# Introduction to AFNI+SUMA+FATCAT, Part III

DTI+tractography for data exploration and complementing functional connectivity

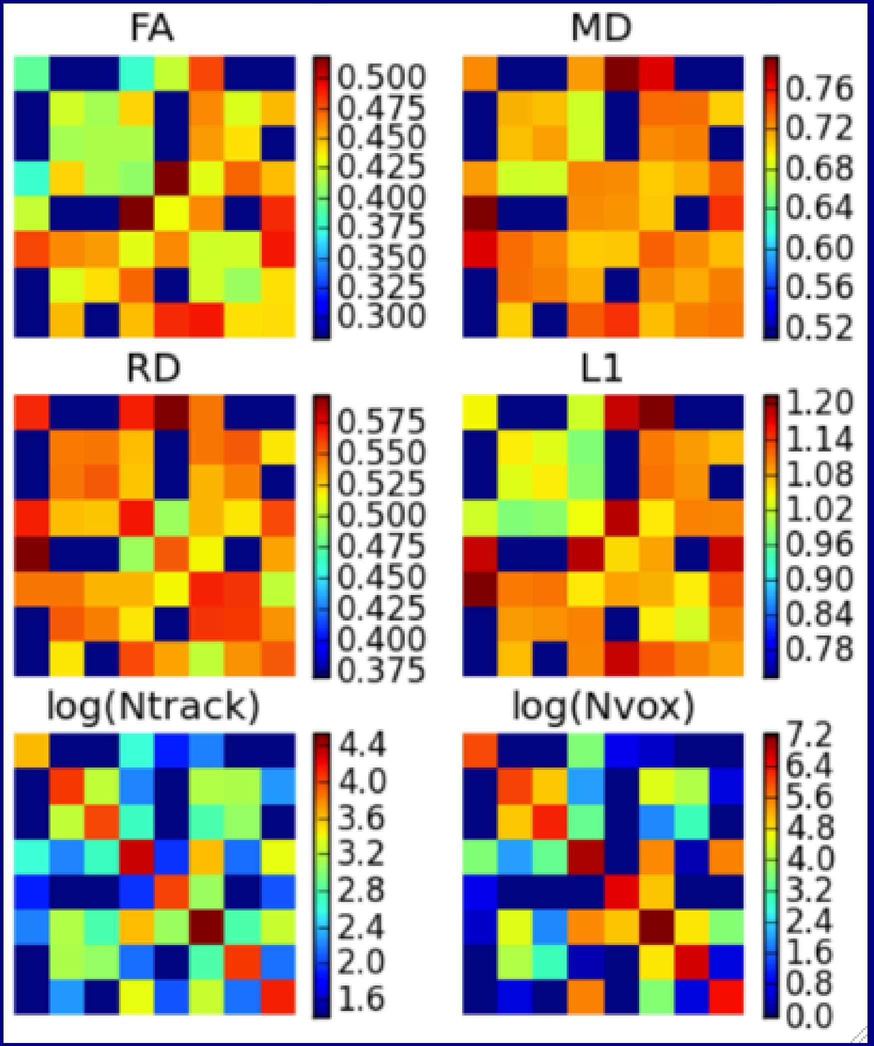
Combining MRI results (SC matrices) with non-MRI data (e.g., age, test scores, characteristics, etc.) for group analysis

# 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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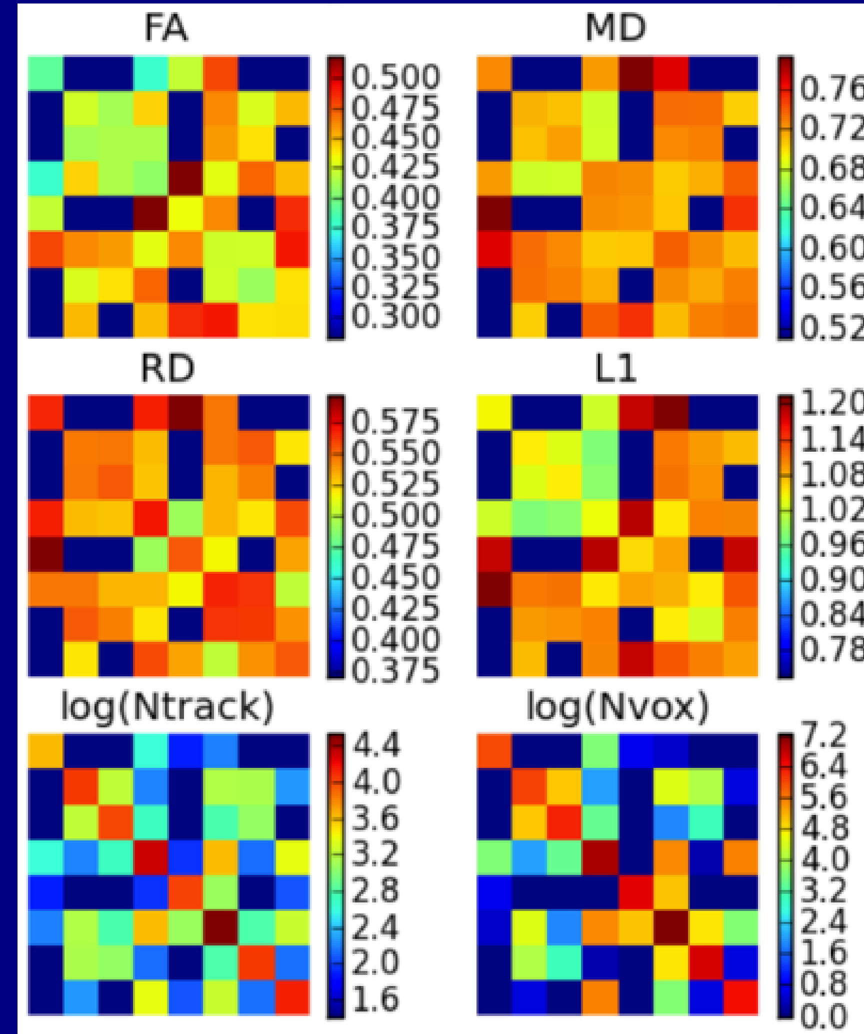
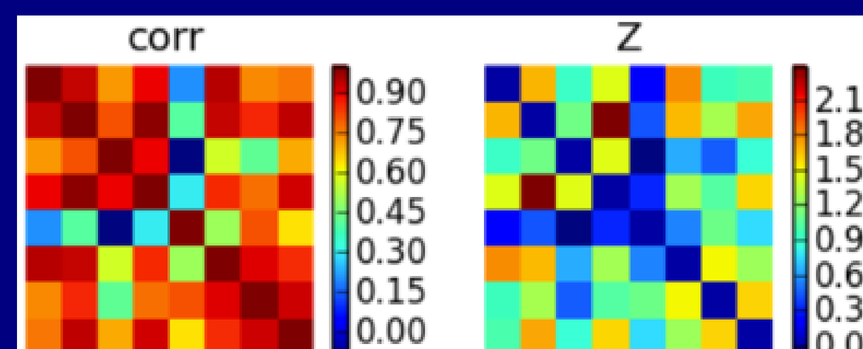



Have produced sets of localized structural/anatomical quantities for comparison with functional values or behavioral scores, genetics, etc.

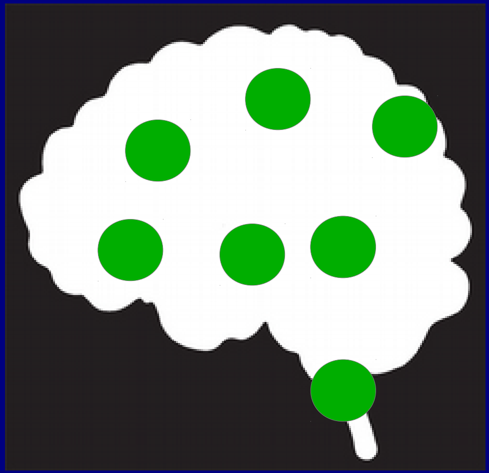
Can use for group or individual comparisons/regressions.

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



# Group Analysis Steps

1) Place network targets



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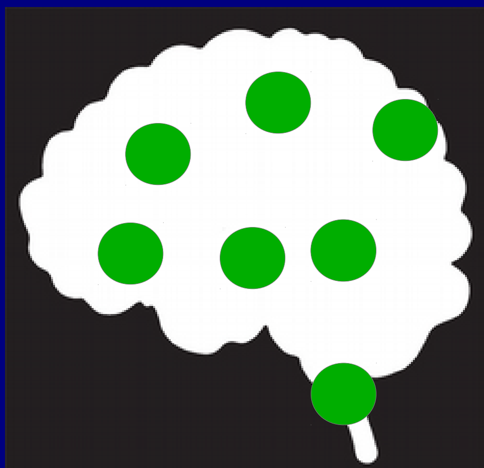
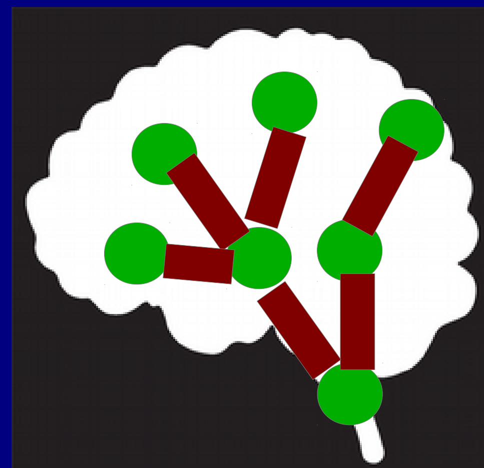


2) Probabilistic tracking



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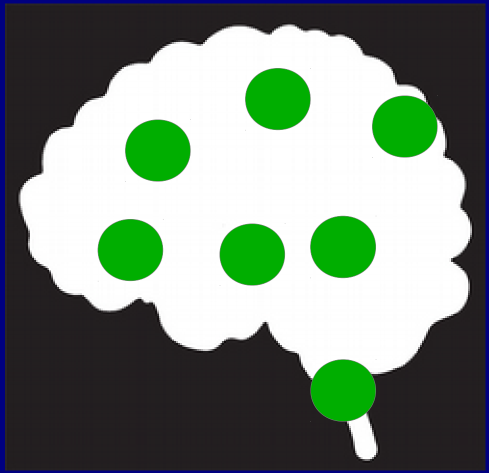

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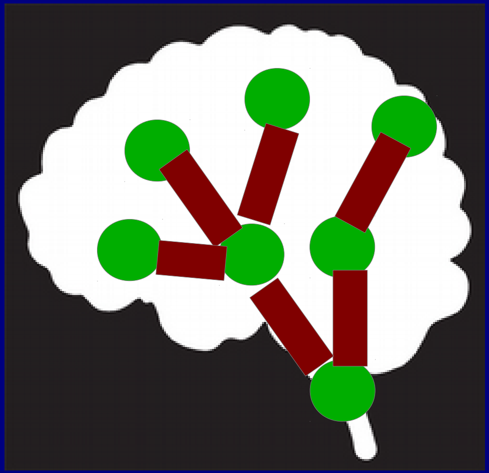
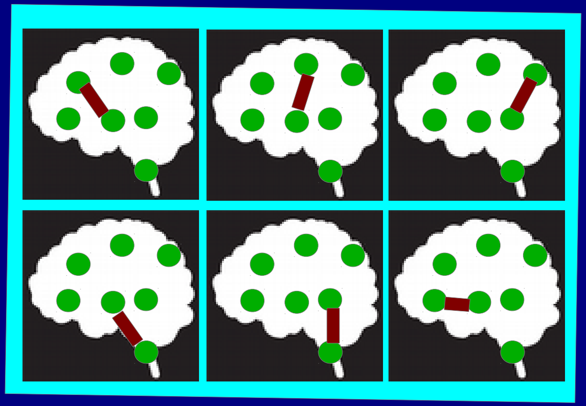


3) set of WM ROIs $\rightarrow$ set of simultaneous measures



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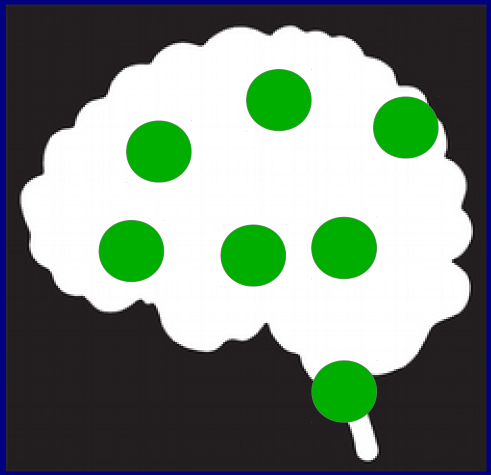

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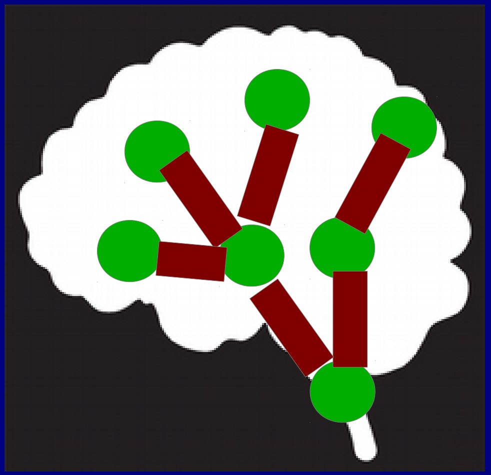

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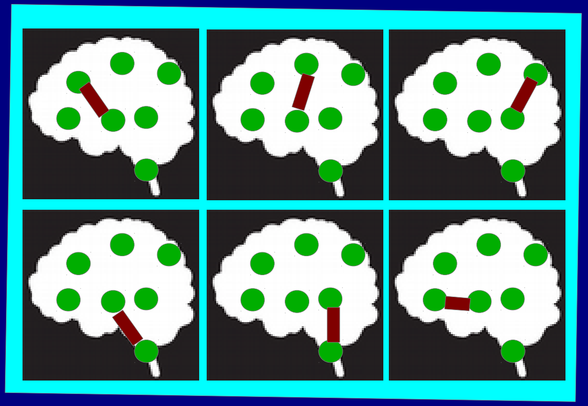

4) Multivariate model

- $\{FA_1, FA_2, FA_3, \ldots\}$
- alc
- infant age
- infant sex
- maternal age
- maternal cig/day

➡ AFNI's 3dMVM, written by G. Chen

# Group Analysis Steps

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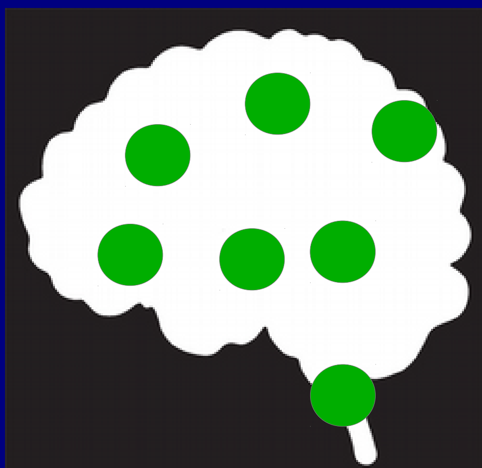

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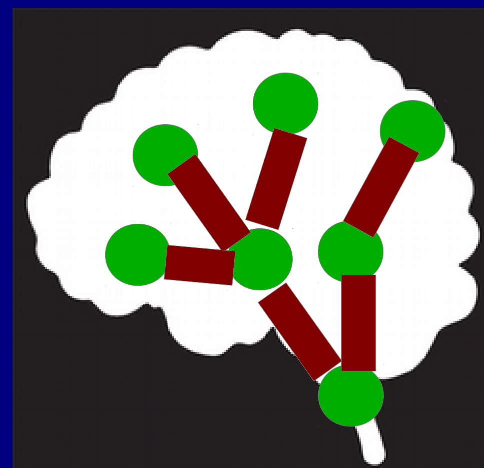

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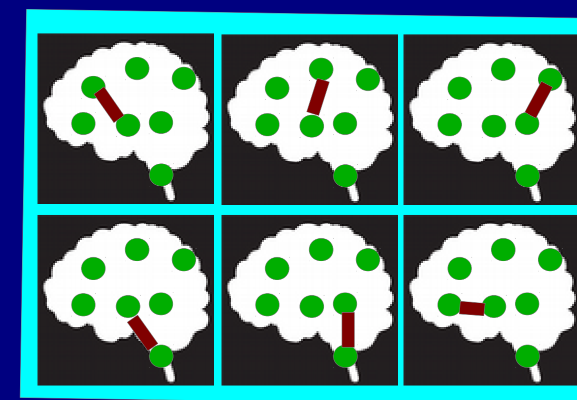
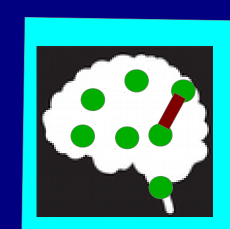
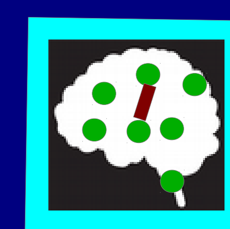


4) Multivariate model

- {$FA_1$, $FA_2$, $FA_3$, ...}
- alc
- infant age
- infant sex
- maternal age
- maternal cig/day

5) Follow-up GLM for each WM ROI

- FA
- alc
- infant age
- infant sex
- maternal age
- maternal cig/day


,

,...

→ AFNI's 3dMVM, written by G. Chen

# Group Analysis Steps

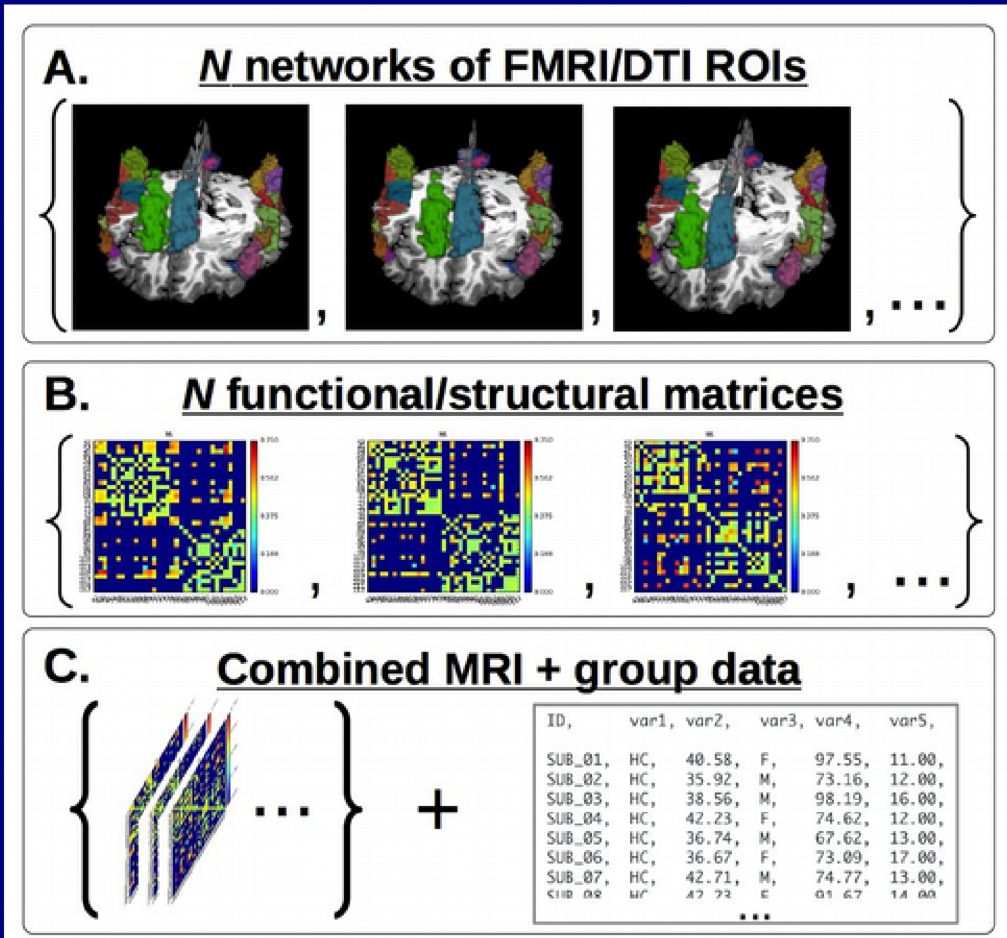
fat_mvm_prep.py
+ make a data table combining:
- a CSV file of subject data with
- a set of *.grid[1] files from 3dTrackID;

+ automatically selects tracked connections found across all groups (future version may have LME modeling that allows missing data)

fat_mvm_scripter.py
+ define a statistical model of variables from CSV file + DTI data
+ build a 3dMVM script to test the model using entire networks, and
+ construct follow-up GLTs to investigate individual regions.

[1]Also works with *.netcc files from 3dNetCorr.

# Group Analysis: Summary




**D. User-defined model(s)**

'measure1 ~ var1 + var2 + var3*var4 + ...'

'measure2 ~ var1 + var2 + var3*var4 + ...'

...

**E. Network-level statistics for each model**

ANOVA table of $\chi^2$, DF, and p-value:

```
# RESULTS: ANOVA table - FA
5 # Number of effects
   # Chisq DF   Pr(>Chisq)
  4.9457216  1 2.615532e-02 # var1
  0.8453055  1 3.578838e-01 # var2
  0.6640459  1 4.151352e-01 # var3
  0.8097606  1 3.681910e-01 # var4
  2.1255675  1 1.448591e-01 # var3:var4
```

**F. Set of ROI statistics for each model**

Post hoc table of value, t-stat, DF and 2-sided p:

```
# RESULTS: Post hoc tests - FA
54 # Number of tests
      # value       t-stat DF    2-sided-P
 -0.0044778181 -0.62834967 14 5.398911e-01 # 001__002-var1(+HC-IL)
 -0.0002940607 -0.23287694 14 8.192272e-01 # 001__002-var2
  0.0011186177  2.13603173 14 5.082097e-02 # 001__002-var3(+F-M)-var4
 -0.0069573895 -1.12411575 14 2.798695e-01 # 001__002-var3(+F-M)
  0.0004507261  1.54181323 14 1.454148e-01 # 001__002-var4
  0.0130966286  1.51536073 14 1.519300e-01 # 003__004-var1(+HC-IL)
  0.0010852927  0.70869270 14 4.901486e-01 # 003__004-var2
```

*(Taylor, Chen, Cox & Saad, 2015?)*

Example:
Group analysis with tracking output
using multivariate statistics

from study:
*A DTI-Based Tractography Study of Effects on Brain Structure Associated with Prenatal Alcohol Exposure in Newborns*,
*Taylor, Jacobson, van der Kouwe, Molteno, Chen, Wintermark, Alhamud, Jacobson, Meintjes (2015)*

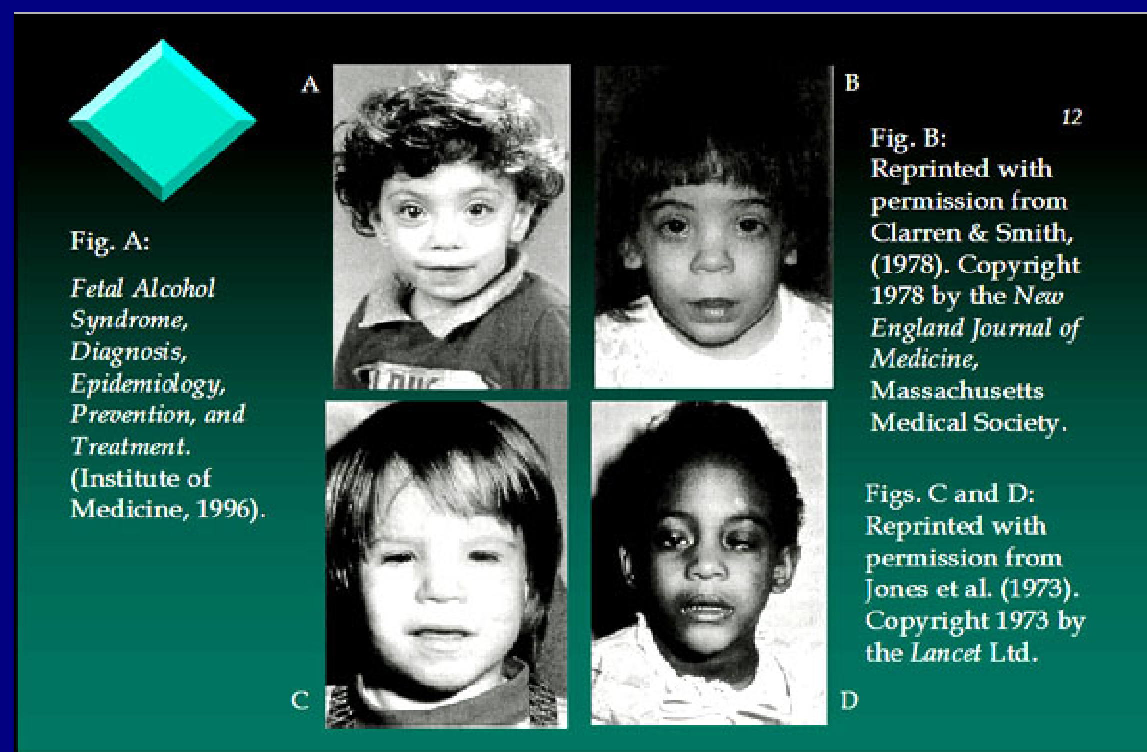
# Prenatal alcohol exposure (PAE)

- Alcohol is a teratogen, disrupting healthy embryonic and fetal development.
  → leads to various Fetal Alcohol Spectrum Disorders (FASD)

- FASD occurs in children whose pregnant mothers binge drank
  - e.g., ≥4 drinks/occasion and/or ≥14 drinks/wk

- Results in *poor*:
  - academic performance
  - language/math skills
  - impulse control
  - abstract reasoning
  - memory, attention

  and facial and skeletal dysmorphology



# Goals of this study

*To:*

1) Use neuroimaging to compare structural brain development in newborns with PAE to that of HC newborns.
2) Quantitatively examine WM properties across the brain
3) Relate changes in (localized) WM properties with PAE, controlling for several confounding effects
   $\rightarrow$ examine several, and see which is/are (most) significant

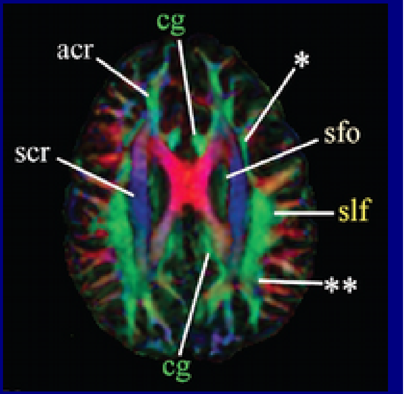
Tools: diffusion tensor imaging (DTI) + tractography

A) delineate similar WM ROIs across all subjects

B) quantify structural properties (FA, MD, T1, ...)

C) statistical modeling for comparisons

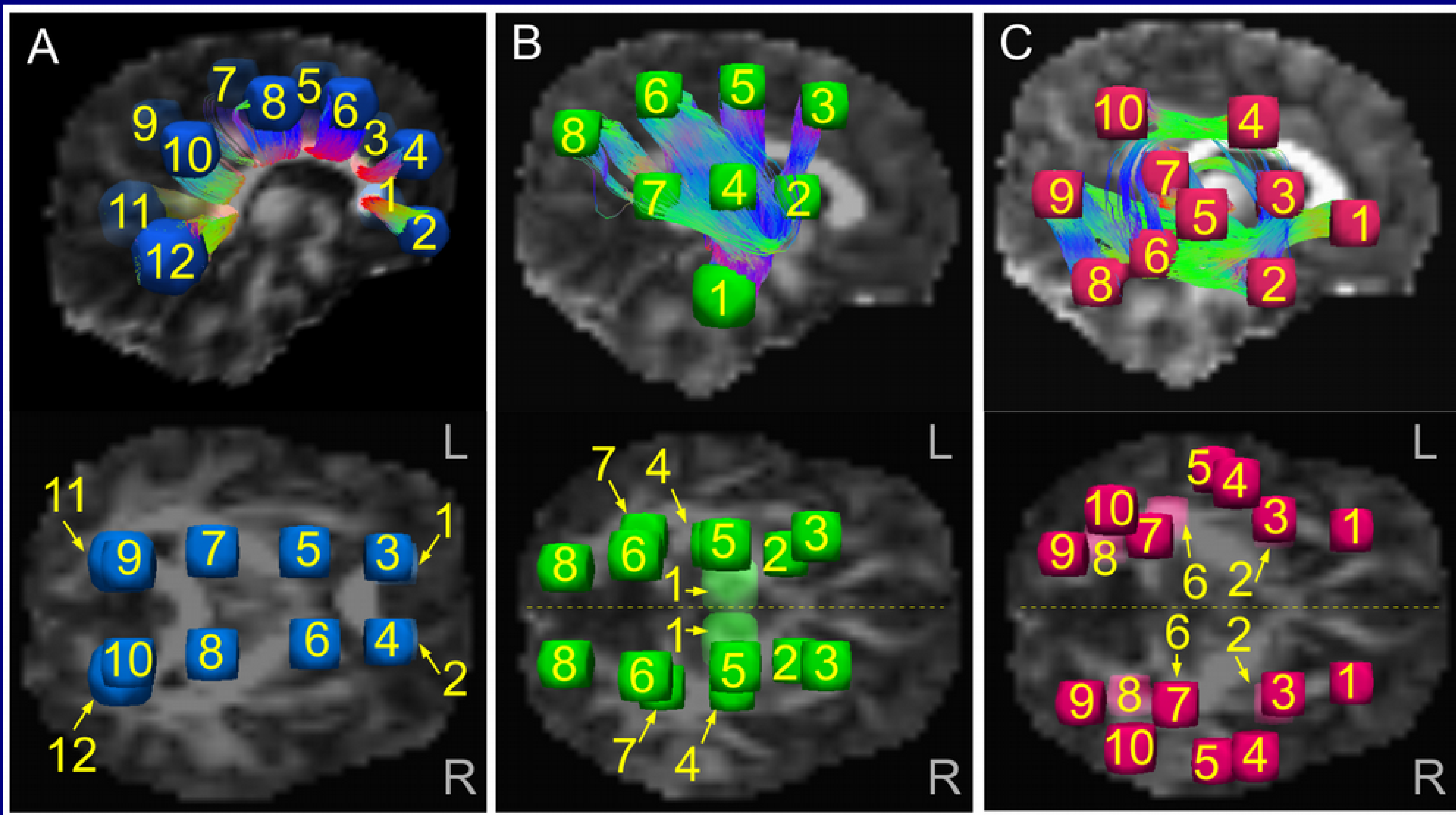
*- at whole brain, network and ROI levels*



# Setting up DTI-tractography

## Location of targets for tractography: 5 WM networks.

| CC and Cor. Rad. (CCCR) | Projection (L/R-PROJ) | Association (L/R-ASSOC) |
|---|---|---|



# II) Results: network level

The questions:

1) which WM networks are affected by PAE?
2) which parameters show effects most strongly?

Answer using:

- (for each network) a multivariate GLM for
  - set of DTI parameters
  - alcohol (frequency: binge/wk)
  - infant age (wks since conception)
  - infant sex (M/F)
  - maternal age (yrs)
  - maternal cigarette smoking (cig/day).

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*Parameters showing at least trends ($p<0.1$) →*

*← Networks*

| | FA | | | | MD | | | | AD | | | | PD | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Network | var. | $\beta_{med}$ | $F\ (df_N, df_D)$ | $p$ | var. | $\beta_{med}$ | $F\ (df_N, df_D)$ | $p$ | var. | $\beta_{med}$ | $F\ (df_N, df_D)$ | $p$ | var. | $\beta_{med}$ | $F\ (df_N, df_D)$ | $p$ |
| CCCR | | | | | alc | -0.70 | 8.6 (1, 14) | 0.011* | alc | -0.72 | 14.0 (1, 14) | 0.002** | | | | |
| | | | | | | | | | cig | -0.27 | 2.5 (6, 9) | 0.101 | cig | 0.47 | 3.5 (1, 14) | 0.083 |
| | | | | | mat_age | 0.56 | 5.5 (1, 14) | 0.034* | mat_age | 0.53 | 6.3 (1, 14) | 0.025* | | | | |
| L-PROJ | | | | | alc | -0.41 | 3.9 (10, 140) | 0.000*** | alc | -0.52 | 4.1 (10, 140) | 0.000*** | | | | |
| | cig | 0.12 | 4.2 (11, 4) | 0.091 | | | | | | | | | cig | 0.52 | 4.0 (1, 14) | 0.066 |
| | | | | | mat_age | 0.37 | 4.4 (1, 14) | 0.056 | mat_age | 0.44 | 6.5 (1, 14) | 0.023* | | | | |
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| | age | 0.33 | 8.6 (13, 2) | 0.109 | age | -0.41 | 5.8 (1, 14) | 0.031* | age | -0.39 | 5.3 (1, 14) | 0.038* | | | | |
| | | | | | sex | -0.20 | 4.3 (1, 14) | 0.056 | sex | -0.39 | 5.9 (1, 14) | 0.029* | | | | |
| | mat_age | -0.16 | 9.2 (13, 2) | 0.103 | | | | | | | | | | | | |
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| R-ASSOC | alc | 0.23 | 1.8 (7, 98) | 0.090 | alc | -0.62 | 10.2 (1, 14) | 0.007** | alc | -0.67 | 14.1 (1, 14) | 0.002** | | | | |
| | | | | | | | | | cig | -0.29 | 3.9 (1, 14) | 0.068 | cig | 0.5 | 3.5 (1, 14) | 0.082 |

** $p<0.05$; ** $p<0.01$; *** $p<0.001$.*

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** p<0.05; ** p<0.01; *** p<0.001.*

→ Statistically significant alcohol exposure associations in ~every WM network

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| | | | | | | | | | cig | -0.29 | 3.9 (1, 14) | 0.068 | cig | 0.5 | 3.5 (1, 14) | 0.082 |

** p<0.05; ** p<0.01; *** p<0.001.*

→ Increased alcohol exposure:
decreased AD
(and decreased MD)

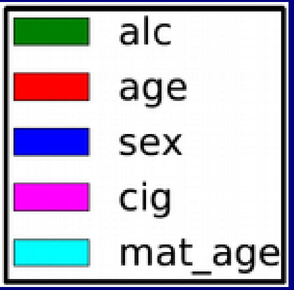
# III) Results: ROI level

The question:

1) where are most significant AD-alcohol relations in each network?

Answer using:

- (for each ROI) a GLM for
  - single DTI parameter
  - alcohol (frequency: binge/wk)
  - infant age (wks since conception)
  - infant sex (M/F)
  - maternal age (yrs)
  - maternal cigarette smoking (cig/day).



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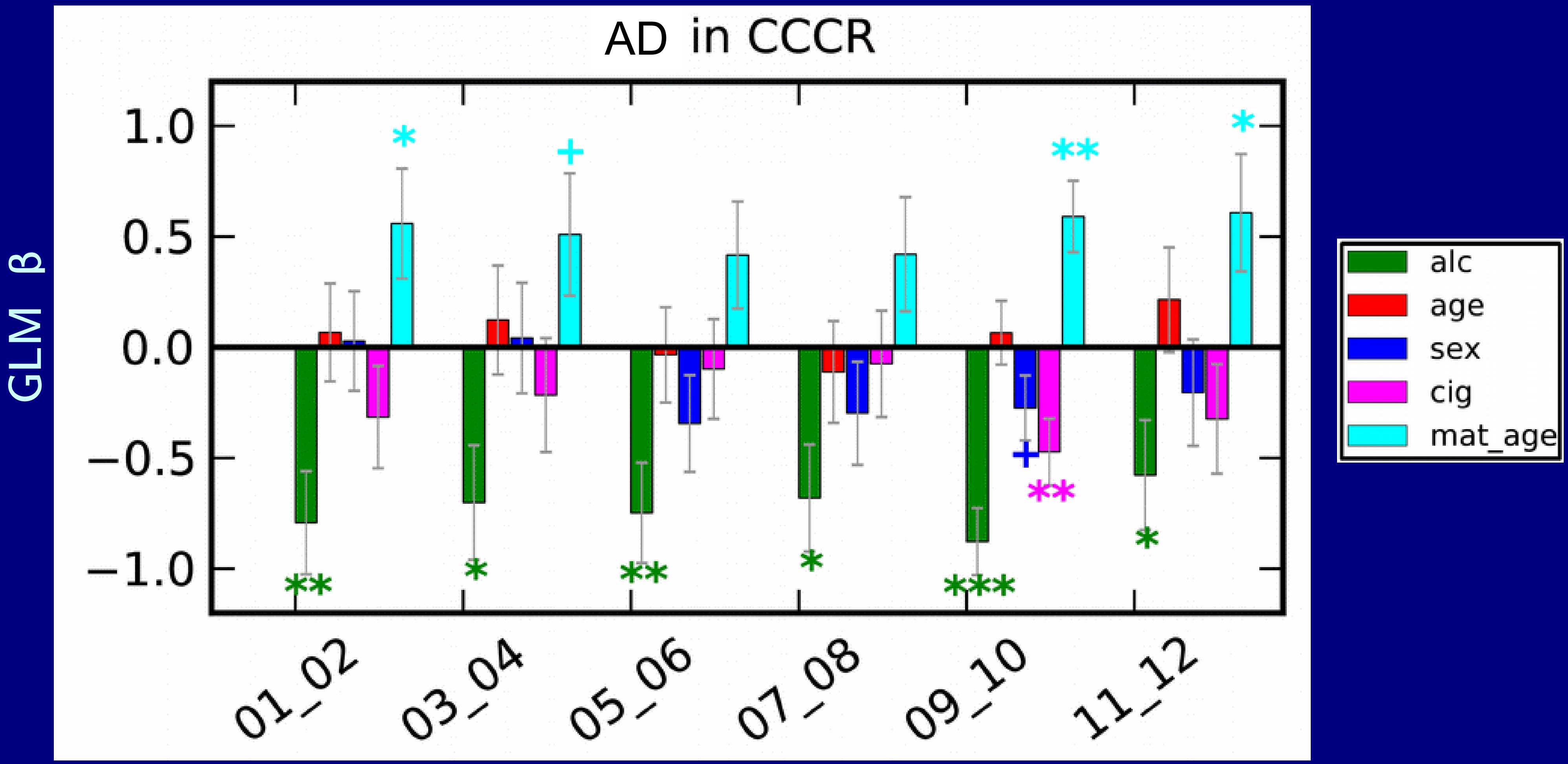
Transcallosal (CC and corona radiata)




anterior → posterior

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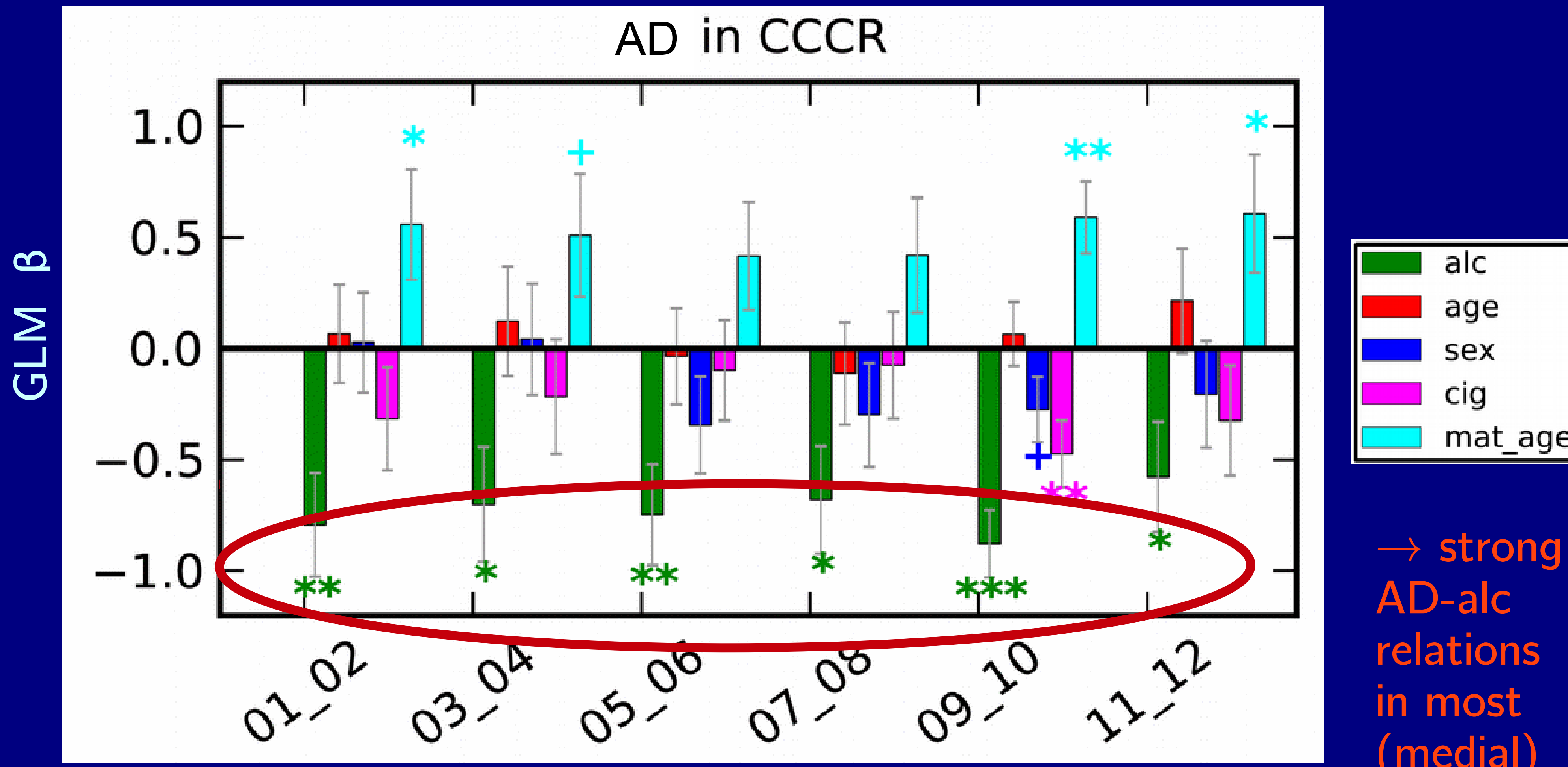


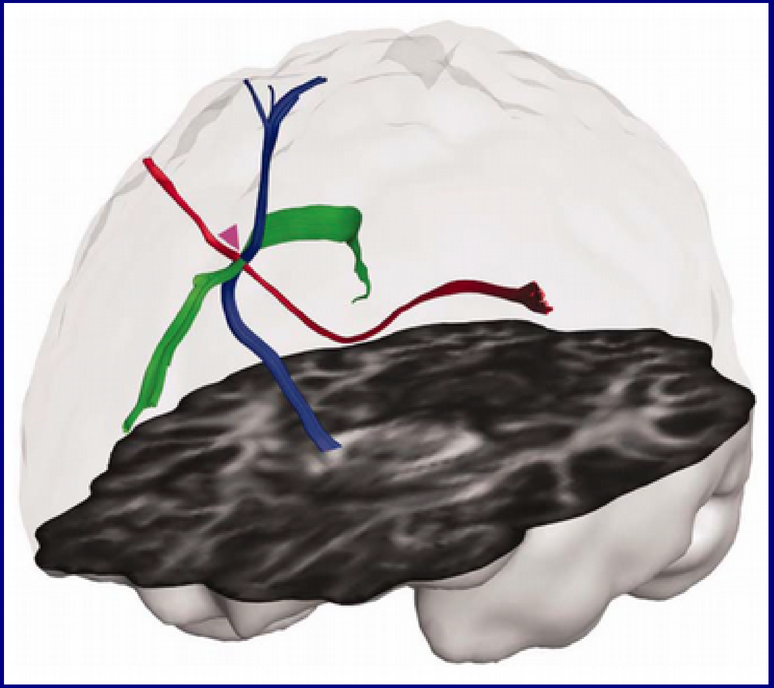

anterior → posterior

→ strong AD-alc relations in most (medial) WM ROIs

FATCAT addenda:
*1) HARDI tracking*

# Higher order models

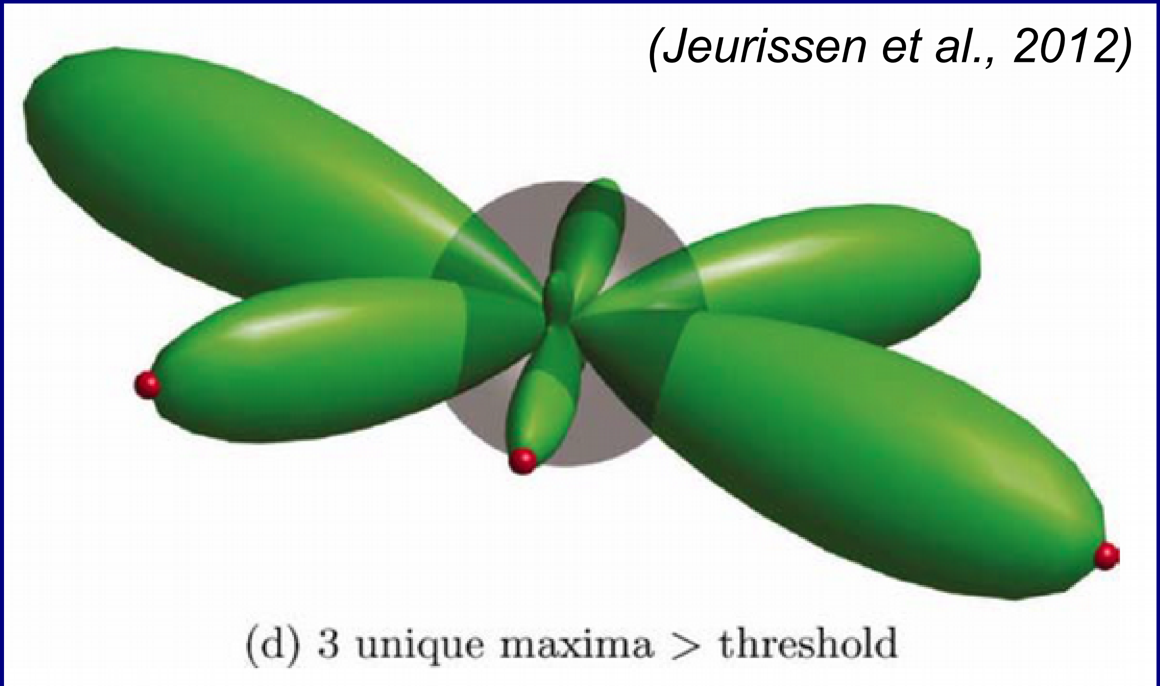
DTI tractography:
+ susceptible to false negatives, difficulty with
  long range tracts (noise/error accumulation)
+ Major diffusion can be average of multiple paths
+ Voxels can have low FA from several WM paths, false ending
+ Can't resolve complex underlying architecture
  - Jeurissen et al. (2012,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

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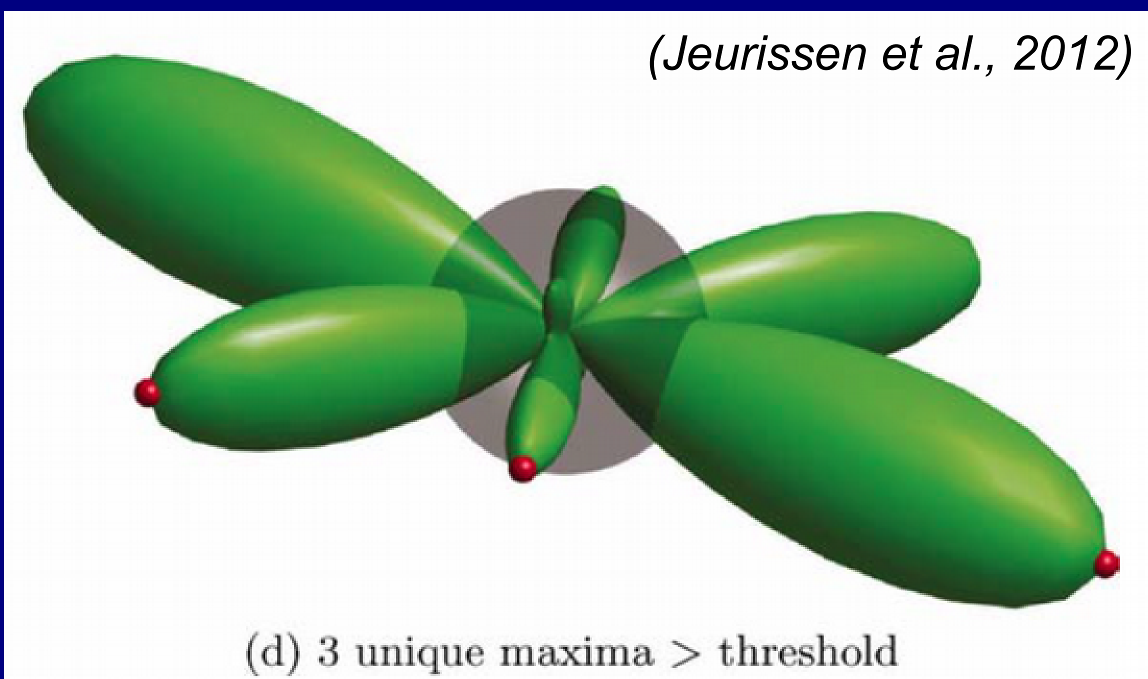
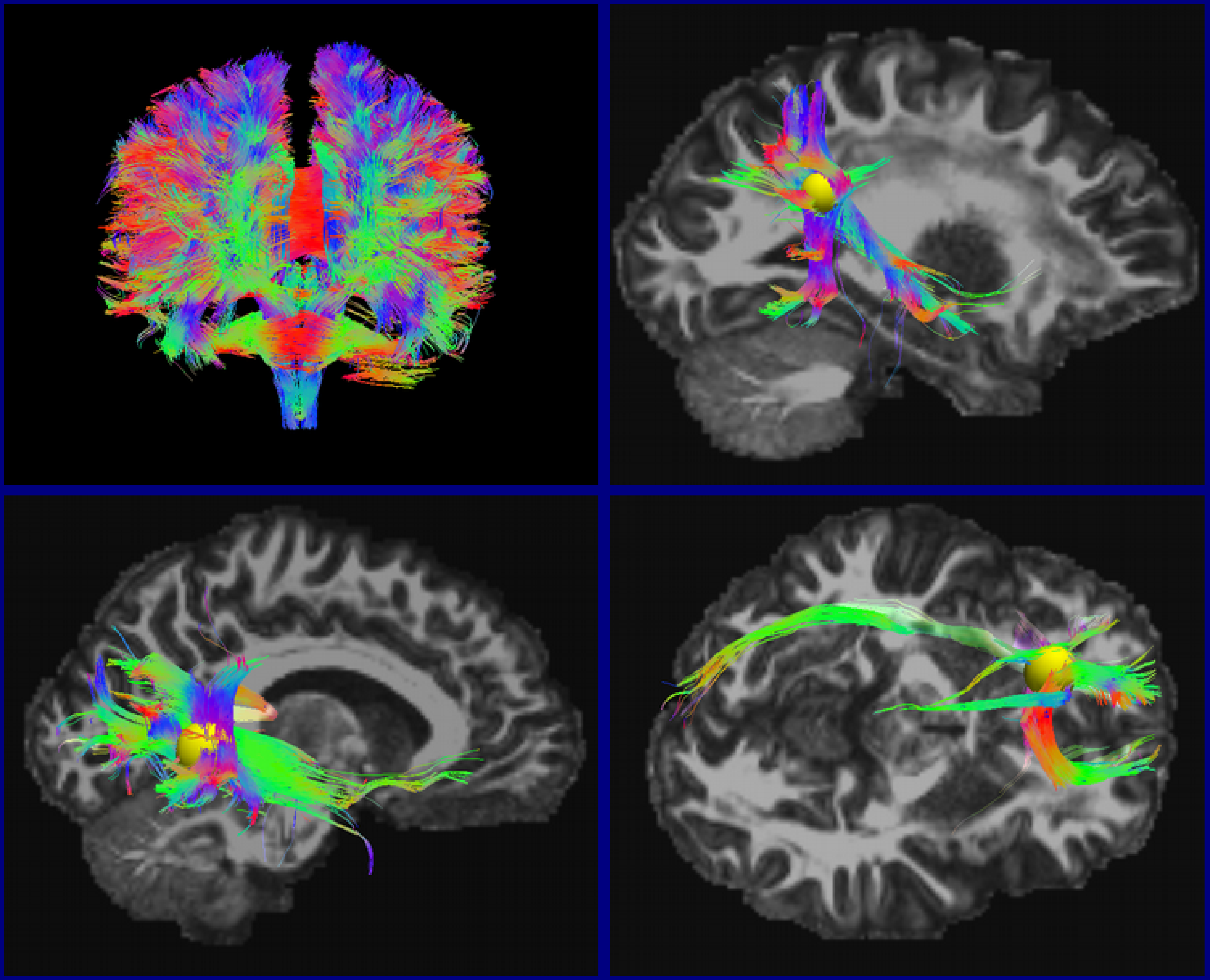



FATCAT can now track through HARDI data

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

# Example: 3dTrackID on HARDI data

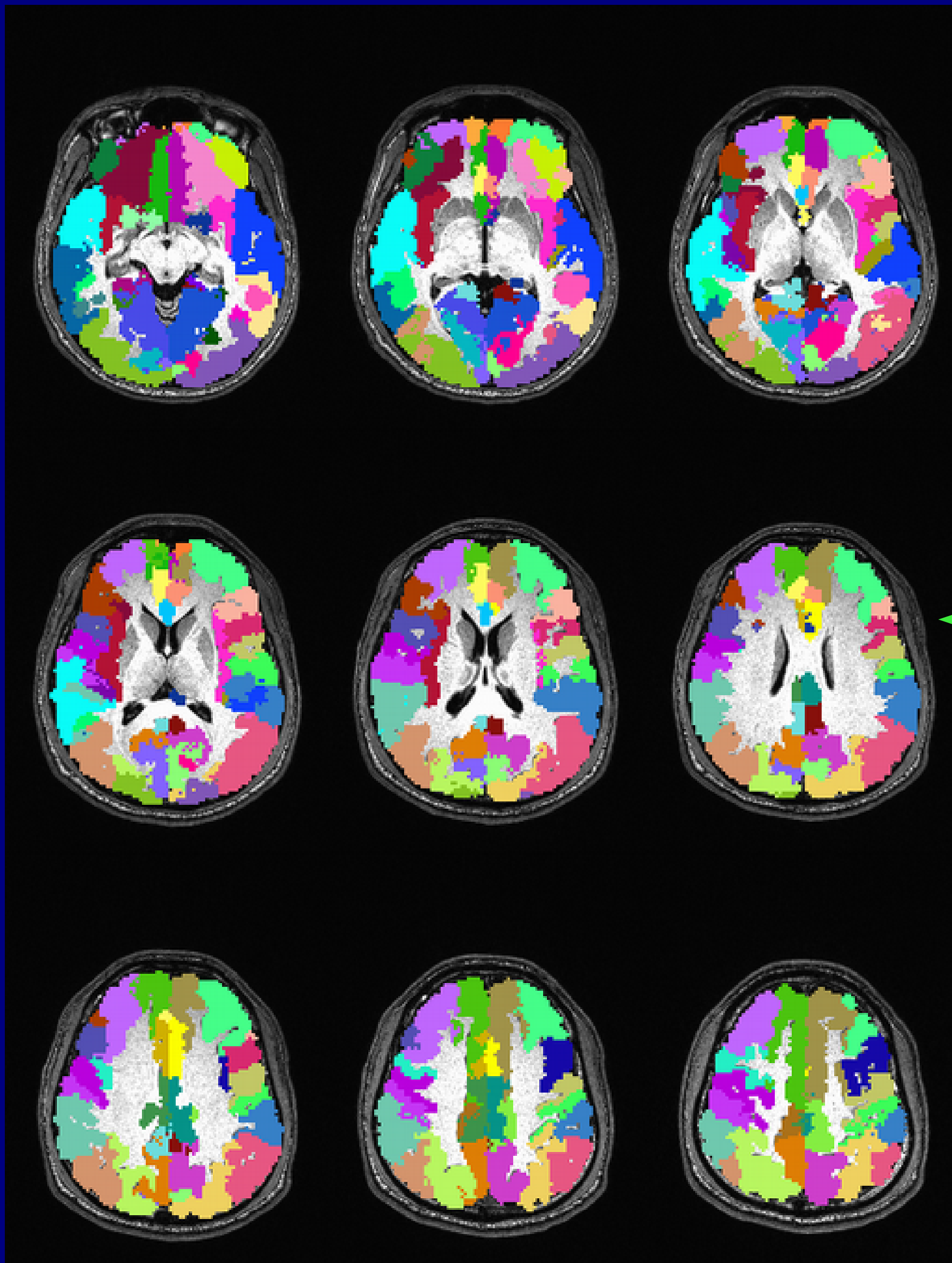
*<u>Ex:</u> Human Connectome Project subject, 288 grads, HARDI reconstructed with GQI in DSI-Studio.*



# FATCAT addenda:

*2) 'Connectome'-type tracking*

# “Connectome”: parcellation of GM



<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 -mode DET' among
  the regions

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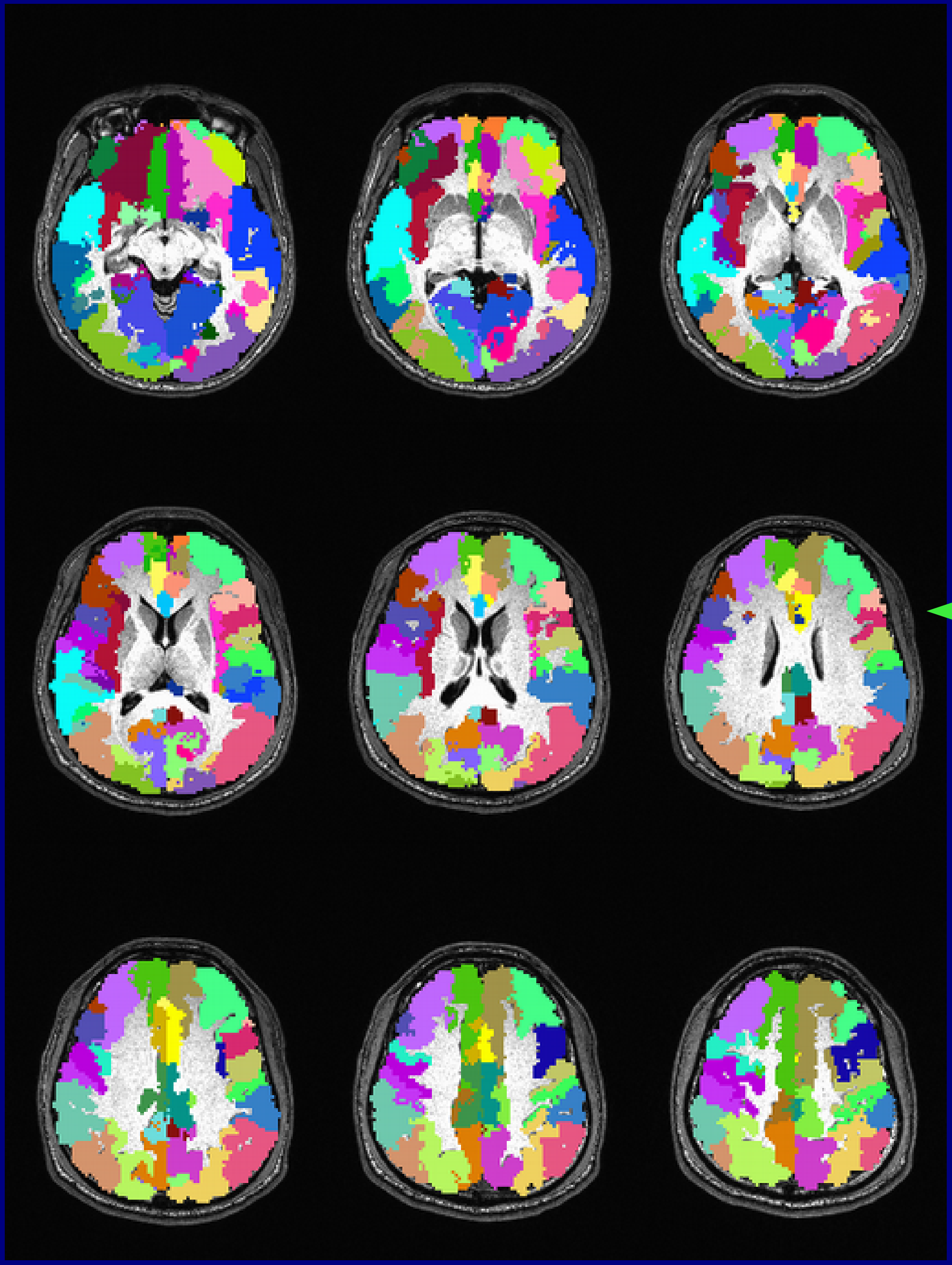

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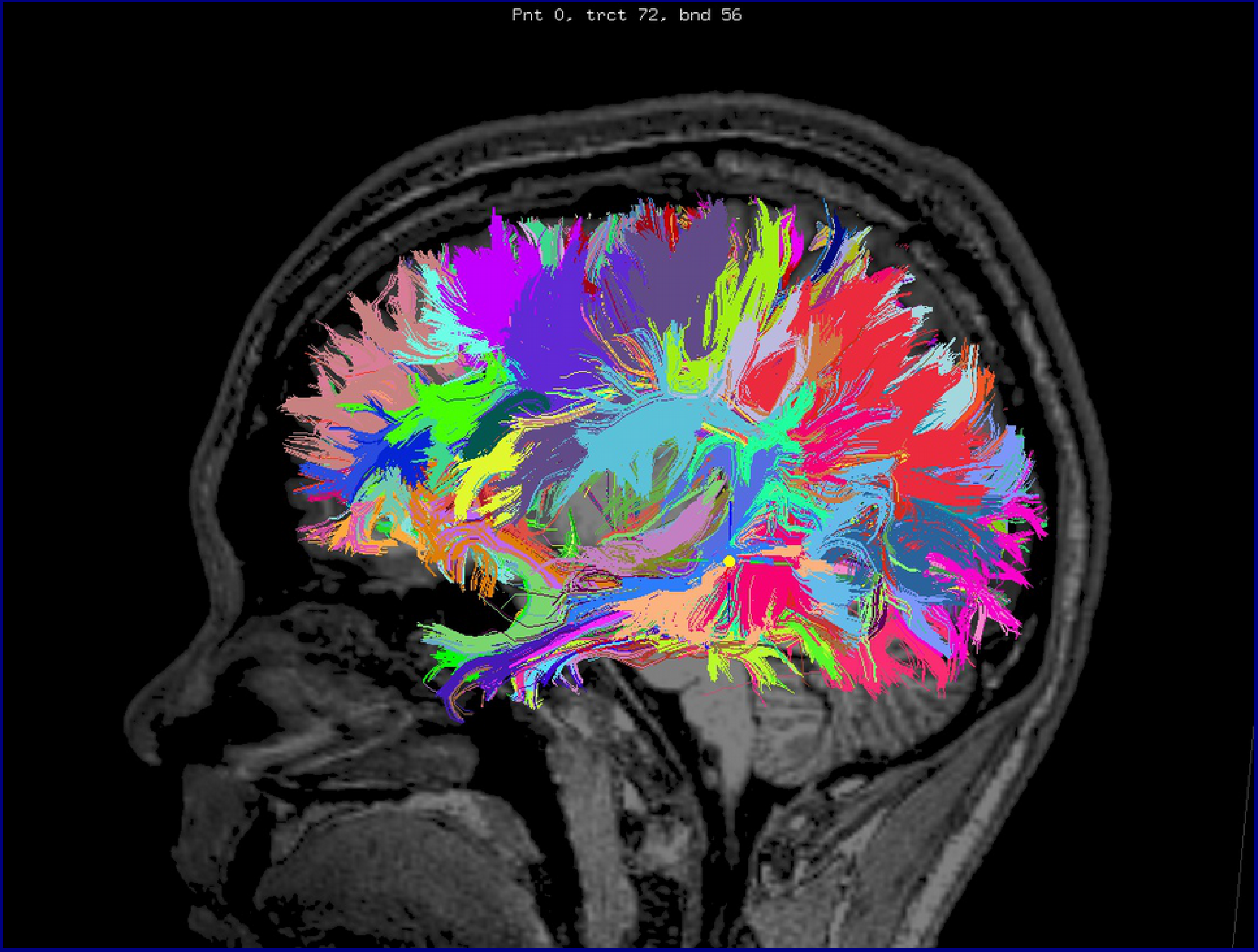
<u>*and a few seconds later...*</u>

# “Connectome”: tracking



FATCAT addenda:

*3) Processing DWI gradients + volumes*
*(including the dreaded*
*Gradient Flip monster)*

# 1dDW_Grad_o_Mat

Before most DTI analysis, useful function for:

+ converting formats of gradient info
    - e.g., row to column, grad to bmatrix, etc.
+ process DWI grads and volumes in same way
    - average b=0 volumes
    - average repeated sets of DWIs
+ use b-value information in processing
+ insert/remove rows of non-weighted grads
+ and ….

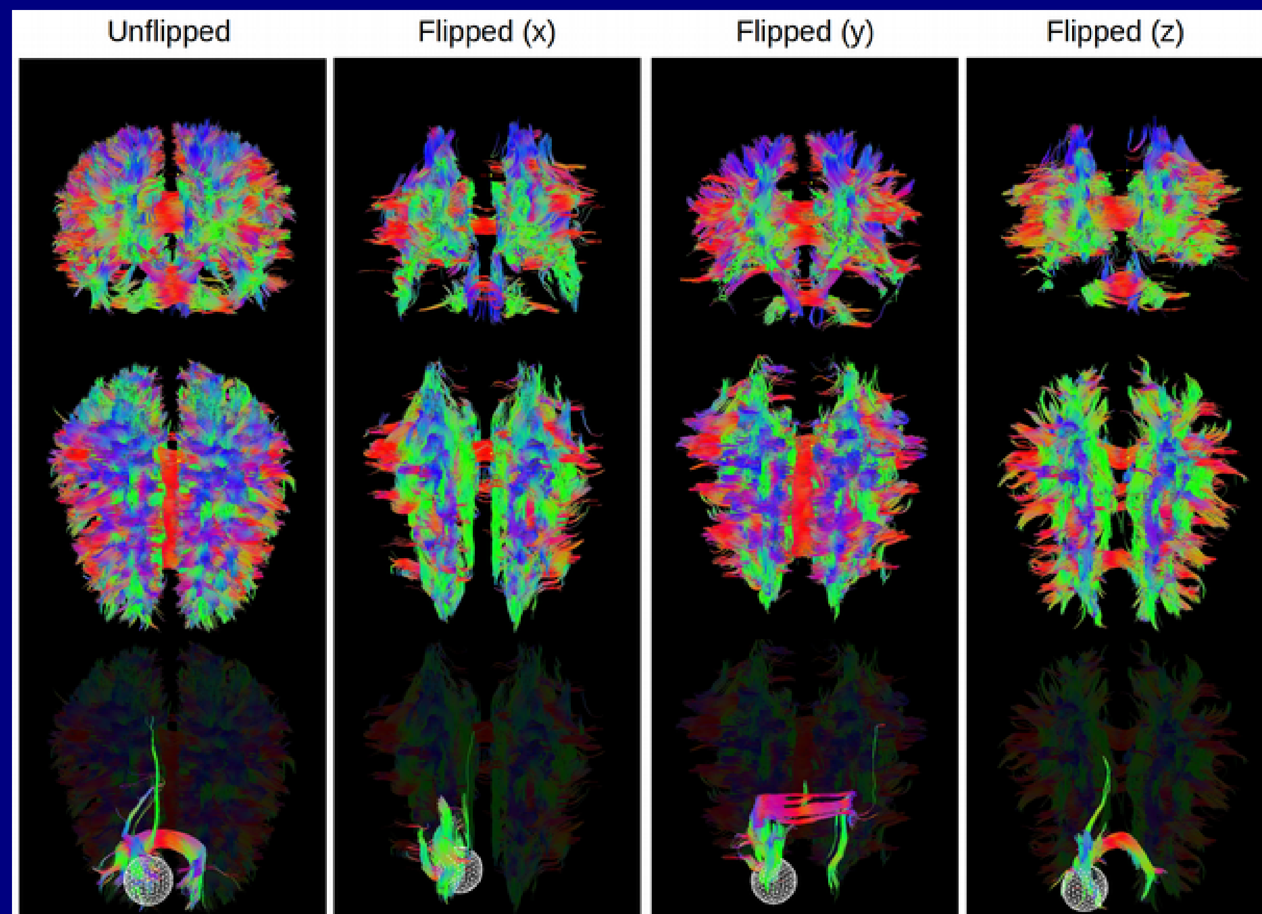
# 1dDW_Grad_o_Mat

… flip a gradient component to convert scanner coordinates to those of the analysis package (*I don't know why they don't necessarily match!*)

- e.g., '-flip_y' converts each y-component to have opposite sign

Example cases:

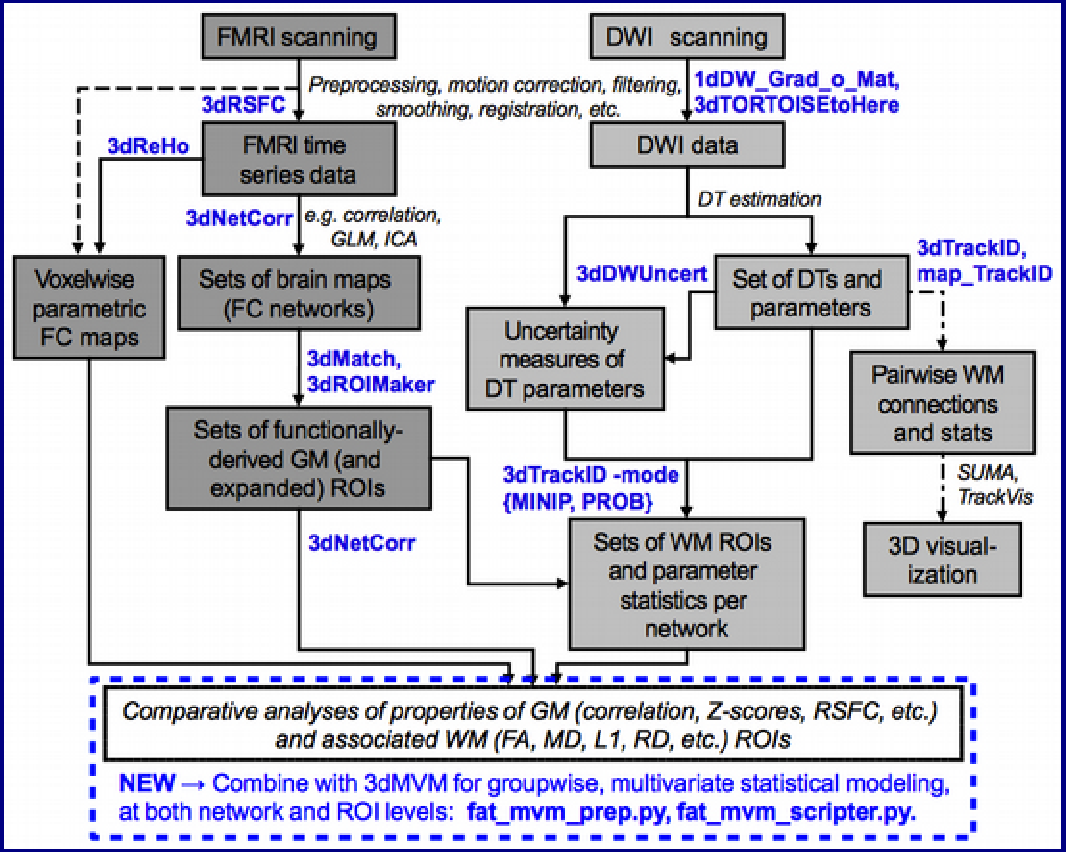
+ note CC structure if x- or z-component has mismatch sign
+ y-flip is least easy to see, but often needed in Siemens scanners, I find (*again, just something to be aware of!*)



# In Summary

We have discussed capabilities and benefits of:

## Combining multimodal data: FC+SC+...



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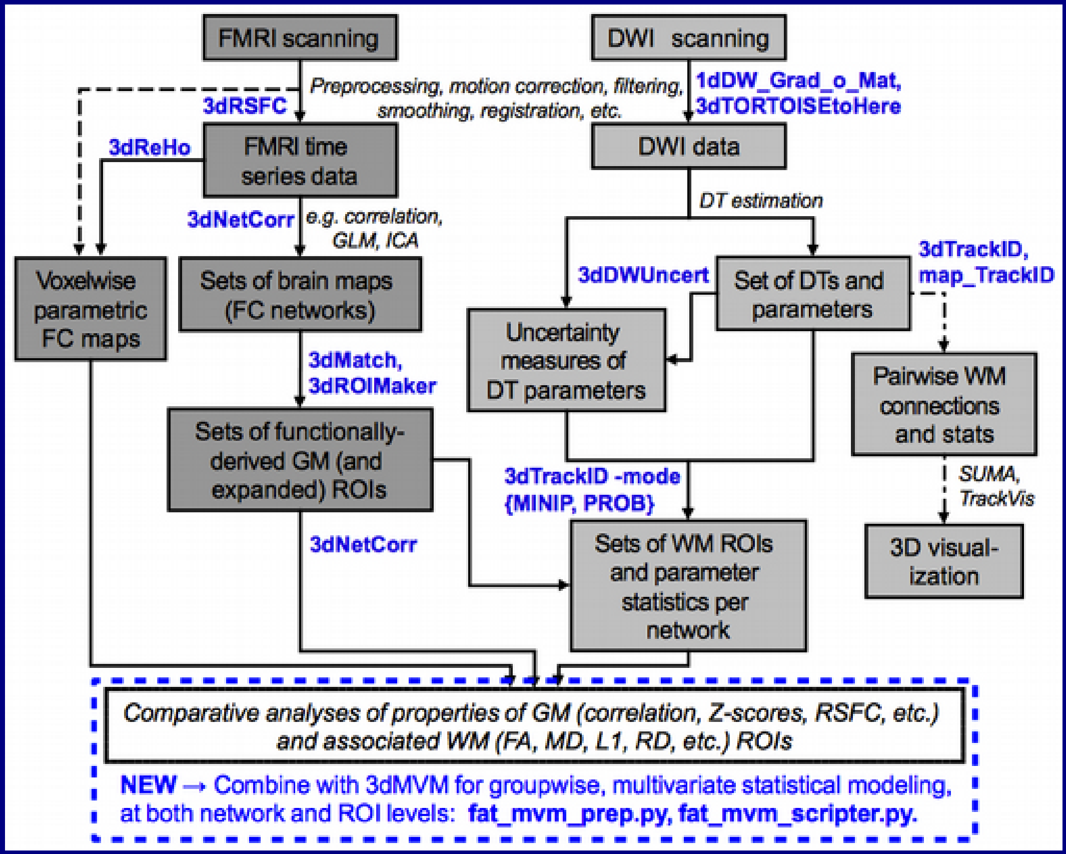
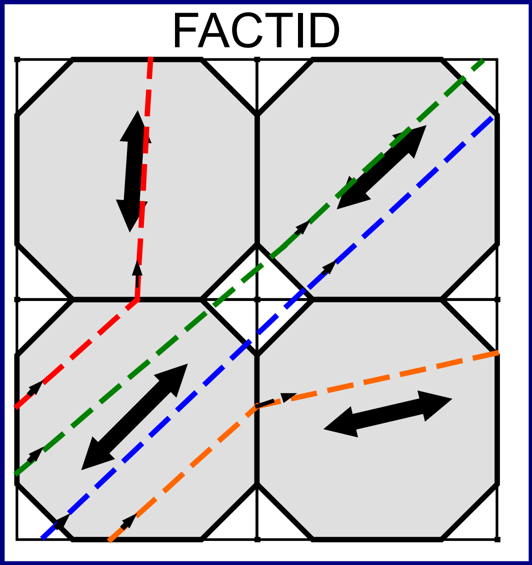



Using an efficient algorithm, reduced bias of propagation



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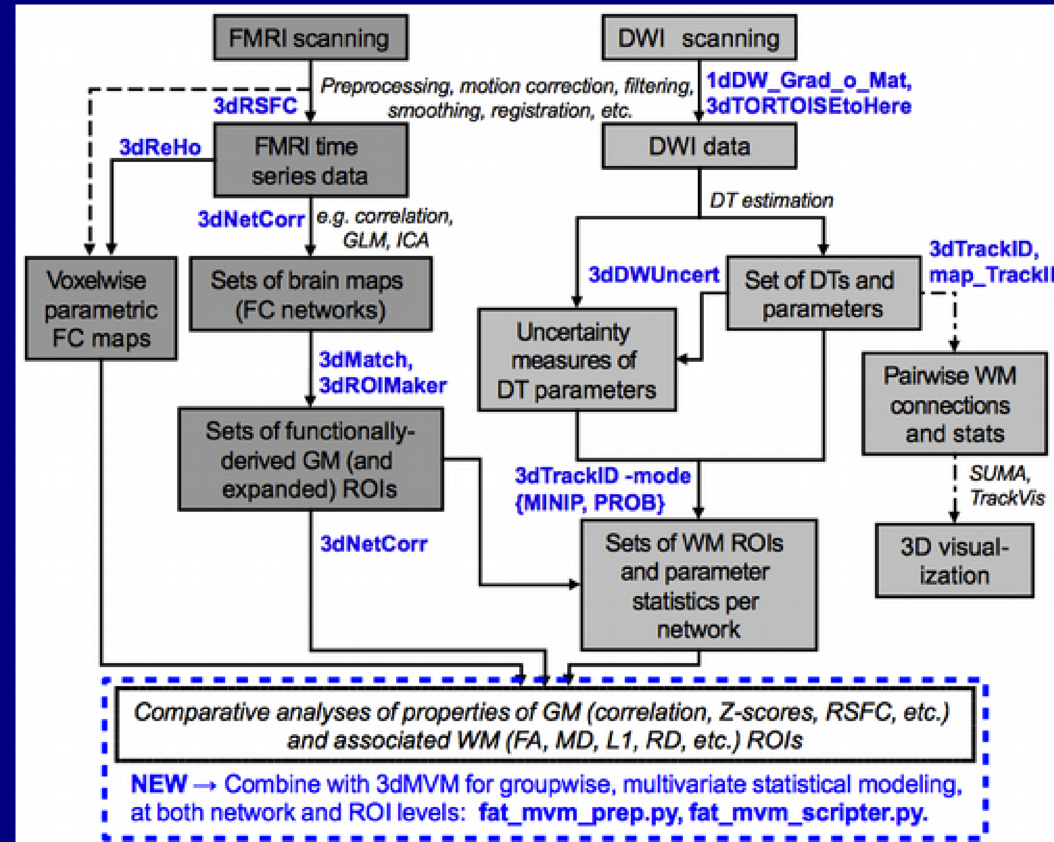


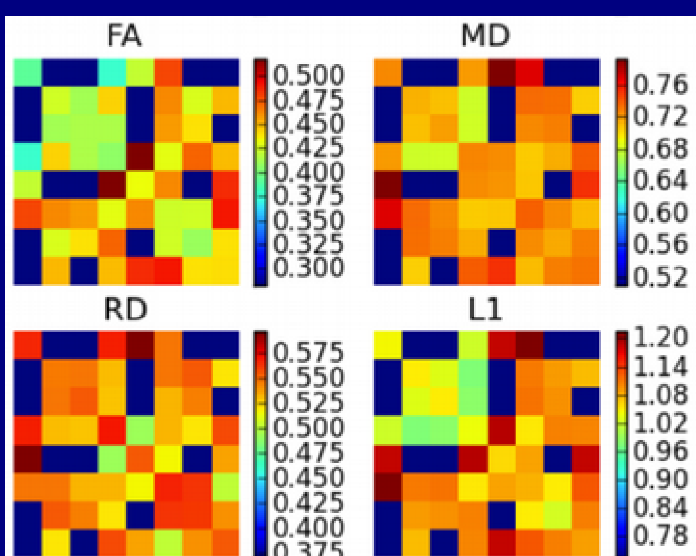


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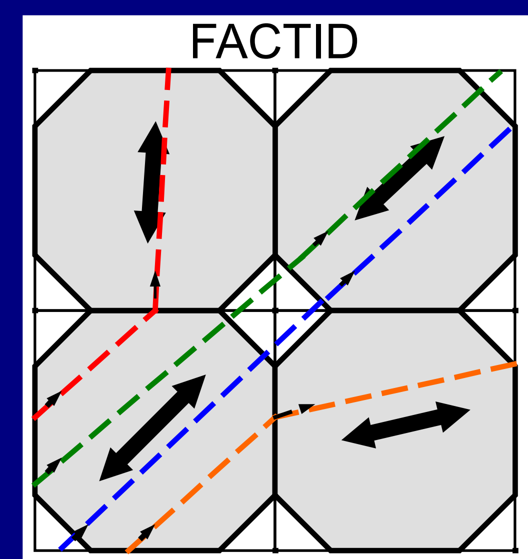


Tracking to define and quantify WM ROIs (with uncertainty/probabilistic) → 3dMVM network stats

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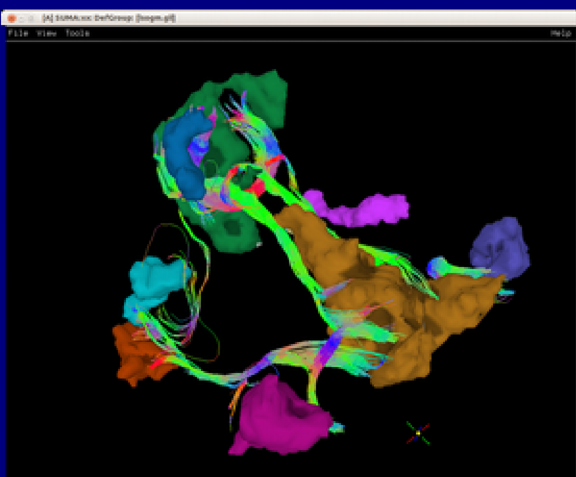
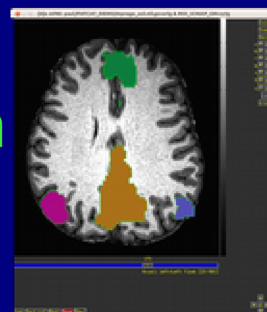
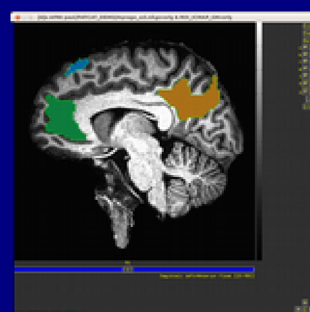
Integrating AFNI-SUMA visualization







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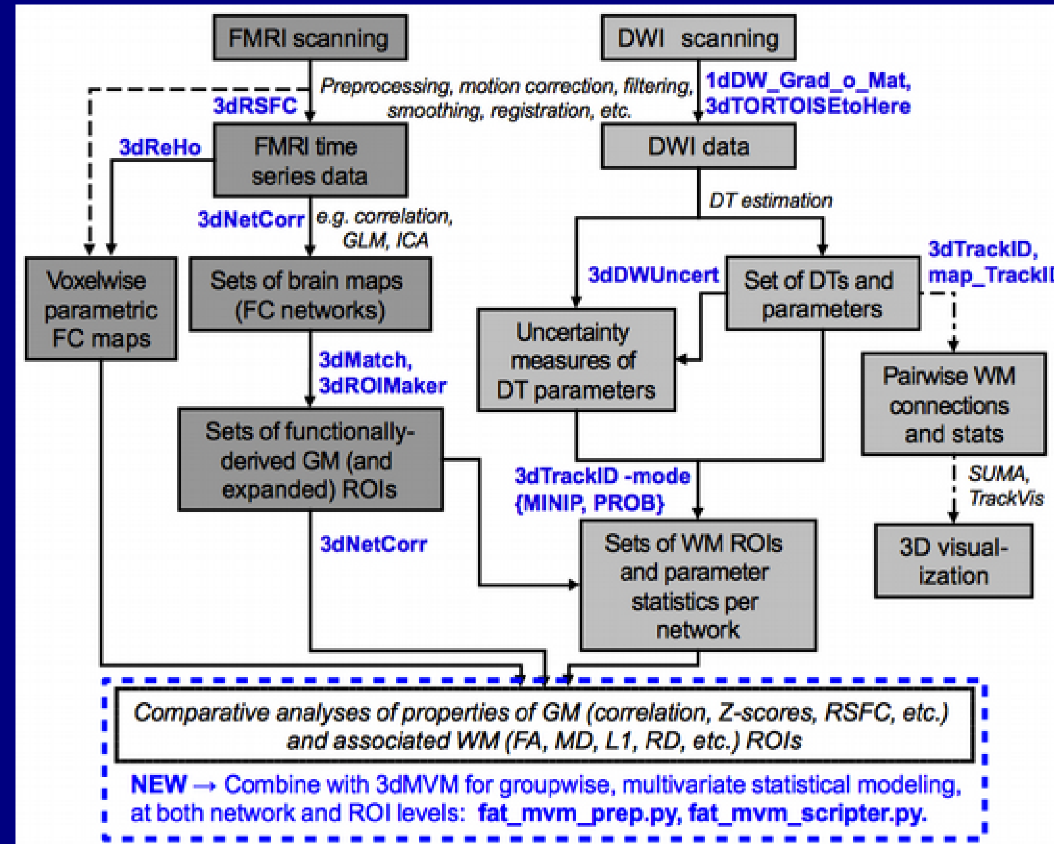


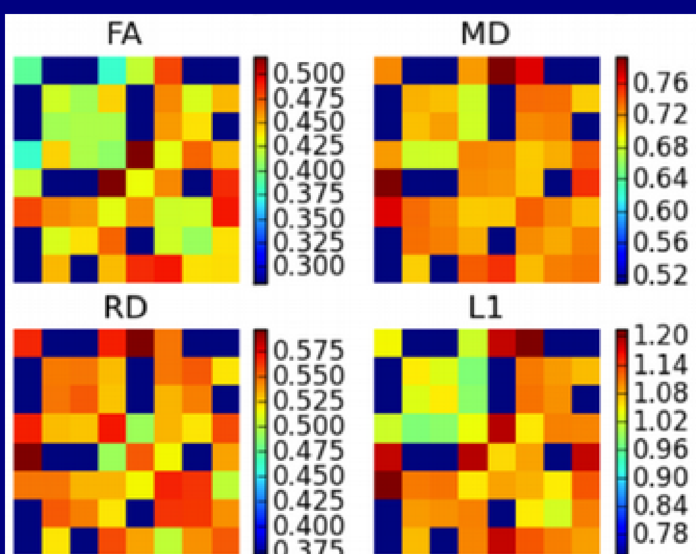


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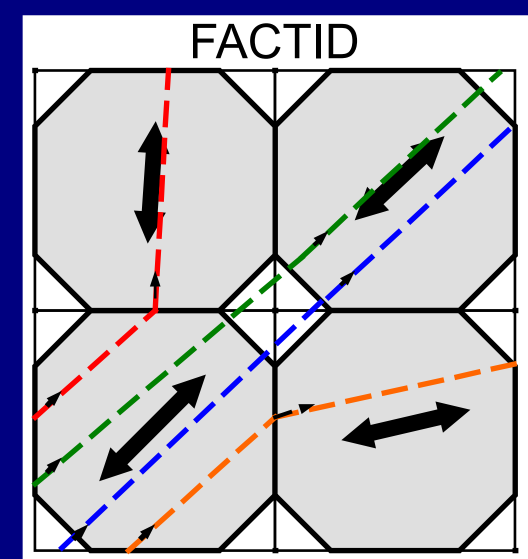


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