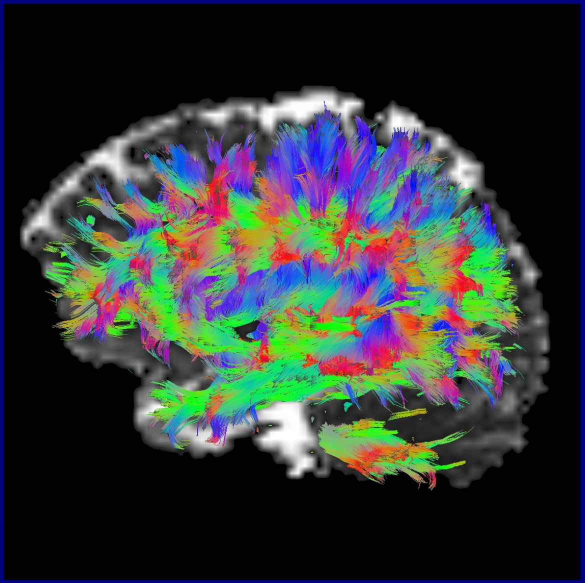
More about DTI-tracking:
Practicalities and programs

AFNI Bootcamp (SSCC, NIMH, NIH)

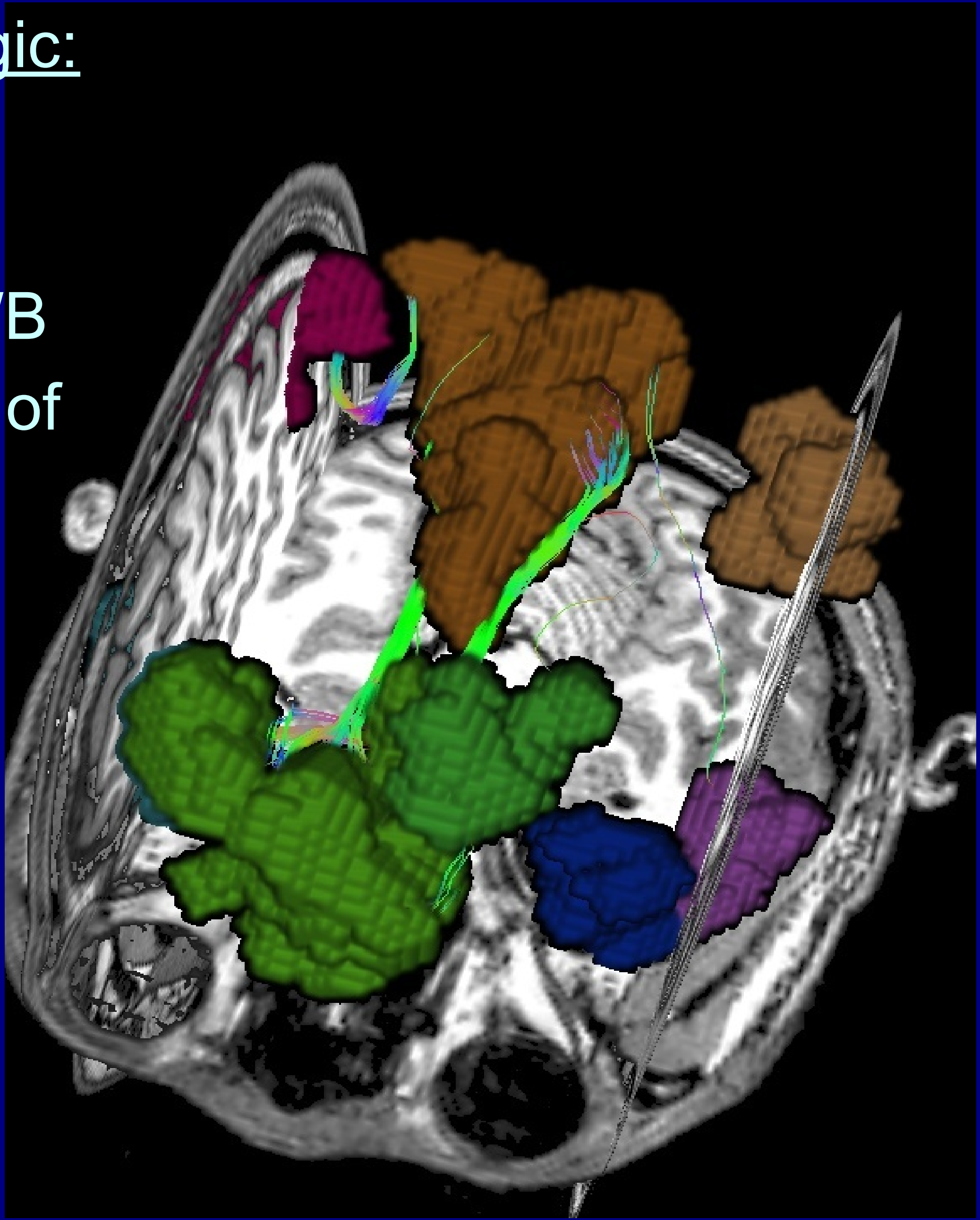


Outline

+ Practicalities around tracking with AFNI/FATCAT
+ 3dTrackID's "modes" (a.k.a. styles or types) of tracking
    - and calculating tensor parameter uncertainty
+ Setting up networks of target ROIs with 3dROIMaker
    - examples from anatomical parc/seg and FMRI
+ Checking gradients
+ Additional tracking features

Network tracking paradigm: recall

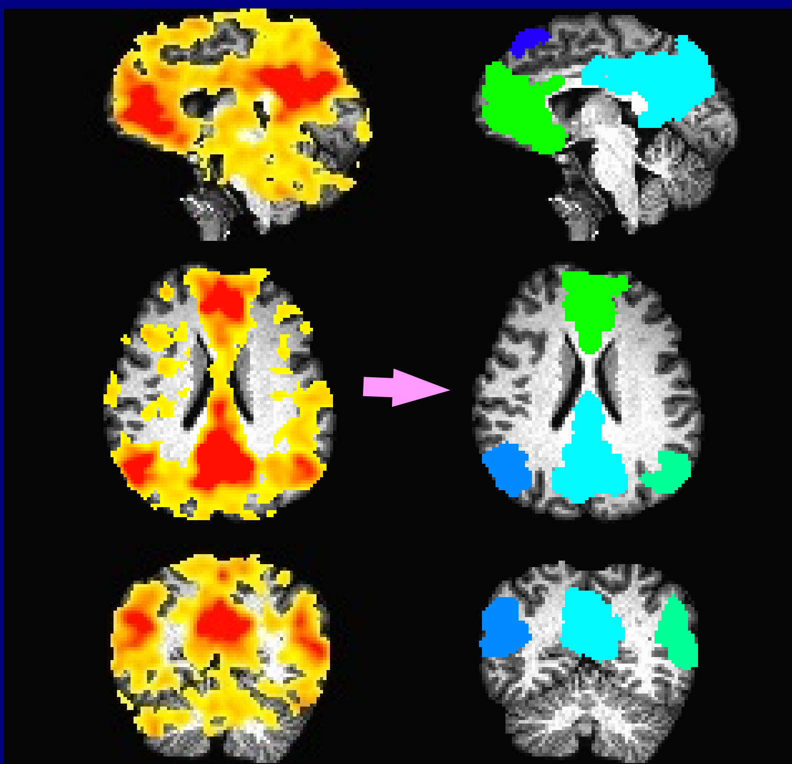
<u>Useful generalization of AND-logic:</u>
“Network tracking”
through several target ROIs simultaneously. Find tracts in WB that go through any pair in a set of targets, where the targets make sense to think about together.



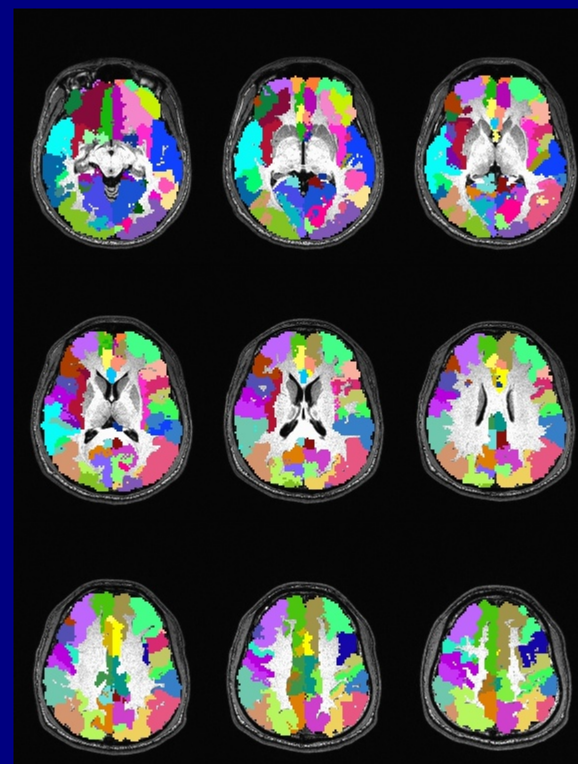
Note that the connections can be “sparse”: not every target is connected to every other target. (Physiologically, we would **not** expect otherwise...)

Network tracking paradigm: recall

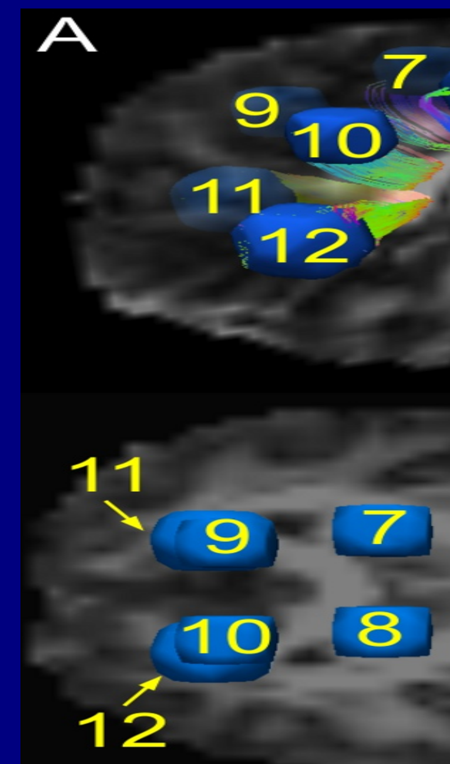
FMRI (e.g., thresholded seed-based or ICA maps)



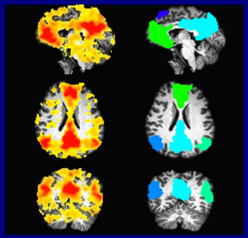
Anatomical parc/seg (e.g., FreeSurfer)

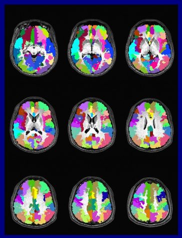


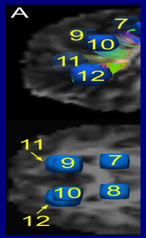
Spheres/simple ROIs (can map across group)



Network tracking paradigm: points



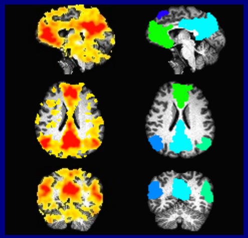


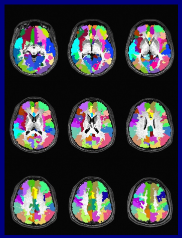


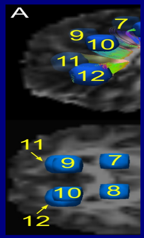
<u>Main criteria for making target ROI networks</u>

+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group

Network tracking paradigm: points







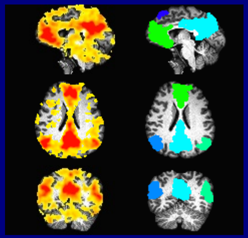
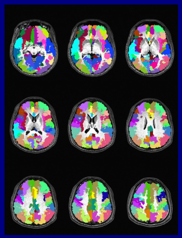
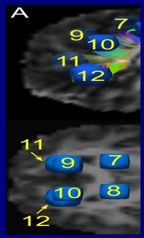
<u>Main criteria for making target ROI networks</u>

+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group

<u>... Then</u>

+ targets can be defined **in** subject's own DTI space
+ main quantity: **matrix of structural properties** for each network

Network tracking paradigm: points

<u>Main criteria for making target ROI networks</u>

+ define meaningful regions (-> sensical to be together for hypothesis)
+ make sure targets border on FA-WM
+ for group analysis, create equivalent/consistent regions across group

<u>... Then</u>

+ targets can be defined **in** subject's own DTI space
+ main quantity: **matrix of structural properties** for each network

<u>Different than "voxelwise comparisons"</u>

+ Here, don't need to warp to standard space/WM skeleton
  -> avoid (some) alignment issues/demands
+ Here: calc "network-wide" properties, then zoom in (big -> small)
  voxelwise comps: calc voxel diffs and build "clusters" (small -> big)
+ Here, WM structure matters; voxelwise comps ignore this.

Combining FMRI and DTI

(much applies to **any** target network)

Tools for combining FC and SC:

Combining functional and tractographic connectivity will require:

+ determining networks from FMRI, parcellation 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...

Tools for combining FC and SC:

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

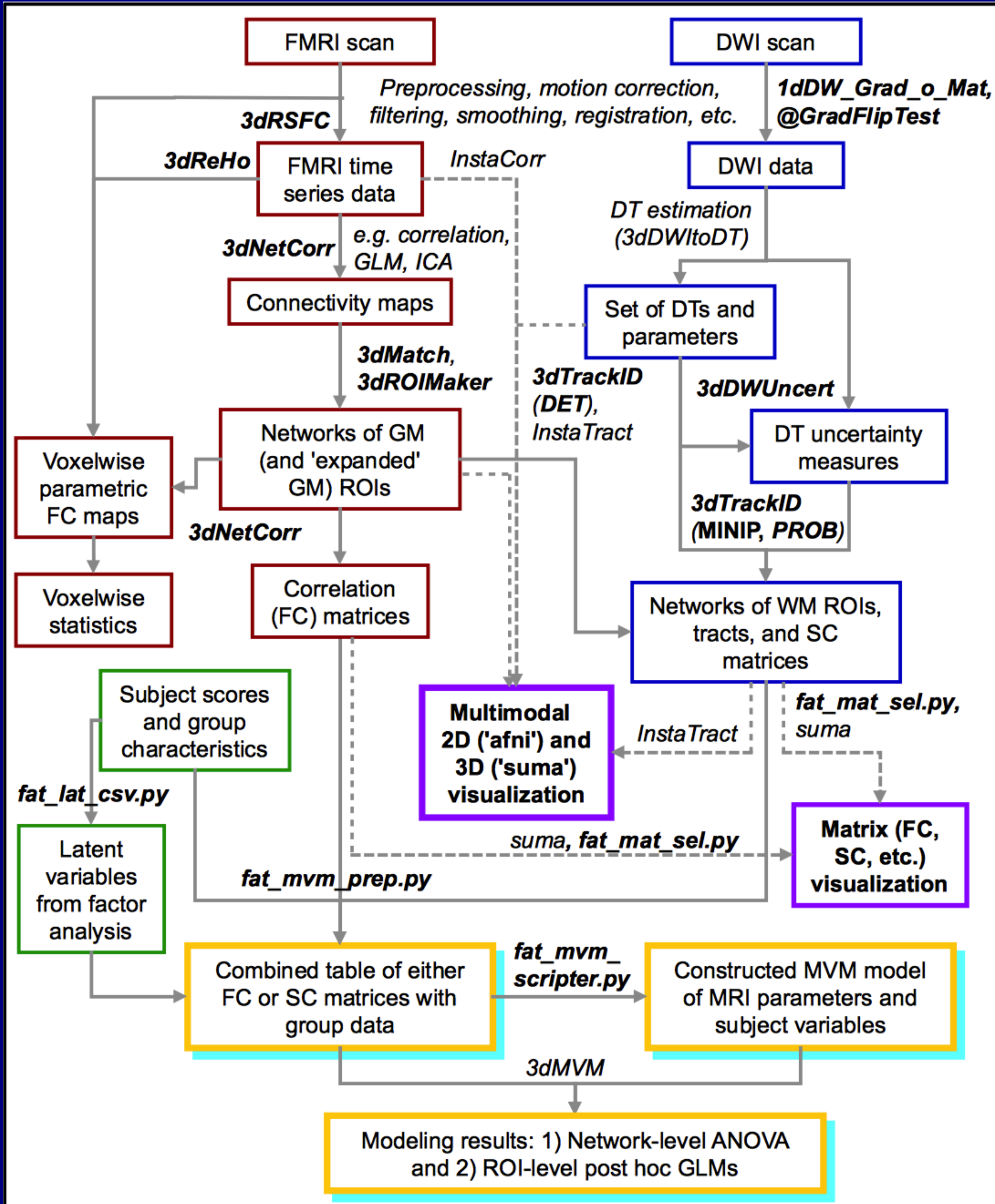
+ determining networks from FMRI, parcellation or other data;
+ finding correlations and local properties of functional networks;
+ turning GM ROIs into targets for tractography;
+ doing reasonable tractography to find WM ROIs;
+ estimating stats on WM ROIs...

FATCAT: Functional And Tractographic Connectivity Analysis Toolbox

(*Taylor & Saad, 2013, BC; Taylor et al. 2015, BC*)

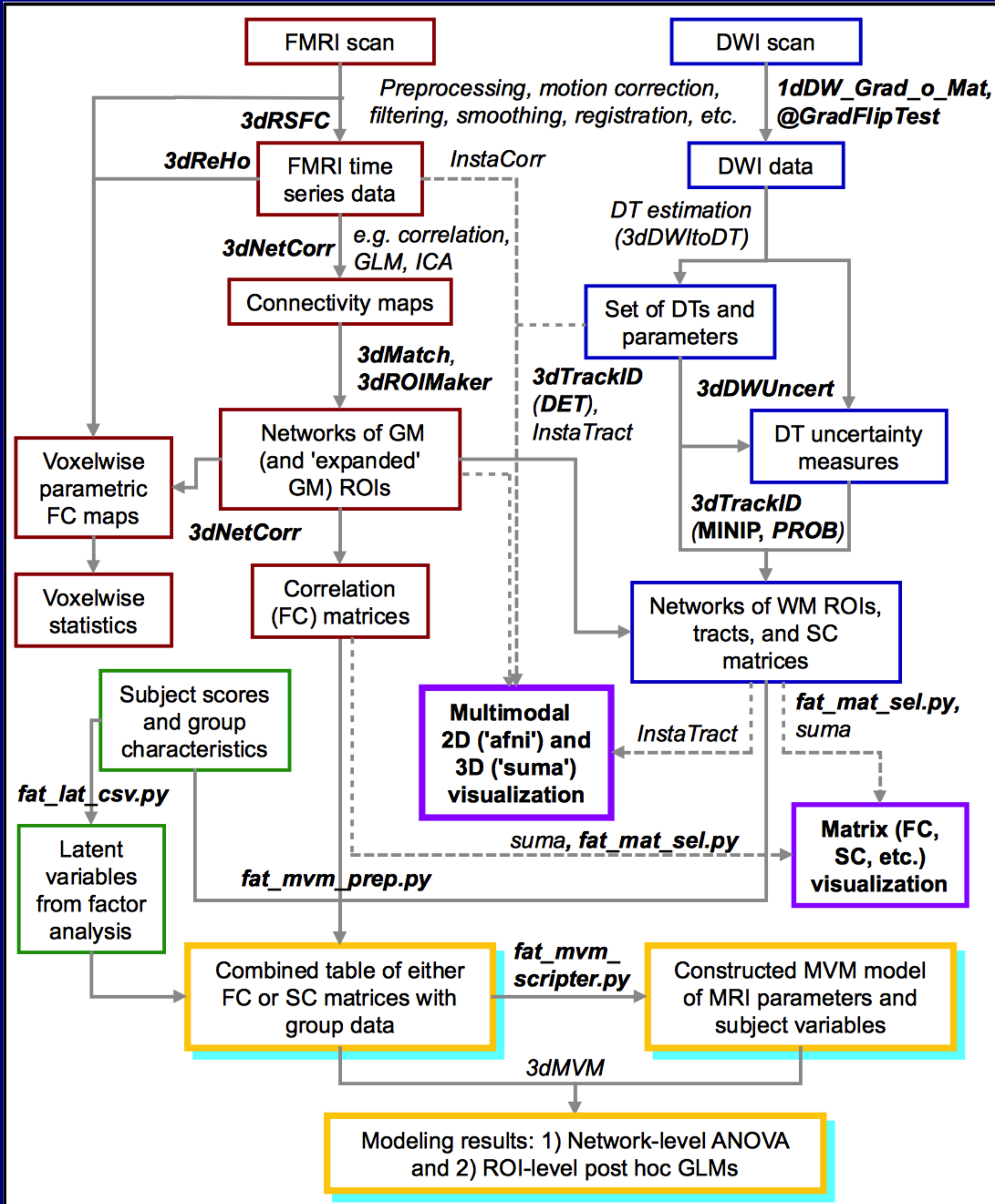
Demos in AFNI: @Install_FATCAT_DEMO, @Install_FATMVM_DEMO

Schematic for combining FMRI and DTI-tractography via FATCAT



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

(Taylor, Chen, Cox & Saad, 2016)



Schematic for combining FMRI and DTI-tractography via FATCAT

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

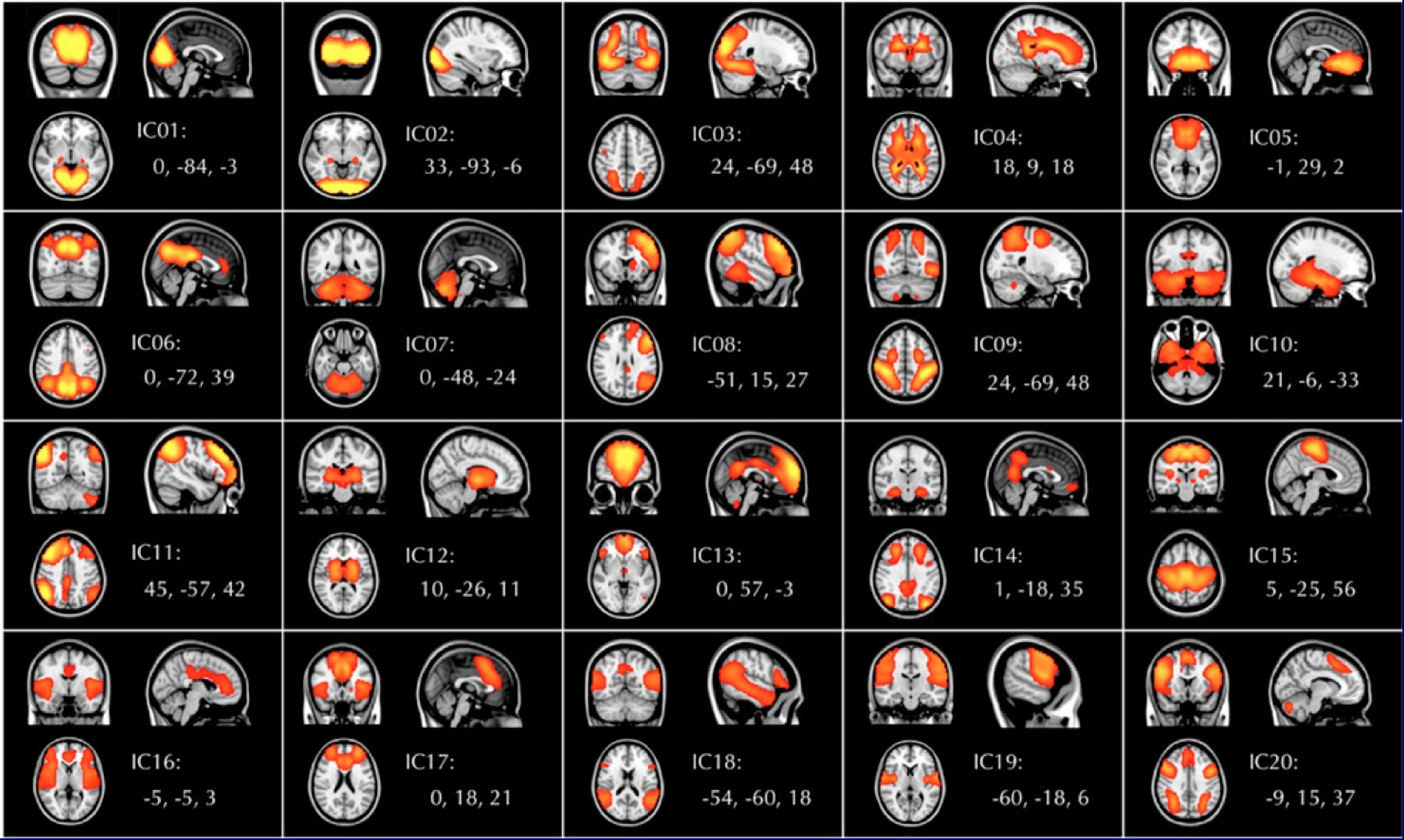
Main focus today on DTI-tractography, including making ROIs from FMRI

(Taylor, Chen, Cox & Saad, 2016)

Motivating example

Network view of both functional and structural data

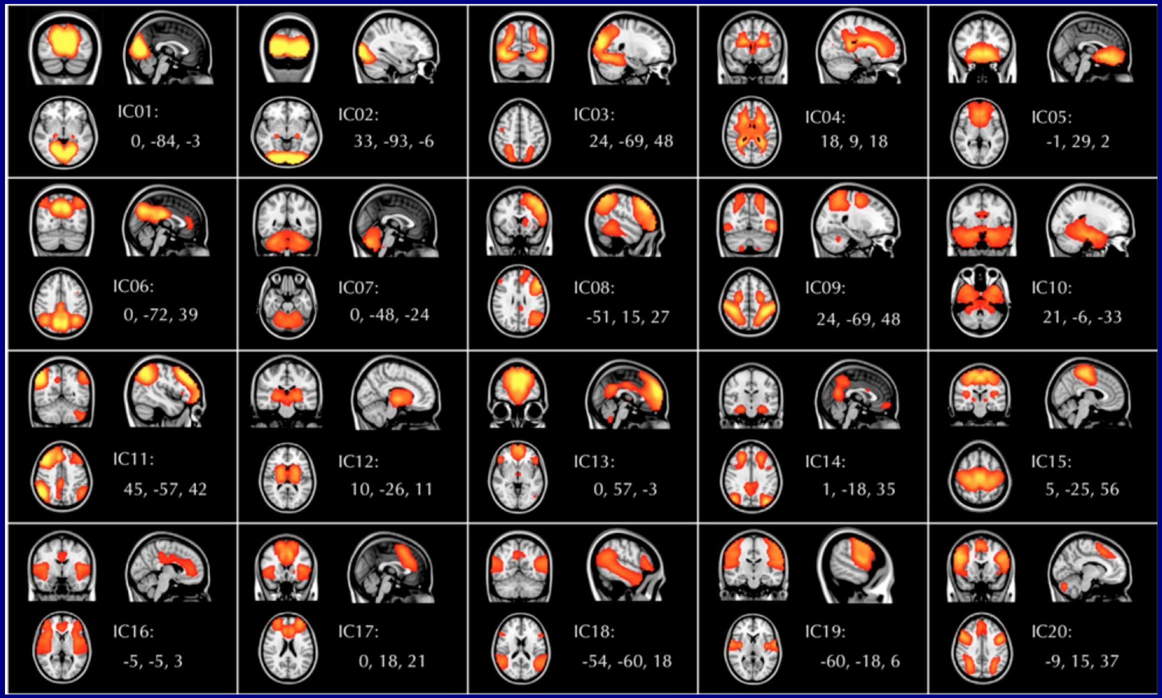
FMRI: GM Networks



(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.

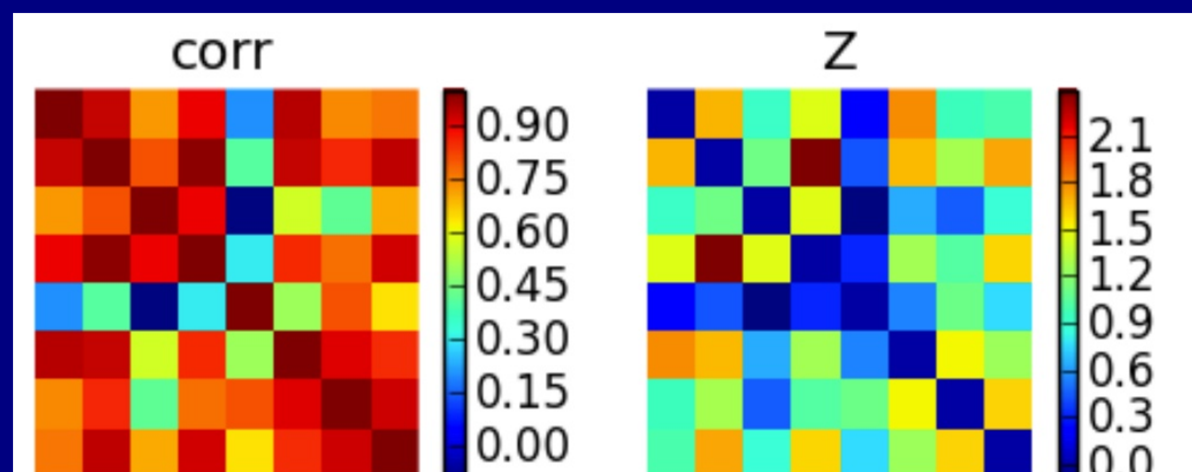
Sidenote:

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)



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

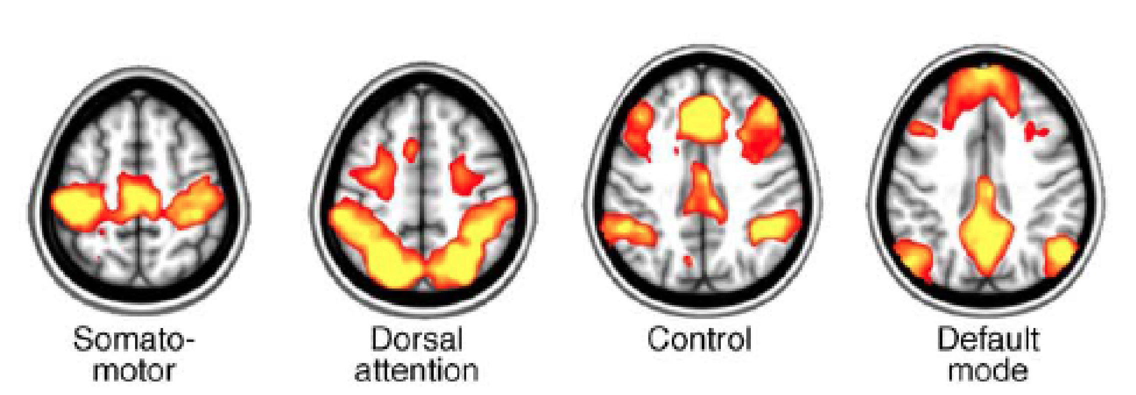
Applying tractography

Structure + Function

Simple example:

FMRI provides:
maps of (GM) regions working together

GM ROIs network:



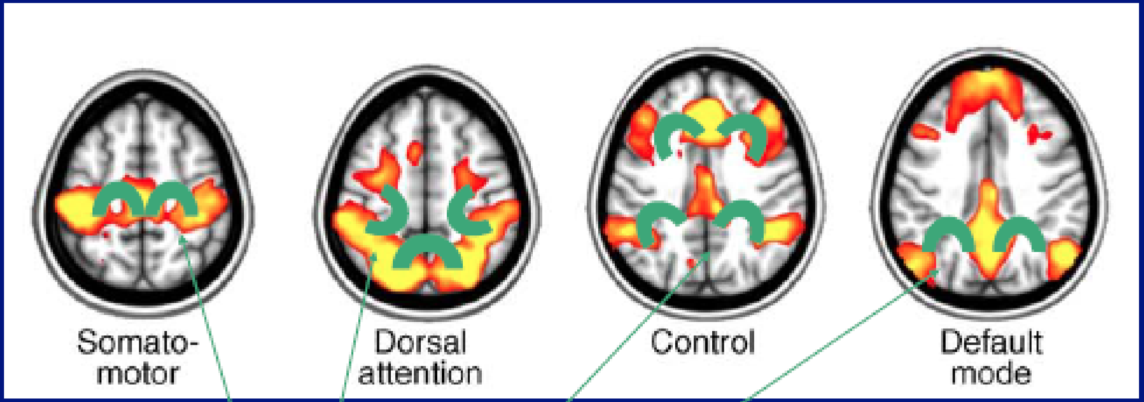
Raichle (2010, TiCS)

Structure + Function

Simple example:

FMRI provides:
maps of (GM) regions working together

GM ROIs network:



Raichle (2010, TiCS)

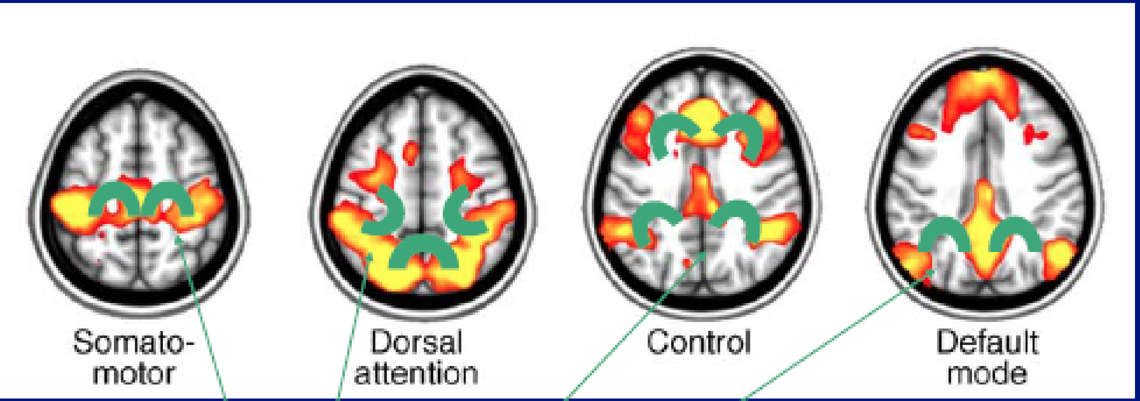
Associated WM ROIs

Structure + Function

Simple example:

FMRI provides:
maps of (GM) regions working together

GM ROIs network:

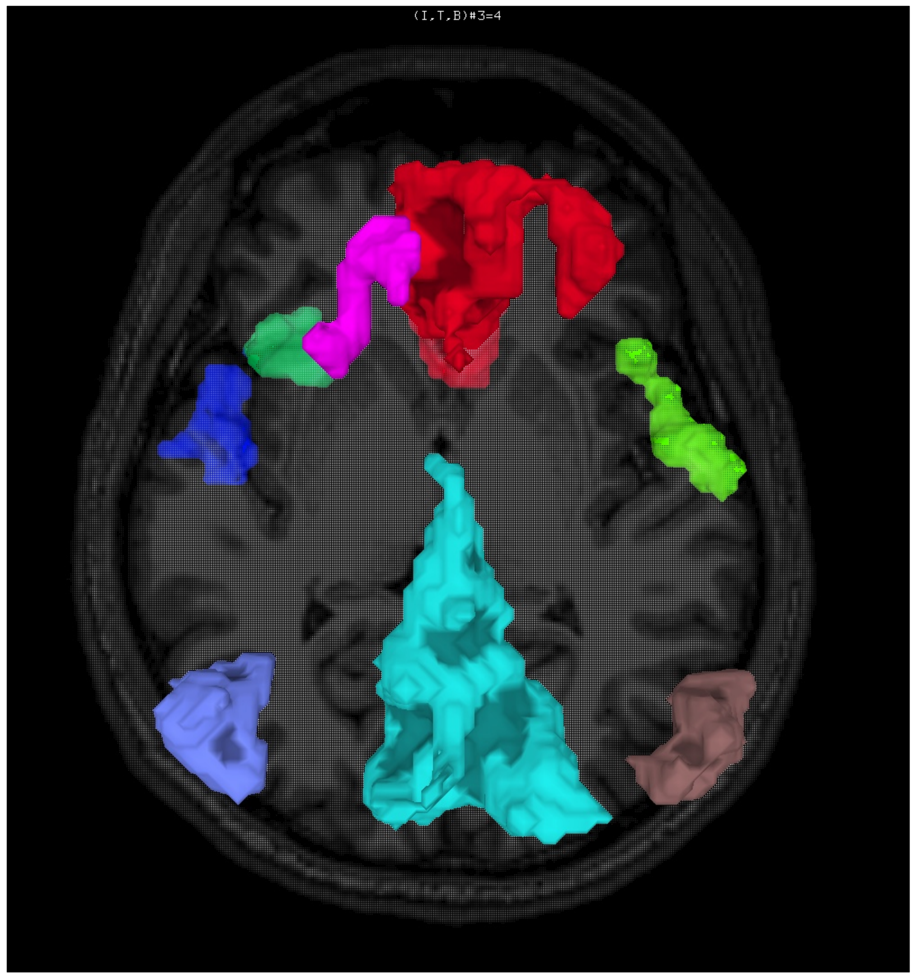


Raichle (2010, TiCS)

Associated WM ROIs

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

Describing and comparing "modes" of tracking in 3dTrackID, with example network of targets:



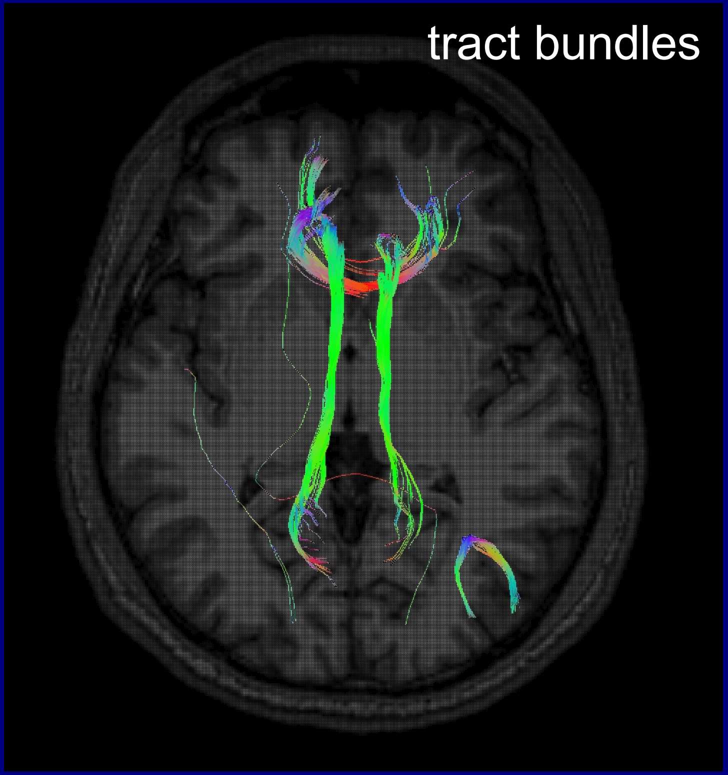
SUMA view of targets from FMRI (axial view, S->I)

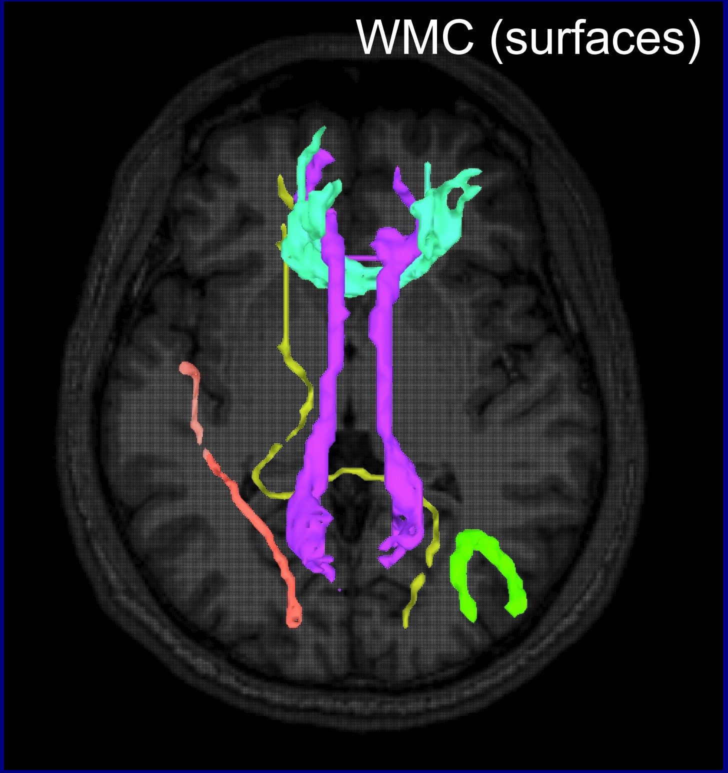
Tracking modes: DET

Deterministic tracking
+ For each FA-WM voxel (e.g., FA>0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic).
+ Can delete "bad" bundles with too few tracts.

+ Output:
 tract bundles,
 volumetric map of WMCs,
 and *matrix of structural properties.*

--> **DET** is OK for quick testing, QC, general data checking, but does not take into account uncertainty; don't know how reliable or noise-dependent results are. Mostly just used for quick, WB QC.





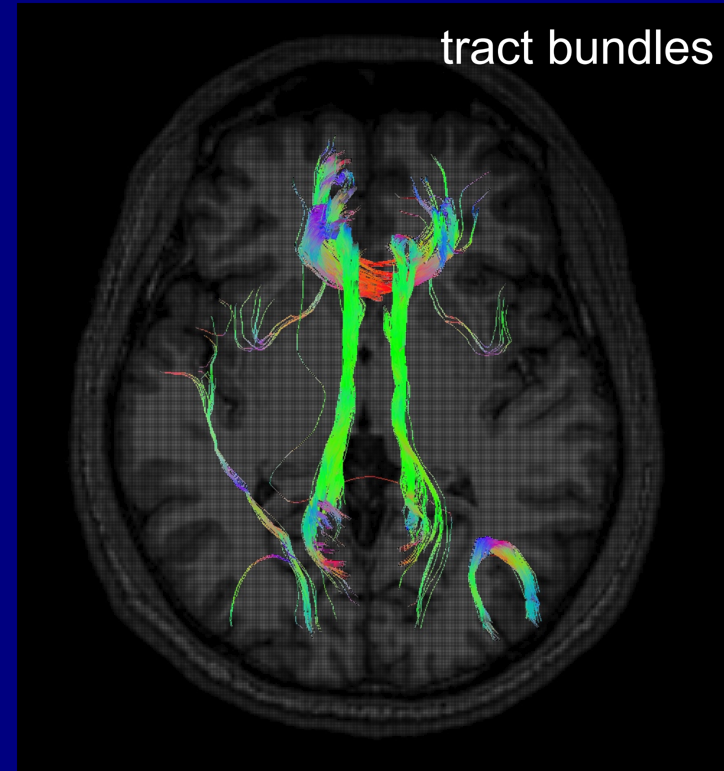
Tracking modes: **MINIP**

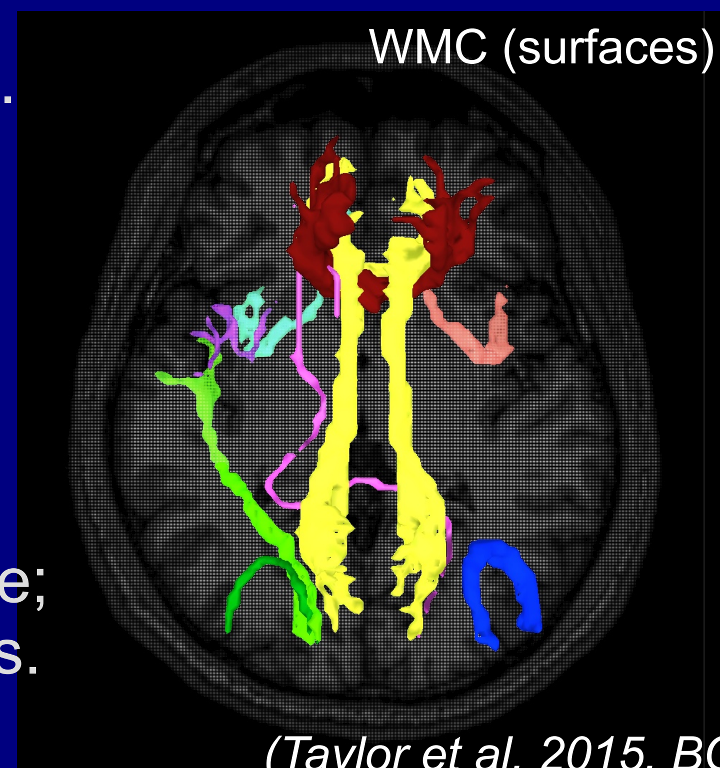
Mini-probabilistic tracking

+ For each FA-WM voxel (e.g., FA>0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic);
+ **Then**, perturb every tensor randomly, according to its estimated uncertainty (-> desc. below), and then do WB tracking. Repeat a few (~5-7) times.
+ Can delete "bad" bundles with too few tracts.

+ Output:
  tract bundles,
  volumetric map of WMCs,
  ***and** matrix of structural properties.*

--> **MINIP** improves on DET: accounts for noise; easier to detect spurious bundles; better vis. than DET. But no voxelwise thresholding...





(Taylor et al. 2015, BC)

Tracking modes: PROB

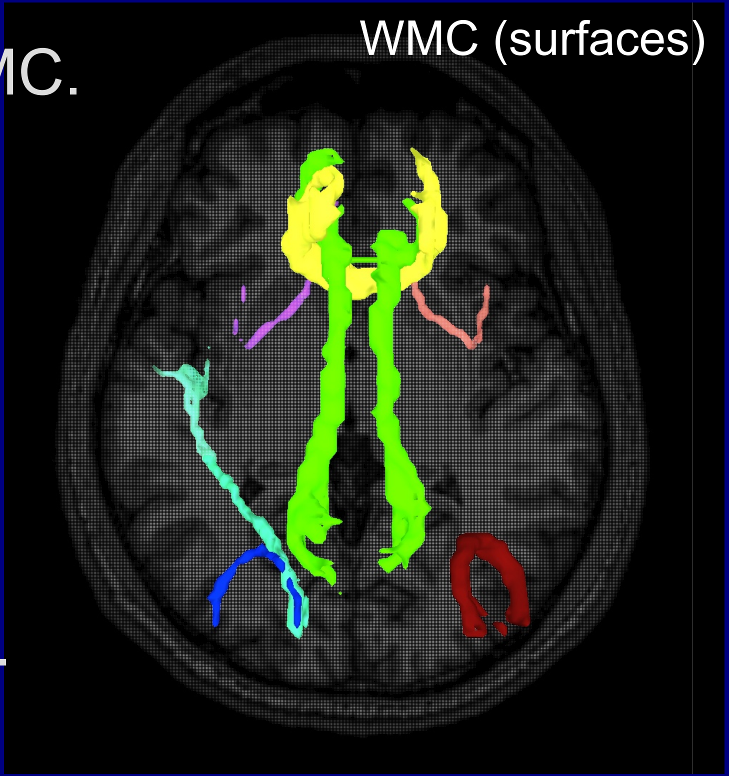
(full) probabilistic tracking

+ For each FA-WM voxel (e.g., FA>0.2), place seedpoint(s), track from each until stop criterion reached, and keep tracts through ROIs (AND- or OR-logic);
+ **Then**, perturb every tensor randomly, according to its estimated uncertainty (-> desc. below), and then do WB tracking. Repeat many (~thousands) times.
+ Threshold tract count **per voxel** to make WMC.

+ Output:
  volumetric map of WMCs,
  ***and** matrix of structural properties.*

--> **PROB** is most robust tracking: noise most strongly accounted for, and each WMC is built with **per voxel** criterion of tract counts. Produces best "likelihood" map of WMC.

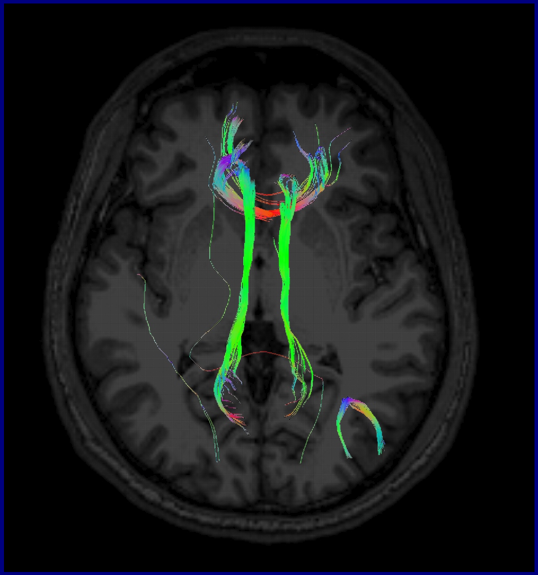
No bundles output
They are only used to build up prob. map

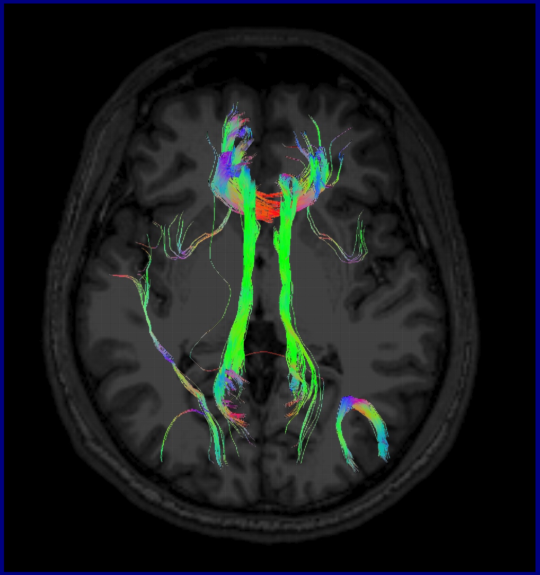


Bundles/WMCs comparisons per mode

DET | **MINIP** | **PROB**

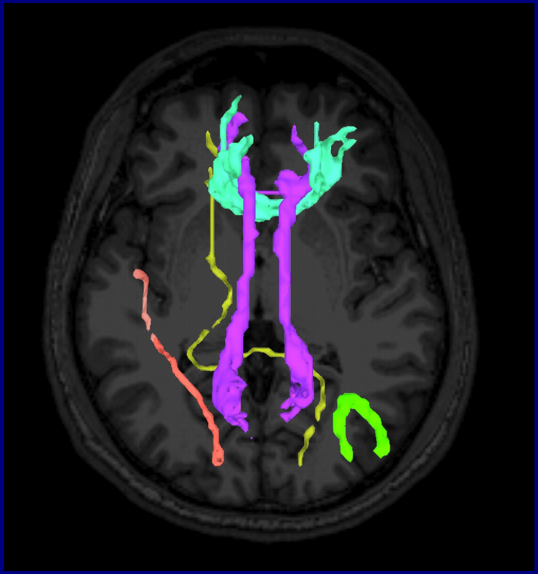
Tract bundles

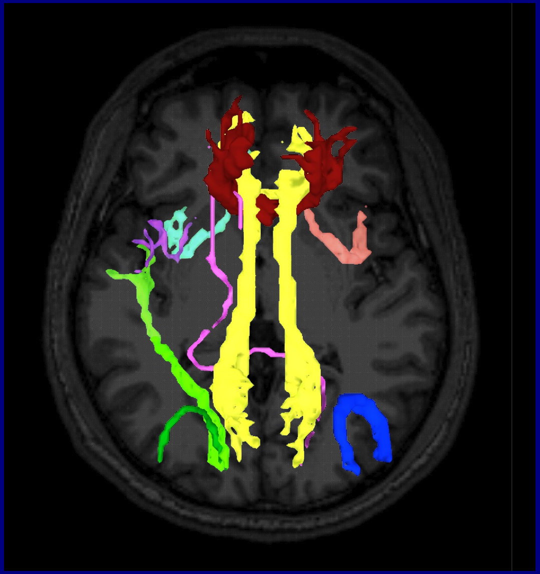


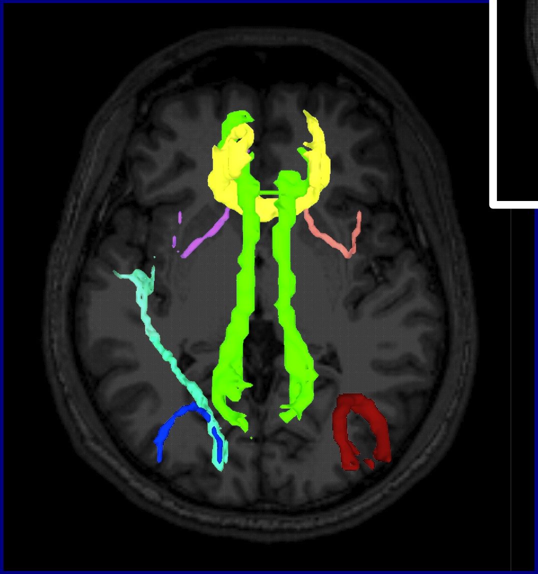


<u>No bundles output</u>
They are only used to build up prob. map

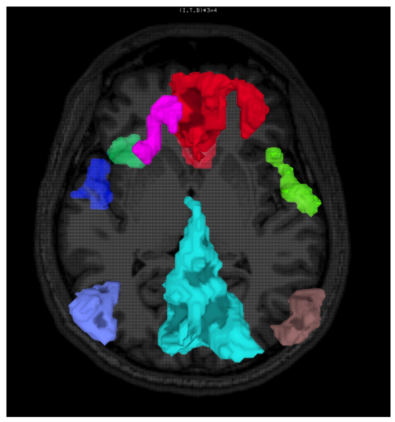
WMC surfaces







Target ROIs



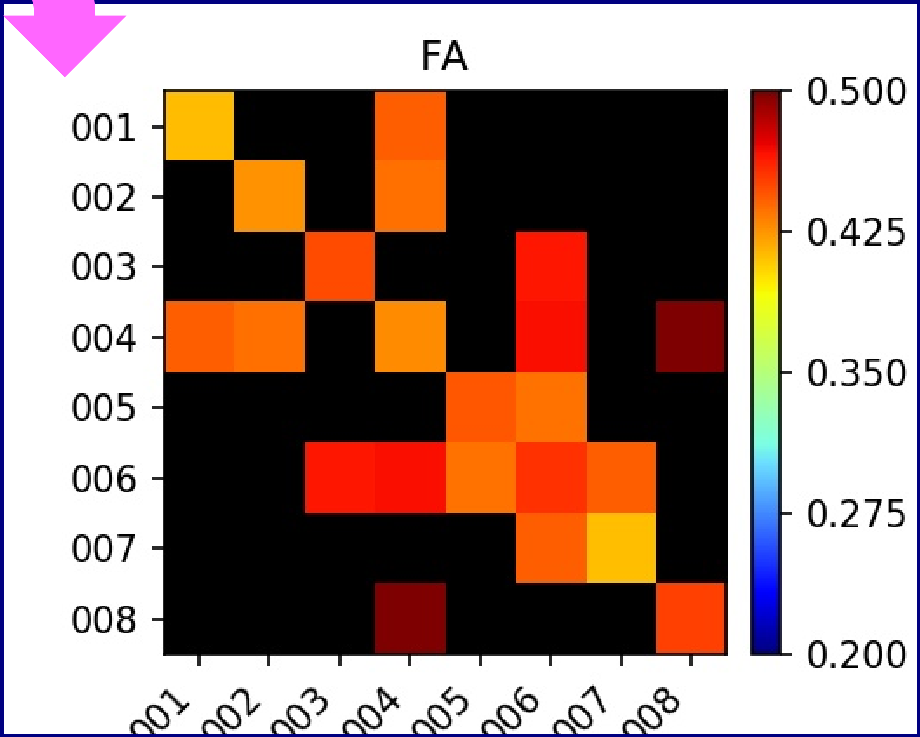
Bundles/WMCs comparisons per mode

DET **MINIP** **PROB**

Importantly, each mode **automatically** makes a file containing matrices of structural properties

-> these will be used quantitative analysis & statistical modeling.

```
# 8  # Number of network ROIs
# 15  # Number of grid matrices
# WITH_ROI_LABELS
        001          002          003          004          005          006          007          008
          1            2            3            4            5            6            7            8
# NT
      56825            0            0           69            0            0            0            0
          0       108697            0           50            0            0            0            0
          0            0        32576            0            0          252            0            0
         69           50            0       609454            0        20305            0         6707
          0            0            0            0       238636         4096            0            0
          0            0          252        20305         4096      1216505           82            0
          0            0            0            0            0           82       264950            0
          0            0            0         6707            0            0            0       201024
# fNT
3.698318e-03 0.000000e+00 0.000000e+00 4.490698e-06 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 7.074281e-03 0.000000e+00 3.254129e-06 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 2.120130e-03 0.000000e+00 0.000000e+00 1.640081e-05 0.000000e+00 0.000000e+00
4.490698e-06 3.254129e-06 0.000000e+00 3.966484e-02 0.000000e+00 1.321502e-03 0.000000e+00 4.365089e-04
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 1.553105e-02 2.665782e-04 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 1.640081e-05 1.321502e-03 2.665782e-04 7.917328e-02 5.336771e-06 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 5.336771e-06 1.724363e-02 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 4.365089e-04 0.000000e+00 0.000000e+00 0.000000e+00 1.308316e-02
# PV
1.241600e+04 0.000000e+00 0.000000e+00 3.360000e+02 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 1.908800e+04 0.000000e+00 3.280000e+02 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 1.578400e+04 0.000000e+00 0.000000e+00 1.176000e+03 0.000000e+00 0.000000e+00
3.360000e+02 3.280000e+02 0.000000e+00 5.860800e+04 0.000000e+00 7.272000e+03 0.000000e+00 4.688000e+03
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 2.372800e+04 1.584000e+03 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 1.176000e+03 7.272000e+03 1.584000e+03 1.087440e+05 3.040000e+02 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 3.040000e+02 2.150400e+04 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 4.688000e+03 0.000000e+00 0.000000e+00 0.000000e+00 2.936000e+04
# fNV
9.200799e-03 0.000000e+00 0.000000e+00 2.489907e-04 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 1.414504e-02 0.000000e+00 2.430623e-04 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 1.169663e-02 0.000000e+00 0.000000e+00 8.714675e-04 0.000000e+00 0.000000e+00
2.489907e-04 2.430623e-04 0.000000e+00 4.343109e-02 0.000000e+00 5.388870e-03 0.000000e+00 3.474013e-03
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 1.758349e-02 1.173813e-03 0.000000e+00 0.000000e+00
0.000000e+00 0.000000e+00 8.714675e-04 5.388870e-03 1.173813e-03 8.058406e-02 2.252773e-04 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00 2.252773e-04 1.593540e-02 0.000000e+00
0.000000e+00 0.000000e+00 0.000000e+00 3.474013e-03 0.000000e+00 0.000000e+00 0.000000e+00 2.175704e-02
# NV
1.552000e+03 0.000000e+00 0.000000e+00 4.200000e+01 0.000000e+00 0.000000e+00 0.000000e+00 0.000000e+00
```



3dTrackID: choosing a "mode"

DET

+ Initial, quick QC of full DWI data (e.g., WB tracking)
+ Check gradient flip (-> @GradFlipTest)

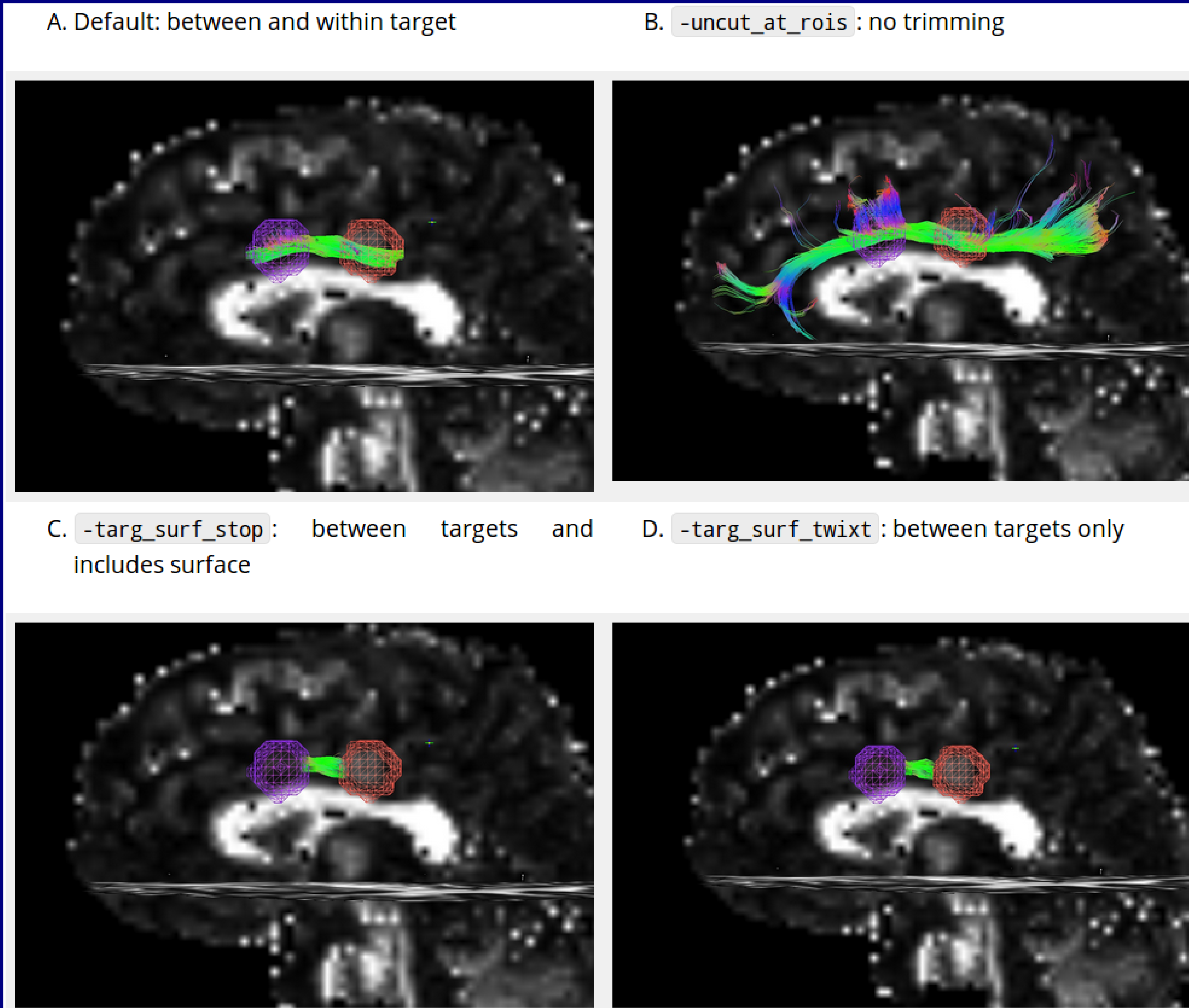
MINIP

+ Quick network check
+ Visualize tract bundles, esp. for example figure
+ Requires uncert. calc. (3dDWUncert)

PROB

+ **The choice for quantitative work**
+ *Can* also visualize WMCs as RGB or per-bundle coloring
+ Requires uncert. calc. (3dDWUncert)
+ Is slower.... but not too bad.

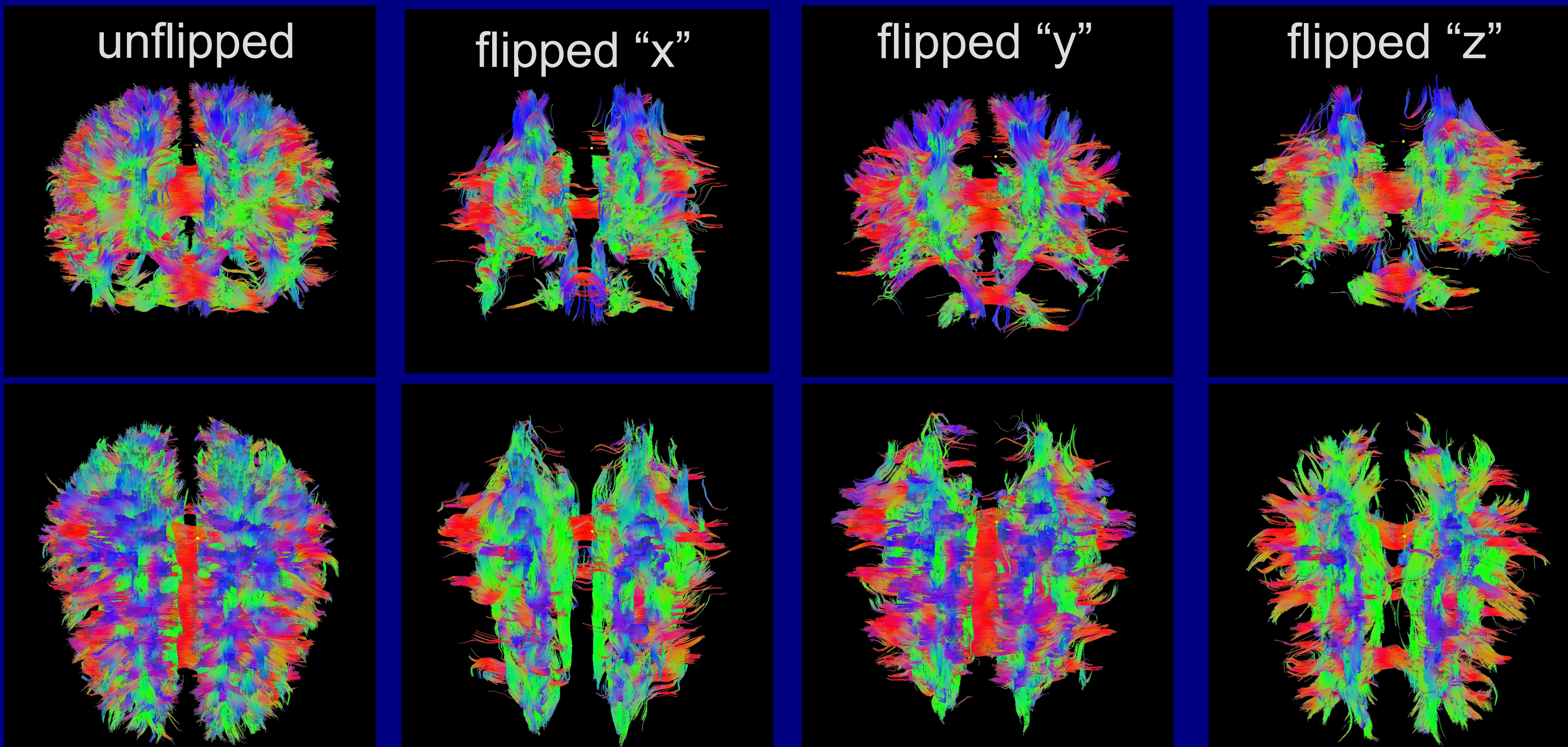
3dTrackID: control tracts at surface boundaries



https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/Tracking.html#using-target-surfaces-to-control-tract-trimming

@GradFlipTest: track WB to check grad format

+ Software and scanners have can have different definitions of +/- when interpreting scan directions. So, use WB tracking via **@GradFlipTest** to check and **1dDW_Grad_o_Mat++** to adjust/fix.



(Taylor et al. 2015, BC)

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/GradFlipTest.html

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/DealingWithGrads.html

Making network of targets for tracking

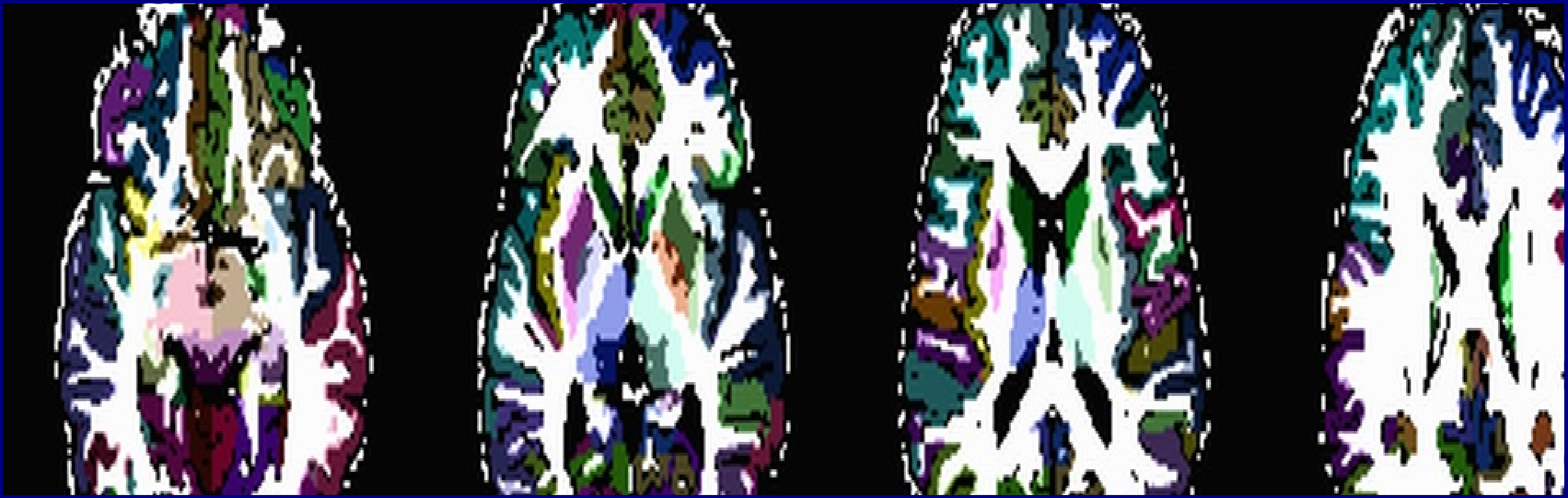
Ex. 1: from FreeSurfer parc/seg

Ex. 2: from FMRI maps

3dROIMaker: (controlled) ROI inflation

+ Target ROIs may be slightly "cut off" from the FA-WM masks, due to thresholding (e.g., FMRI) or alignment/resampling (e.g., FS/template or FMRI).
  Can use **3dROIMaker** to inflate targets a little to fill in gaps while not overrunning WM or other targets.

Ex. 1: olay: FS targets **pre-**inflation; ulay: FA>0.2 mask



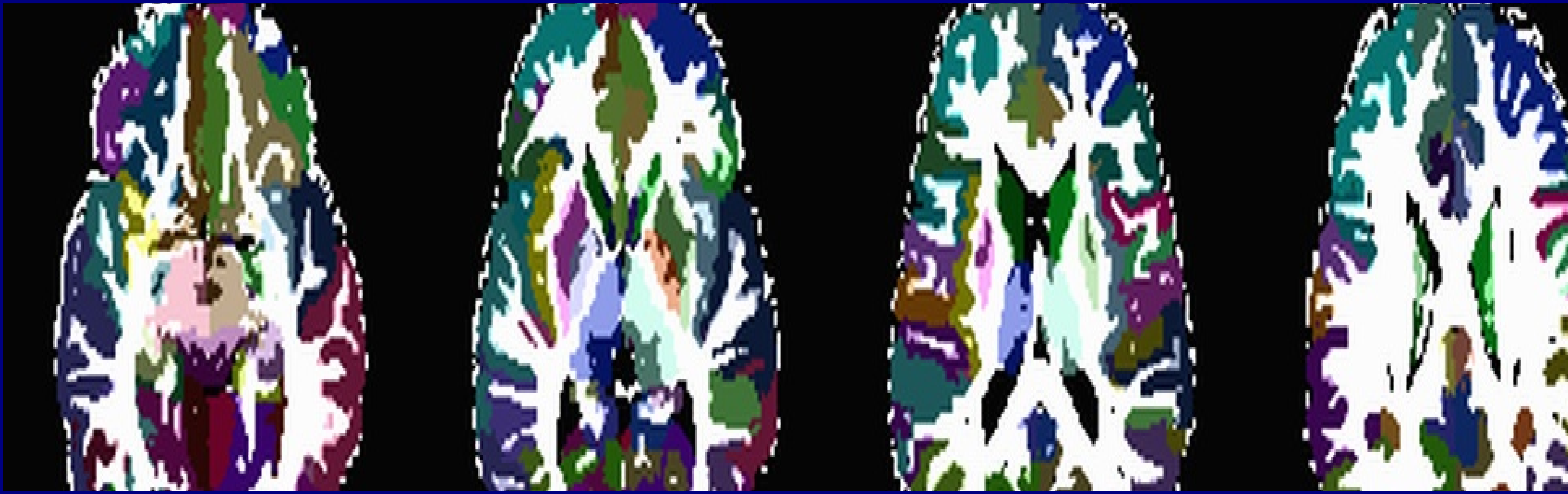
https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/MakingROIs.html

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/tutorials/fatcat_prep/Postprocessing_III.html

3dROIMaker: (controlled) ROI inflation

+ Target ROIs may be slightly "cut off" from the FA-WM masks, due to thresholding (e.g., FMRI) or alignment/resampling (e.g., FS/template or FMRI).
  Can use **3dROIMaker** to inflate targets a little to fill in gaps while not overrunning WM or other targets.

Ex. 1: olay: FS targets **pre-**inflation; ulay: FA>0.2 mask

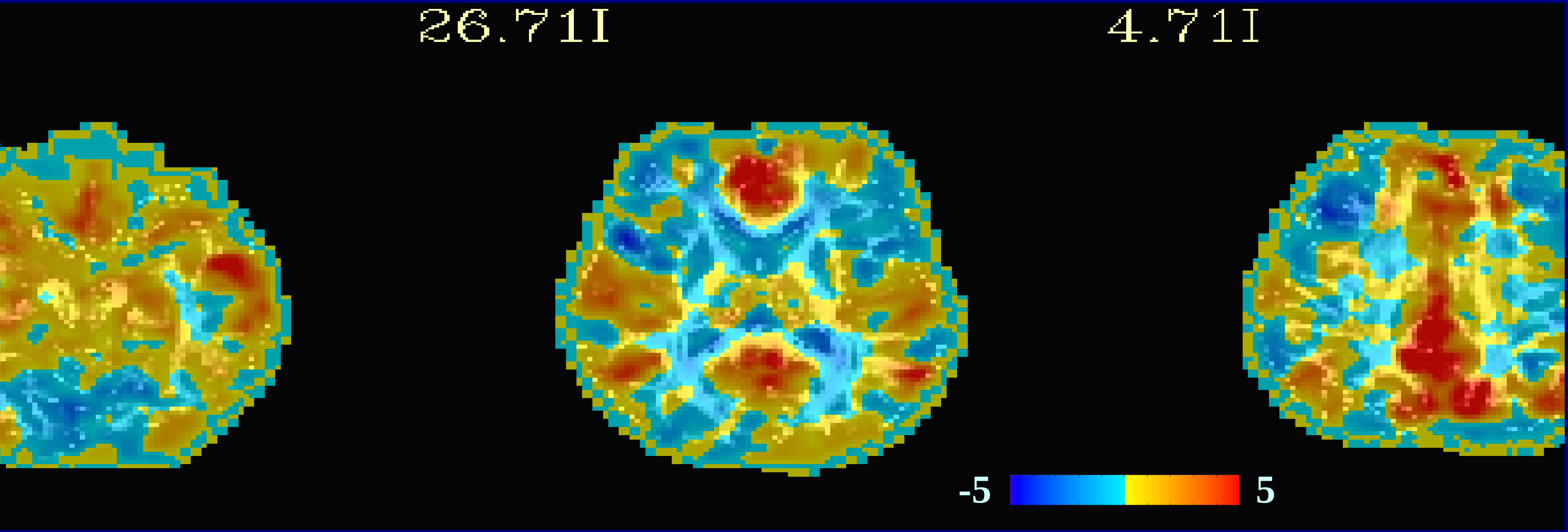


https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/FATCAT/MakingROIs.html

https://afni.nimh.nih.gov/pub/dist/doc/htmldoc/tutorials/fatcat_prep/Postprocessing_III.html

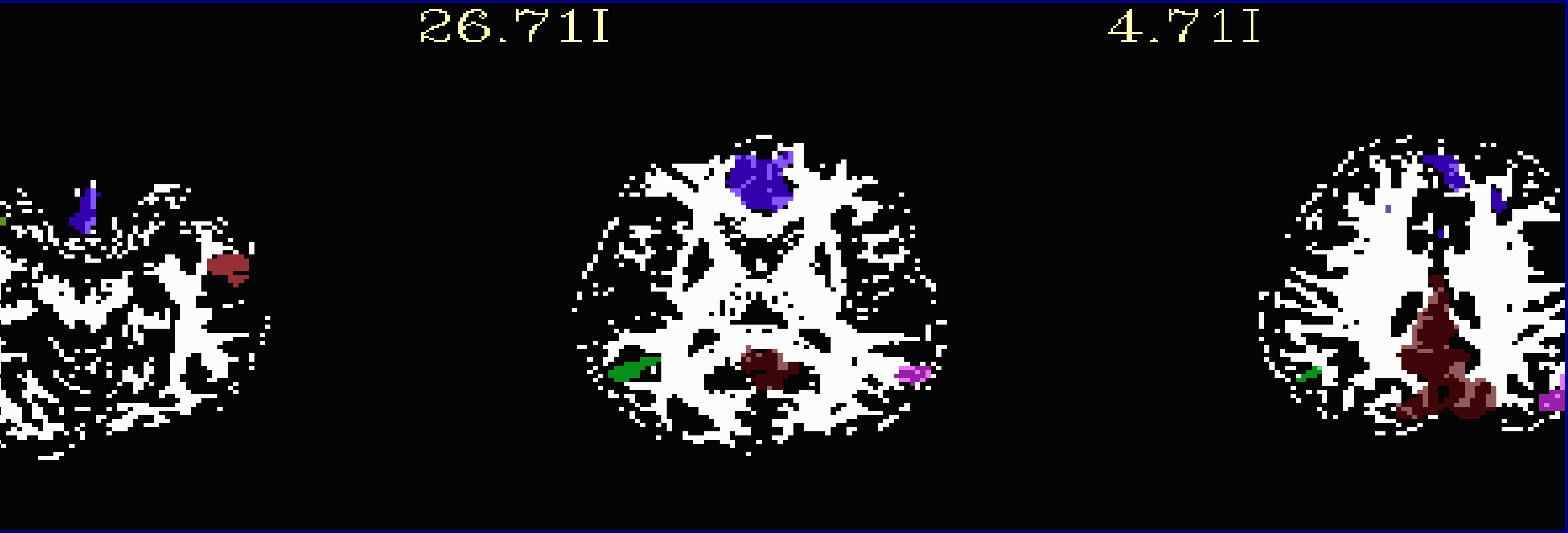
Ex. 2: FMRI-derived targets

1) Start with some FC map (seed-based correlation, ICA, etc.)
Here: olay = ICA map (Z-score values)
ulay = FA map



Ex. 2: FMRI-derived targets

2) Threshold FC map voxelwise and for size of clusters -> isolated ROIs
Here: olay = map of regions after thresholding
ulay = mask of FA>0.2 (-> FA-WM)

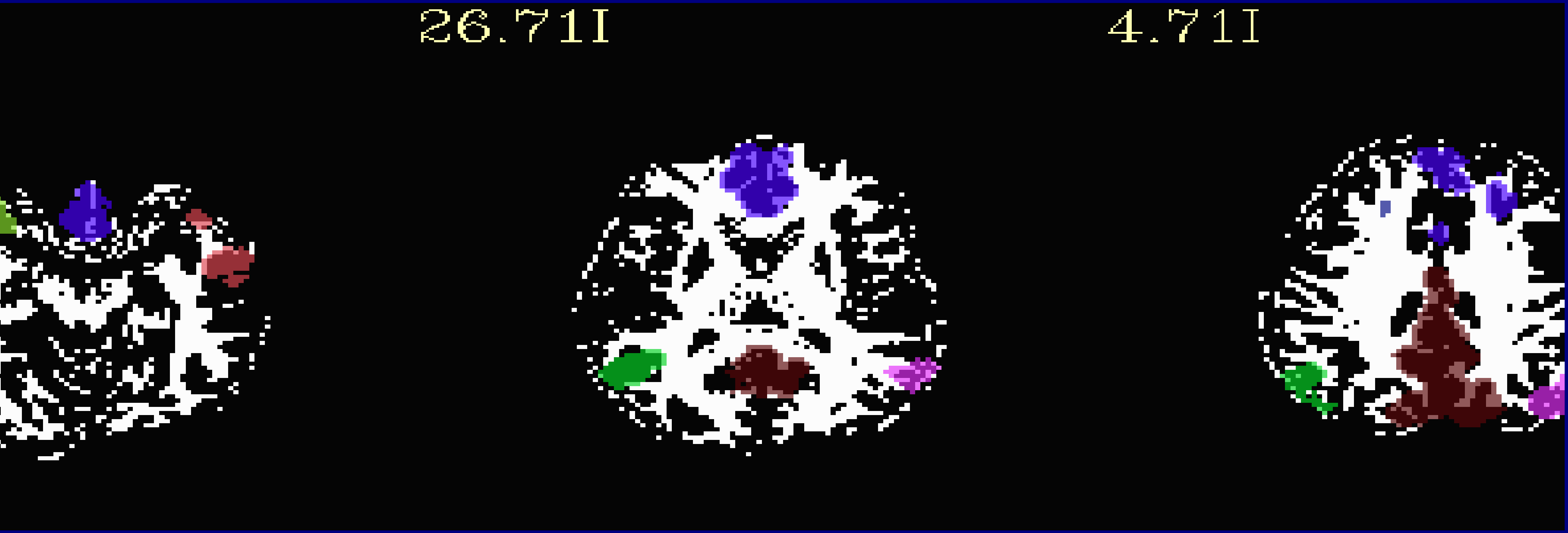


Ex. 2: FMRI-derived targets

3) Inflate isolated targets a small amount, constrain with FA-WM

Here: olay = inflated ROIs -> targets for tracking

ulay = mask of FA>0.2 (-> FA-WM)



3dROIMaker: additional features

+ Can remove overlap of regions with WM or CSF

+ Inflation options: inflation can stop just before or just after overlapping with FA-WM

+ Select subsets of ROIs with *N* highest values

+ Apply a “refset” to have consistent numbering+labelling of ROIs

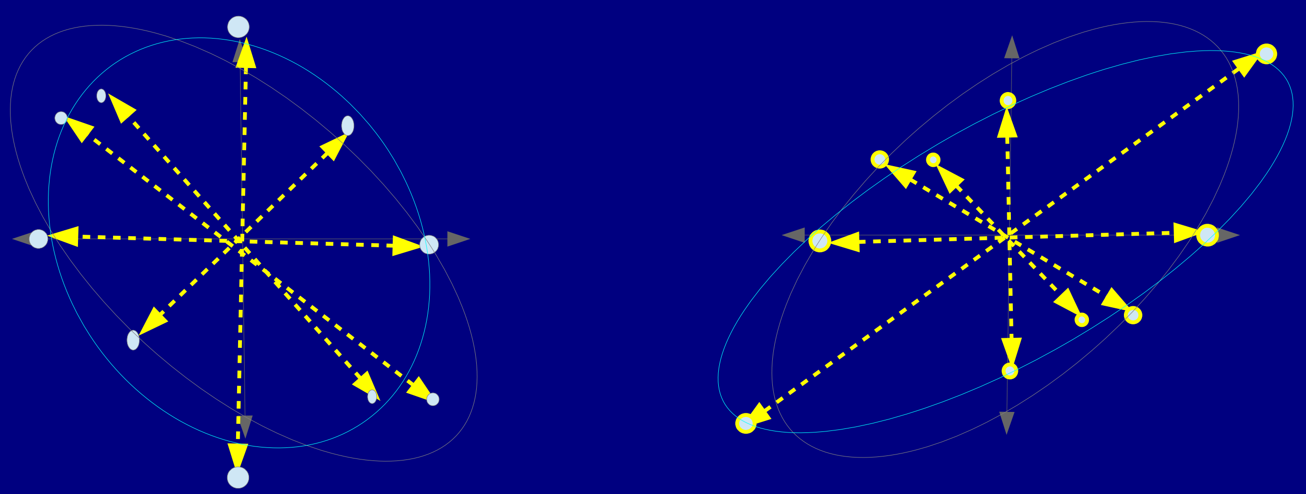
How do we estimate tensor parameter noise/uncertainty for MINIP and PROB tracking?

Recall: 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.

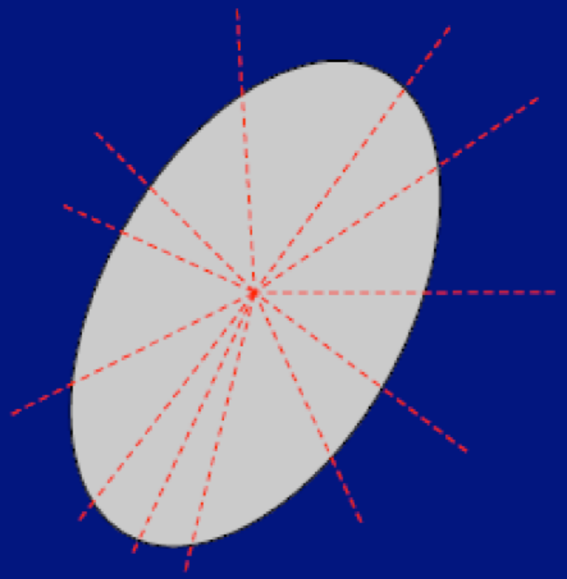
DTI Uncertainty

- 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

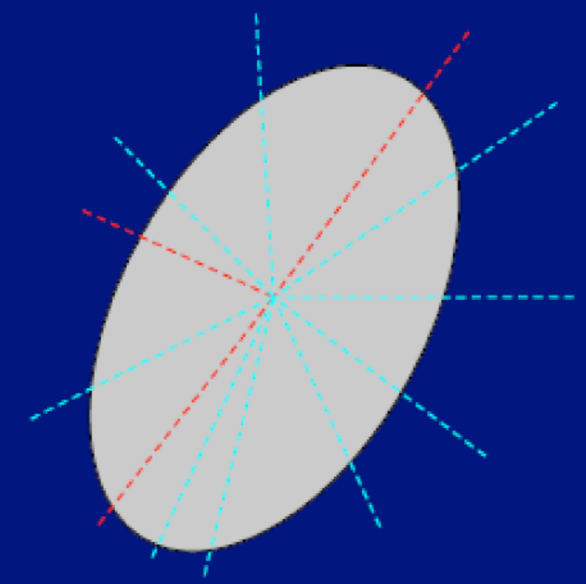
e.g., M=12



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

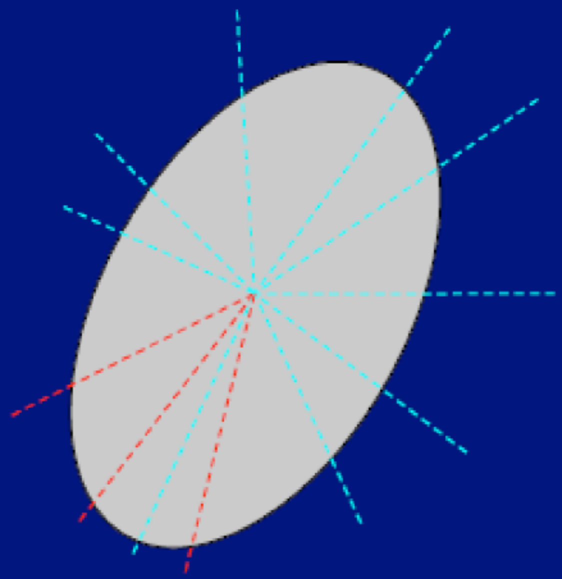


$$[D_{11}\ \ D_{22}\ \ D_{33}\ \ D_{12}\ \ D_{13}\ \ D_{23}] = \ldots$$

Jackknifing

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

e.g., M=12
M_J=9



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

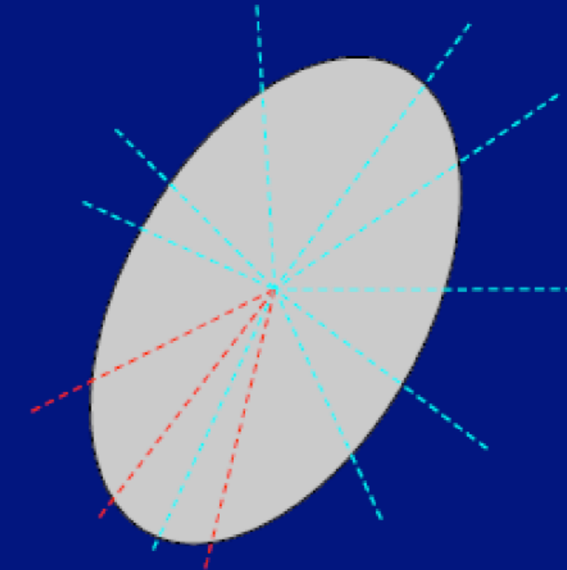
....

Jackknifing

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

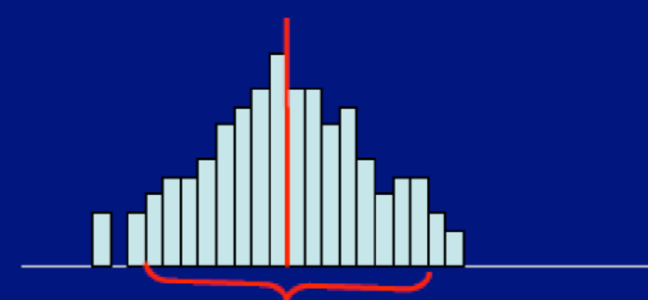
e.g., $M=12$

$M_J=9$



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

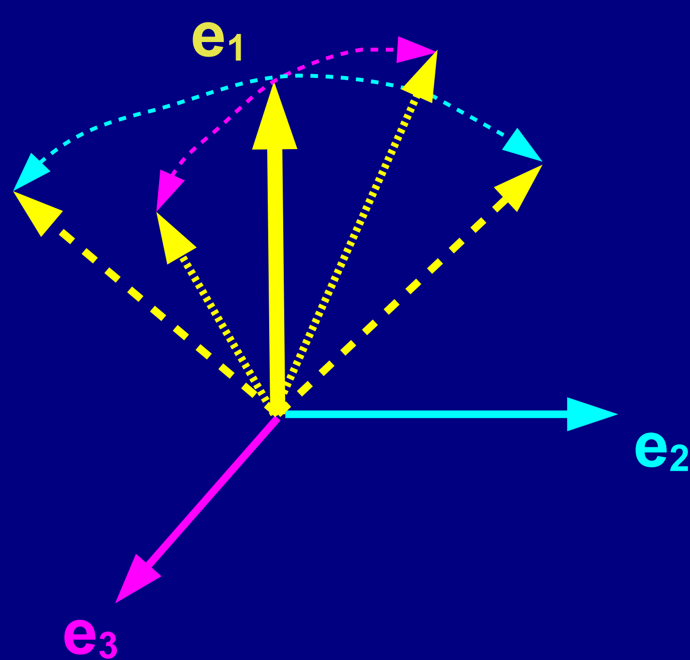
....



Uncertainty estimation

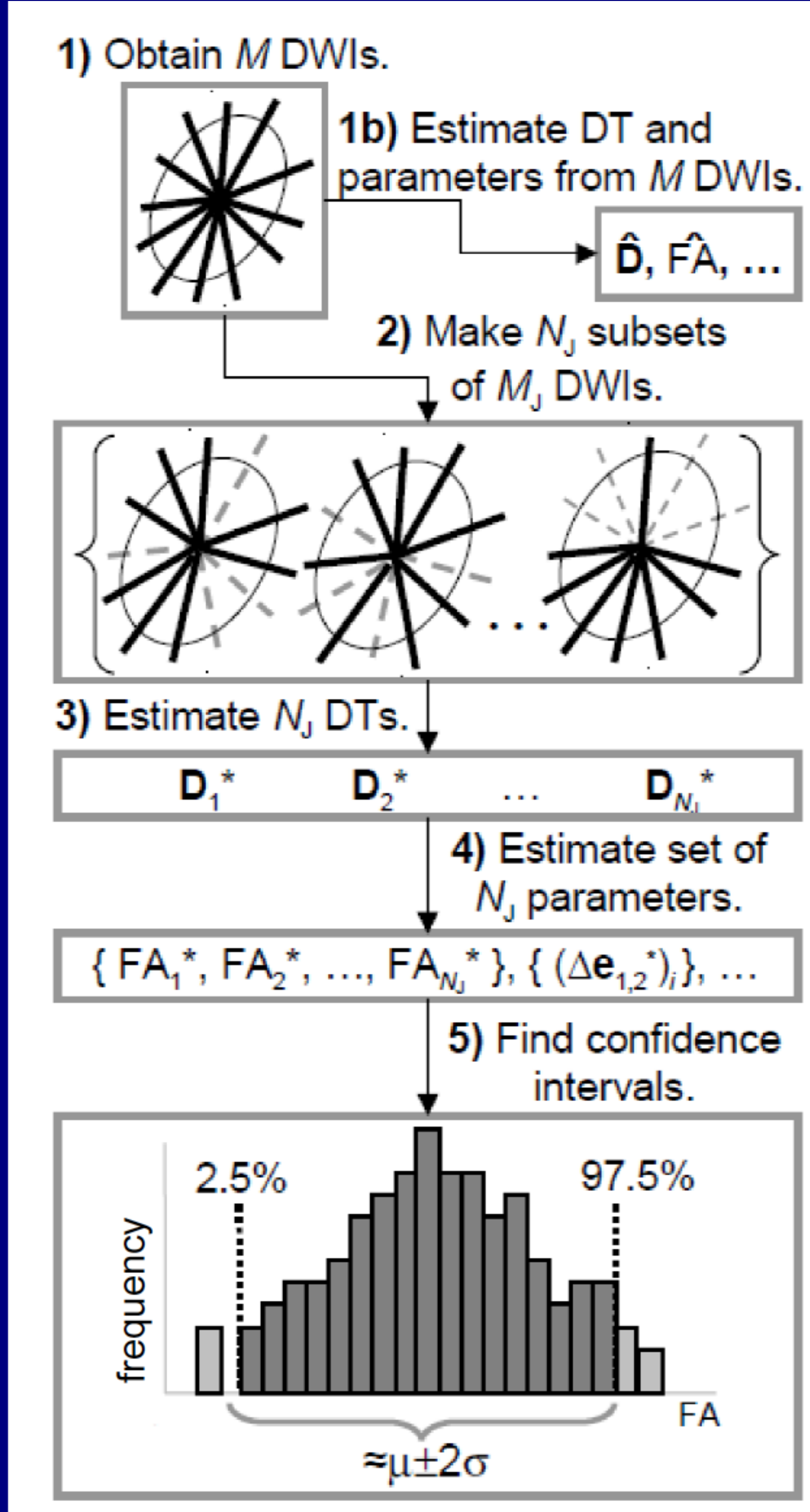
+ 3dDWUncert estimates

1) bias and σ of the first eigenvector $\mathbf{e_1}$ (main direction of diffusion), for two degrees of freedom: how much it could tip toward either $\mathbf{e_2}$ or $\mathbf{e_3}$:



2) and the bias and σ of (scalar) FA.

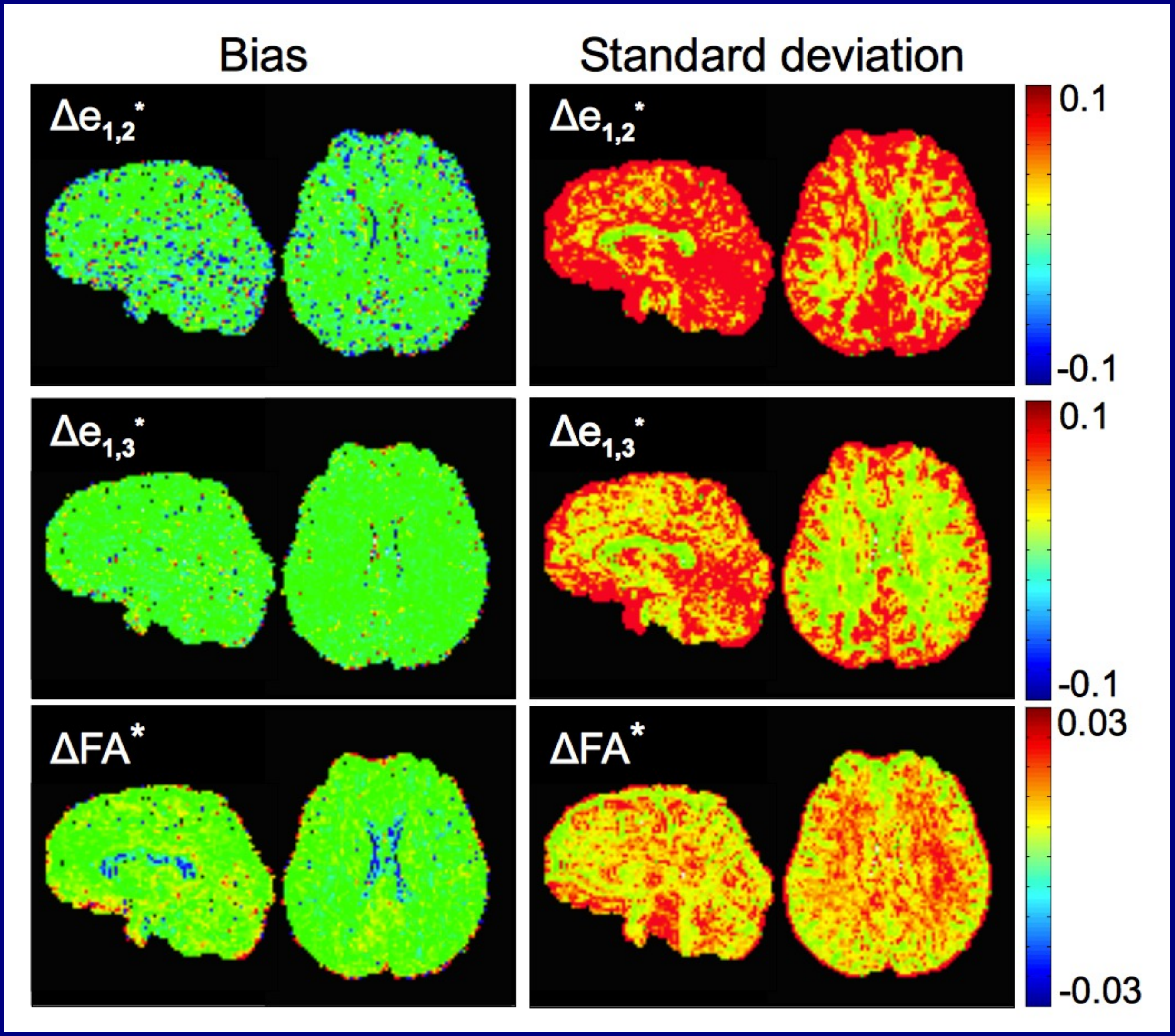
(Taylor & Saad. 2013, BC)



Uncertainty example

+ Can see difference in e_1 uncertainty along e_2 and e_3 (in rads).

+ Tissue-dependent differences in FA uncertainty.



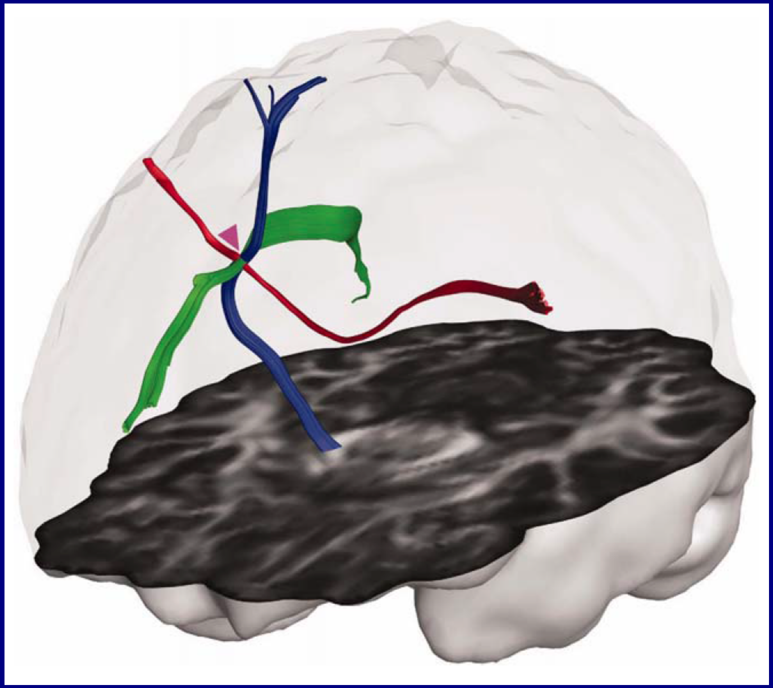
(Taylor & Saad. 2013, BC)

FATCAT addenda:

1) HARDI tracking

Higher order models

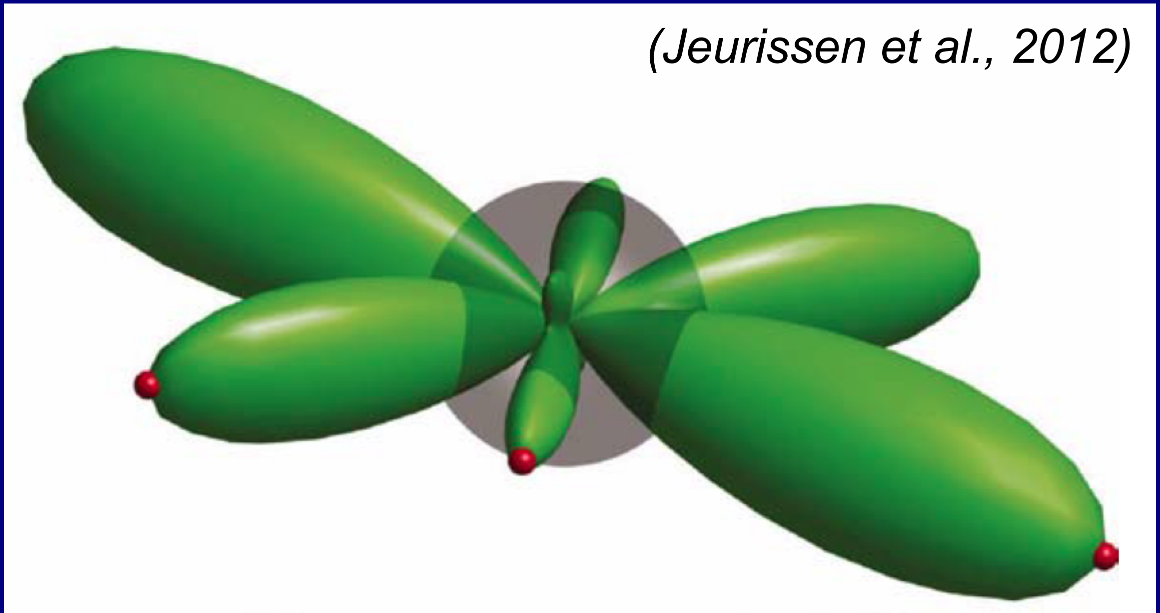
DTI tractography:
+ susceptible to false negatives, difficulty with
    long range tracts (noise/error accumulation)
+ Major diffusion can be average of multiple paths
+ Voxels can have low FA from several WM paths, false ending
+ Can't resolve complex underlying architecture
    - Jeurissen et al. (2012,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



(Jeurissen et al., 2012)

HARDI

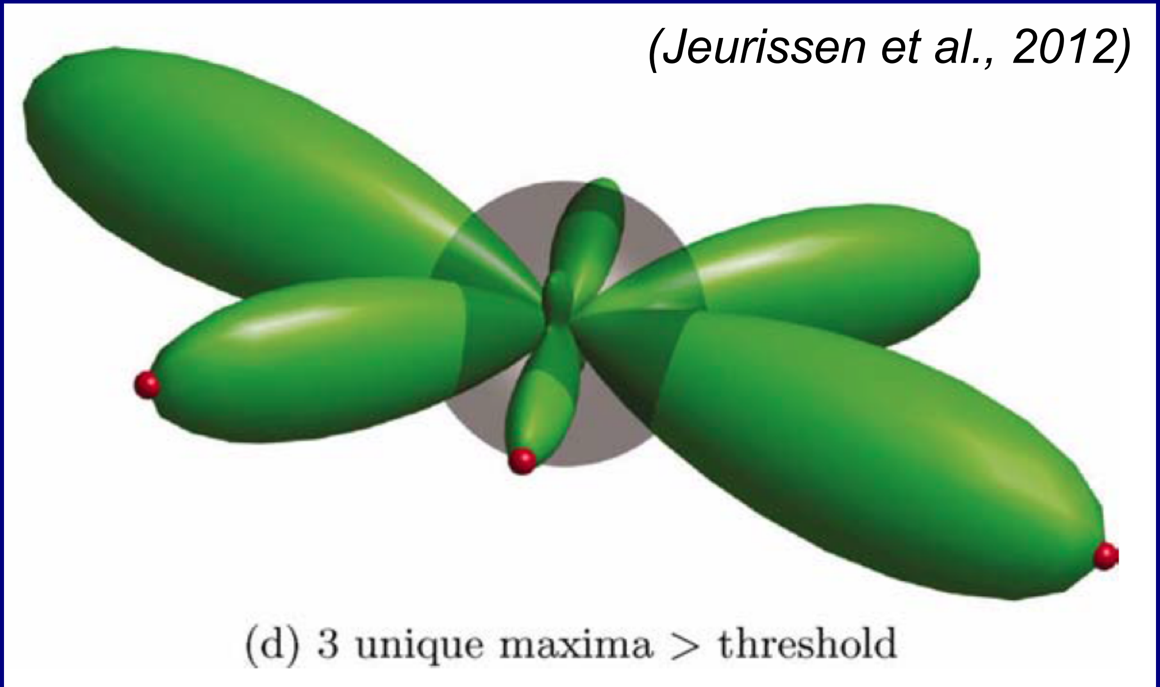
+ High Angular Resolution Diffusion Imaging:
    - DSI, ODF, Qball, FOD...
    - model multiple fiber bundle directions per voxel
    - generally need more scan time and acquisitions and computational power, much higher b-values
    - still can't resolve intravoxel tract behavior (which of multiple paths?)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



(d) 3 unique maxima > threshold

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

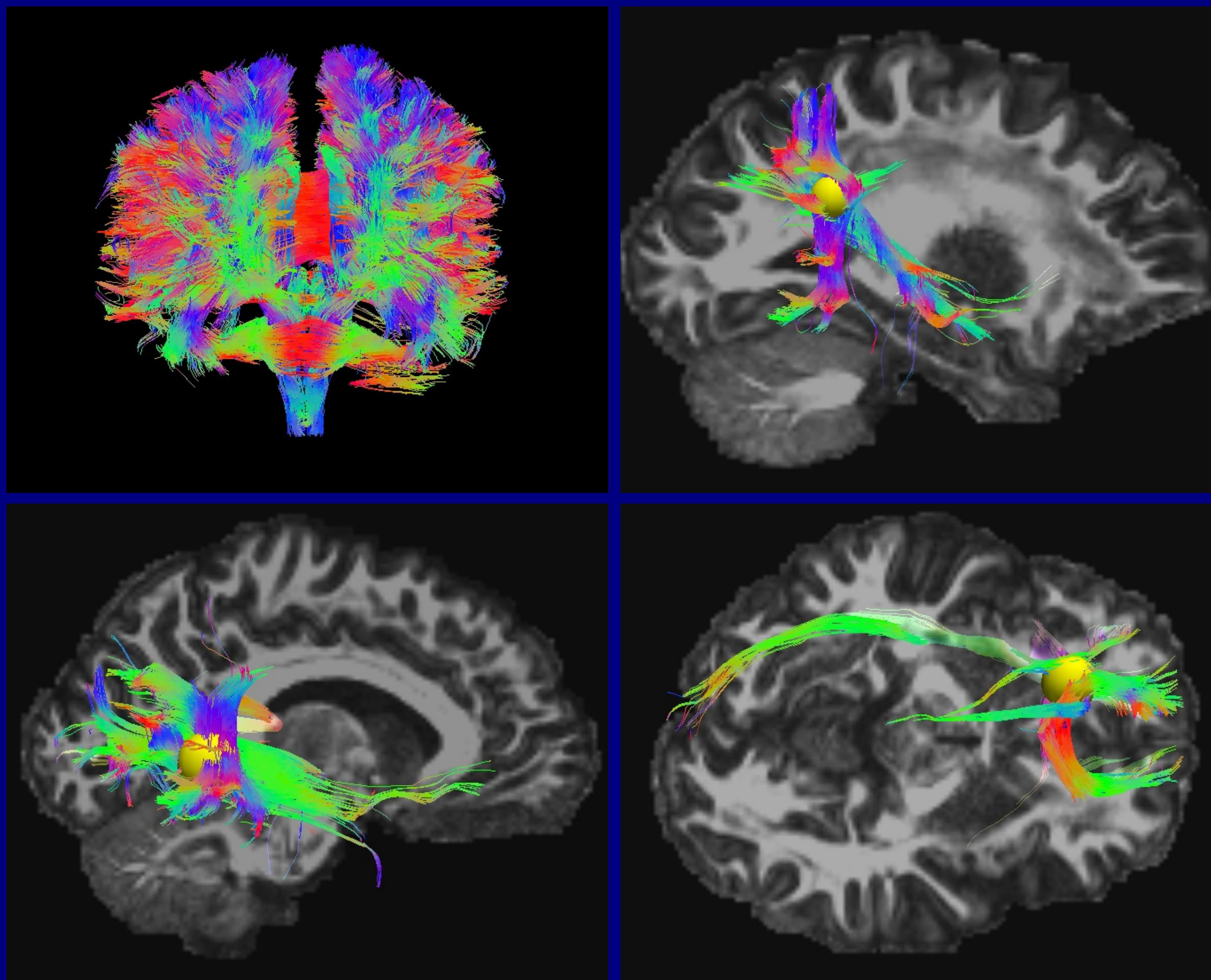


FATCAT can now track through HARDI data

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

Example: 3dTrackID on HARDI data

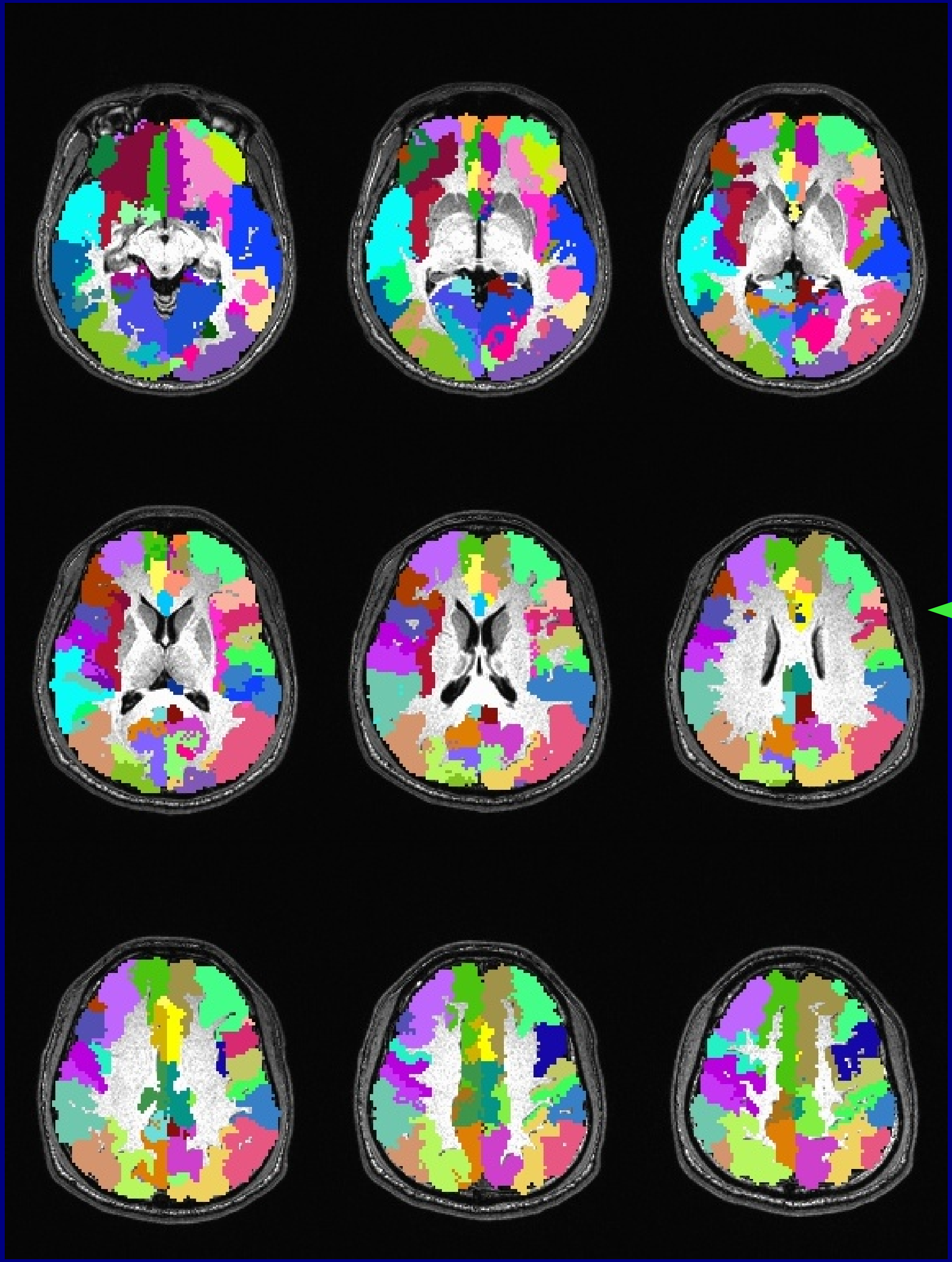
<u>Ex:</u> Human Connectome Project subject, 288 grads, HARDI reconstructed with GQI in DSI-Studio.



FATCAT addenda:

2) 'Connectome'-type tracking

“Connectome”: parcellation of GM



Example (script available in FATCAT_DEMO):

+ FreeSurfer parcellation into >112 ROIs.

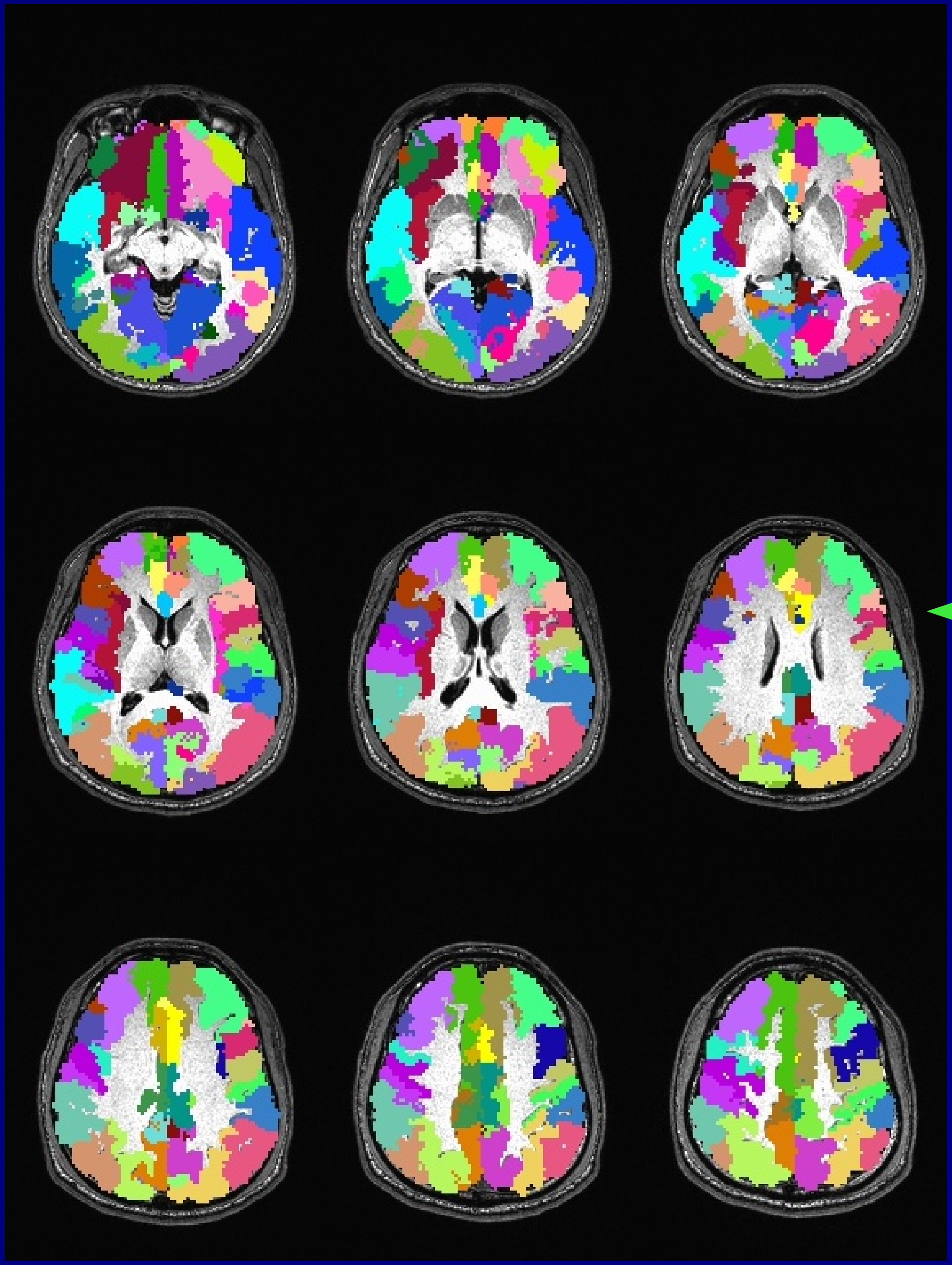
+ Selected 80 cortical GM ROIs.

+ Used 3dROIMaker to inflate by 1 voxel, up to FA>0.2.

(+ NEW: keep labeltable labels and use them in output.)

+ '3dTrackID' among the regions

"Connectome": parcellation of GM



<u>Example (script available in FATCAT_DEMO):</u>

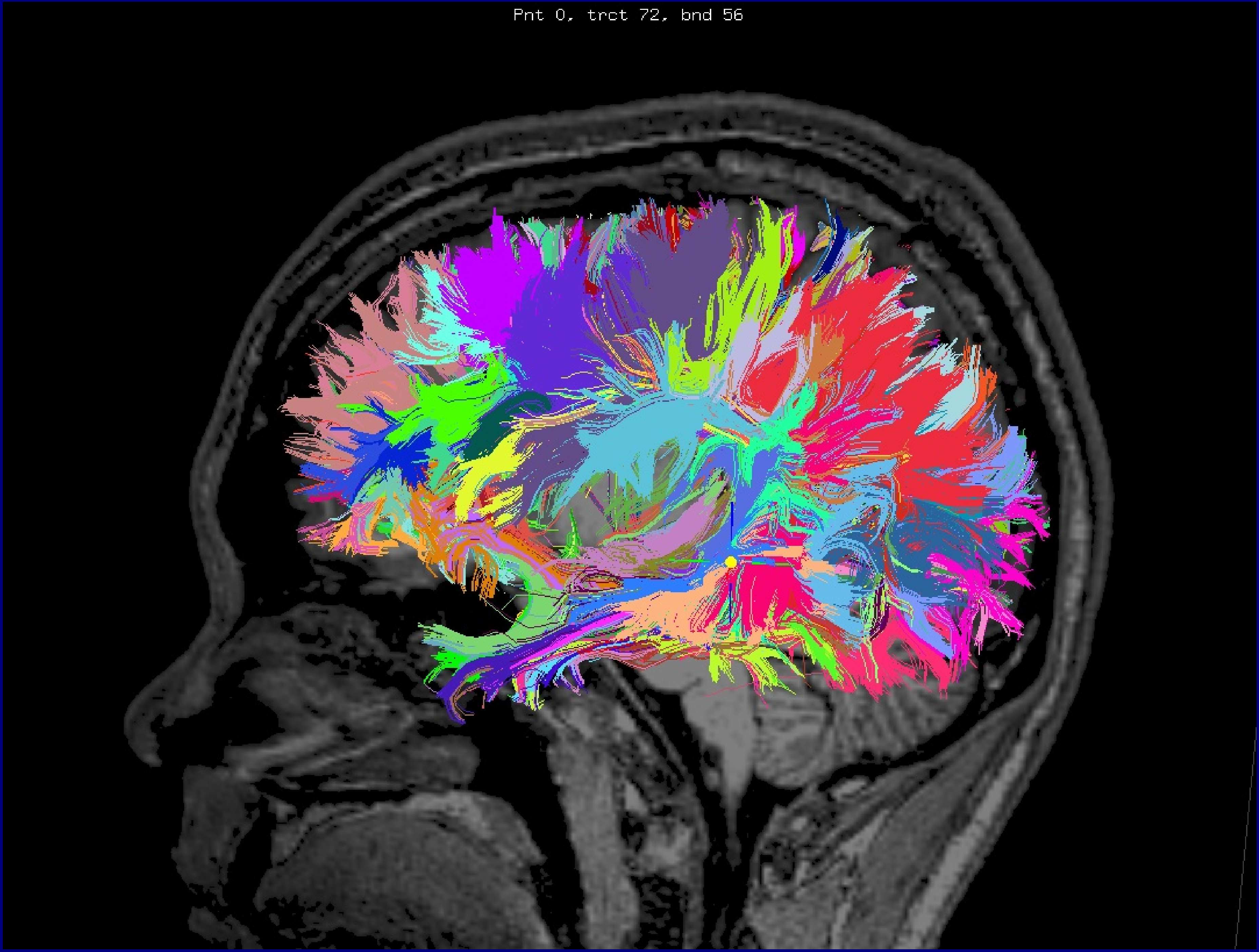
+ FreeSurfer parcellation into >112 ROIs.
+ Selected 80 cortical GM ROIs.
+ Used 3dROIMaker to inflate by 1 voxel, up to FA>0.2.

(+ NEW: keep labeltable labels and use them in output.)

+ '3dTrackID' among the regions

<u>and a few seconds later...</u>

“Connectome”: tracking



SUMMARY

+ We motivated using subject data to make networks of targets
    - e.g., FMRI or anatomical parcellation
+ Tracking estimates most likely locations of WMCs
    - Use **PROB** mode in 3dTrackID for best estimation
    - 3dDWUncert to estimate DT parameter uncertainty
+ Quantitative output: matrices of properties in tracked WMCs
+ 3dROIMaker is useful for making target ROIs
+ Checking/fixing grads: @GradFlipTest + 1dDW_Grad_o_Mat
+ 3dTrackID also has HARDI-compatible functionality