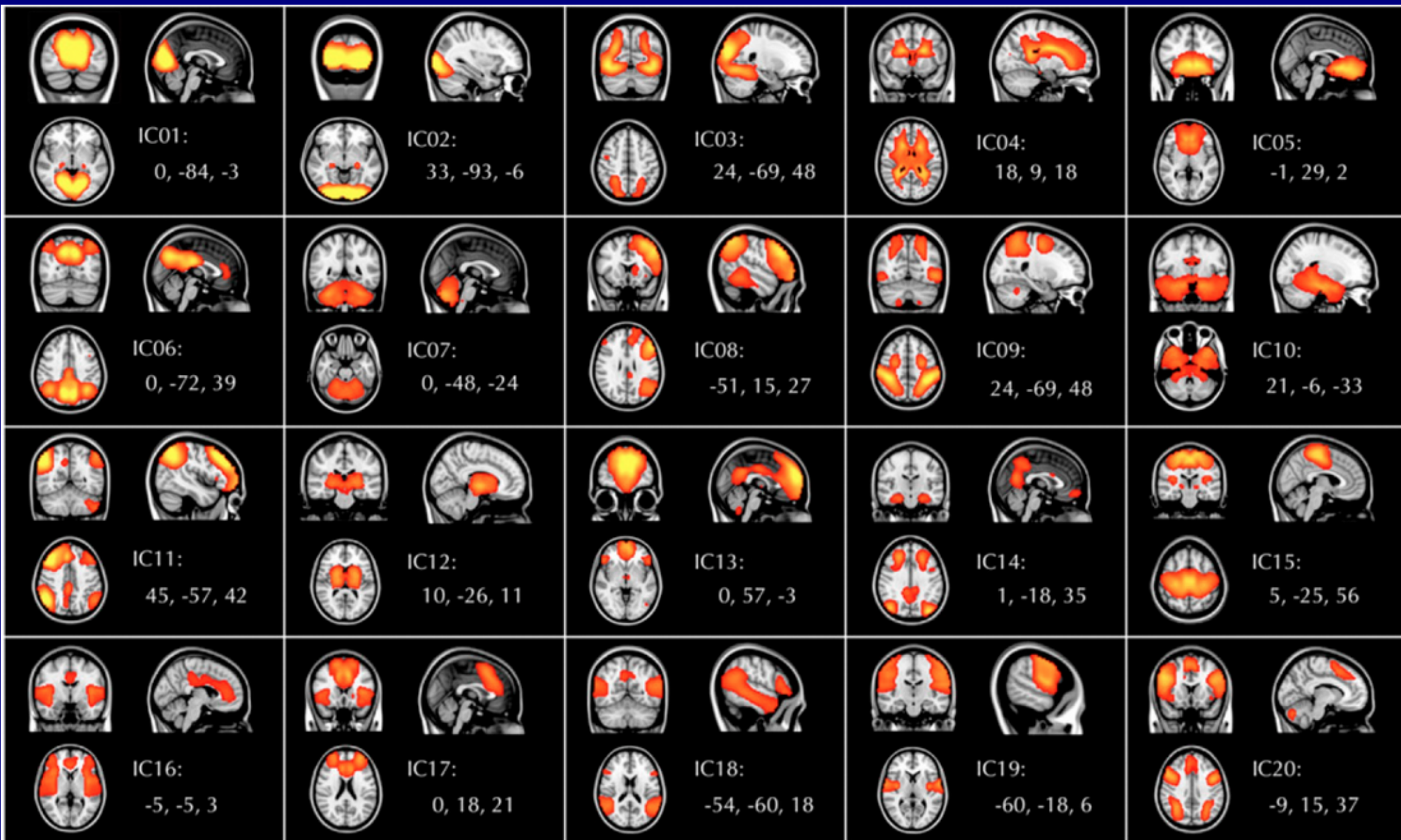# Introduction to AFNI+SUMA+FATCAT, Part I

DTI+tractography for data exploration and complementing functional connectivity

Outline

+ Why Function+Structure

+ DWI and DTI ($\rightarrow$ local structures)

    - Brief diffusion imaging basics and parameters

    - Role of noise $\rightarrow$ DTI parameter uncertainty

+ Using tractography ($\rightarrow$ estimate extended structures)

    - goals of tracking.

    - algorithms/properties

   - final thoughts on interpretation

FMRI: GM Networks

IC01: 0, -84, -3
IC02: 33, -93, -6
IC03: 24, -69, 48
IC04: 18, 9, 18
IC05: -1, 29, 2
IC06: 0, -72, 39
IC07: 0, -48, -24
IC08: -51, 15, 27
IC09: 24, -69, 48
IC10: 21, -6, -33
IC11: 45, -57, 42
IC12: 10, -26, 11
IC13: 0, 57, -3
IC14: 1, -18, 35
IC15: 5, -25, 56
IC16: -5, -5, 3
IC17: 0, 18, 21
IC18: -54, -60, 18
IC19: -60, -18, 6
IC20: -9, 15, 37

(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,
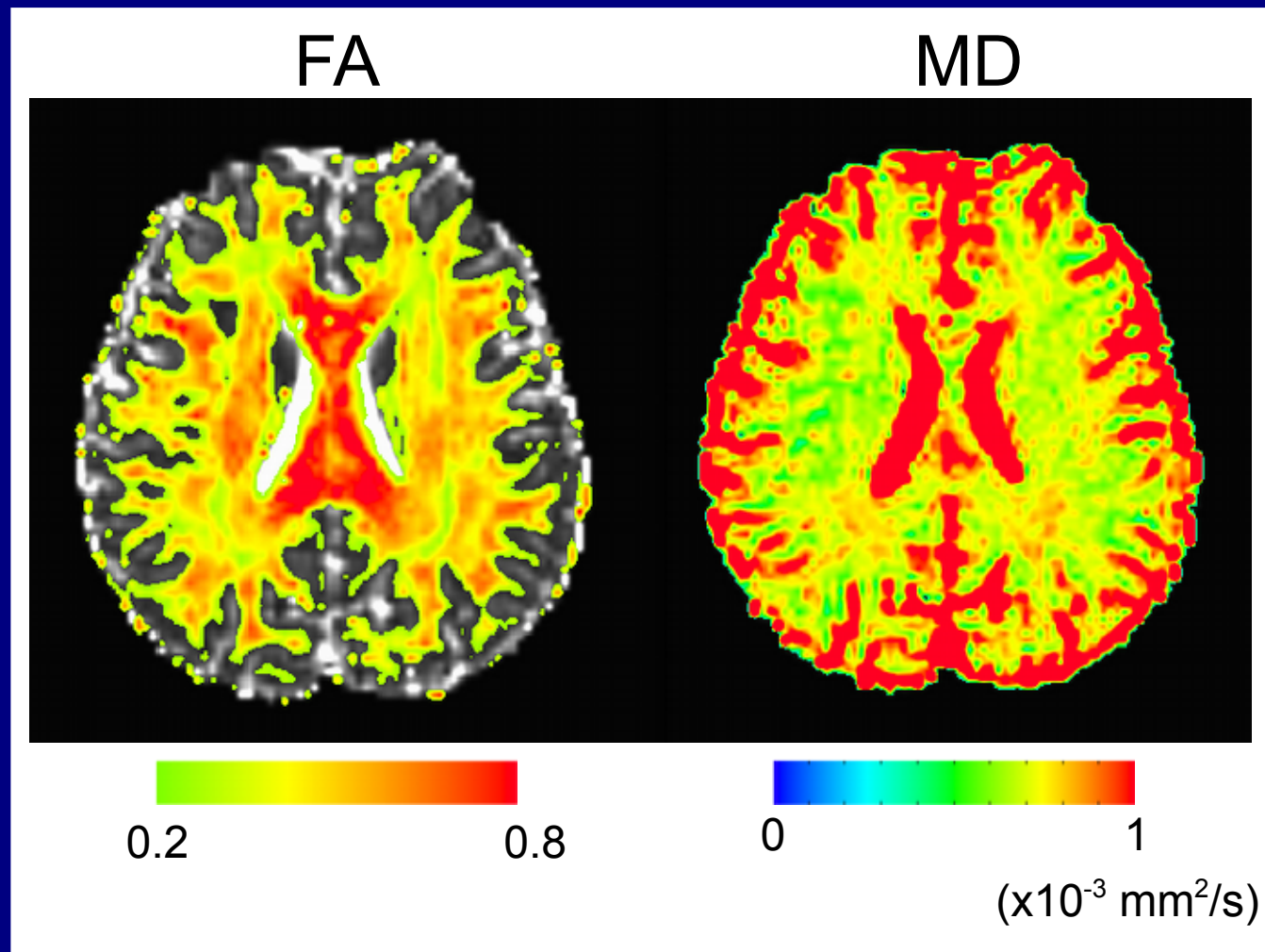   ICA, graph theoretical
    measures, etc.
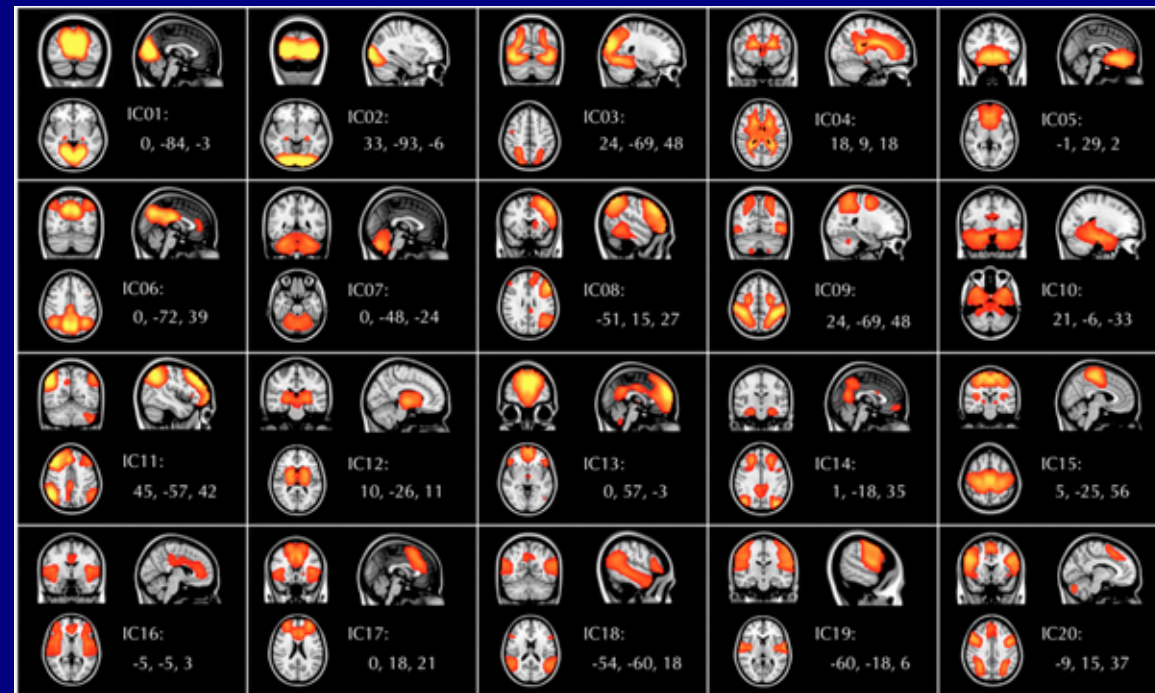
DTI: WM structure

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

FA   MD

0.2   0.8   0   1

$(\times 10^{-3}\ mm^2/s)$

Structure + Function

Simple example:

GM ROIs
network:

Somato-motor   Dorsal attention   Control   Default mode
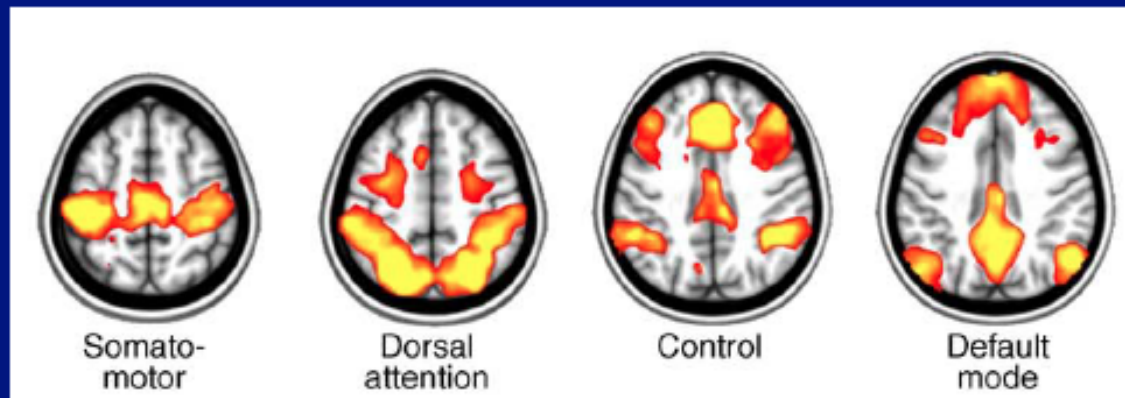
Raichle (2010, TiCS)

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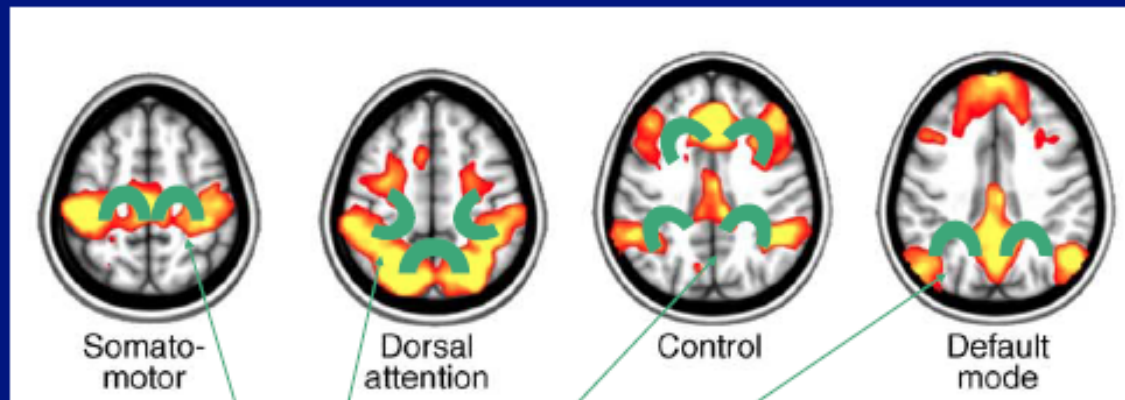
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Associated WM ROIs

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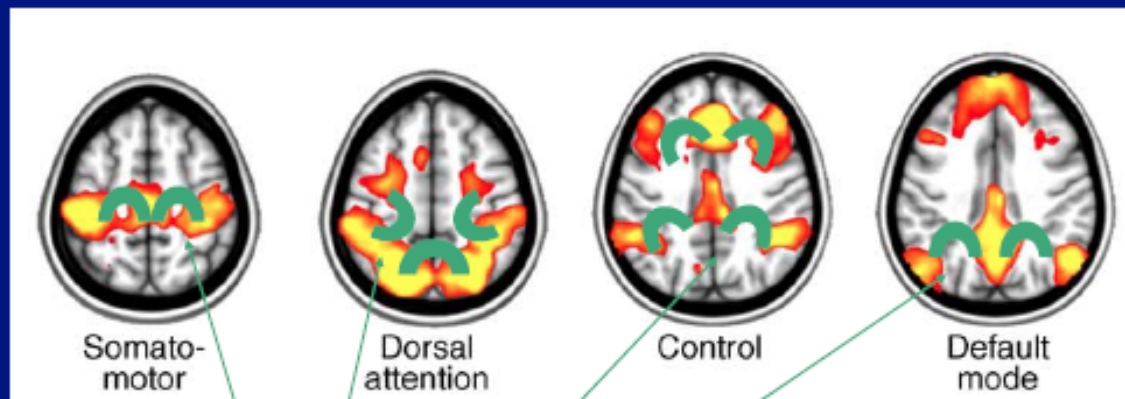
Raichle (2010, TiCS)

Associated WM ROIs

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

Combining FC and SC

+ How to combine *quantitatively*?

    - FMRI has measures of functional connectivity and 'strength'

        (e.g., correlation, network parameters)

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$\rightarrow$ 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:

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...

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+ 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

Schematic for combining FMRI and DTI-tractography via FATCAT
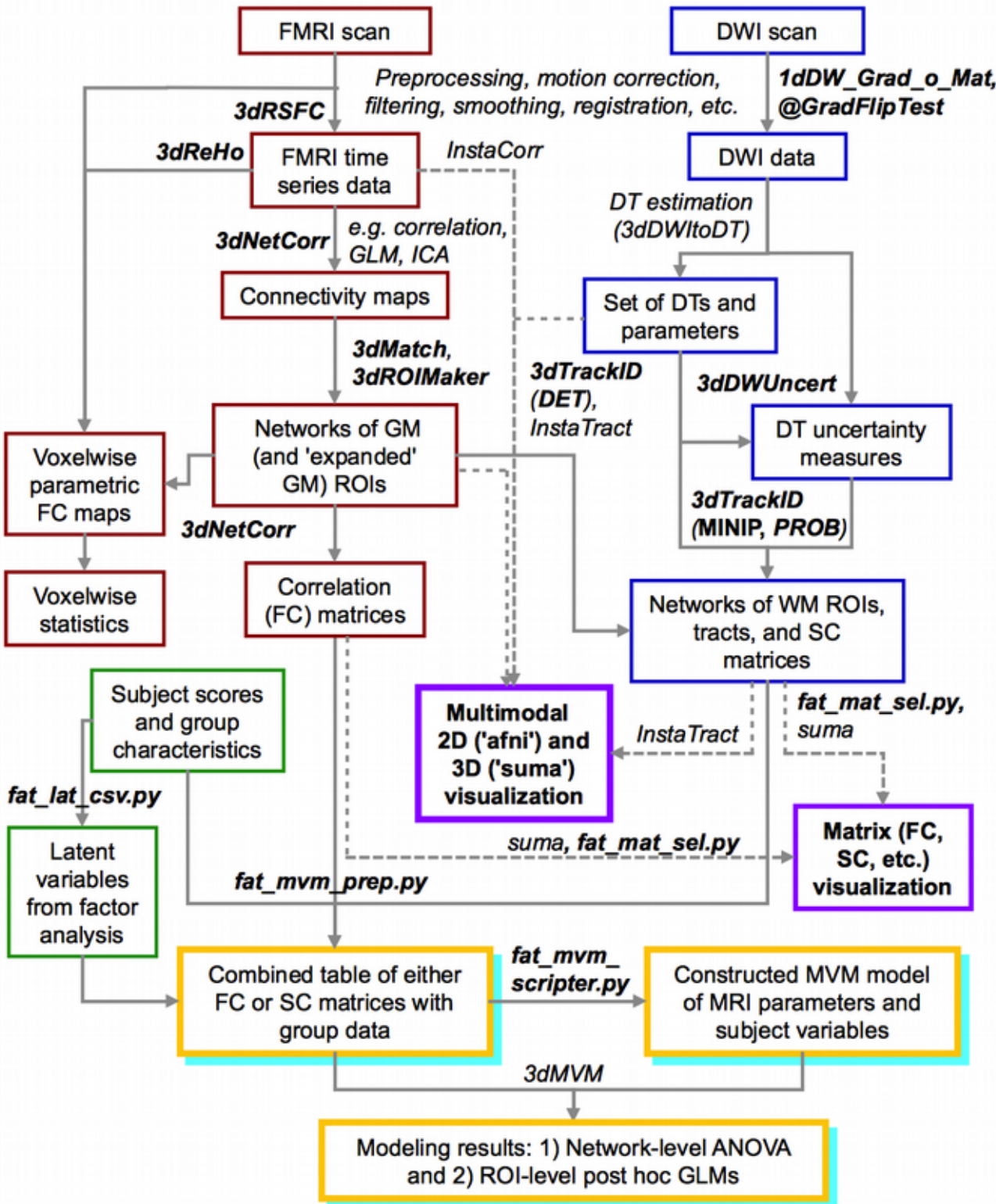
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FATCAT goals:
+ Do useful tasks
+ Integrate with existing pipelines/software
+ **Derive/use information from the data itself**
+ Be "simple" to implement
+ Be network-oriented, when possible
+ Be efficient
+ Be flexible and able to grow
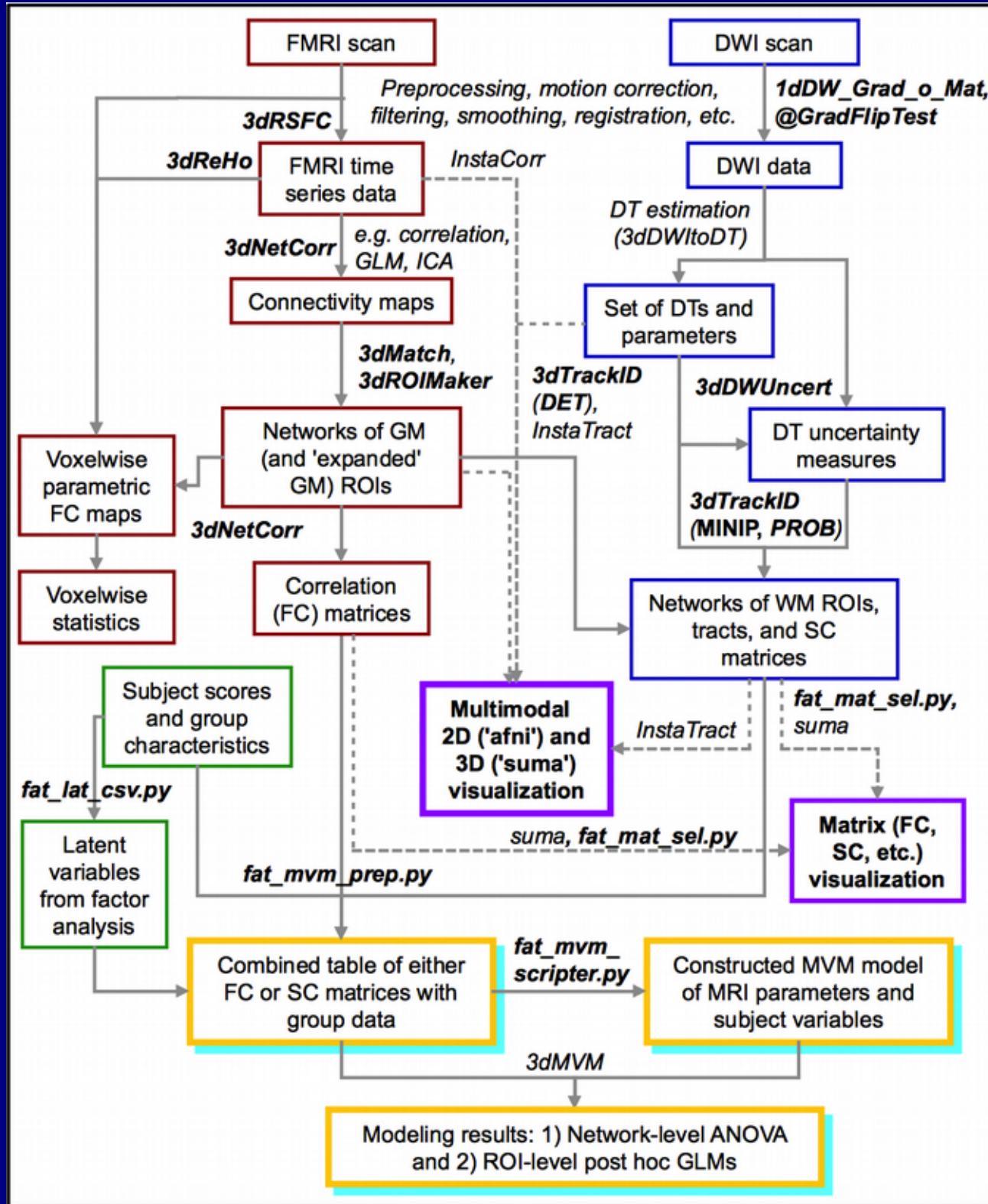
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Main focus today on DTI-tractography, including making ROIs from FMRI

(Taylor, Chen, Cox & Saad, 2015?)
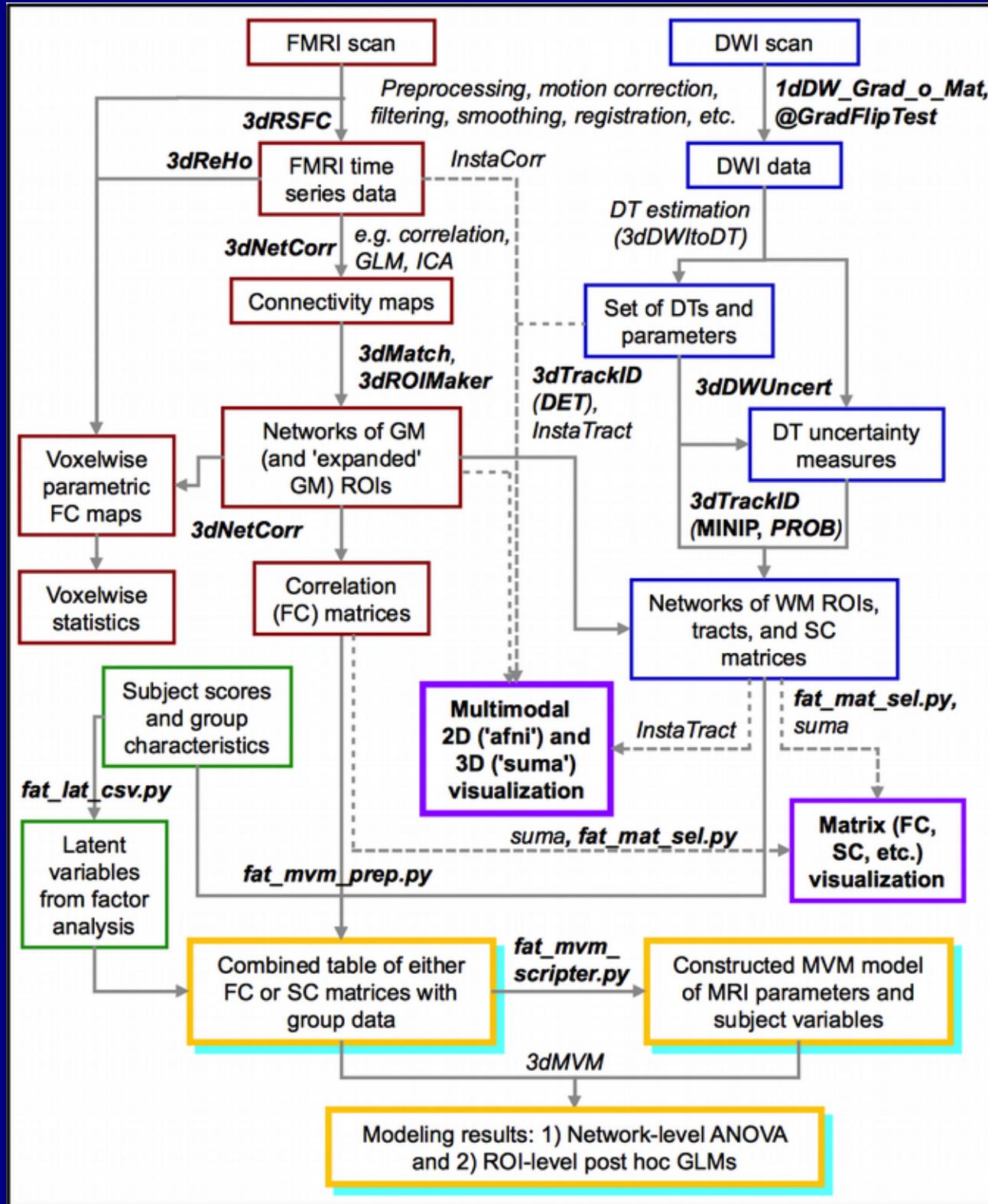
Sidenote:

Mention of a few of the FMRI tools

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)
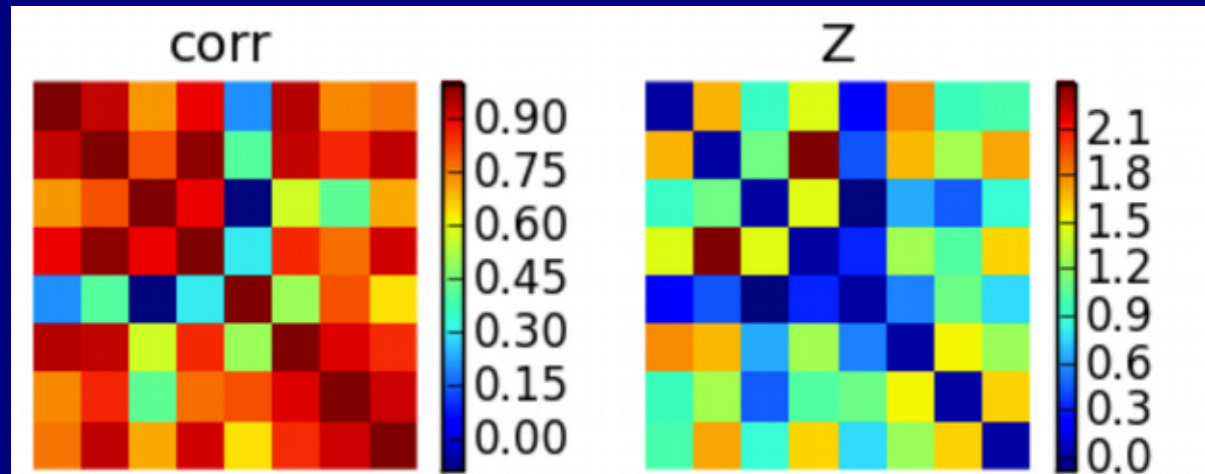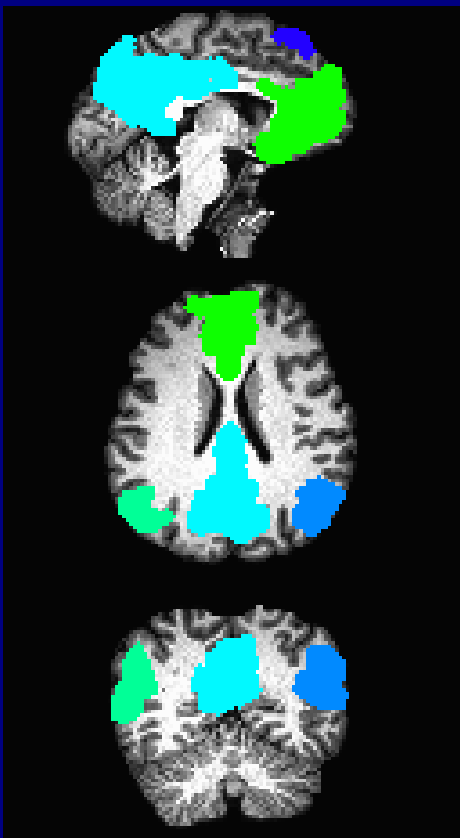
Diffusion tensor and parameters:
local measure of structure

Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures
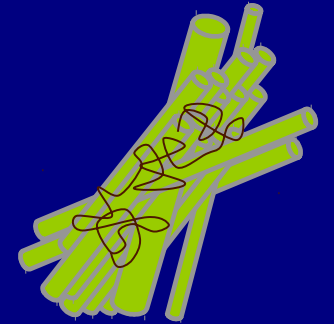
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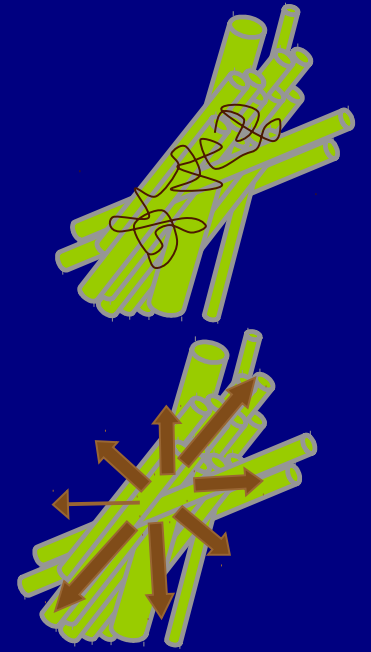
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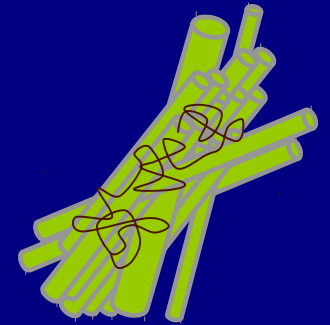
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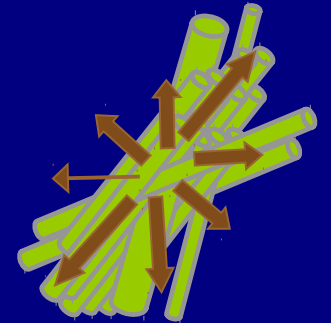
3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:

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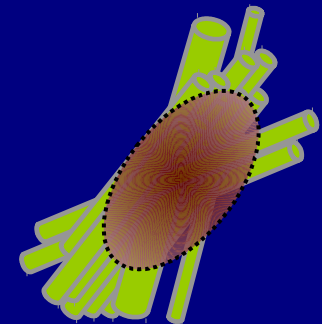
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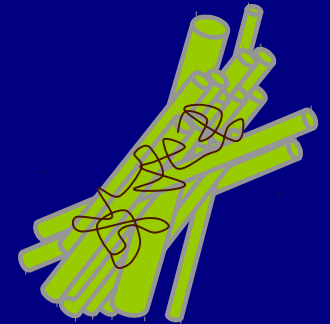
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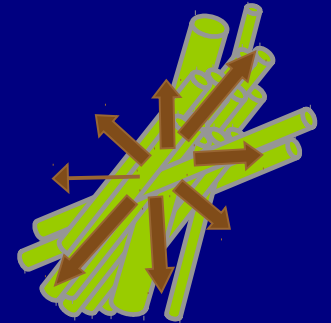
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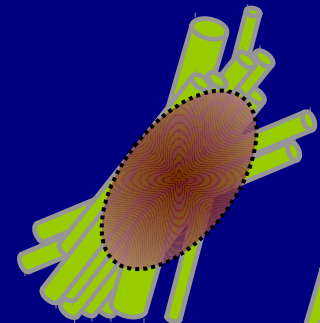
   + >=1 direction:
     HARDI (High Angular Resolution Diffusion Imaging)
     Qball, DSI, ODFs, ball-and-stick, multi-tensor, CSD, ...
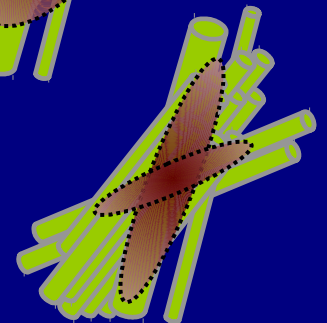
Diffusion in MRI

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 ($\mathbf{r^T D r} > 0$)
         $\mathbf{De}_i = \lambda_i \mathbf{e}_i$, $\lambda_i > 0$

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

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$$D e_i = \lambda_i e_i, \qquad \lambda_i > 0$$

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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
$\lambda_1 = \lambda_2 = \lambda_3$

$[\lambda_1]^{-1/2}$
$[\lambda_2]^{-1/2}$
e_i
$[\lambda_3]^{-1/2}$
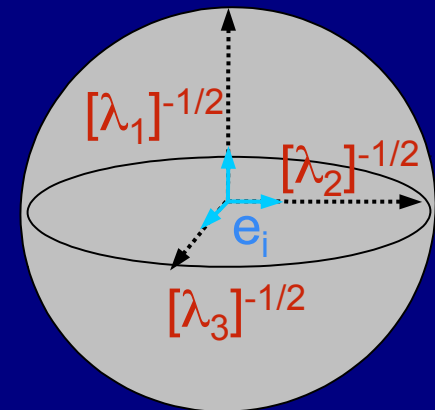
anisotropic case
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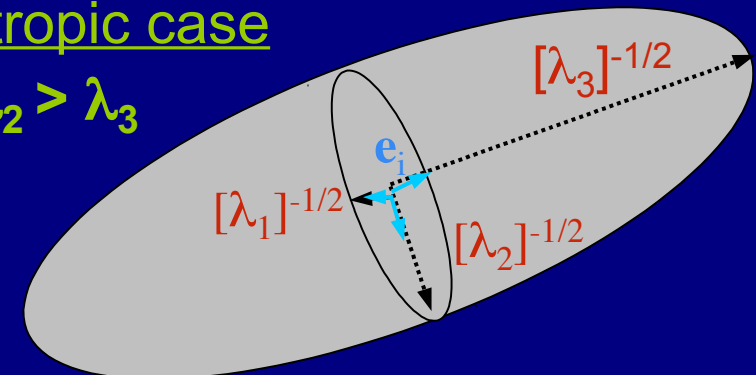
DTI: ellipsoids

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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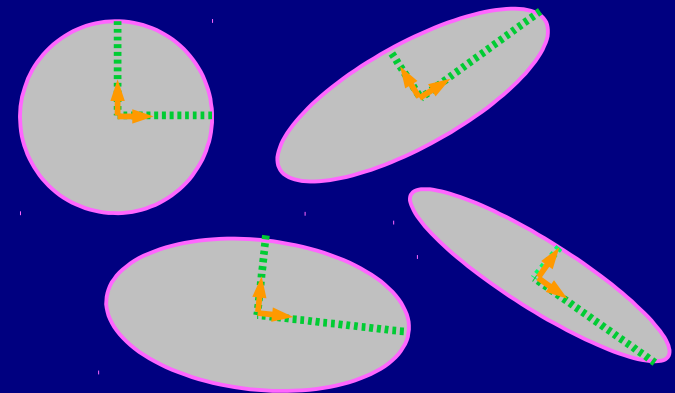
+ Determine the minimum number of

DWIs measures needed (6 + baseline)

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+ Determine much of the processing and
  noise minimization steps

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"Big 5" DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)

$$L1_1 \quad < \quad L1_2$$

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e_1 e_1

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(stdev of eigenvalues)

$$FA \approx 0 \qquad FA \approx 1$$

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Radial diffusivity, RD
($= (\lambda_2 + \lambda_3)/2$)

$$RD_1 \quad > \quad RD_2$$

Cartoon examples: white matter ↔ FA

GM   vs   WM

Cartoon examples: white matter ↔ FA

GM   vs   WM

FA ↑

Cartoon examples: white matter ↔ FA

GM vs WM

WM bundle organization

FA ↑

Cartoon examples: white matter ↔ FA
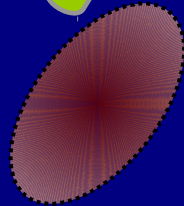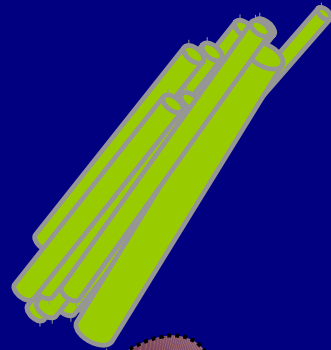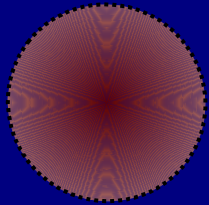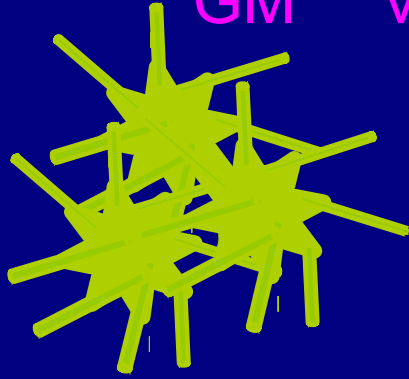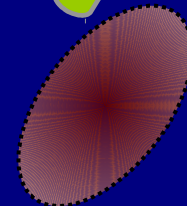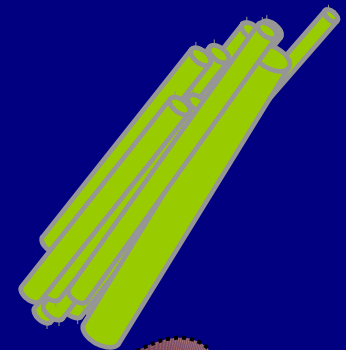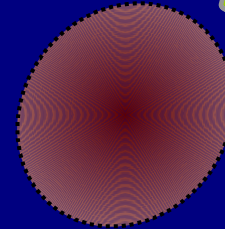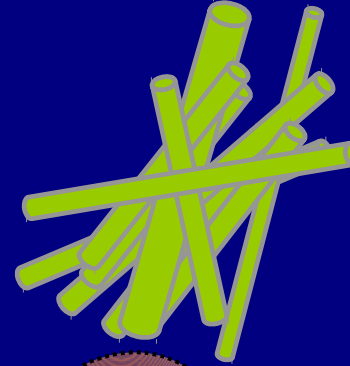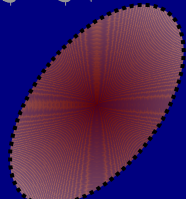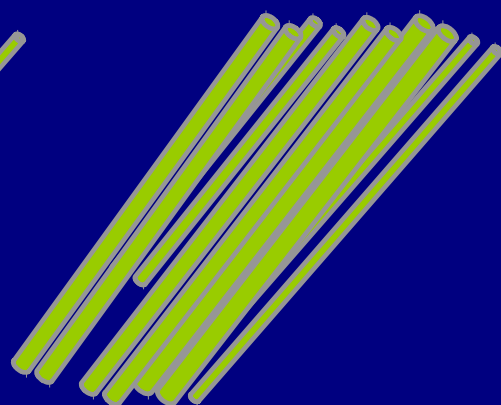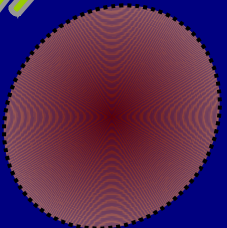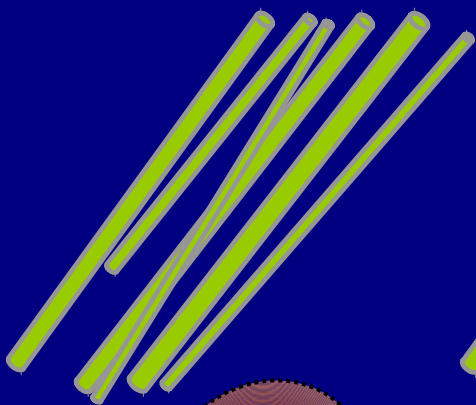
GM   vs   WM

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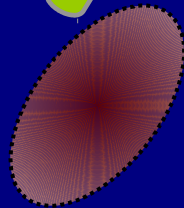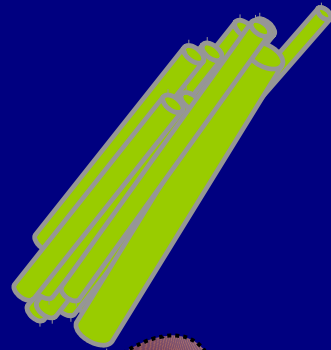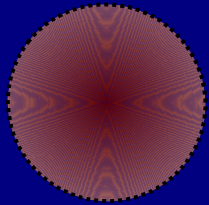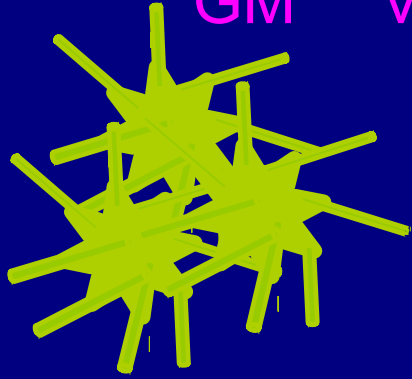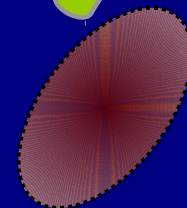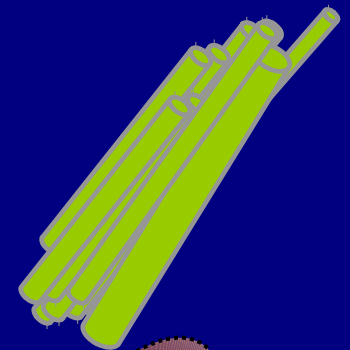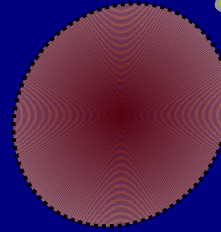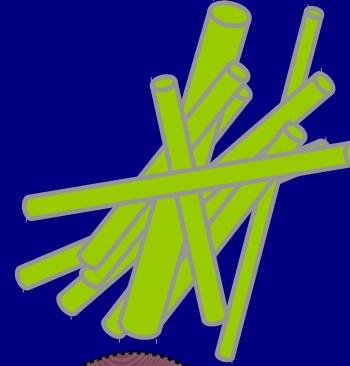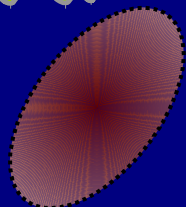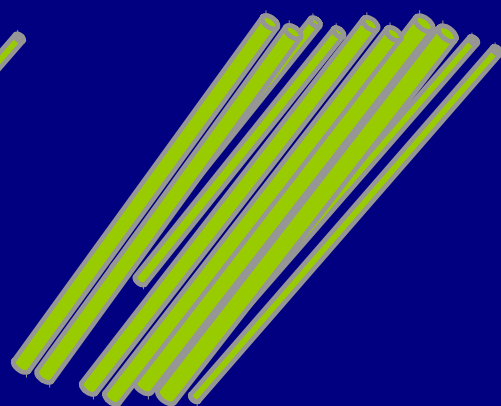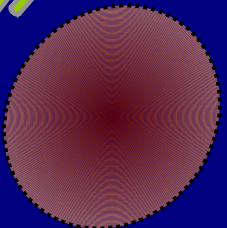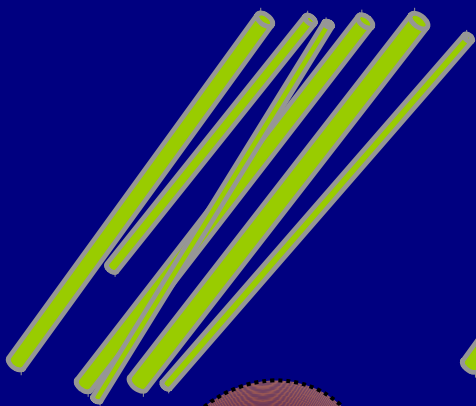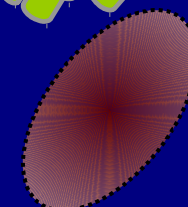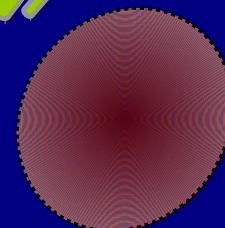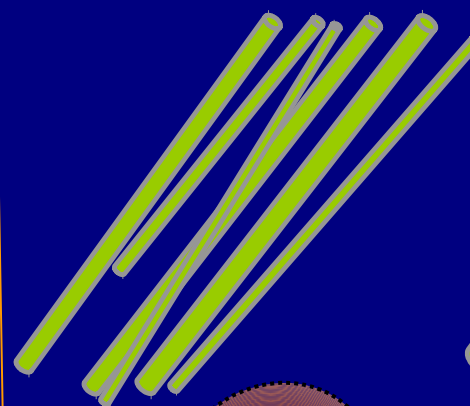
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Interpreting DTI parameters

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e_1: orientation of major bundles

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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

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.

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

where ε is (Rician) noise.

$\rightarrow$ Leads to errors in surface fit, equivalent to *rotations* and *rescalings* of ellipsoids:
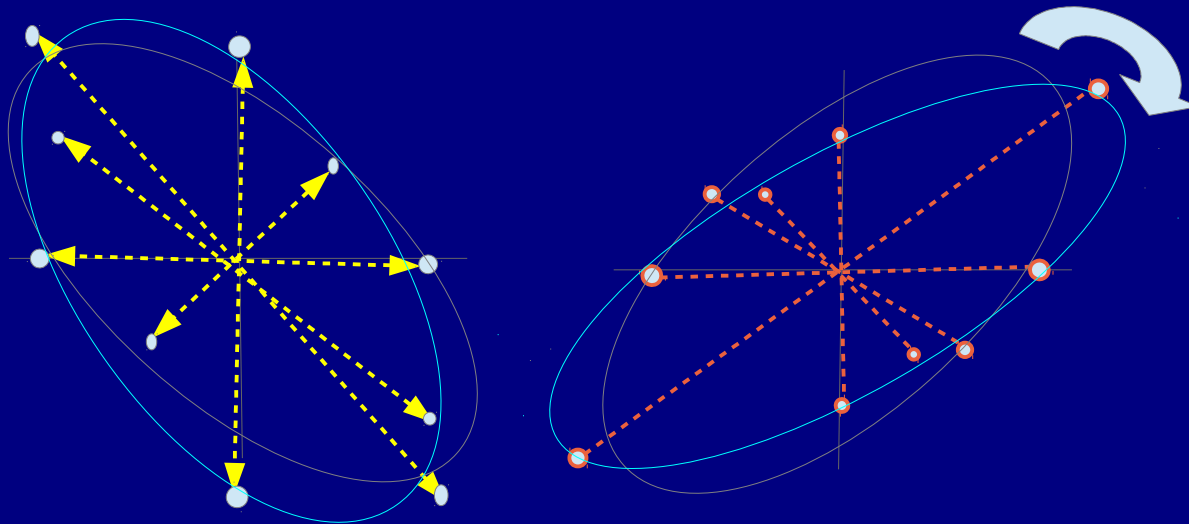

'Un-noisy' vs perturbed/noisy fit

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.

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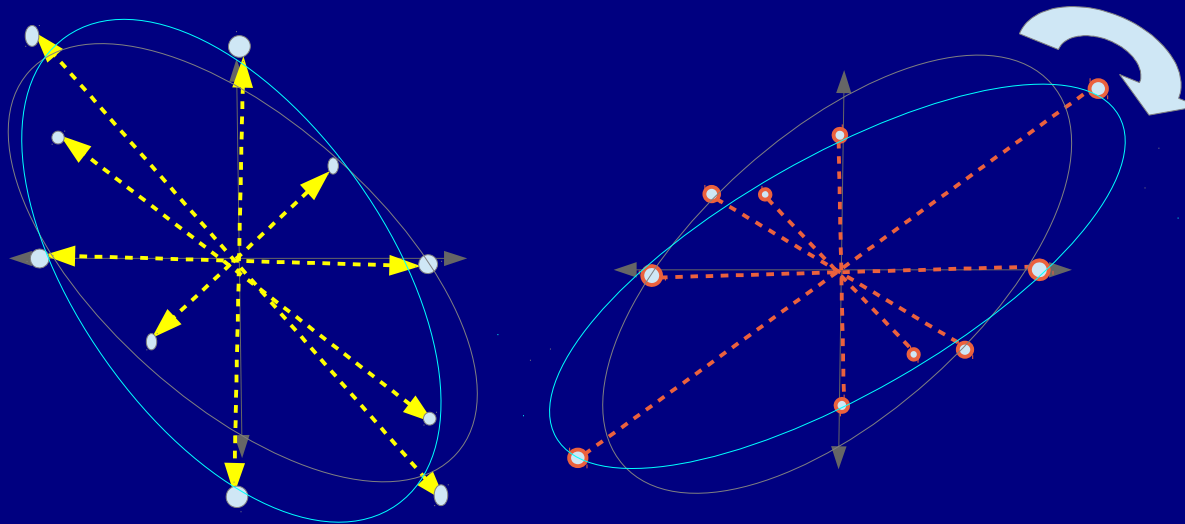
Leads to standard:
+ 30 DWs (~12 clinical)
+ repetitions of b=0
+ DW b chosen by:
    MD * $b \approx 0.84$
+ nonlinear fitting

'Un-noisy' vs perturbed/noisy fit

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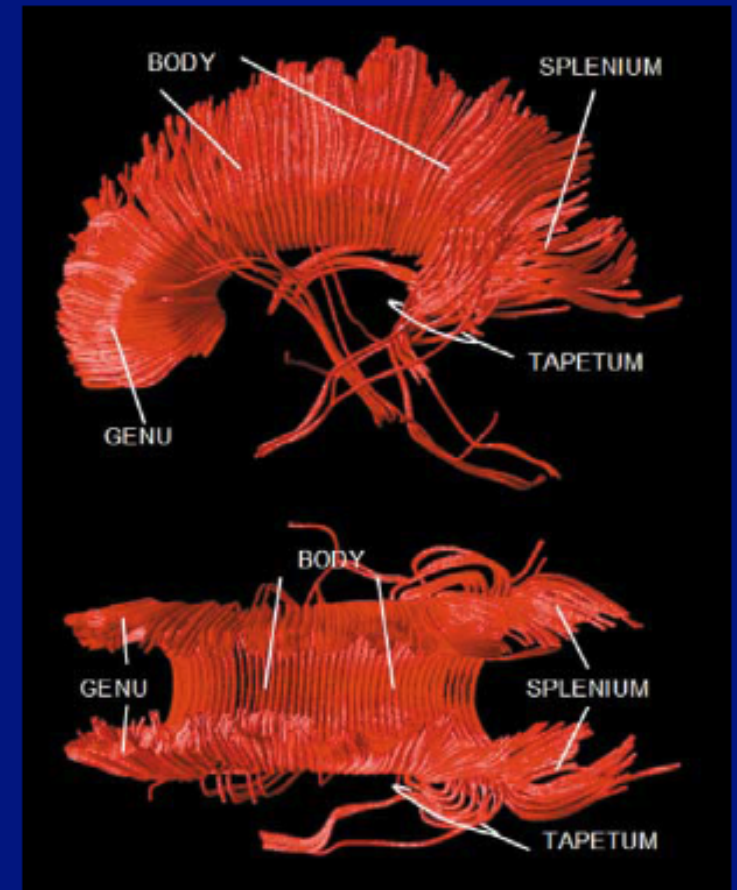WM tractography

Tractography in brief

old, invasive

new(er), theoretical

stain and preserve brain, get some

Idea of structure… non-ideal:

brain physiology changes postmortem, also `mortem' aspect

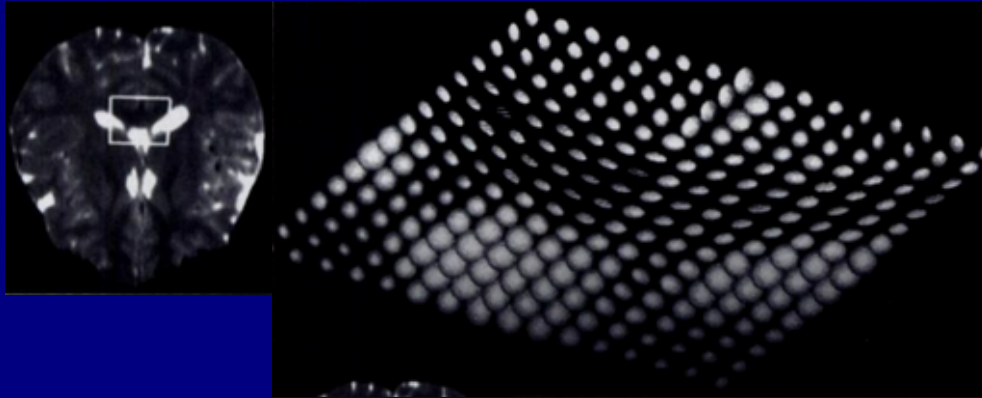(images from Iowa Virtual Hospital and Bammer et al. 2003)
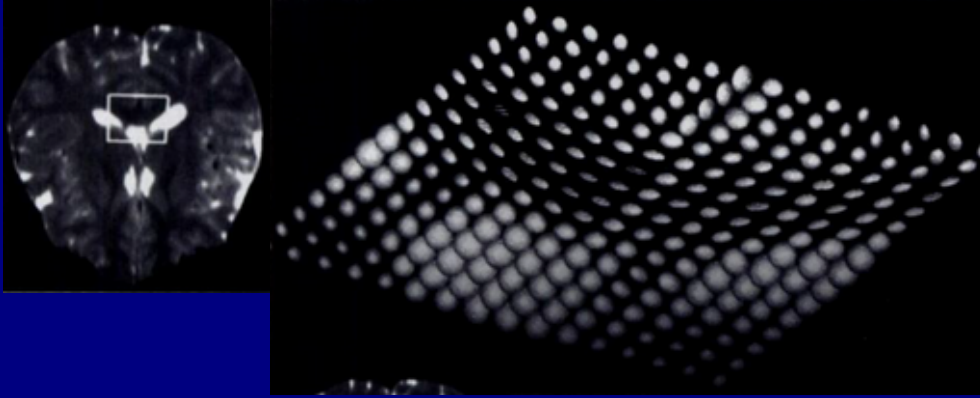
Local DTs → extended tracts

Field of local diffusion parameters

Local DTs $\rightarrow$ extended tracts

Field of local diffusion parameters

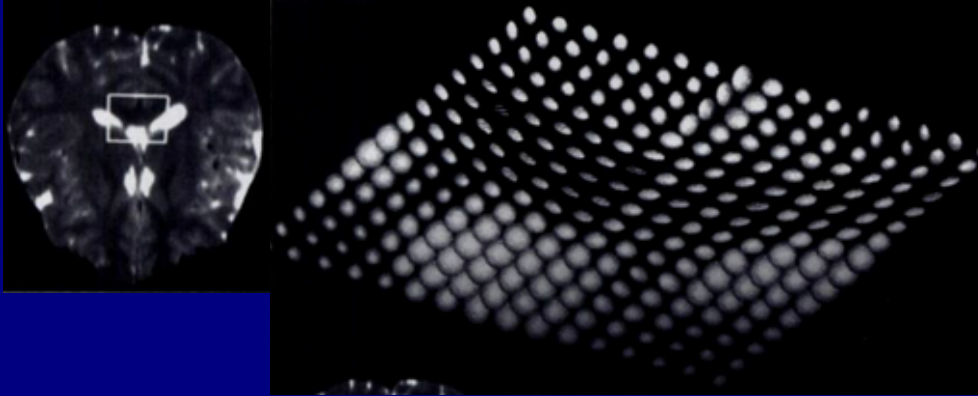$\rightarrow$ individual ellipsoids

Local DTs → extended tracts

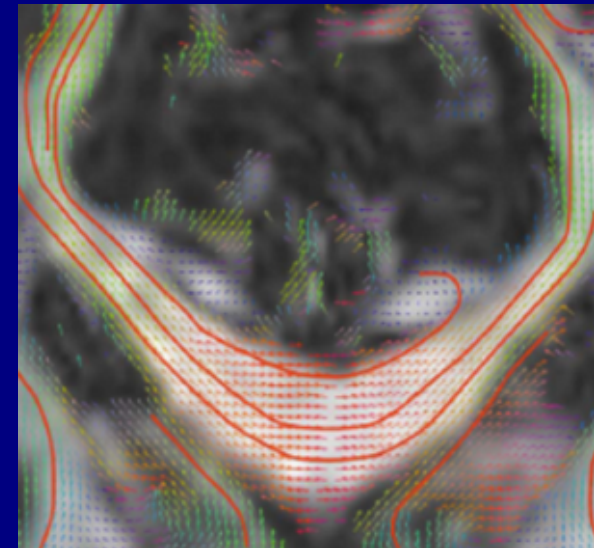**Field of local diffusion parameters**

→ individual ellipsoids

Connect to form extended tracts
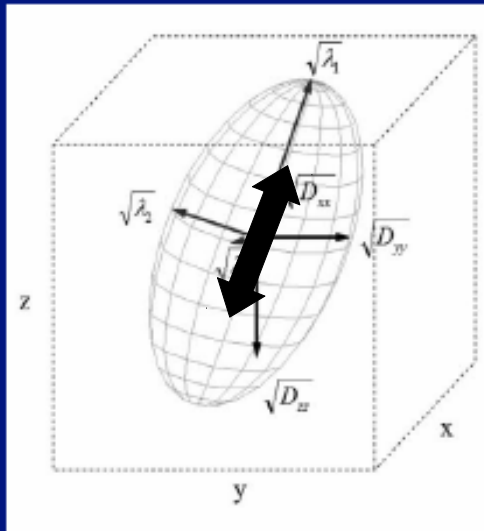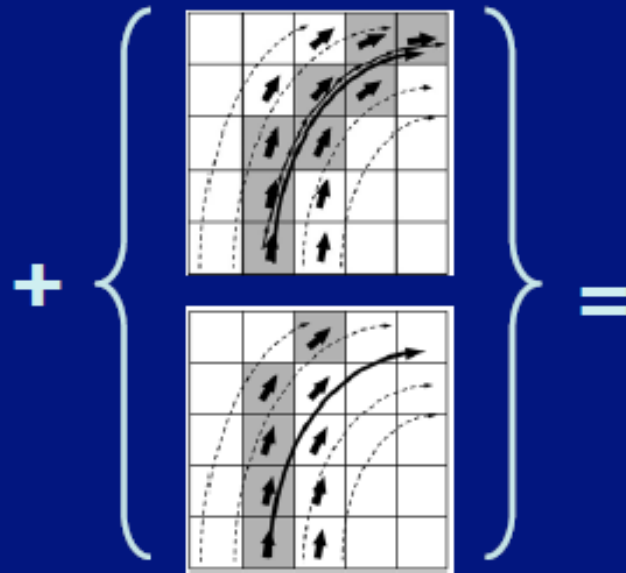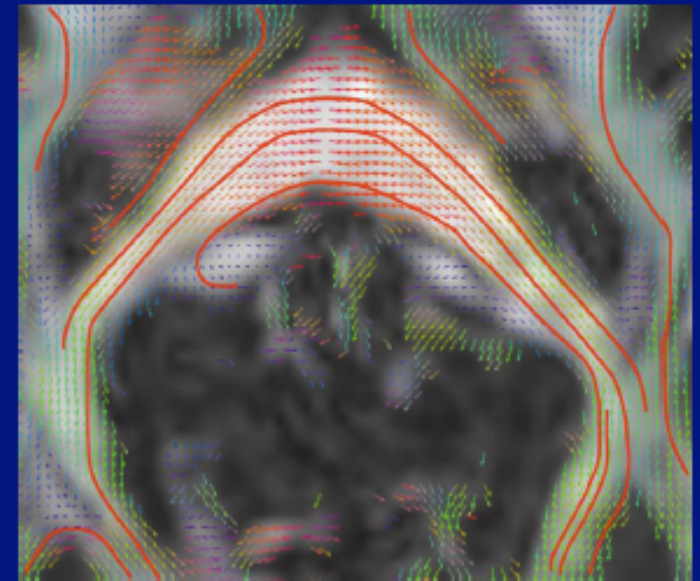

→ linked structures

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; Taylor et al. 2012; ….)

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 e_1s is <45 deg
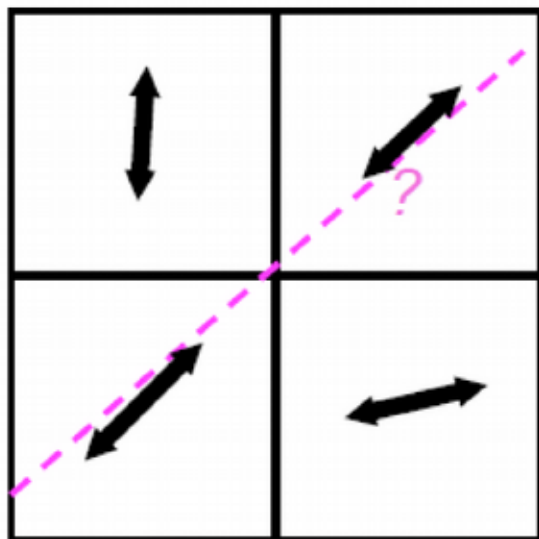
Ex.:

FACT (in 2D)

FACT (in 3D)
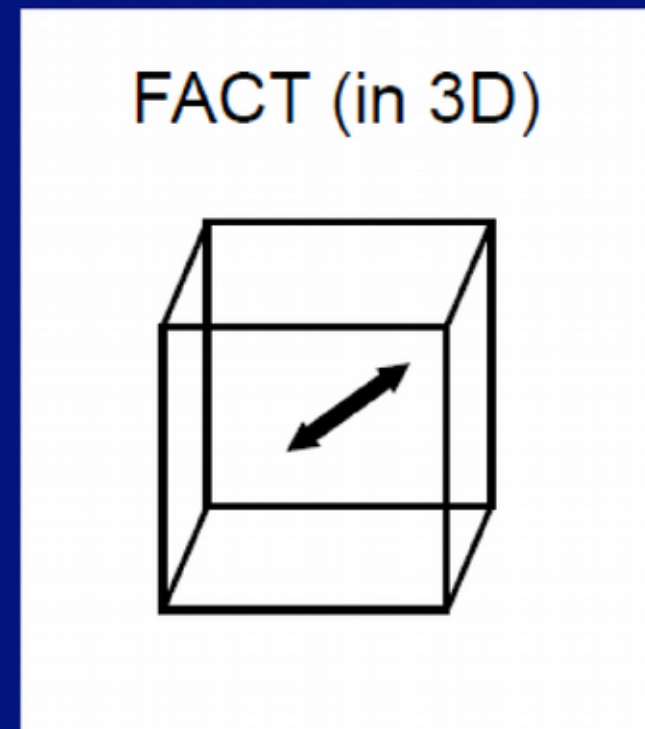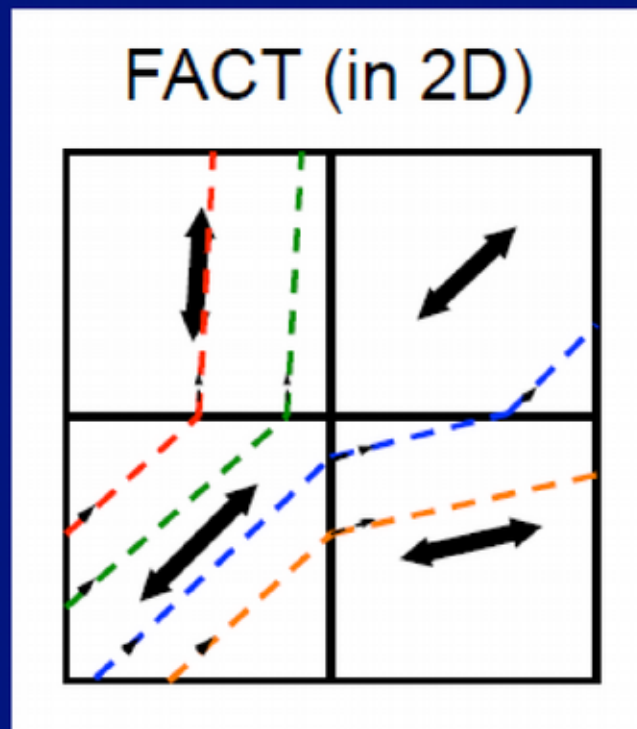
Very simple, but actually, gives some decent results, e.g. many known tracts

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FACT (in 3D)

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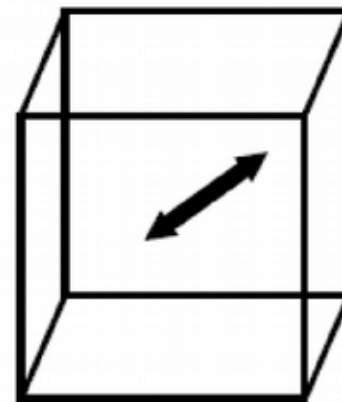
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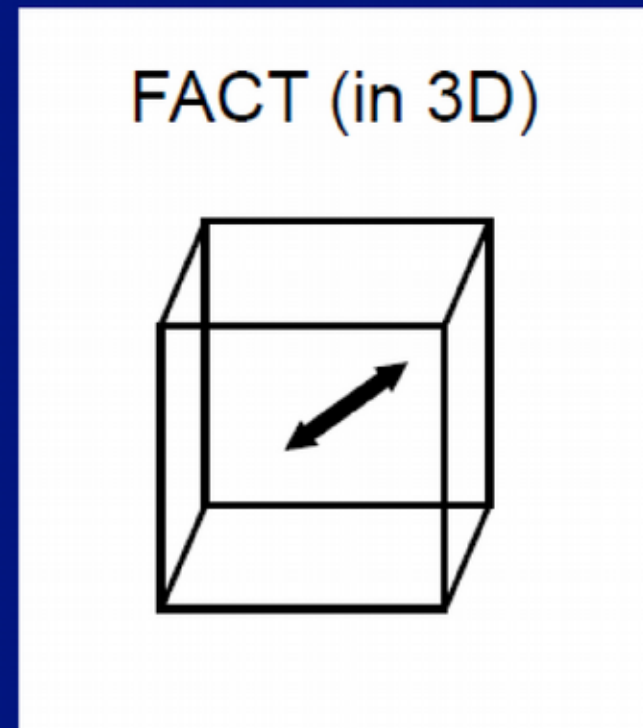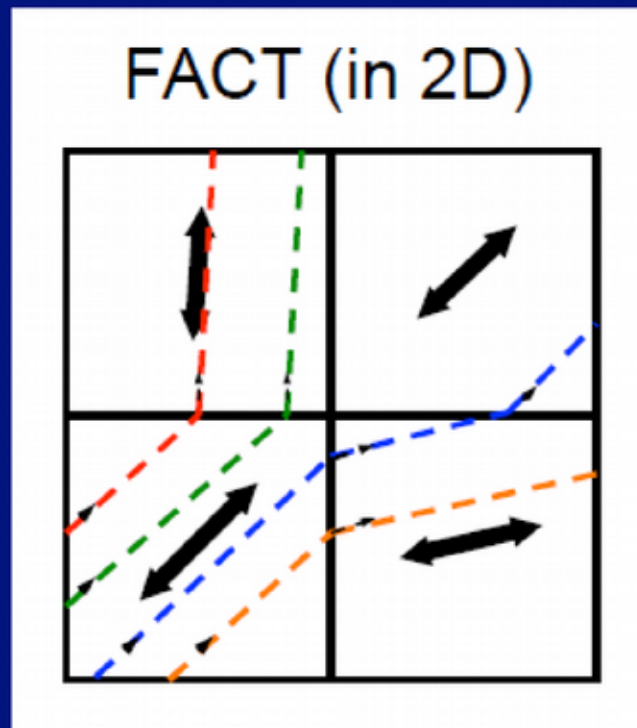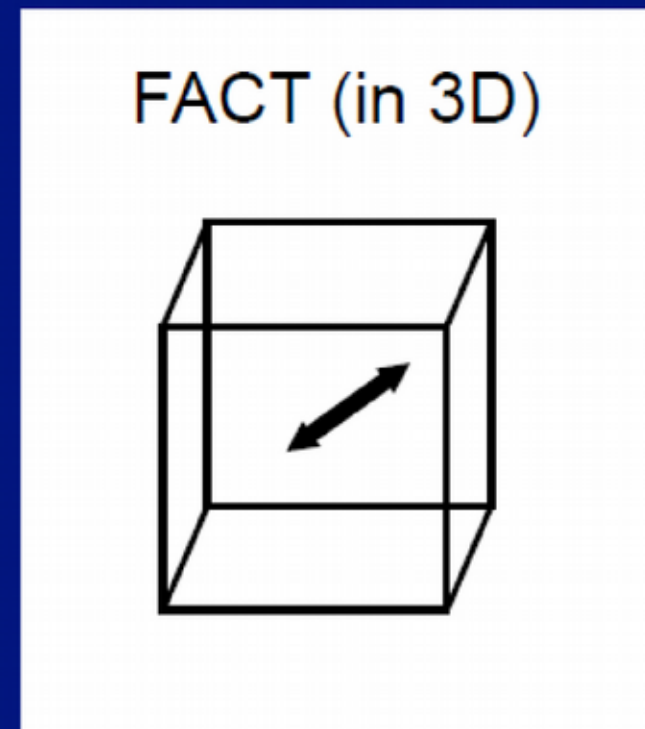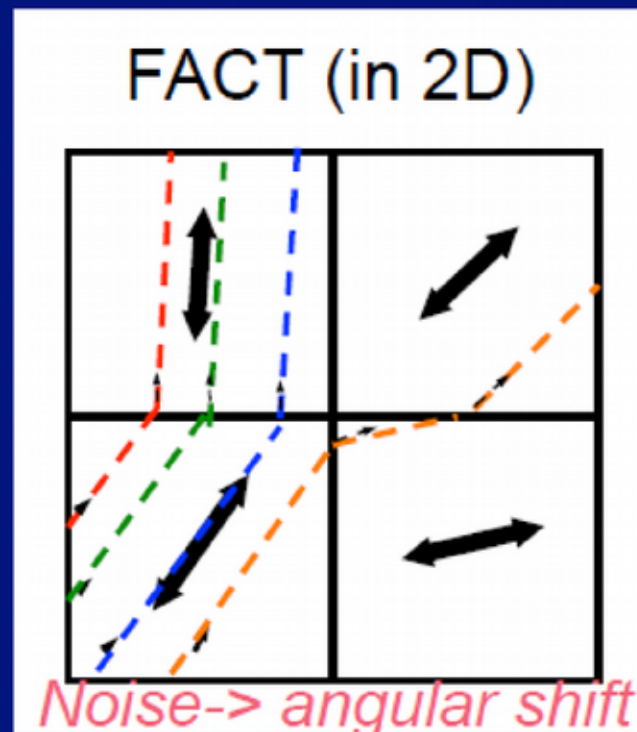
Ex.:

FACT (in 2D)

FACT (in 3D)

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Ex.:

FACT (in 2D)

Noise-> angular shift

FACT (in 3D)

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

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)

 4) Should not have strong instability with or dependence on noise

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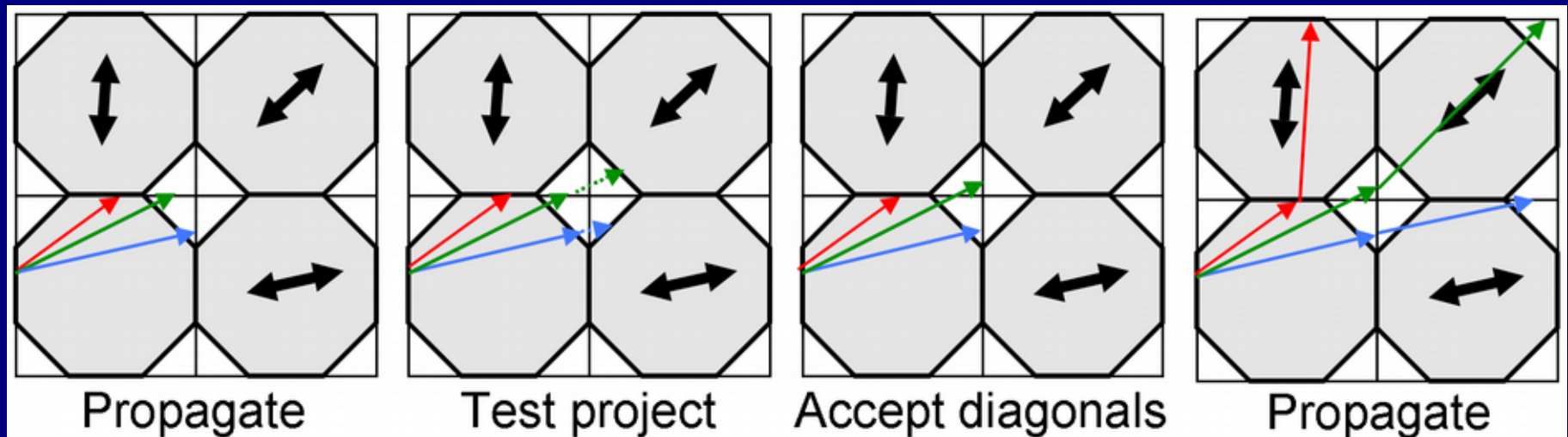Posit: including diagonal (ID) propagation helps 1 and 4, check about other props.

FACTID (in 2D)
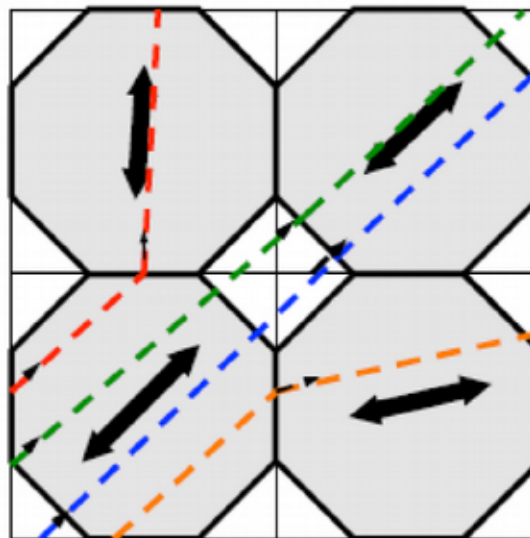
FACTID (in 3D)
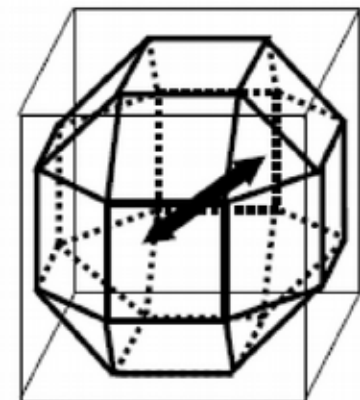
FACTID (FACT Including Diagonals):

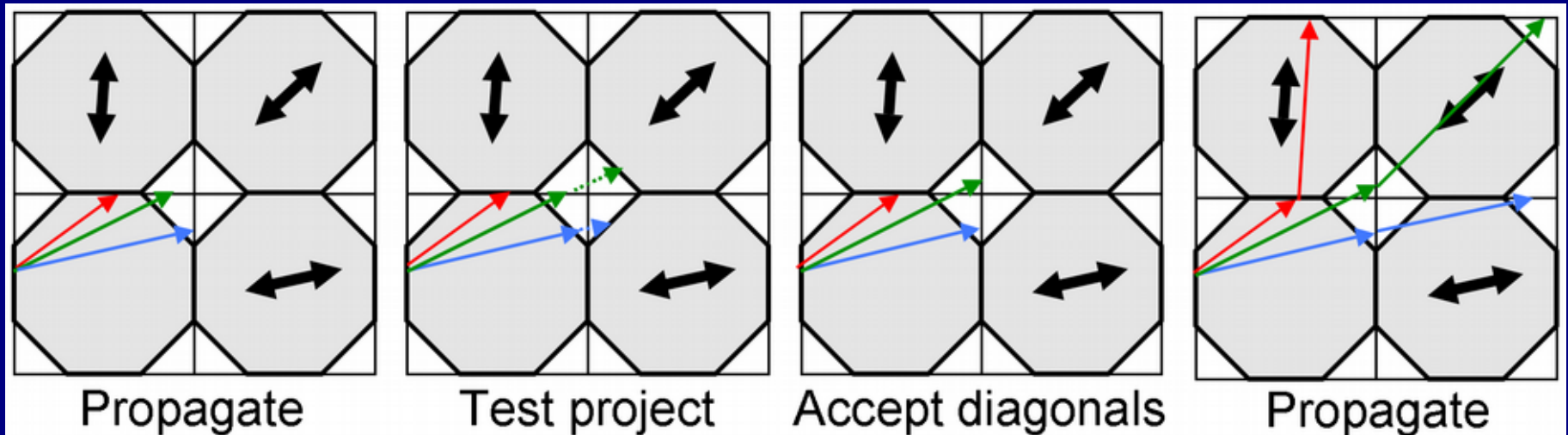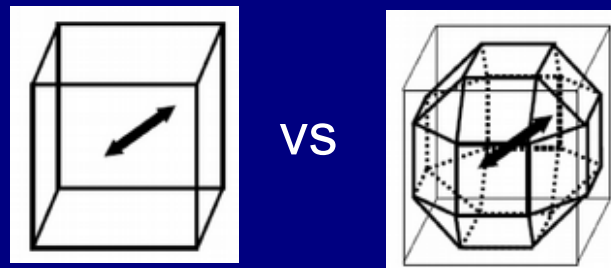+ Utilize simple check for diagonals.

(2D) Schematic:

Propagate   Test project   Accept diagonals   Propagate

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+ Utilize simple check for diagonals.

(2D) Schematic:

Propagate   Test project   Accept diagonals   Propagate

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

 vs

(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)
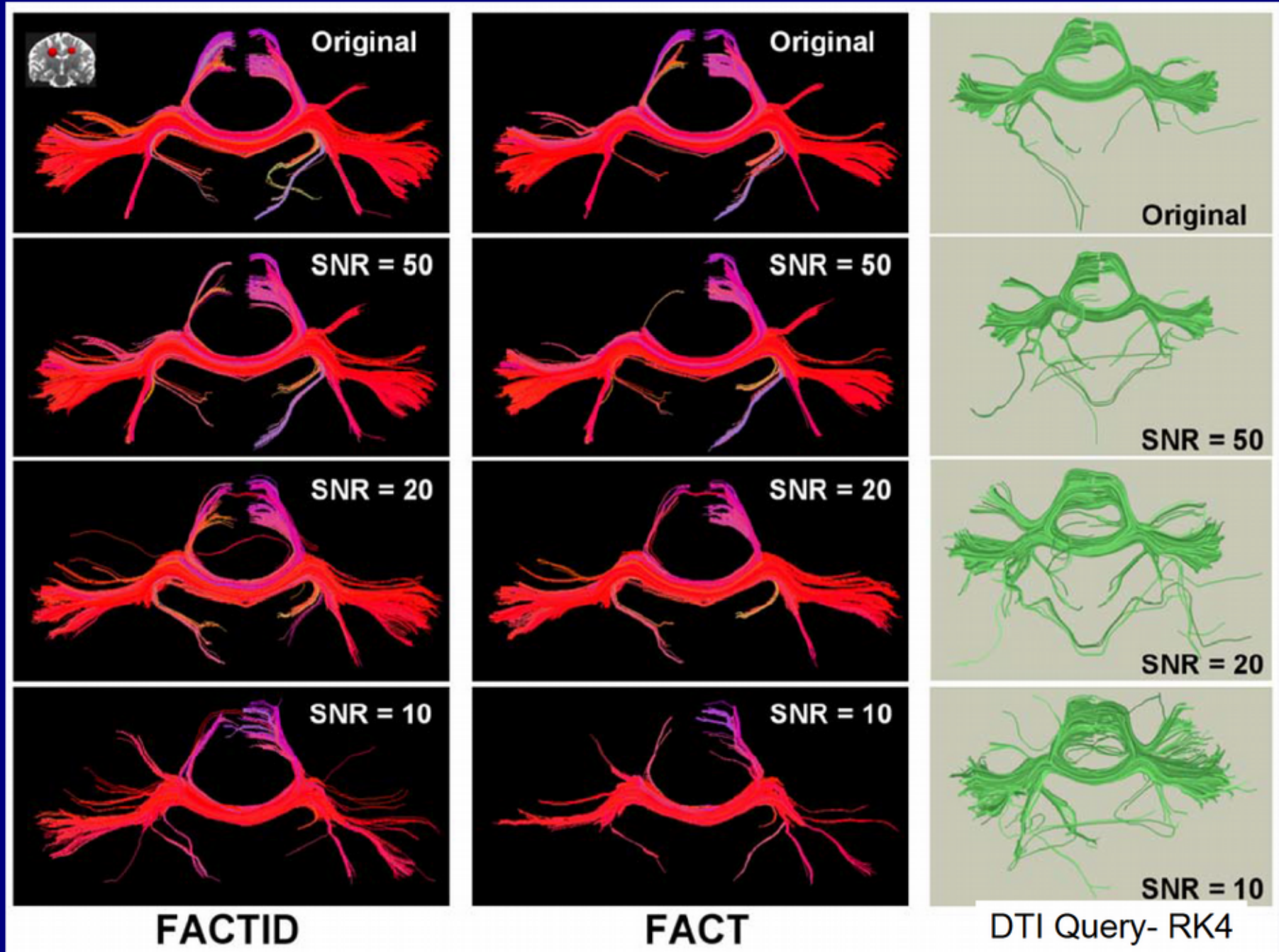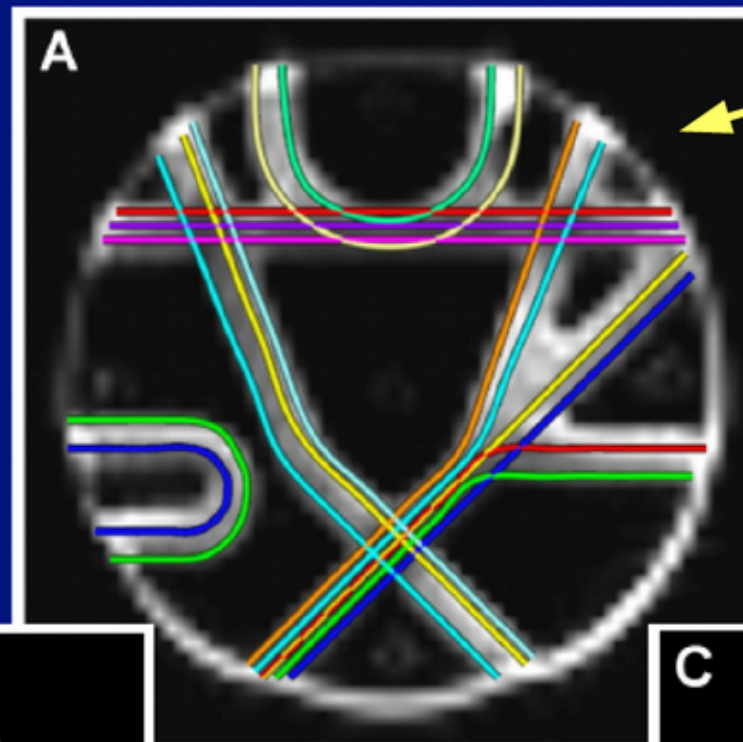
FACTID

FACT

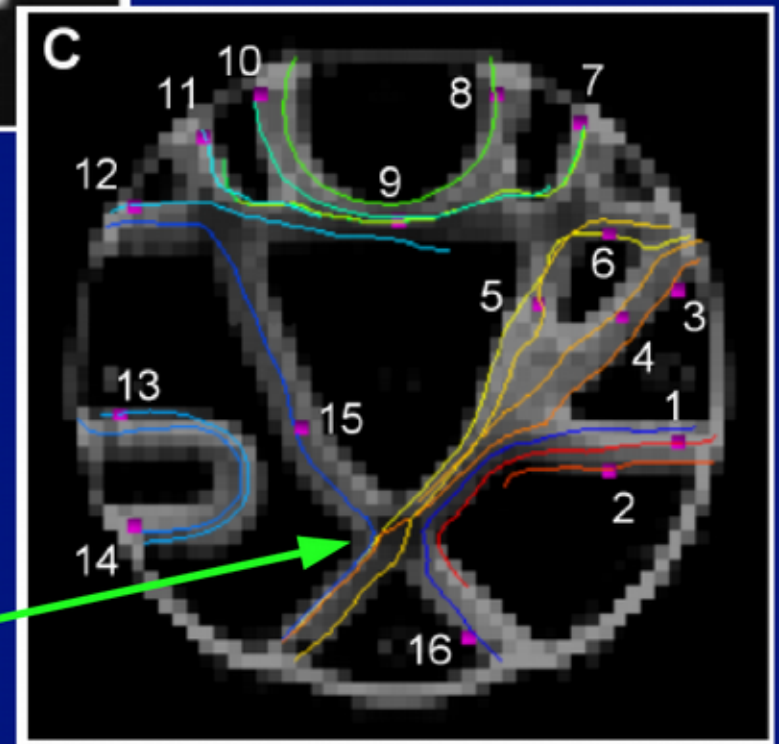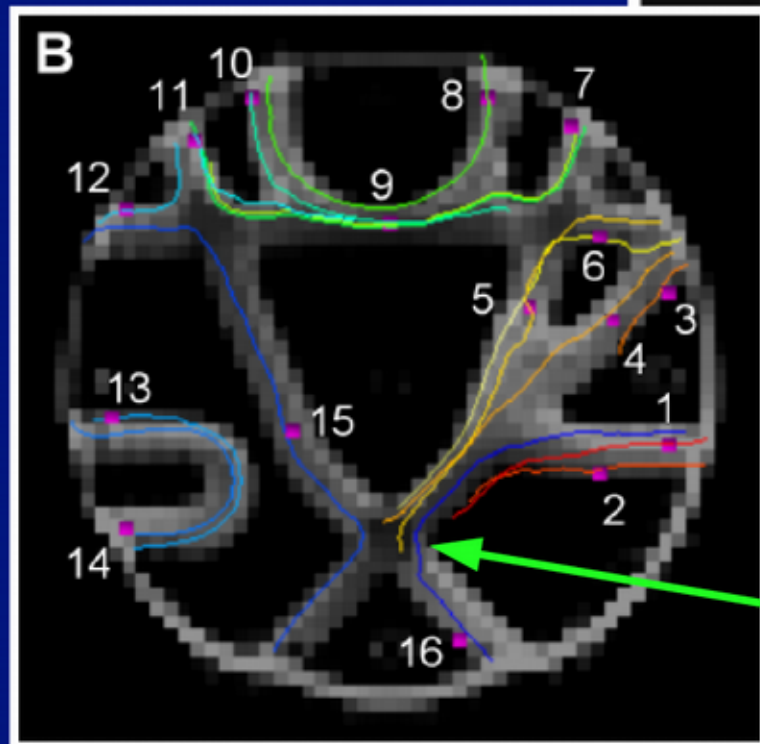*(Taylor, Cho, Lin & Biswal, 2012)*

Test 3: Noise sensitivity

FACTID | FACT | DTI Query- RK4

(Taylor, Cho, Lin & Biswal, 2012)

Test 5: Phantom Set

Fillard et al. (2011, NI) test phantom

A "ANSWER"

FACT

B

FACTID

C

(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.

—Charles Babbage, <u>Passages from the Life of a Philosopher</u>

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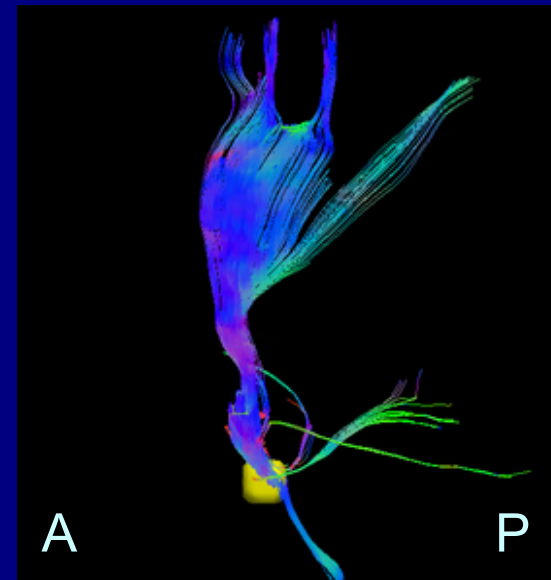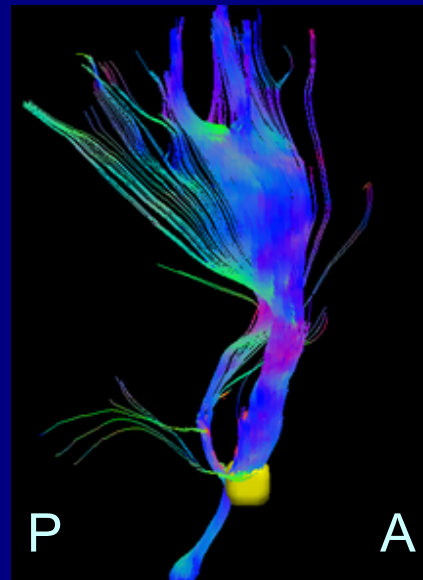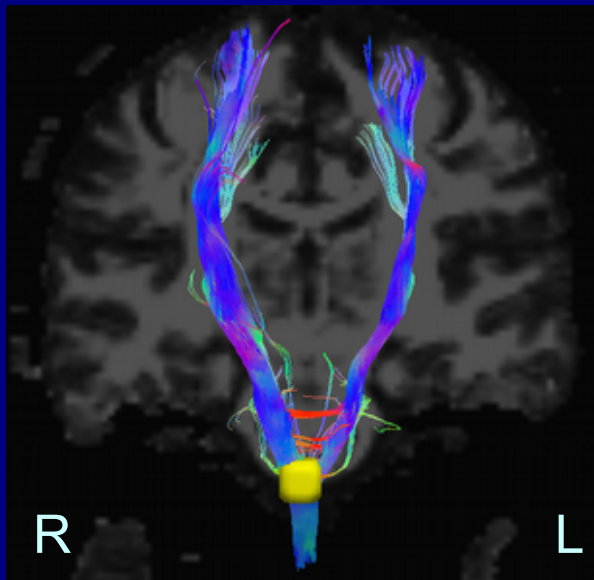—Charles Babbage, <u>Passages from the Life of a Philosopher</u>

→   In addition to the tracking algorithm, the quality of data acquisition and preparation matter quite a bit (as seen in morning TORTOISE session).
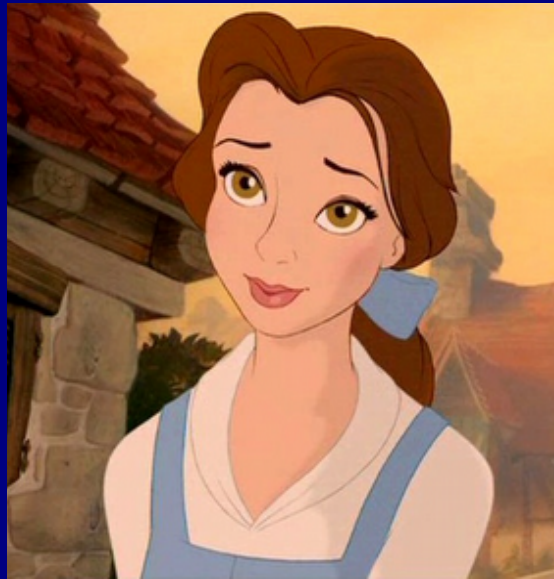
Importance of being processed (in earnest)
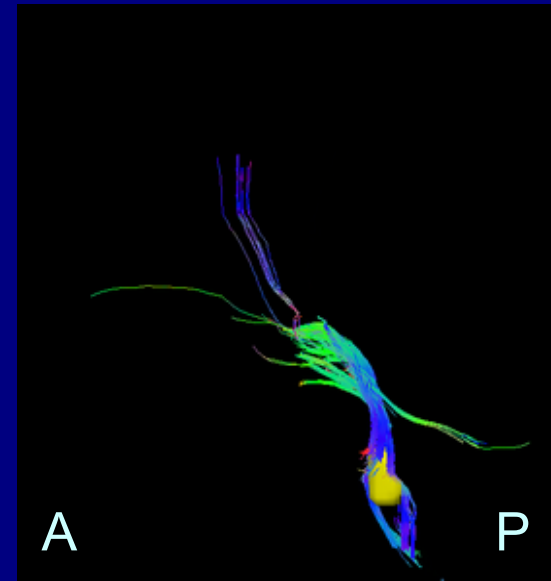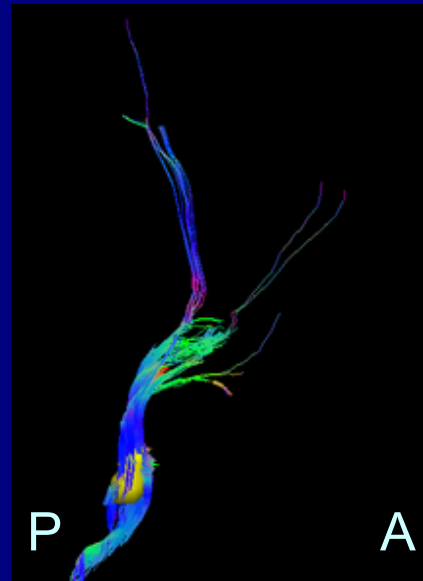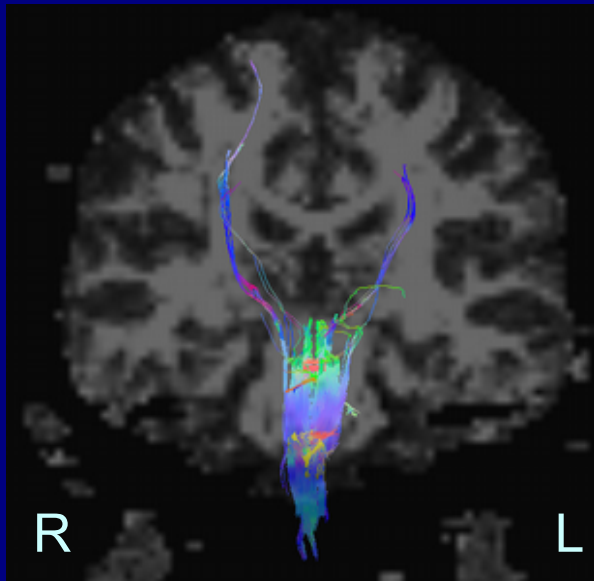
Data from the morning session, same target ROI in brainstem.
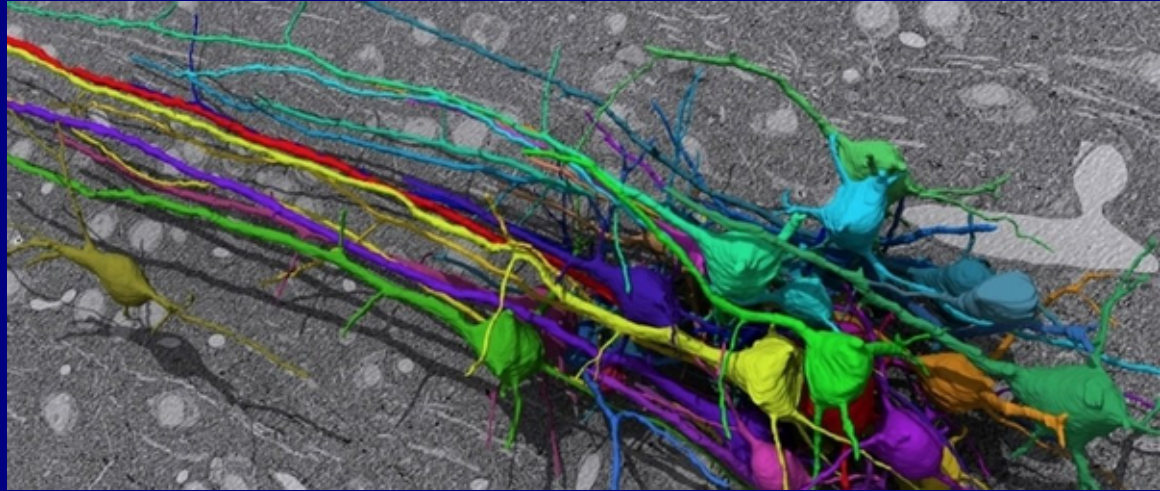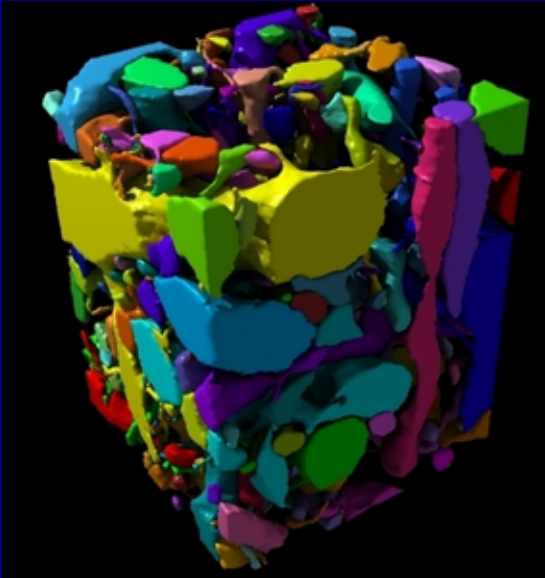Consider reach of tracts, symmetry, physiology, etc.

Cinematic side note:

La Belle et la Bête of tractography

Known Challenges for Tracking

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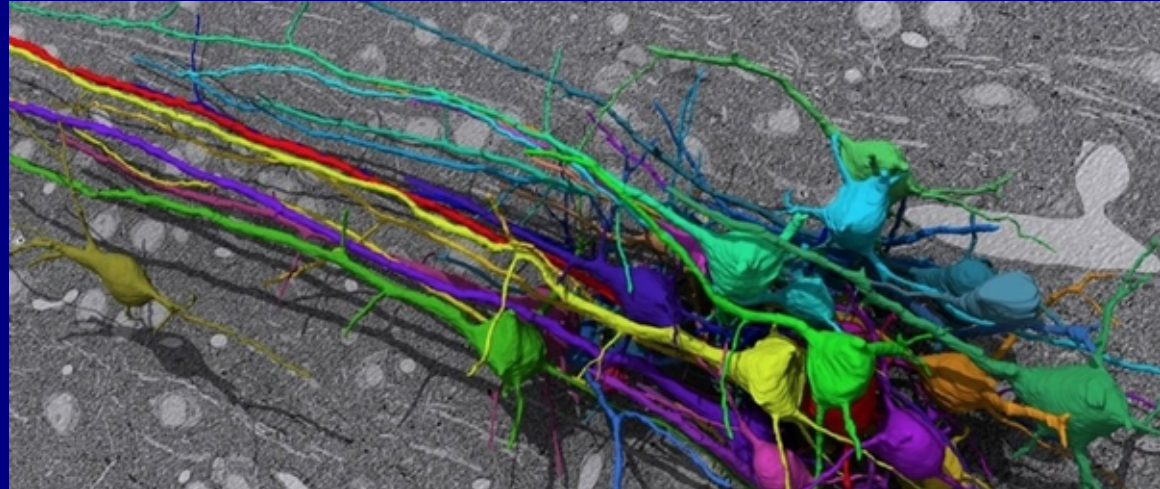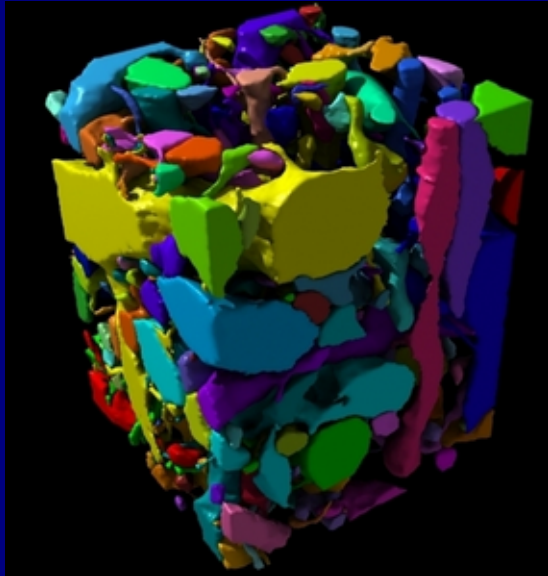+ MRI voxel size is of order millimeters

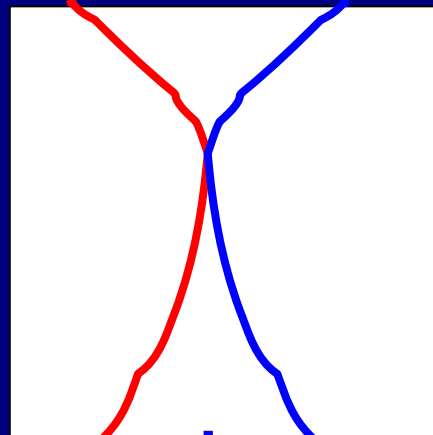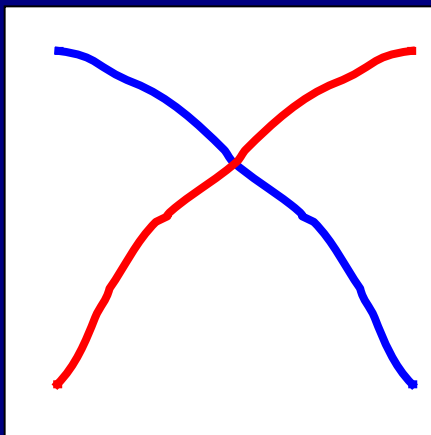*(images of Eyewire data via NPR website)*

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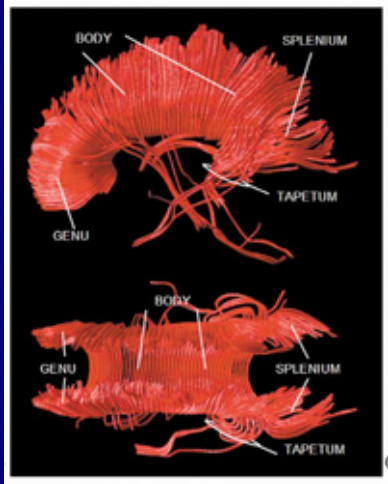+ WM regions are tightly packed, with many connections and potentially complicated sub-voxel scale structure

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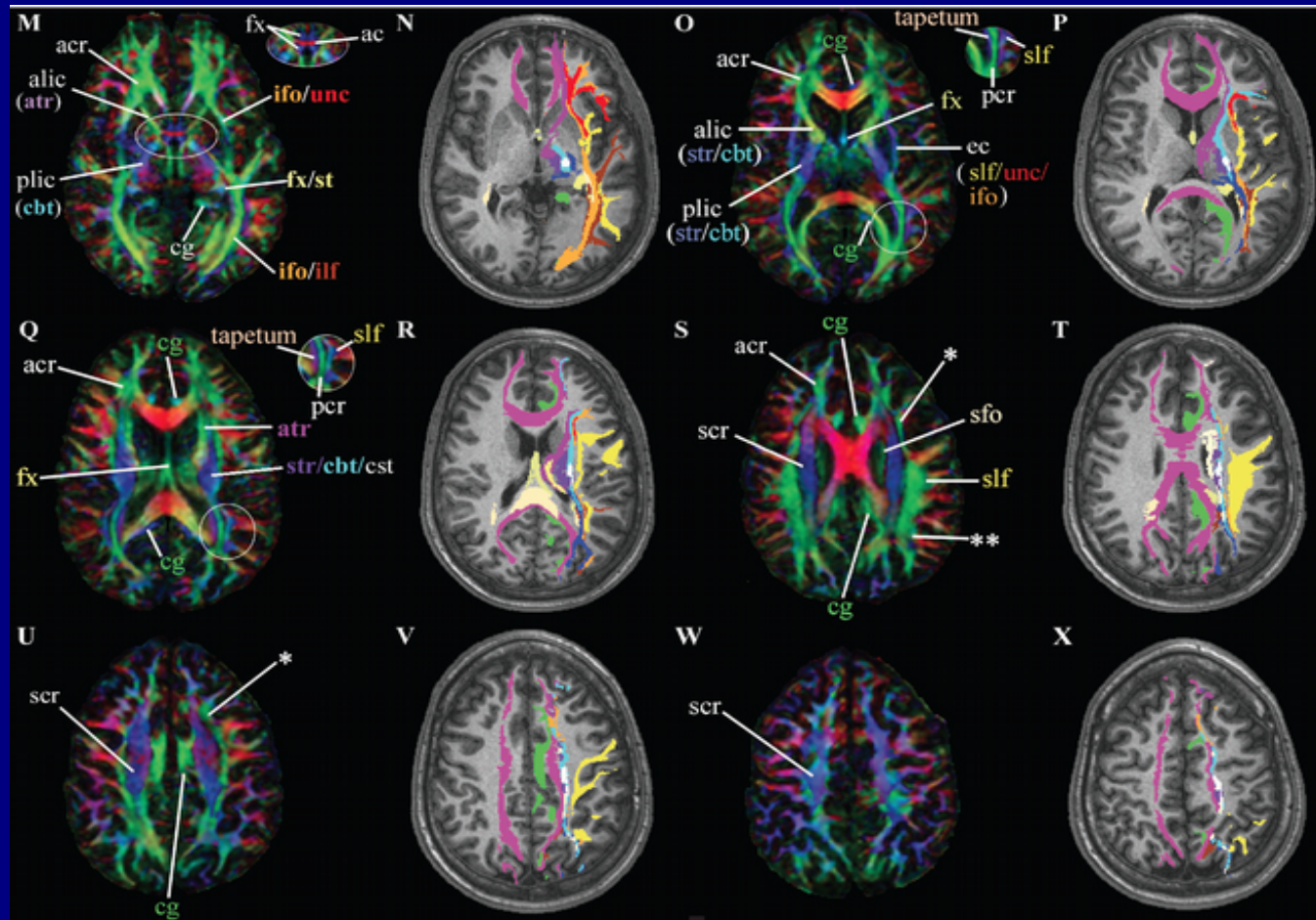- Redirect (or *not*) tracking incorrectly.

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?

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.