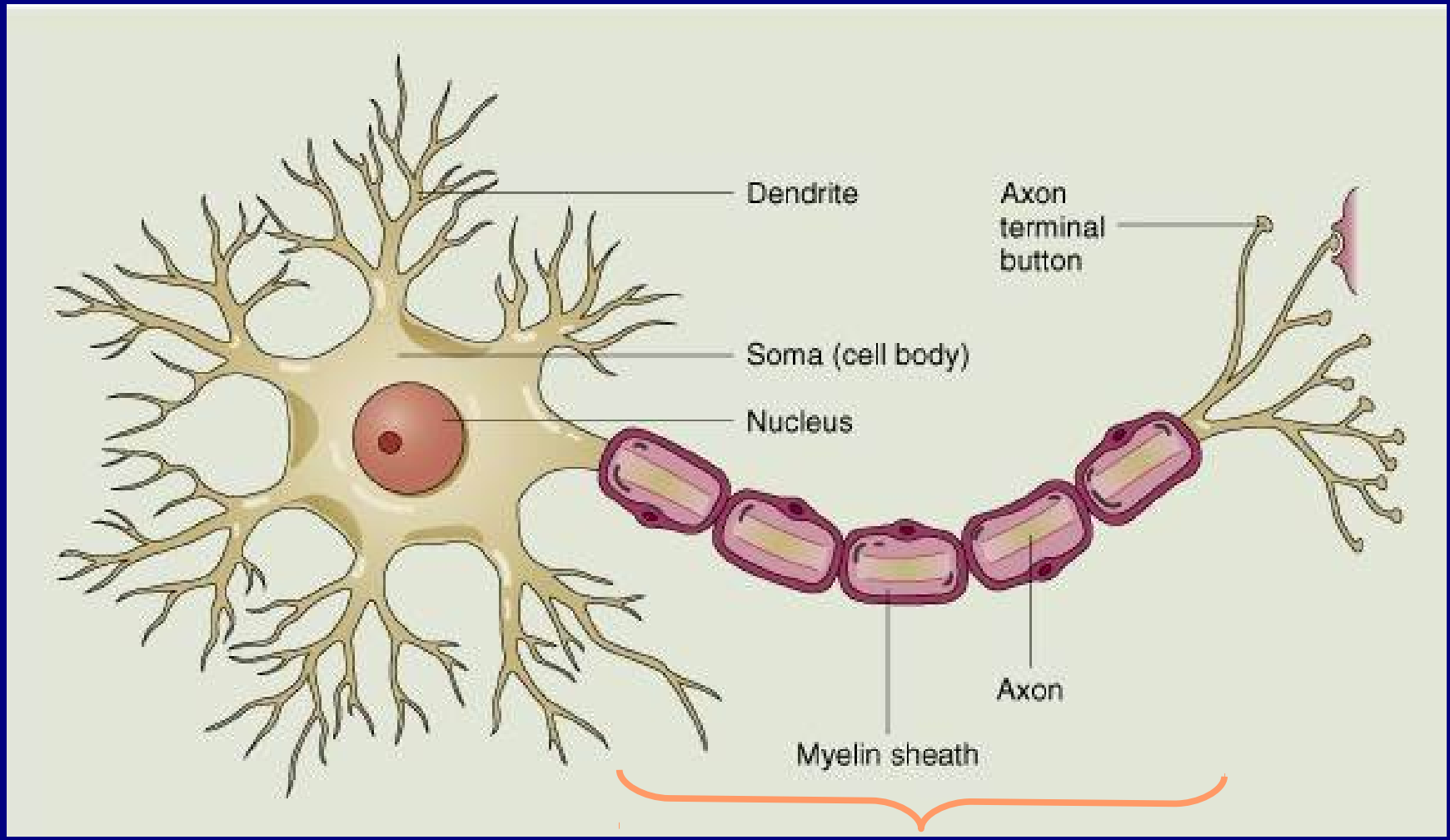
Can quantify structural (esp. WM) properties using:
FA, MD, RD, L1, etc.

Can investigate (and Quantify?) network relations with:
tractography



Structural connections in the brain

The (schematic) structure of neurons

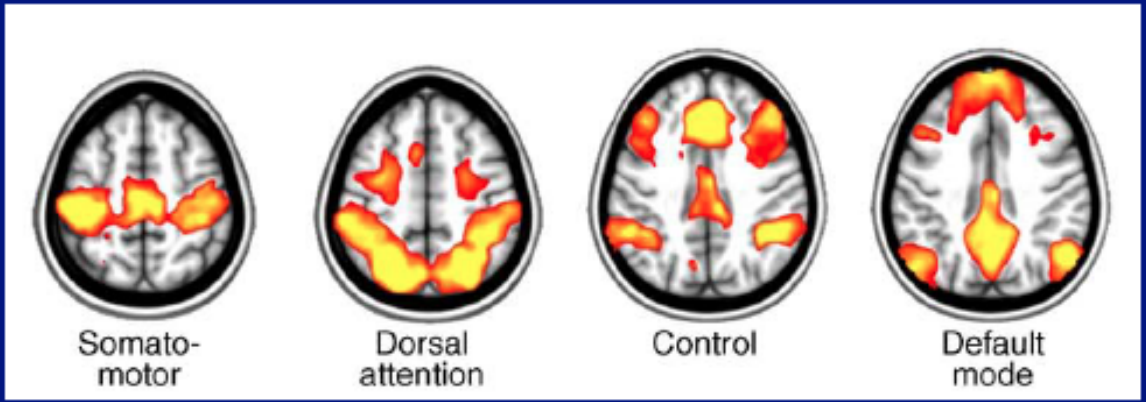


Extended white matter fibers, often organized in bundles

Structure + Function

Simple example:

GM ROIs network:



Raichle (2010, TiCS)

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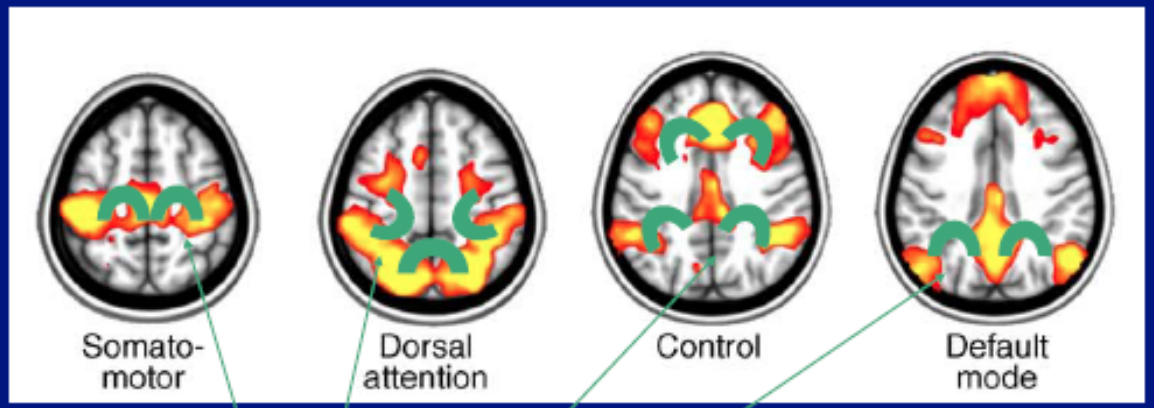

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Associated WM ROIs

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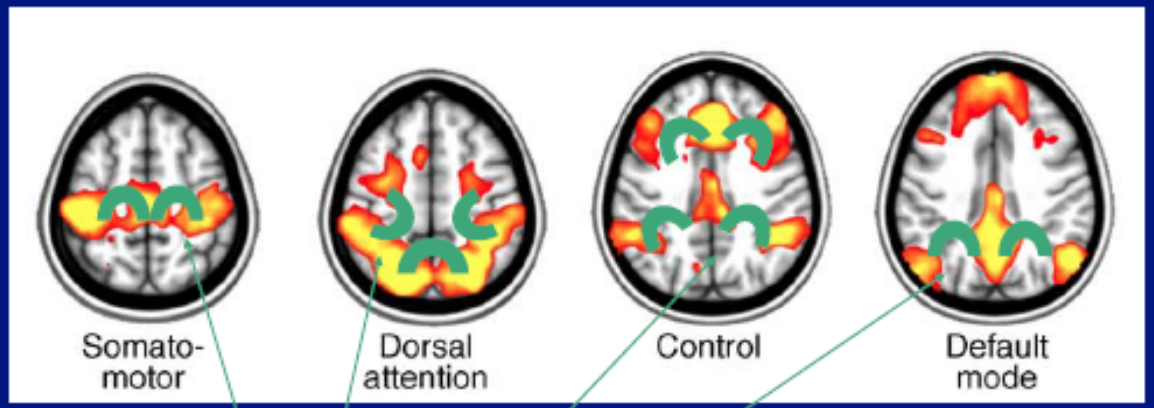

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Associated WM ROIs

Our goal for tractography->
estimate likely/probable locations of WM associated with GM, and relate ROI quantities with functional/GM properties

AFNI tools for combining FC and SC:

Combining functional and tractographic connectivity will require:

+ determining networks from FMRI (or other) data;
+ finding correlations and local properties of functional networks;
+ turning GM ROIs into targets for tractography;
+ doing reasonable tractography to find WM ROIs;
+ estimating stats on WM ROIs...

FATCAT: Functional And Tractographic Connectivity Analysis Toolbox (Taylor & Saad, 2013), available in AFNI with demo data+scripts.

*picture from google search, not from/of either author

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

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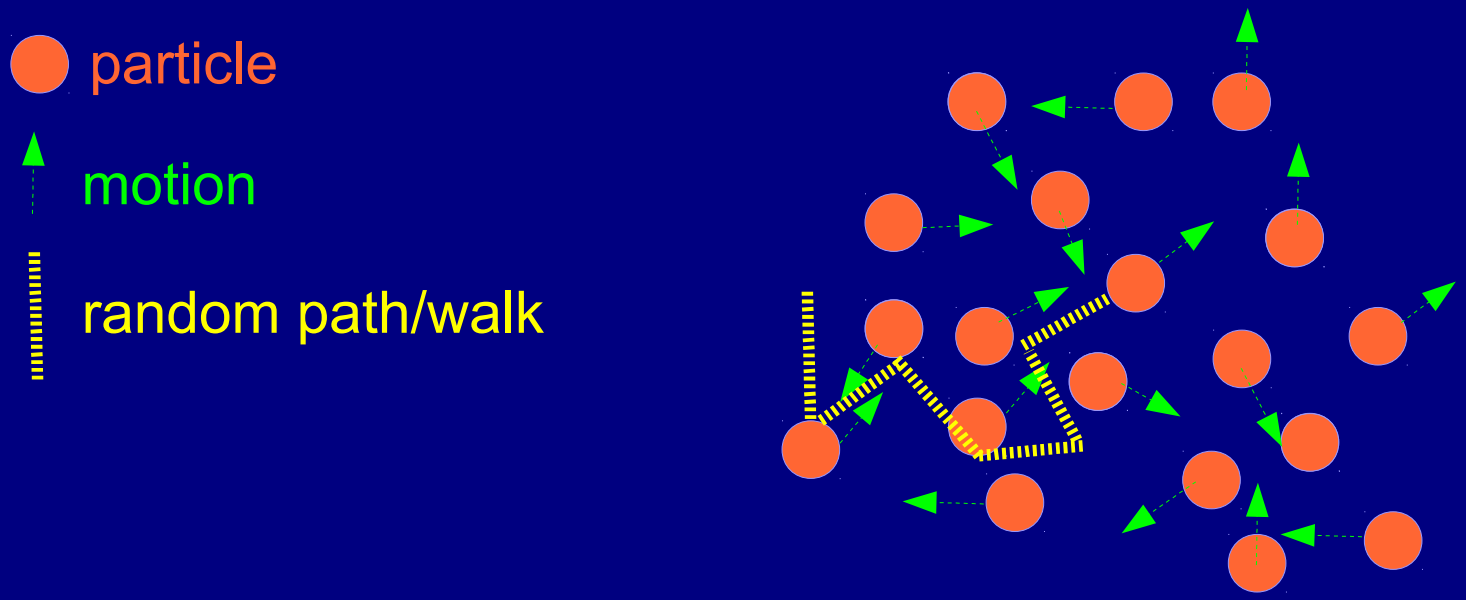
*D*iffusion: random motion of particles, tending to spread out

$\rightarrow$ here, hydrogen atoms in aqueous brain tissue



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*T*ensor: a mathematical object (a matrix) to store information

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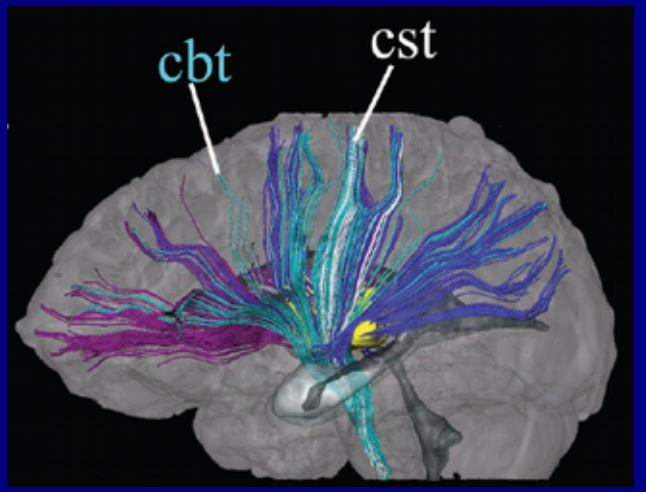
→ here, quantifying particle spread in all directions

*I*maging: 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):

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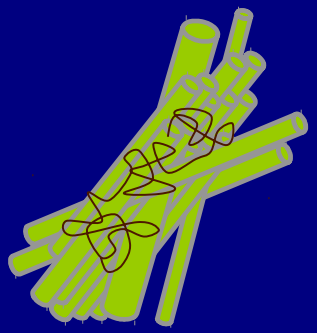
$\rightarrow$ *Diffusion shape tells of structure presence and spatial orientation*

Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures

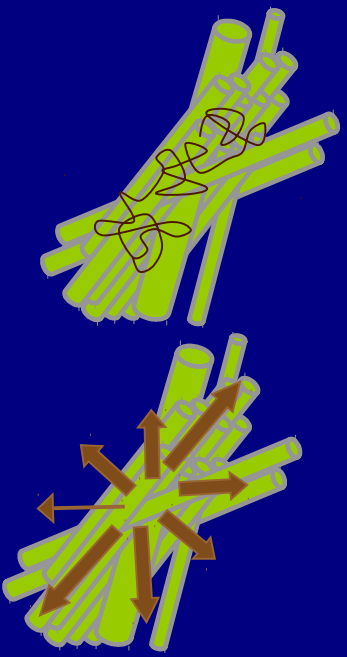


Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures

2) Statistical motion measured using diffusion weighted MRI



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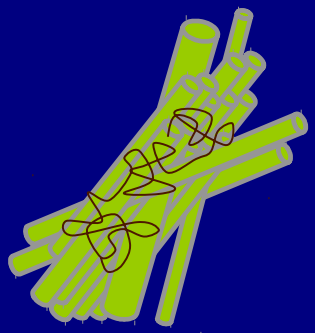

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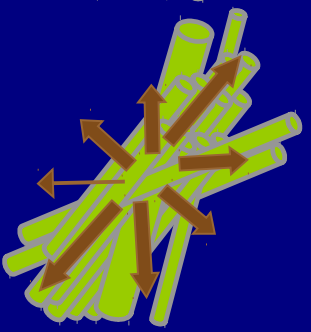
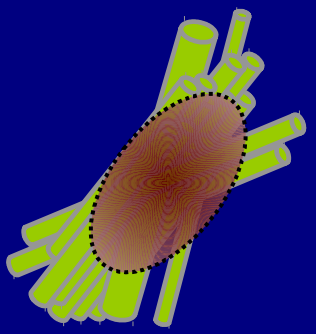


3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:

+ one direction:
  DTI (Diffusion Tensor Imaging)



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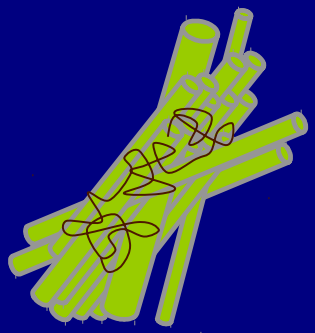

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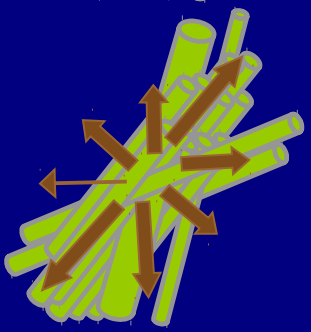

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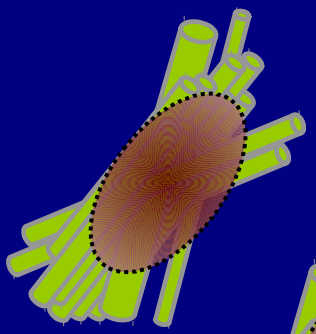

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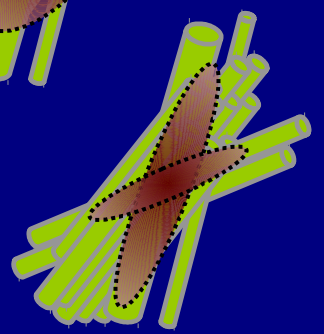

+ >=1 direction:
  HARDI (High Angular Resolution Diffusion Imaging)
  Qball, DSI, ODFs, ball-and-stick, multi-tensor, CSD, ...

Diffusion in MRI

Mathematical properties
of the matrix/tensor:

$$\mathbf{D} = \begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

Having: 3 eigenvectors: $\mathbf{e}_i$
3 eigenvalues: λ_i

- Real-valued
- Positive definite ($\mathbf{r}^T\mathbf{D}\mathbf{r} > 0$)

$\mathbf{D}\mathbf{e}_i = \lambda_i \mathbf{e}_i, \quad \lambda_i > 0$

- Symmetric ($D_{12} = D_{21}$, etc),
6 independent values

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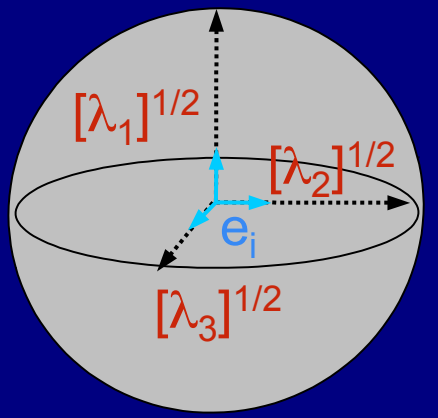
6 independent values

Geometrically, this describes an ellipsoid surface:

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

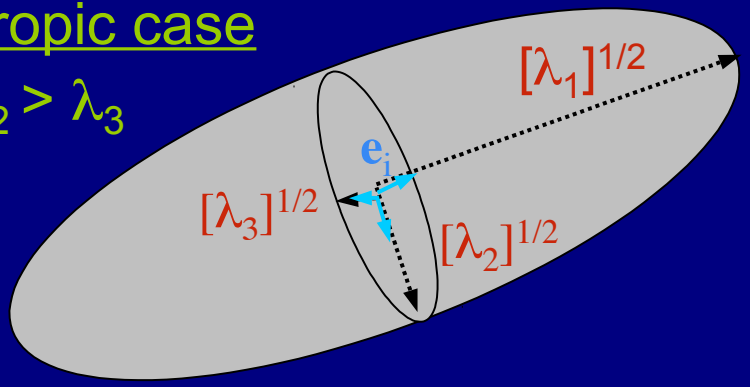
isotropic case

$\lambda_1 = \lambda_2 = \lambda_3$



anisotropic case

$\lambda_1 > \lambda_2 > \lambda_3$



DTI: ellipsoids

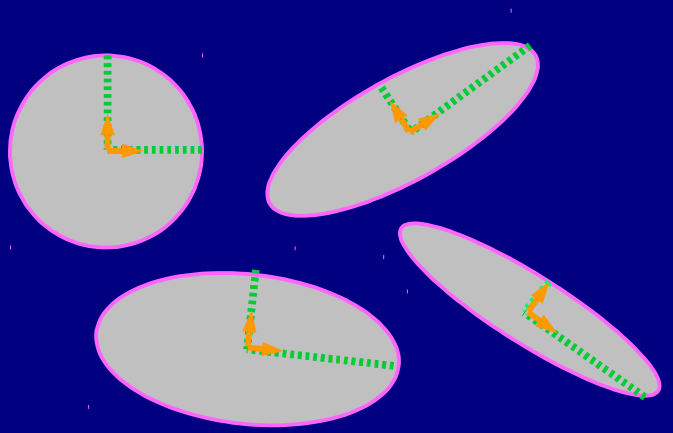
Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:

  tensor **D** → **ellipsoid surface**

  eigenvectors → orientation in space

  eigenvalues → 'pointiness' + 'size'



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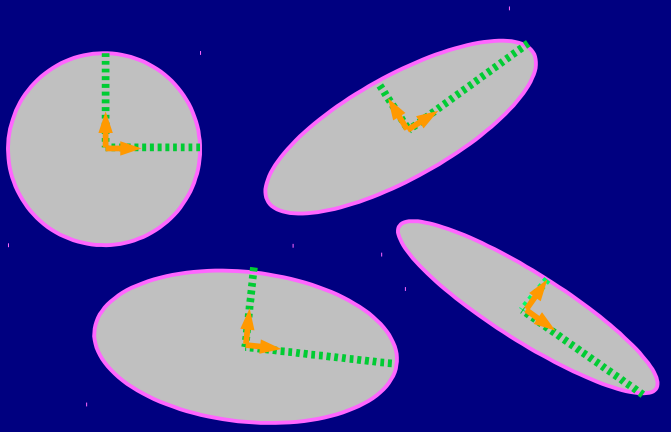

+ Determine the minimum number of

  DWIs measures needed (6 + baseline)

$$\begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

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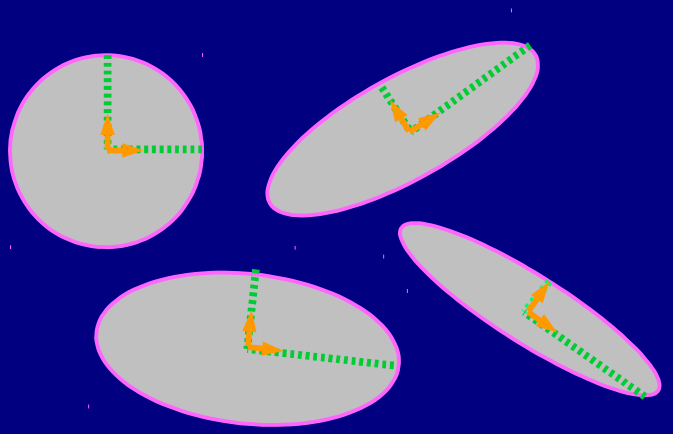
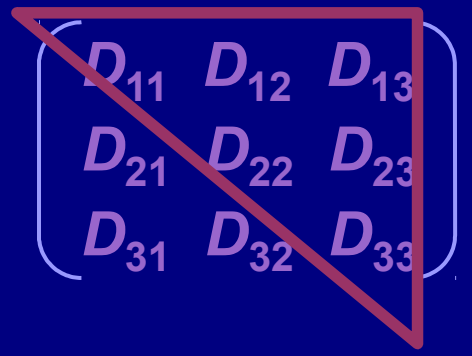
  - eigenvectors → orientation in space
  - eigenvalues → 'pointiness' + 'size'

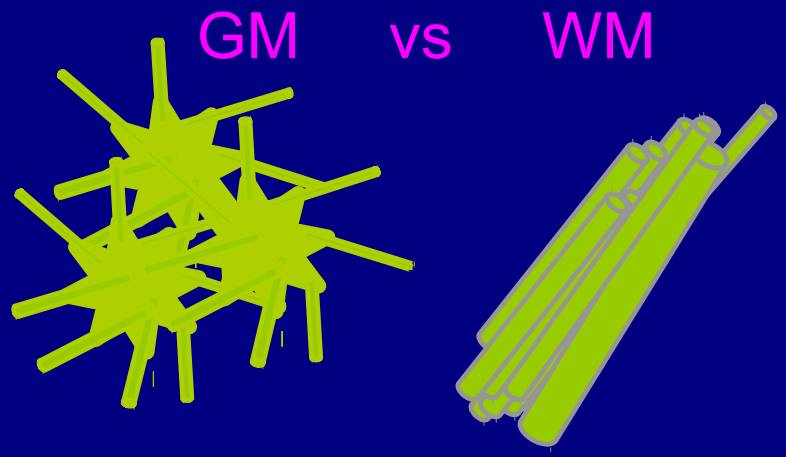


+ Determine the minimum number of
  - DWIs measures needed (6 + baseline)

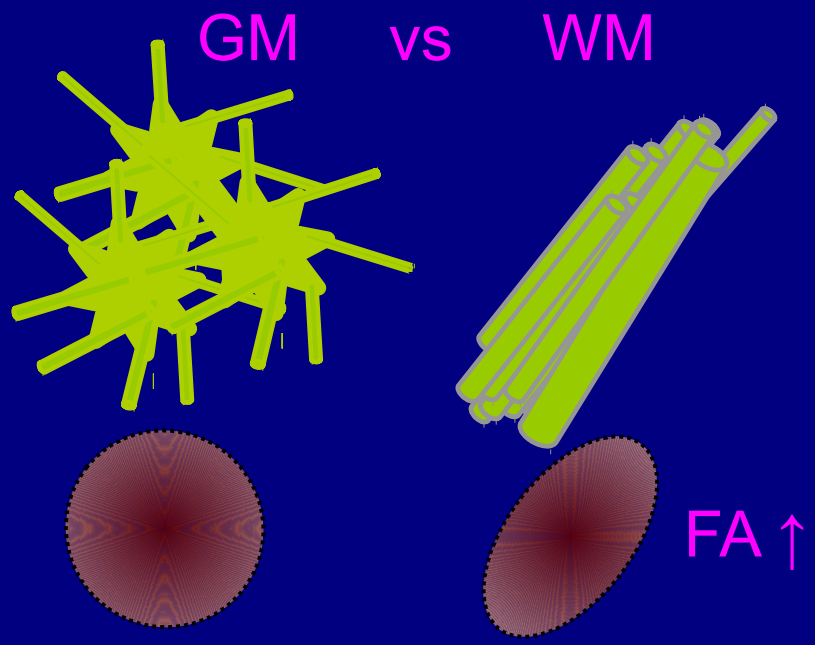


+ Determine much of the processing and
  - noise minimization steps

Cartoon examples: white matter ↔ FA

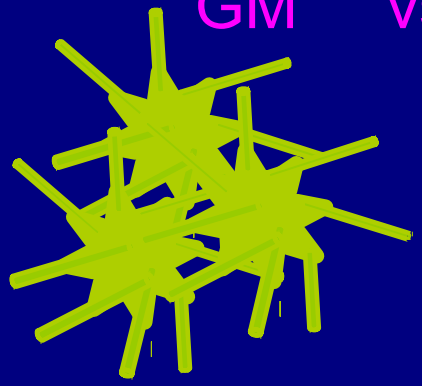


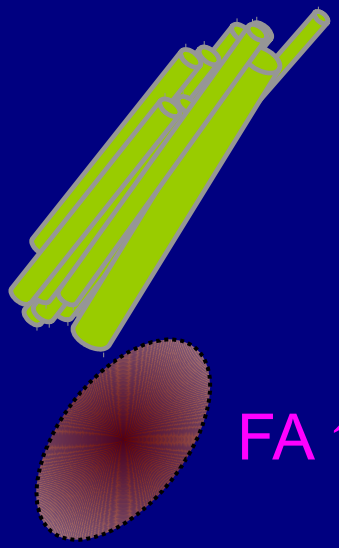
Cartoon examples: white matter ↔ FA



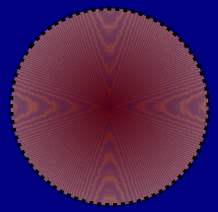
Cartoon examples: white matter ↔ FA

GM vs WM

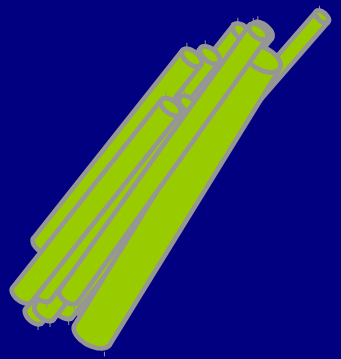




FA ↑



WM bundle organization



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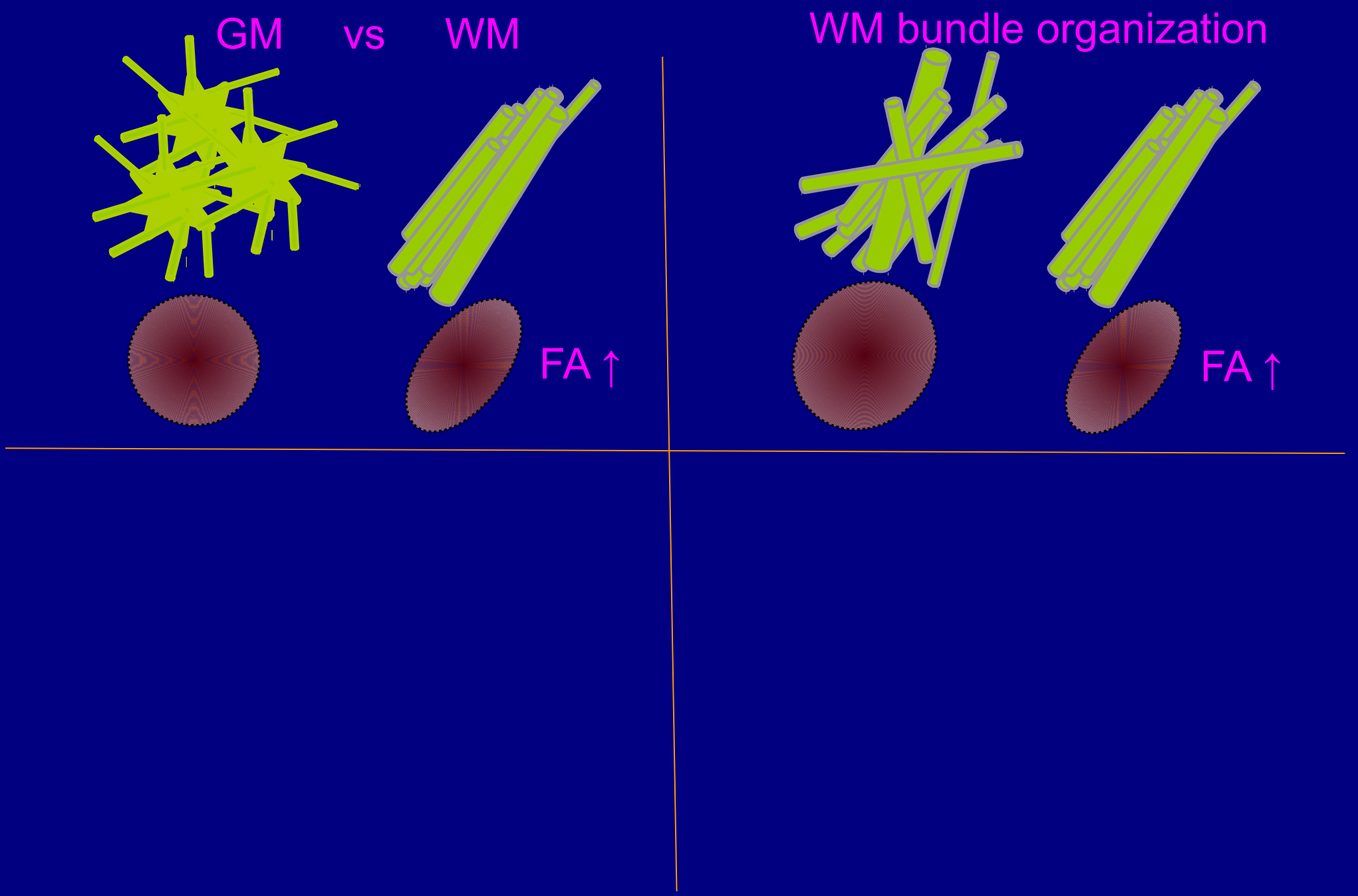
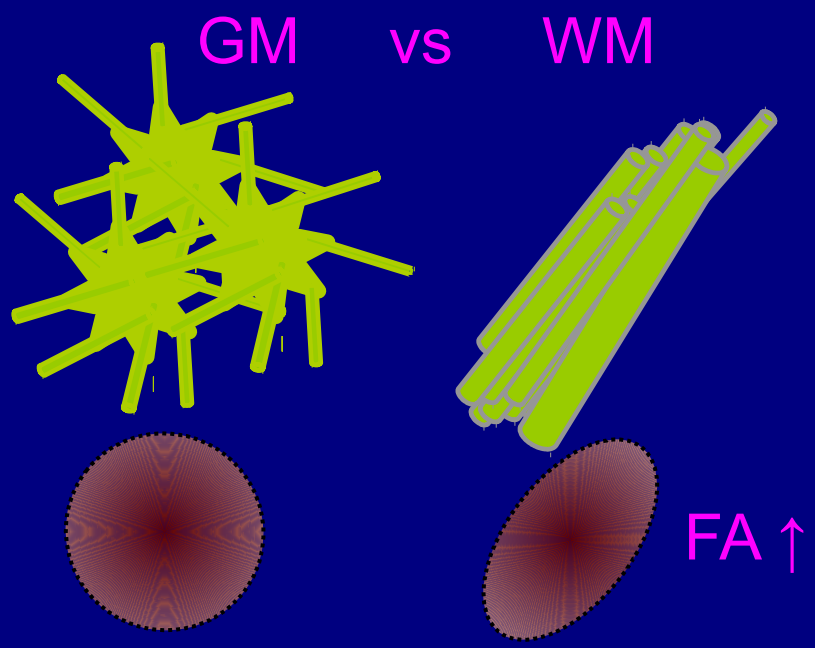
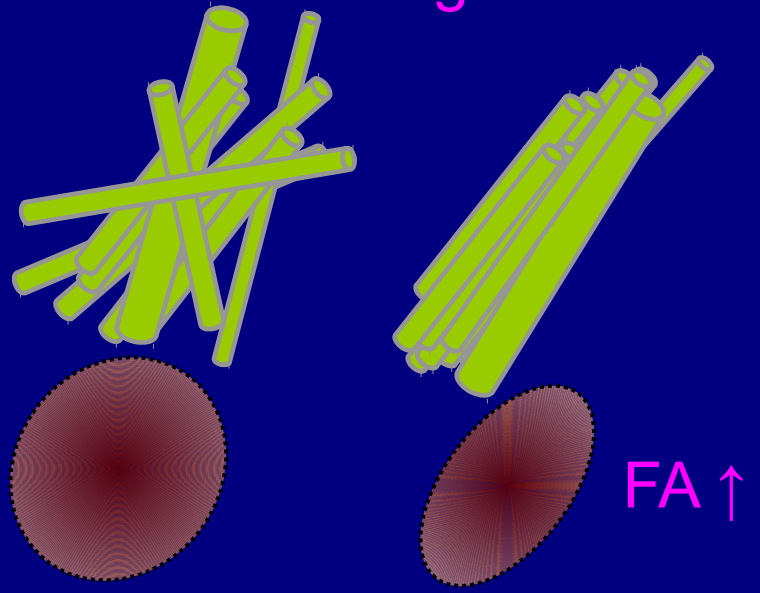
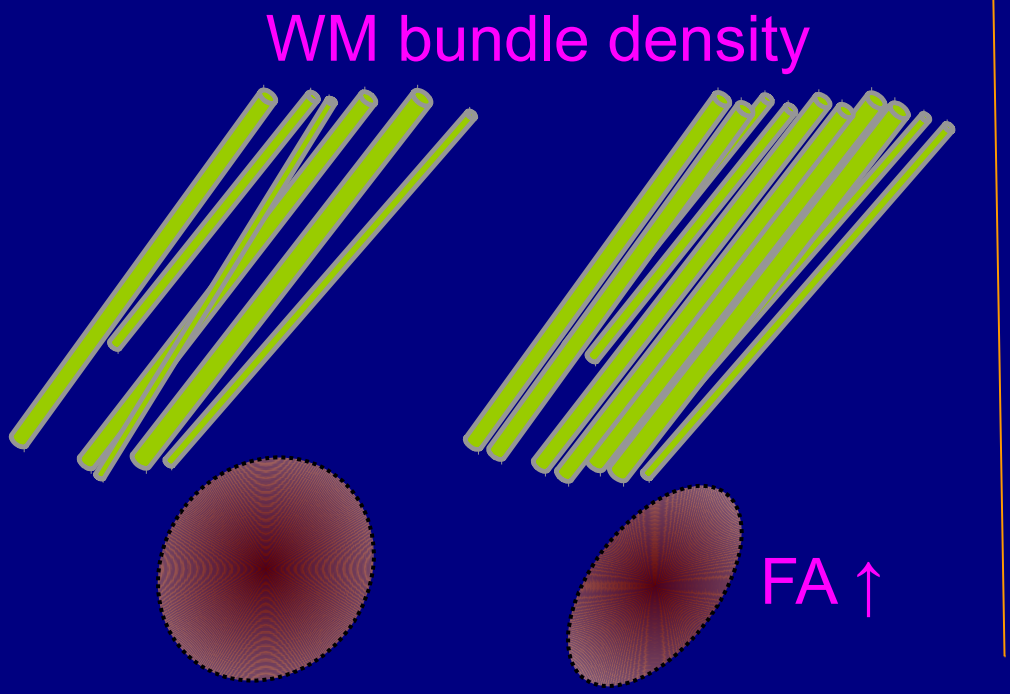


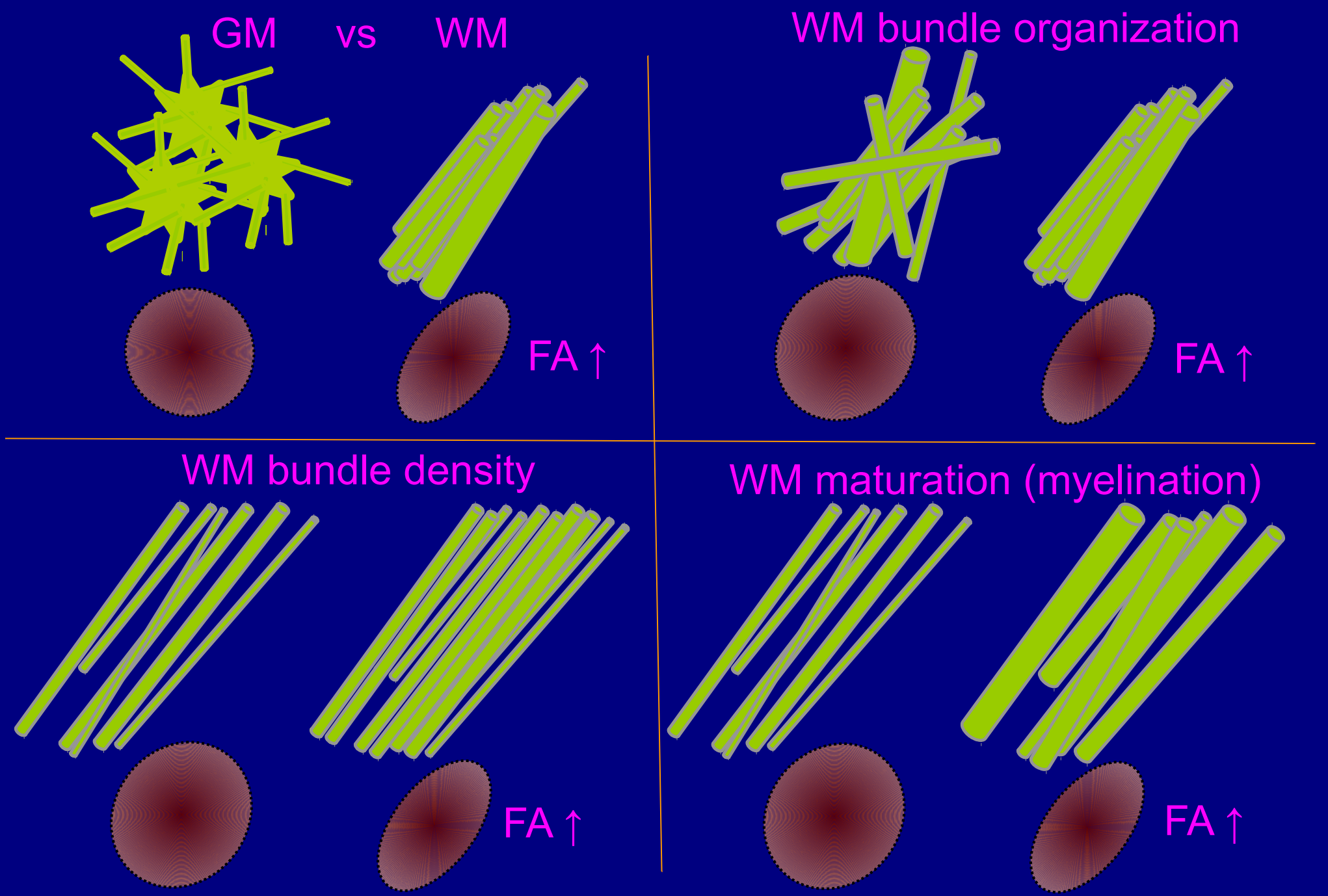
Cartoon examples: white matter ↔ FA







Cartoon examples: white matter ↔ 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

- in adults, FA>0.2 is proxy for WM

MD, L1, RD: local density of structure

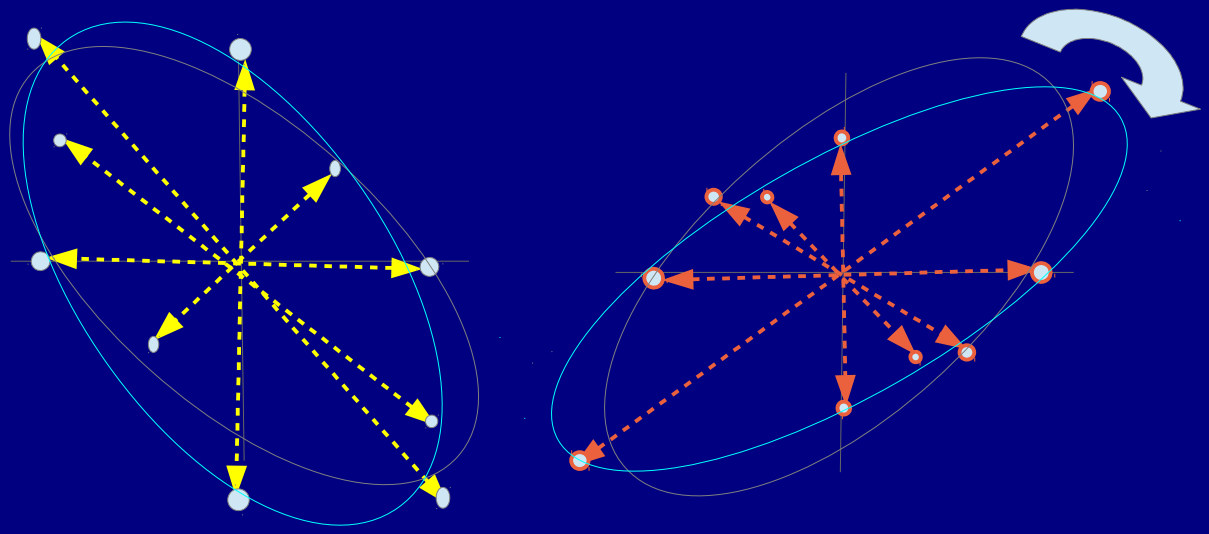
e_1: orientation of major bundles

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

Noise in DW signals

→ Leads to errors in surface fit, equivalent to *rotations* and *rescalings* of ellipsoids:



'Un-noisy' vs perturbed/noisy fit

Now discuss using *local* structure information
to generate/estimate *nonlocal* structures:
WM tractography

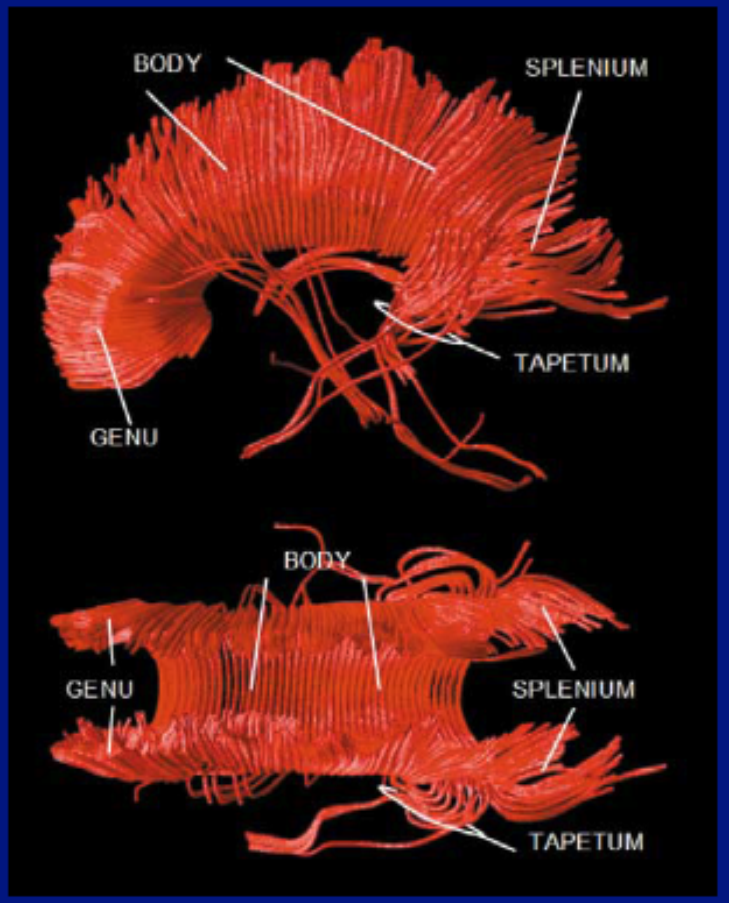
Tractography in brief

old, invasive

stain and preserve brain, get some Idea of structure… non-ideal:

brain physiology changes postmortem, also `mortem' aspect

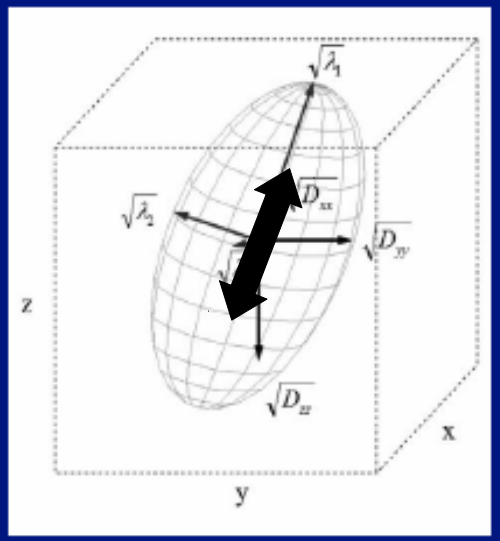
new(er), theoretical



(images from Iowa Virtual Hospital and Bammer et al. 2003)

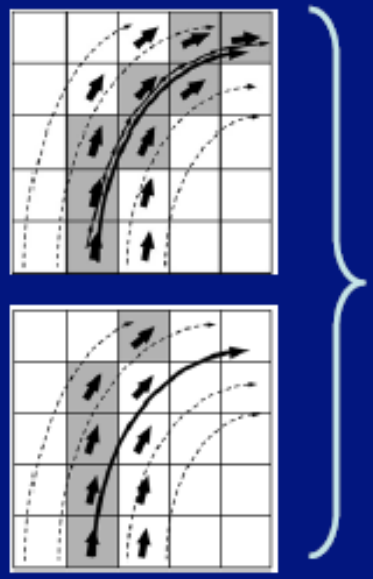
Tractography

Estimate WM structure (fiber tract locations)



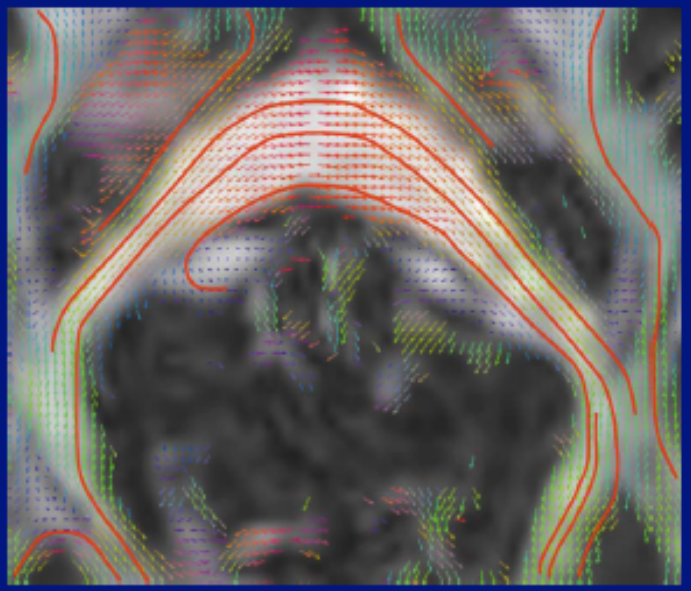
ellipsoid measures (*~smoothing of real structures*)

+



some kind of algorithm for connecting

=

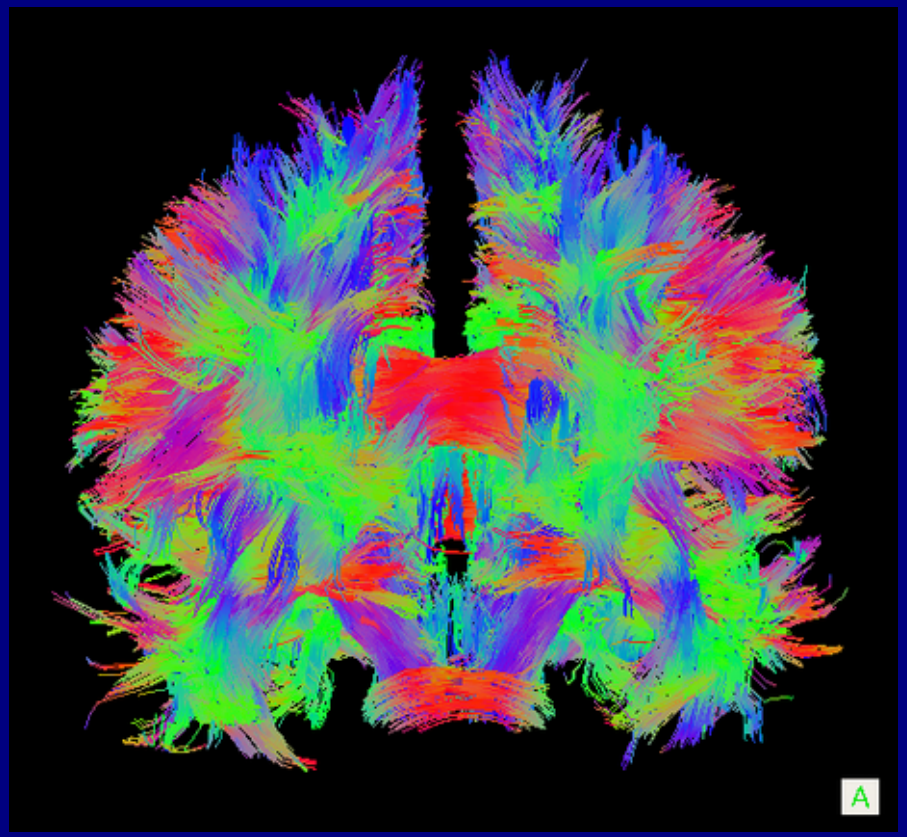


estimate spatial extents of WM 'tracts' in vivo

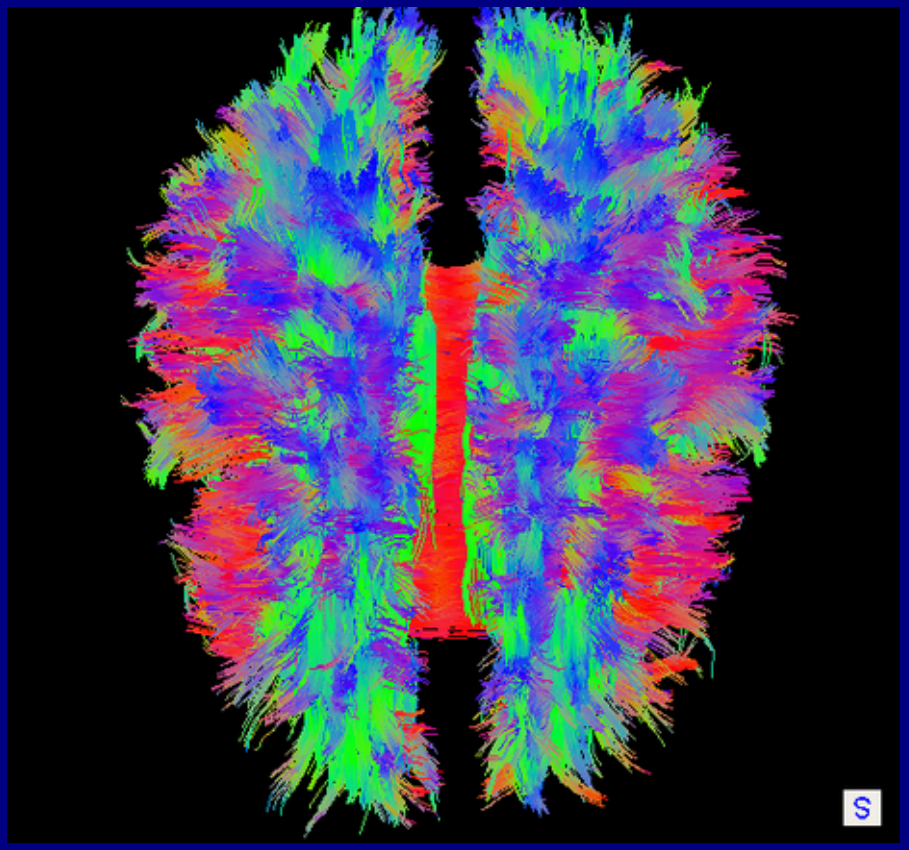
(images from Bammer et al. 2003)

Tractography: connecting the brain

(looking at you)



(looking downward)



Importance of being processed (in earnest)

NB words of wisdom from wikipedia GIGO entry:

On two occasions I have been asked, "Pray, Mr. Babbage, if you put into the machine wrong figures, will the right answers come out?" ... I am not able rightly to apprehend the kind of confusion of ideas that could provoke such a question.

—Charles Babbage, Passages from the Life of a Philosopher

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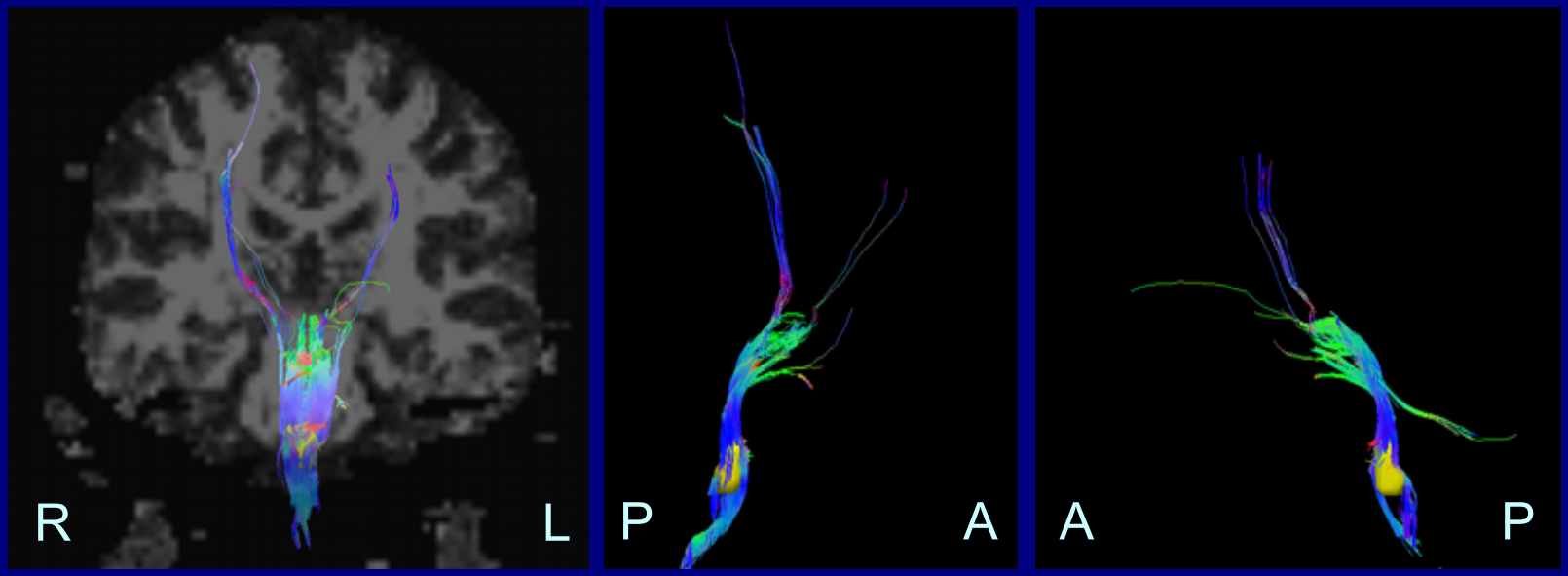
In addition to the tracking algorithm, the quality of data acquisition and preparation matter quite a bit

→ see the *TORTOISE* tool (Pierpaoli et al., 2010)

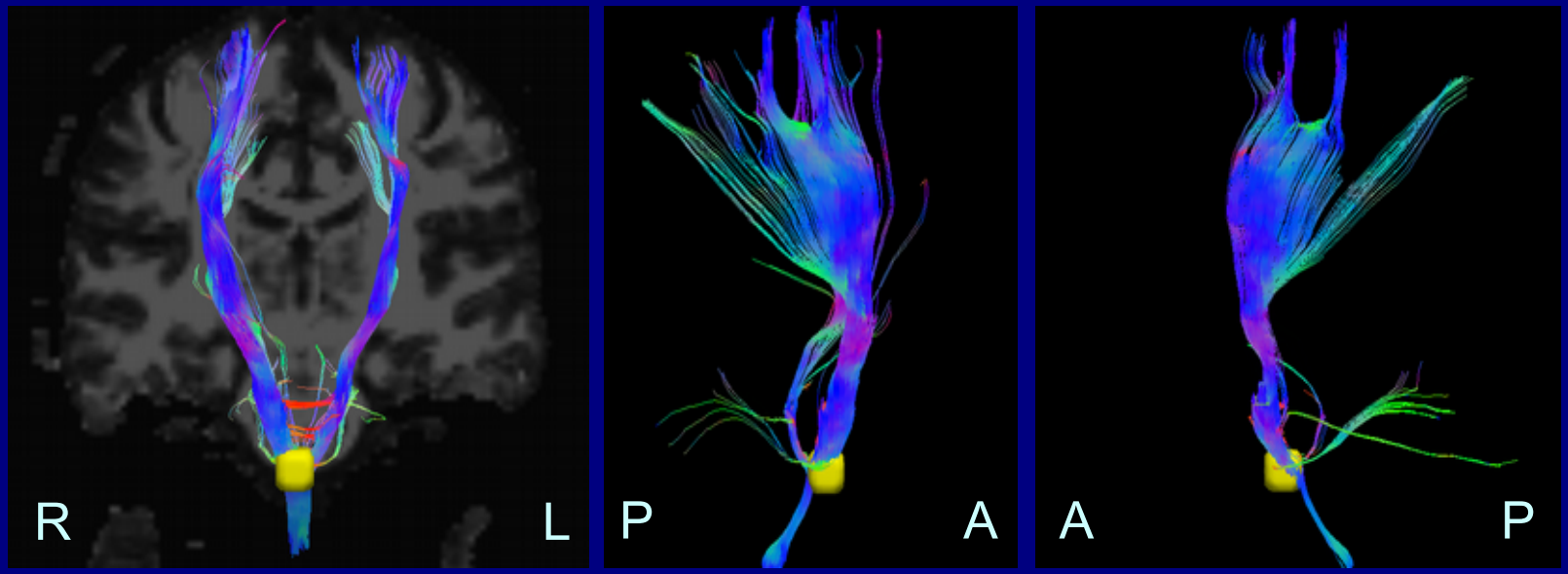
https://science.nichd.nih.gov/confluence/display/nihpd/TORTOISE

Importance of being processed (in earnest)

unprocessed



TORTOISEd



Data from the morning session, same target ROI in brainstem.

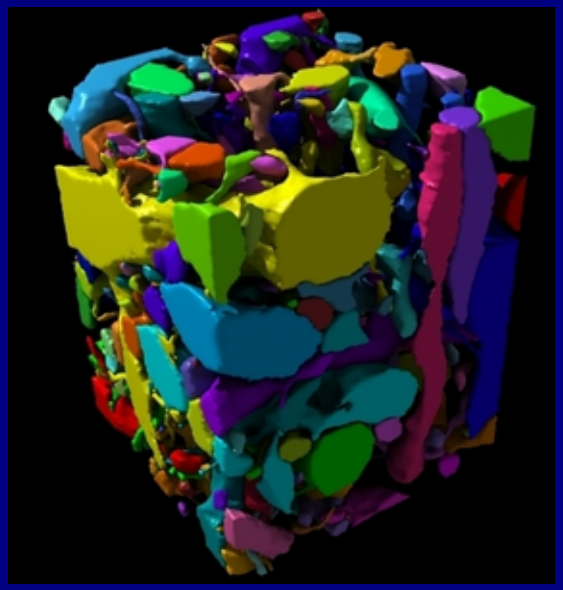
Consider reach of tracts, symmetry, physiology, etc.

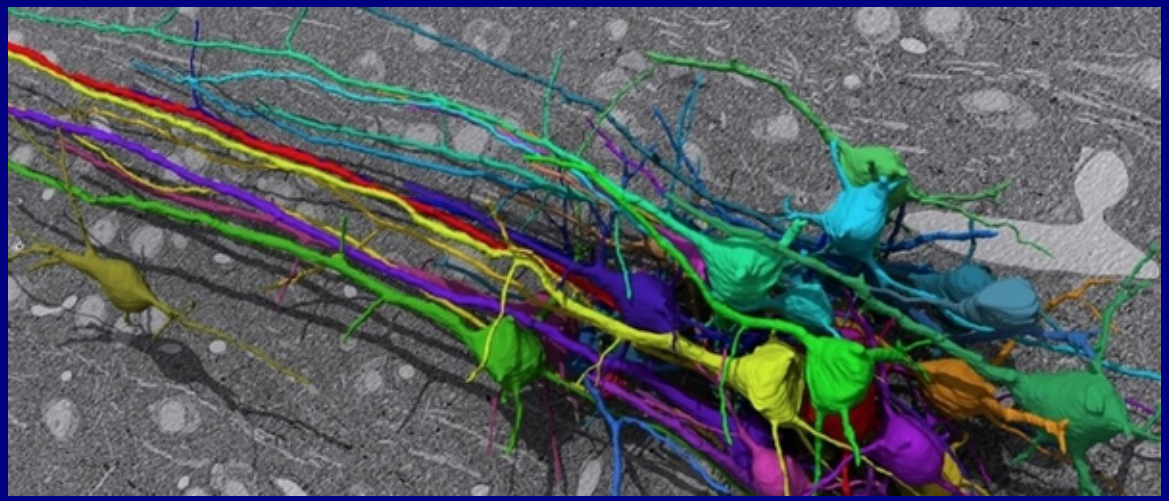
Cinematic side note:

La Belle et la Bête of tractography

Known Challenges for Tracking

+ Axon diameters are of order a few micrometers
+ MRI voxel size is of order millimeters





(images of Eyewire data via NPR website)

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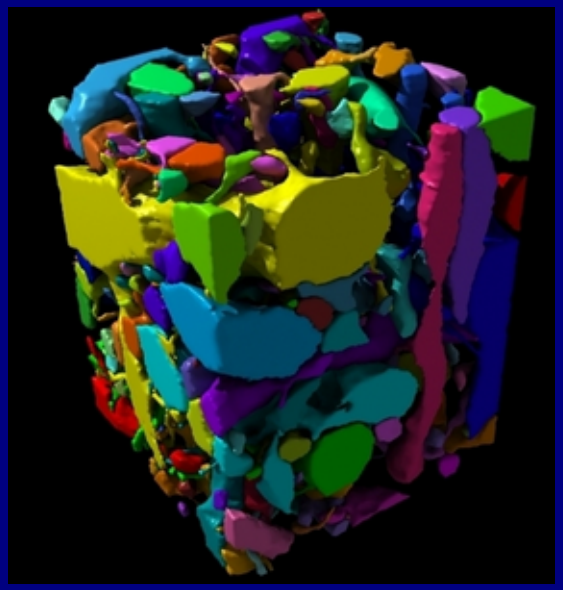
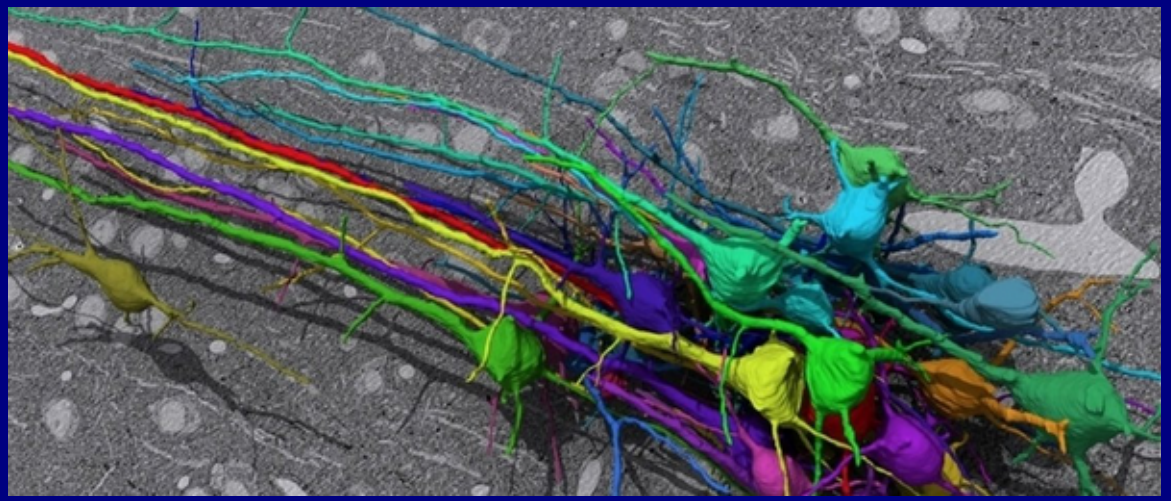
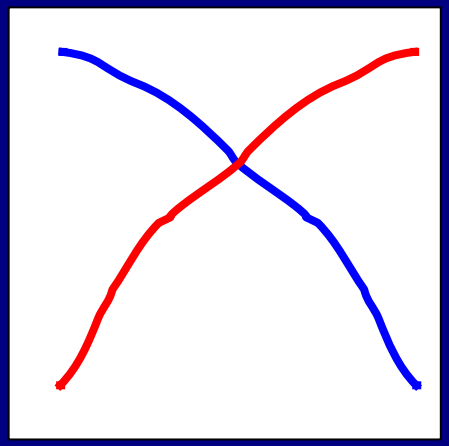
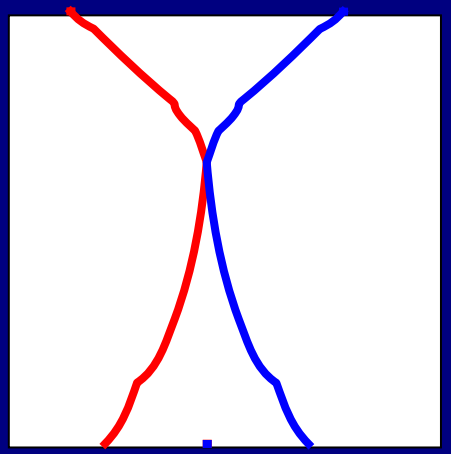




(images of Eyewire data via NPR website)

+ WM regions are tightly packed, with many connections and potentially complicated sub-voxel scale structure





Crossing/kissing fibers can:
- Lower FA (stop tracking)
- Redirect (or *not*) tracking incorrectly.

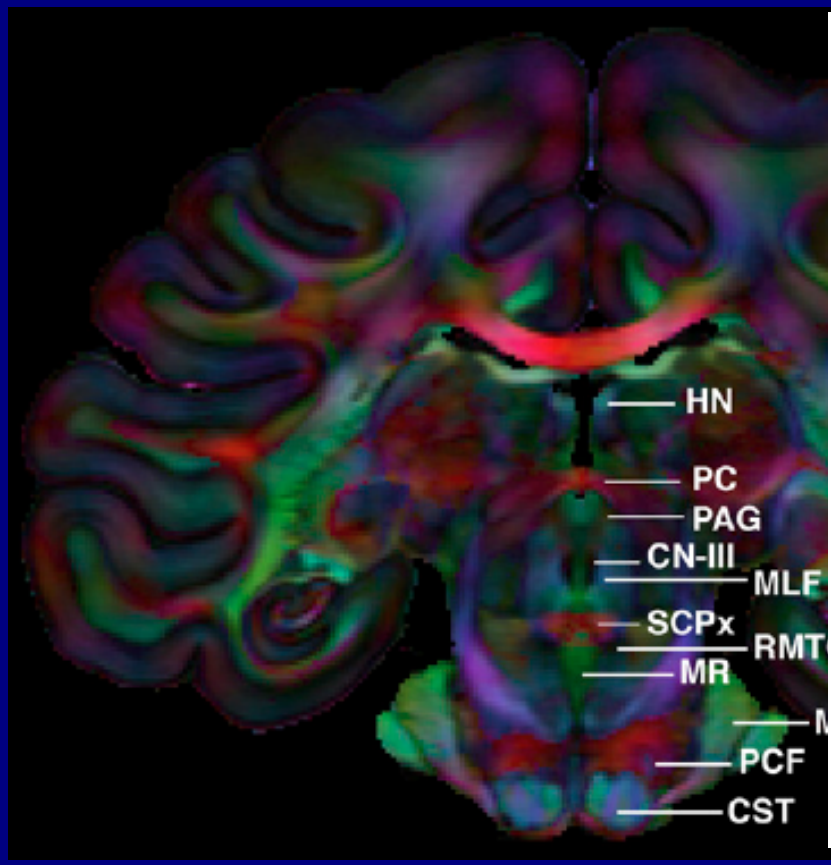
Known Challenges for Tracking

+ Comparisons: high res DTI with tracer anatomy

CrossMark click for updates

Anatomical accuracy of brain connections derived from diffusion MRI tractography is inherently limited

Cibu Thomas[a,b,1], Frank Q. Ye[c,d], M. Okan Irfanoglu[a,b], Pooja Modi[a], Kadharbatcha S. Saleem[e], David A. Leopold[c,d], and Carlo Pierpaoli[a,b]



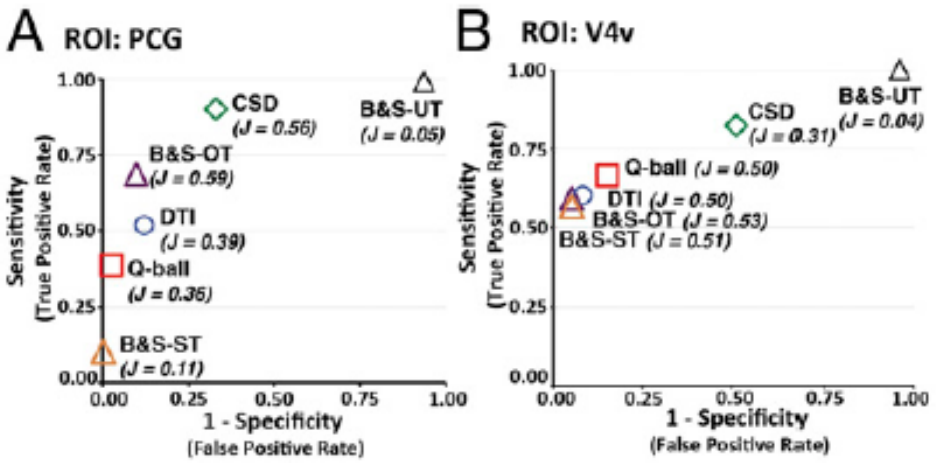
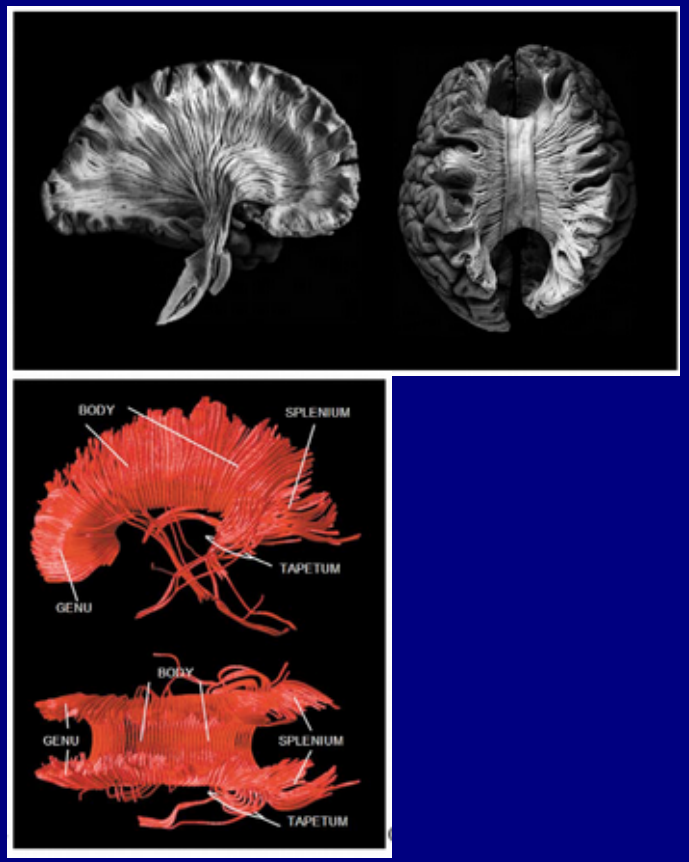


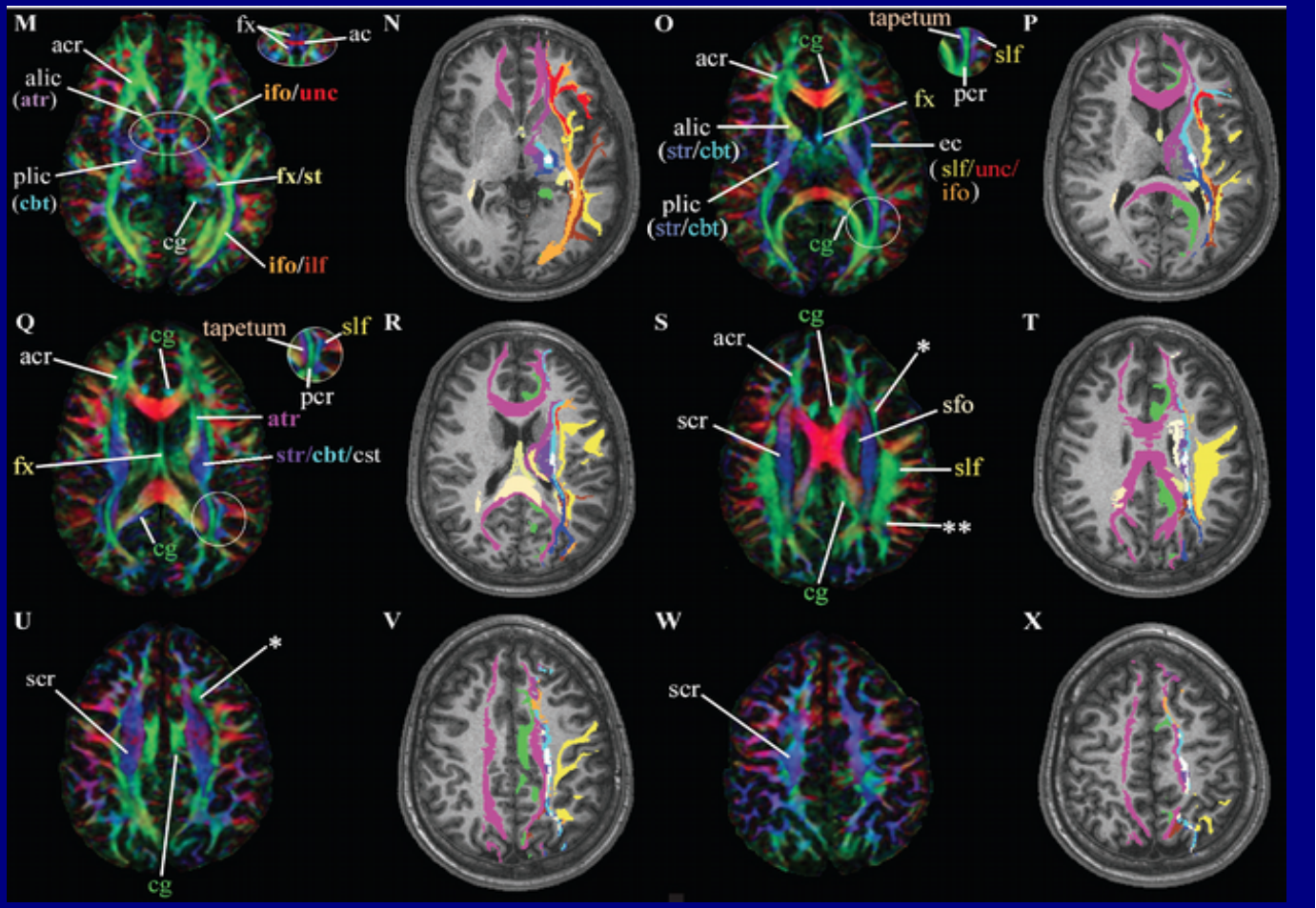
Fig. 2. The specificity and sensitivity of diffusion tractography techniques differ by diffusion model and location of the seed ROI. Specificity and sensitivity for seed ROI-PCG (*A*) and seed ROI-V4v (*B*). For all four types of diffusion models tested, the seed ROI was a sphere with a radius of 10 voxels, and the default angular threshold was used for deterministic (45°) and probabilistic (80°) tractography techniques. The Youden index value (J), which summarizes the performance of each tractography technique, is noted.

Achievements of Tracking

+ Reproduction of many known pathways
+ In vivo vs post-mortem information



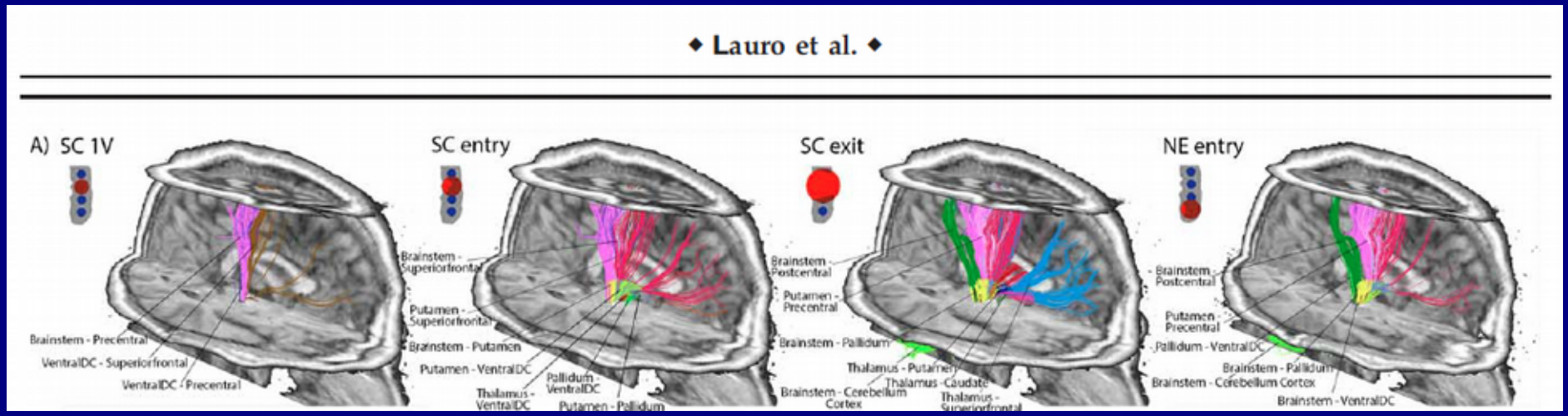
(Bammer et al., 2003)



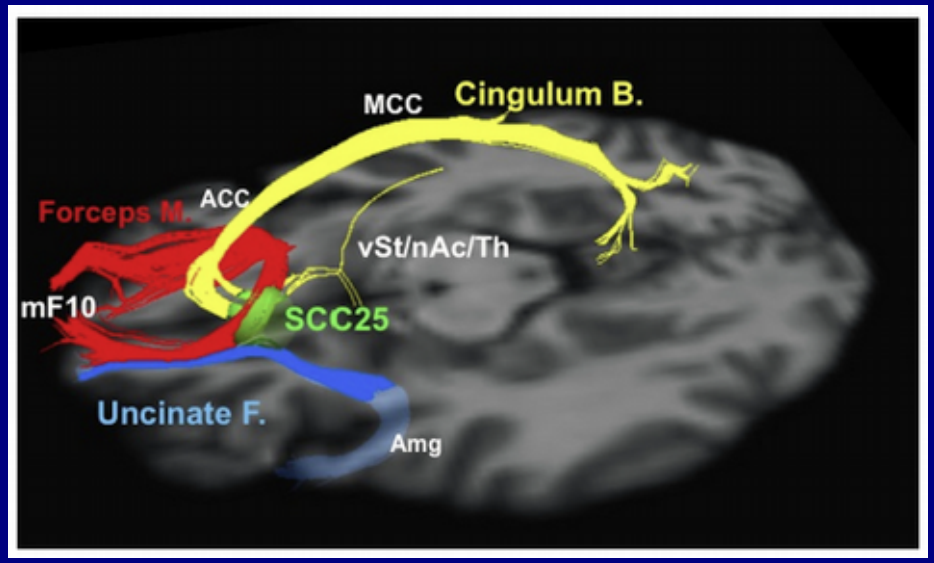
(Wakana et al., 2004)

Achievements of Tracking

+ Helping in planning electrode placement in deep brain stimulation (DBS)



DBS application: Parkinsons disease (Lauro et al., 2015)



DBS application: treatment-resistant depression (Rive-Posse et al., 2014)

Light at the end of the tunnel?

Tractography seems useful and logically consistent as follows:

1) GM ROIs *are* connected by WM skeleton.
2) We can use tracking to estimate and highlight WM *likely* to be associated with GM ROIs.
3) One can then use DTI parameters in the tracked 'WM ROIs' for quantitative comparisons (or use ROIs as masks for other data).
4) Tractography can parcellate the WM skeleton based on the subject's own data.
5) Avoid interpreting reconstructed tracks to represent literal, underlying fibers.

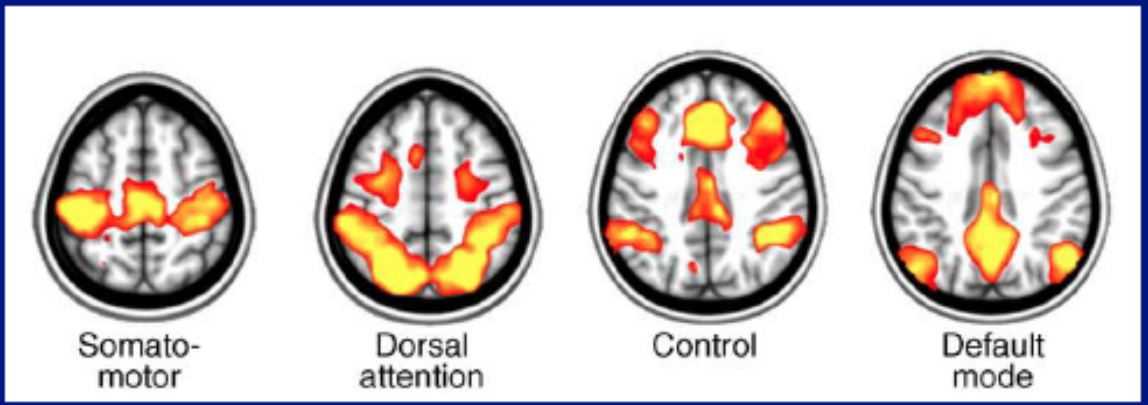
Applying tractography

Structure + Function

Simple example:

FMRI provides:
maps of (GM) regions working together

GM ROIs network:



Raichle (2010, TiCS)

Structure + Function

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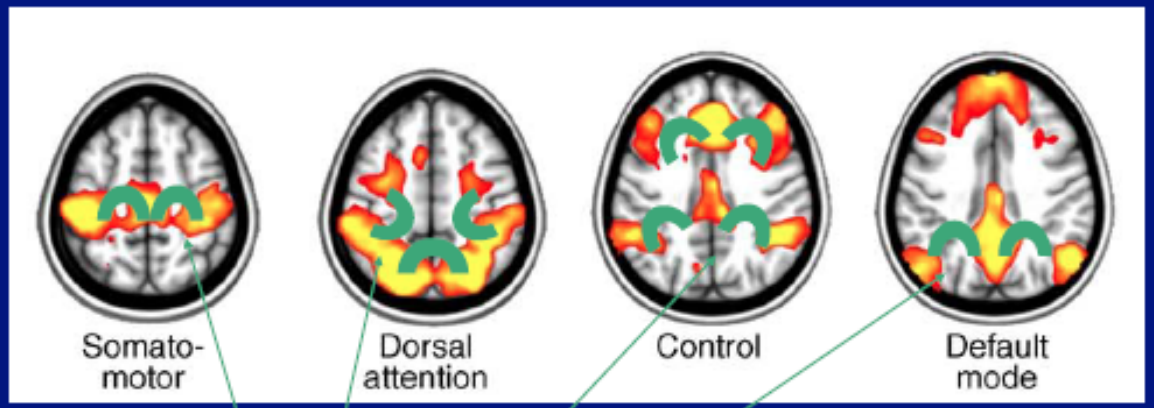

Raichle (2010, TiCS)

Associated WM ROIs

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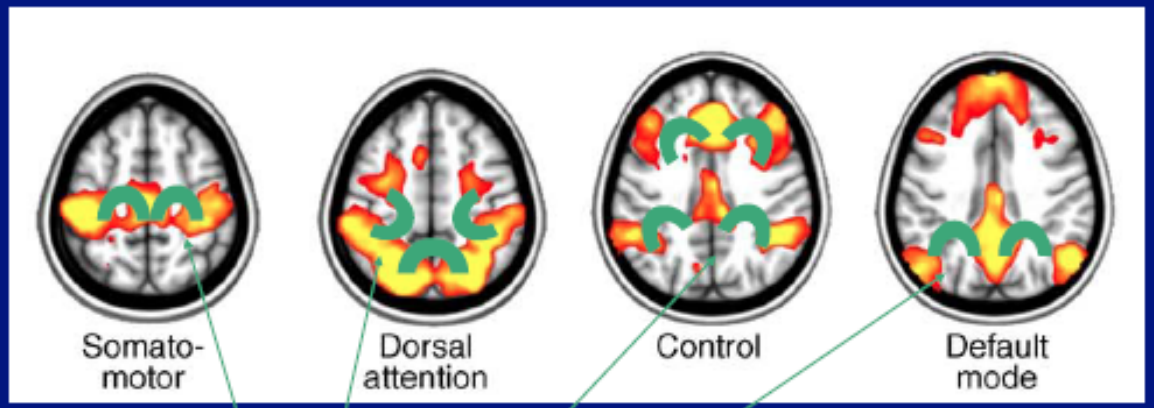


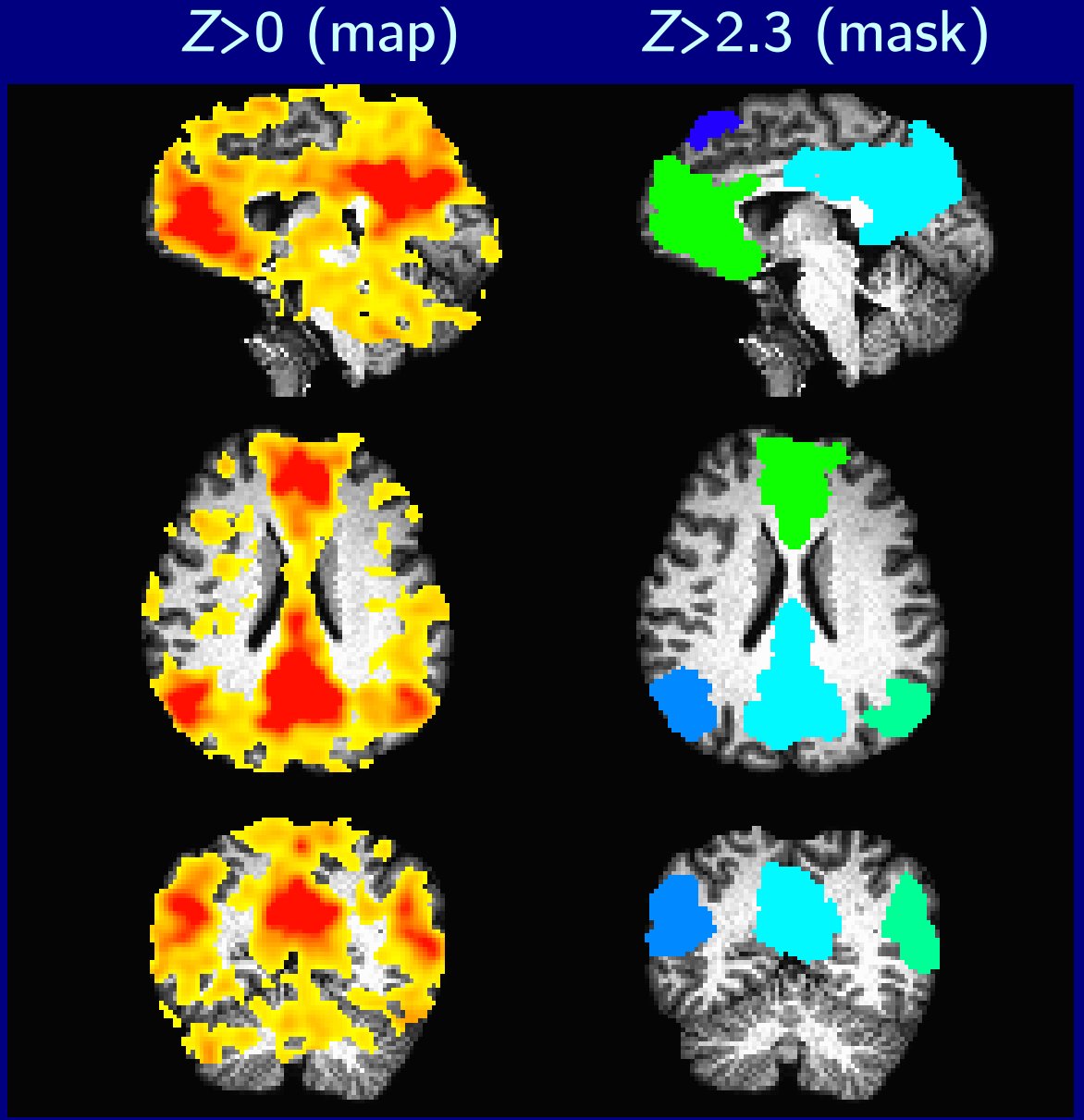
Raichle (2010, TiCS)

Associated WM ROIs

Our goal for tractography->
estimate likely/probable locations of WM associated with GM, and relate ROI quantities with functional/GM properties

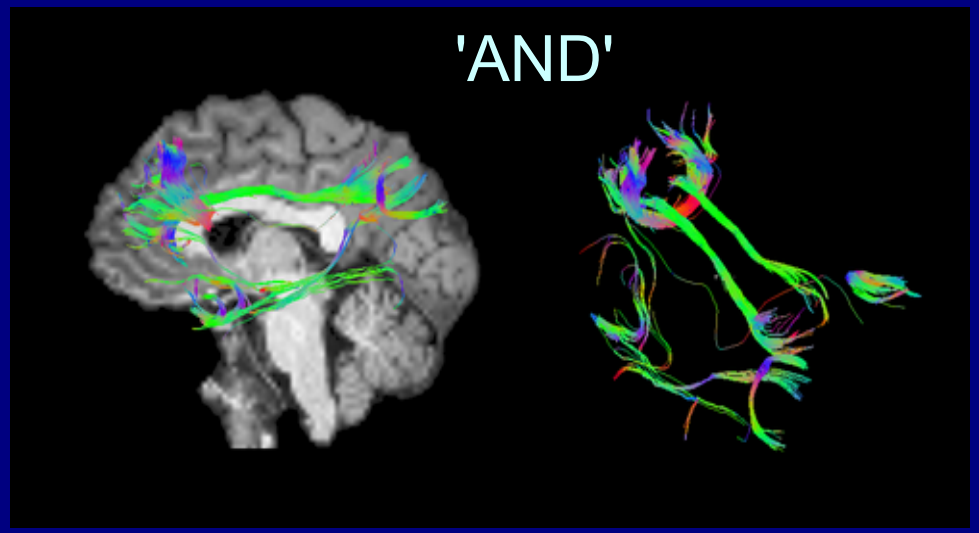
Example: Tractographic selections of WM

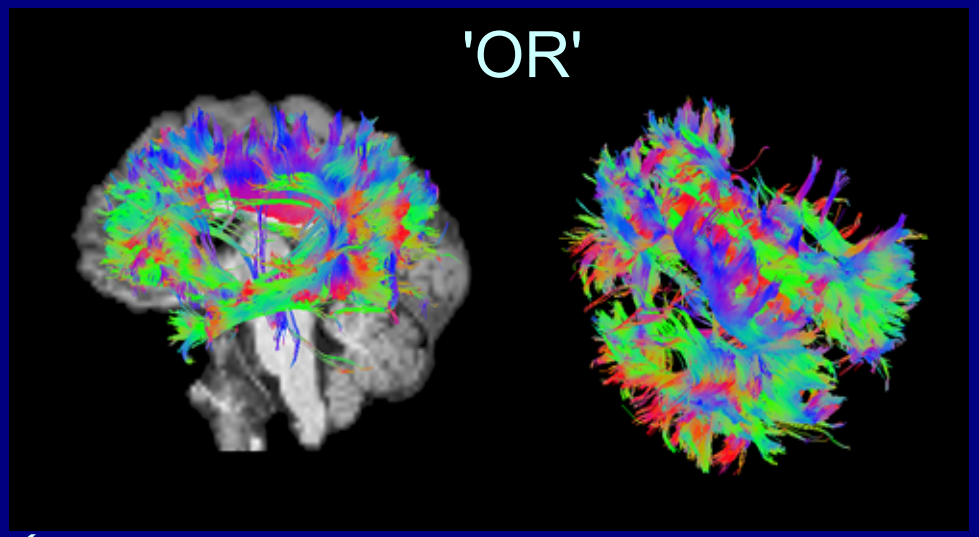
1) Start with FMRI:
$\rightarrow$ threshold to obtain
networks of GM ROIs

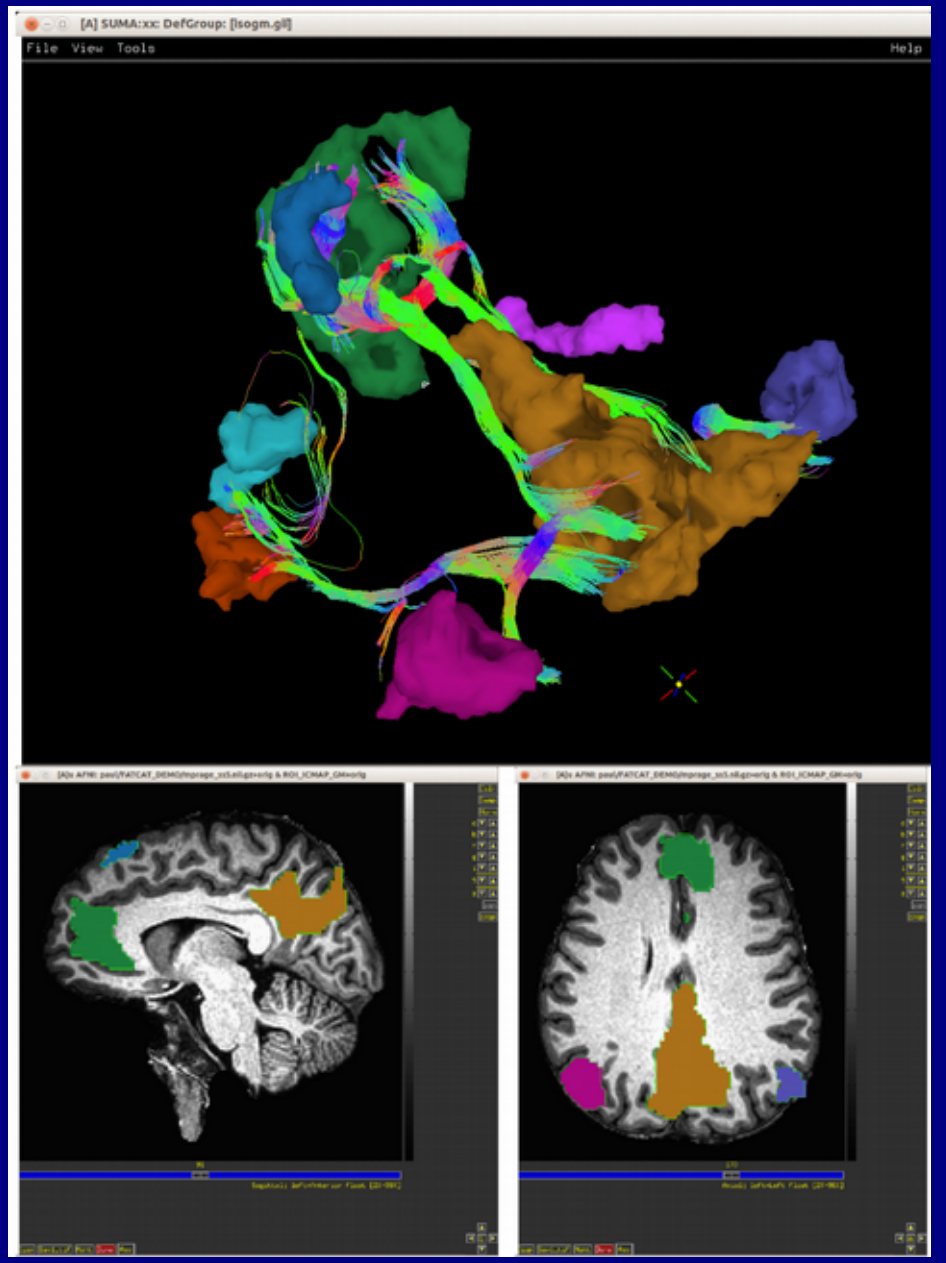


Example: Tractographic selections of WM

2) Use DTI-tractography to find likely location of WM associated with these 'targets'





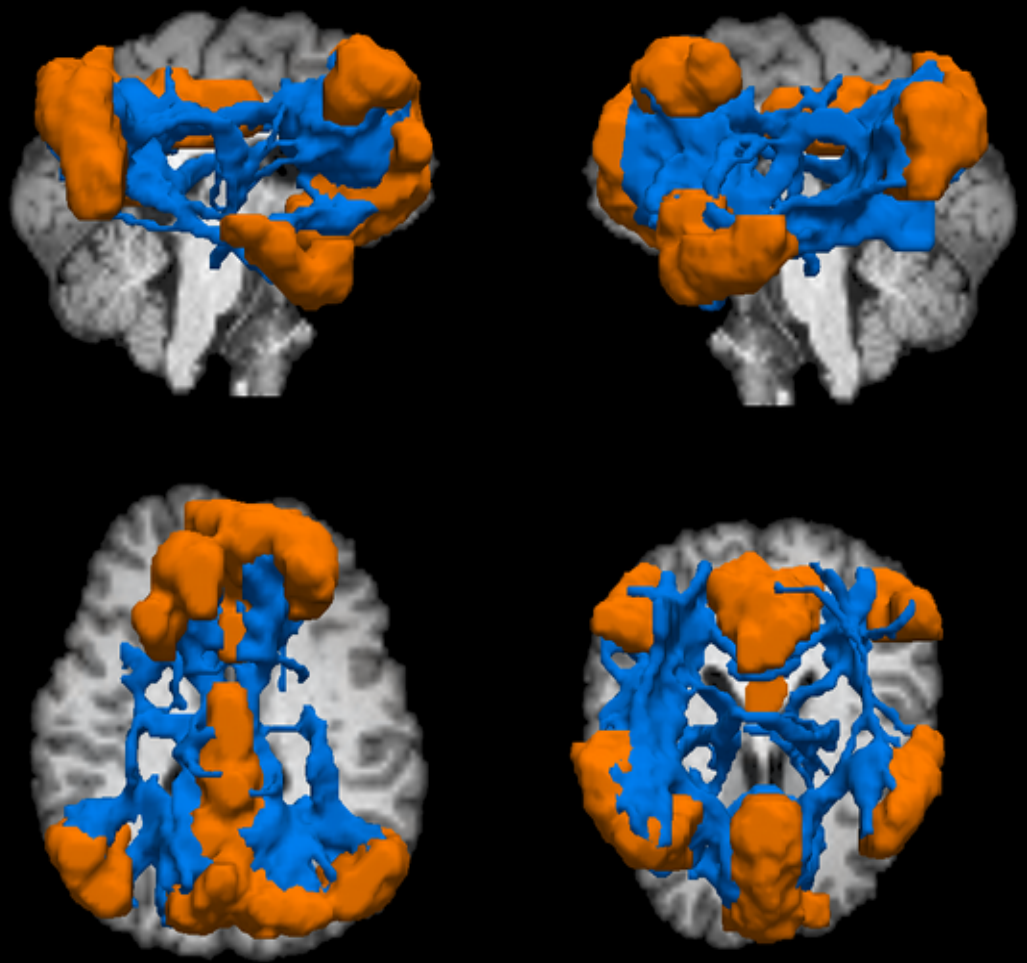


(Deterministic tracking using publicly available AFNI-FATCAT software)

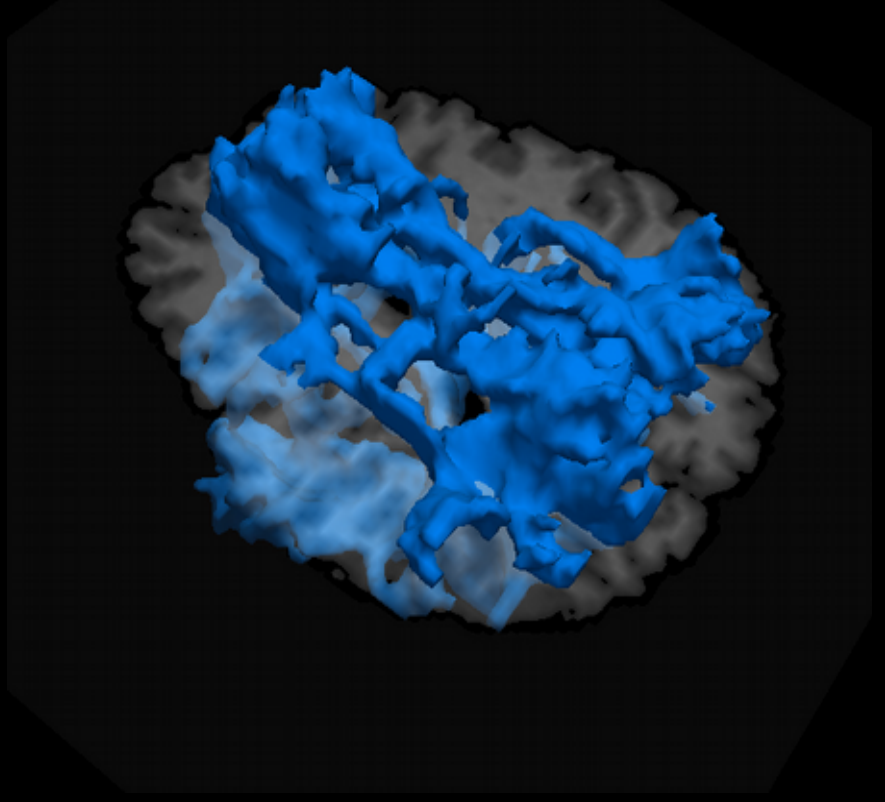
Example: Probabilistic tractography

More robust tracking method (many Monte Carlo iterations)

→ '***most likely***' locations of WM



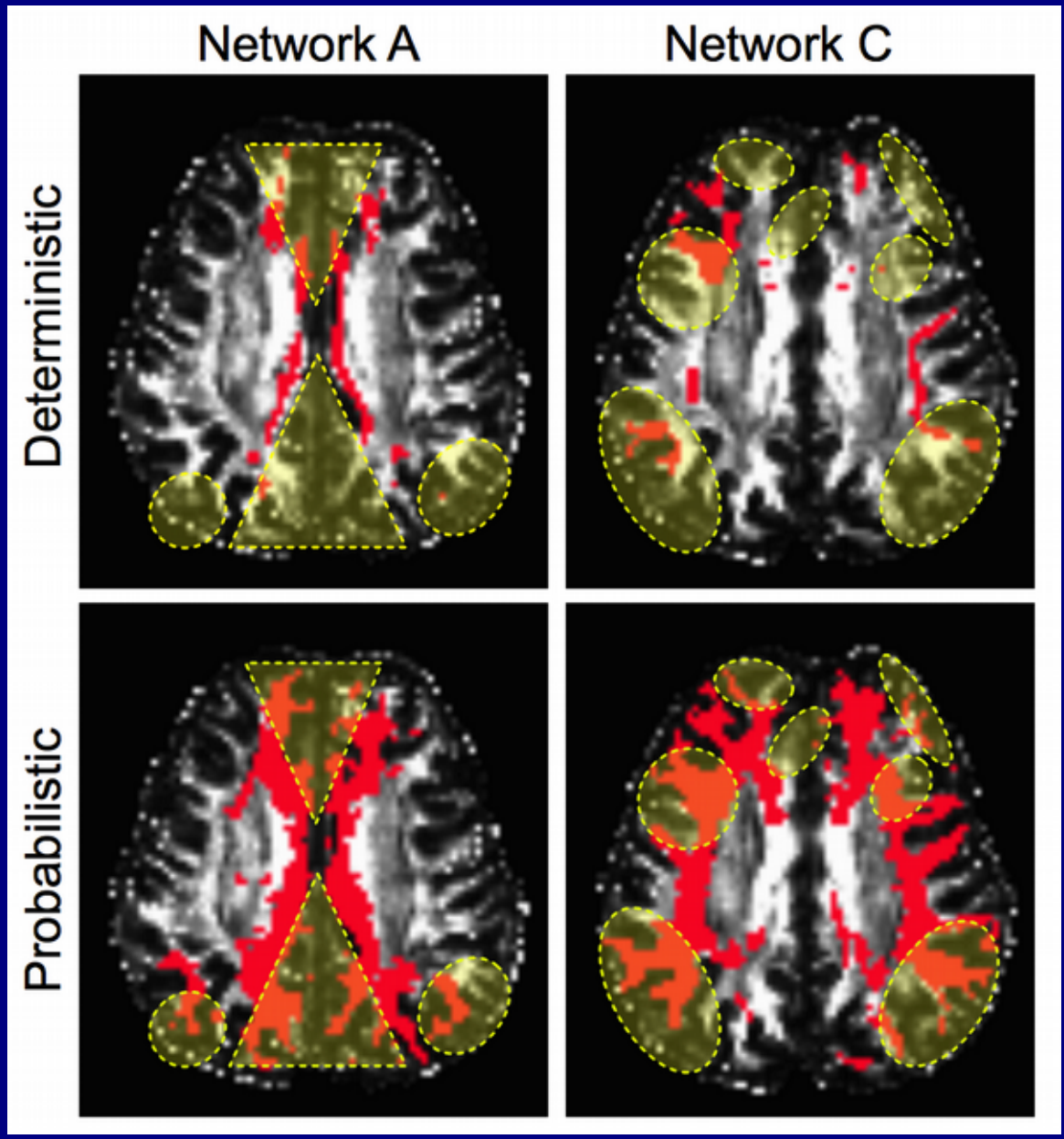
orange = GM ROIs
blue = WM estimates
(via AFNI-FATCAT)



Deterministic vs Probabilistic

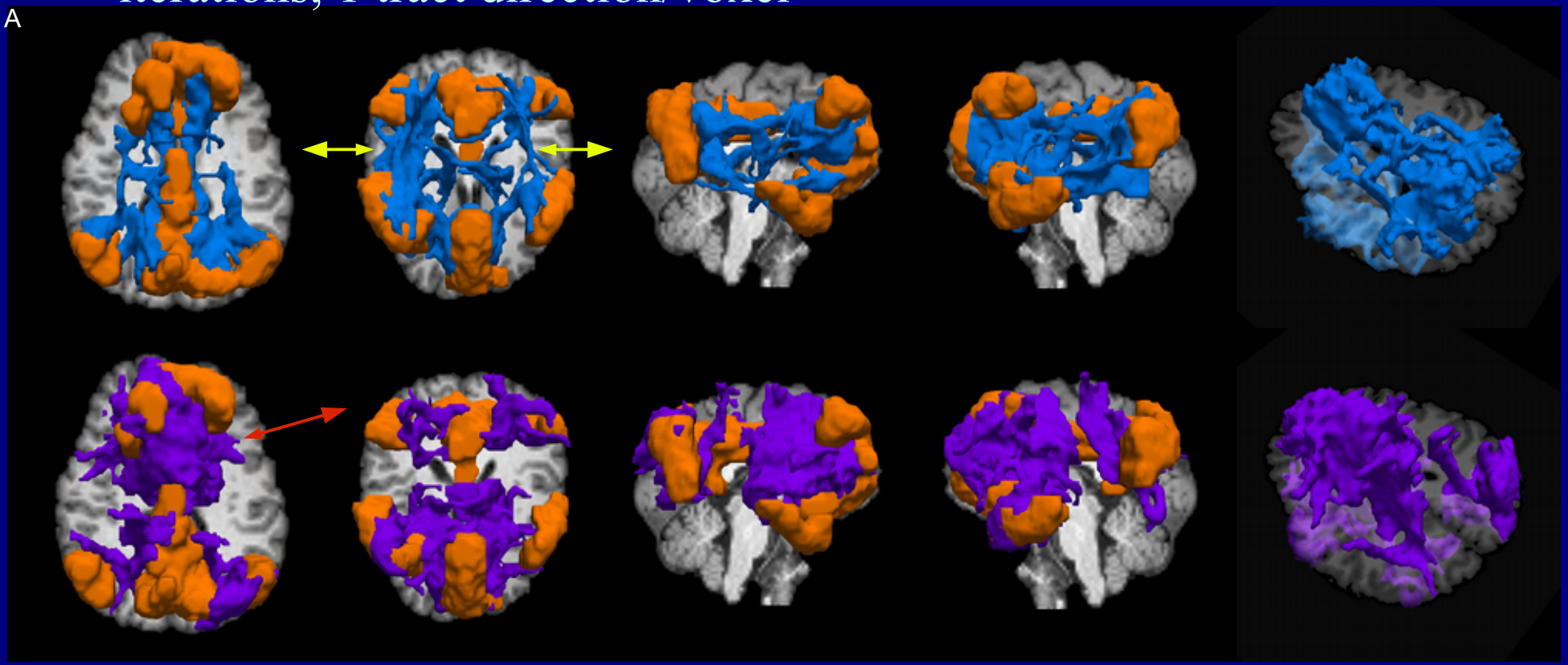
+ NB: coverage and connectivity differences between tractography types

+ Deterministic can be useful for initial investigations, but is more susceptible to noise/errors and truncation



3dTrackID: Probabilistic tractography

+ compare with existing algorithms:
  - purple: FSL-probtrackX (and FSL-bedpostX for uncertainty)
  - same parameters: FA>0.2, max angle 60deg, 5000 Monte Carlo iterations; 1 tract direction/voxel



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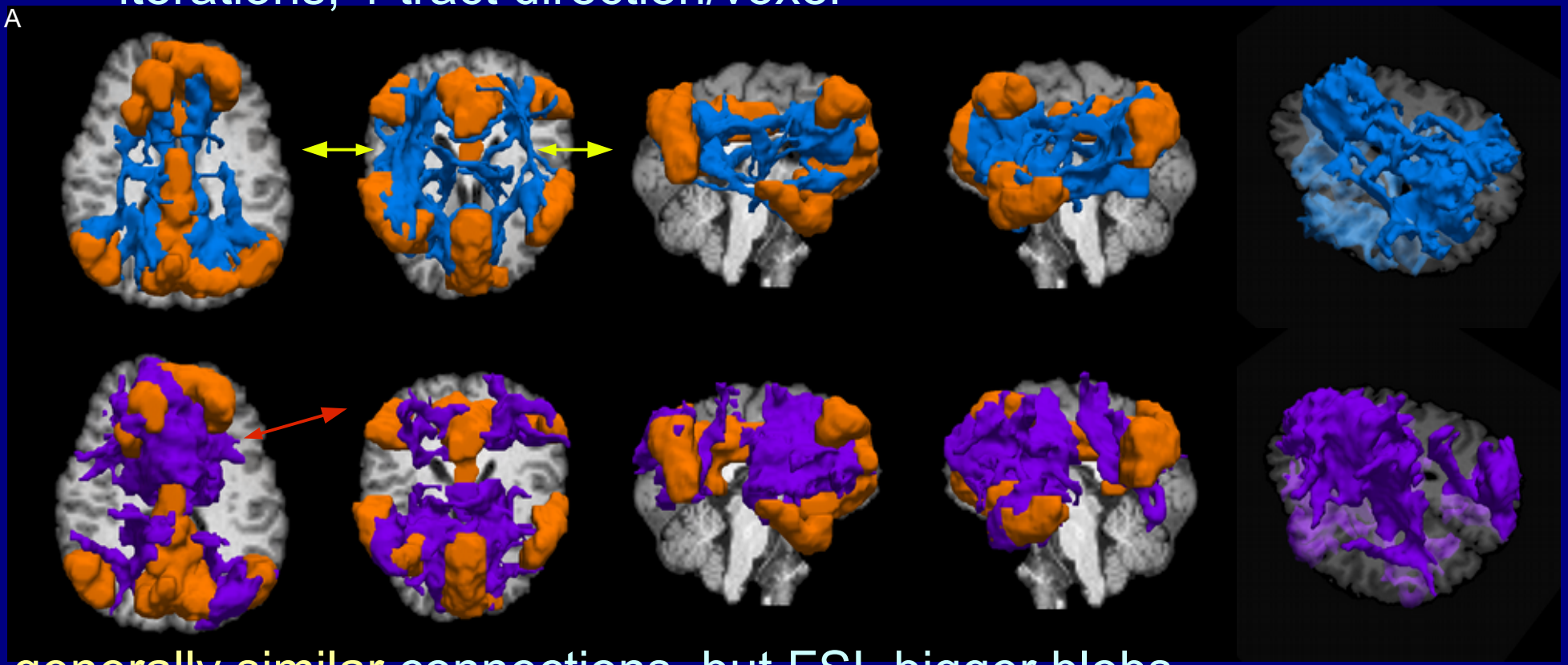

+ generally similar connections, but FSL bigger blobs
+ FSL took several hours for uncertainty, and then >24 hours for tracking this single network (and had to run 4 for this study)

3dTrackID: Probabilistic tractography

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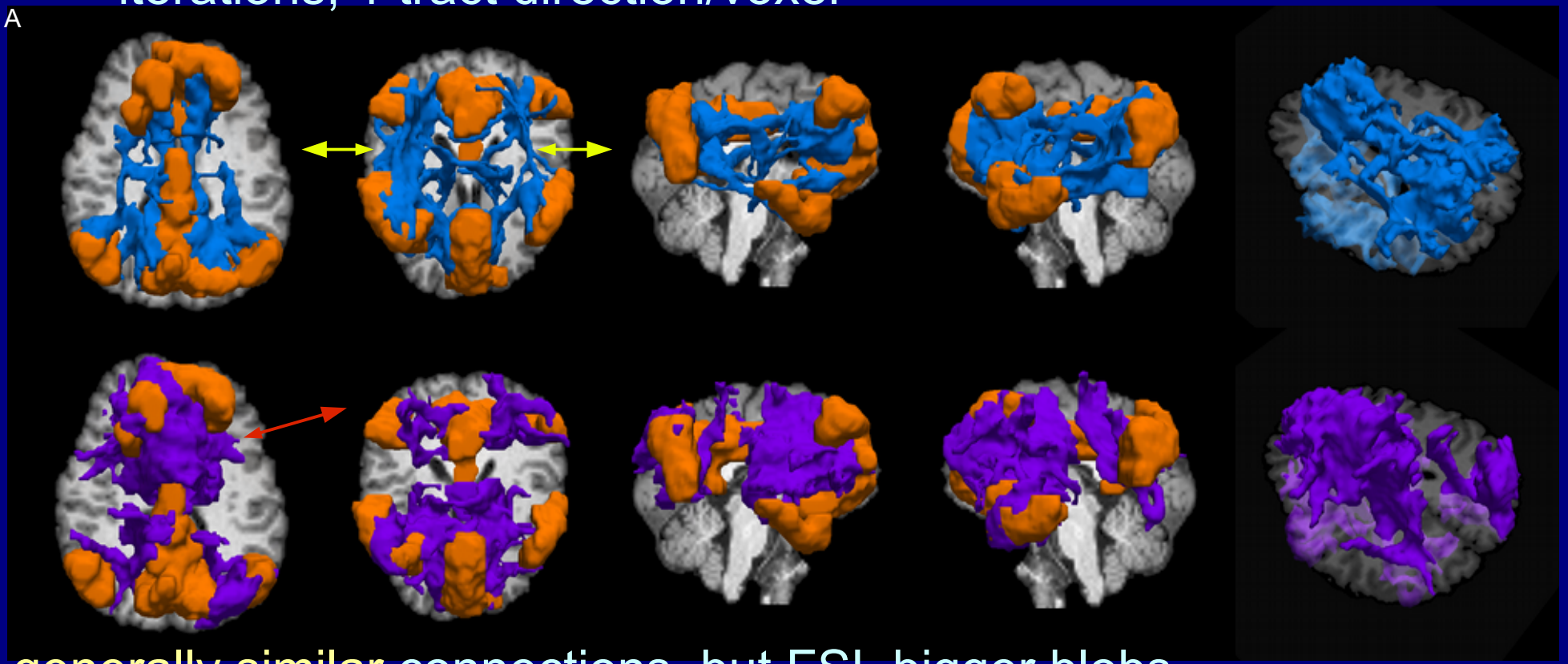
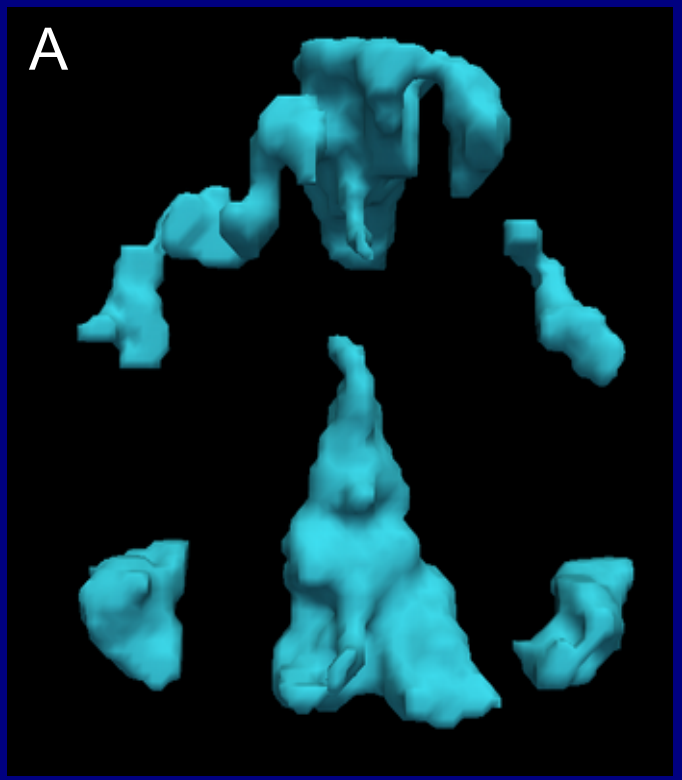
  - purple: FSL-probtrackX (and FSL-bedpostX for uncertainty)
  - same parameters: FA>0.2, max angle 60deg, 5000 Monte Carlo iterations; 1 tract direction/voxel



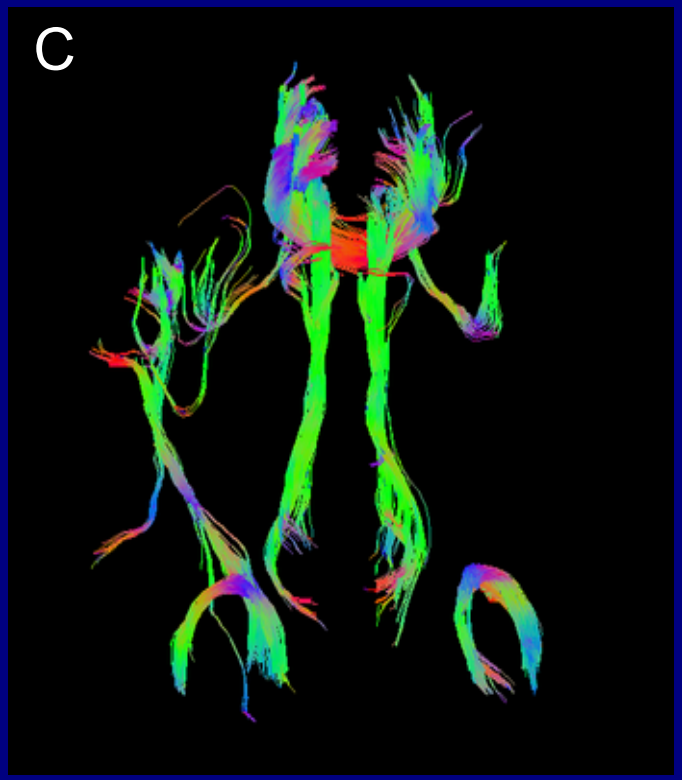
+ generally similar connections, but FSL bigger blobs
+ FSL took several hours for uncertainty, and then >24 hours for tracking this single network (and had to run 4 for this study)
+ 3dDWUncert took 7***min***; 3dTrackID took 25***mins*** total for 4 netw.

Mini-Probabilistic Tracking

+ Full probabilistic methods generate voxelwise brain maps without linear track structure
+ 'Mini-probabilistic' tracking performs a few extra iterations of' deterministic' tracking on uncertainty-perturbed data sets
    - track structure is retained,
    - results generally exhibit more robust tracks and fewer false negatives than deterministic tracking alone
    - false positives tend to be isolated and visually apparent.



Deterministic (AND)



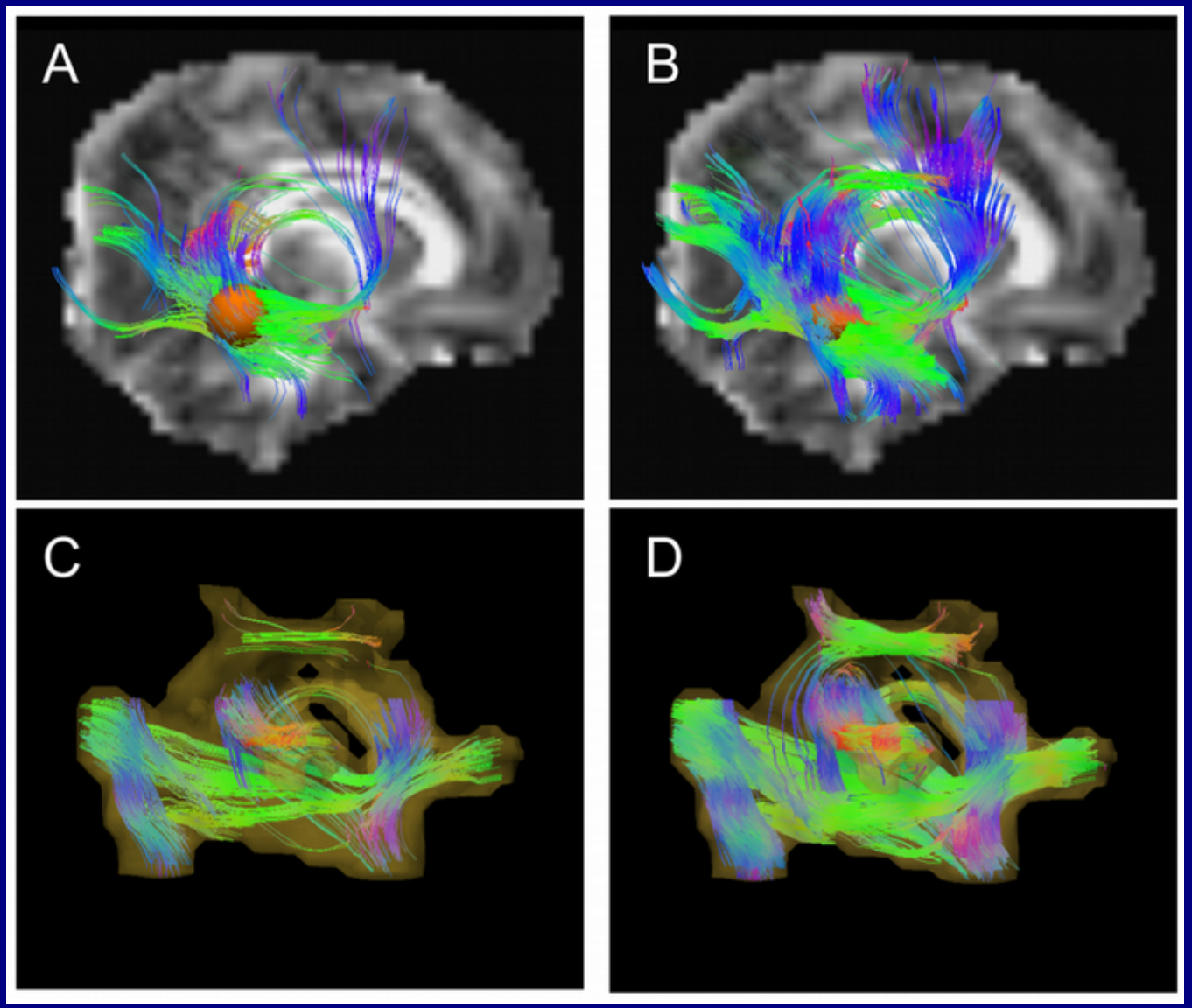
with `-mini_prob 7'

Mini-Probabilistic Tracking

Deterministic vs mini-Probabilistic

Through single ROI

AND logic through network, cf with full-prob results

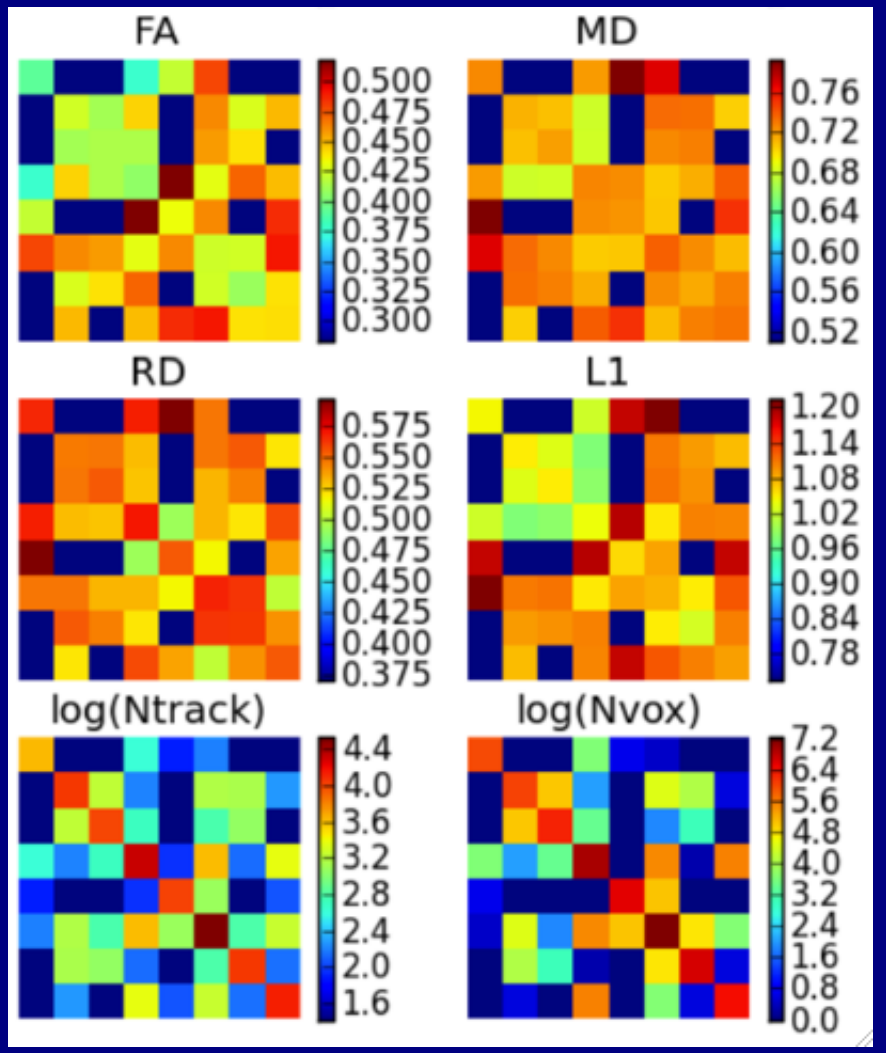


WM (ROI) Quantities

For connected pairs of GM ROIs in a network, have an average WM property (or can map to T1, PD...) →

Have produced sets of localized structural/anatomical quantities for comparison with functional values or behavioral scores, genetics, etc.

Can use for group or individual comparisons/regressions.



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3dNetCorr: correlation matrices Of average time series in ROIs (e.g., uninflated GM ROIs from 3dROIMaker)