Introduction to AFNI-FATCAT, Part I

Tractography for data exploration and complementing functional connectivity

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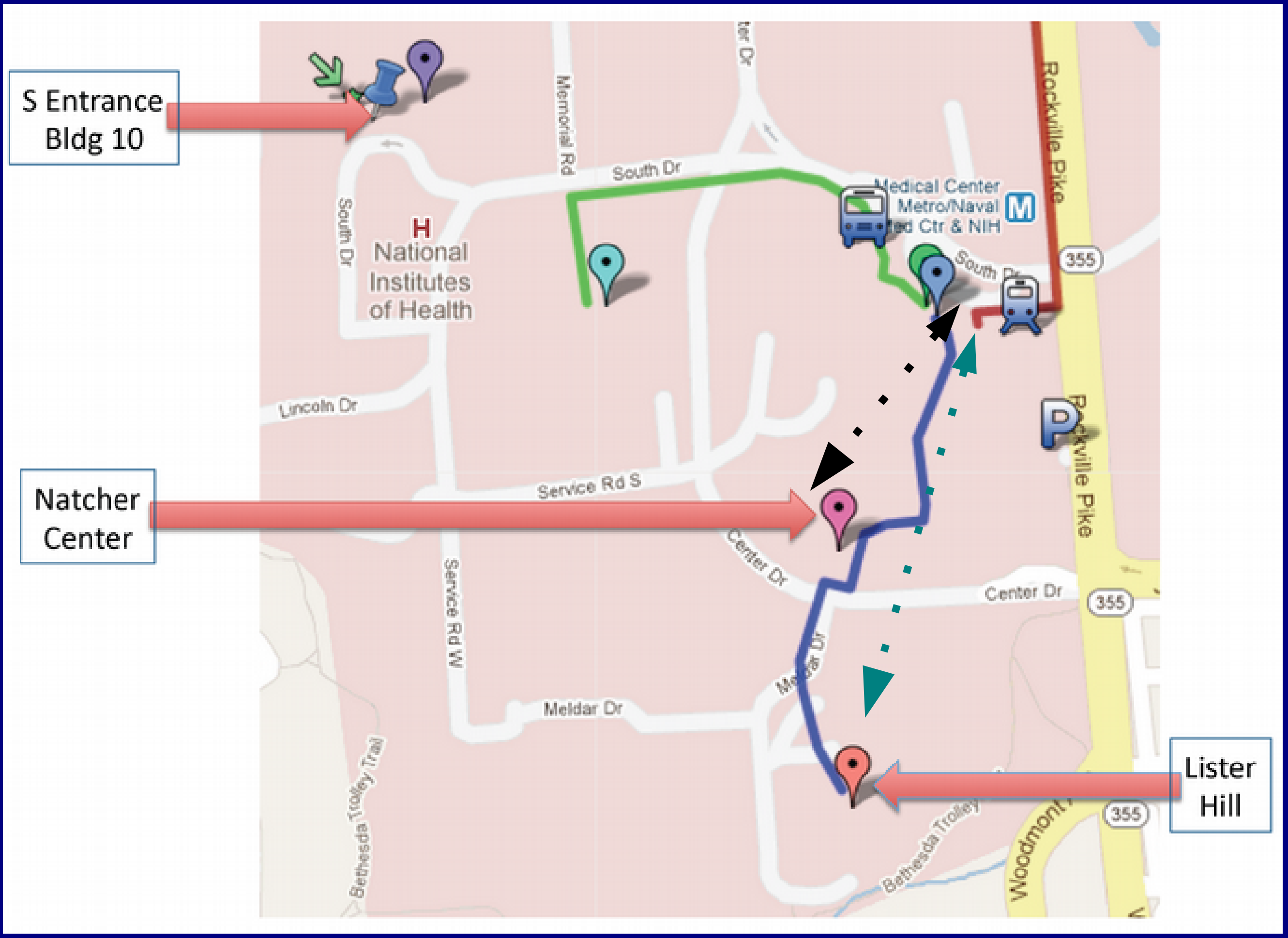
or

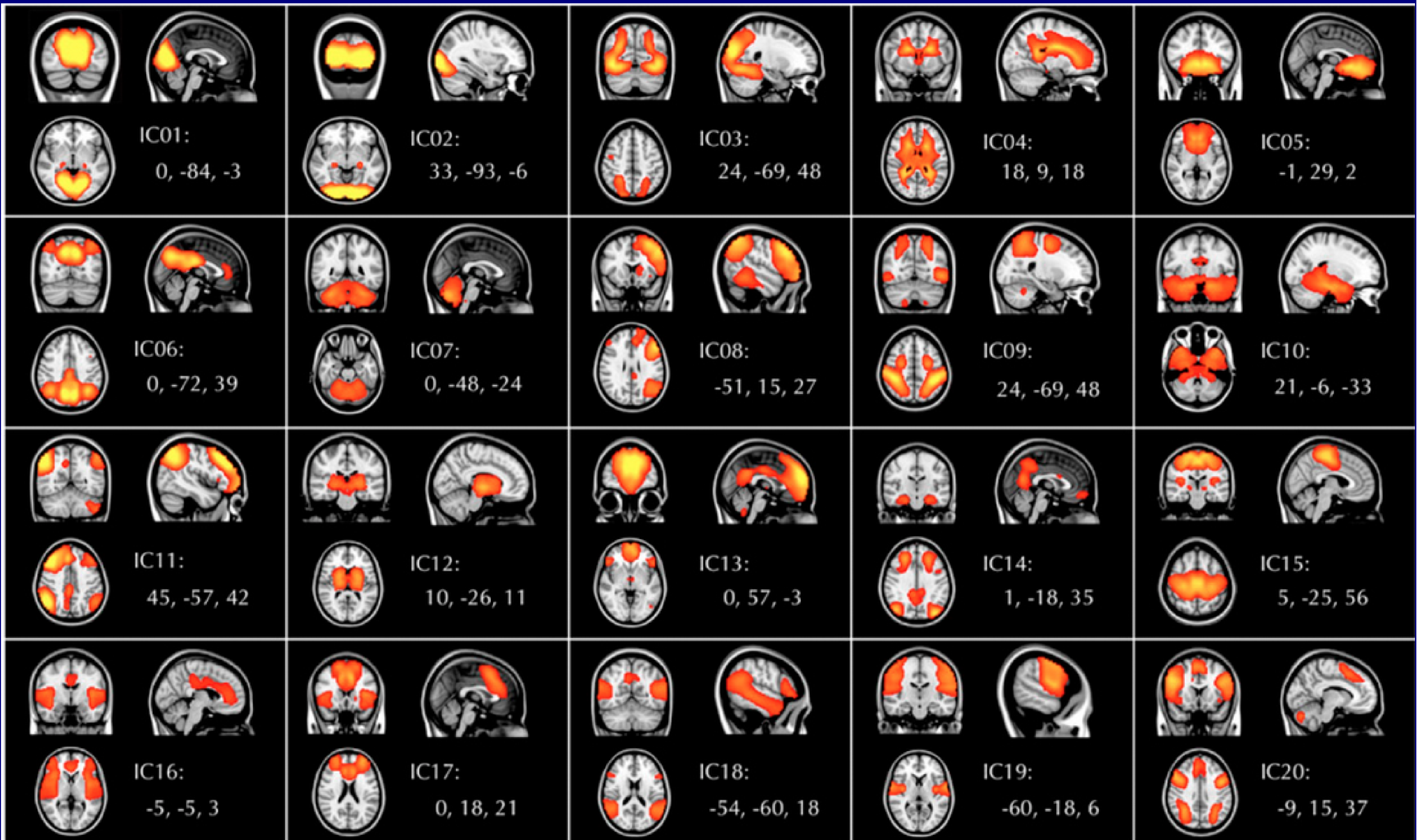
(the not-so) Long Walk to FATCAT



Outline

+ Why Function+Structure
+ DWI and DTI (very brief, following morning session)
  - Diffusion imaging basics and parameters
+ Using tractography to estimate WM connections
  - Making targets from functional data
  - Deterministic, probabilistic (or both?)
  - using WM region properties for quantitative comparison
+ Brief example – newborn alcohol exposure study
+ Further FATCAT:
  - HARDI tracking
  - LFF calculation+RSFC parameters, ReHo

FMRI: GM Networks



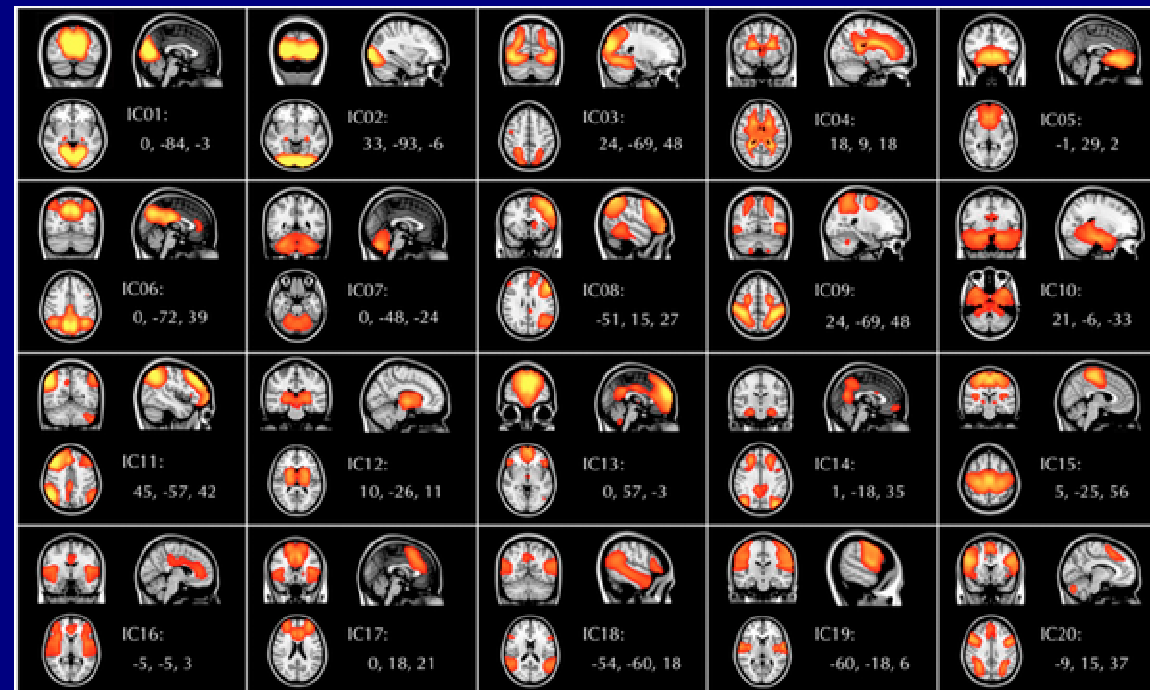
(Biswal et al., 2010 PNAS)

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.

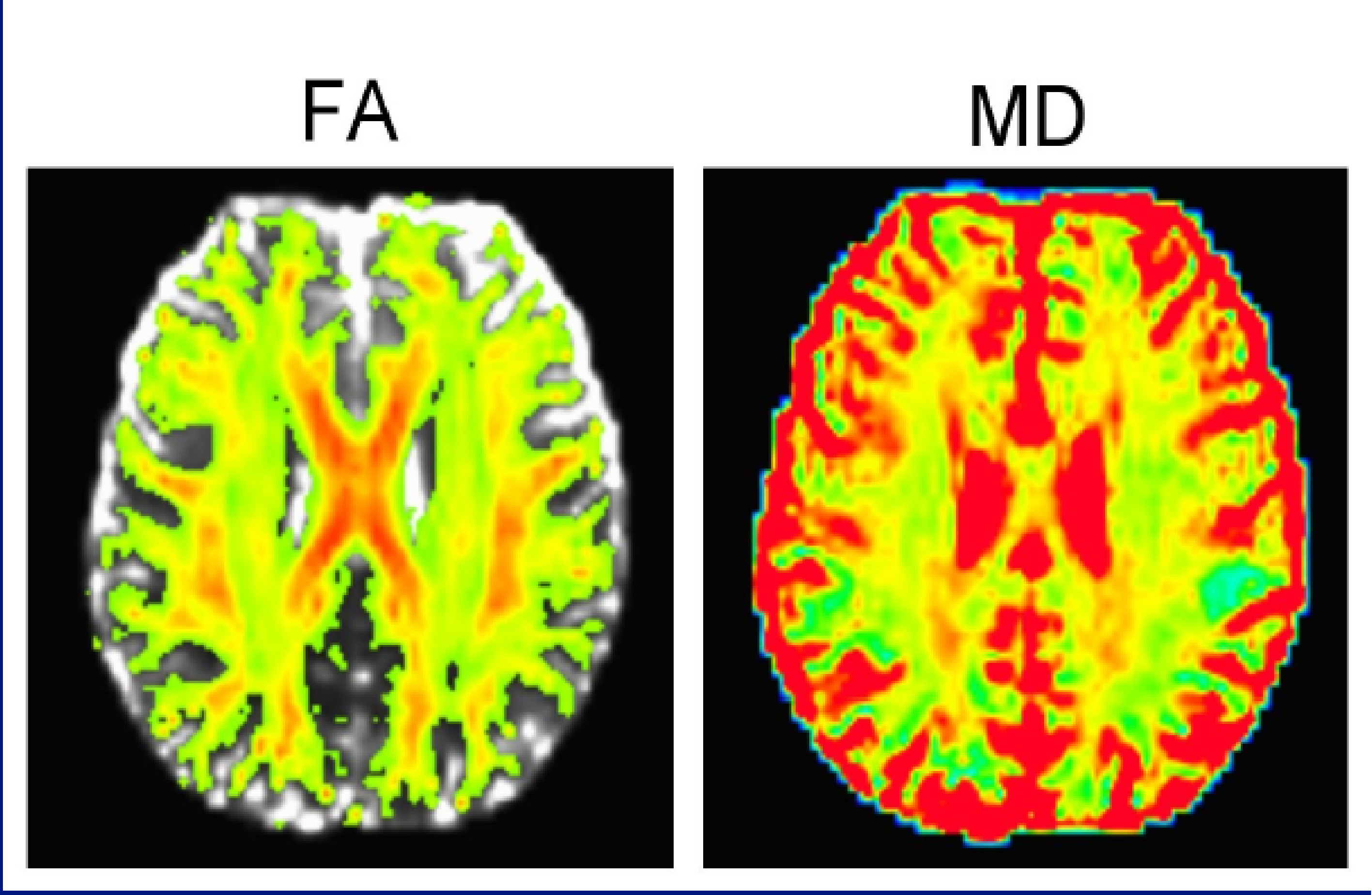


Structural (WM)

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

Can investigate and quantify WM properties with:
FA, MD, RD, L1, etc.

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

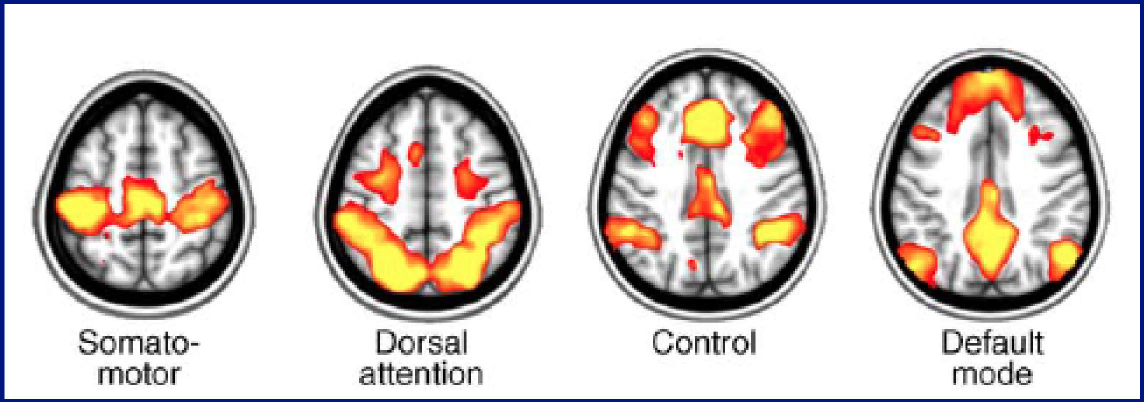


(FA>0.2)

Structure + Function

Simple example:

GM ROIs network:



Raichle (2010, TiCS)

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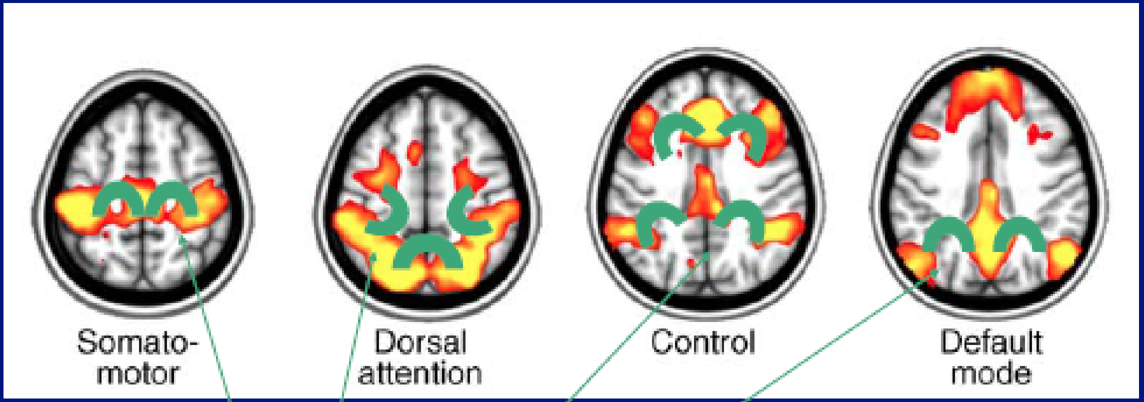

Raichle (2010, TiCS)

Associated WM ROIs

Structure + Function

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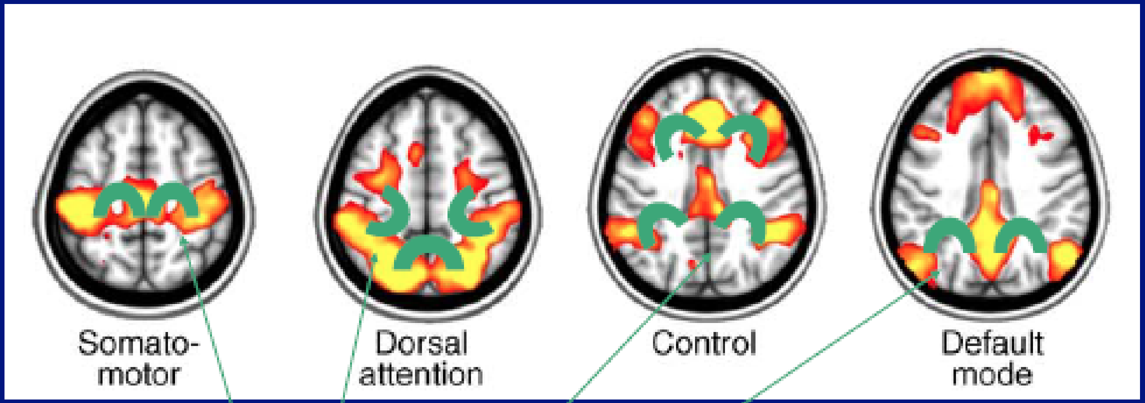

Raichle (2010, TiCS)

Associated WM ROIs

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

Combining FC and SC

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  - FMRI has measures of functional connectivity and 'strength' (e.g., correlation, network parameters)

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→ FC+SC provides sets of complementary quantities to describe a network, and can be further combined with behavioral/other measures (statistical modeling).

Tools for combining FC and SC:

<u>Combining functional and tractographic connectivity will require:</u>

+ determining networks from FMRI 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...

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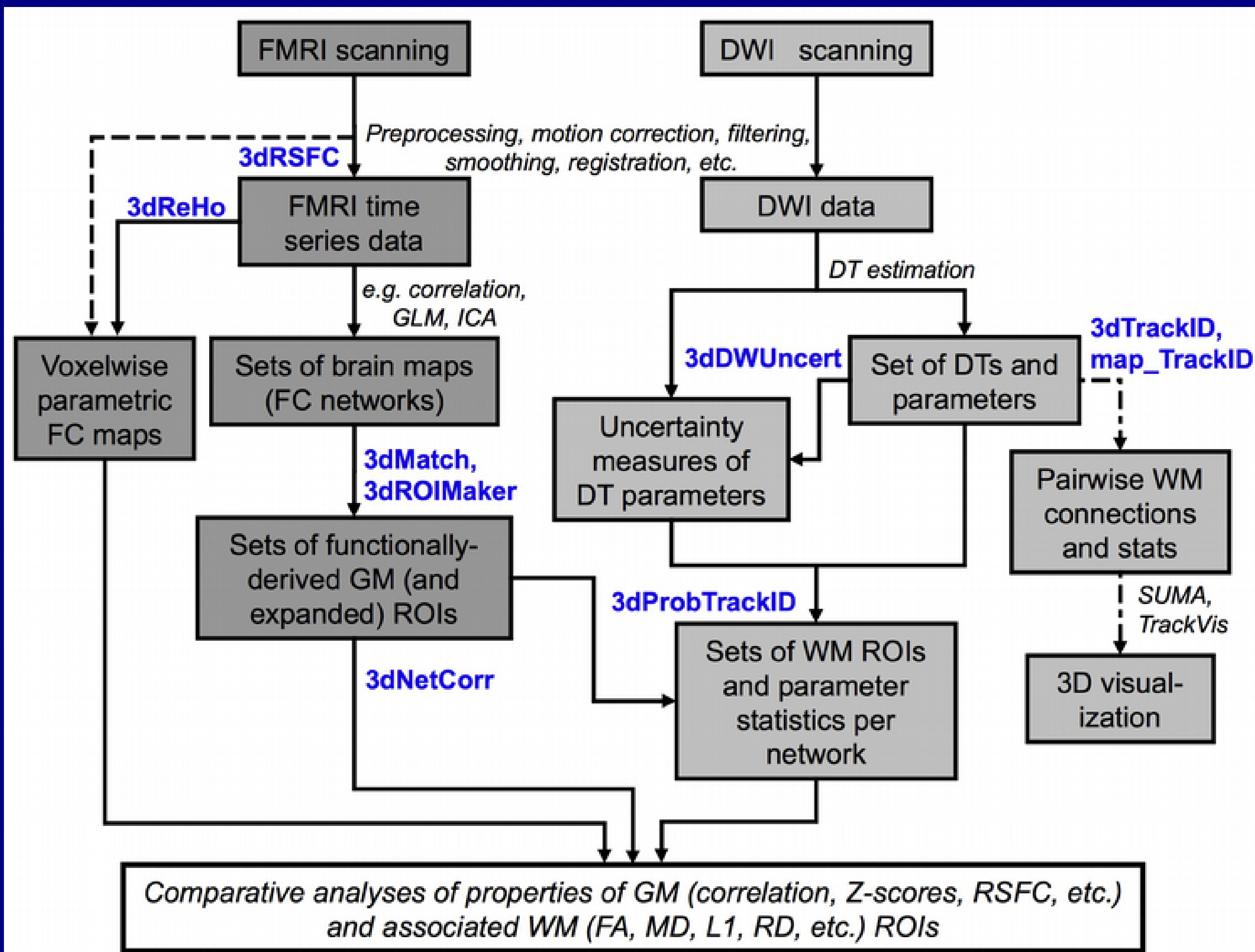
FATCAT: Functional And Tractographic Connectivity Analysis Toolbox (Taylor & Saad, 2013), now available in AFNI with demo data.

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

Functional and structural processing

Schematic for combining FMRI and DTI-tractography via FATCAT:



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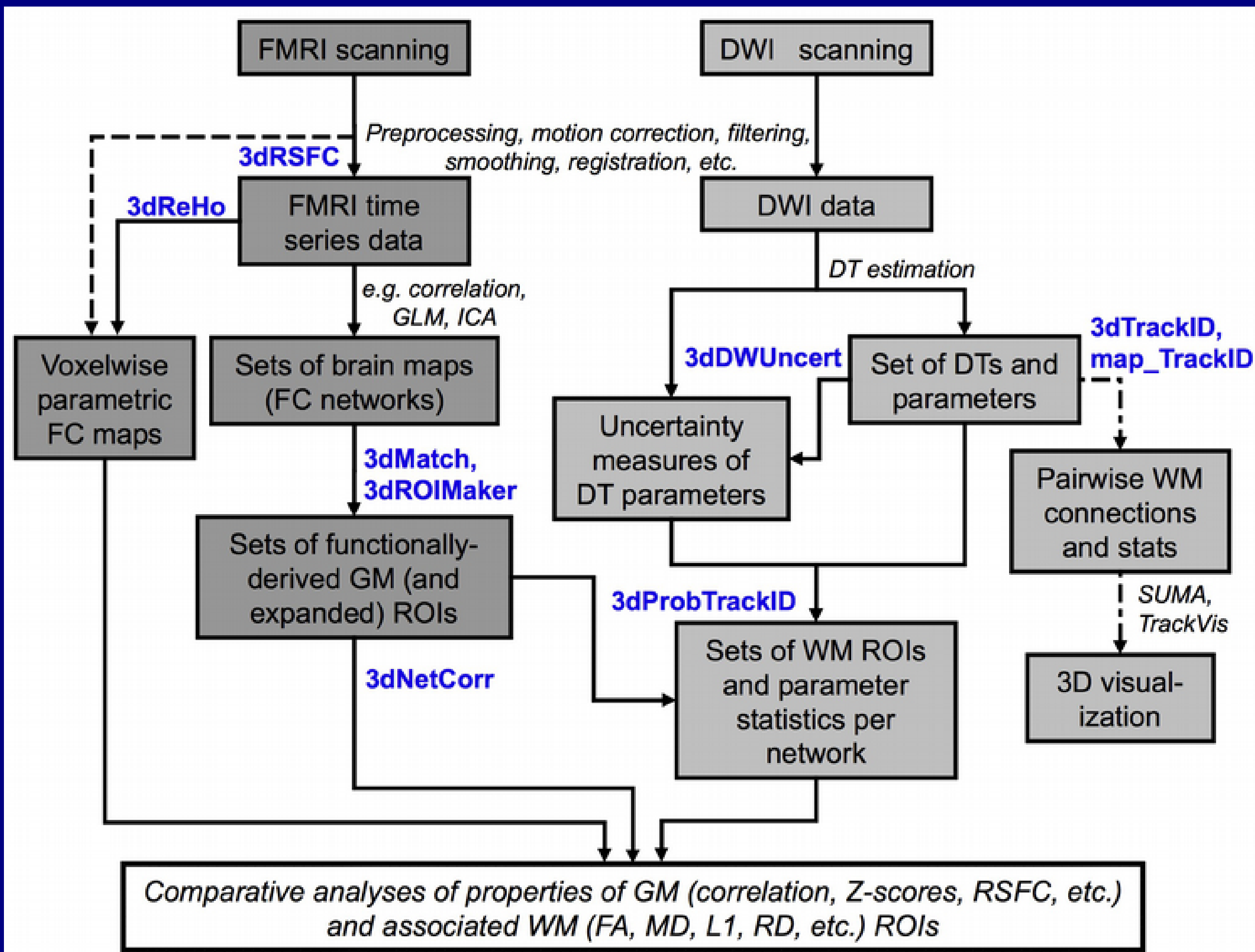

FATCAT goals:

+ do useful tasks
+ integrate with existing pipelines/software
+ **derive/use information from the data itself**
+ be simple to implement
+ be efficient
+ be flexible and able to grow

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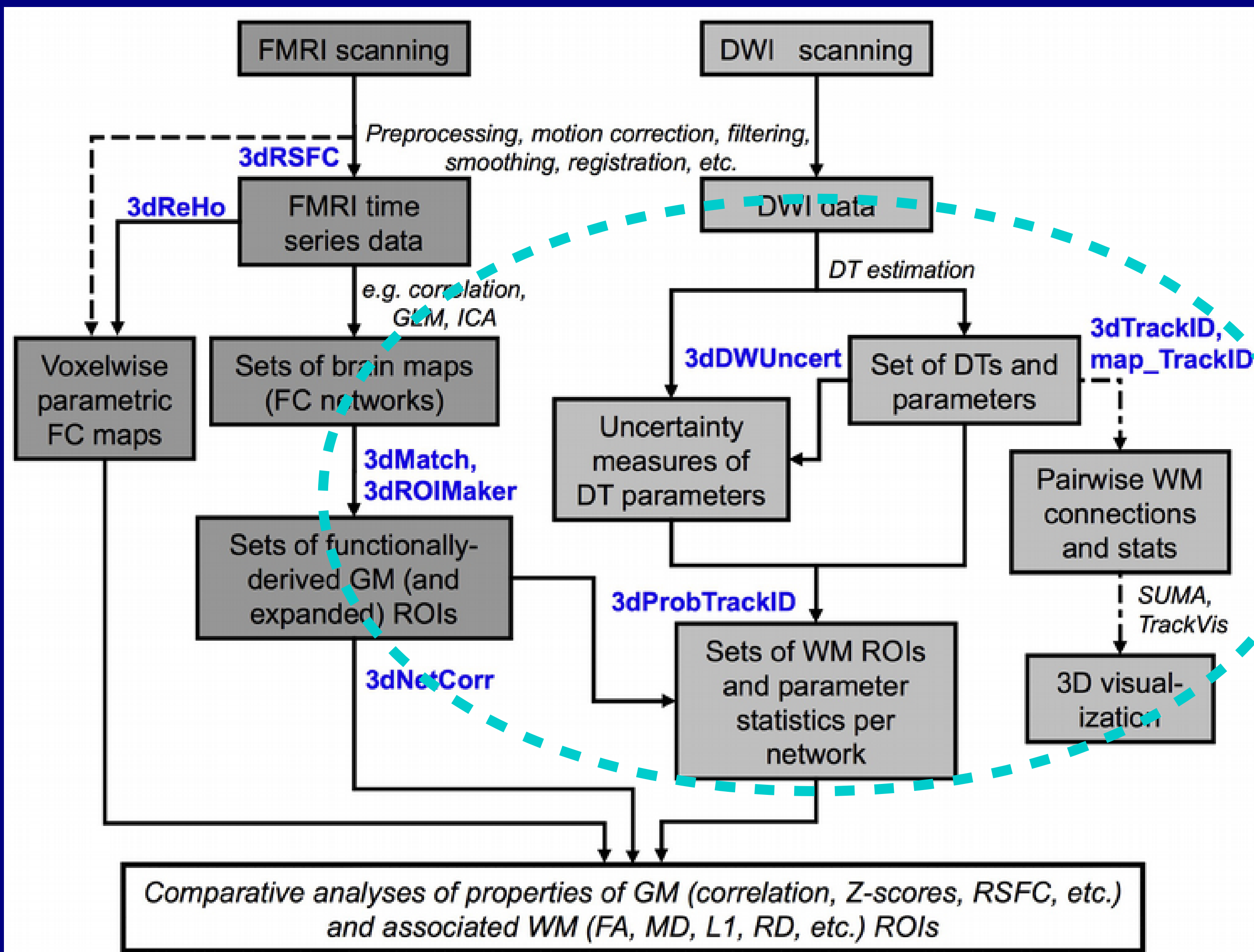

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Main focus today on DTI-tractography, including making ROIs from FMRI

Sidenote:

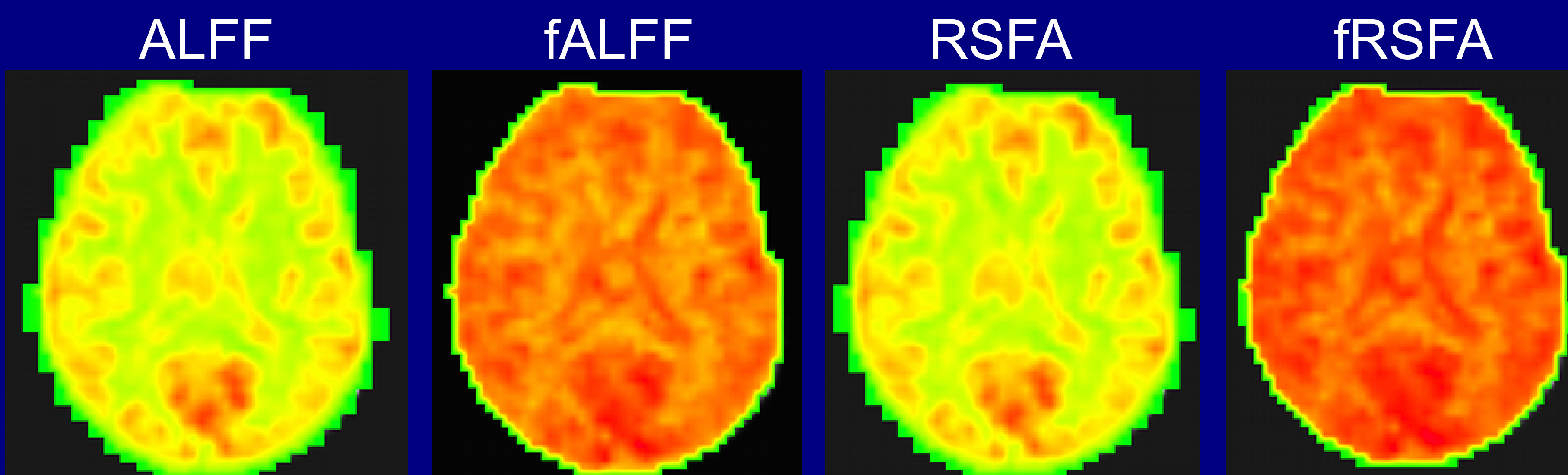
Mention of a few of the FMRI tools

Functional processing, 1

For RS-FMRI: RSFC parameters (and processing considerations)

+ Frequency-based parameters: ALFF, fALFF, mALFF, RSFA (,fRSFA, mRSF)
  - fALFF = fractional of amplitudes before and after bandpass filtering
    → needs to be calculated **during** filtering process

+ 3dRSFC is a wrapper for 3dBandpass, which calculates above frequency-based parameters while processing.
  - available to use in afni_proc.py processing with '-regress_RSFC'
    + *see afni_proc example 10b (NB: no censoring)*

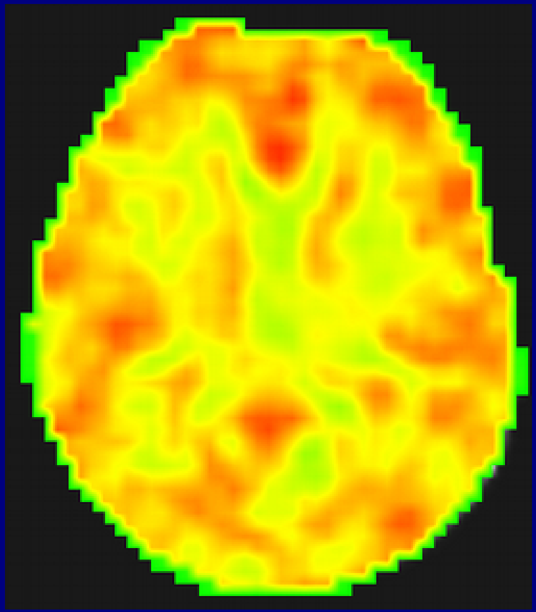


Functional processing, 2

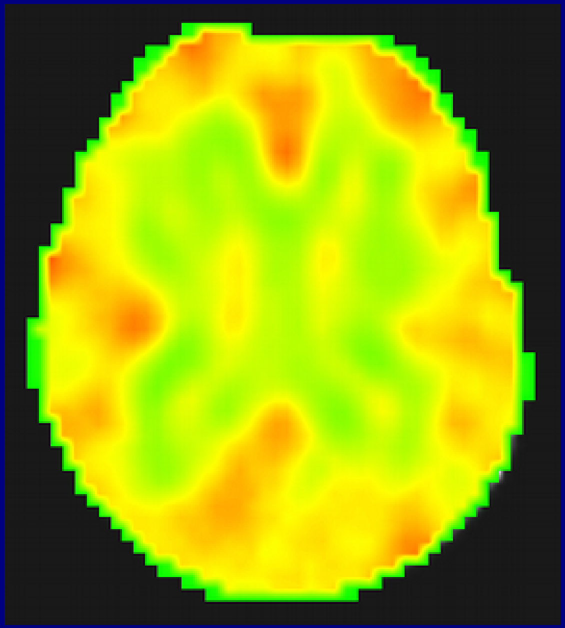
For {RS- | TB-}FMRI: ReHo
    (KCC, Kendall's Coefficient of Concordance)

+ 3dReHo: calculated post-processing, input time series data
  - can calculate for any shape spheroid/ellipsoid
  - can calculate within ROI shapes ('-in_rois' option) → list of values + voxelwise

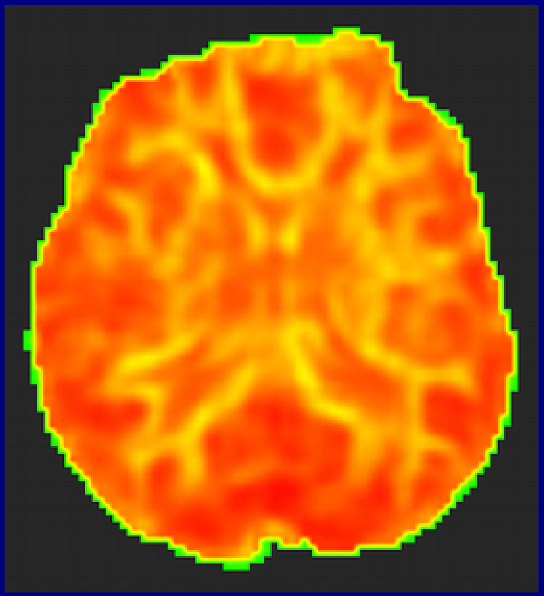
LFF (standard sphere neighbors)



LFF (ellipsoid neighborhood)



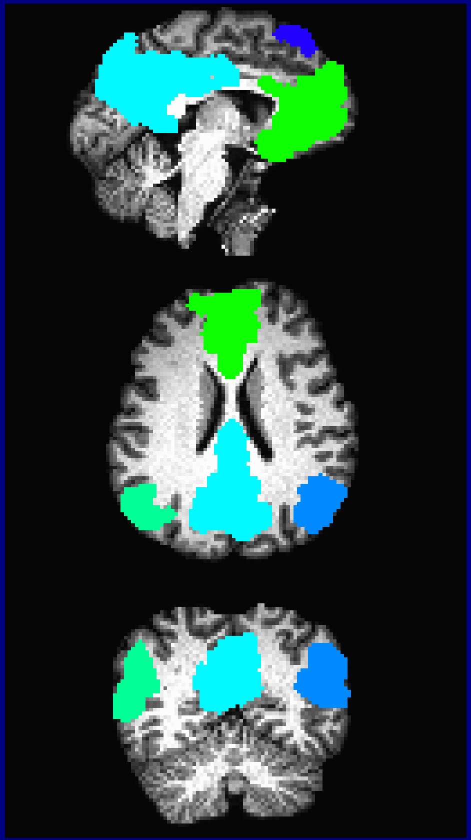
Unfiltered RS-FMRI (sphere neighborhood)

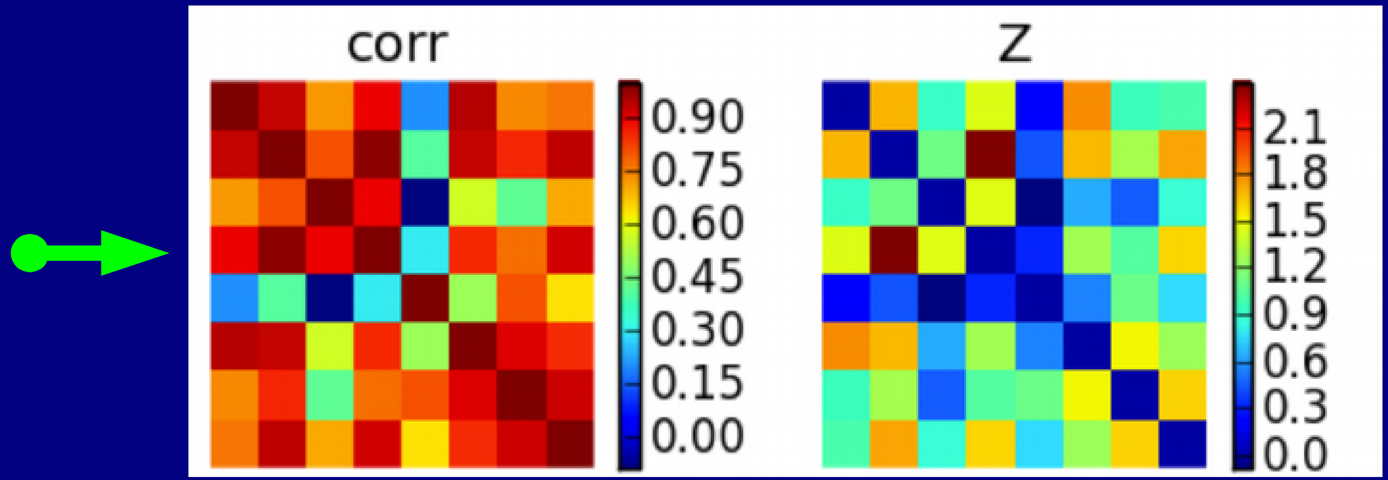


Functional processing, 3

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

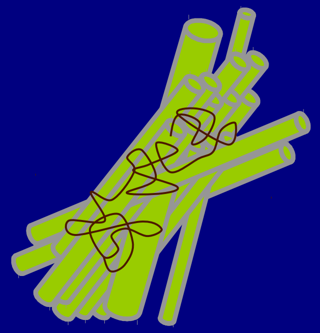
+ 3dNetCorr: calculated post-processing, input time series data + network maps
    - can be multi-brick maps, 1 network per brick
    - calculate average time series per ROI, correlation among network ROIs
    - outputs correlation matrix/matrices, (can also do Fisher-Z transform output)





(Back to diffusion)

Local Structure via Diffusion MRI



(In brief)

1) Random motion of molecules affected by local structures

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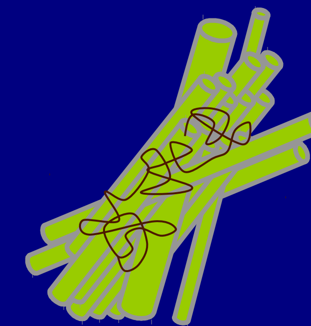
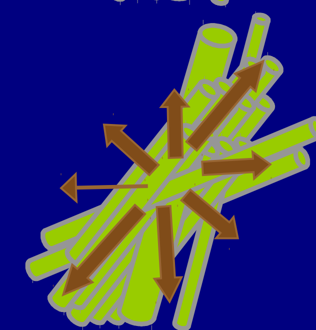


2) Statistical motion measured using diffusion weighted MRI



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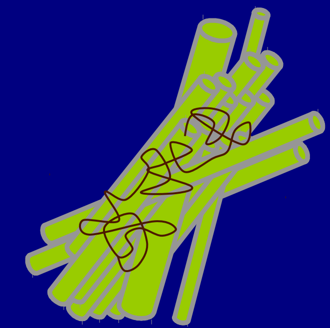

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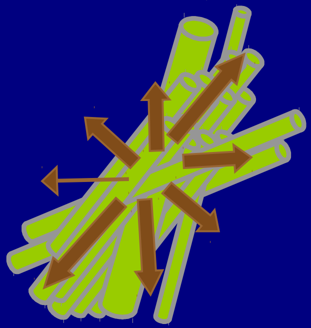
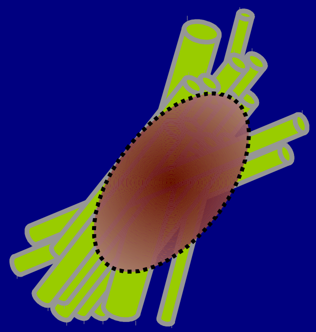


2) Statistical motion measured using diffusion weighted MRI

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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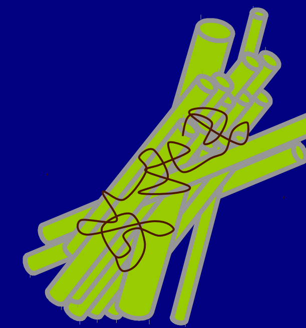

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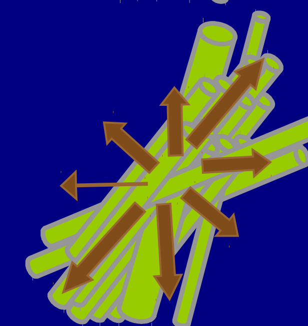

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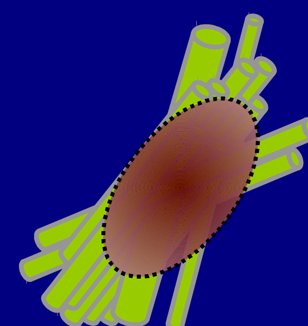

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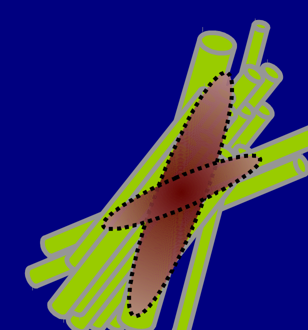

- >=1 direction:
  HARDI (High Angular Resolution Diffusion Imaging)
  Qball, DSI, ODFs, ball-and-stick, multi-tensor, CSD, ...

DWI → Diffusion Tensors (DTs)

Mathematically, the 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 ($\mathbf{r}^T\mathbf{D}\mathbf{r} > 0$)

  $\mathbf{D}\mathbf{e}_i = \lambda_i \mathbf{e}_i, \qquad \lambda_i > 0$
- Symmetric ($D_{12} = D_{21}$, etc),

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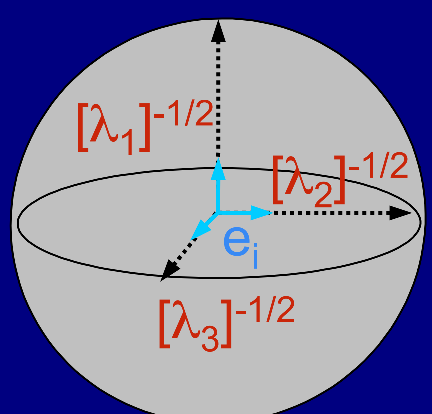
Geometrically, this describes ellipsoid surface, with $\mathbf{r} = (x, y, z)$:

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



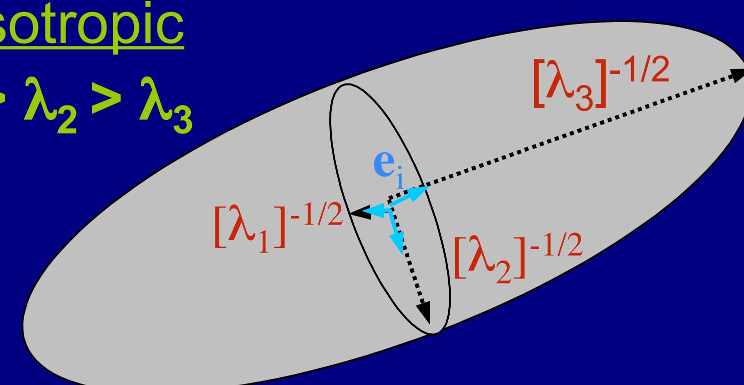
isotropic

$\lambda_1 = \lambda_2 = \lambda_3$

anisotropic

$\lambda_1 > \lambda_2 > \lambda_3$

`Diffusion measure' surfaces



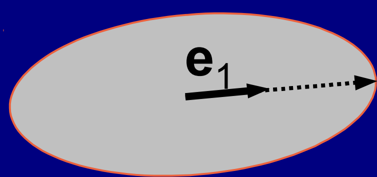
$\boldsymbol{\lambda_i}$ describe length of semiaxes; $\mathbf{e}_i$ are spatial orientation of semiaxes

'Big 5' DTI ellipsoid parameters

~Main quantities of diffusion (<u>motion</u>) surface:

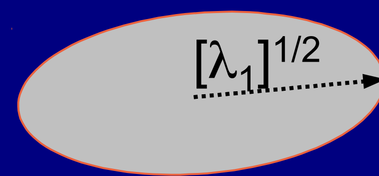
<u>Direction of max diffusion</u>

(unit) first eigenvector: $\mathbf{e}_1$



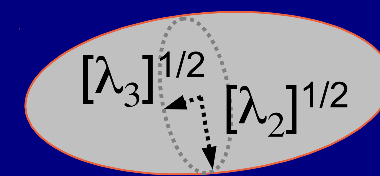
<u>Maximum diffusion</u>

first eigenvalue: λ_1, L1



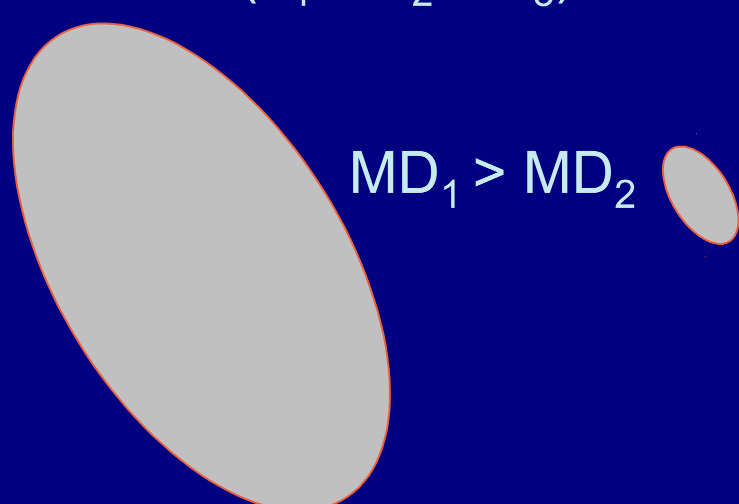
<u>Radial/perp. diffusion</u>

RD = $(\lambda_2 + \lambda_3)/2$



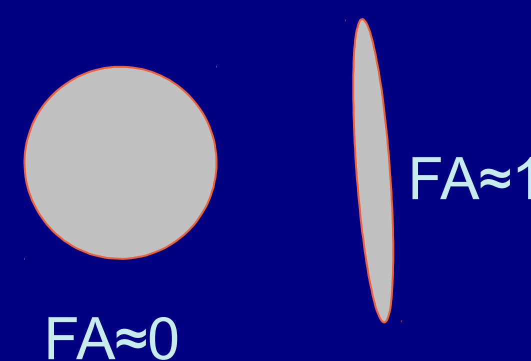
<u>Mean diffusivity</u>

MD = $(\lambda_1 + \lambda_2 + \lambda_3)/3$



<u>Fractional anisotropy</u>

$$FA = \left[\frac{3[(\lambda_1 - MD)^2 + (\lambda_2 - MD)^2 + (\lambda_3 - MD)^2]}{2\,[\lambda_1^2 + \lambda_2^2 + \lambda_3^2]}\right]^{1/2}$$



Interpreting DTI parameters

General literature:

FA: measure of fiber bundle coherence and myelination

- in adults, FA>0.2 is proxy for WM (strong segment. overlap)

MD, RD, L1: local density of structure

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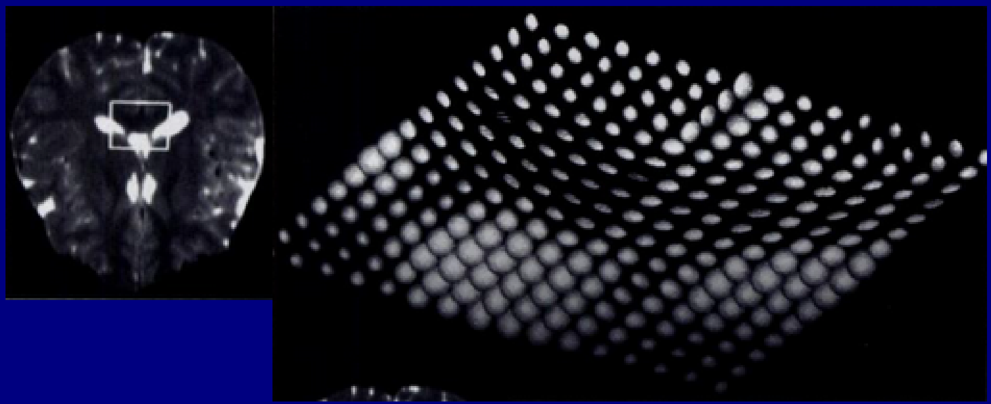
Cautionary notes:

+ 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 just structure-- i.e., fluid properties
+ Noise, distortions, etc. in measures

Local DTs → Extended Tracts

Field of local diffusion parameters



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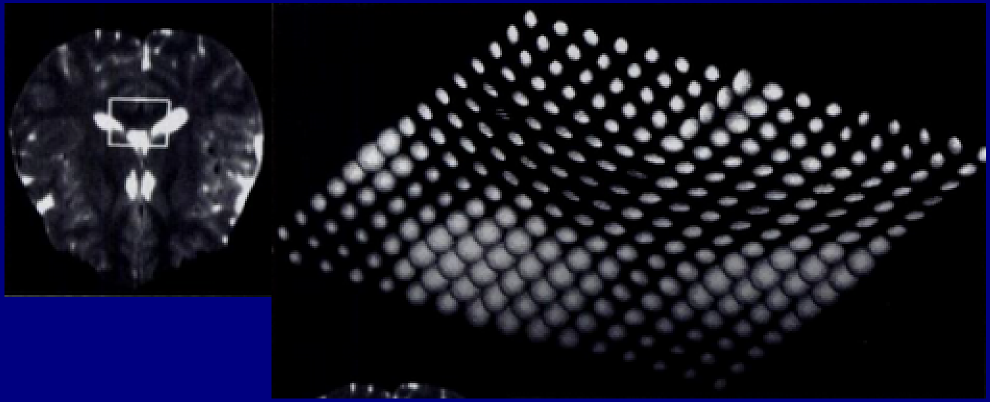
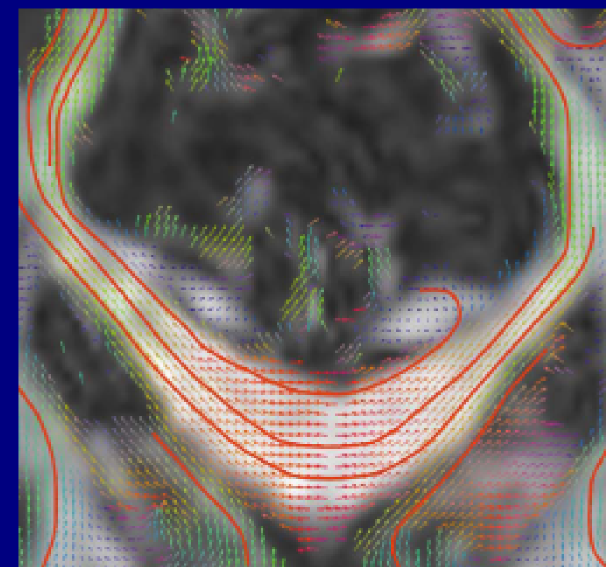


→ individual ellipsoids

Local DTs → Extended Tracts

Field of local diffusion parameters

Connect to form extended tracts

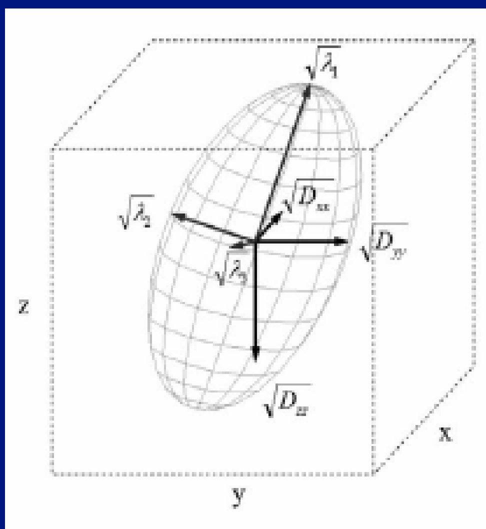


→ individual ellipsoids

→ linked structures

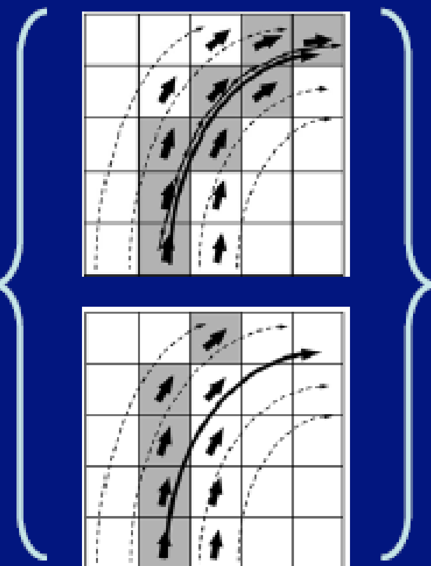
Tractography

Estimate WM structure (fiber tract locations)



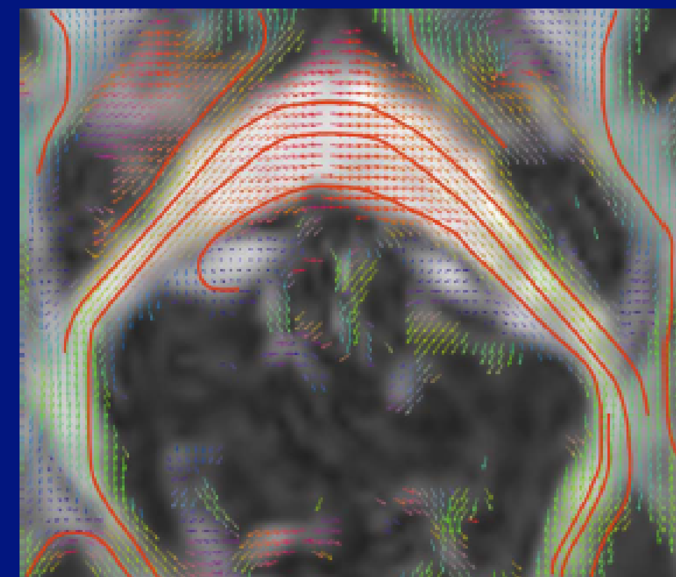
ellipsoid measures (~*smoothing of real structures*)

+



some kind of algorithm for connecting

=



estimate spatial extents of WM ‘tracts’ in vivo

(images from Bammer et al. 2003)

Diversity in tractography

Series of (mostly) logical, simple rules for estimating tracts
→ *many* methods/algorithms and kinds of parameters to choose:
(Mori et al., 1999; Conturo et al. 1999; Weinstein et al. 1999; Basser et al. 2000; Poupon et al. 2001; Mangin et al. 2002; Lazar et al. 2003; ….)

Propagation via, e.g.:
smoothing diffusion vectors and solving differential equations; deflecting propagating tracts; allowing tracts themselves to 'diffuse'; solving for global minimum energy of connections…

To date, no single 'best' algorithm, work continues:
- histology can't give perfect answers.
- some test models (phantoms) exist, but not brain-complex

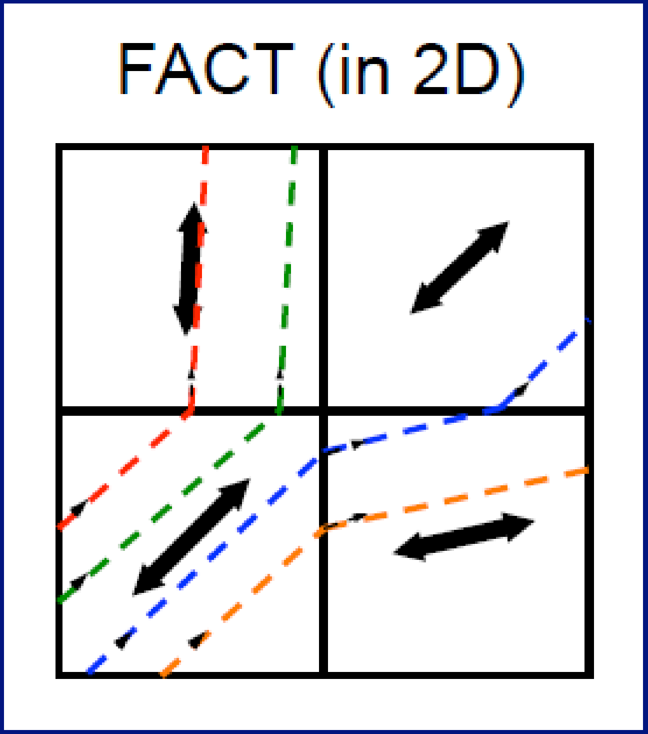
So, first question for using tractography in a study:

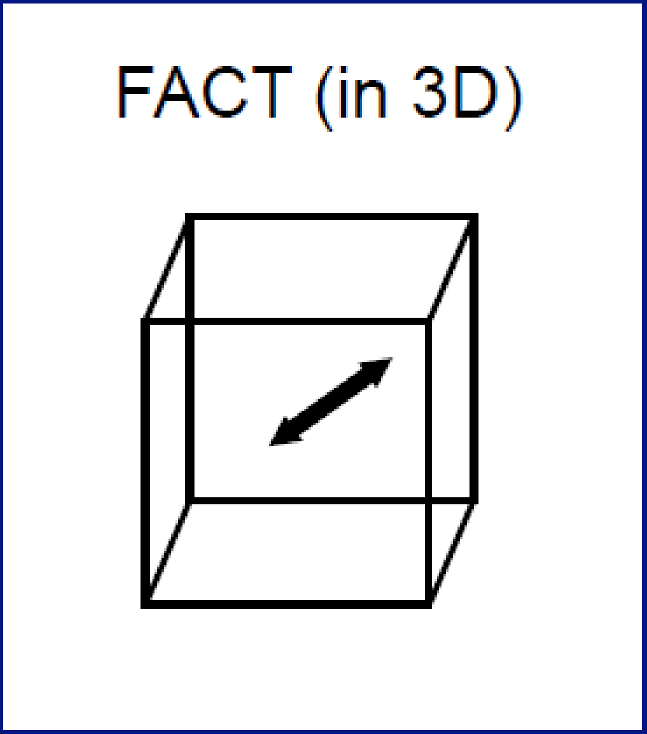
Which algorithm to choose?

Popular technique: FACT

- FACT = Fiber Assessment by Continuous Tracking (Mori et al. 1999) [used more than 200 times in past 1.5 yrs]
  - Start in voxel with FA>0.2 (proxy definition for WM)
  - Follow 1st eigenvector/greatest diffusion direction to next voxel
  - Continue if FA stays>0.2 and angle between $\mathbf{e}_1$s is <45 deg

Ex.:





Very simple, but actually, gives some decent results, e.g.many known tracts

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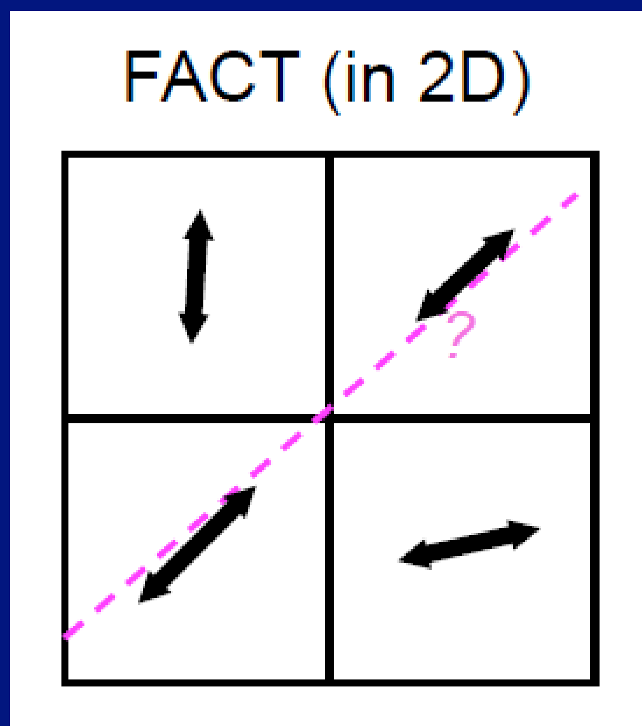

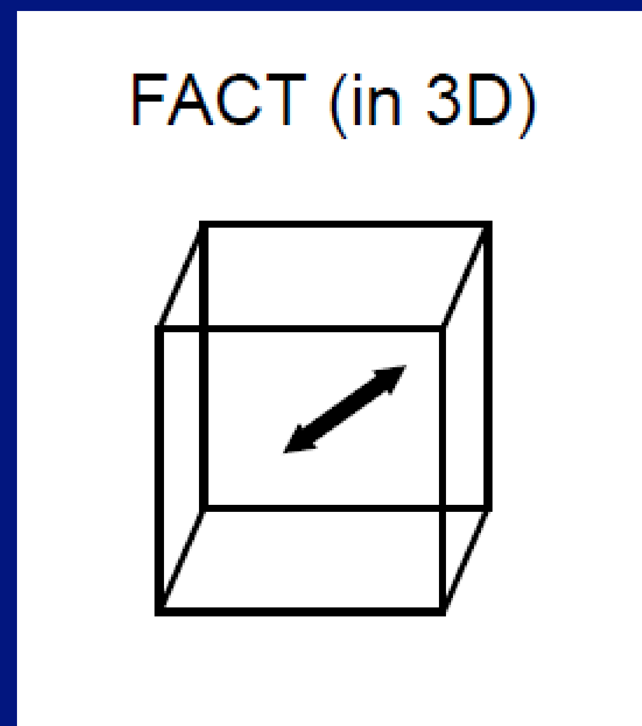

Very simple, but actually, gives some decent results, e.g.many known tracts **however… e..g bias?*

Popular technique: FACT

- FACT = Fiber Assessment by Continuous Tracking (Mori et al. 1999) [used more than 200 times in past 1.5 yrs]
  - Start in voxel with FA>0.2 (proxy definition for WM)
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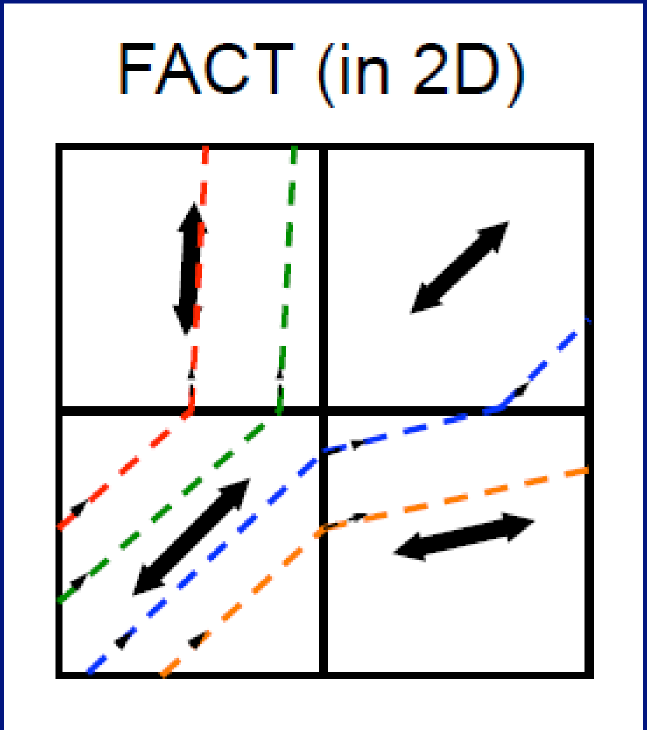
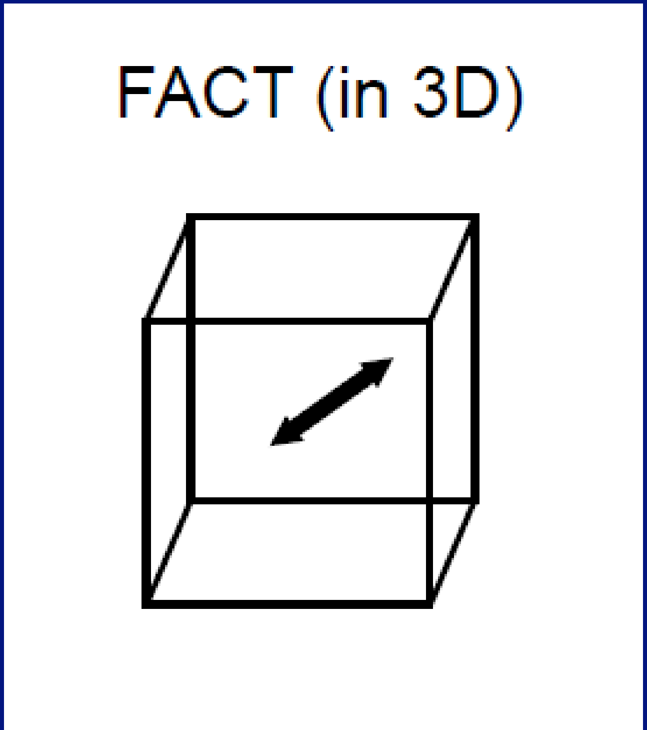
Ex.:





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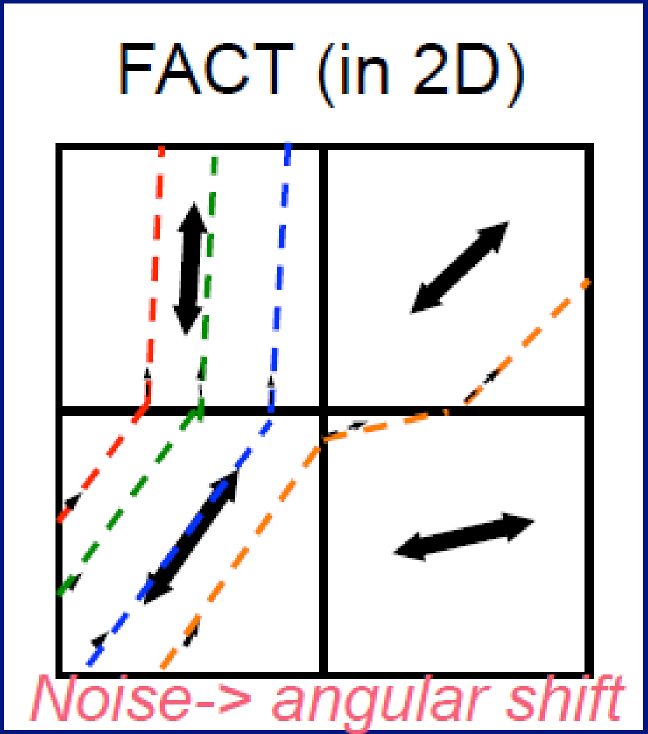

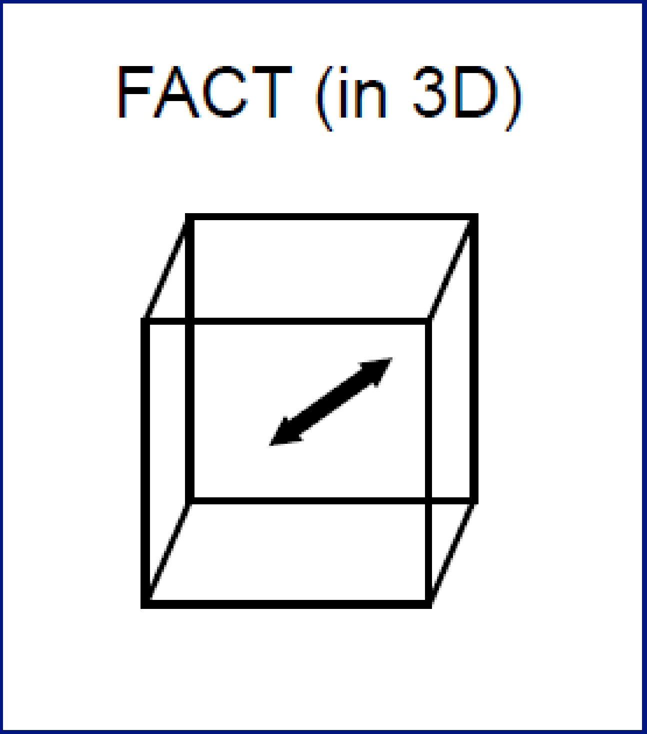

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Improving FACT->

- Start by thinking: what properties a ‘good’ algorithm should have?
  1) Should be independent of coordinate axes (i.e., results invariant to rotation of data set)
  2) Should improve with spatial resolution (convergence in resolution)
     e.g., like in calculus, diagonals are better approximated with small grid steps
  3) Should improve with SNR (converge in SNR)
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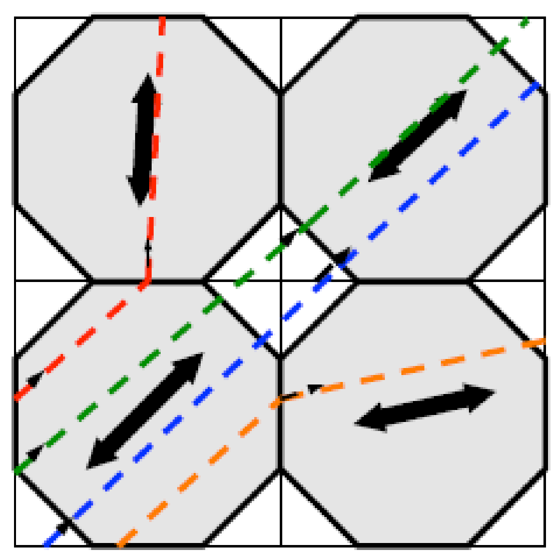
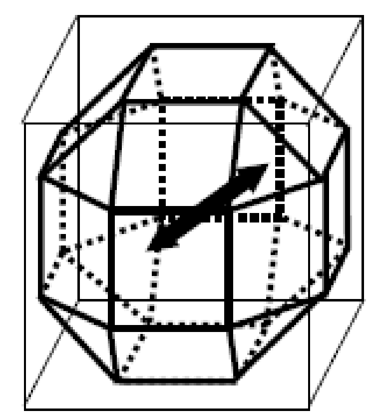
Posit: including diagonal (ID) propagation helps 1 and 4, check about other props.

FACTID (in 2D)



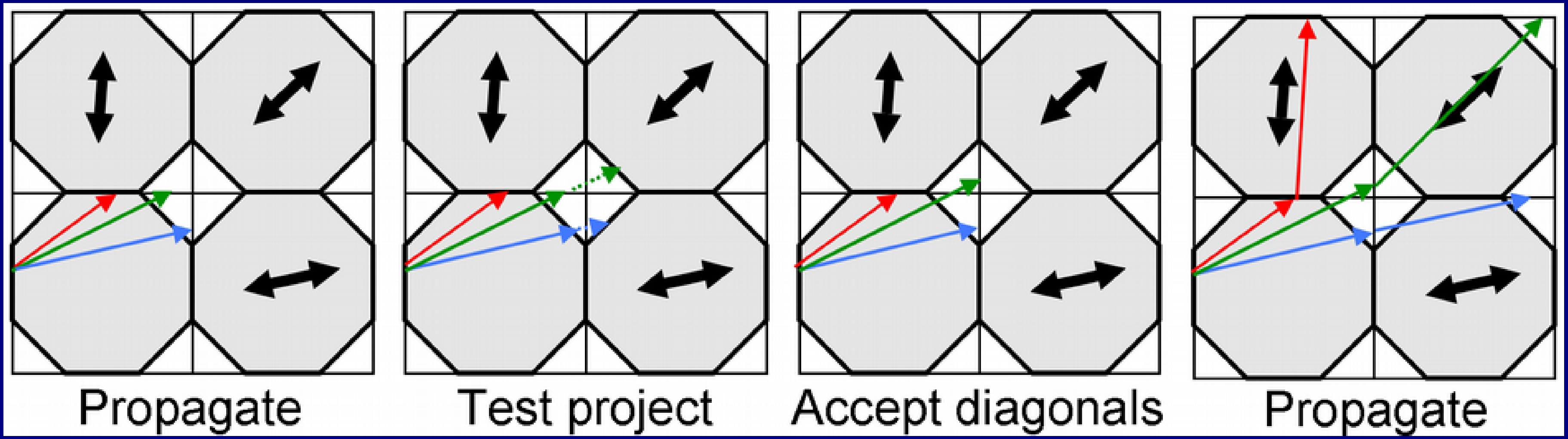
FACTID (in 3D)



FACTID (FACT Including Diagonals):

+ Utilize simple check for diagonals.

(2D) Schematic:



(Taylor, Cho, Lin & Biswal, 2012)

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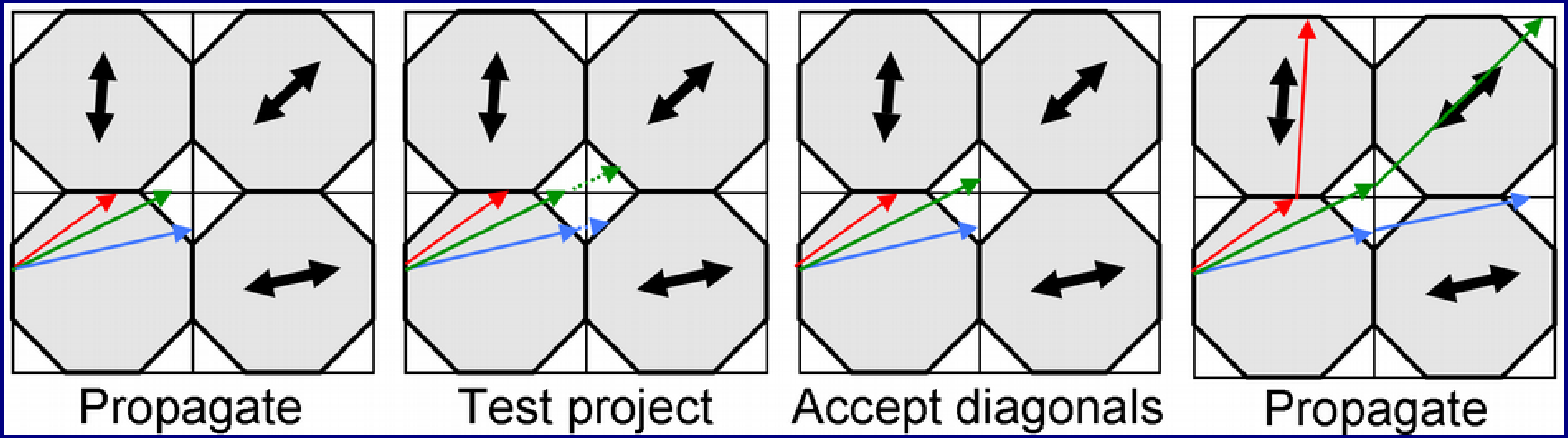


NB that in (3D) FACT, a single voxel has 6 neighbors for propagation, while in FACTID, a voxel has 26 neighbors propagation.

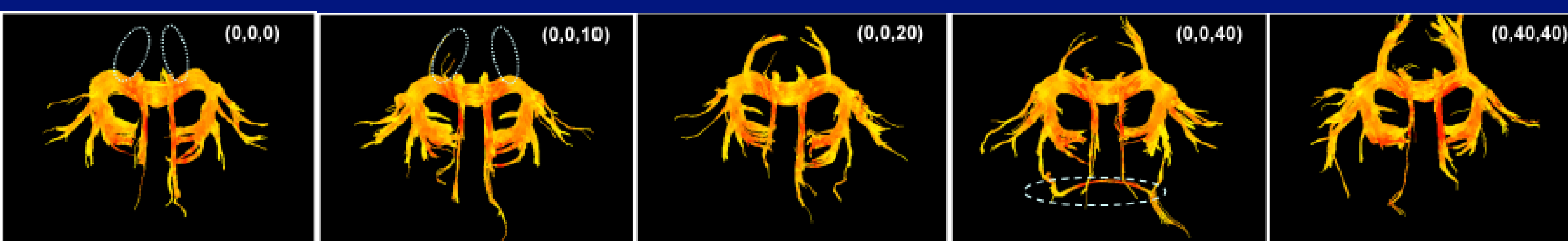
(Taylor, Cho, Lin & Biswal, 2012)

Test 1: Rotational invariance

A test for consistency of results when axes of data have been rotated; here, using data from a real subject (scan axes rotated)

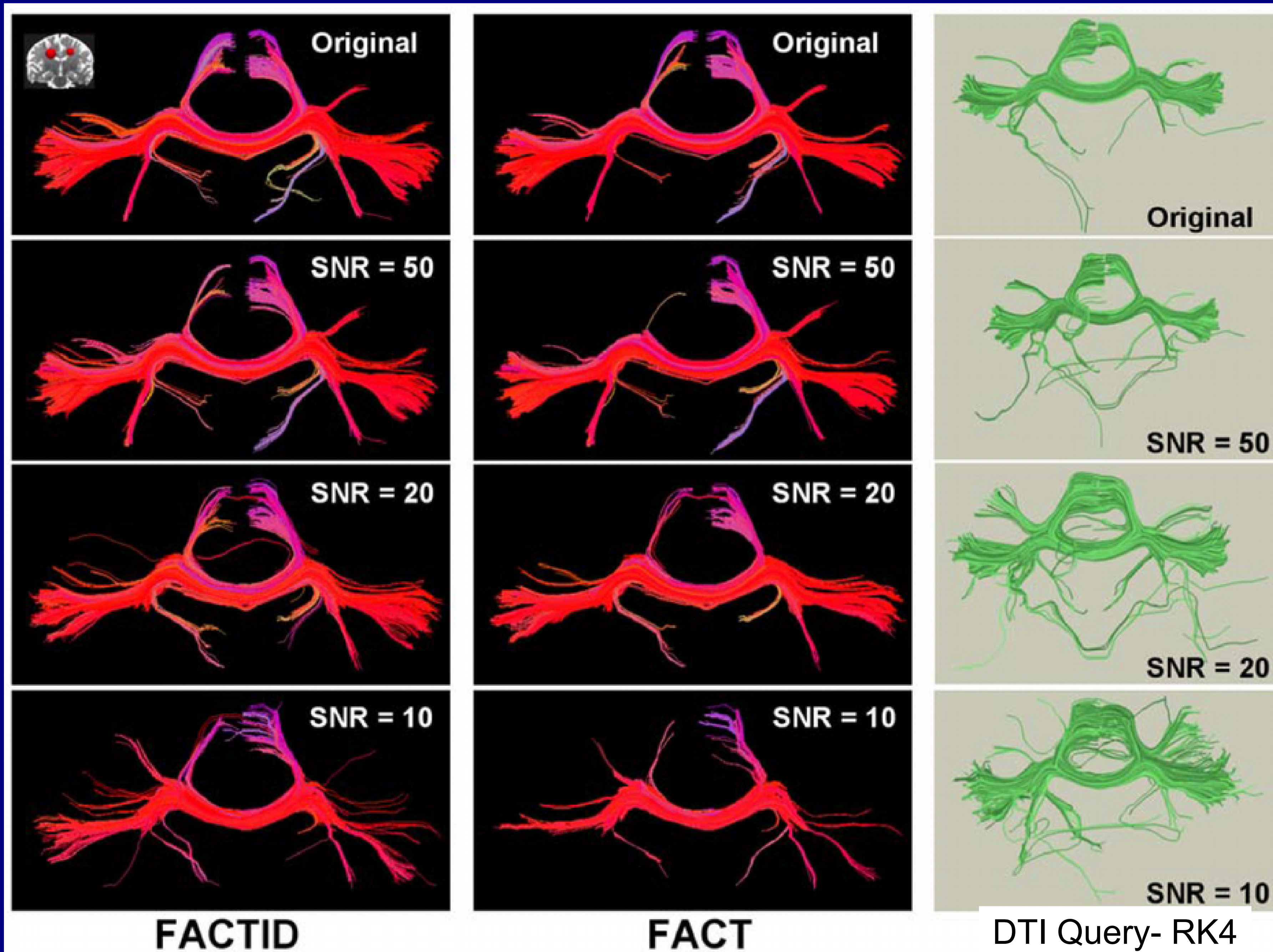
FACTID

FACT



(Taylor, Cho, Lin & Biswal, 2012)

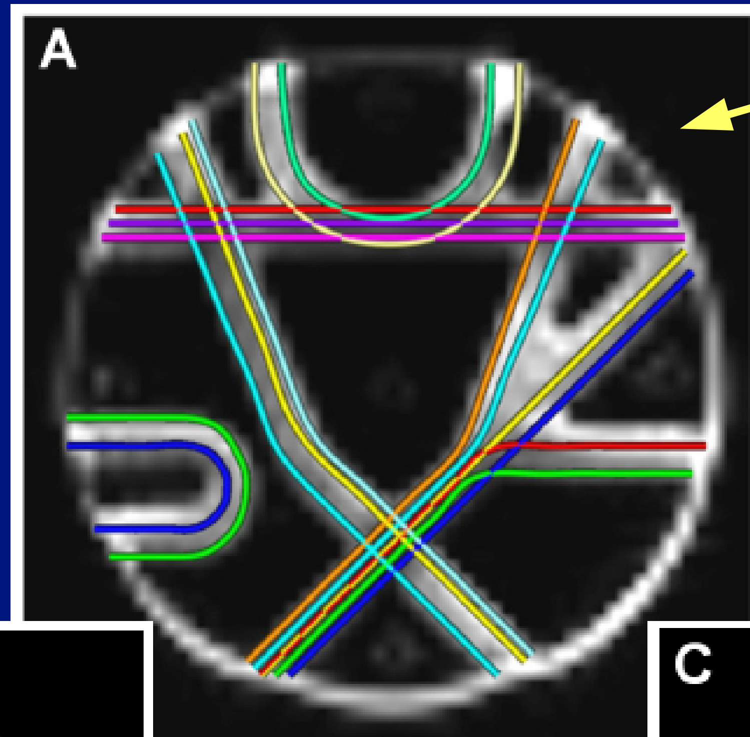
Test 3: Noise sensitivity



(Taylor, Cho, Lin & Biswal, 2012)

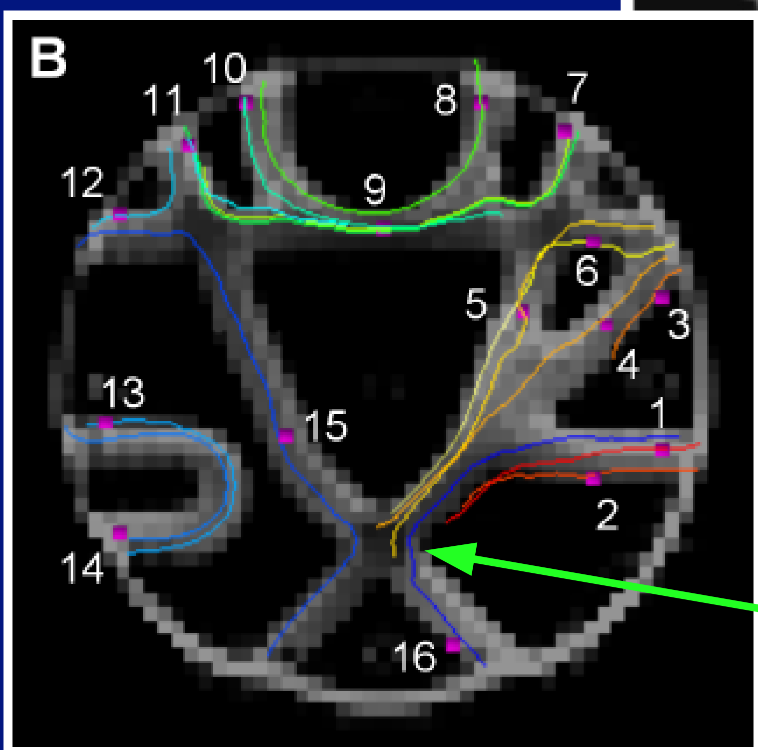
Test 5: Phantom Set

Fillard et al.
(2011, NI)
test phantom

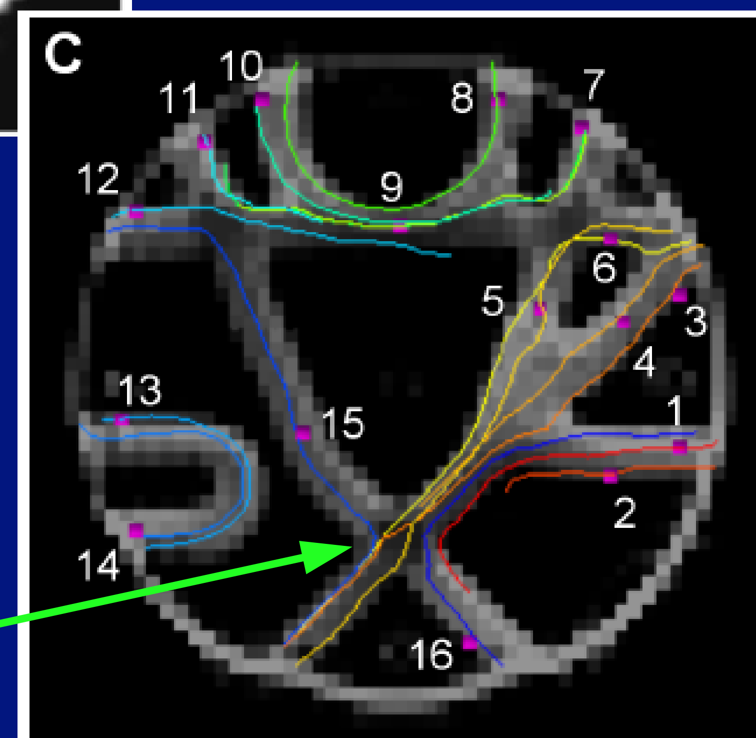


"ANSWER"

FACT



FACTID



(Taylor, Cho, Lin & Biswal, 2012)

e.g. compare

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.

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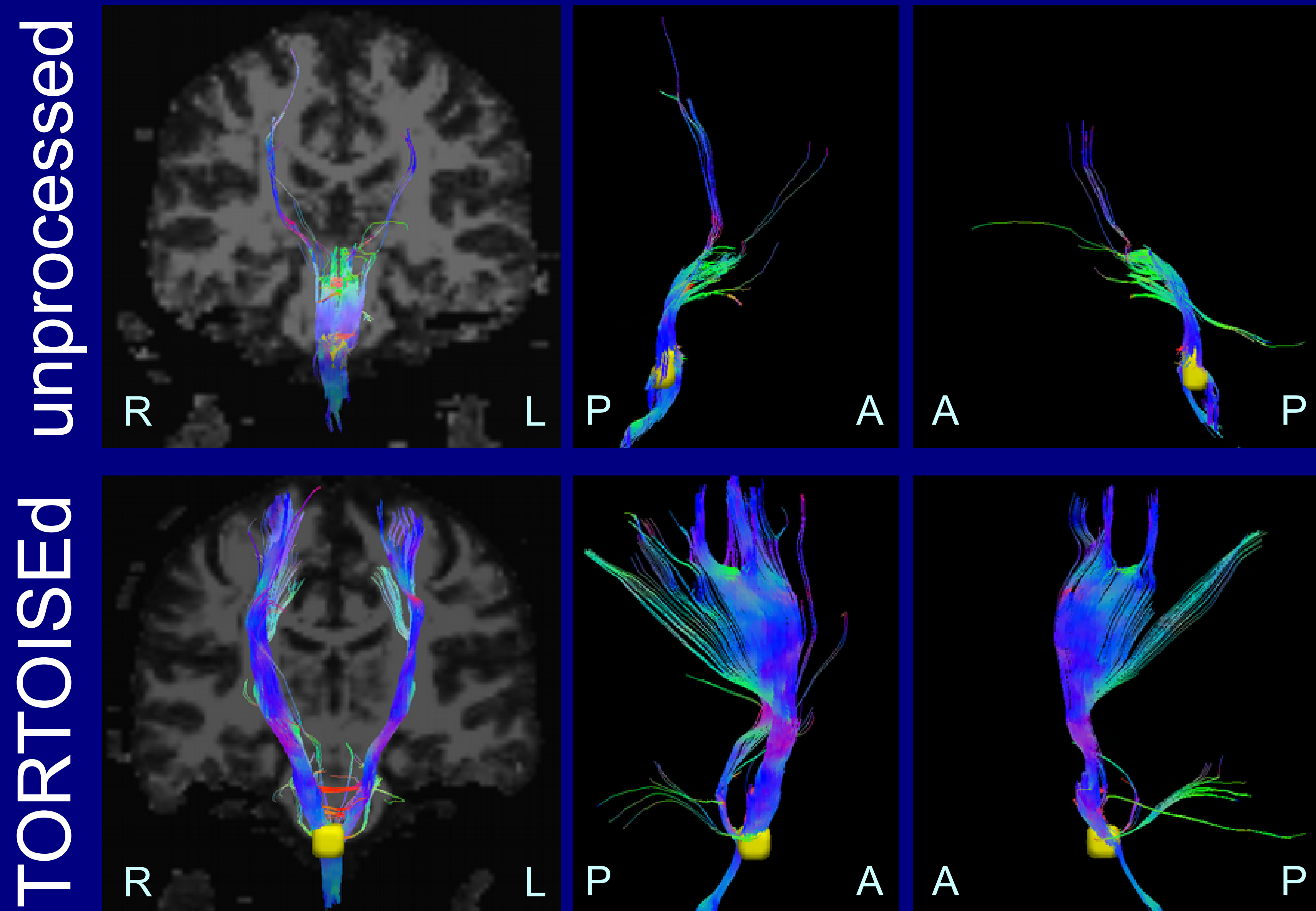
→ ** In addition to the tracking algorithm, the quality of data acquisition and preparation matter quite a bit (as seen in morning TORTOISE session). **

Importance of being processed (in earnest)



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

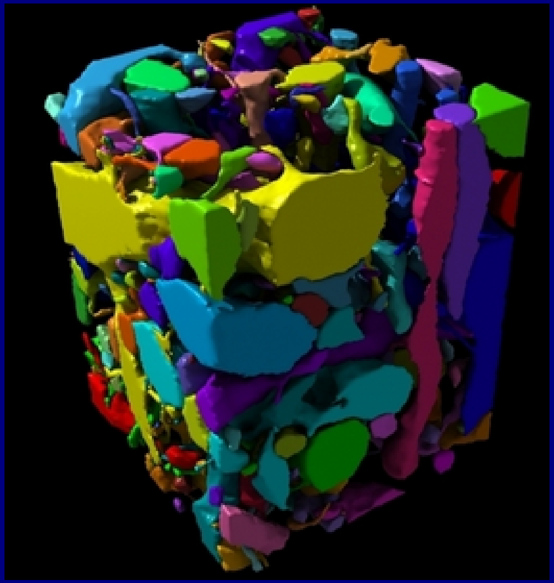
Consider reach of tracks, symmetry, physiology, etc.

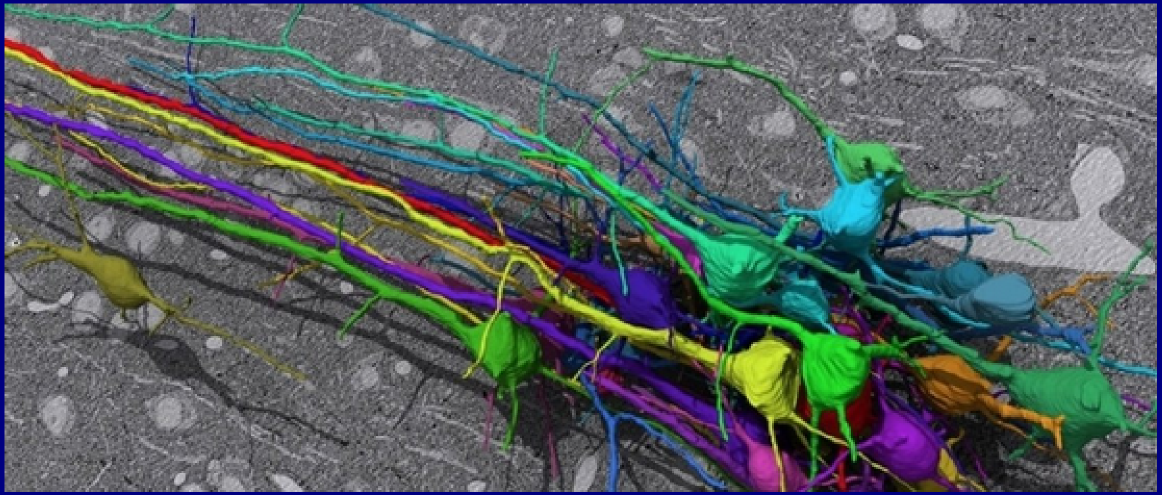
Cinematic side note:

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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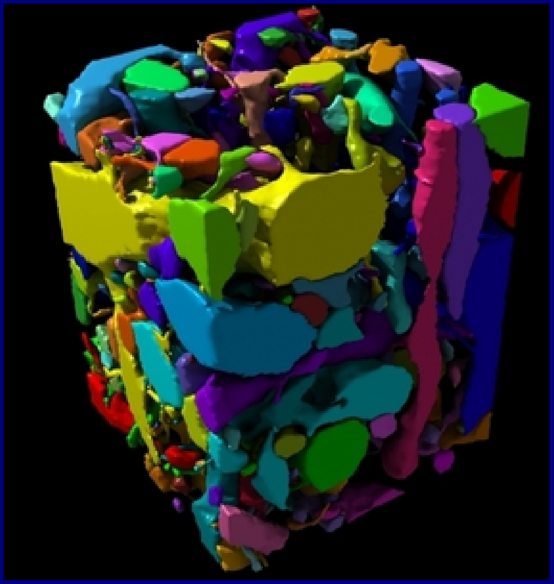
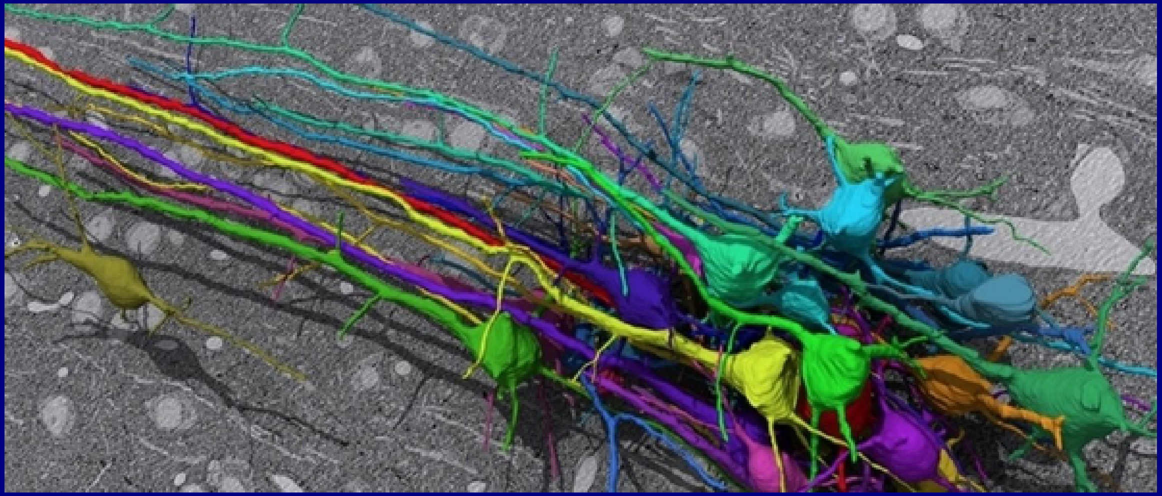
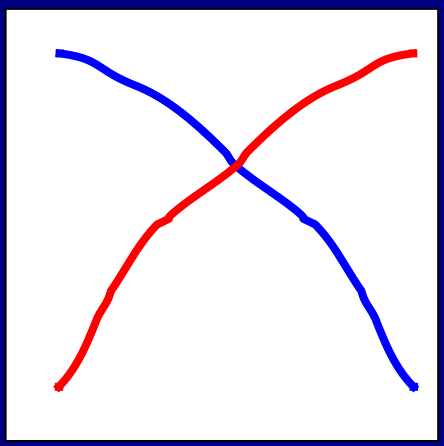
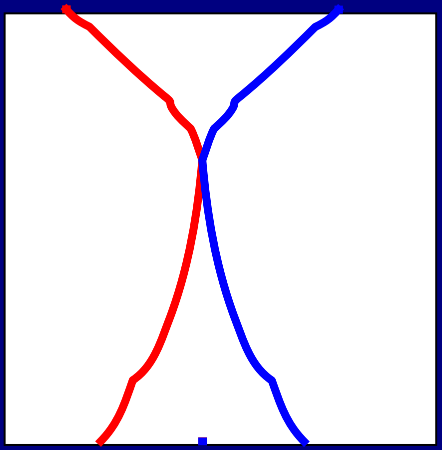




(images of Eyewire data via NPR website)

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

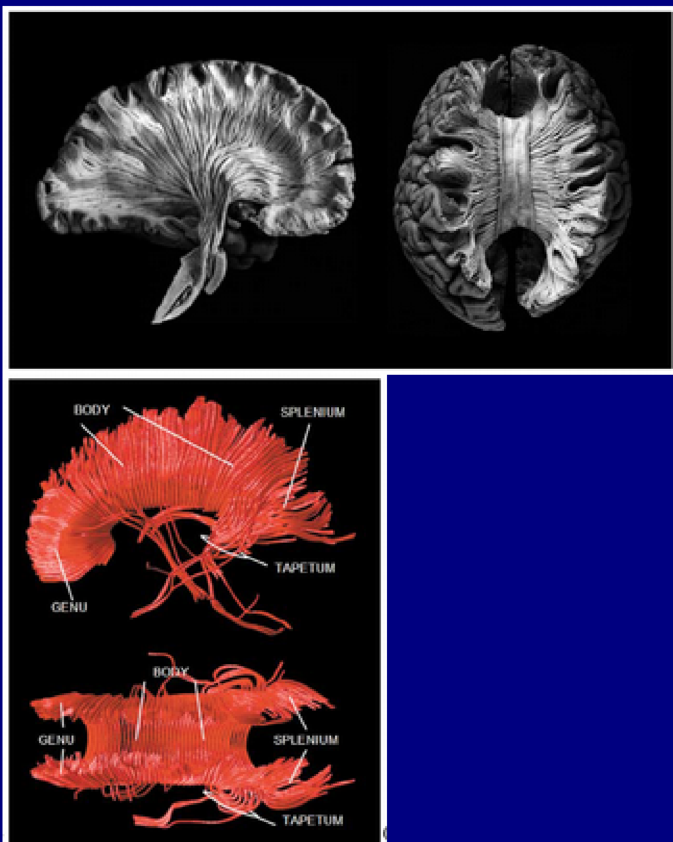




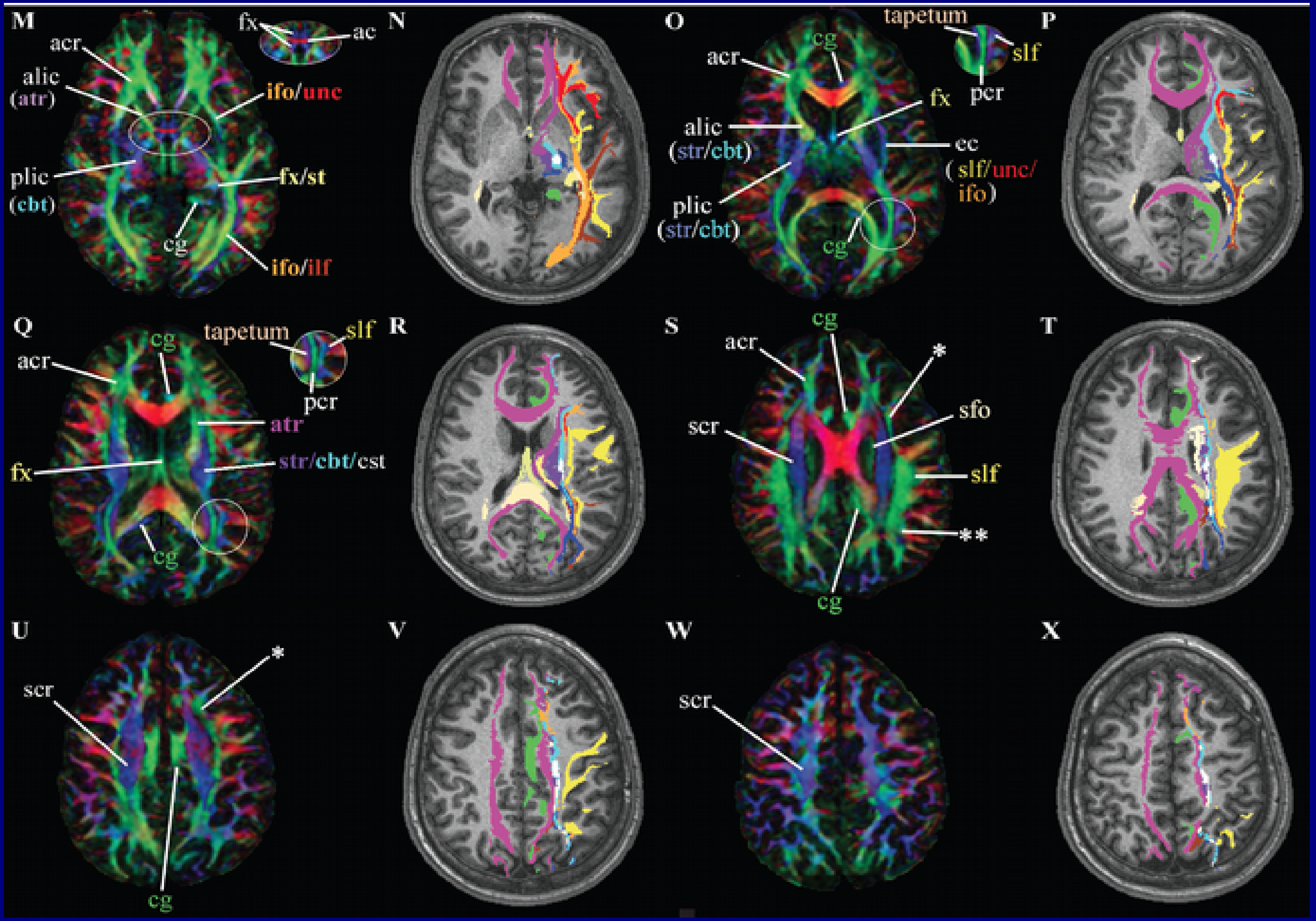
Crossing/kissing fibers can:
- Lower FA (stop tracking)
- Redirect (or *not*) tracking incorrectly.

Achievements of Tracking

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



(Bammer et al., 2003)



(Wakana et al., 2004)

Light at the end of the tunnel?

Application of tractography seems useful and logically consistent as follows:

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

Next question for doing tractography:

where does one go to get the ROIs to try to connect?

Next question for doing tractography:

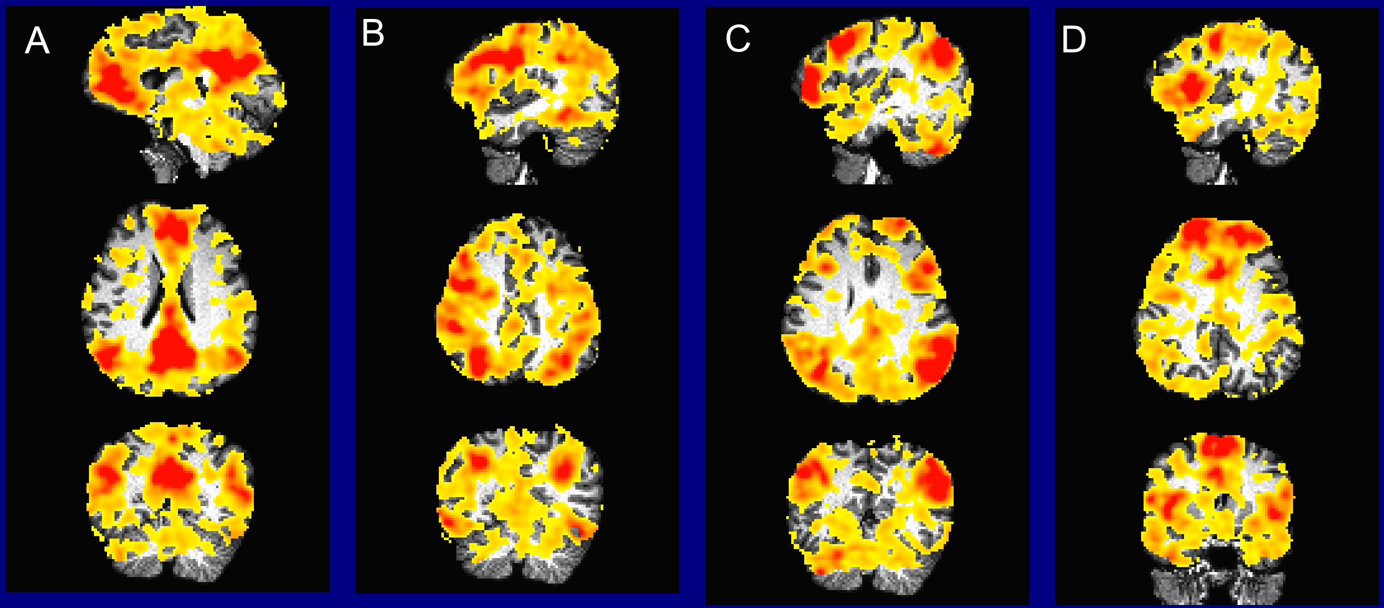
where does one go to get the ROIs to try to connect?

-> could go to atlases and standard maps,
or to exploratory spheres dotted around,

FMRI measures -> networks of ROIs

+ For example, one can perform ICA on a resting state study, resulting in several functional networks:

(each IC is map of Z-scores; here, shown for Z>0)



...

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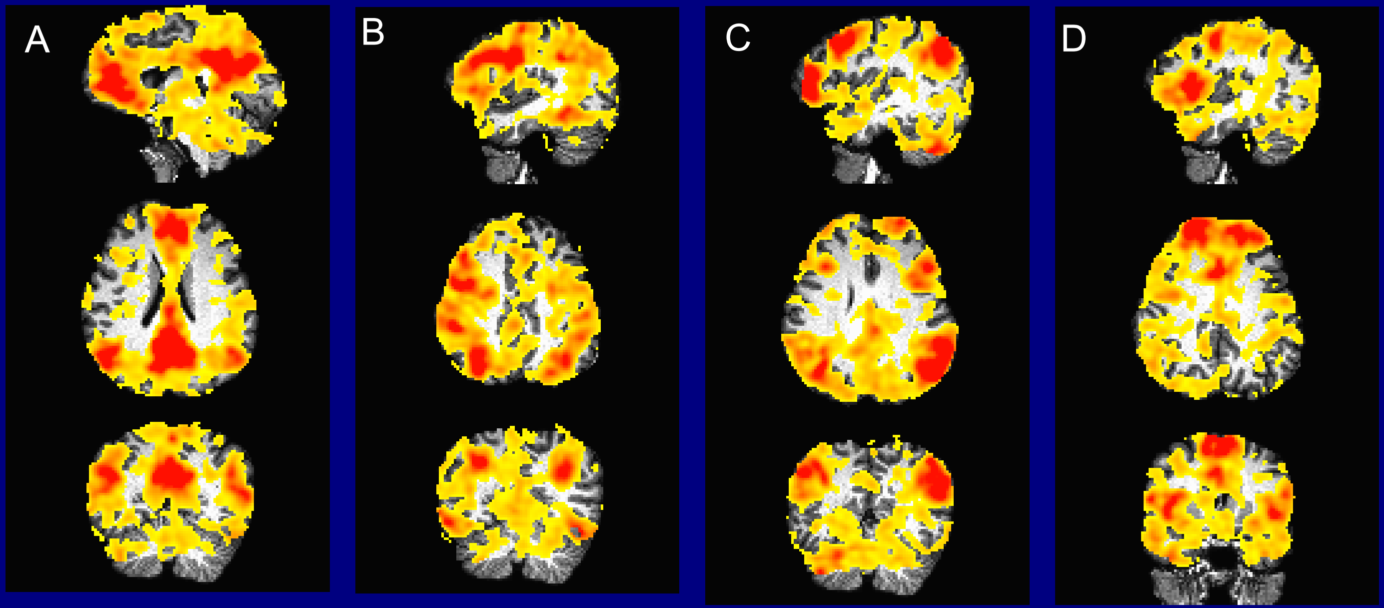

...

+ want to isolate GM ROIs, and then to expand each to make sure that they are at least touching nearby (*associated?*) WM voxels to have any hope to connect tracts

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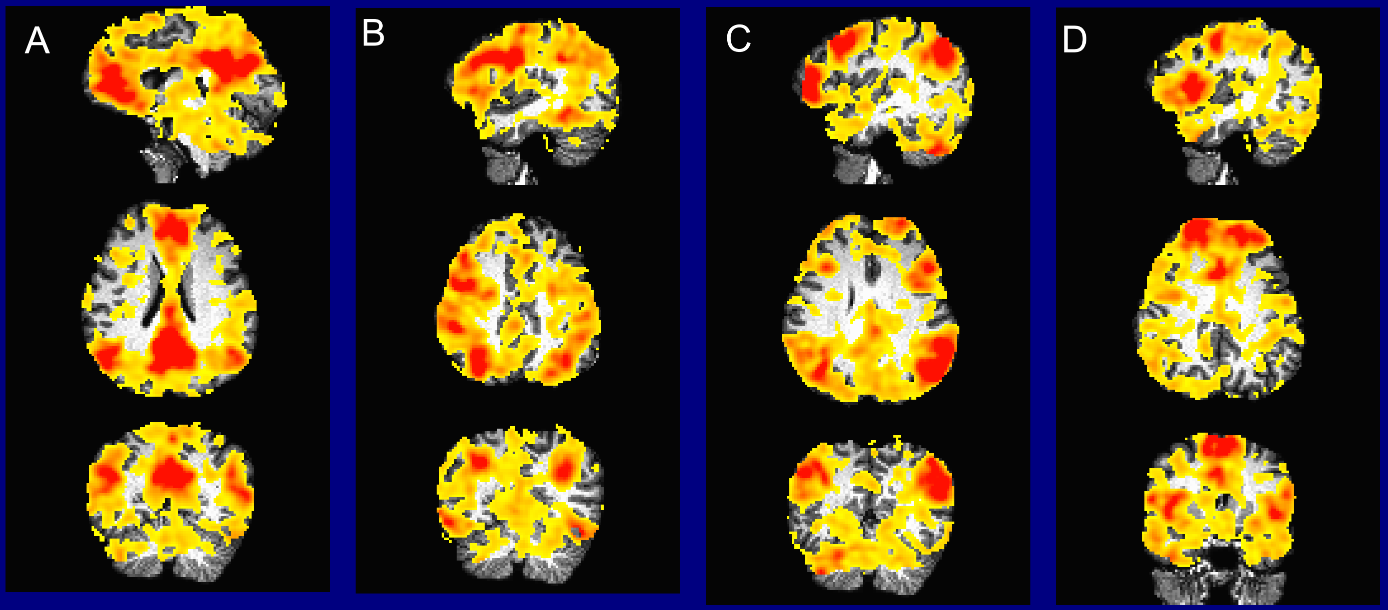
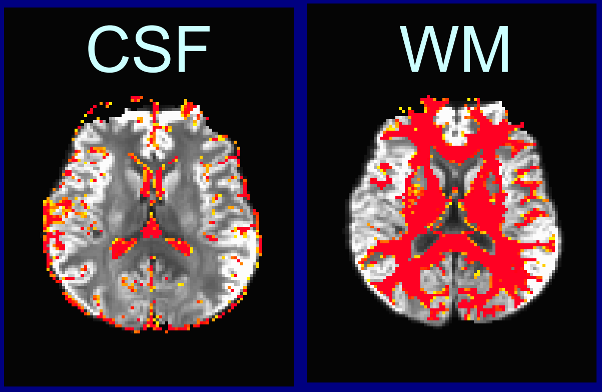


...

+ 3dROIMaker can parcellate into GM ROIs based on:
  - thresholding voxel values
  - thresholding cluster size
  - subtract away CSF and WM voxels from segmentation maps
  - expand each GM ROI to location of WM (don't want to *overexpand* unphysically)

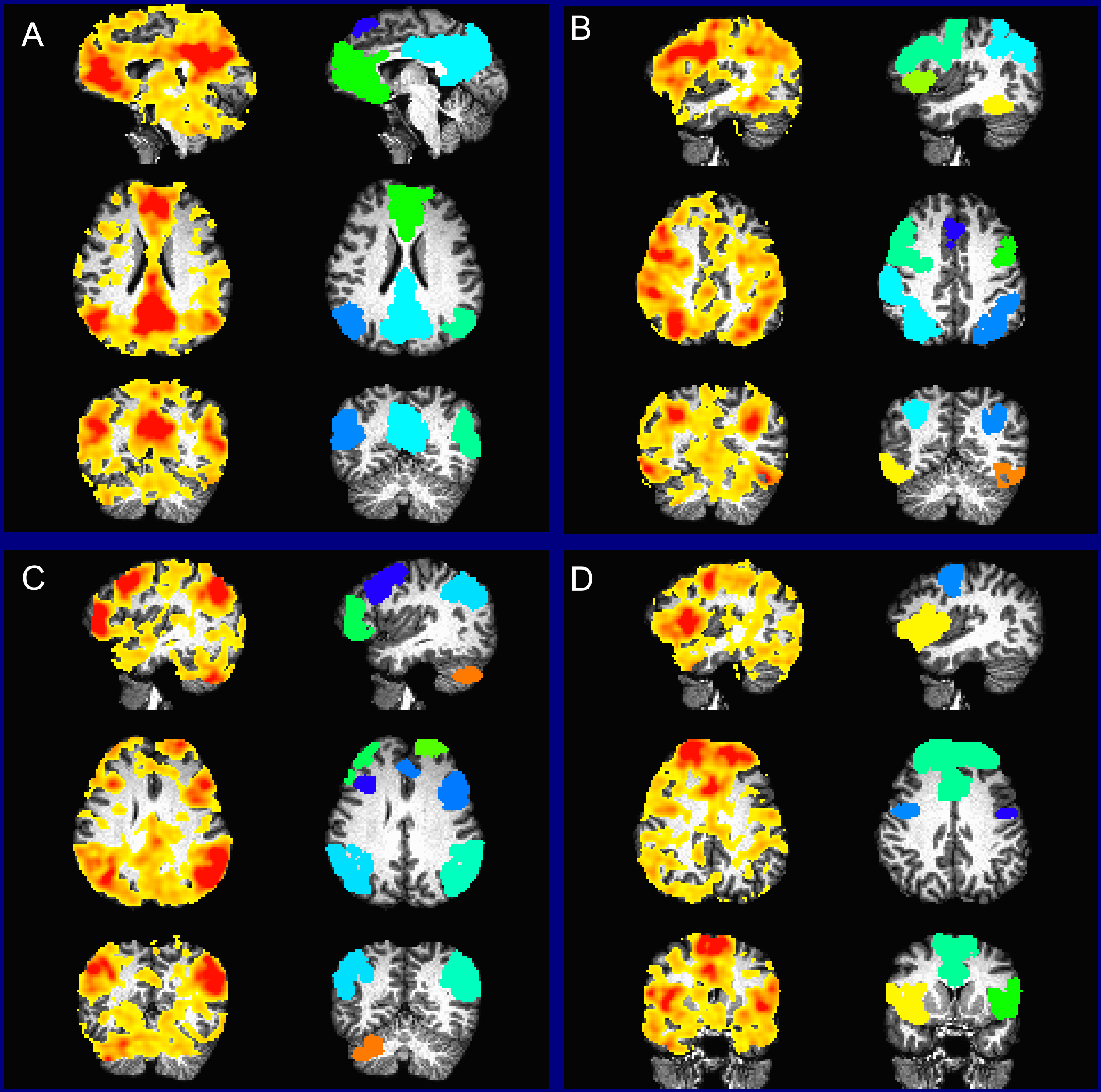


FMRI measures -> networks of ROIs

Example case for ICA networks:

thresholded Z>3.0
cluster volume > 130 voxels
expand clusters +2 voxels
limit expansion with WM map

(NB: this involved mapping FMRI data of ICs and T1 tissue segmentation results into DWI space; used 3dAllineate)



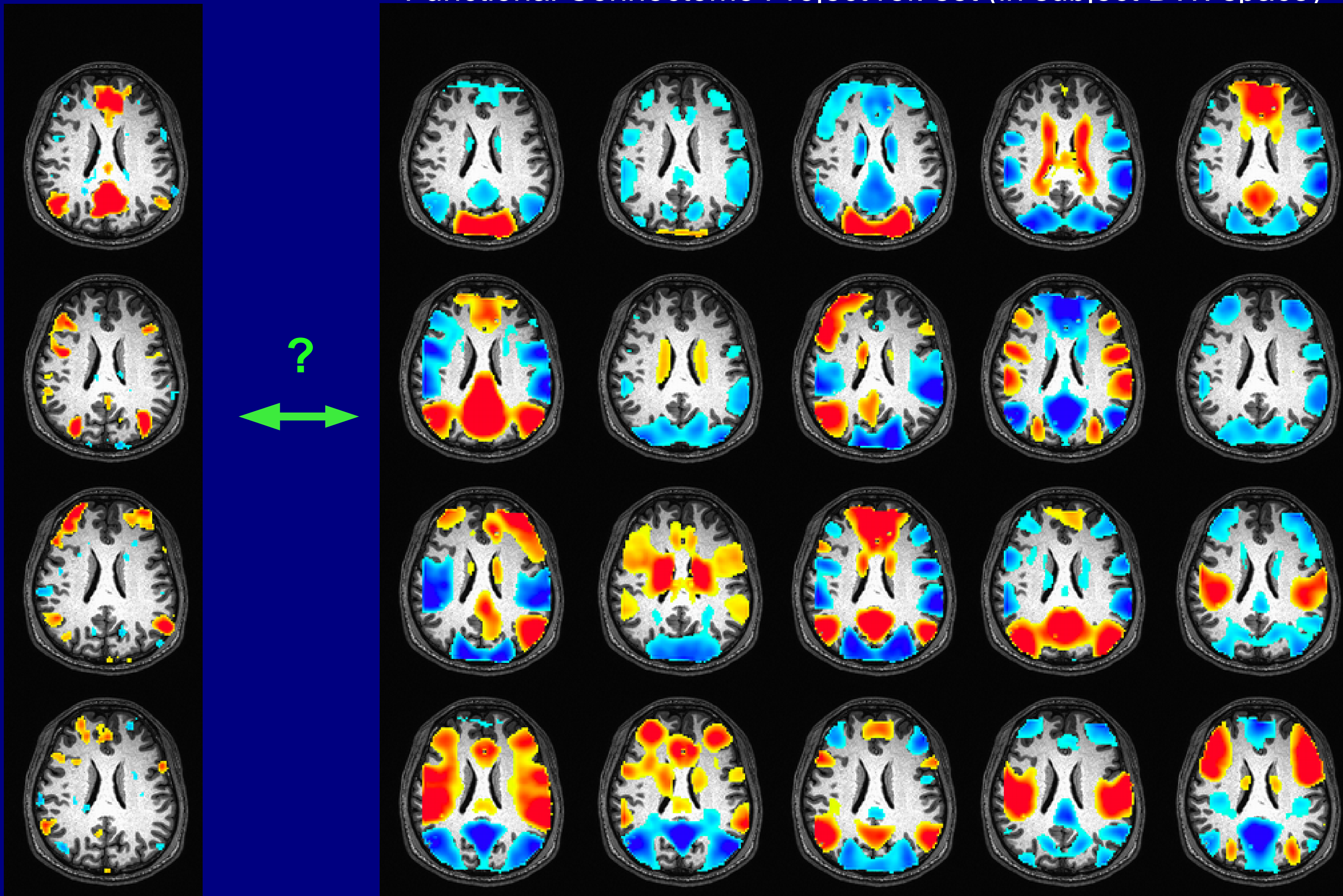
Sidenote:

How to identify network maps, or match them with reference/group set?

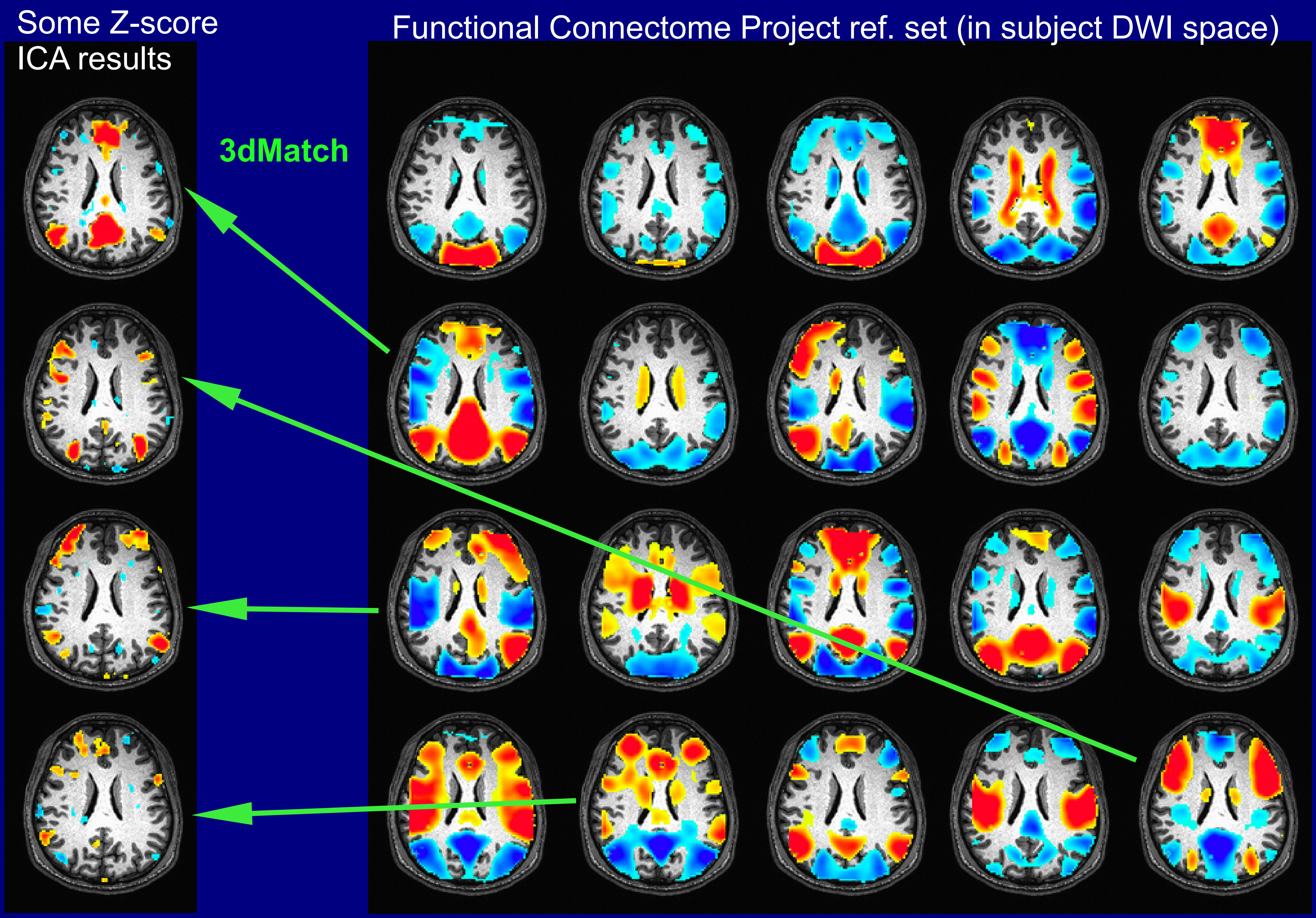
Matching Network maps

Some Z-score

Functional Connectome Project ref. set (in subject DWI space)



Matching Network maps



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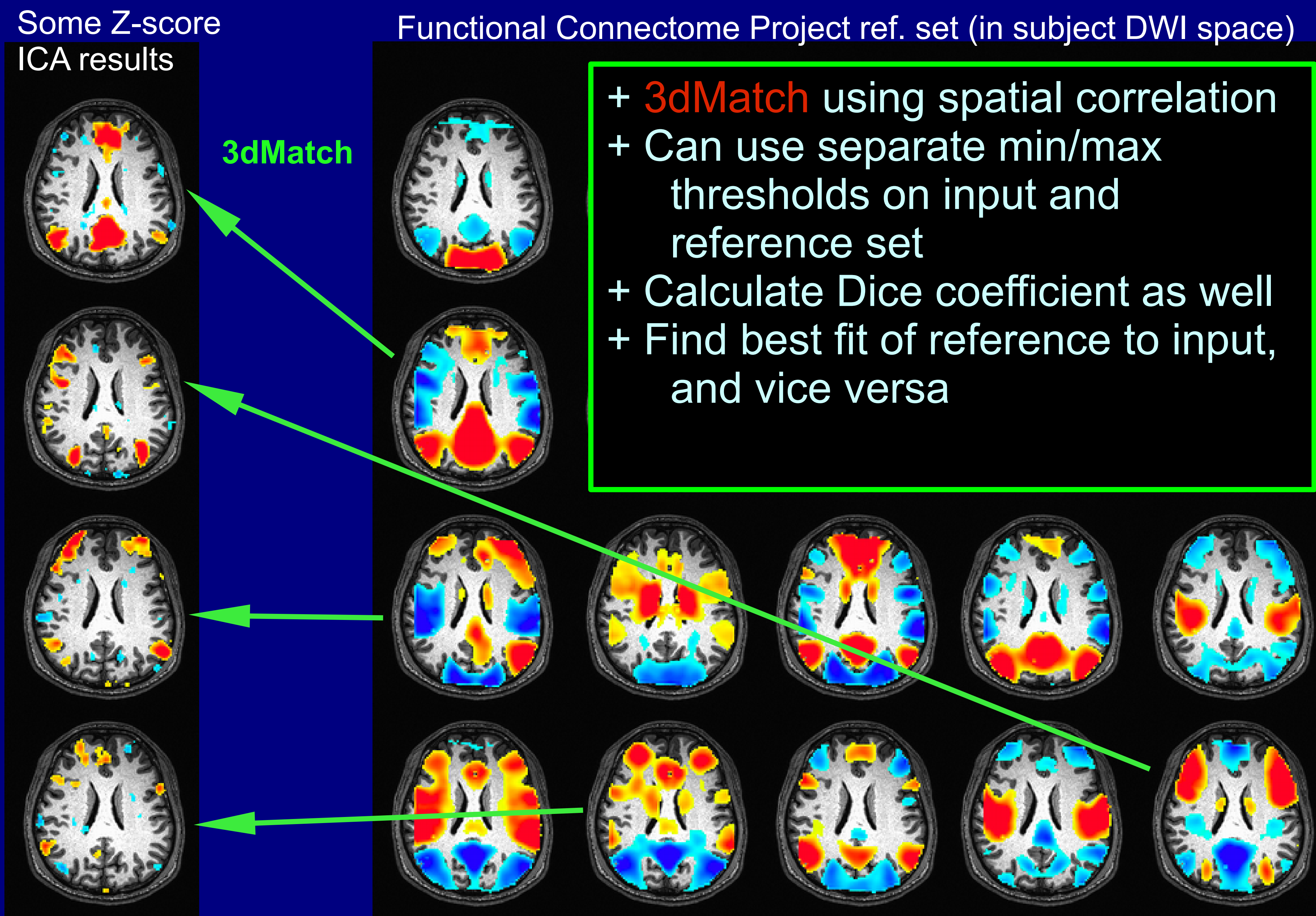
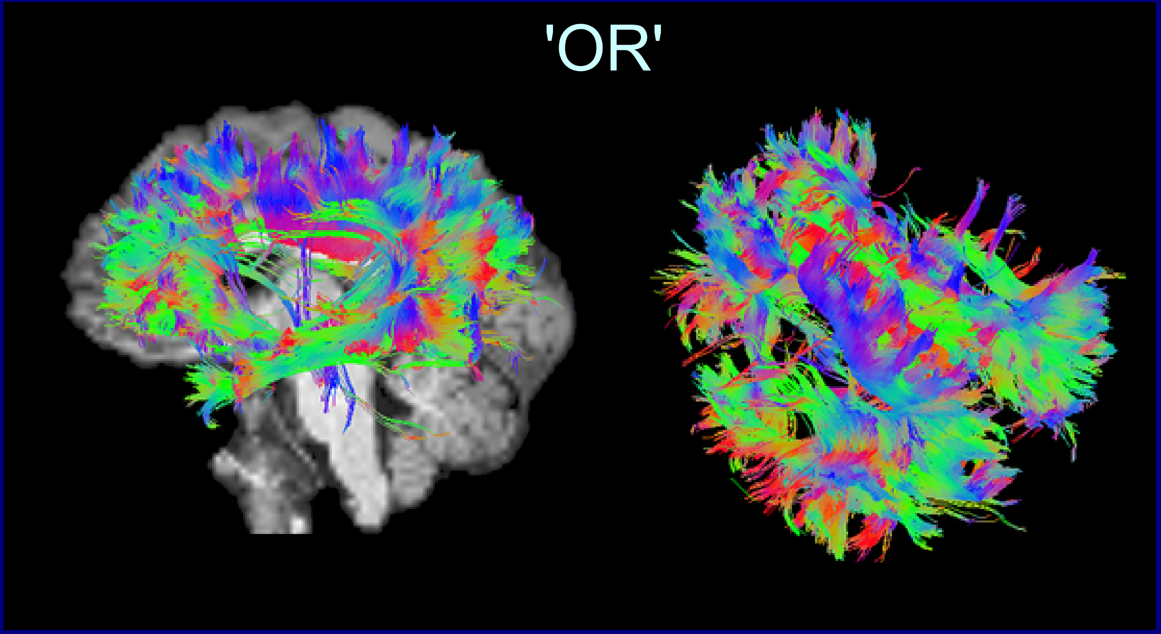
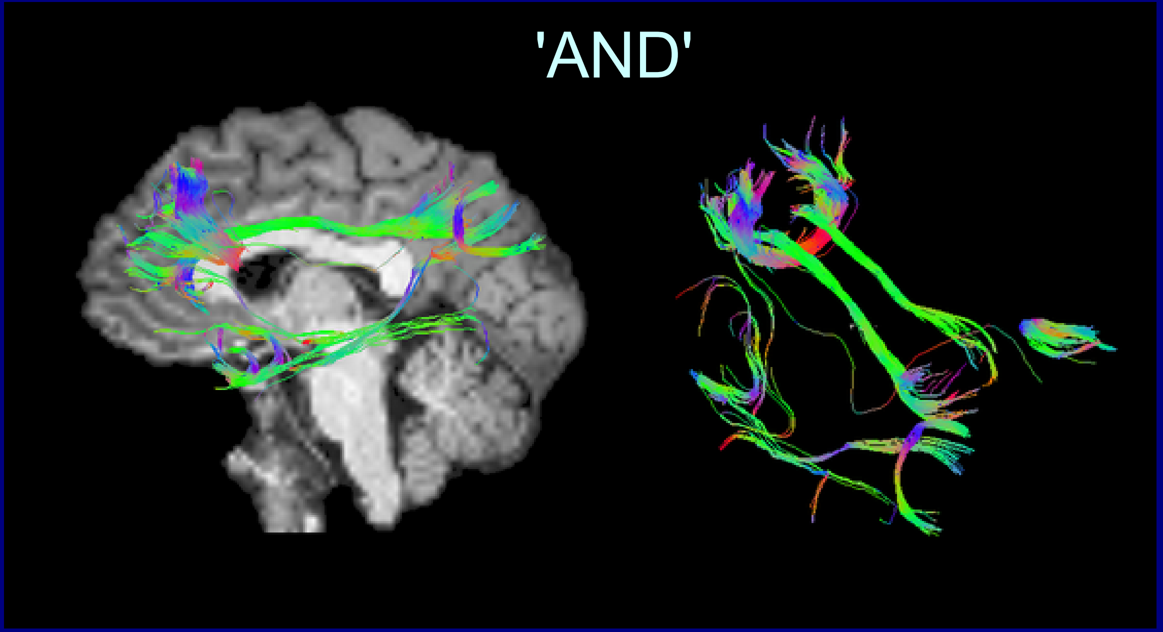


+ 3dMatch using spatial correlation
+ Can use separate min/max thresholds on input and reference set
+ Calculate Dice coefficient as well
+ Find best fit of reference to input, and vice versa

Deterministic tractography

+ 3dProbTrackID -detnet { OR | AND }
  using FACTID
+ good for exploratory
  analysis and visualization
  of results



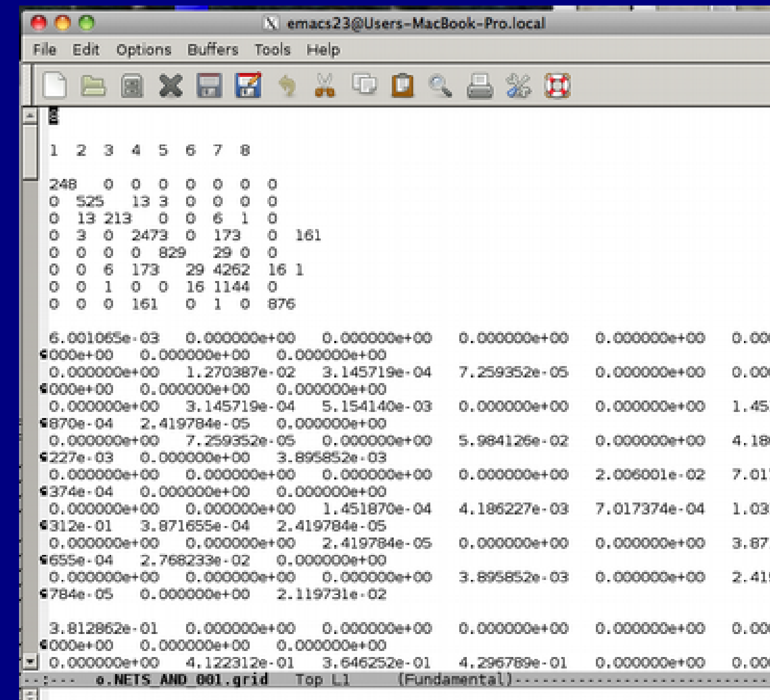


ex.: DMN network tractography results using ROIs from 3dROIMaker
(FA>0.2; max angle 60deg; 8 seeds/voxel)

Deterministic tractography

+ 3dProbTrackID -detnet { OR | AND }

+ Automatically produces statistics of WM ROIs where voxels pass (Nvox, Ntracks, mean/std FA, MD, RD, L1): *.grid file.



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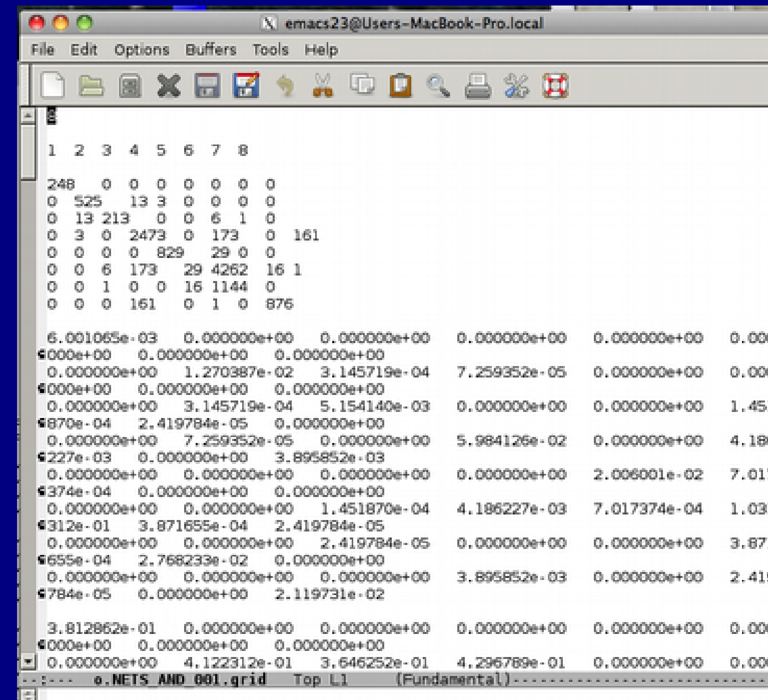

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8

1  2  3  4  5  6  7  8

248   0  0  0  0  0  0  0
0  525   13 3  0  0  0  0
0  13 213   0  0  6  1  0
0  3  0  2473  0  173   0  161
0  0  0  0  829   29 0  0
0  0  6  173   29 4262  16 1
0  0  1  0  0  16 1144  0
0  0  0  161   0  1  0  876

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000e+00   0.000000e+00   0.000000e+00
0.000000e+00   1.270387e-02   3.145719e-04   7.259352e-05   0.000000e+00   0.000
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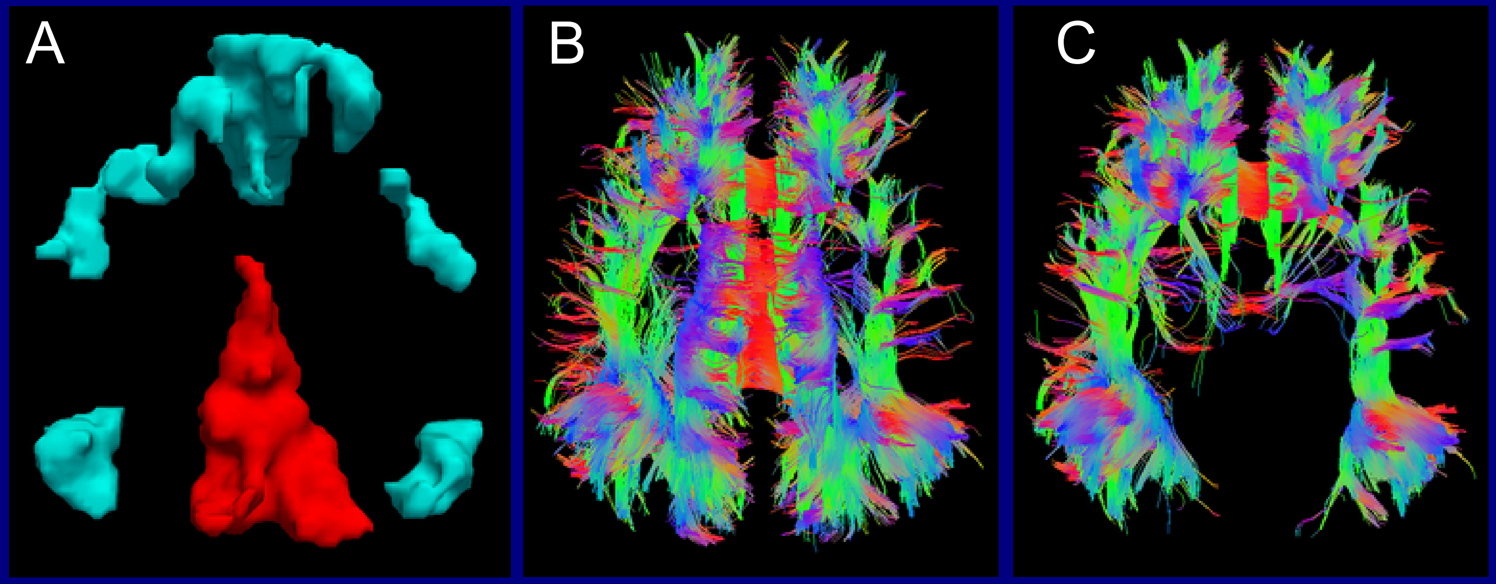
000e+00   0.000000e+00   0.000000e+00
0.000000e+00   4.122312e-01   3.646252e-01   4.296789e-01   0.000000e+00   0.000
--:---   o.NETS_AND_001.grid   Top L1   (Fundamental)----------
```

Control tracks with `anti-mask' regions, simply defined by voxels =-1:



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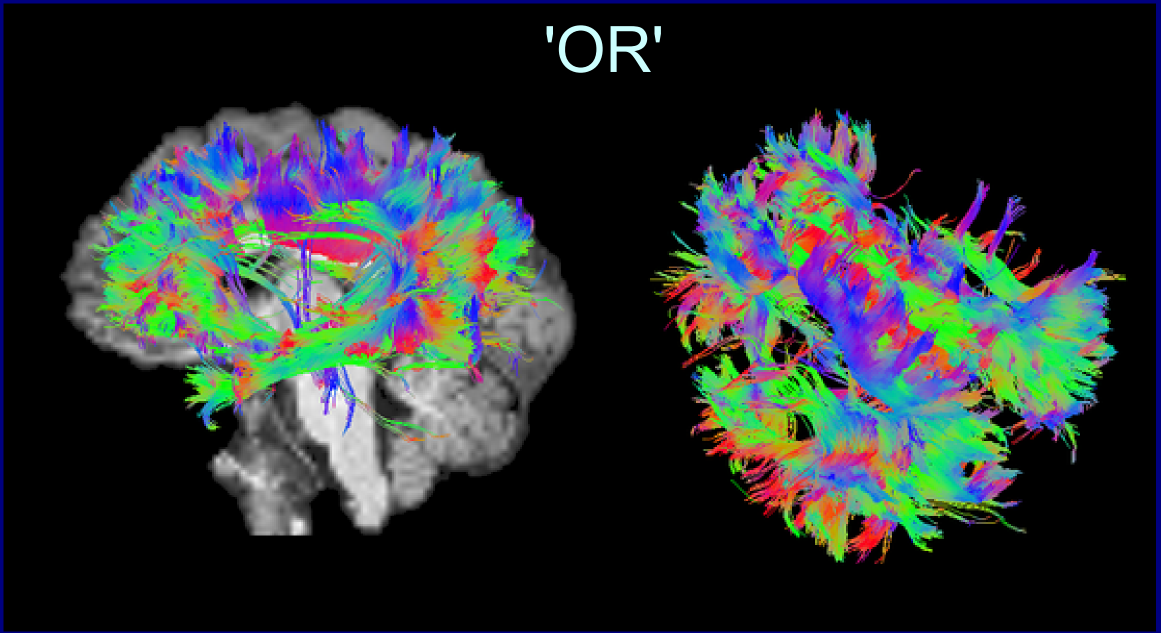

ex.: DMN network tractography
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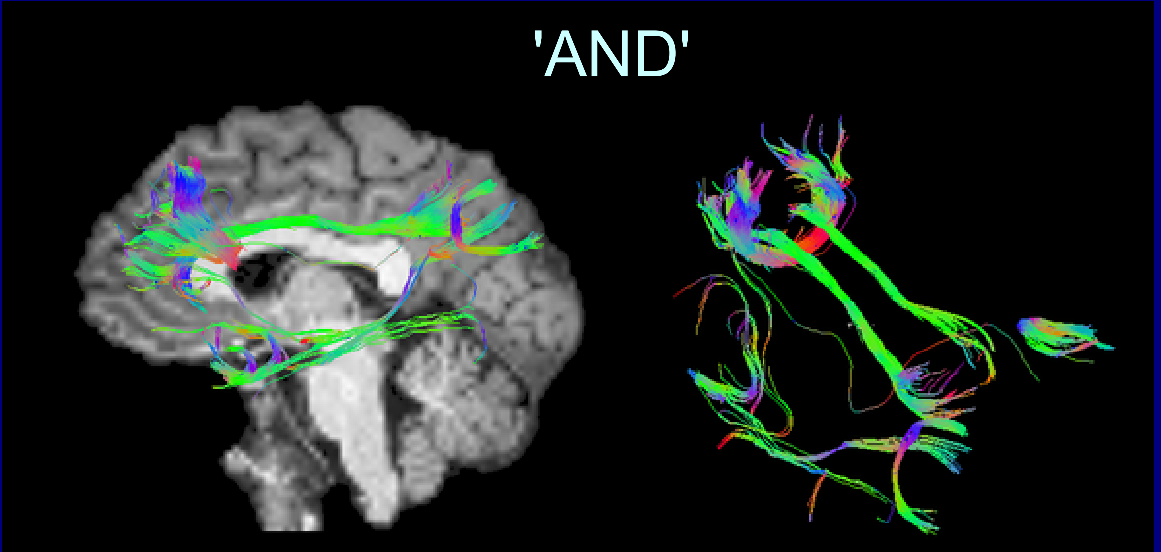


*Tract results may seem 'fine',
but is **noise** affecting them?
Are these the **most likely/robust** regions where tracts go?*

Brings up next question for doing tractography:

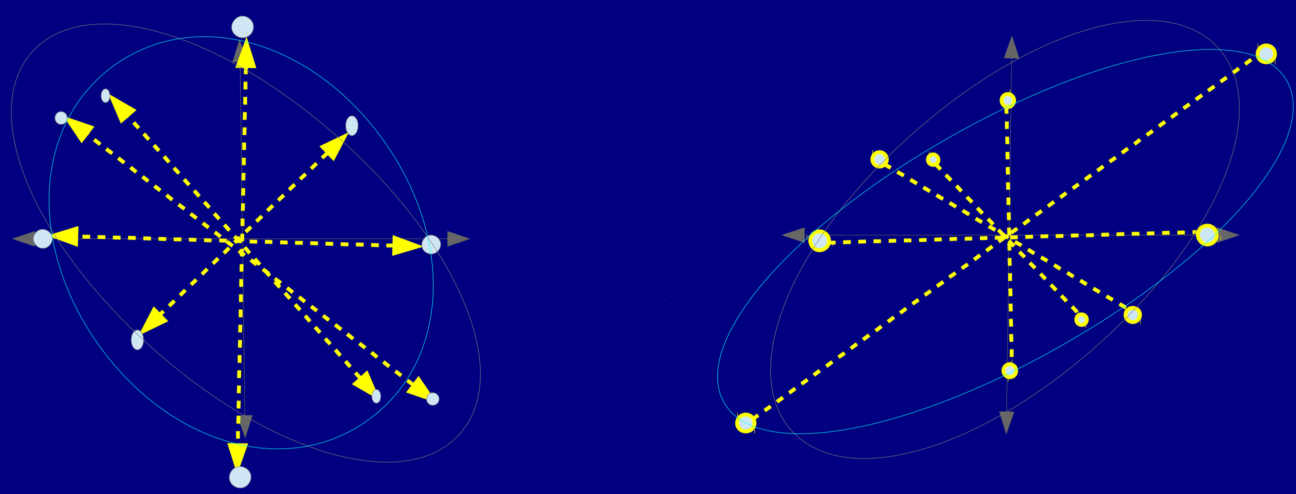
How do we estimate tensor parameter noise/uncertainty?

Noise in DW signals

MRI signals have additive noise

$$S_i = S_0\, e^{-b\, \mathbf{g}_i^T \mathbf{D}\, \mathbf{g}_i} + \varepsilon,$$

where ε is (Rician) noise, with the effect of leading to errors in surface fit, equivalent to *rotations* and *rescalings* of ellipsoids:



'Un-noisy' vs perturbed/noisy fit

EPI distortions, subject motion, et al. also warp ellipsoids.

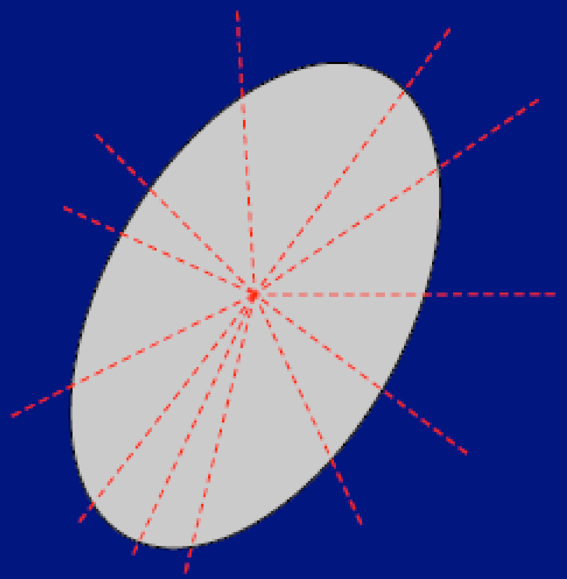
DTI Uncertainty

- We use jackknife resampling (e.g., Efron 1982)
  - Other studies have used bootstrapping (e.g., Jones 2003), or theoretical estimates (Jeong & Anderson 2008)
  - Jackknifing is efficient (just need one data set unlike bootstrap), simpler than theory, since, e.g., SNR is likely not constant across voxels

Jackknifing

- Basically, take M acquisitions

e.g., M=12

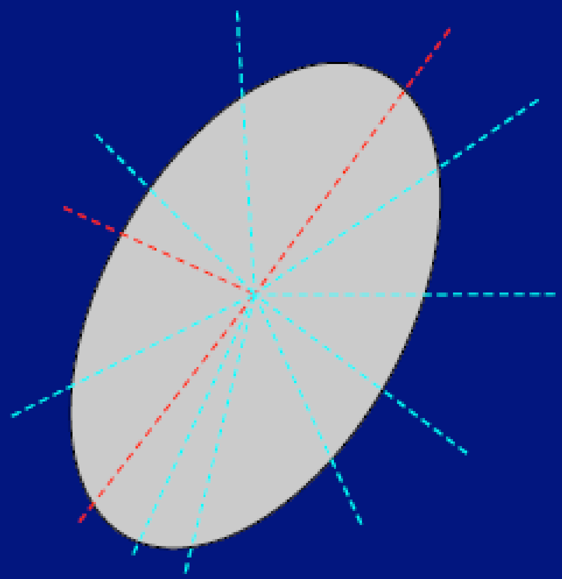


Jackknifing

- Basically, take M acquisitions
- Randomly select $M_J < M$ to use to calculate quantity of interest
  - standard nonlinear fits

e.g., $M=12$

$M_J=9$



$$[D_{11} \;\; D_{22} \;\; D_{33} \;\; D_{12} \;\; D_{13} \;\; D_{23}] = \ldots$$

Jackknifing

- Basically, take M acquisitions
- Randomly select $M_J < M$ to use to calculate quantity of interest
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- Repeatedly subsample large number (~10^3-10^4 times)

e.g., $M=12$

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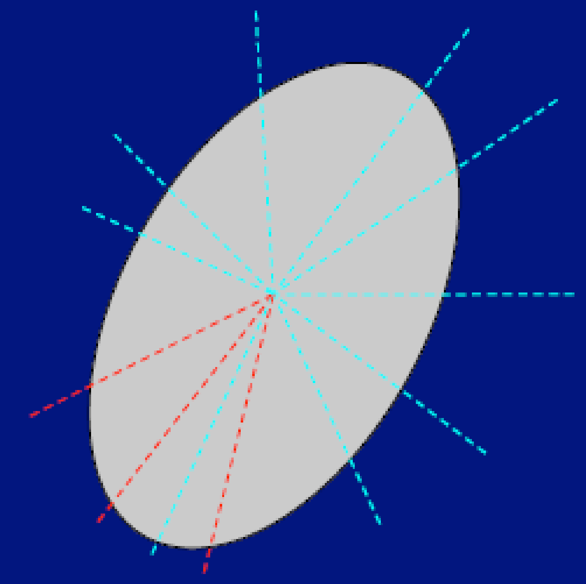

$$[D_{11}\ \ D_{22}\ \ D_{33}\ \ D_{12}\ \ D_{13}\ \ D_{23}] = \ldots.$$
$$[D_{11}\ \ D_{22}\ \ D_{33}\ \ D_{12}\ \ D_{13}\ \ D_{23}] = \ldots.$$
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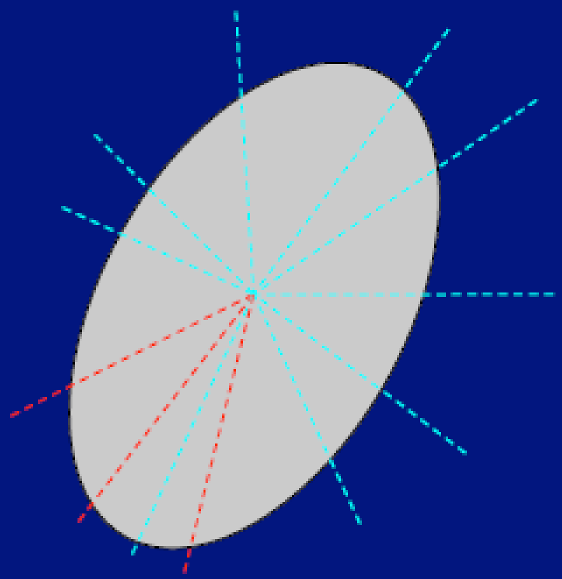
....

Jackknifing

- Basically, take M acquisitions
- Randomly select $M_J < M$ to use to calculate quantity of interest
  - standard nonlinear fits
- Repeatedly subsample large number (~10^3-10^4 times)
- Analyze distribution of values for estimator (mean) and confidence interval
  - sort/%iles
    - (not so efficient)
  - if Gaussian, e.g. $\mu \pm 2\sigma$
    - simple

e.g., M=12

M_J=9



$[D_{11} \ \ D_{22} \ \ D_{33} \ \ D_{12} \ \ D_{13} \ \ D_{23}] = ...$

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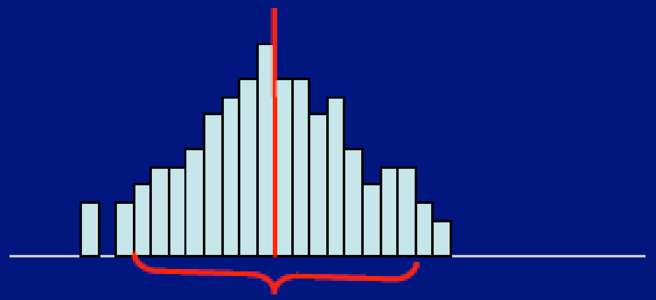
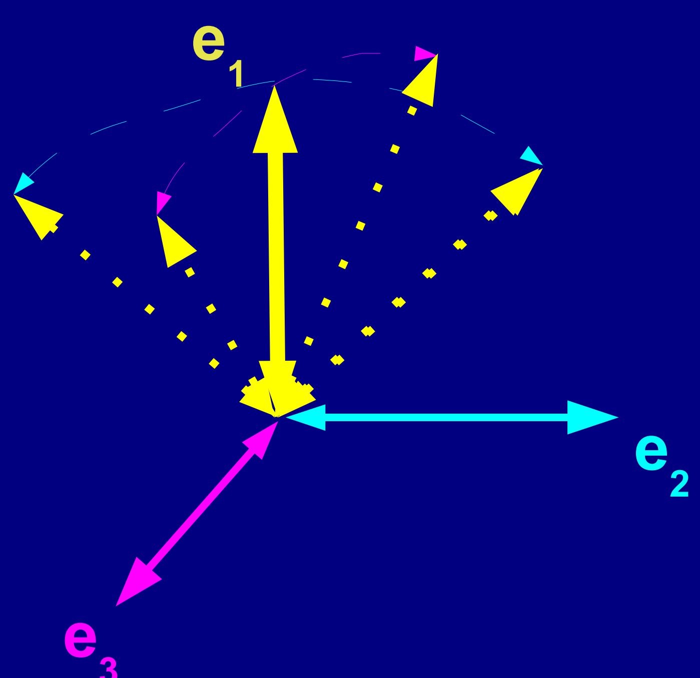
....

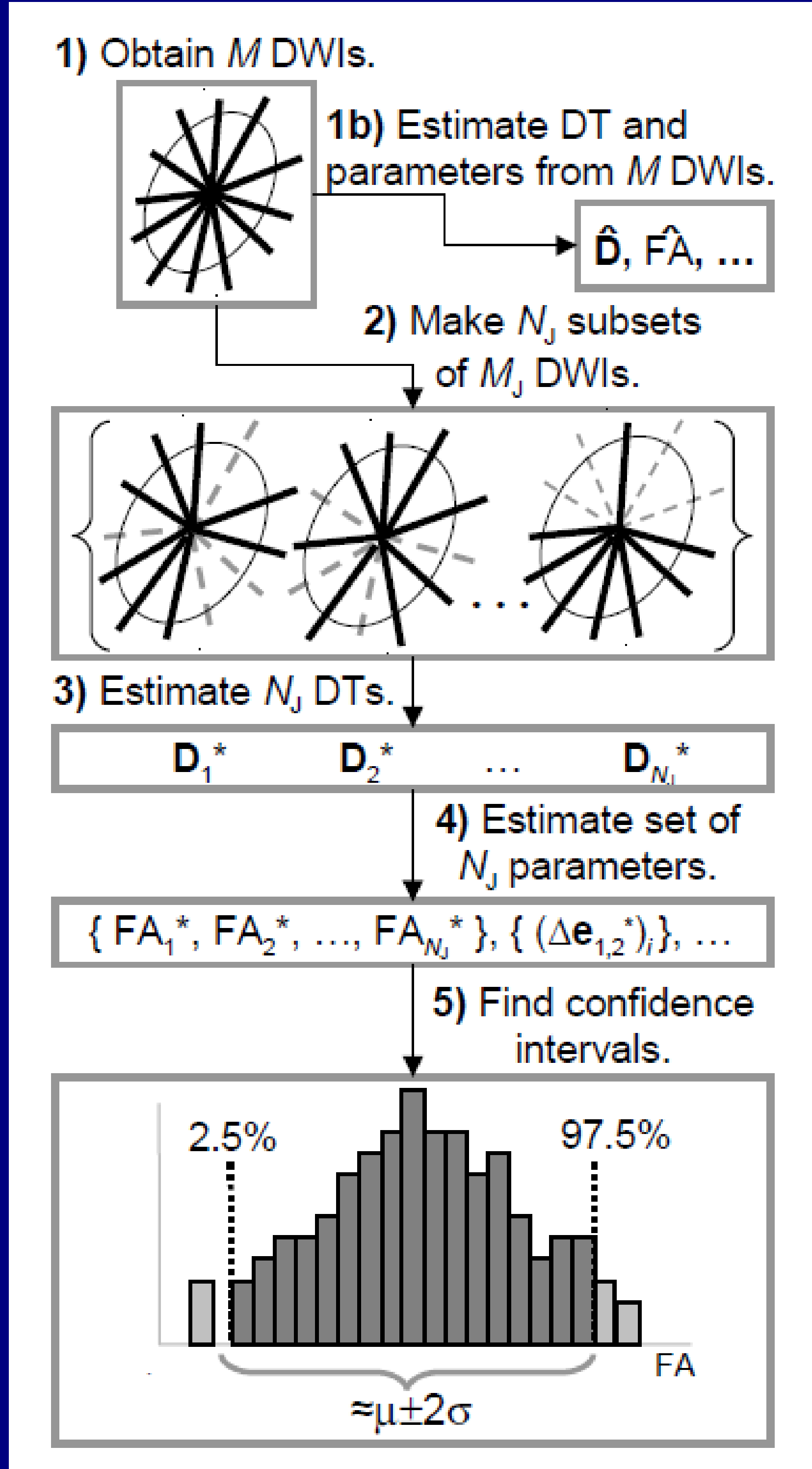


Uncertainty estimation

+ 3dDWUncert estimates bias and σ of first eigenvector $\mathbf{e}_1$ (main direction of diffusion), based on how much it could tip toward either $\mathbf{e}_2$ or $\mathbf{e}_3$:

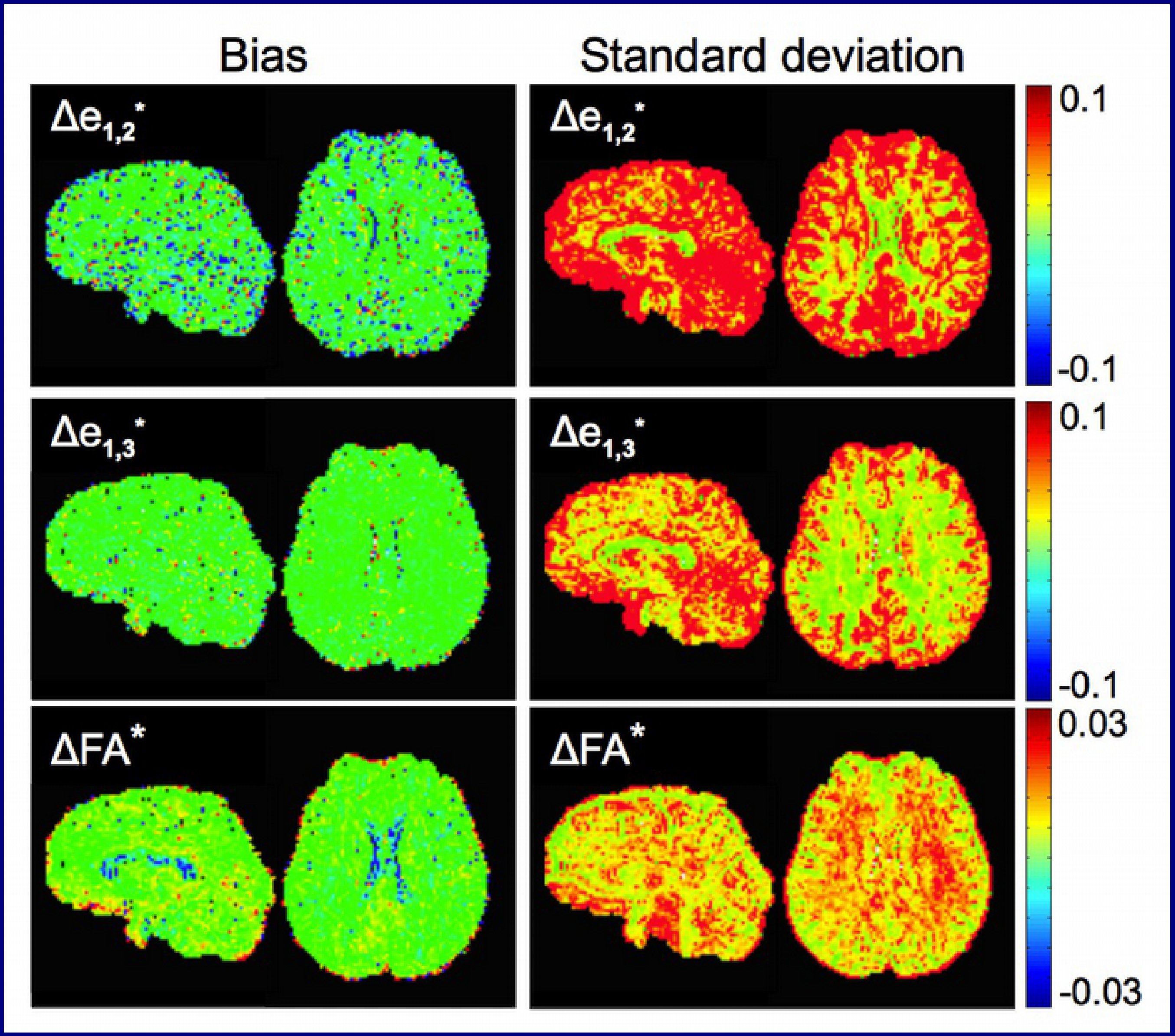


.... and the bias and σ of FA



Uncertainty example

- Can see difference in e1 uncertainty along e2 and e3
- Tissue-dependent differences in FA uncertainty



Next question for doing tractography:

How do we take into account noise/uncertainty during tracking?

Probabilistic Tractography

- We know that estimates of DTI ellipsoids are not exactly representing tracts/bundles
  - Size scale differences between voxel/tracts, multiple tracts, complex structure, signal noise, eddy currents, nonlinear fits, etc.
- How to include errors/uncertainty in interpretation and usage?

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  - Size scale differences between voxel/tracts, multiple tracts, complex structure, signal noise, eddy currents, nonlinear fits, etc.
- How to include errors/uncertainty in interpretation and usage?
- *Probabilistic tractography*: use uncertainty in ellipsoid measures with Monte Carlo-esque simulations and build up large ~population of possible trajectories
  - E.g., Parker et al. (2003); Behrens et al. (2003)
  - Do DTI estimates; do whole brain tractography; keep track of number of tracks through relevant voxels; perturb DTI voxel estimates based on uncertainty values; do whole brain tract… [repeat many ~1000 times] … find voxels which had lots of traffic, define relative ‘connectivity’ based on traffic

(Side note before continuing with
'full' probabilistic tracking)

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'

(Track visualization tools)

(Back to the feature:
full probabilistic tracking)

Probabilistic Tractography

- Note on interpretation: most reports define a parameter to be the probability of connection between voxels A and X:

  $\Psi(X,A)=\mu(X,A)/N$

  - N: number of iterations
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-> for example, how literally can one equate a numerically-constructed tract through a ~2x2x2mm voxel with a fiber bundle with orders-of-magnitude smaller diameter?

-> or how can one compare this 'connectivity' between ROIs of different sizes on equal footing?

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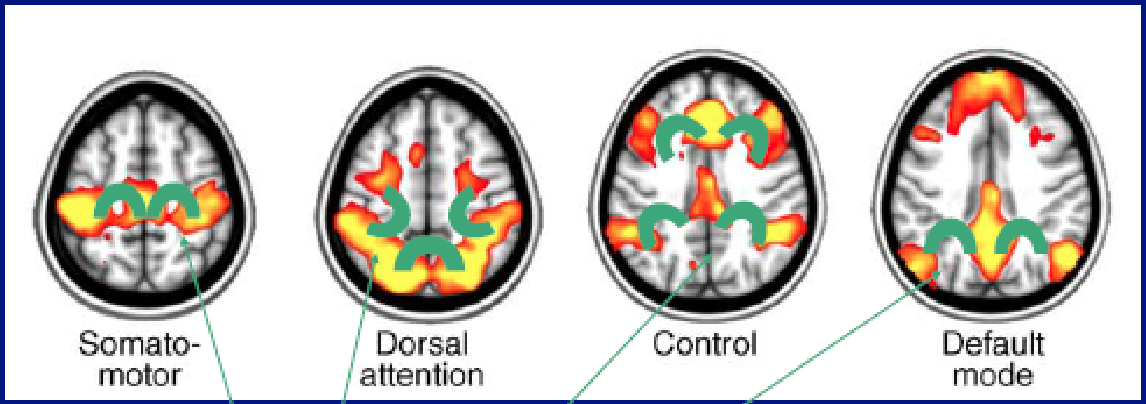
- While this quantity is somehow relevant in representing what relative 'connectivity' which can be estimated, exact interpretation as 'probability of connectivity' is tricky
- Prefer to think of Ψ more loosely as a probability of that voxel being a part of WM volume related to the two ROI-voxels.
  - Not probability of *connectivity* of A and X, but more *likelihood of a voxel being part of associated WM*

Probabilistic Tractography

- This interpretation more useful for working with GM networks. Recall interest:

GM ROIs network:



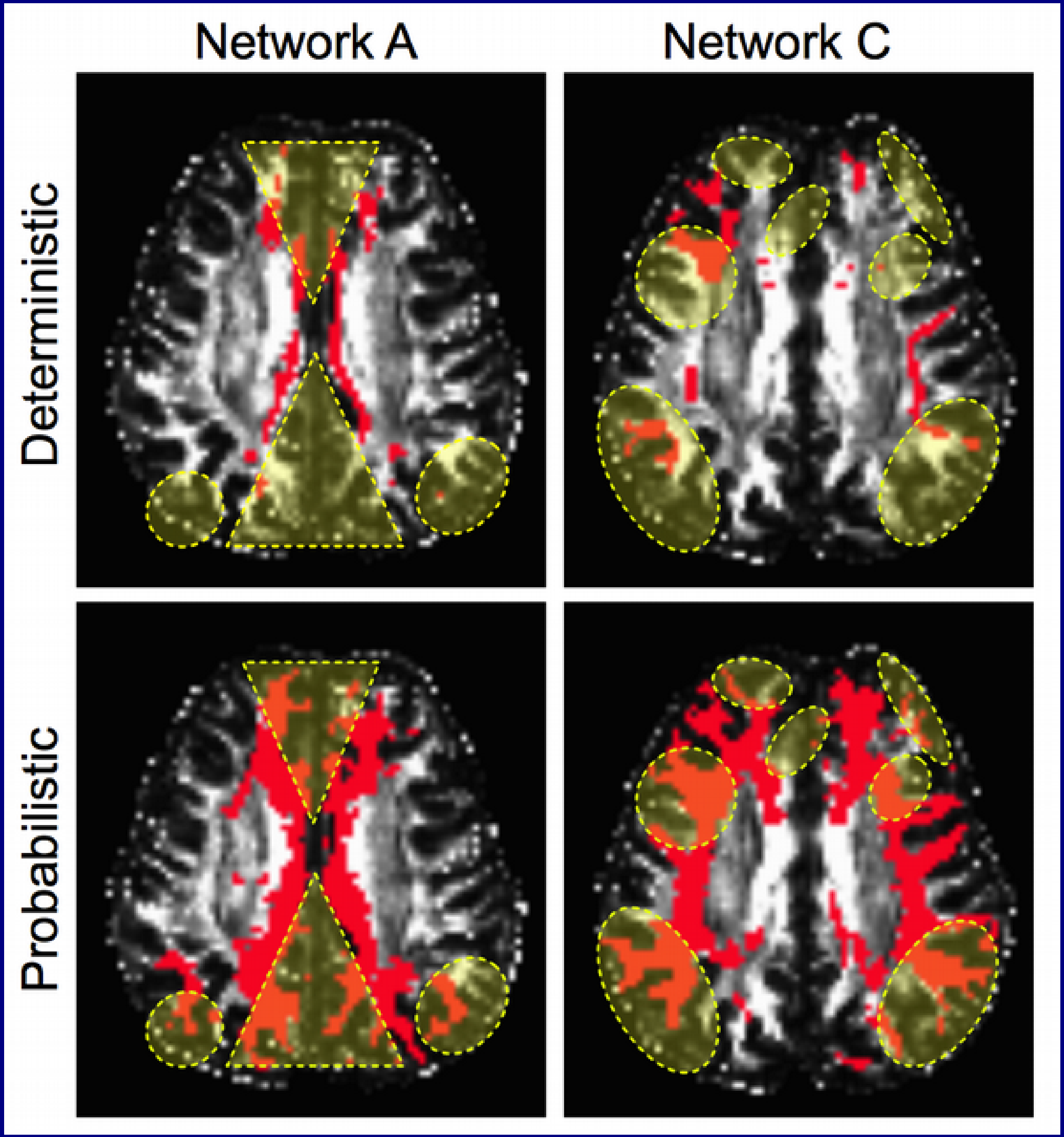
Associated WM ROIs

- Threshold Ψ per voxel after probabilistic tracking, use to define WM ROI between GM ROIs

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



Probabilistic tractography

+ with networks of ROIs from 3dROIMaker and uncertainty from 3dDWUncert (as well as tensor estimates from, e.g., 3dDWItoDT), can finally do probabilistic tractography
+ 3dProbTrackID
  - does lots of Monte Carlo simulations: wholebrain tractography -> perturb FA & e1 based on uncertainty -> wholebrain tracking -> perturb -> wholebrain tracking -> etc.

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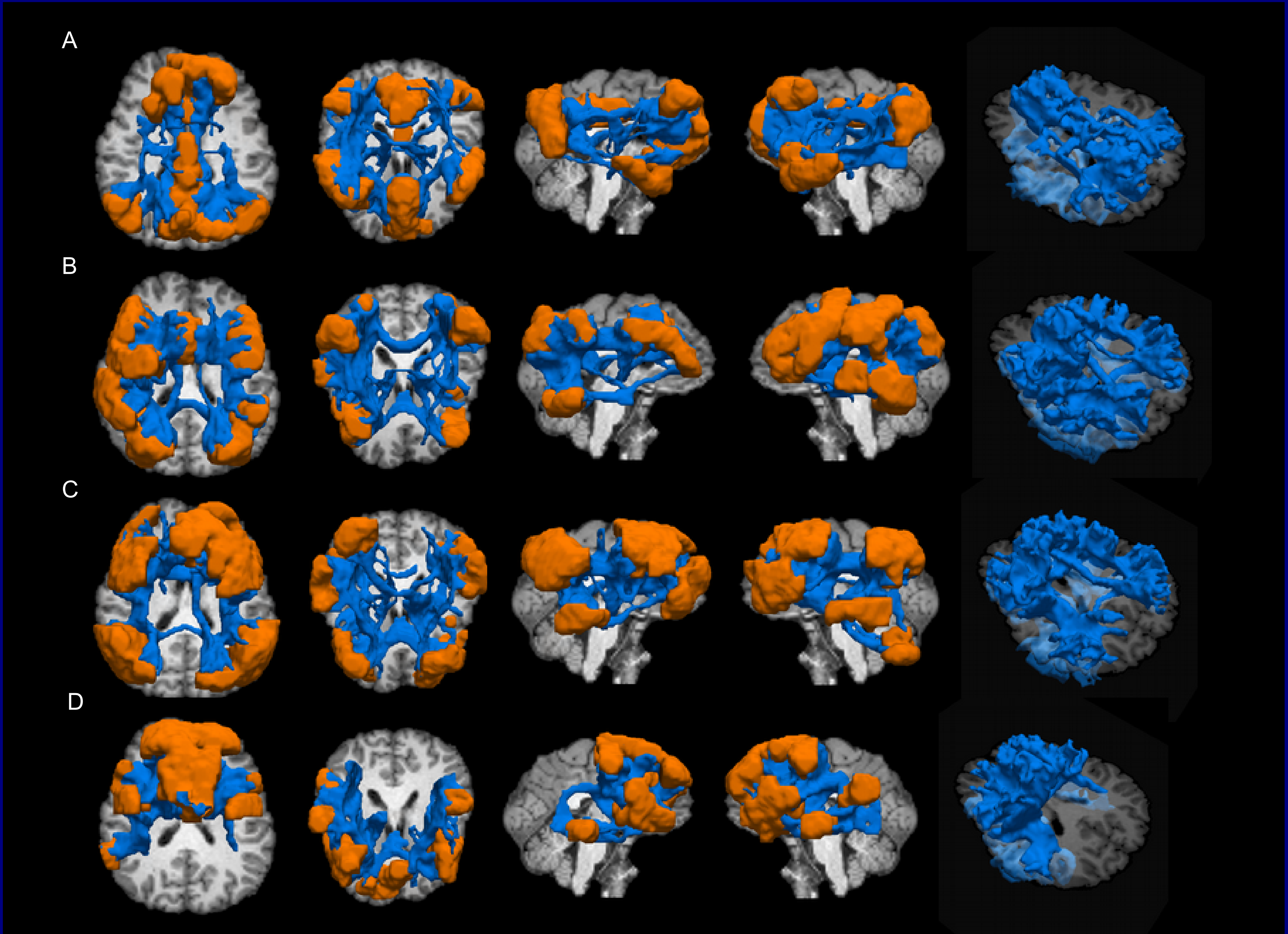
  - calculate stats on final WM ROIs found
  - analyze multiple networks **simultaneously** for efficiency (i.e., very little extra cost)

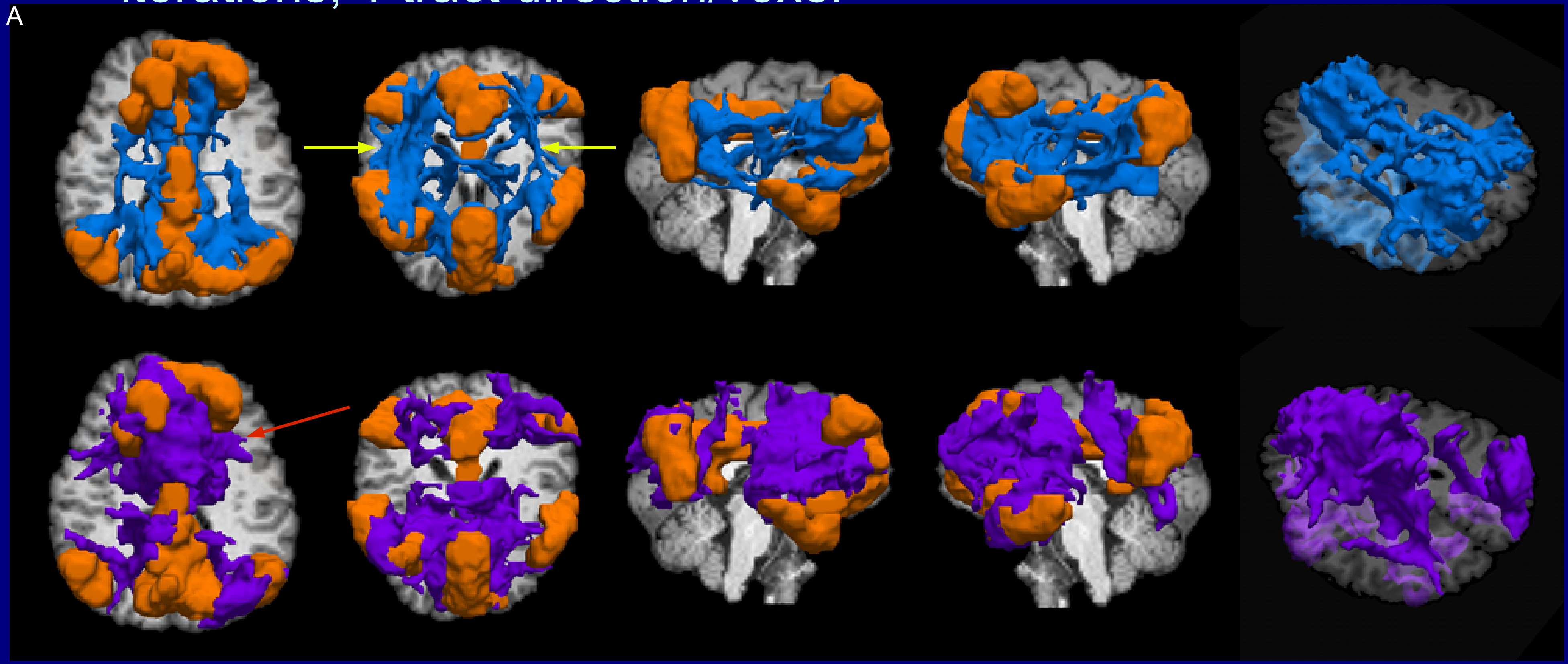
3dProbTrackID: Probabilistic tractography



(orange is ROI; blue is set of WM regions with tracts connecting)

3dProbTrackID: 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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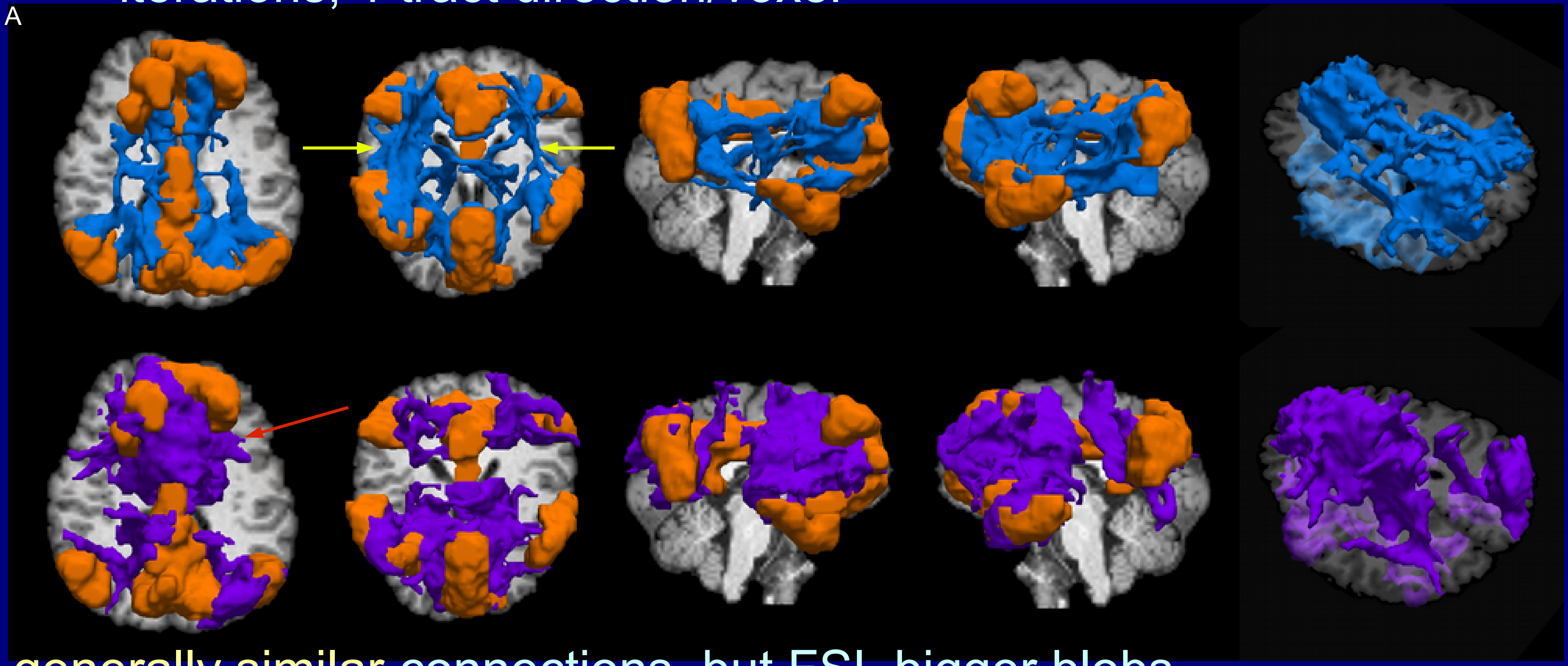

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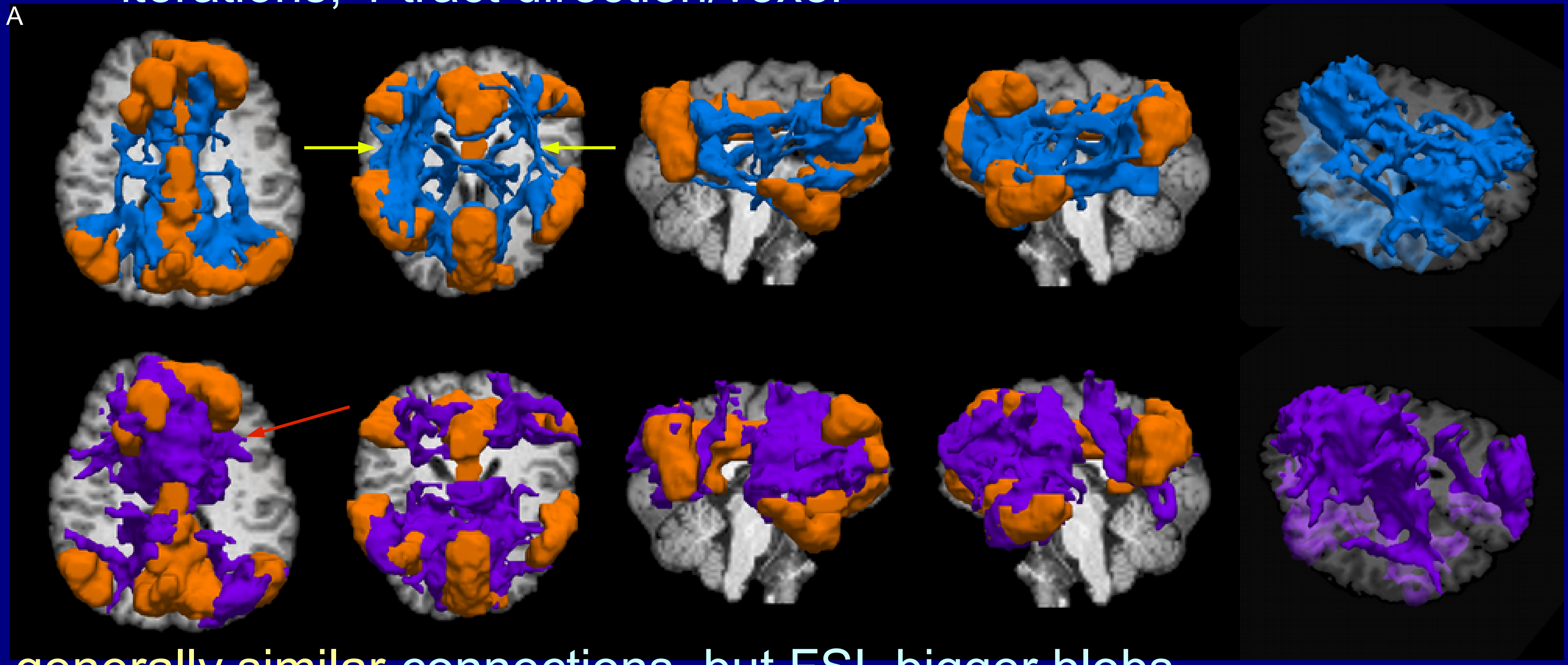

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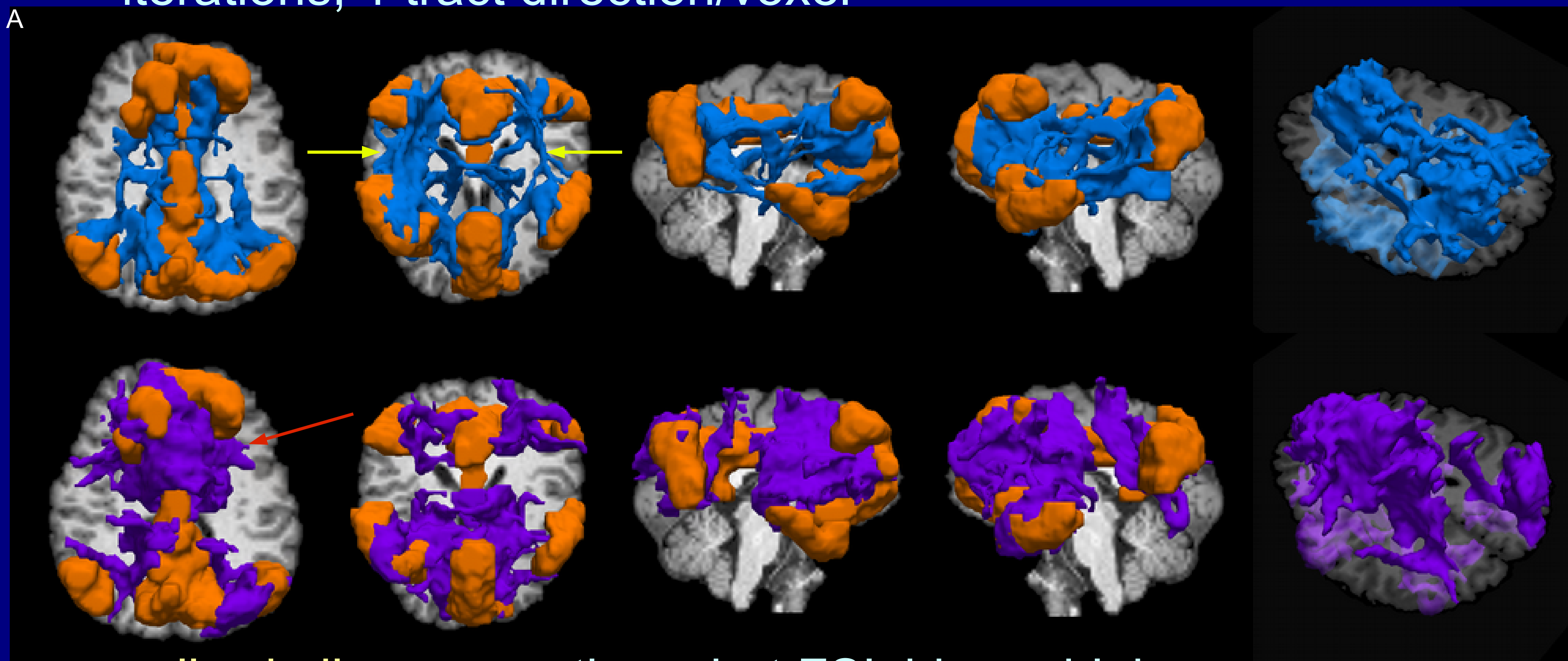
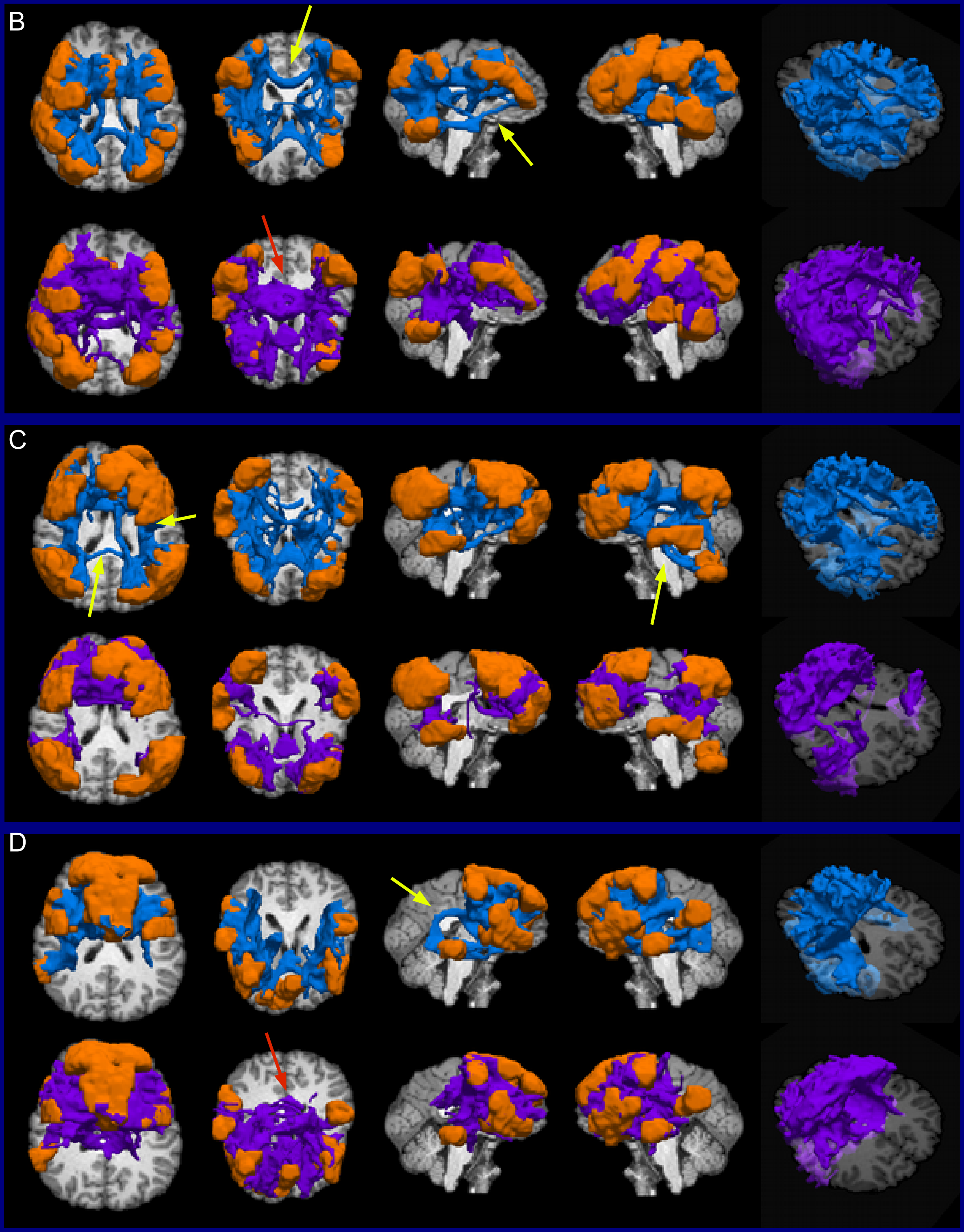


+ generally similar connections, but FSL bigger blobs
+ FSL took several hours for uncertainty, and then >24 hours for tracking this single network (and had to run 4 for this study)
+ 3dDWUncert took *7min*; 3dProbTrackID took *25mins* total for 4 netw.

3dProbTrackID:

(other networks show similar results in terms of:

- narrow/wide regions of tracts;
- broadly similar locations;
- each program shows some tracks which the other doesn't)



3dProbTrackID:

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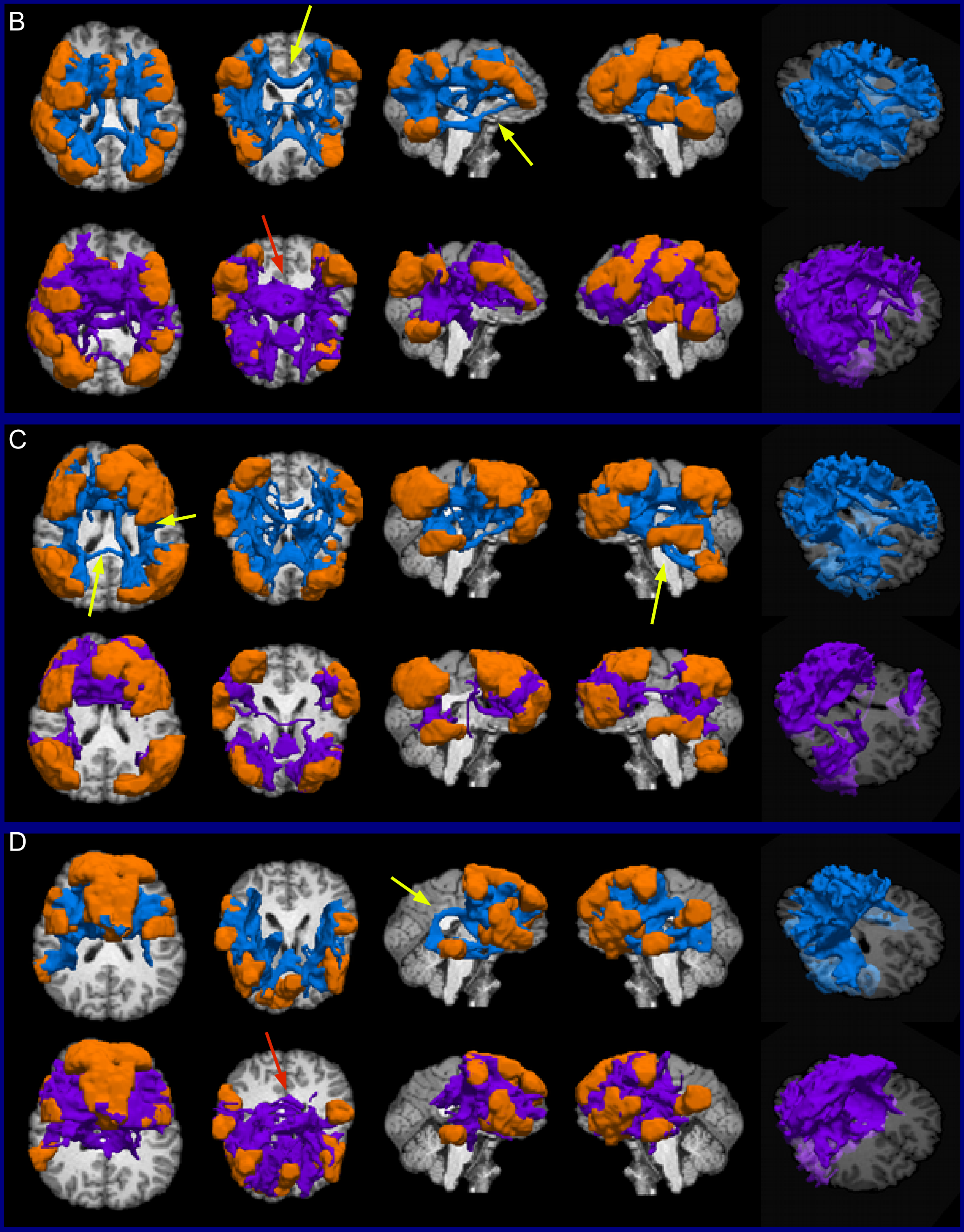
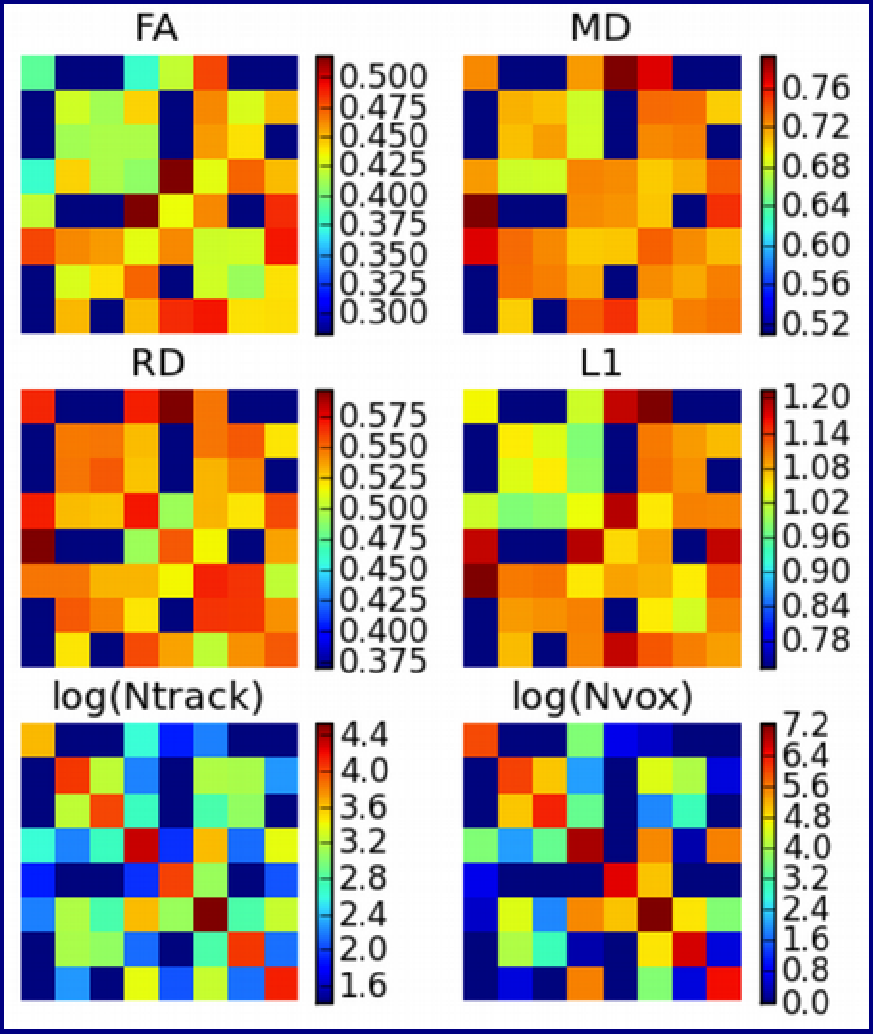
(Also, 3dProbTrackID automatically calculates values of mean/std FA, MD, RD, L1, Ntracks, Nvox per WM ROI, stores these as matrices, similar to RSFC connectivity matrices)



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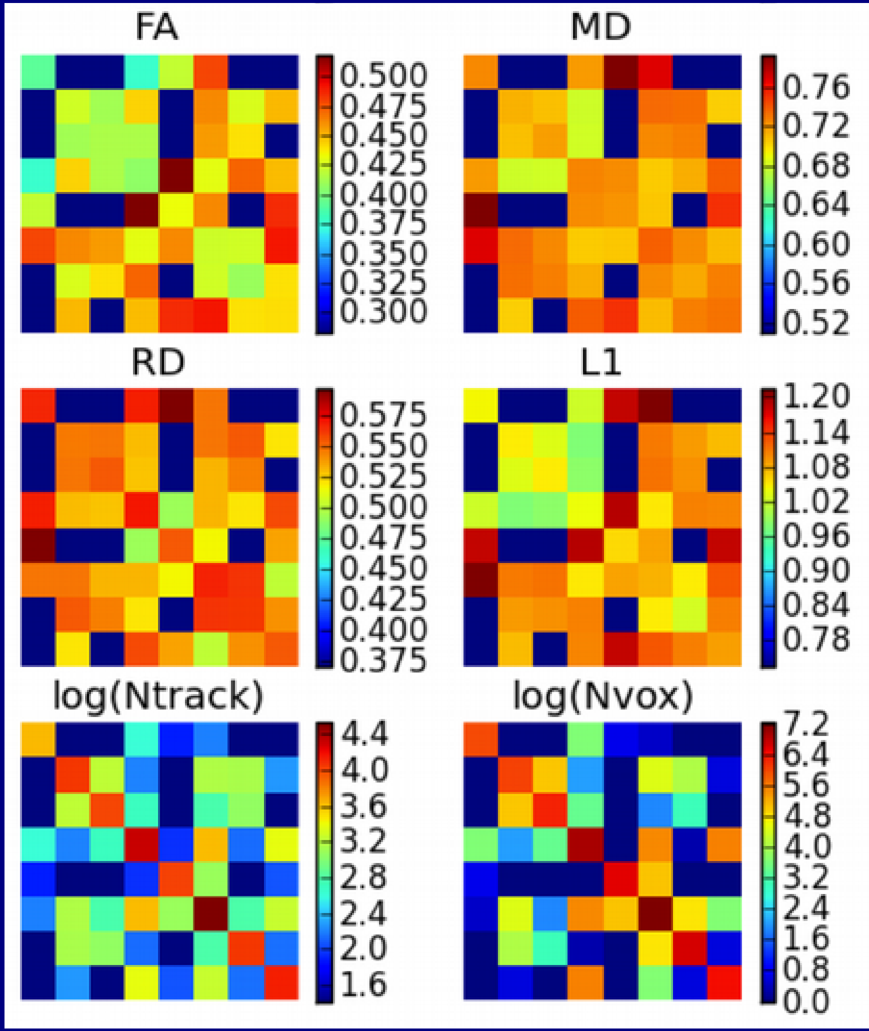
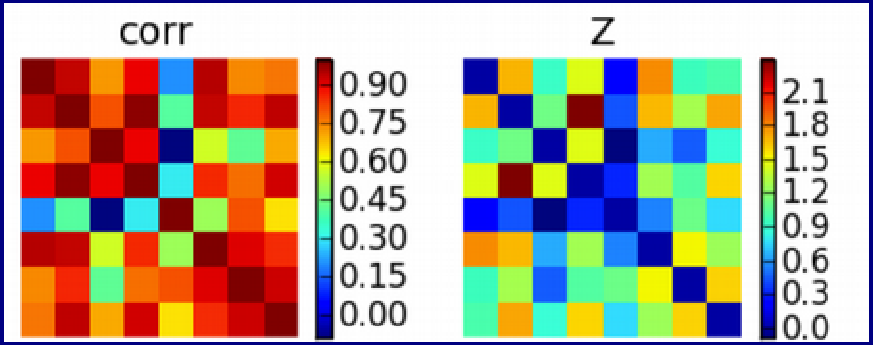
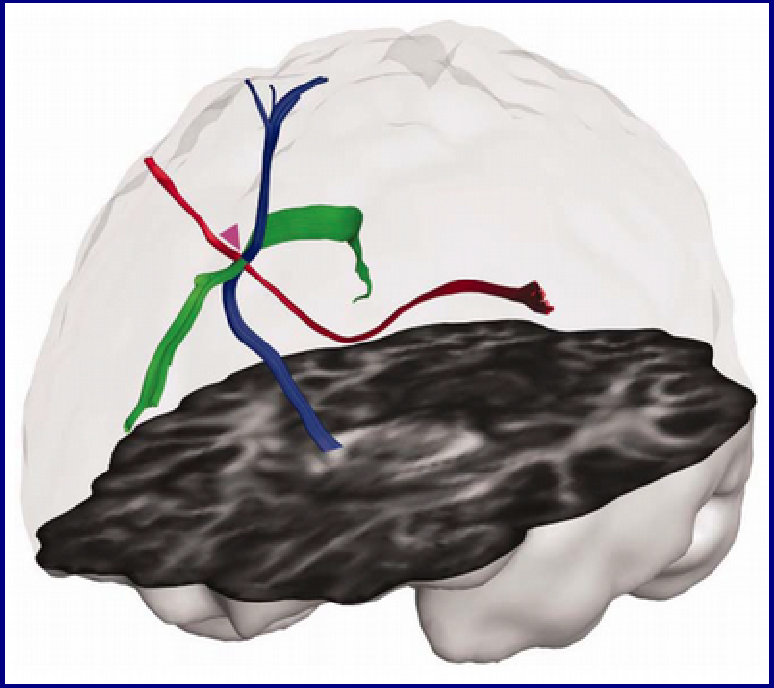
3dNetCorr: correlation matrices Of average time series in ROIs (e.g., uninflated GM ROIs from 3dROIMaker)





Higher order models

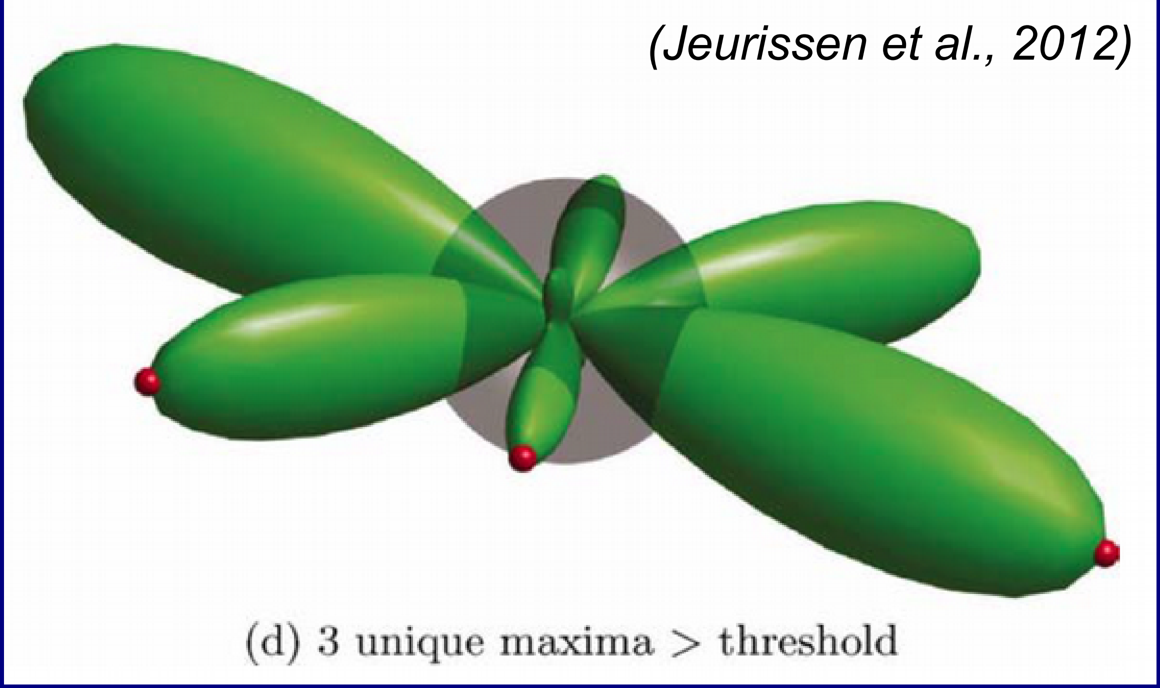
DTI tractography:
+ susceptible to false negatives, difficulty with
  long range tracts (noise/error accumulation)
+ Major diffusion can be average of multiple paths
+ Voxels can have low FA from several WM paths, false ending
+ Can't resolve complex underlying architecture
  - Jeurissen et al. (2012, HBM): 60-90% of WM voxels estimated
    to have multiple fibers



(Jeurissen et al., 2012)

HARDI

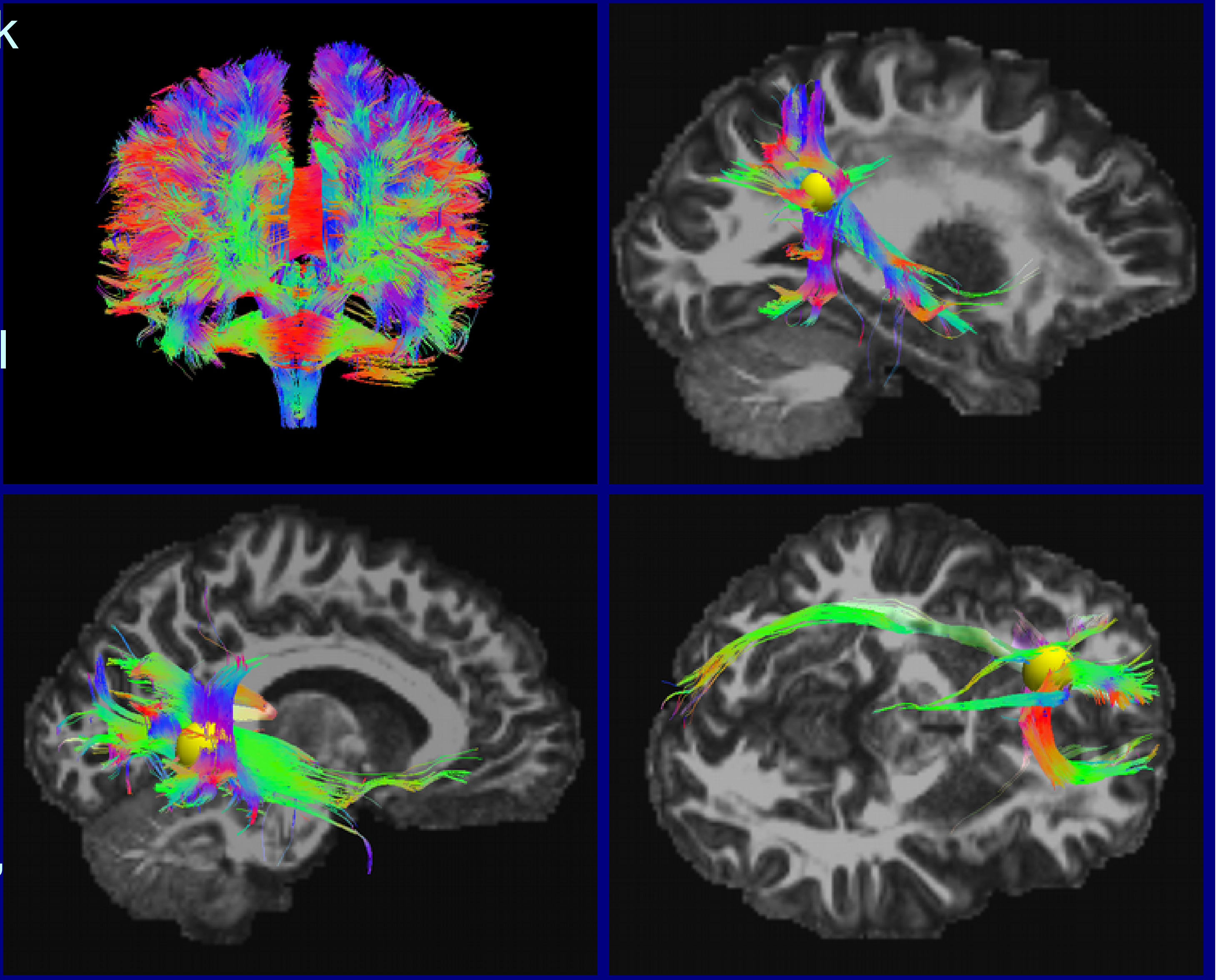
+ High Angular Resolution Diffusion Imaging:
  - DSI, ODF, Qball, FOD...
  - model multiple fiber bundle directions per voxel
  - generally need more scan time and acquisitions and computational power, much higher b-values
  - still can't resolve intravoxel tract behavior (which of multiple paths?)
  - higher DW → lower signal, so susceptible to noise



HARDI + multidirectional tracking

FATCAT can now track through HARDI data, such as Qball, DSI, GQI, ODF, ball-stick, etc., where each voxel has >=1 propagation direction.

HARDI reconstruction done outside AFNI (e.g., DSI-Studio, Diffusion Toolkit, FSL), and outputs tracked in FATCAT.



<u>Ex:</u> Human Connectome Project subject, 288 grads, reconstructed with GQI in DSI-Studio.

A brief example for statistical analysis

\+ Networks + probabilistic tractography
\+ from the Cape Town FASD Newborn Neuroimaging Study
- first newborn (<47 days) DTI tractography study on FASD
- conducted in South Africa

(Taylor, Jacobson, van der Kouwe, Molteno, Wintermark, Alhamud, Meintjes, Jacobson; in progress)

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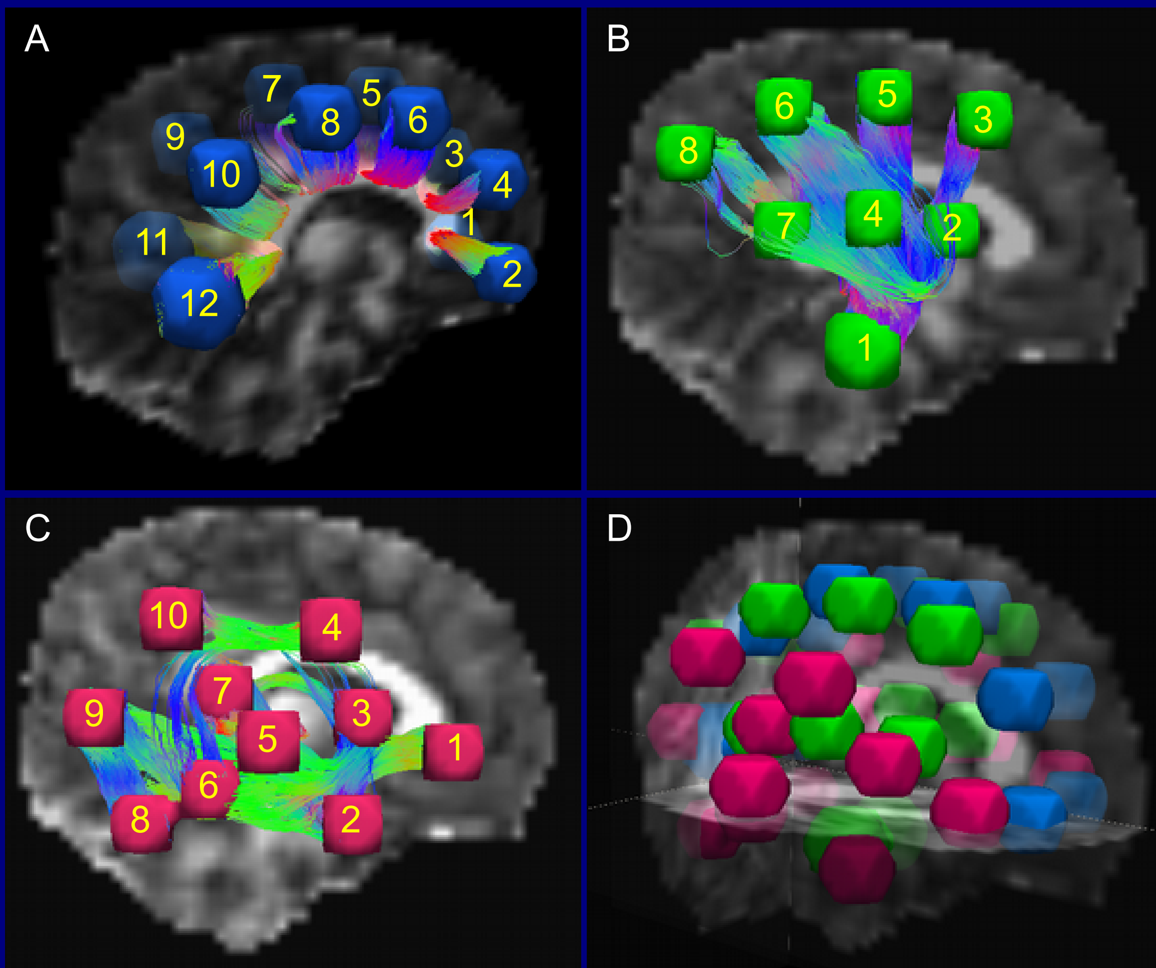
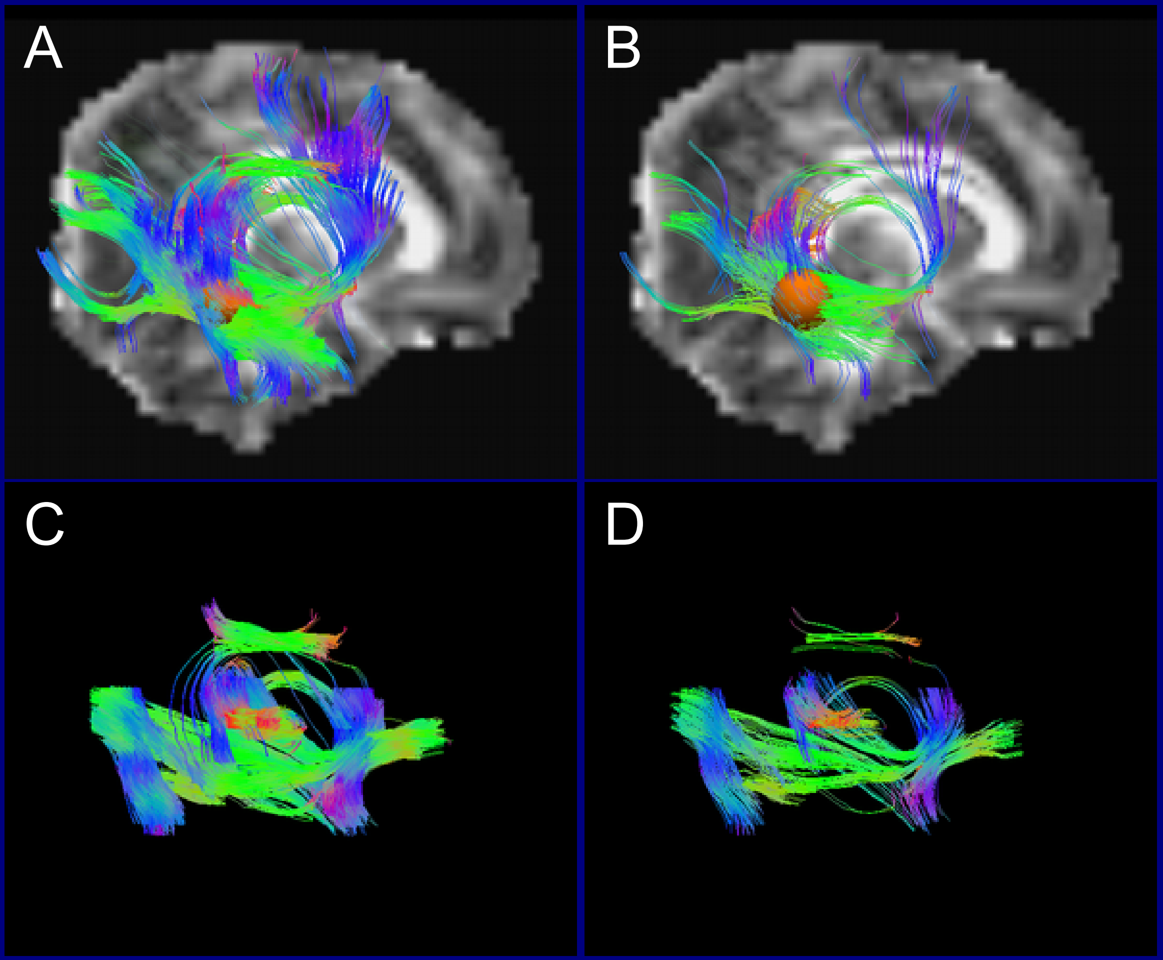


Location of ROIs for tractography.
A) Transcallosal
B) Projection (both L and R).
C) Association (both L and R).
D) All.
ROIs were mapped among subjects.

(NB: no RS-FMRI for this study)

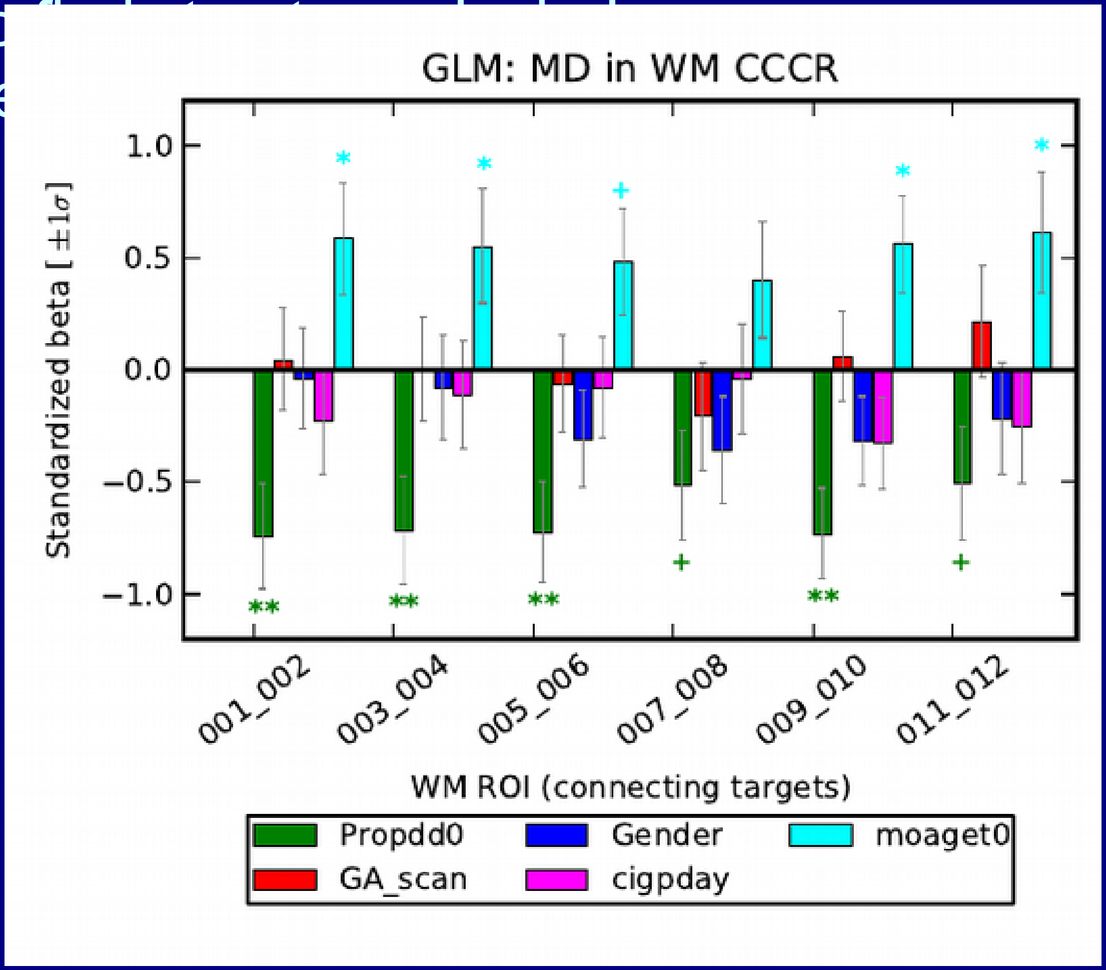
A brief example for statistical analysis



Mini-prob tracking was useful in placing ROIs at likely junctures of tracks. A and C show miniprob locations, while B and D are purely deterministic.

A brief example for statistical analysis

+ Combining tractography, quantitative DTI and subject measures
with GLM to
consumption re



Significant (*p<0.05; **p<0.01) explanation of DTI measures MD in specific WM regions of CC by alcohol measure (Propdd0) in GLMs which controlled for several other factors.

In Summary

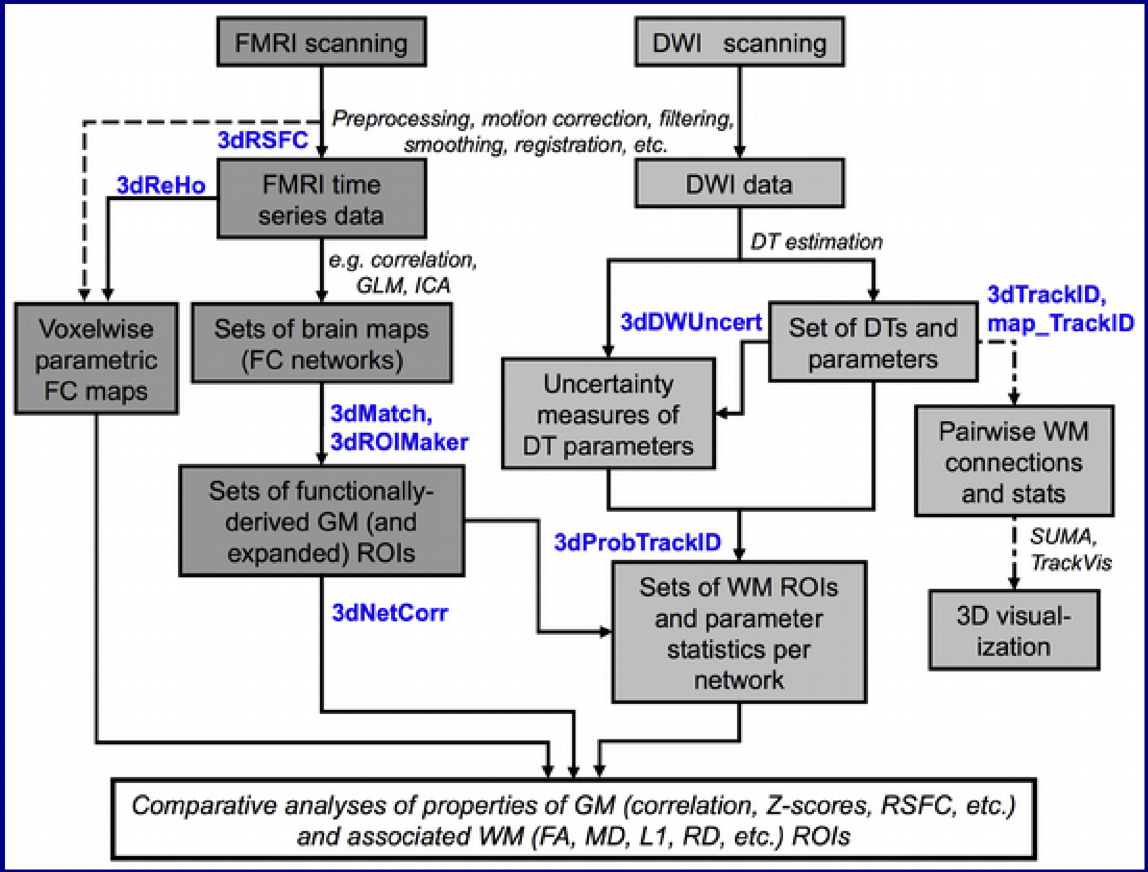
+ Have motivated ways of combining FC and SC analyses
    - FMRI to define networks of GM ROIs
    - find locations of connections within/across networks -> WM ROIs
    - calculate stats of DTI/anatomical properties there
    - combine structural quantities of, e.g., mean FA, with FMRI connectivity matrices; behavioral measures; genetic values, etc.

+ Diffusion-based tractography is useful complement to FMRI
    - probabilistic tractography is more robust than deterministic
    - different types of quantities than FMRI, not necessarily 'strengths'

In Summary

We have discussed capabilities
and benefits of:

Combining multimodal data: FC+SC+...



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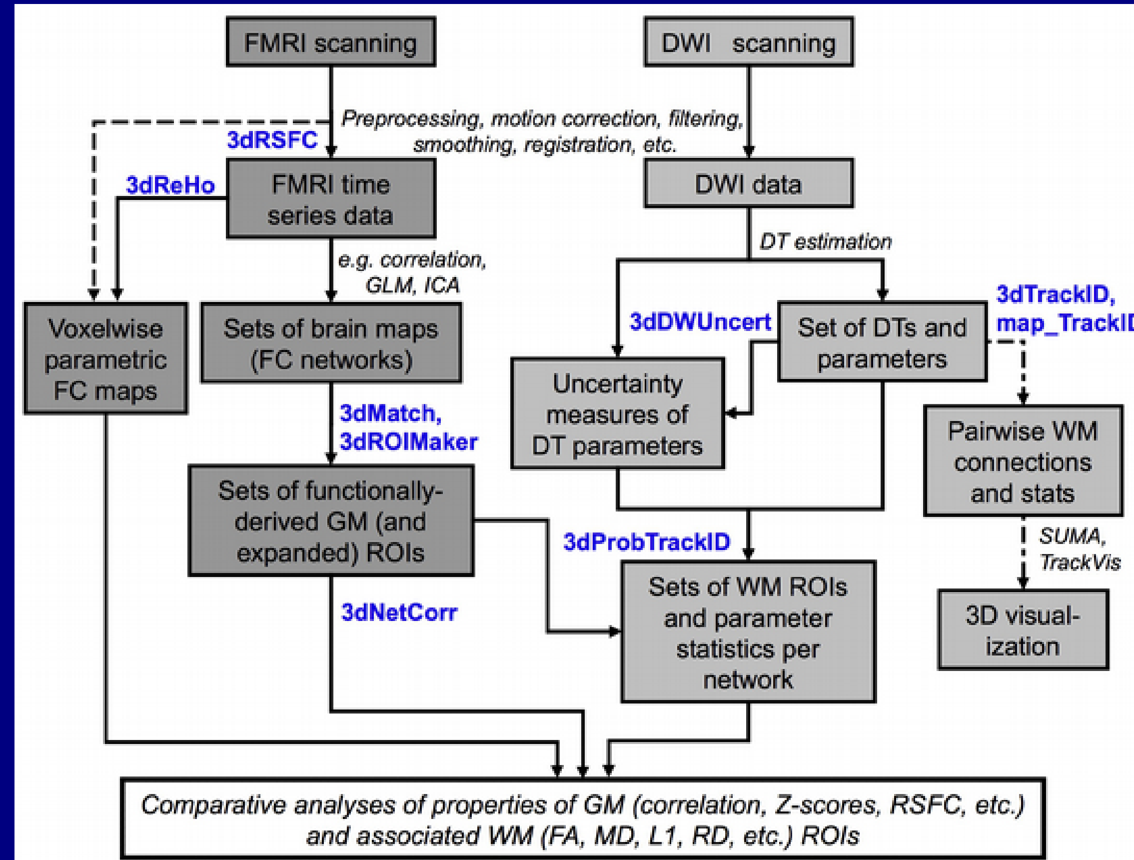
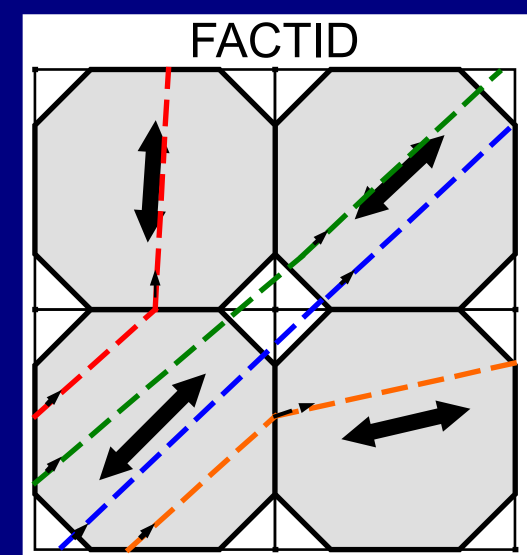


Using an efficient algorithm, reduced bias of propagation



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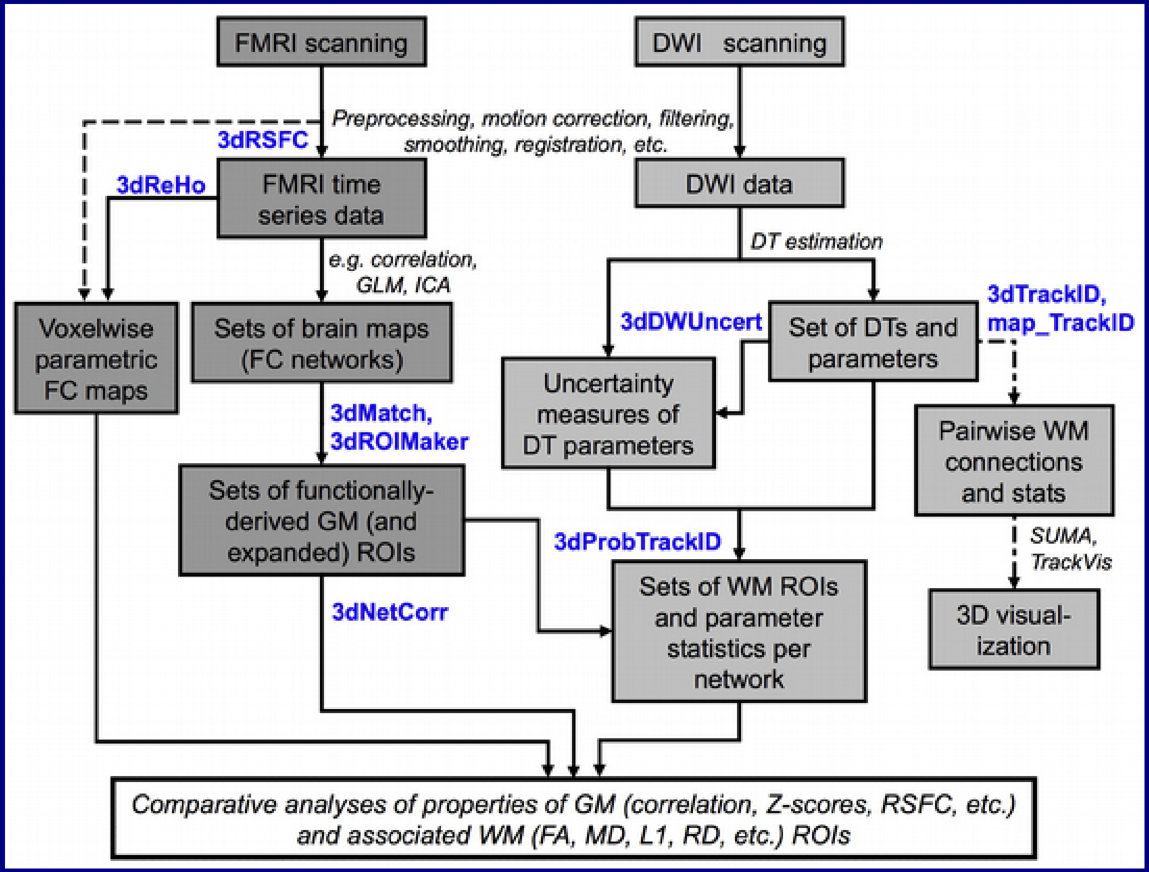

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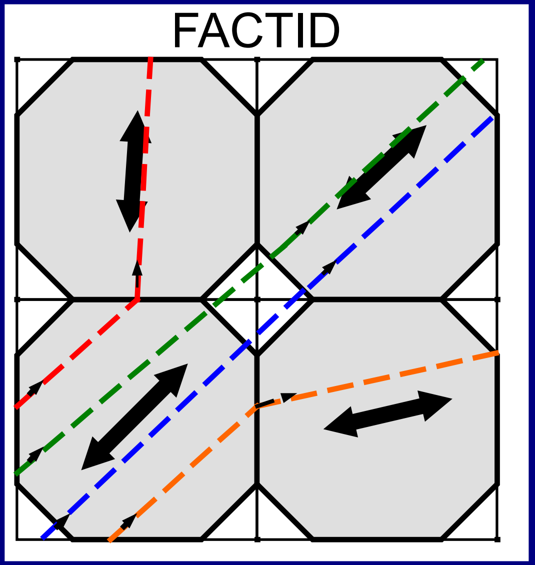
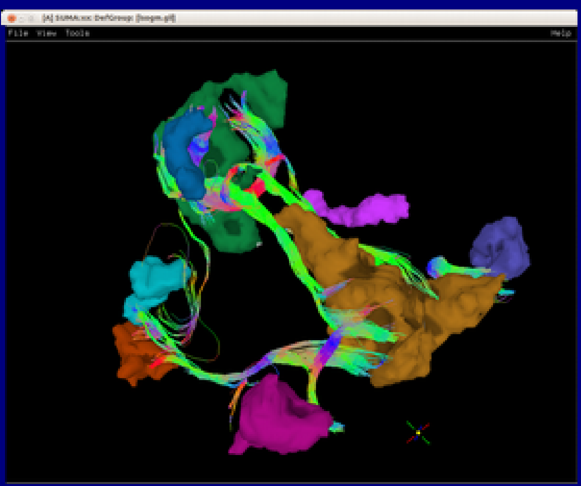


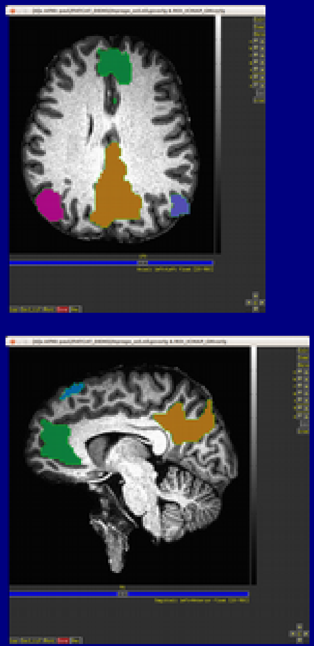
Tracking to define and quantify WM ROIs (with uncertainty/probabilistic)

In Summary

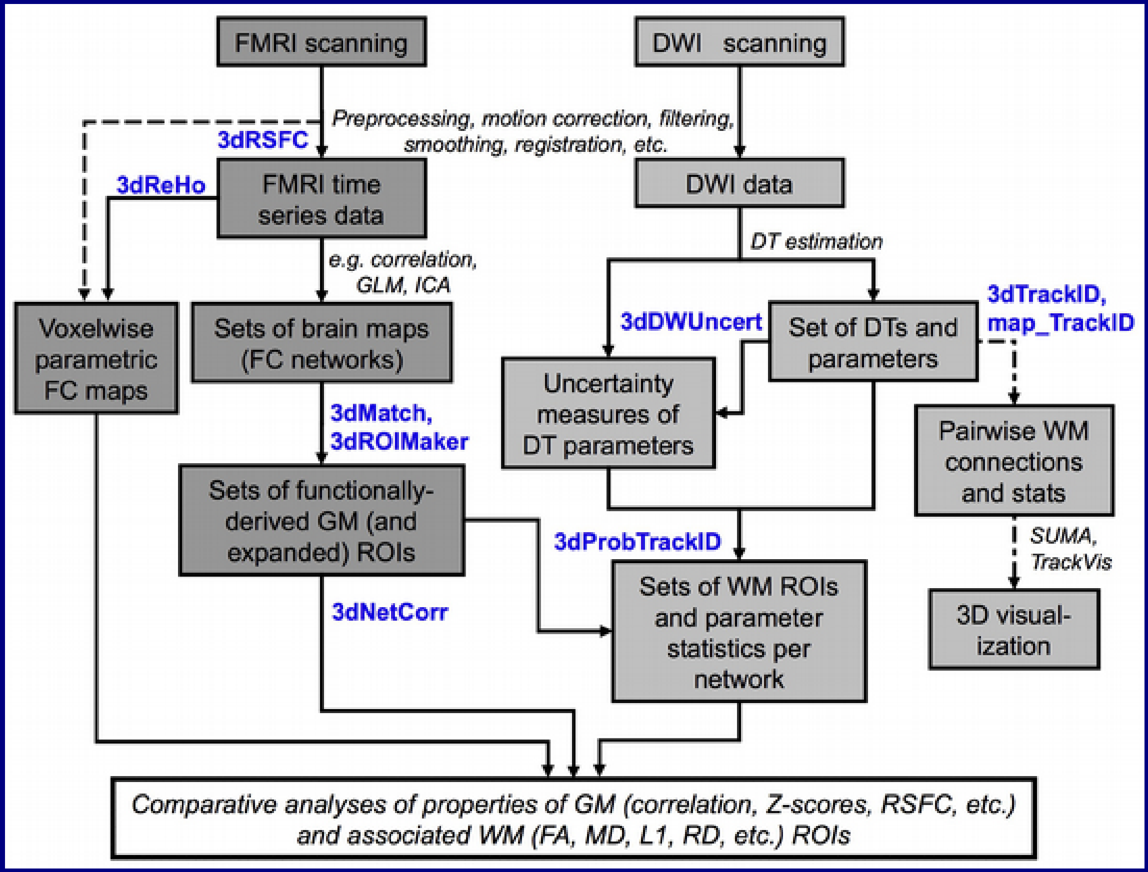
We have discussed capabilities and benefits of:

Integrating AFNI-SUMA visualization





Combining multimodal data: FC+SC+...



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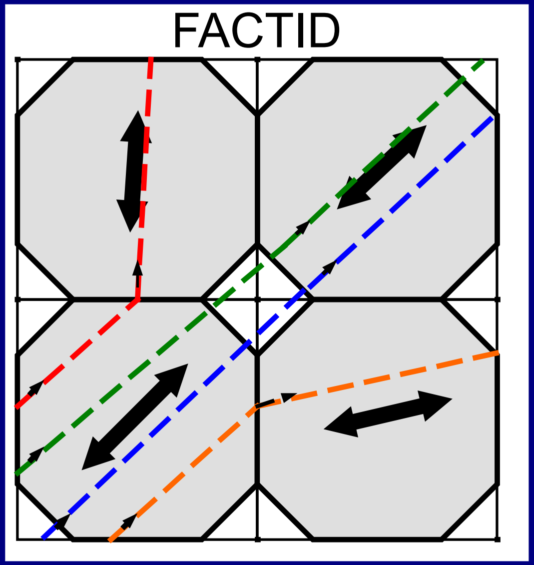

Tracking to define and quantify WM ROIs (with uncertainty/probabilistic)

Thanks

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UMDNJ/NJIT:
Bharat Biswal
Suril Gohel
Xin Di

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Rick Reynolds
Gang Chen
Bob Cox

UCT:
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Alkathafi Alhamud
Chris Molteno
Fleur Warton

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Joseph L. Jacobson (Wayne St.)
Andre van der Kouwe (Harvard/MGH)
Pia Wintermark (Montreal Children's)