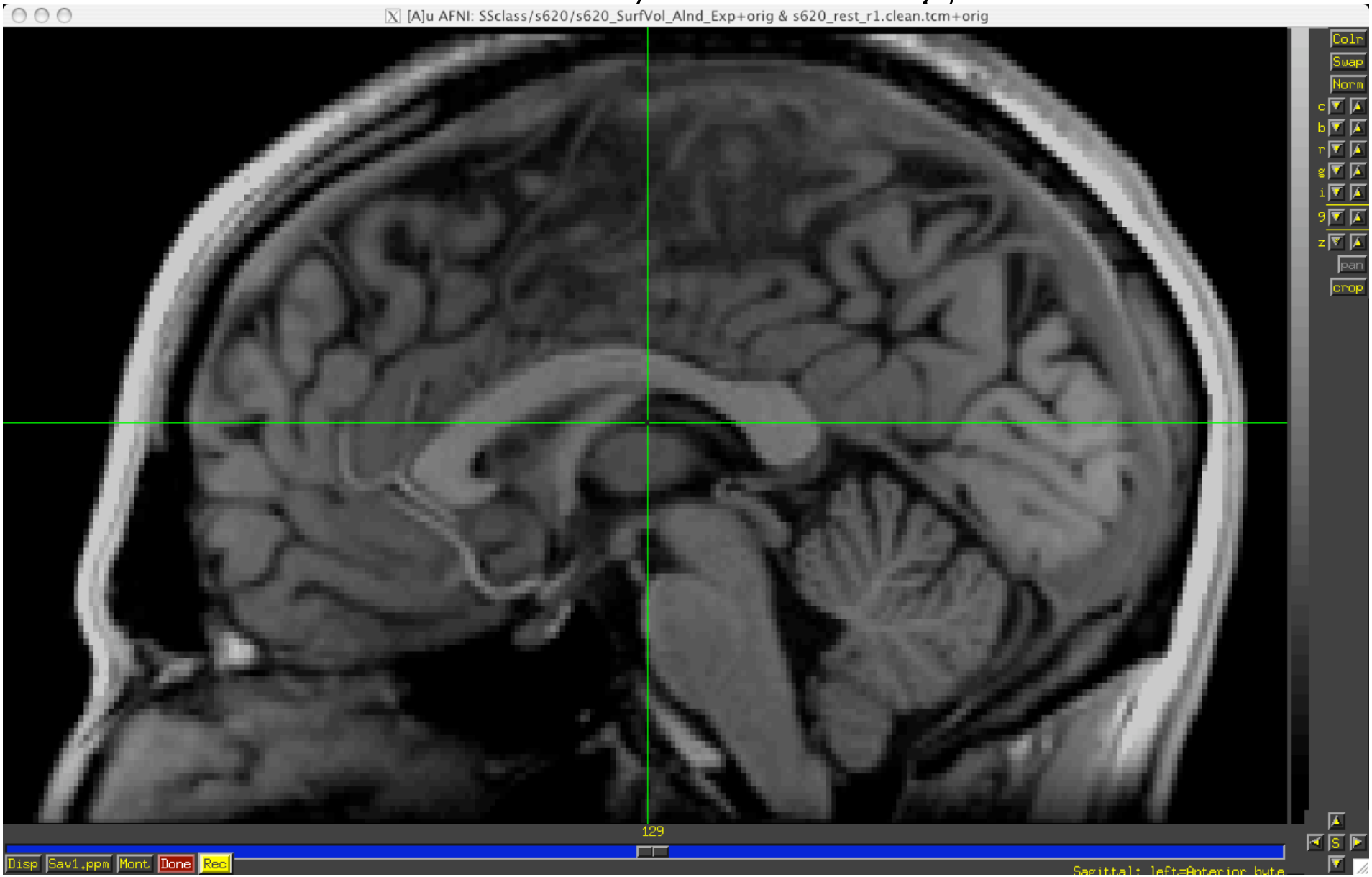
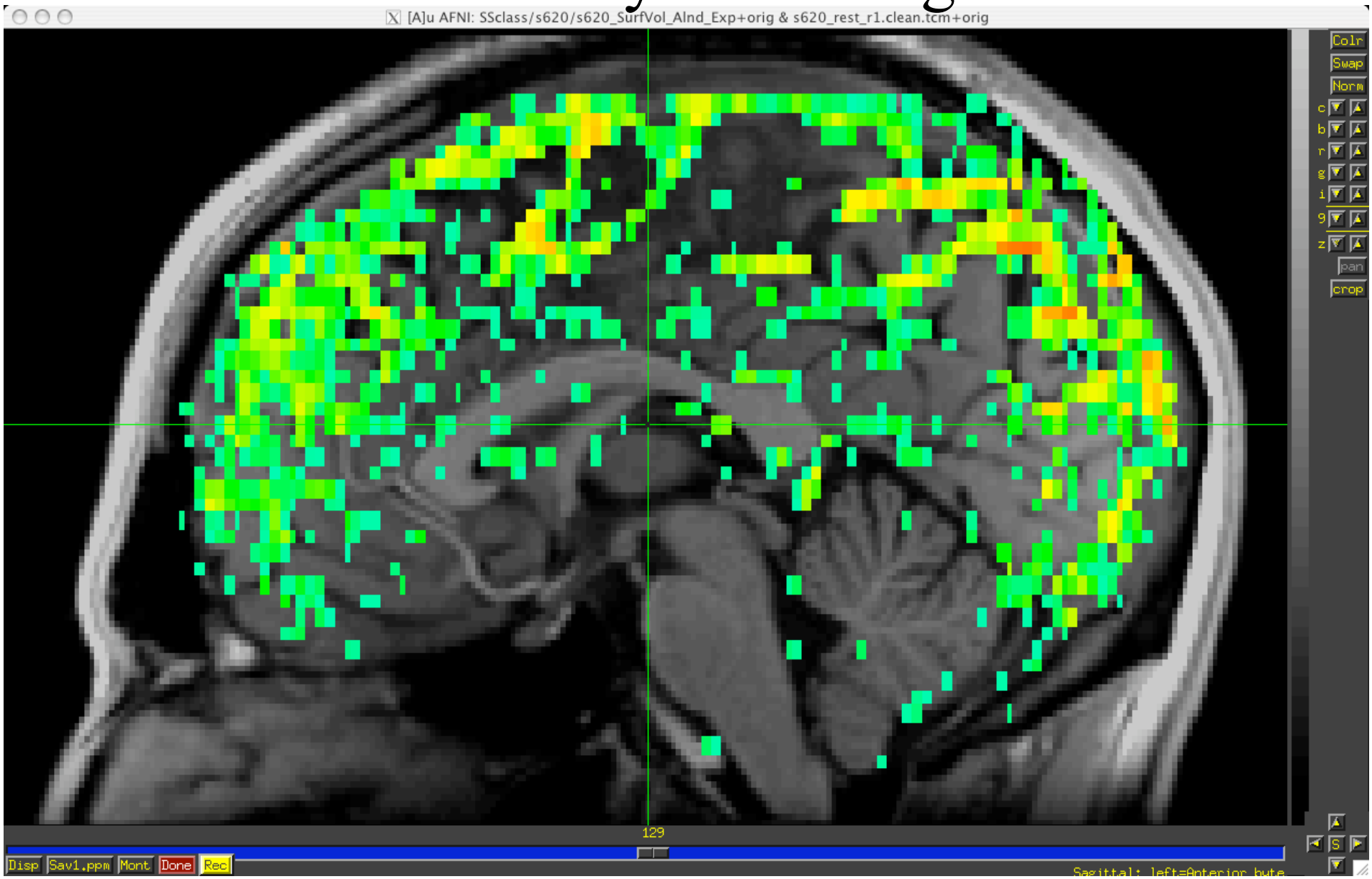
Single Subject Analysis in the context of functional connectivity

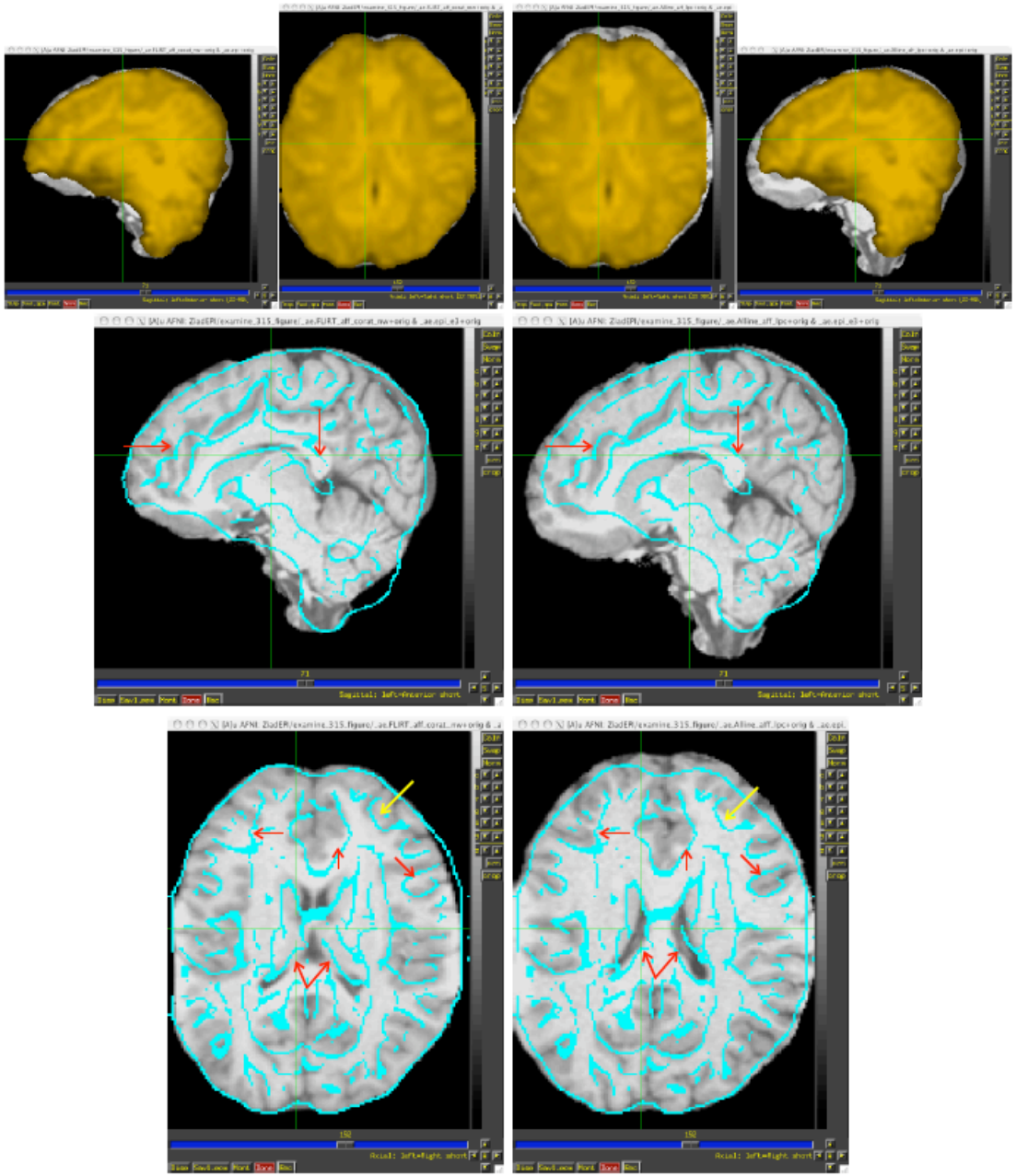
- Precise Anatomy to EPI registration
  - New approach
  - Examining results
  - Tough cases, and more than T1 to EPI
- RETROICOR and RVT correction
  - Creating RONIs
  - Interface for RONI cleanup
  - Reduction in variance
- Volume- and Surface- based ROIs From FreeSurfer
- Interactive Seed-Based Correlation
  - In the volume
  - On the surface
- Correlation Matrices

Precise Anatomy to EPI registration



Precise Anatomy to EPI registration

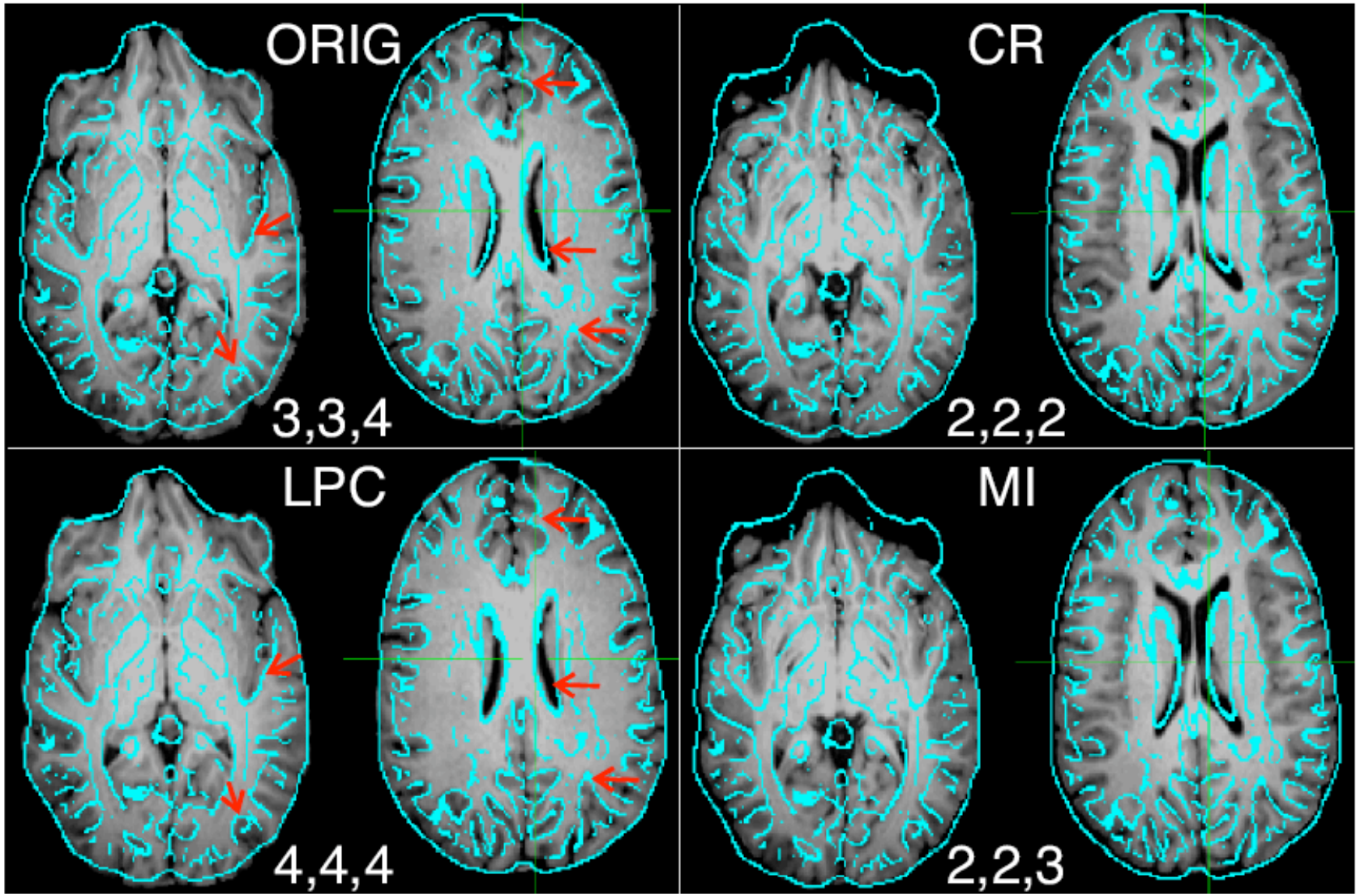




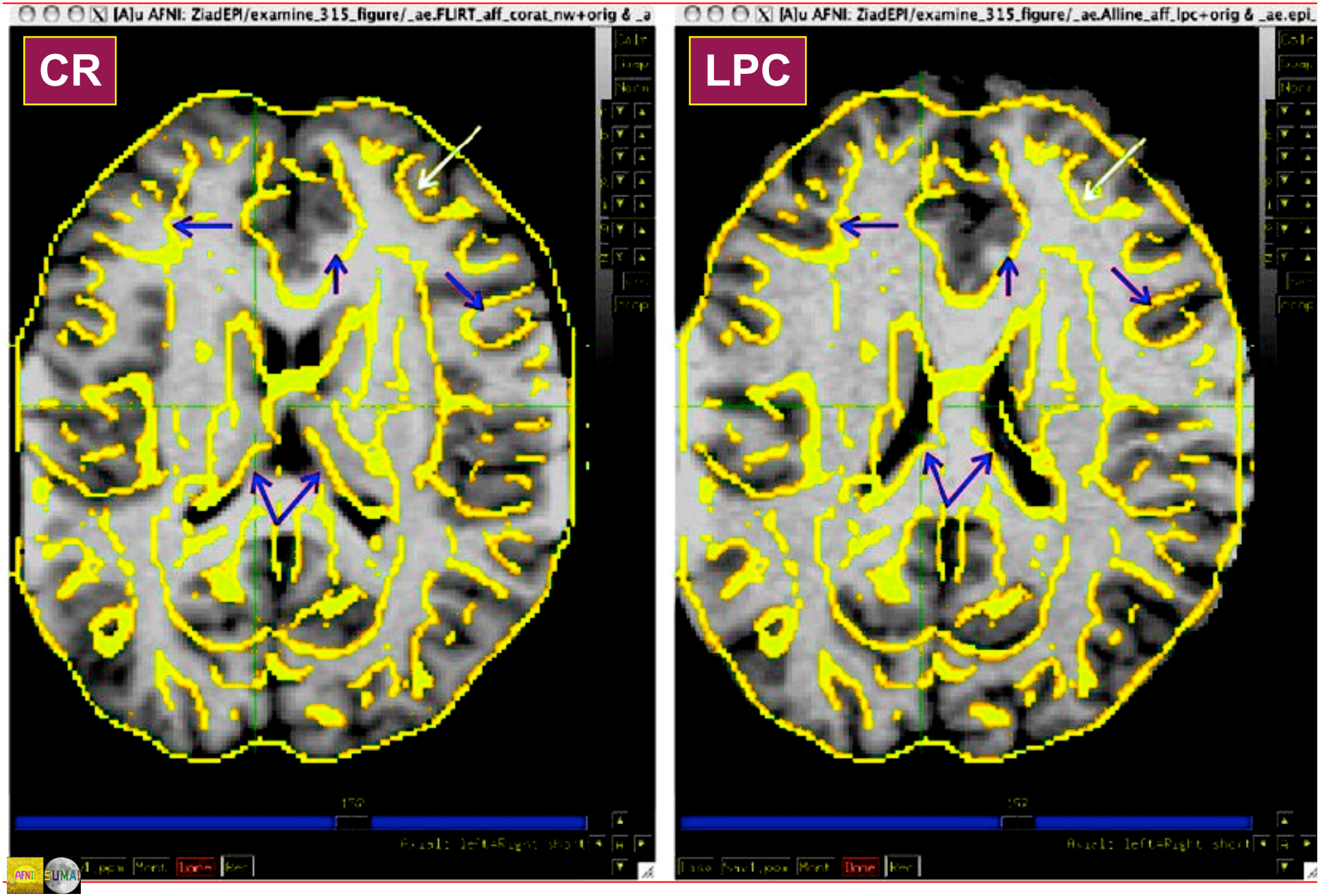
CR LPC
3,3,3 4,4,4

Alignment of EPI and Anatomical Datasets

New LPC method gives consistently better alignment—based on visual inspection—over other cost functionals, including MI and CR



Results: EPI Edges Atop Anatomical Slices



align_epi_anat

Aligning EPI and T1-weighted structural volumes

Alignment of EPI and Anatomical Data in AFNI

align_epi_anat.py and @AddEdge scripts

Alignment – Basics

- Want to align anat and EPI

LPC method – Local Pearson Correlation to match dark CSF in anatomical data with bright CSF in EPI data.

- align_epi_anat.py script – preprocessing and calls 3dAllineate for alignment
- @AddEdge – for visualization

Assessing alignment visually

- Multiple controllers and crosshairs
- Overlay - opacity and threshold
- Overlay toggling
- Underlay toggling
- Edge detection in underlay
- @AddEdge

Align_epi_anat.py basic example

Align anatomical dataset to EPI

```
align_epi_anat.py
 -anat s620_t1+orig
 -epi s620_rest_r1+orig.
 -epi_base 4 -suffix _al2epi
 -AddEdge
```

```
afni -niml -yesplugouts &
@AddEdge
```

or

```
@AddEdge -single_edge
```

Basic example 2

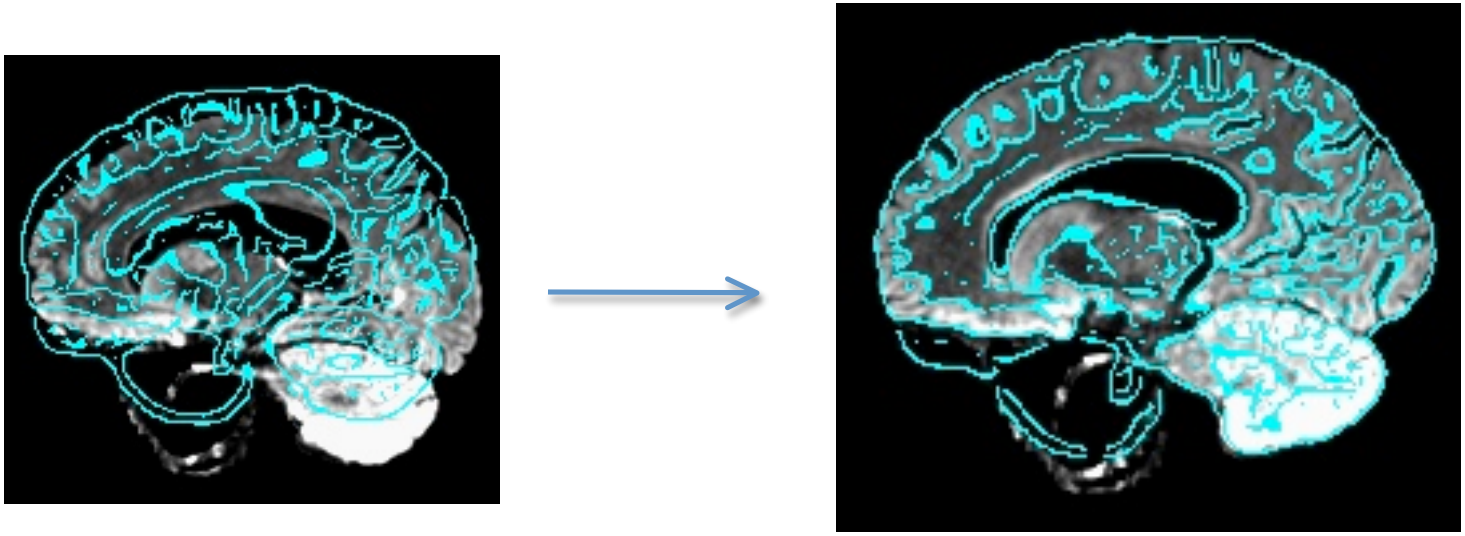
Align multiple EPI runs to anat, and create Talairached version of EPI datasets

```
align_epi_anat.py
  -anat anat+orig -epi epi+orig.
  -epi_base 4 -AddEdge
  -epi2anat -suffix _al2anat
  -child_epi epi_r*+orig.HEAD
  -tlrc_apar anat_at+tlrc
```

“Tough” Cases…

Alignment Examples 1

Structural longitudinal alignment-
3T FLAIR Day 2 aligned to 3T FLAIR Day 1

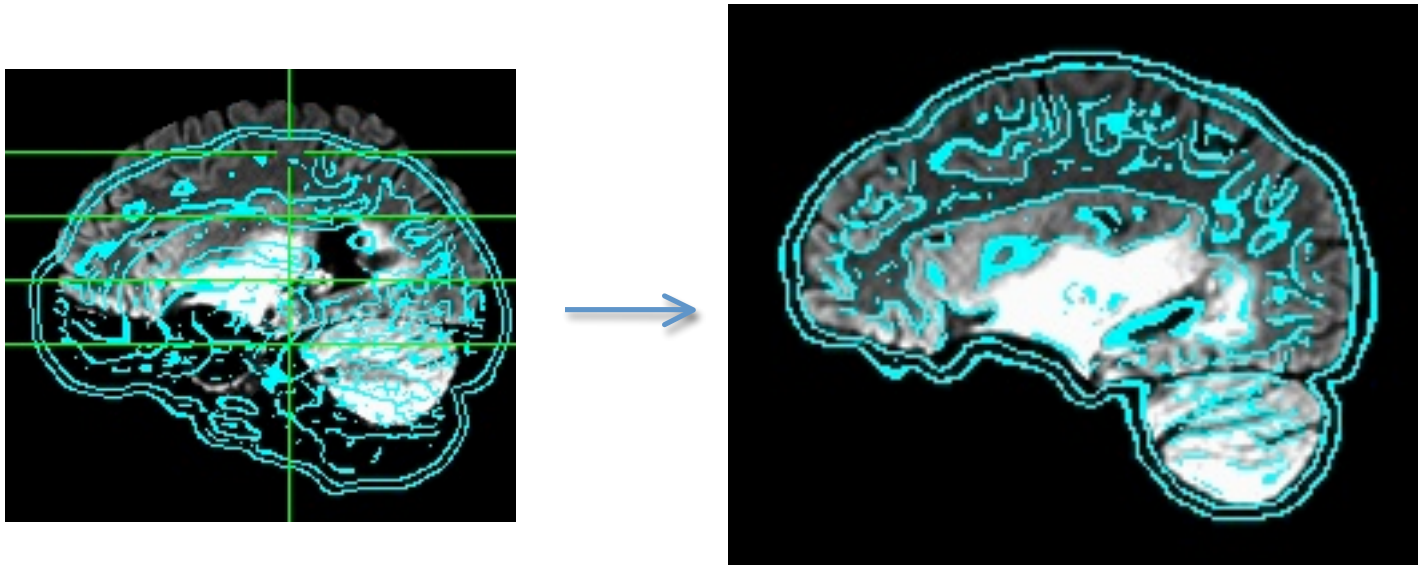


```
align_epi_anat.py -anat 3T_F2+orig
  -epi  3T_F1+orig -epi_base 0
  -cost lpa -big_move -suffix _al1 -AddEdge
```

Data from John Butman
(CC/Radiology)

Alignment Examples 2

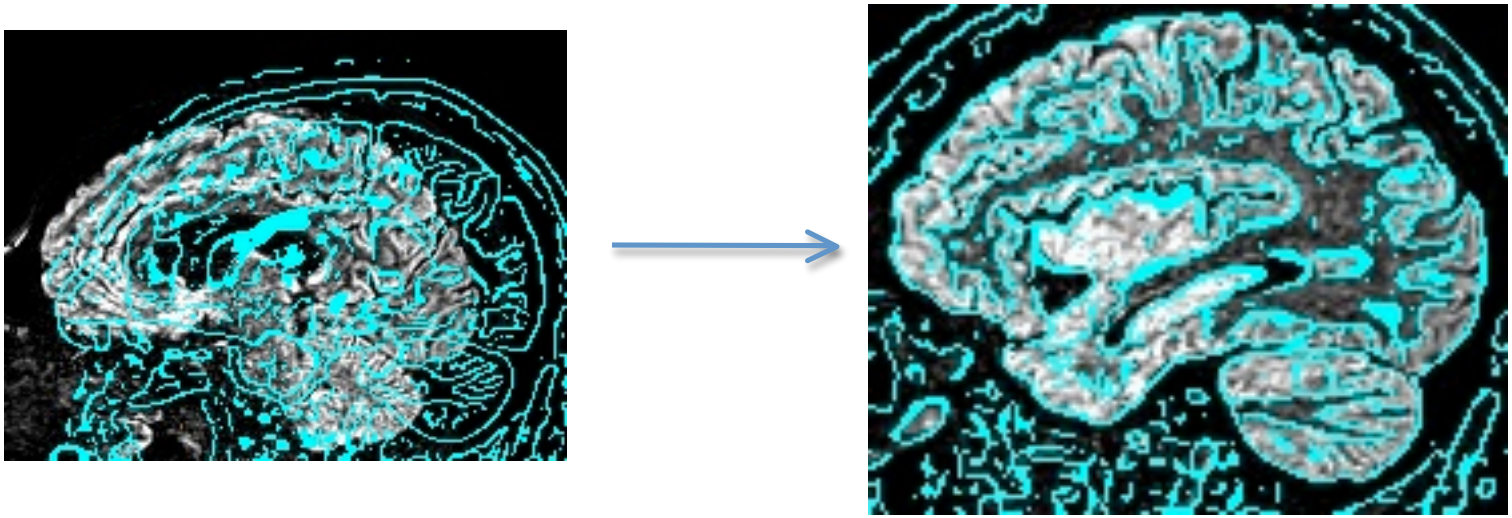
3T FLAIR aligned to 1.5T FLAIR



```
align_epi_anat.py -anat 3T_F1+orig.
 -epi 15T_F1_rs+orig
 -epi_base 0 -cost lpa -big_move
 -suffix _al215T_F1 -prep_off
 -cmass cmass -AddEdge
```

Data from John Butman
(CC/Radiology)

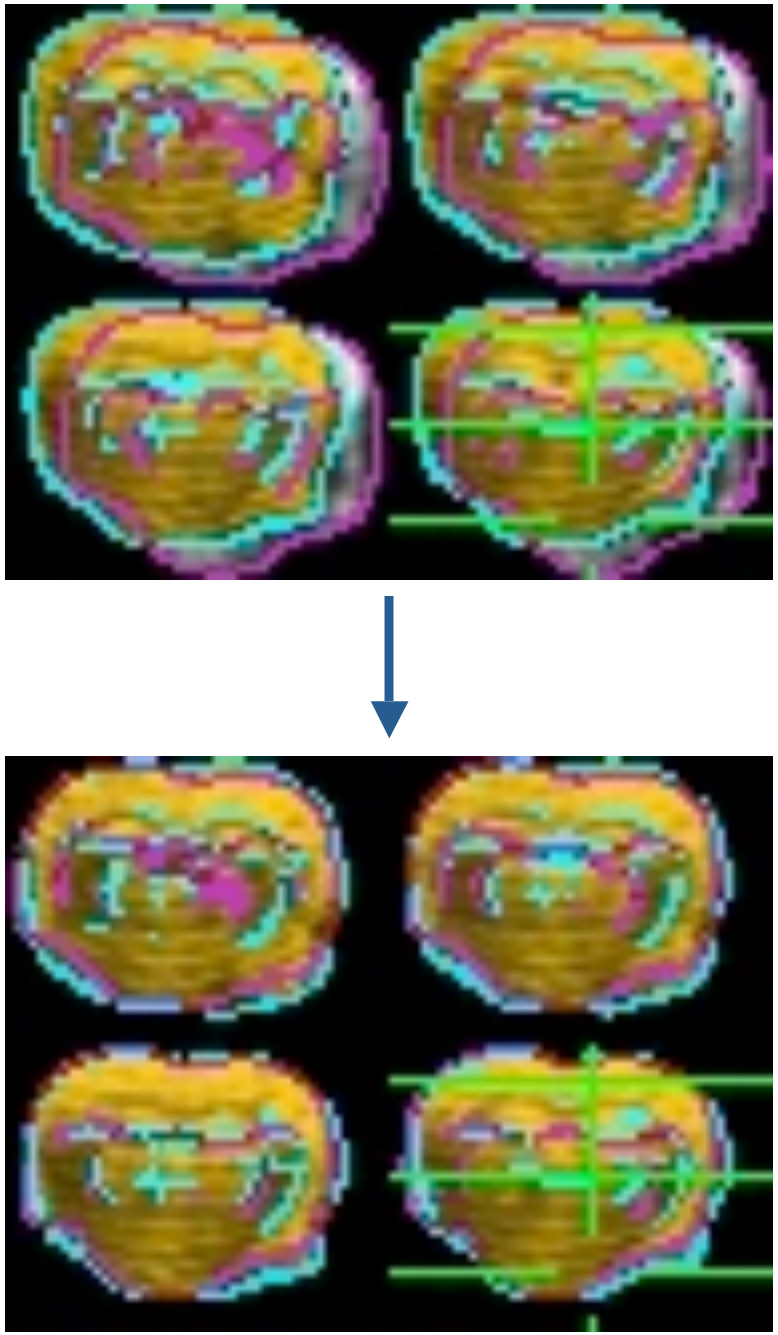
Alignment Examples 3



1.5T FLAIR Day 1 to 1.5T FLAIR Day 2 (longitudinal)

```
align_epi_anat.py -anat 15T_F2_rs+orig
  -epi 15T_F1_rs+orig -epi_base 0
  -cmass cmass -big_move
  -suffix _al_F1 -prep_off
  -epi_strip None -anat_has_skull no
  -cost lpa   -AddEdge
```

Data from John Butman
(CC/Radiology)



Rat EPI

EPI time series from multiple rats aligned to a single rat EPI template

Motion correction and alignment combined

```
align_epi_anat.py
 -anat epi_template+orig
 -epi 07262008.36.1_al+orig
 -epi_base 0
 -suffix _rat5
 -rat_align -cost lpa -epi2anat
 -big_move
```

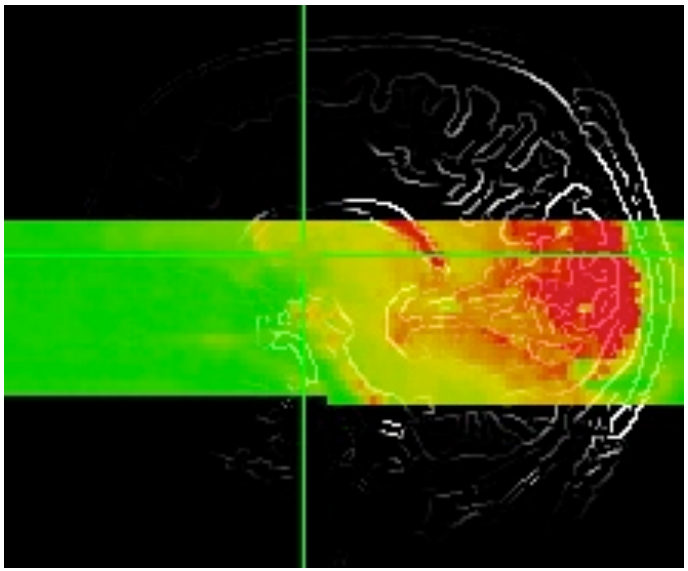
Data from Xin Yu (NINDS)

More alignment examples

Partial axial EPI data with surface coil

Slice timing, motion correction applied to child epi

```
# uniformity correction (use first
sub-brick)
3dUniformize -prefix r1sb0u
   -anat r1+orig'[0]'
align_epi_anat.py -partial_coverage
 -anat anat+orig -epi r1sb0u+orig.
 -suffix _al2anat -epi_base 0
  -epi2anat -child_epi r1+orig.
```

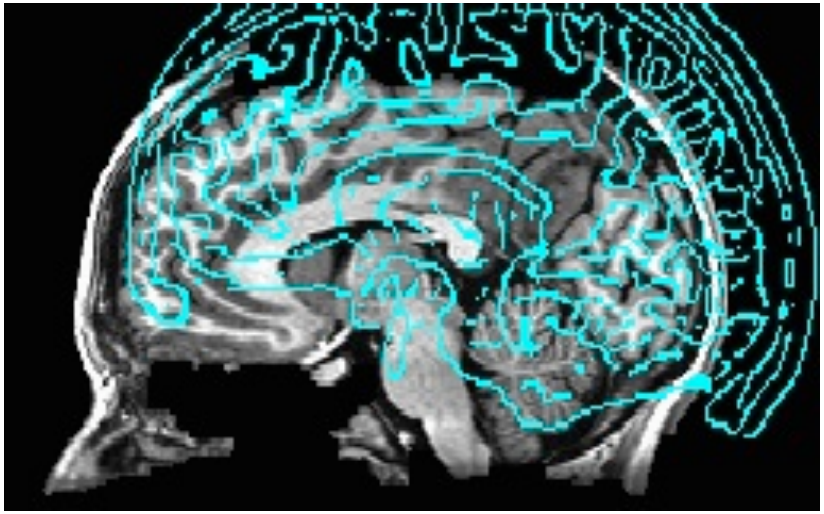


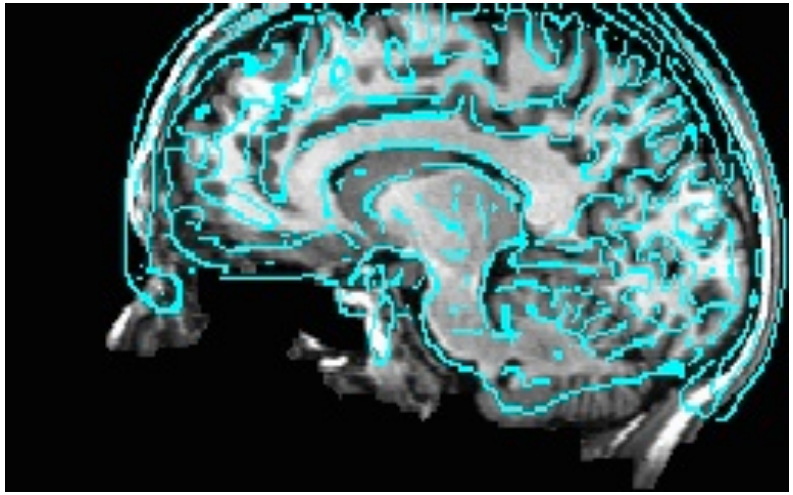
Data from James Bjork, NIMH, Stephanie McMains, Princeton

More alignment examples

MP-RAGE to older SPGR alignment

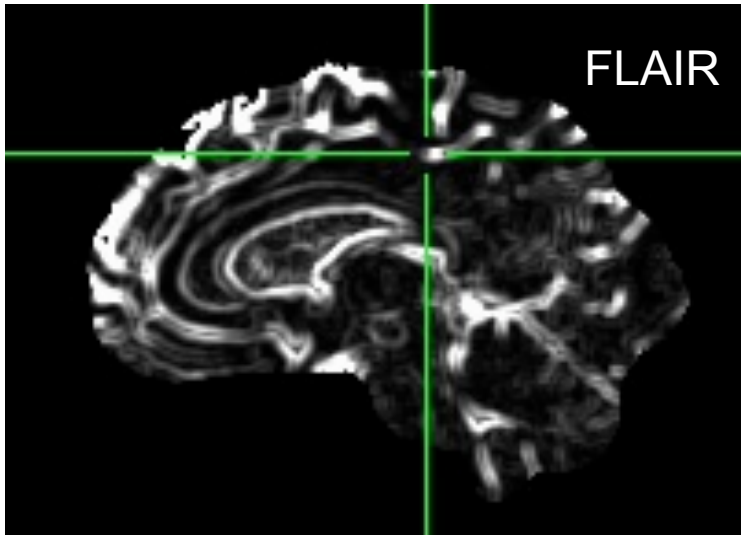
```
align_epi_anat.py
 -anat PythonTest+orig. -epi mprage_series003+orig.
 -epi_base 0 -cost lpa
 -prep_off -anat_has_skull no
 -epi_strip None -giant_move
 -suffix _gm2 -AddEdge
```

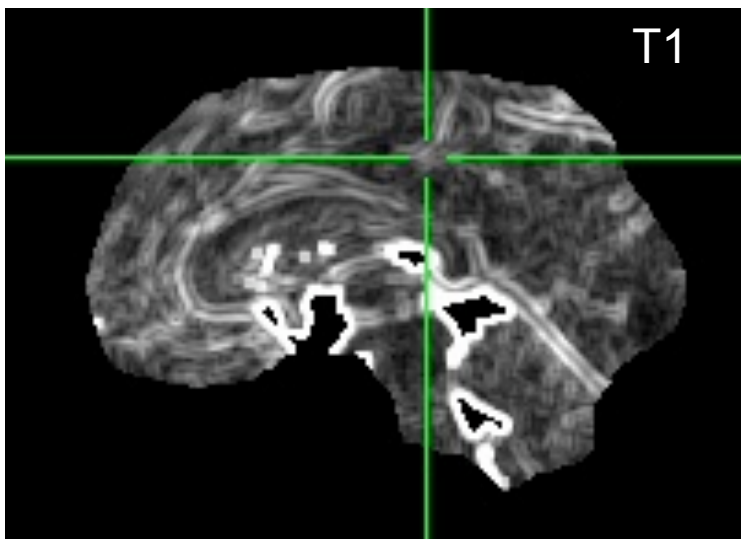


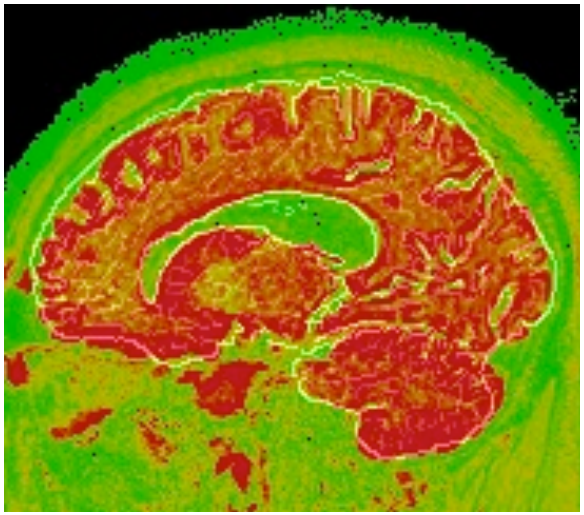


Data from James Bjork, NIMH

Edge Alignment Example 1





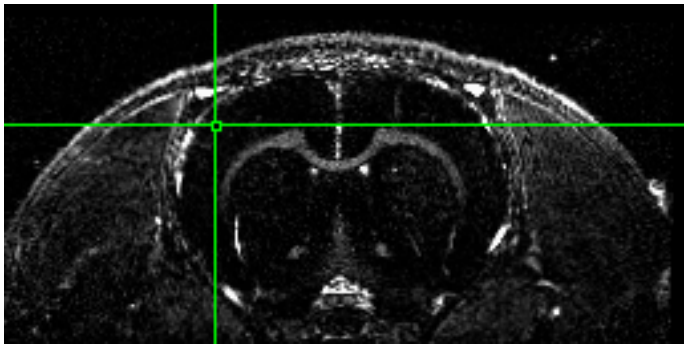


3T T1 to 3T FLAIR (multi-modality)

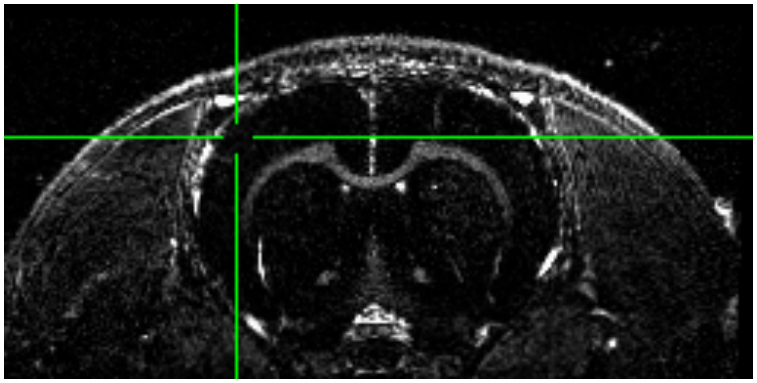
```
align_epi_anat.py -anat 3T_T1_short+orig
 -epi 3T_F1_ns+orig -epi_base 0 -big_move -cmass cmass
 -cost lpa -master_anat 1 -suffix _al_3TF1e  -prep_off
 -epi_strip None -edge
```

Data from John Butman (CC/Radiology)

Rat Brains



Alignment of 12 hour Manganese enhanced MRI scan (MEMRI) to start



```
#!/bin/tcsh
# align_times.csh
set basedset = 14_pre+orig
foreach timedset ( 14_*hr+orig.HEAD)
  align_epi_anat.py -prep_off -anat $timedset -epi $basedset \
  -epi_base 0 -anat_has_skull no -epi_strip None -suffix _edge2prep \
  -cost lpa -overwrite -edge -rat_align
end
3dTcat -prefix 14_timealigned_edge 14_pre+orig. 14*edge2prep+orig.HEAD
```

Data from Der-Yow Chen, Xin Yu (NINDS)

Other cases for alignment

child_epi datasets can include statistical datasets (unlikely to be useful for the alignment itself)

child_anat datasets transformed to match epi data. Can be used if resampled or zeropadded anat dataset is used for alignment (to save memory and time) and apply transformation to original anat.

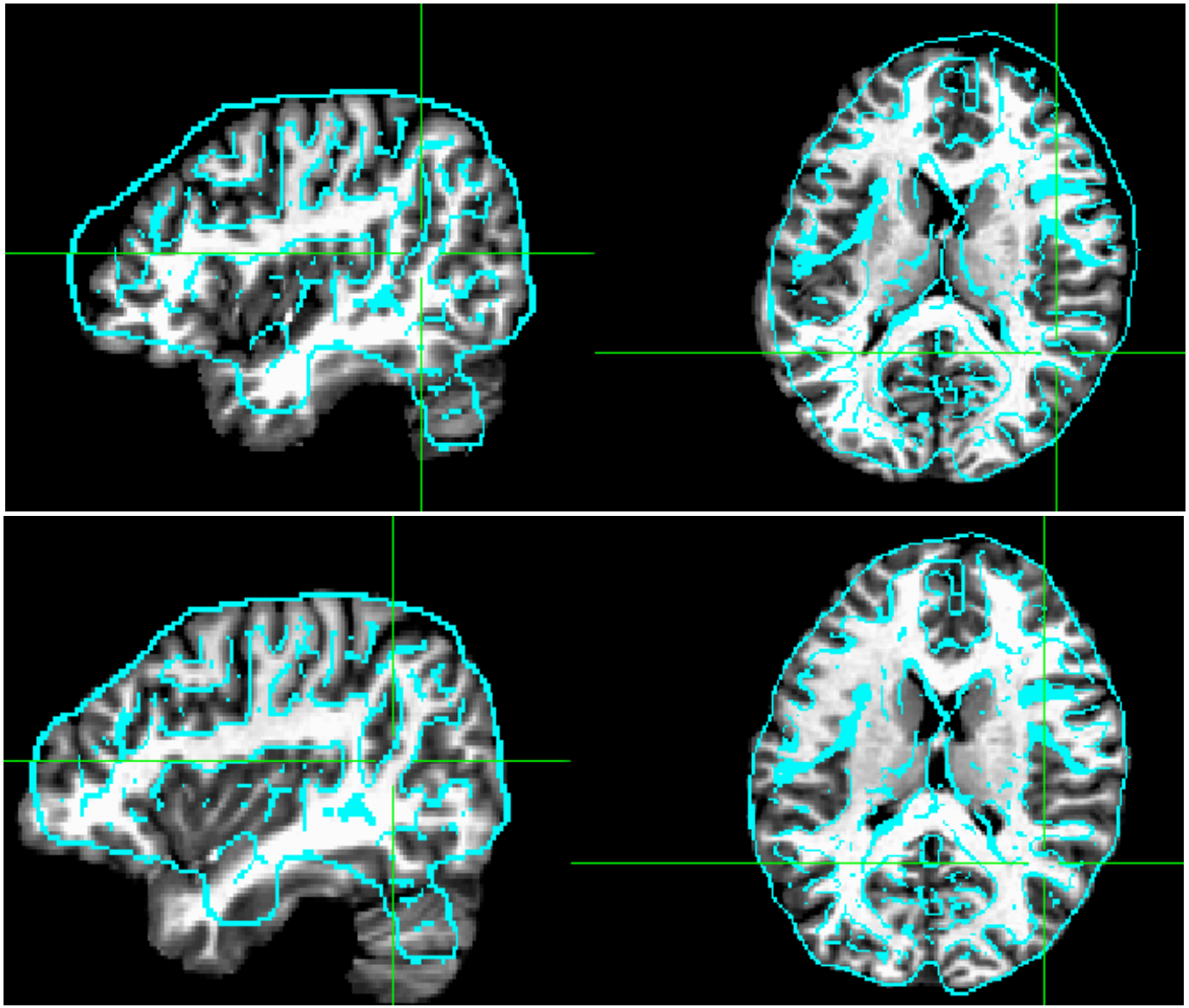
Partial coverage (-partial_coverage, partial_axial, partial_sagittal, partial_coronal)

DTI registration (-volreg_method 3dWarpDrive)

align_epi_anat.py example output

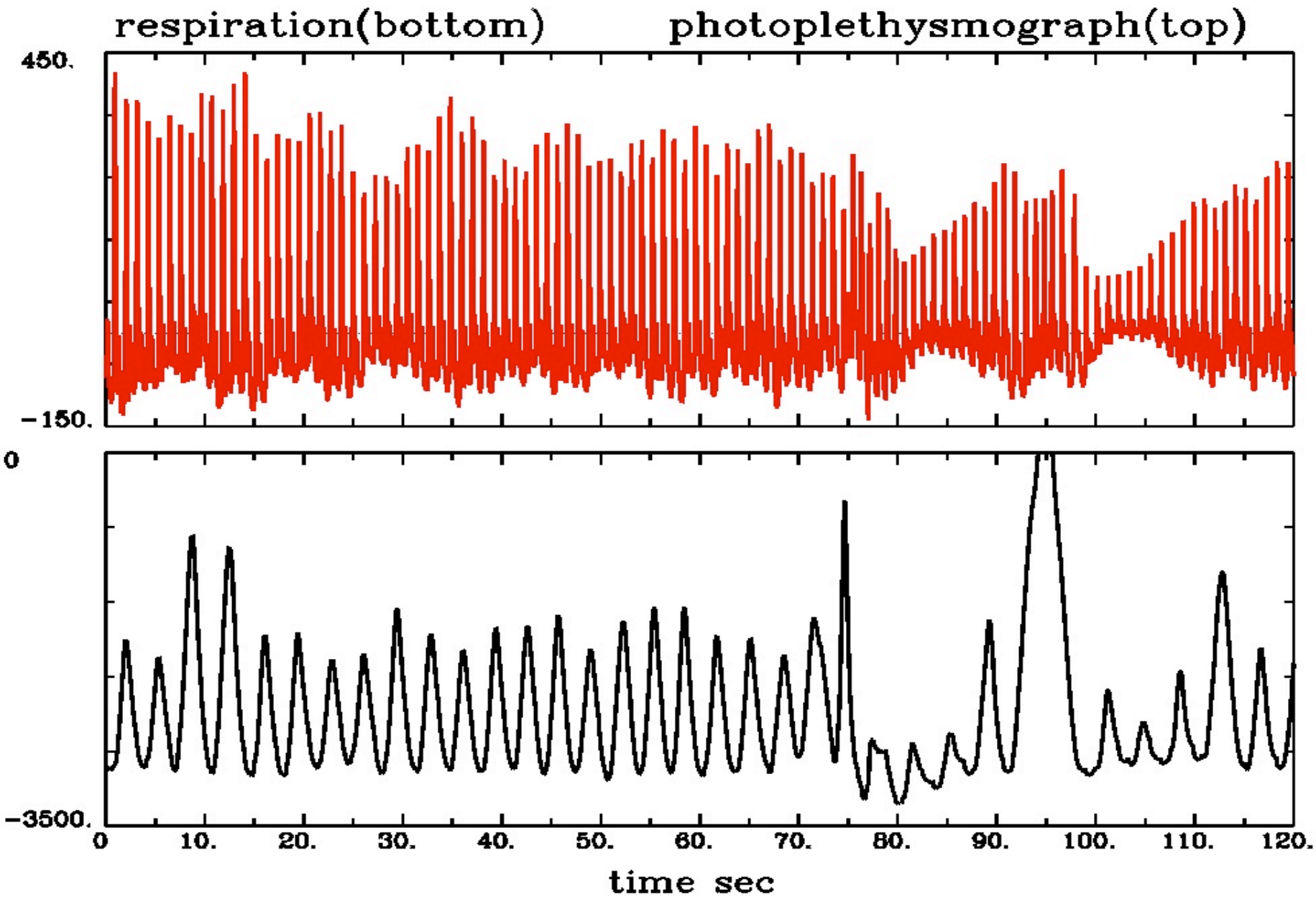
Pre-alignment

Post-alignment



@AddEdge -single-edge display shows before and after with edges from transformed EPI dataset as overlay

RETROICOR and RVT correction



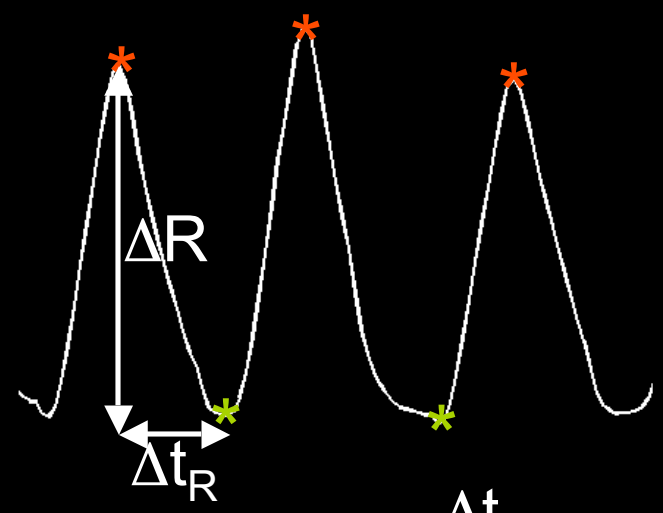
Physiologic rate regressors: modeling issues

The phase and the shape of the expected fMRI signal changes due to fluctuations in the rates of respiratory and cardiac pulsation are not fully understood…

Respiration volume per unit time (RVT) regressor

$$\sim \frac{\Delta R}{\Delta t_R}$$

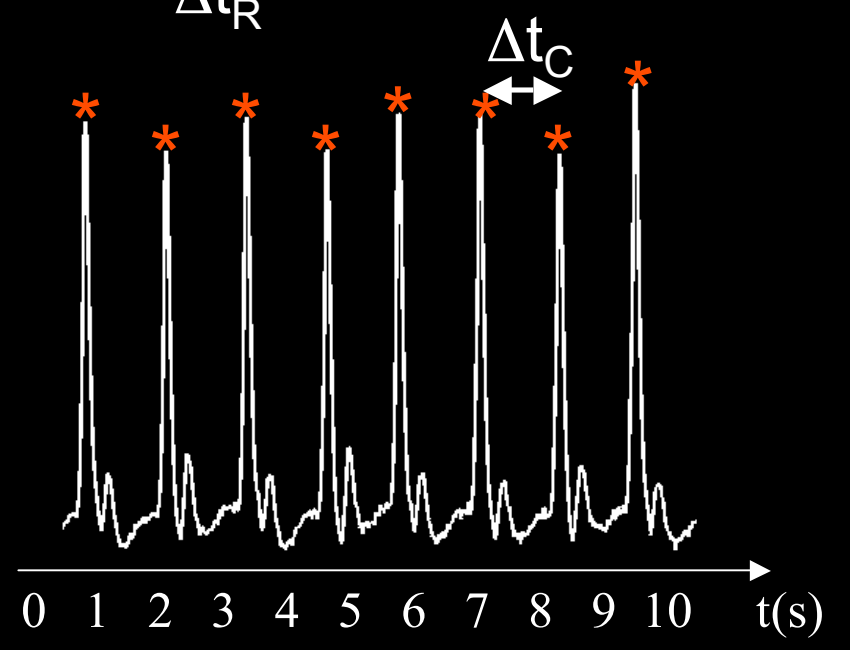
Birn et al., NI, 2006



Cardiac rate (CR) regressor

$$\sim \frac{1}{\Delta t_C}$$

Shmueli et al, NI, 2007

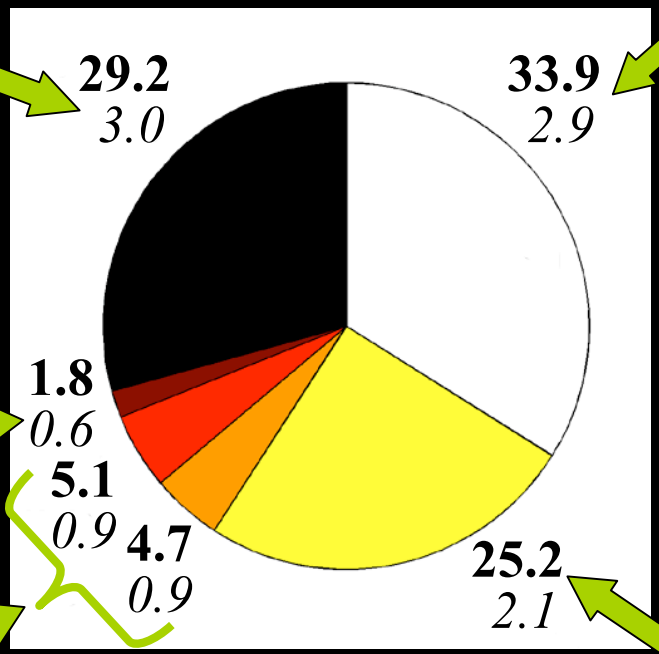


Results

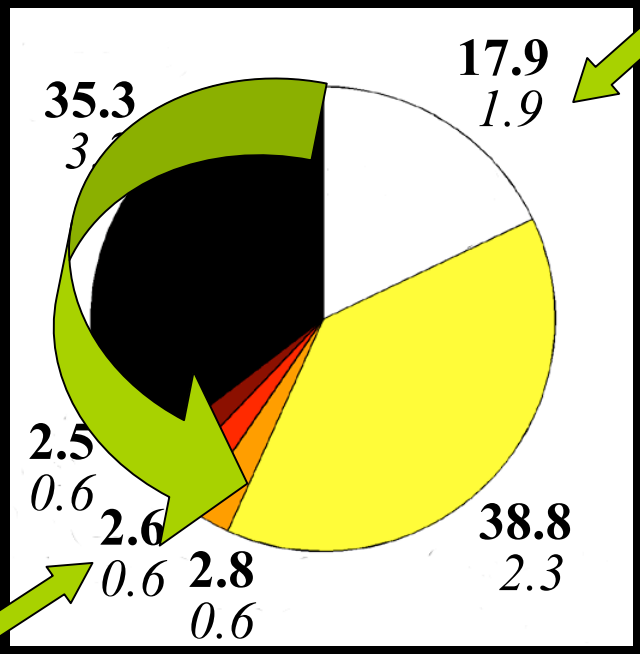
VARIANCE EXPLAINED (%)
% SIGNAL CHANGE relative to baseline

Mean (s.e.)
n = 8

VISUAL CORTEX



GRAY MATTER



- Instrumental drifts
- Physiologic cycles
- RVT (lags: -9s, +9s)
- Cardiac-rate (lags: -3s, +9s)
- Thermal noise
- Spontaneous activity

GRAY MATTER

Total % signal change = 5.1%
tSNR: ~20 → ~30

Bianciardi et al., MRI 2009

AFNI's RETROICOR

- Current implementation is in RetroTS.m
- To specify the options for RetroTS

```
Opt.PhysFS=1./0.02;
Opt.Nslices=42;
Opt.VolTR=3.5;

Opt.Respfile = 's620_respir_rest.dat';
Opt.Cardfile = 's620_ecg_rest.dat';
Opt.Prefix = 's620_RTS';
[Opt1(i), OptR1(i), OptE1(i)] = RetroTS(Opt);
```

- For a demo:

```
tcsh @run_ShowRetroTS
```

RETROICOR with afni_proc.py

recall: afni_proc.py creates processing scripts

suggested processing block order is despike, ricor, everything else

volreg would significantly alter timing in a voxel

process respiratory/cardiac regressors per run (though only 1 run)

run example **`s1.afni_proc.ricor`** under **`ap.examples`**

```
cd ap.examples        (recall use of the <tab> key)
tcsh s1.afni_proc.ricor
tcsh -xef proc.s620.1.RICOR.perrun |& tee output.ricor
```

allow processing script to run while we discuss it (8-20 minutes)

note use of higher degree poly in ‘ricor’ compared to ‘regress’

view both scripts using **`‘less’`** (or some editor, or just watch)

```
less proc.s620.1.RICOR.perrun
```

results are under **`s620.1.RICOR.perrun.results`**

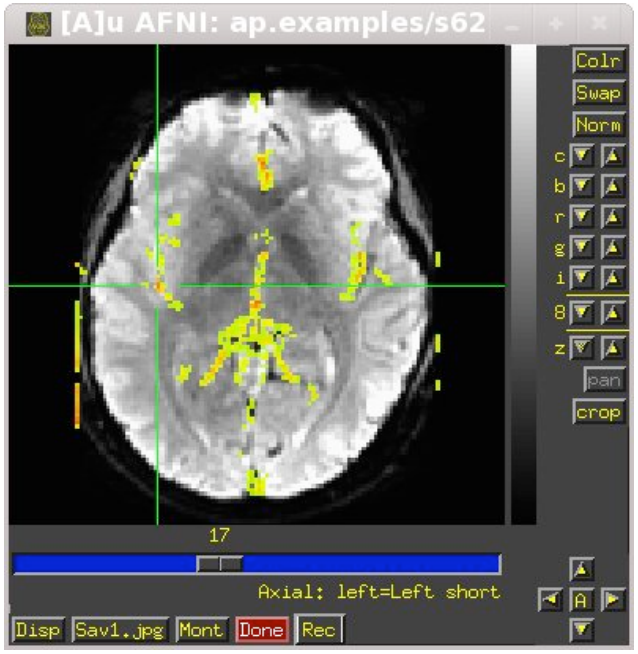
How much variance have we gotten rid of?

`s2.ap.baseonly` does same processing, but no RETROICOR

compare ratio of variances

run script 3 to compute:

```
tcsh s3.ss.ratio
cd s620.1.RICOR.perrun.results
afni
```



- **`all_runs`** is underlay dataset
- **`sos.ratio`** is overlay dataset
- threshold at 1.5
- basic 20 voxel cluster

- **`jump to (xyz)`**: 32 -30 12

- F-stat might be 4 times as large here

RETROICOR with regressors of interest

consider with class data: AFNI_data4

- 9 runs, 9 regressors of interest, typical processing
- note effect of processing per-run:
  - adds 117 regressors (9 runs * 13 regressors per run)

```
cd AFNI_data4
cat s.ricor.1.per-run
less proc.s.RICOR.1
```

- processing across-runs:
  - adds 13 regressors (each catenated across 9 runs)
  - similar to typical processing of motion regressors

```
cat s.ricor.2.across-runs
less proc.s.RICOR.2
```

Interlude: **afni_proc.py** updates

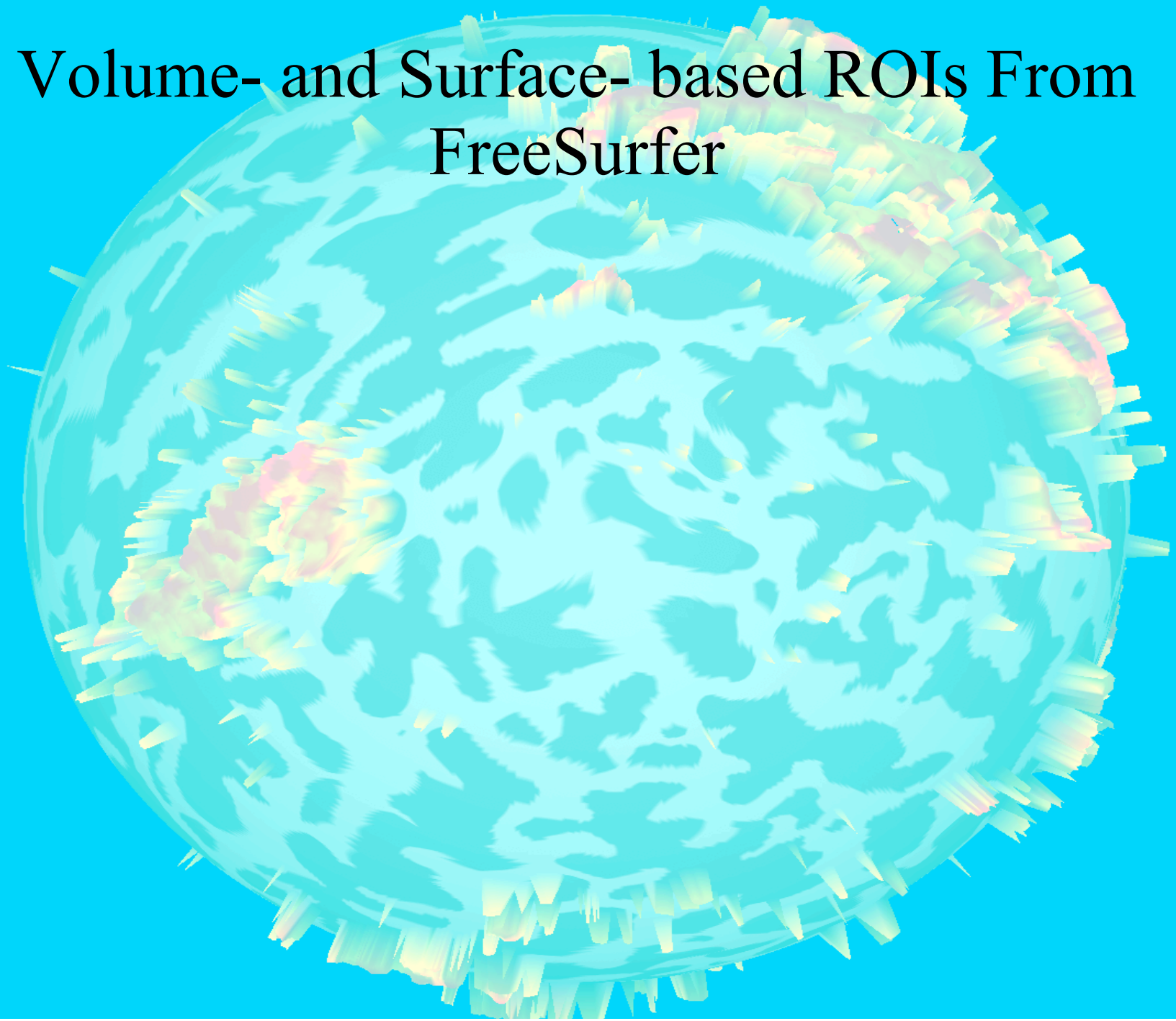
select recent updates (as of version 1.44 : May 8, 2009)

- estimation of smoothness for **AlphaSim**
- run regression via **3dREMLfit** (and/or **3dDeconvolve**)
- by default, the EPI mask is NOT applied in regression
  - suggest masking in group space from anatomical template
  - see **'MASKING NOTE'** section of **'afni_proc.py -help'**
- can now process +tlrc data
- can process of RETROICOR regressors (per run or across runs)
- motion parameters can be processed per run

in the near future (order may vary)

- warp to standard space as part of volume registration step
  - using single interpolation of data
  - could compare time series data across subjects
  - could apply standard masks/atlases to EPI data
  - with **`3dBlurToFWHM`**, could use **`AlphaSim`** lookup table
  - needed to avoid interpolation of stats for use with **`3dMEMA.R`**
- deoblique data at volreg step
- align EPI to anat (you guessed it, via **`align_epi_anat.py`**)
- roiregs processing block
  - automatically create regressors from ROIs or atlases
  - as time series averages or (multiple?) principle components
  - as regressors of interest / no interest
- use **`3dBlurToFWHM`** (instead of **`3dmerge`**)
- allow list of basis functions (this has been too slow in coming)
- allow for **`stim_times_AM1/2`**

Volume- and Surface- based ROIs From FreeSurfer



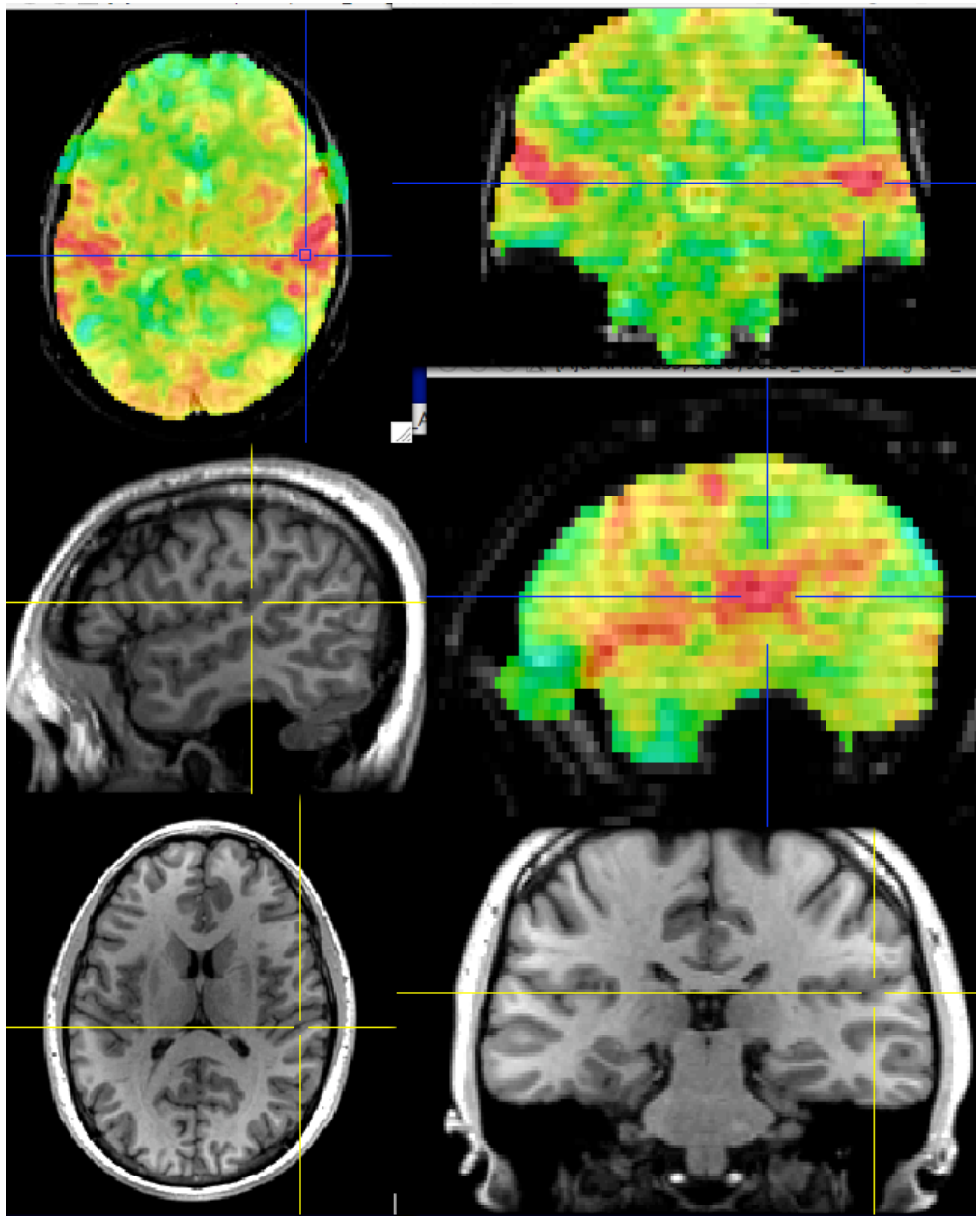
Volume- and Surface- based ROIs From FreeSurfer

- @SUMA_Make_Spec_FS now ports:
  - Surface models from FreeSurfer
  - Surface and volume parcellations
  - Other segmentation volumes
- Parcellation integer labels are not contiguous
  - For ease of display we rank them
    - **`3dRank`** or **`3dmerge -1rank`**
  - To recover labels from ranked or unranked data
    - **`@FS_roi_label`**
- Demo:

  `@run_ViewParcellation`

AFNI! InstaCorr

All data herein from Alex Martin, *et al.* [NIMH IRP]



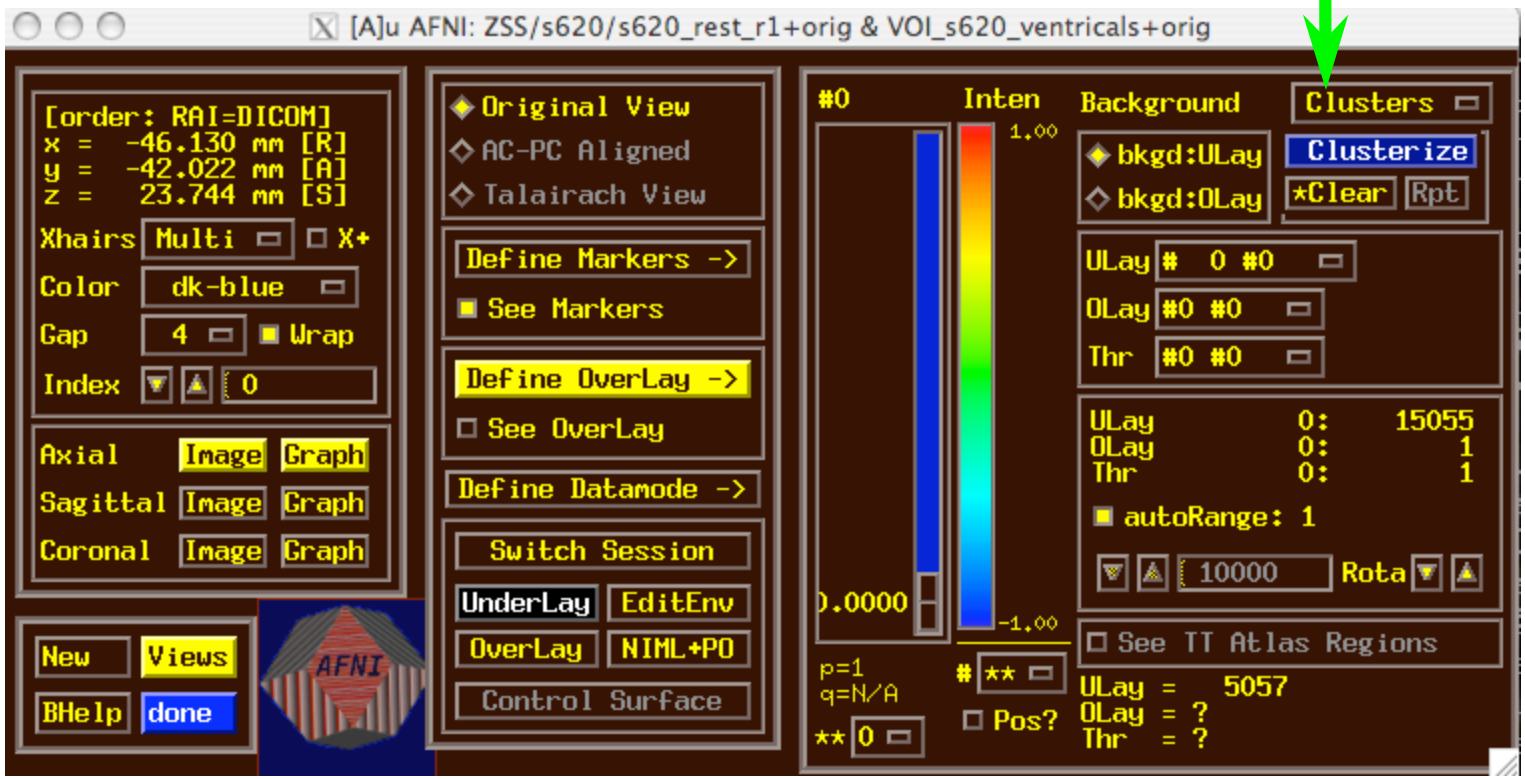
- On-the-fly **insta**ntaneous **corr**elation map of resting state data with interactively selected seed voxel
- **Setup phase**: prepares data for correlations (several-to-10+ seconds)
- **Correlation phase**: you select seed voxel, correlation map appears by *magic*

InstaCorr: Processing Outline

- **Setup phase**:
  - ★ Masking: user-selected *or* Automask
  - ★ Bandpass and other filtering of voxel time series
  - ★ Blurring inside mask = the slowest part
- **Correlation phase**:
  - ★ Correlate selected seed voxel time series with all other prepared voxel time series
  - ★ Make new dataset, if needed, to store results
  - ★ Save seed time series for graphing
  - ★ Redisplay color overlay
  - ★ Optional: compute FDR curve for correlations
    - o This can be slow, so is not turned on by default

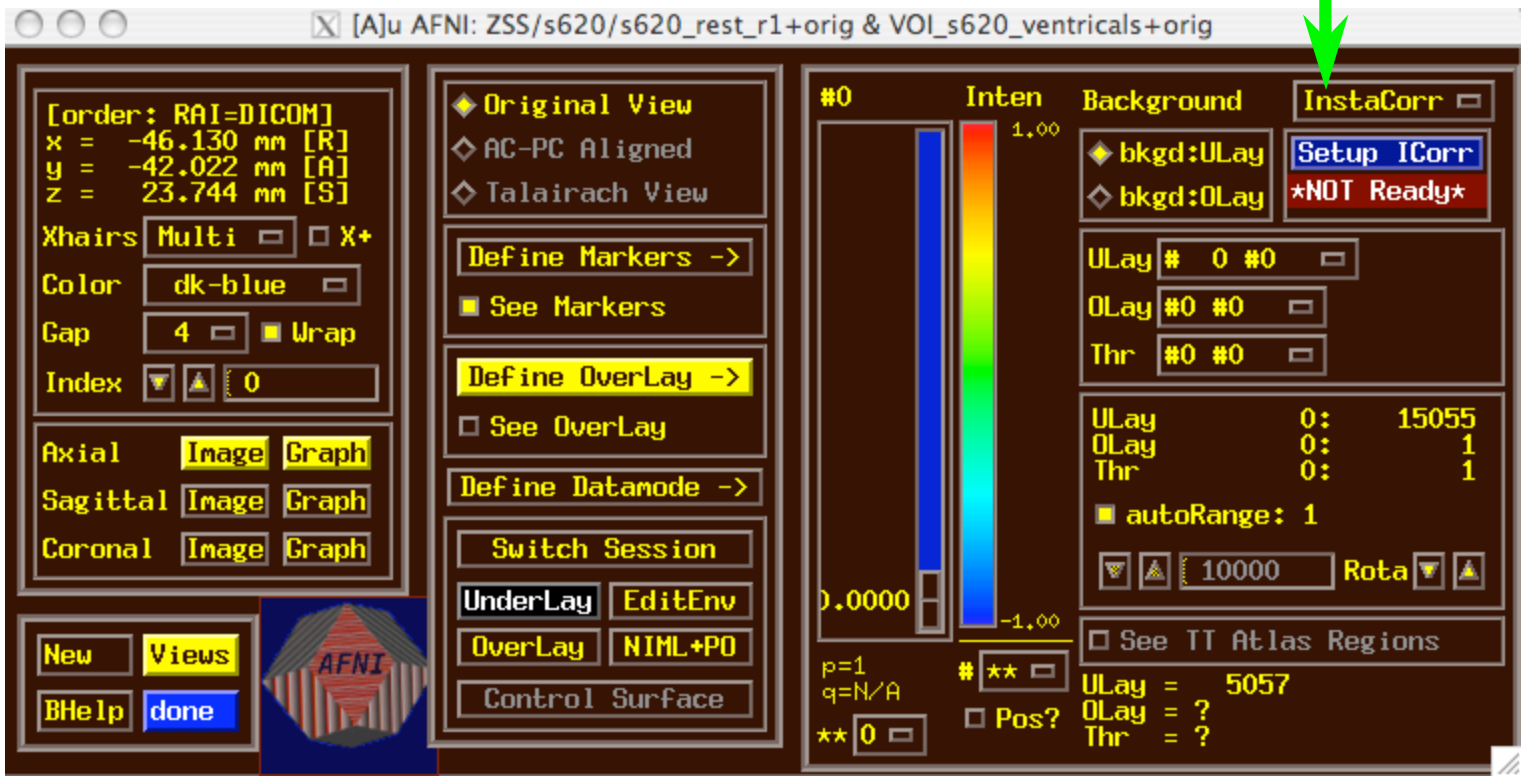
InstaCorr: Setup - 1

- Open Define Overlay, choose InstaCorr from menu in top right corner



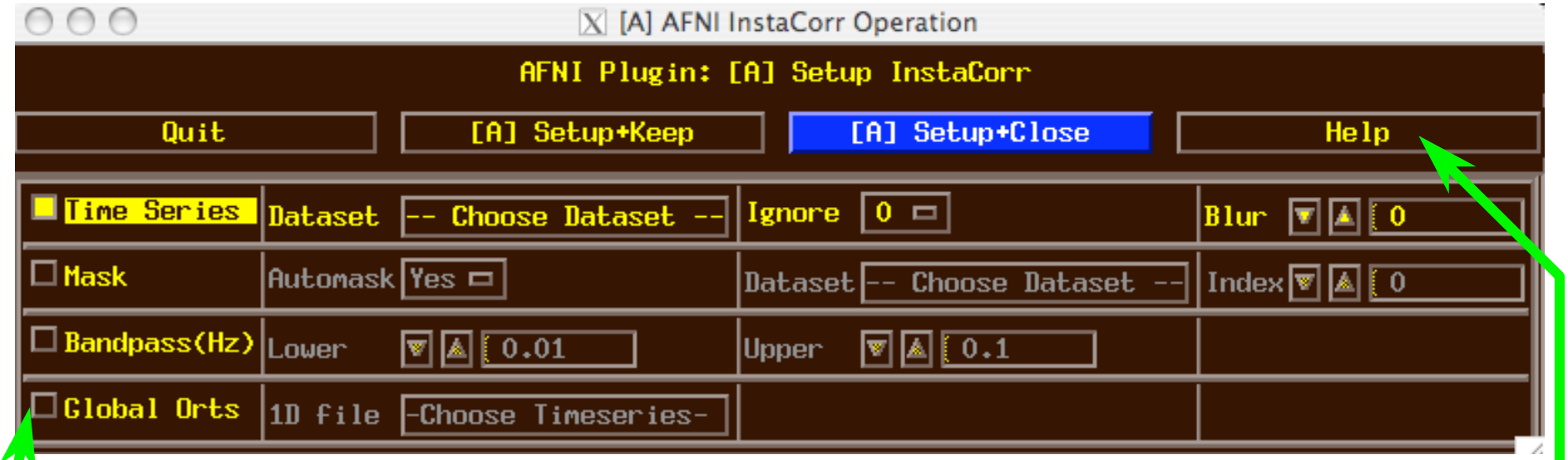
InstaCorr: Setup - 2

- Open Define Overlay, choose InstaCorr from menu in top right corner



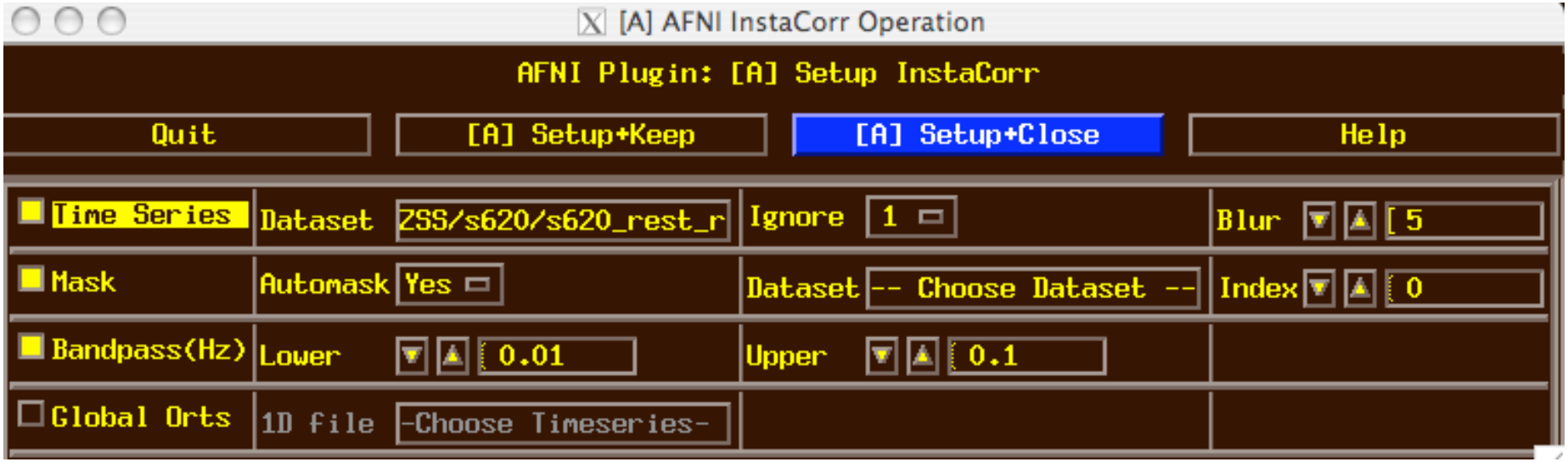
- Then press Setup ICorr button to get control panel

InstaCorr: Setup - 3



- Mostly self-explanatory (I hope) — *cf.* Help
- Global Orts = extra time series to be projected out of dataset before correlation
  - ★ All columns in selected 1D file
  - ★ The first Ignore rows (time points) will be skipped
  - ★ *e.g.*, movement parameters
- When ready, press one of the Setup buttons

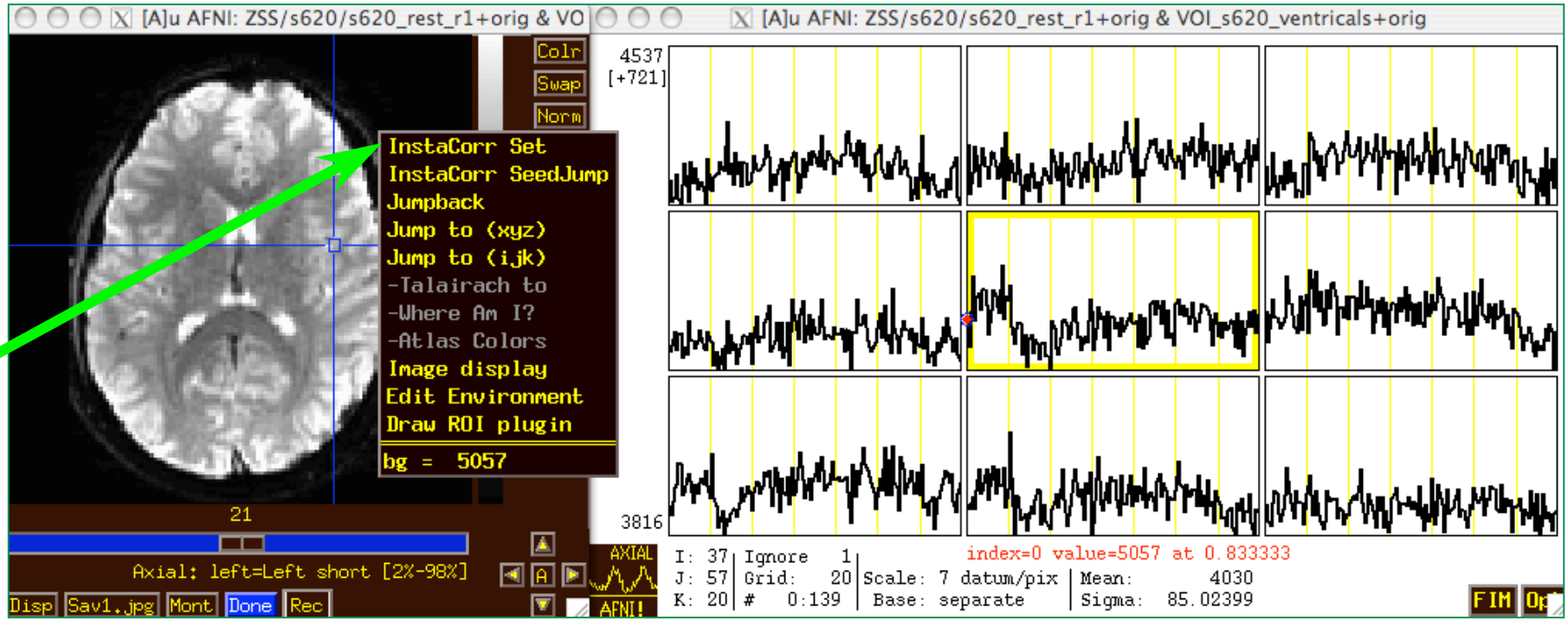
InstaCorr: Setup - 4



- Text output to shell window details the setup process:
- **++ InstaCorr preparations:**
- **+ Automask from '/Users/rwcox/data/Resting/ZSS/s620/s620_rest_r1+orig.BRIK' has 19723**
- **+ Extracting dataset time series**
- **+ Filtering 197234 dataset time series**

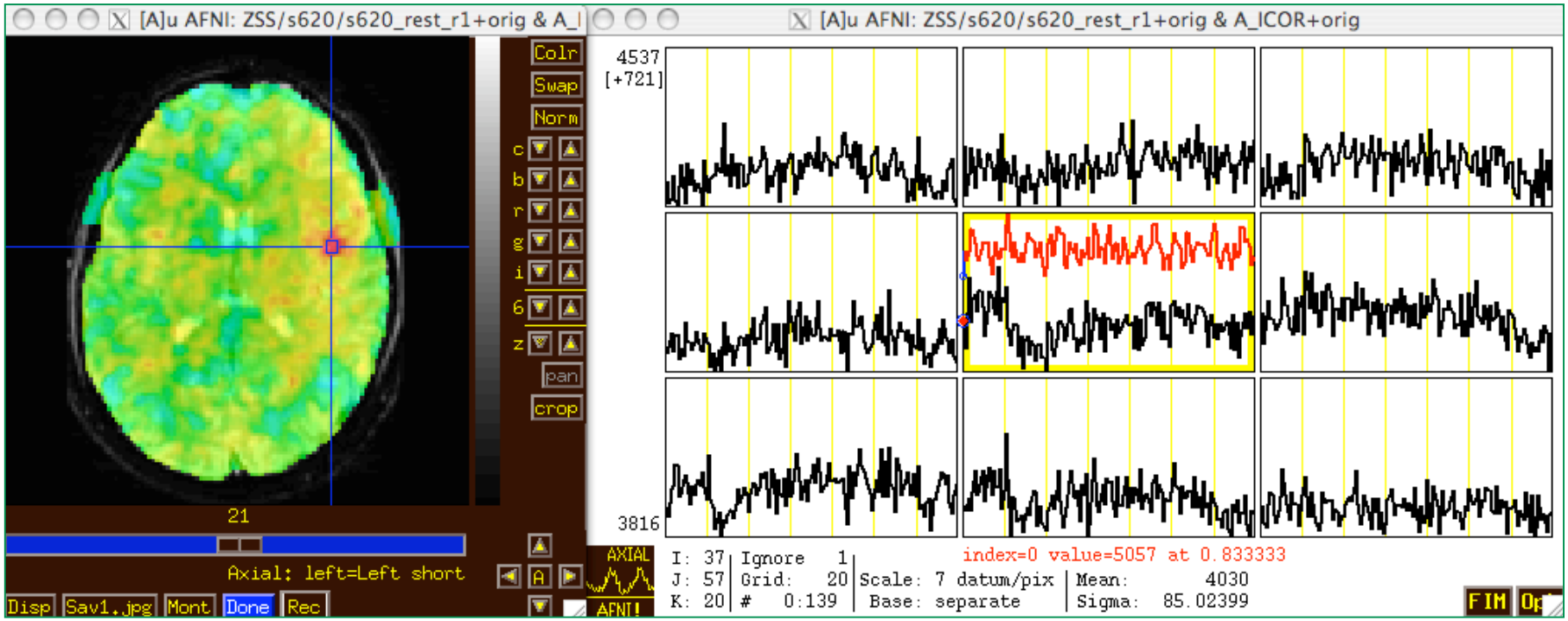
Most of the CPU time

InstaCorr: The Fun Part - 1



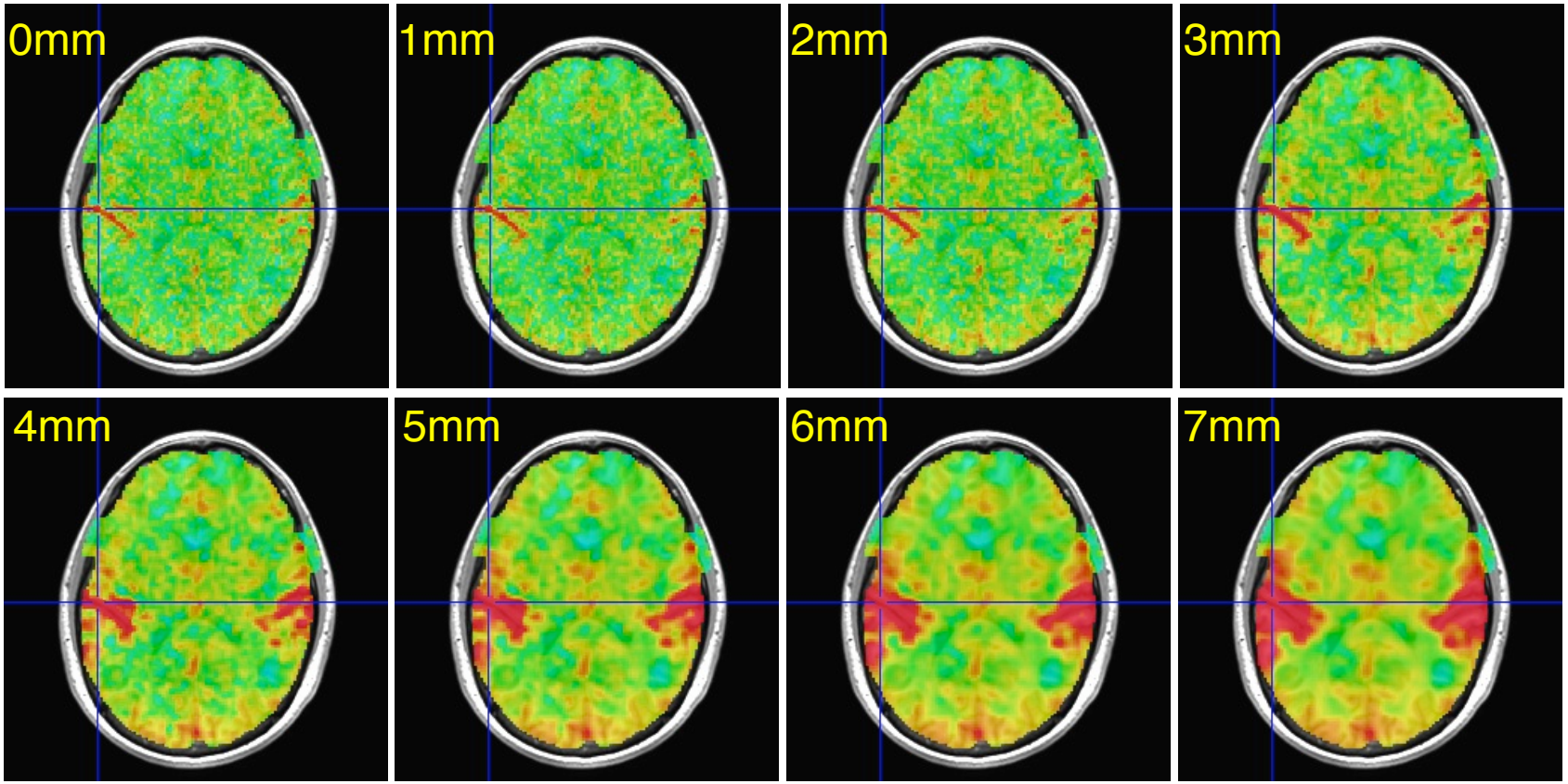
- In image viewer, set crosshairs to desired seed voxel
- **Right-click** popup menu → InstaCorr Set
- Shortcut: **Shift+Ctrl+Left-click** sets new crosshair location, then does InstaCorr Set
- InstaCorr SeedJump jumps focus to current seed

InstaCorr: The Fun Part - 2



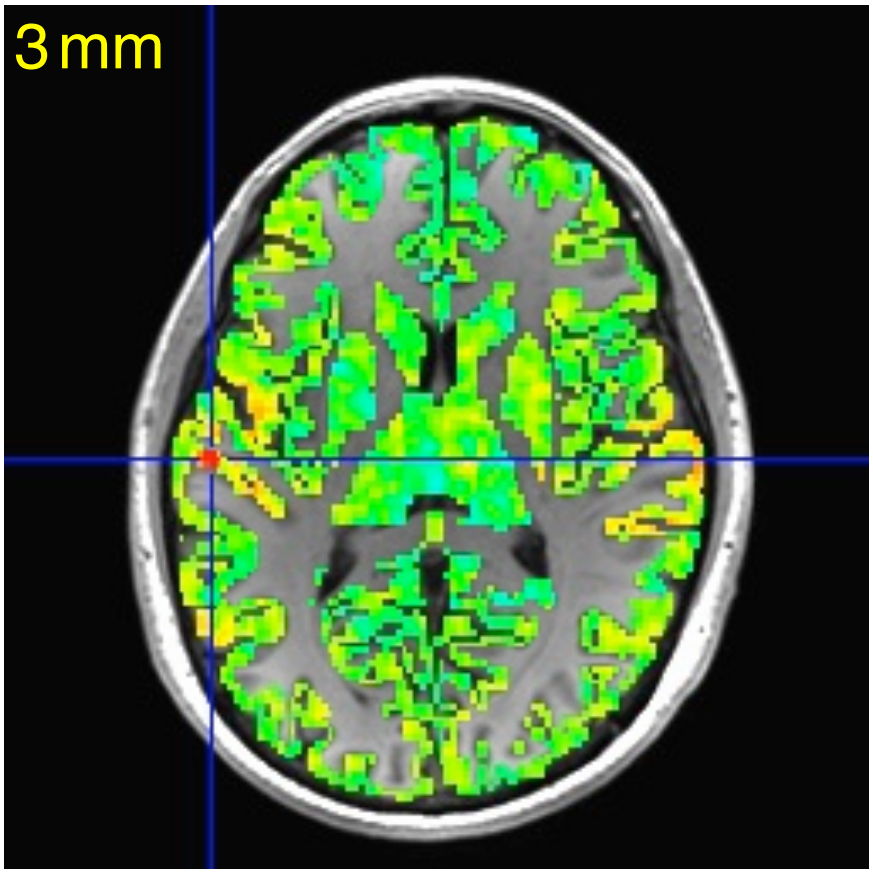
- In graph window:
  - ★ Set Ignore with FIM→Ignore menu (or I key)
  - ★ Set seed overlay with FIM→Pick Ideal menu
- When you change seed voxel, saved overlay time series will change (but you have to refresh graph to see it)

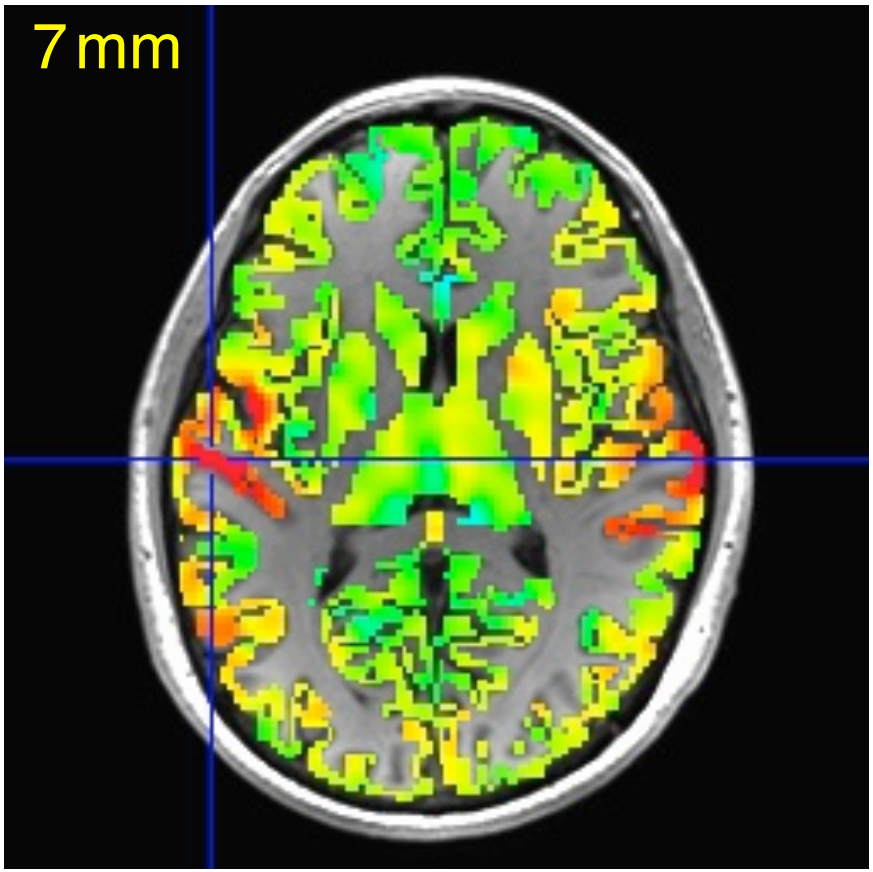
InstaCorr: Effects of Blurring - 1



- Is this a pure vascular/cardiac effect being progressively smeared? Or real neural correlations seen via BOLD? Or some of both? *Venograms*?
  - ★ Dataset was RETROICOR-ized; mask is whole brain

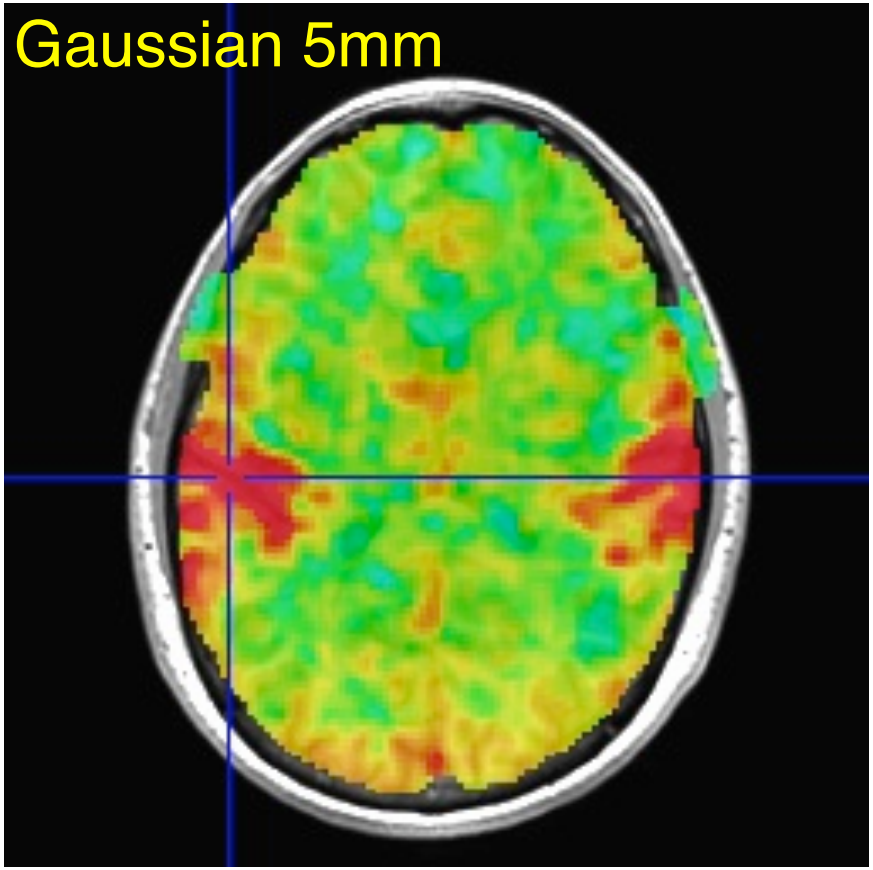
InstaCorr: Effects of Blurring - 2

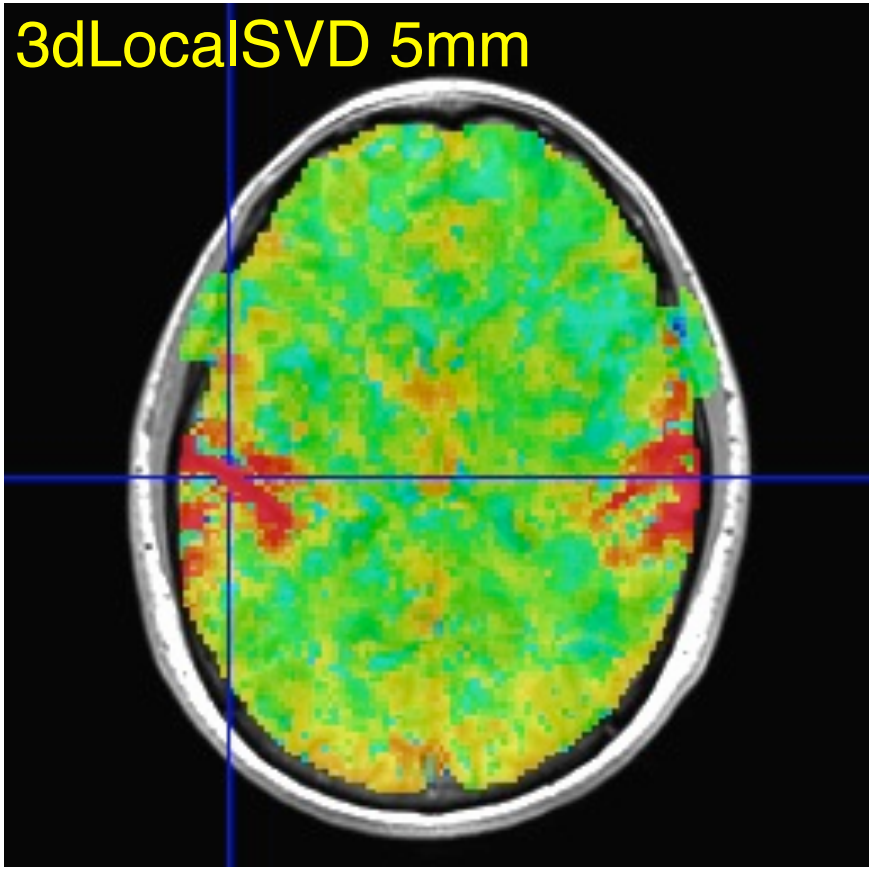




- Similar calculations, but with FreeSurfer-generated gray matter mask instead of Automask from EPI data
  - ★ Blurring is done only inside the mask
    - o Using a discrete PDE-based iterative approach

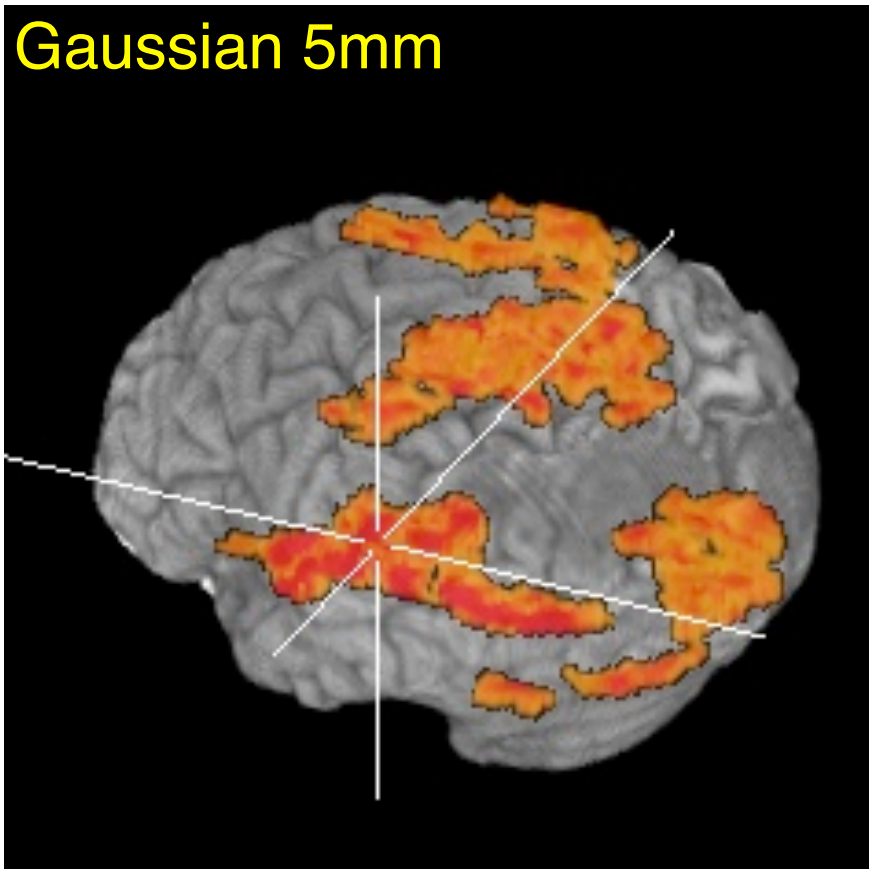
InstaCorr: SVD-based "Blurring" - 1

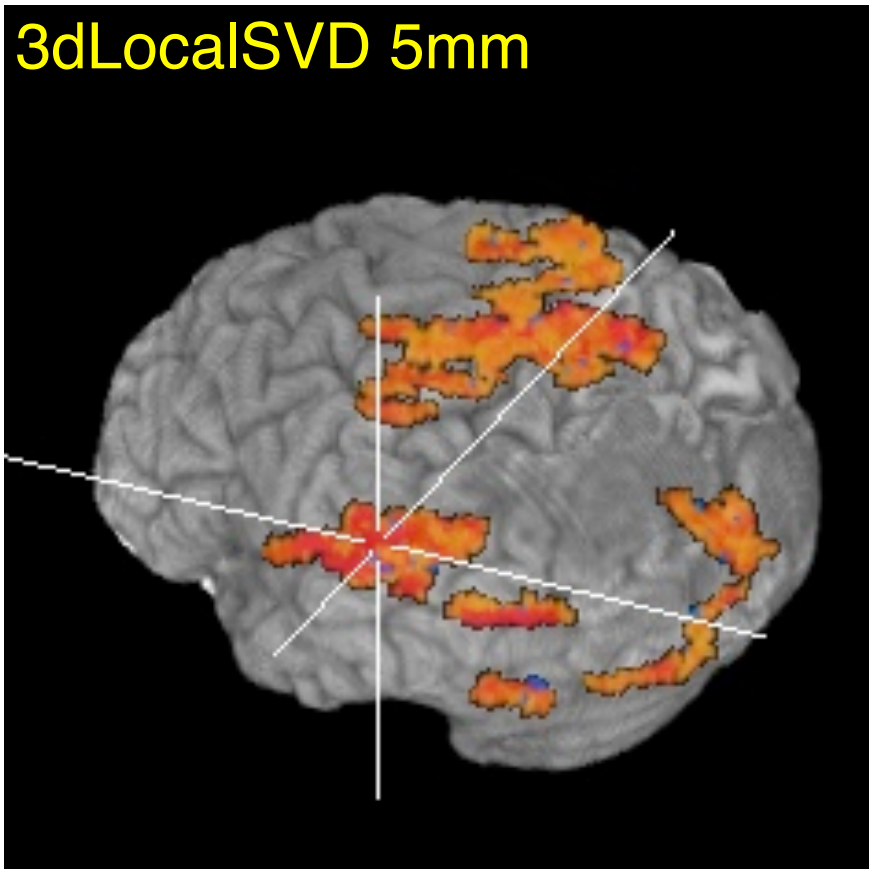




- Similar calculations, with Automask from EPI data, using 3dLocalSVD over 5 mm radius sphere (67 voxels)
  - ★ Project each vector onto 2-dim principal subspace
  - ★ Too slow to do interactively (at this time)

InstaCorr: SVD-based "Blurring" - 2





- Volume rendering of InstaCorr maps (threshold at r=0.5)
  - ⋆ Renderer updates automatically if DynaDraw is on
- SVD smoothing has cleaner spatial structure?
  - ⋆ Or has it lost some information?

InstaCorr: Options and Notions

- Underlay doesn't have to be EPI data; could be anat
  - ★ Can use InstaCorr in multiple AFNI controllers
- FDR: setenv AFNI_INSTACORR_FDR YES
  - ★ Will slow things down by a significant factor
- Saving A_ICOR dataset: overwrites previous copies

- Future Possibilities:
  - ★ Select ROI-based Orts to be detrended?
    - o Based on ROIs from FreeSurfer or atlases?
  - ★ Or multiple seeds (partial + multiple correlations)?
  - ★ Interactive local SVD "smoothing"? (needs speedup)
  - ★ Group analysis InstaCorr (in standardized space)
    - o Not quite "Insta" any more; ≈ 0.1×#Subjects sec per seed
    - o External script to do subject setups?
  - ★ Use time series subsets? (*e.g.*, for block design data)

InstaCorr on the surface

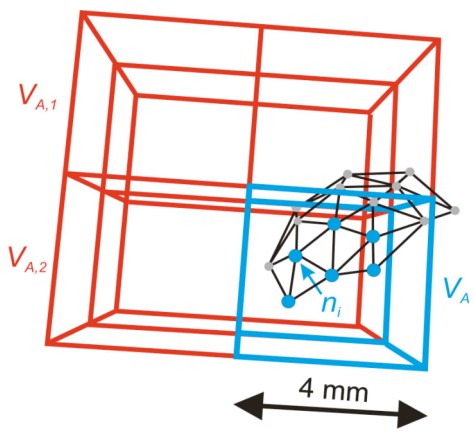
- Concept quite similar to AFNI's
  - with enough difference to keep me employed.
- I assume you are familiar with SUMA's interface
- First a few words on the data (thanks be to A. Martin, and K. Simmons)

  `@run_Vol2Surf` creates surface-based time series data
  - Maps volumetric time series onto surface
  - Blur time series along the cortical surface
- Launch SUMA, load the time series, get rid of unwanted hair with:

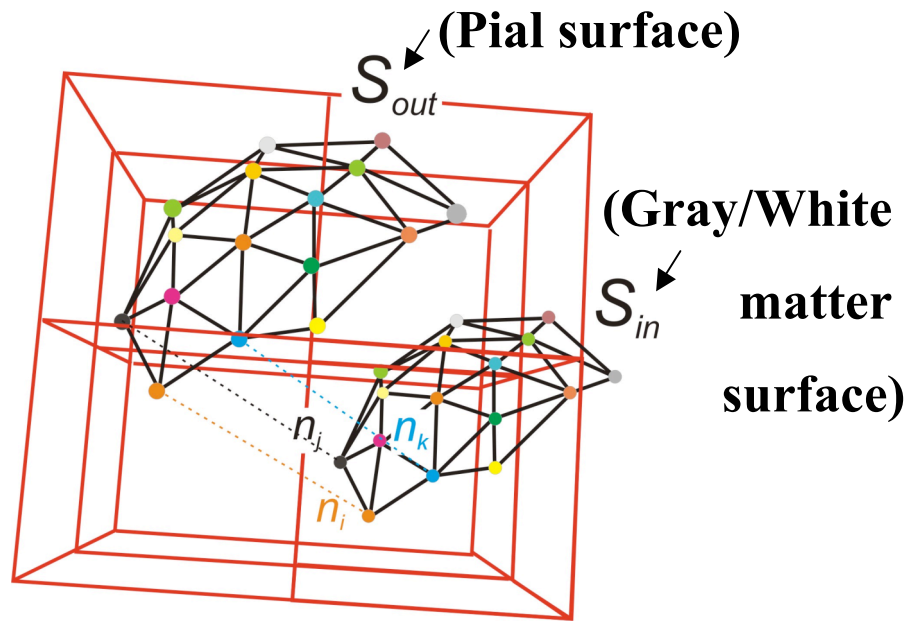
  `@run_suma_ic`

Mapping options

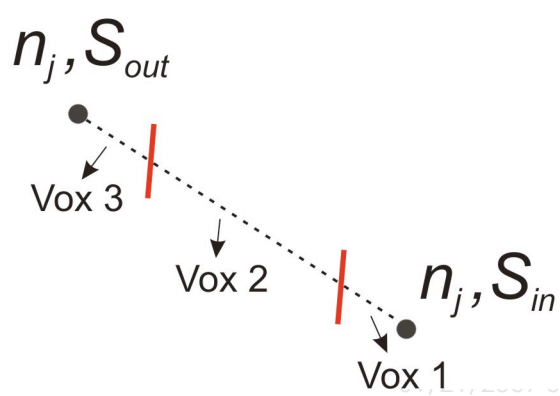
- Surface/volume Intersection
  - ★ One voxel per node

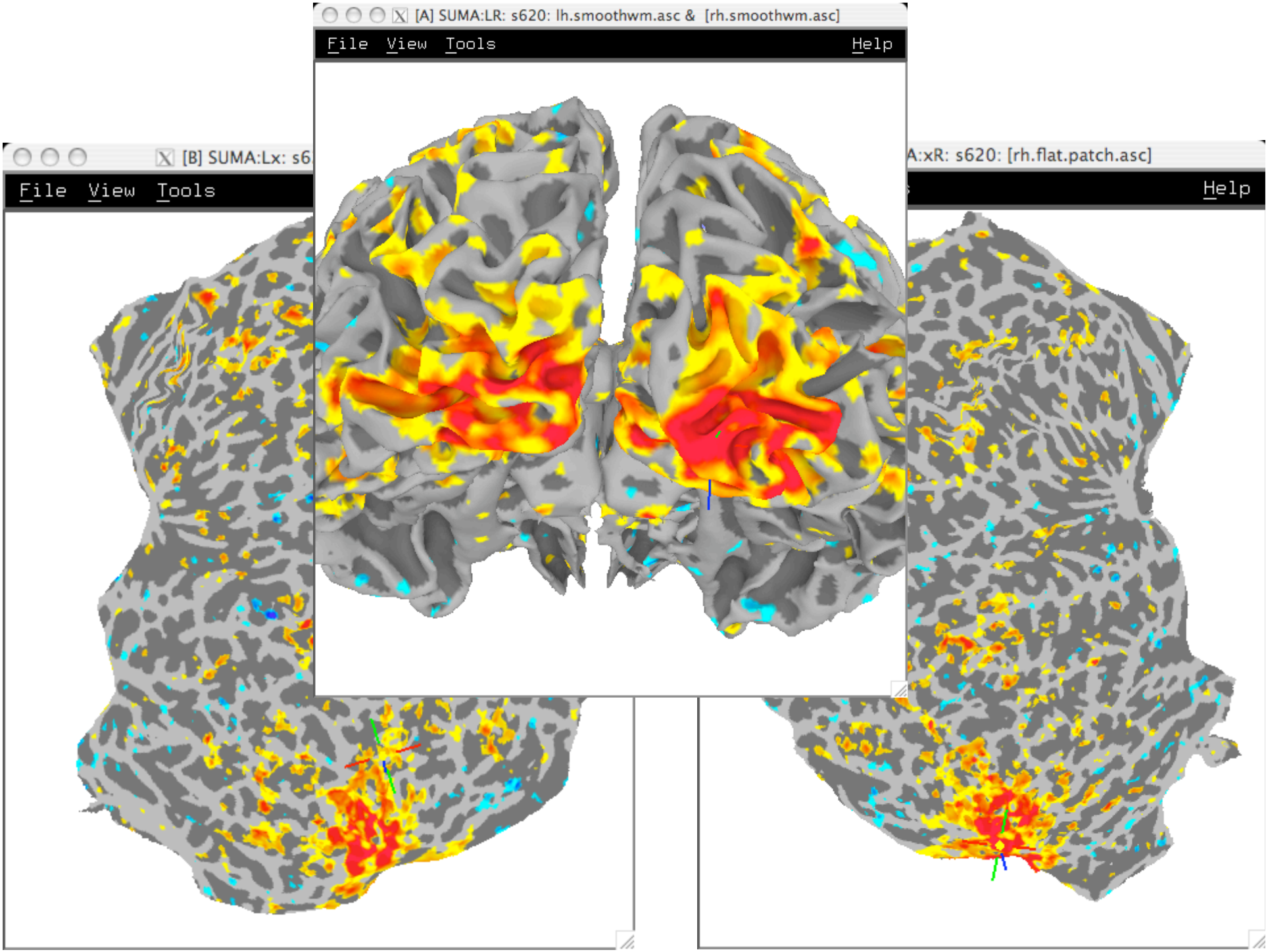


- Shell/volume Intersection
  - λ Multiple voxels possible per node



Node segment intersecting 3 voxels

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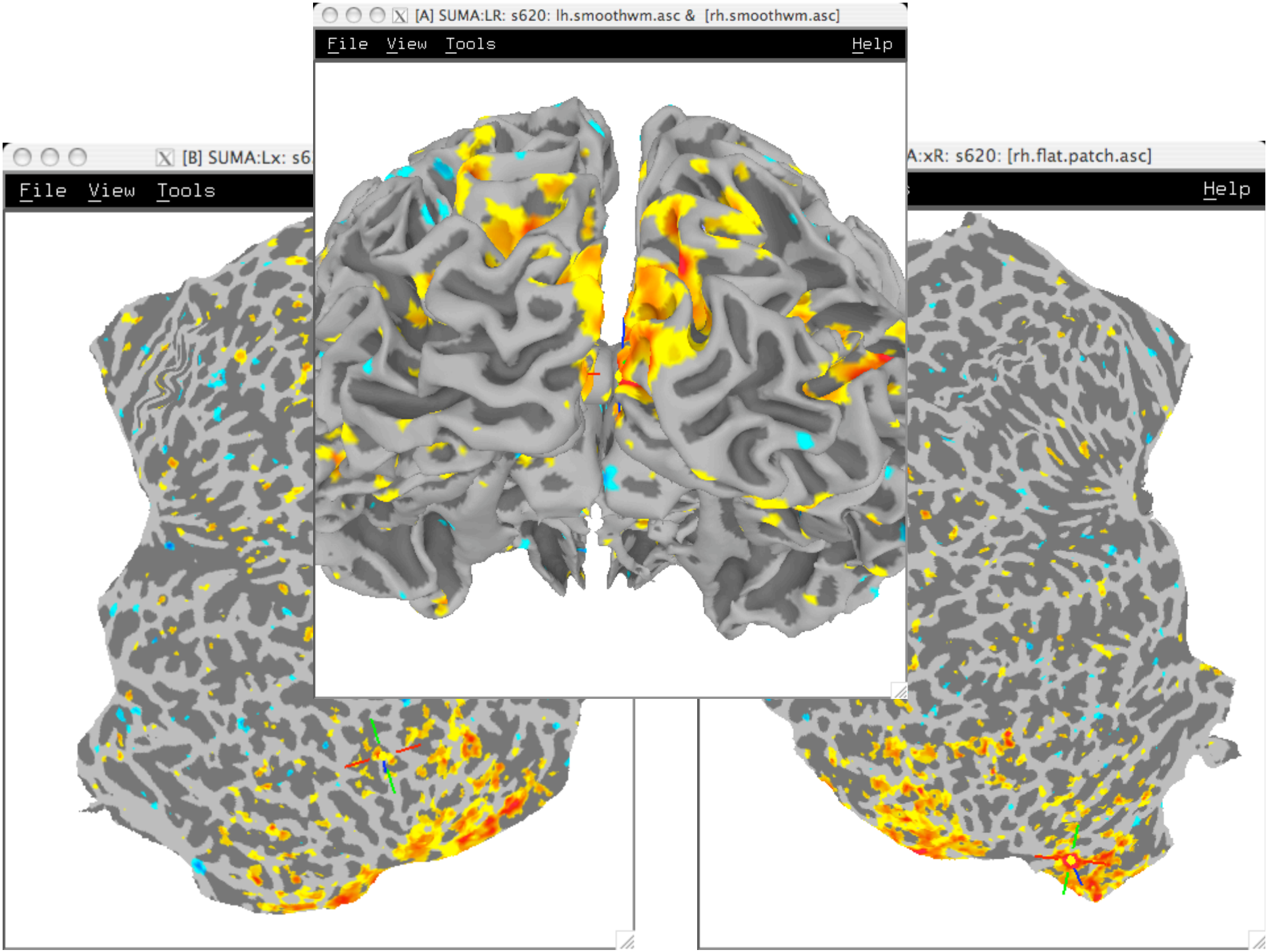
File View Tools Help
[B] SUMA:Lx: s6
File View Tools
A:xR: s620: [rh.flat.patch.asc]
Help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File View Tools Help
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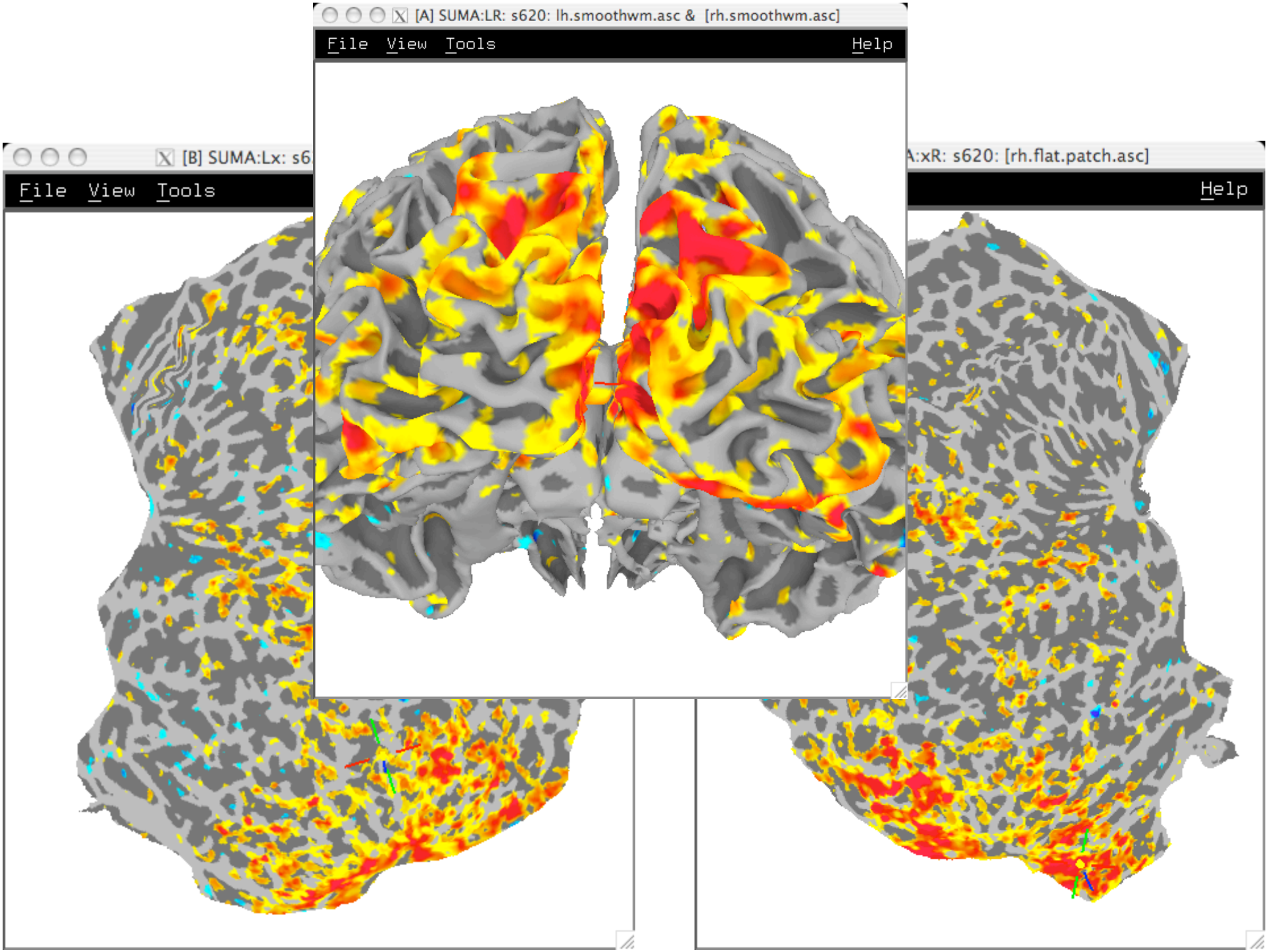
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File View Tools Help
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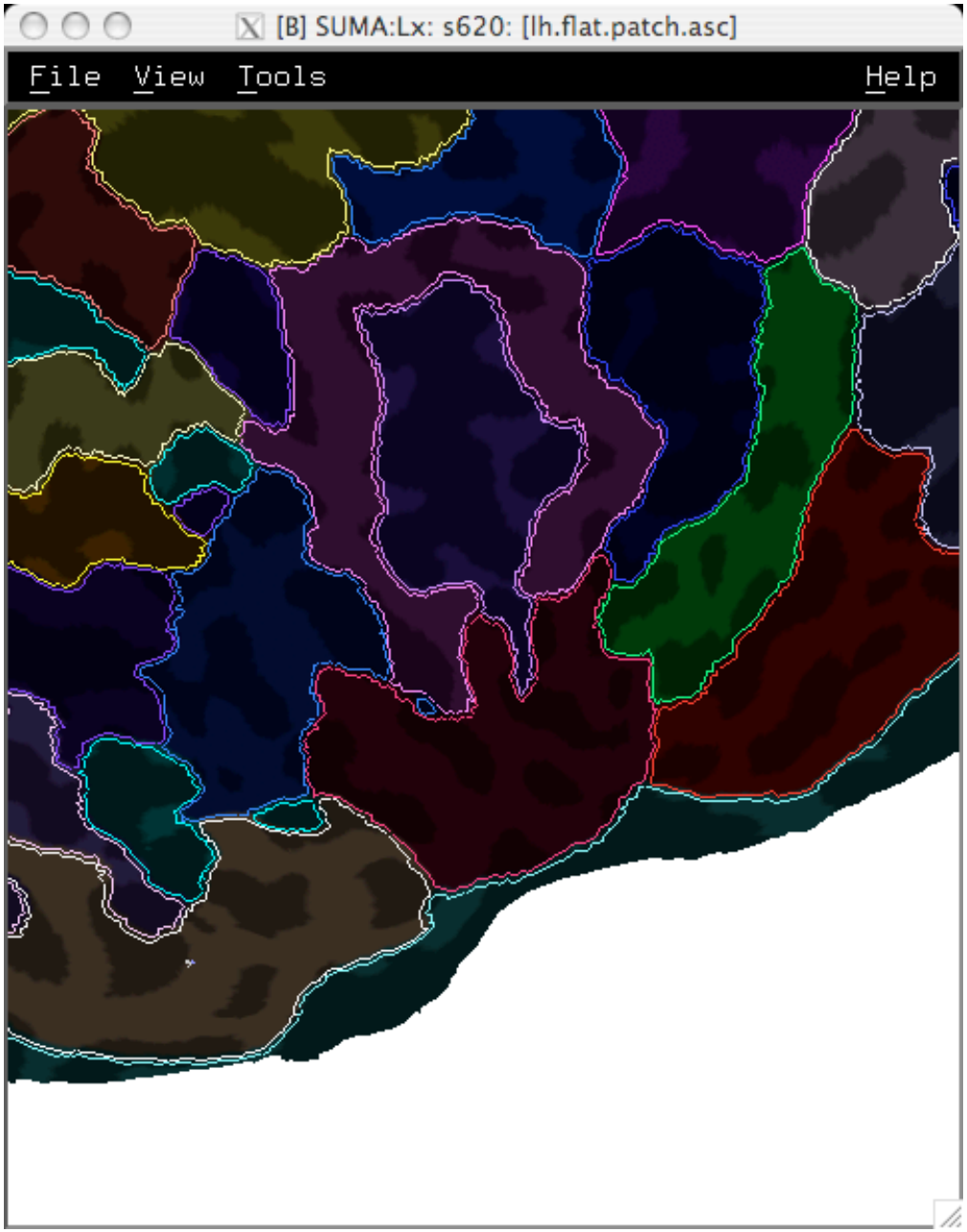
File View Tools
A:xR: s620: [rh.flat.patch.asc]
Help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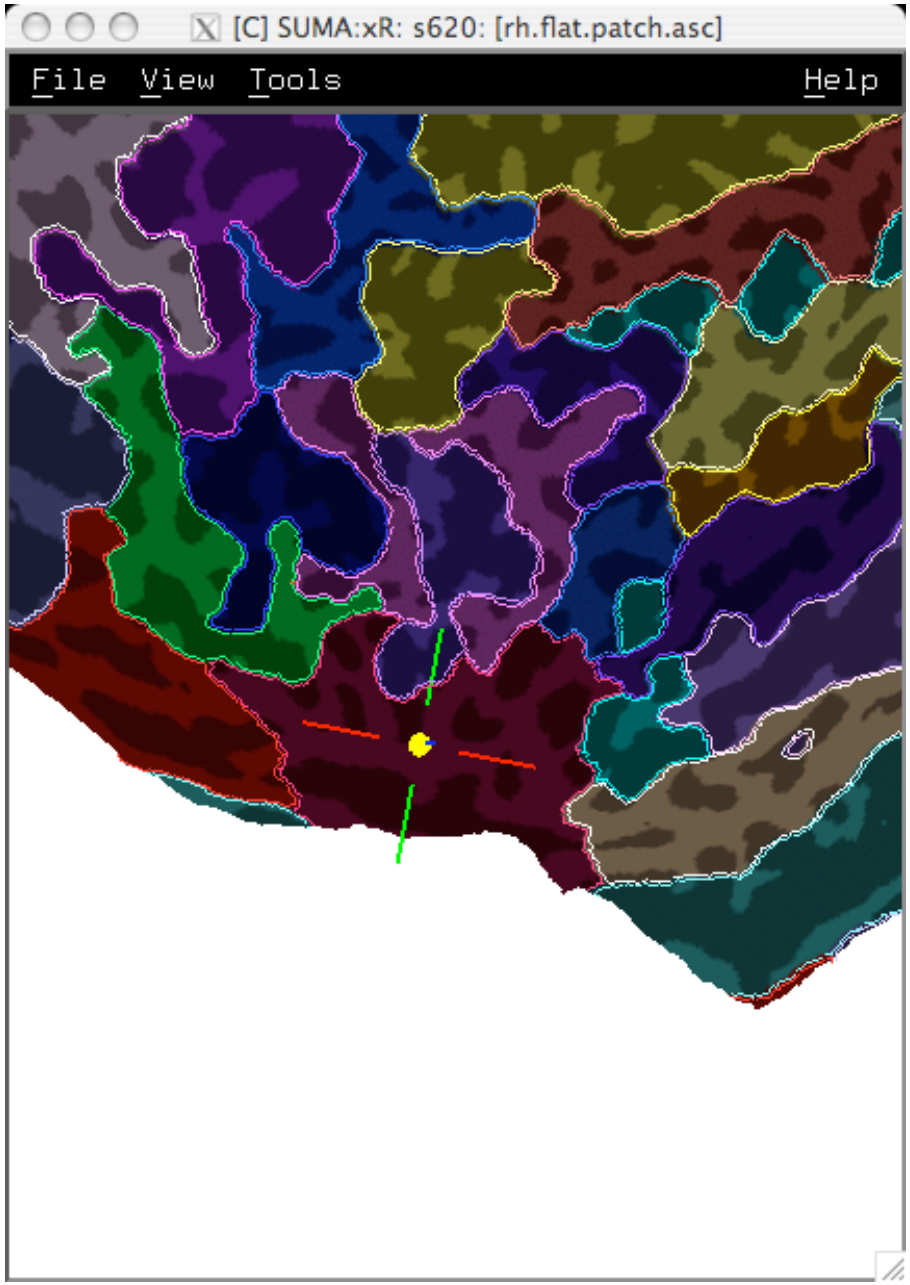
File View Tools Help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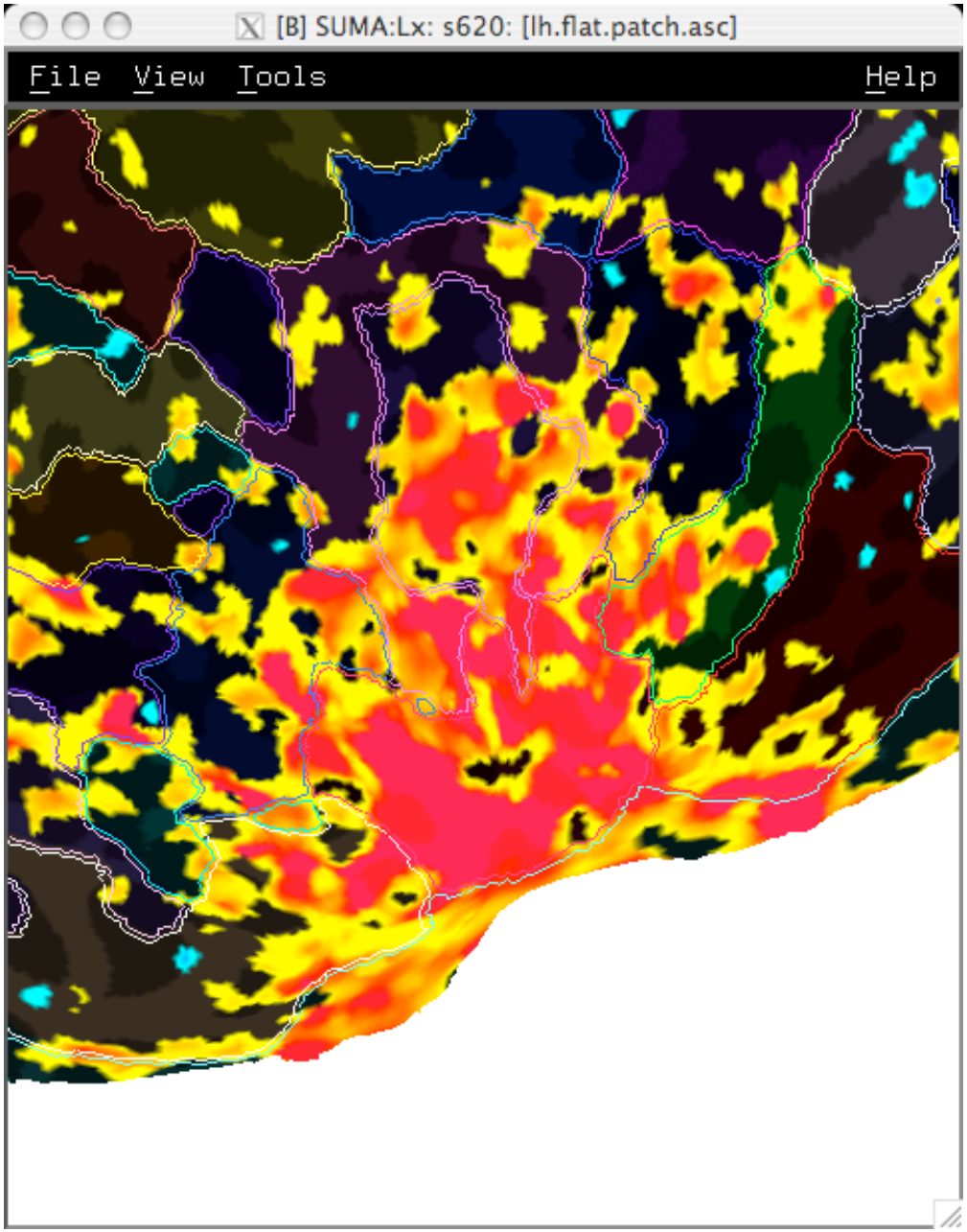
File View Tools Help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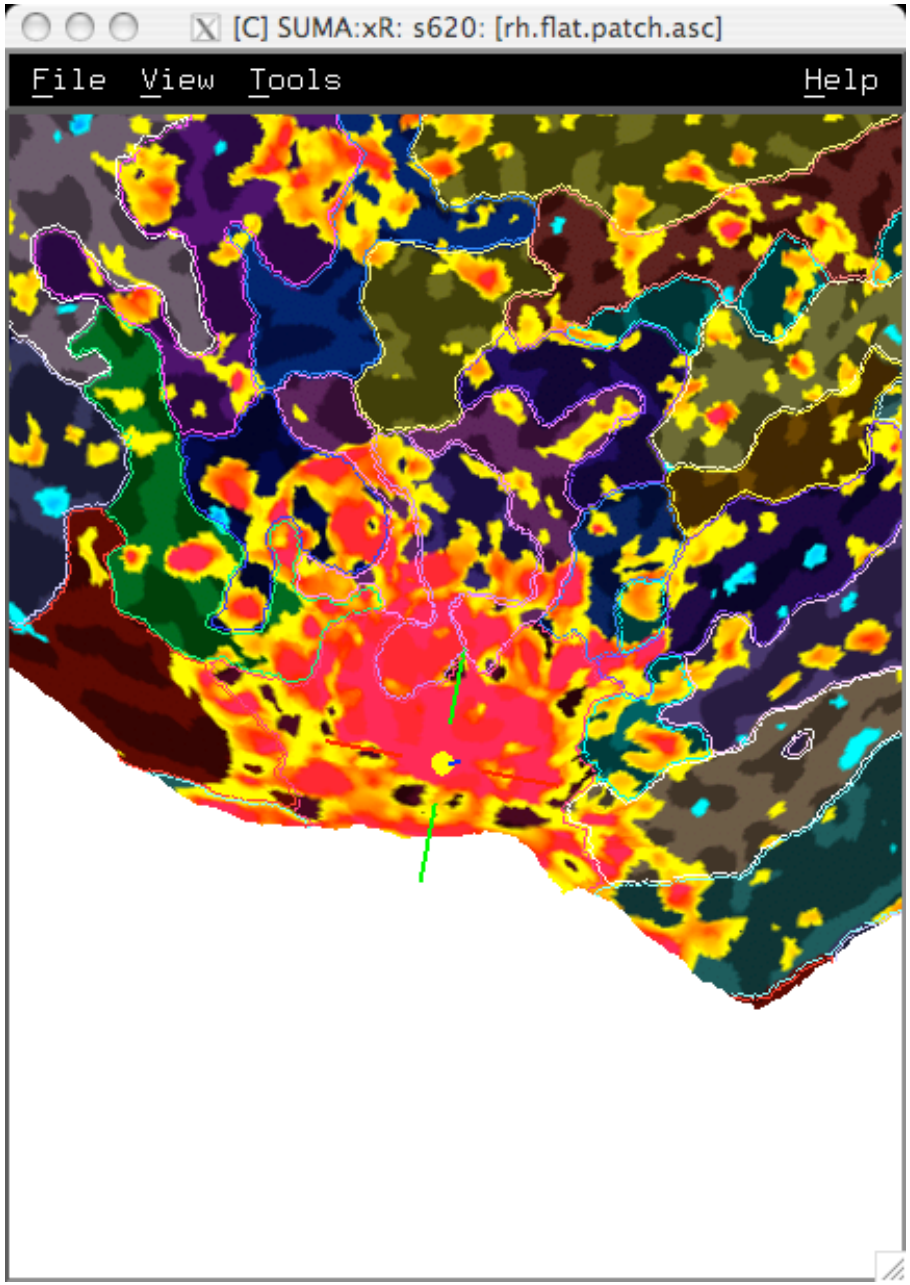
File View Tools Help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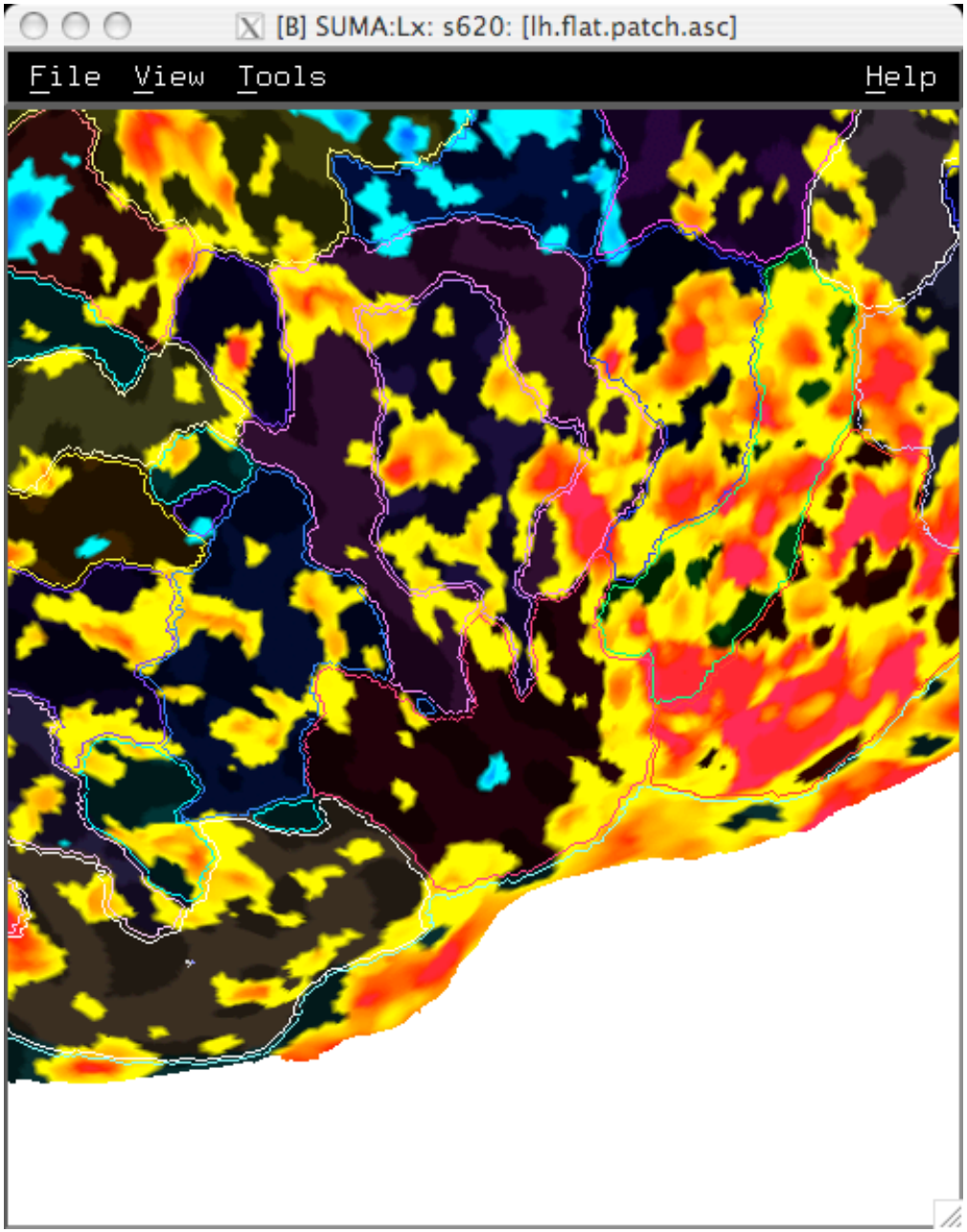
File View Tools Help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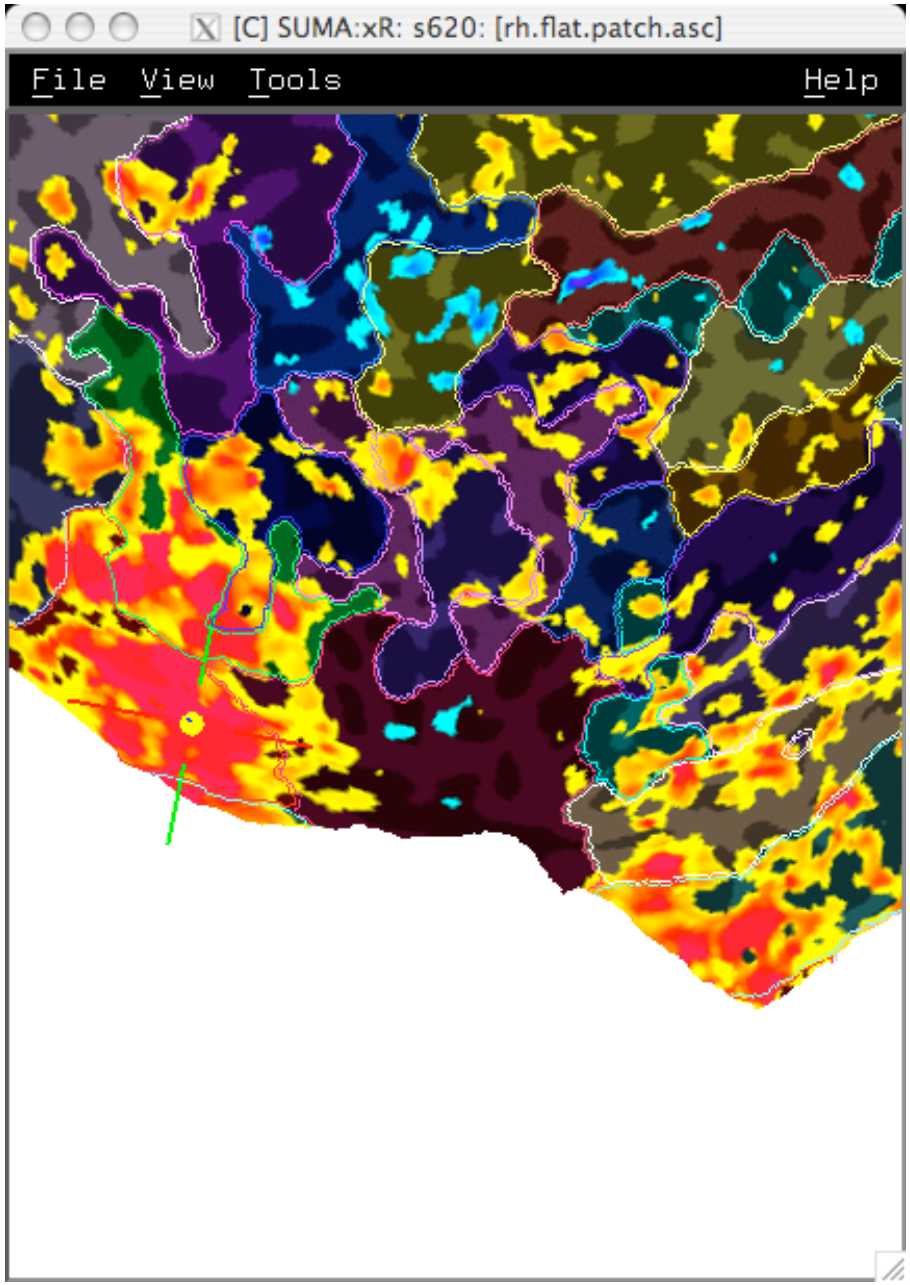
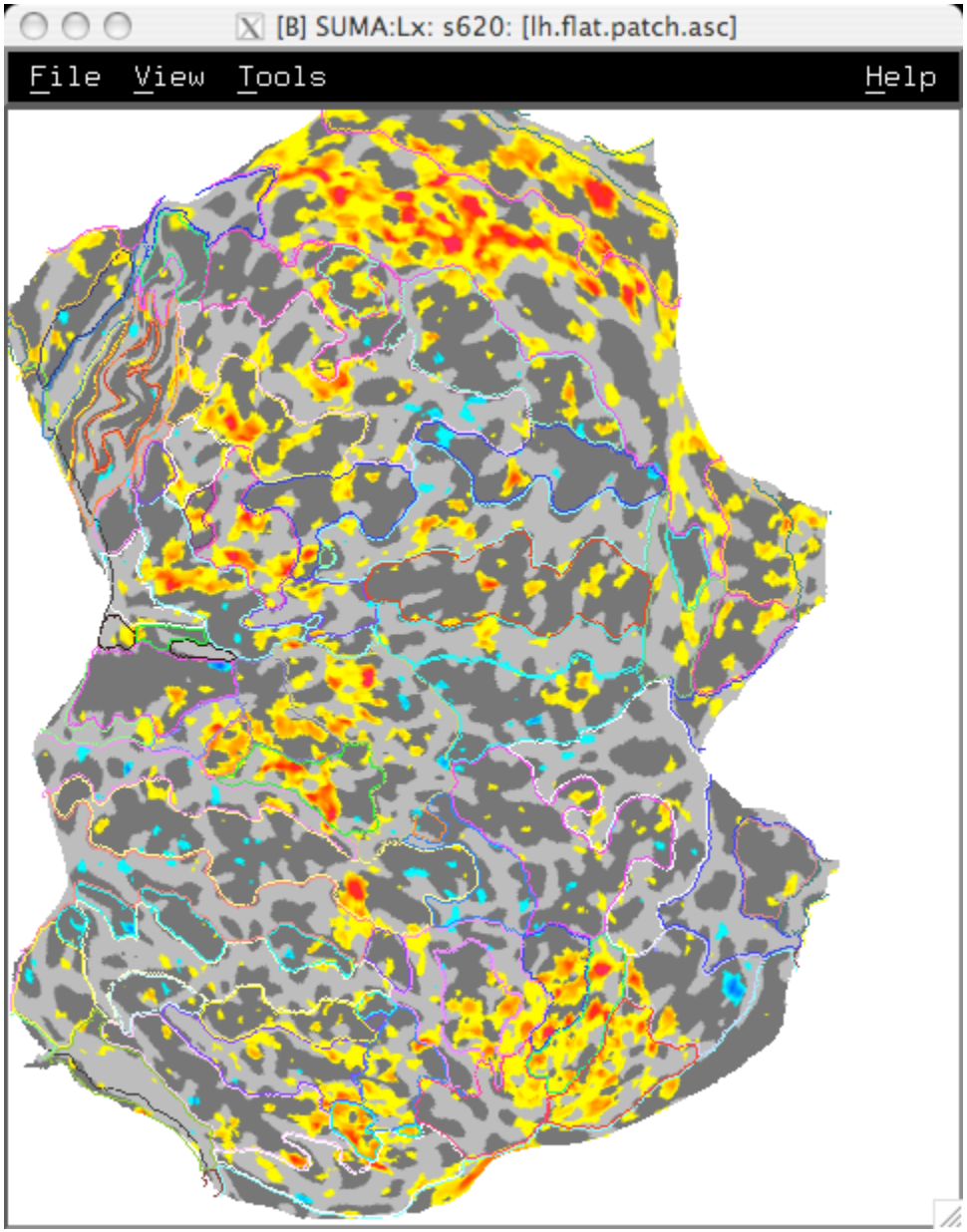
File View Tools Help

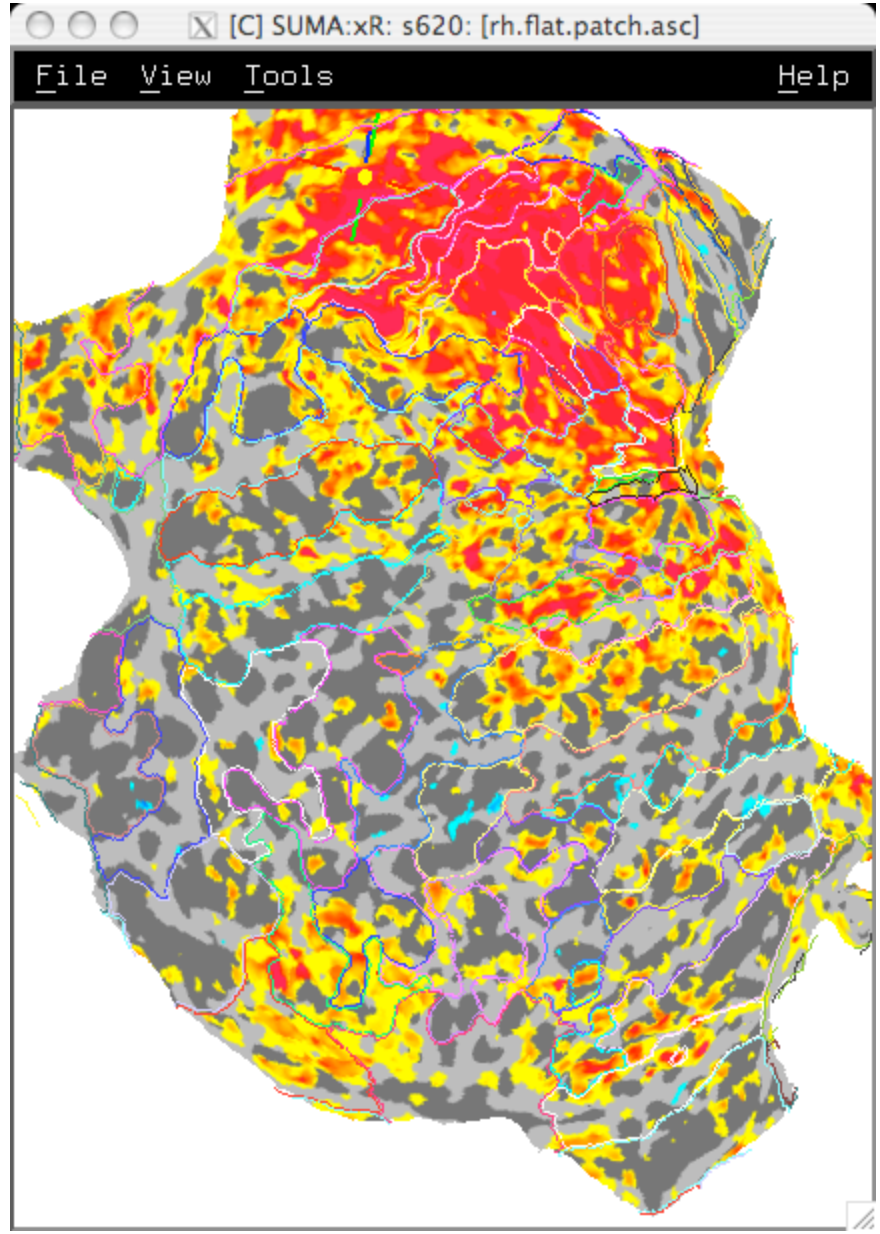

[C] SUMA:xR: s620: [rh.flat.patch.asc]
File View Tools Help

That looks promising, now for some weird stuff

- On the right hemisphere, use ‘j’ to jump to node 162329

That looks promising, now for some weird stuff





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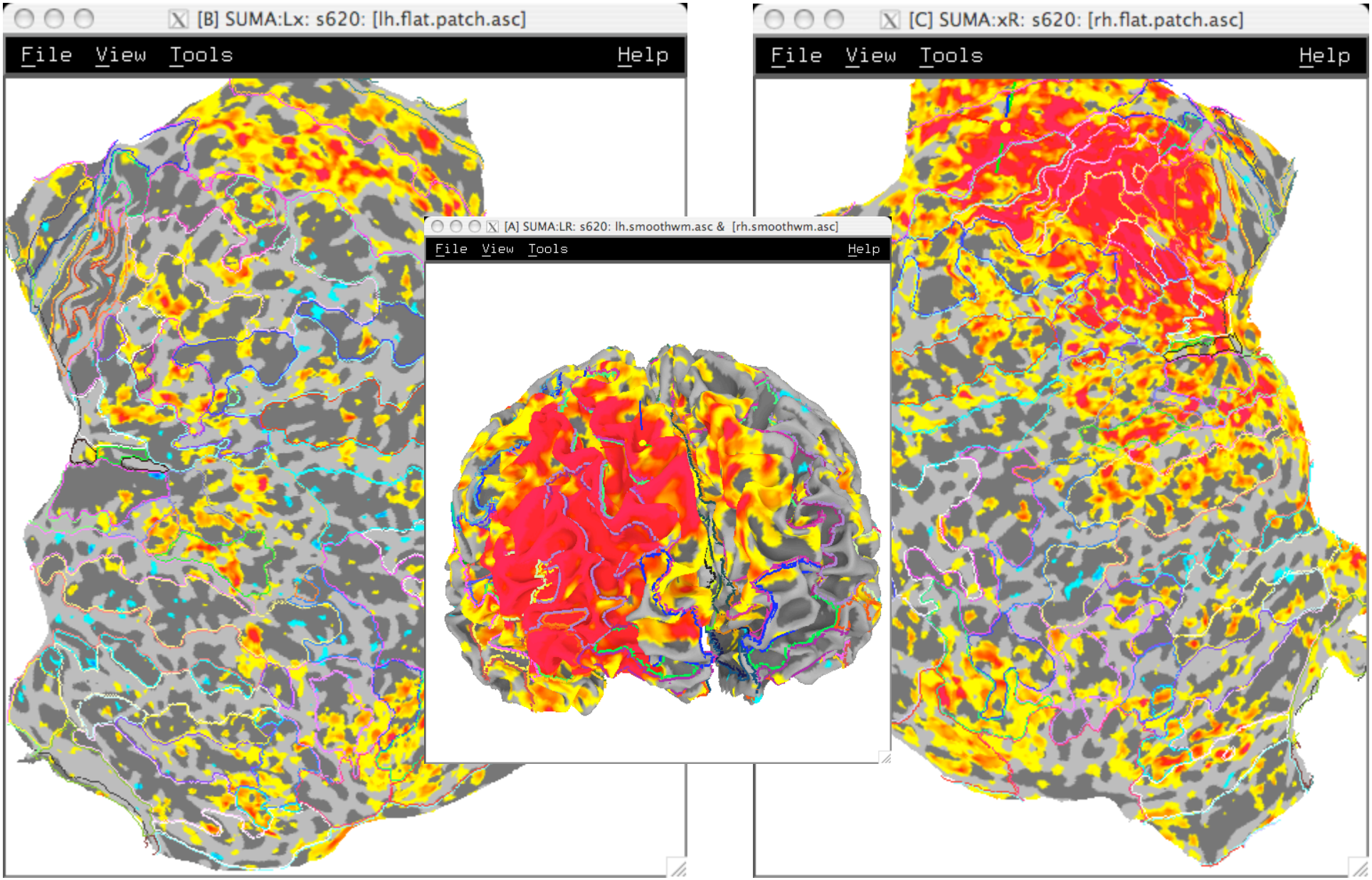

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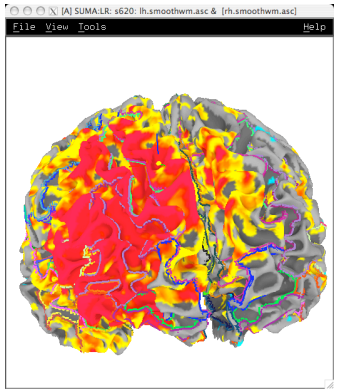
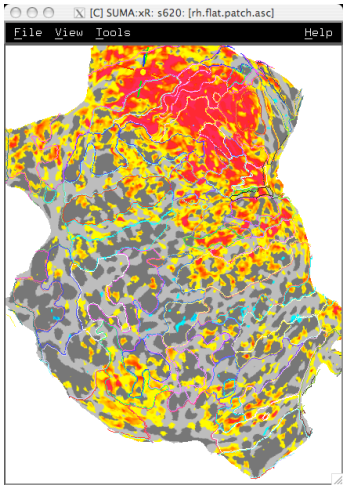
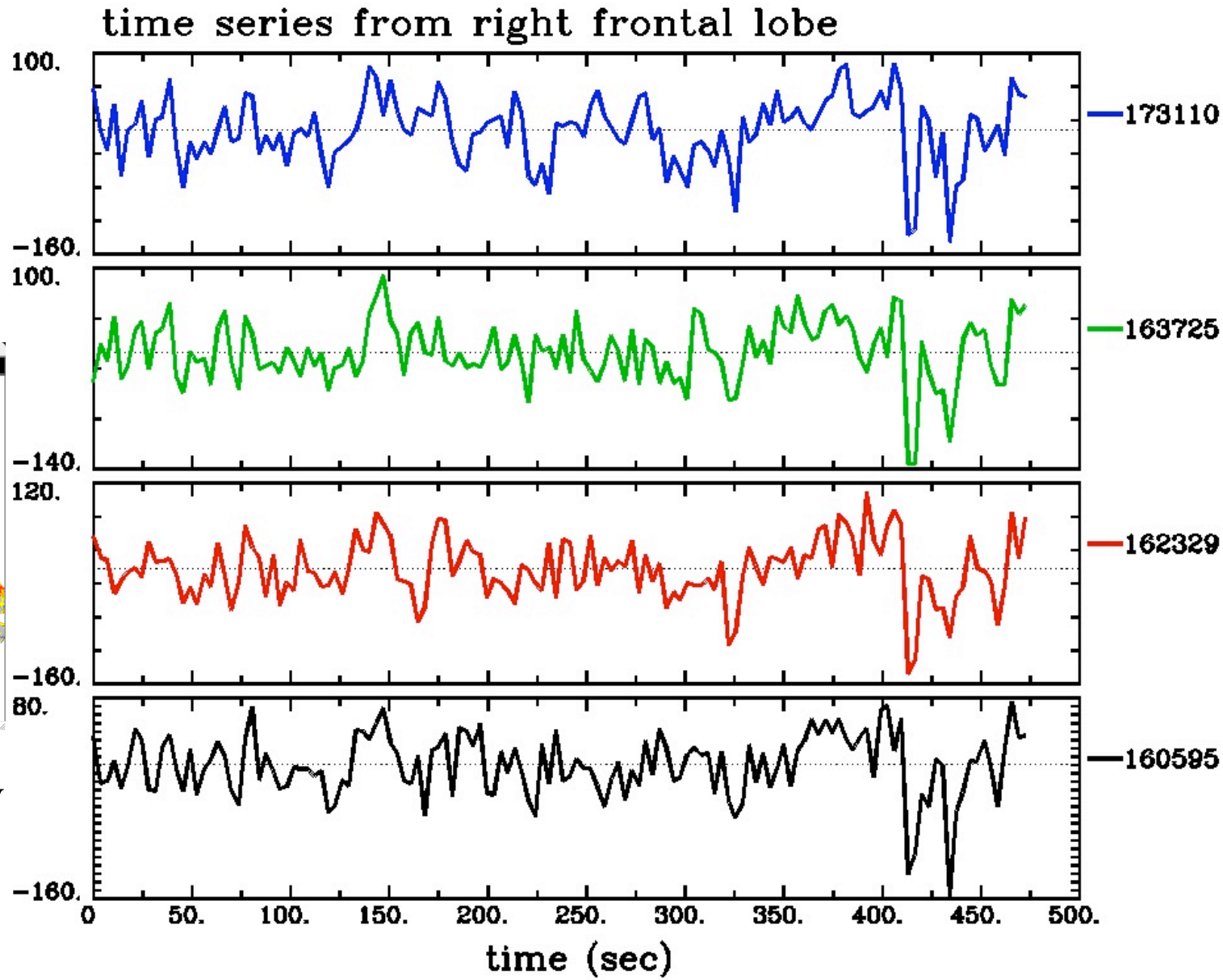


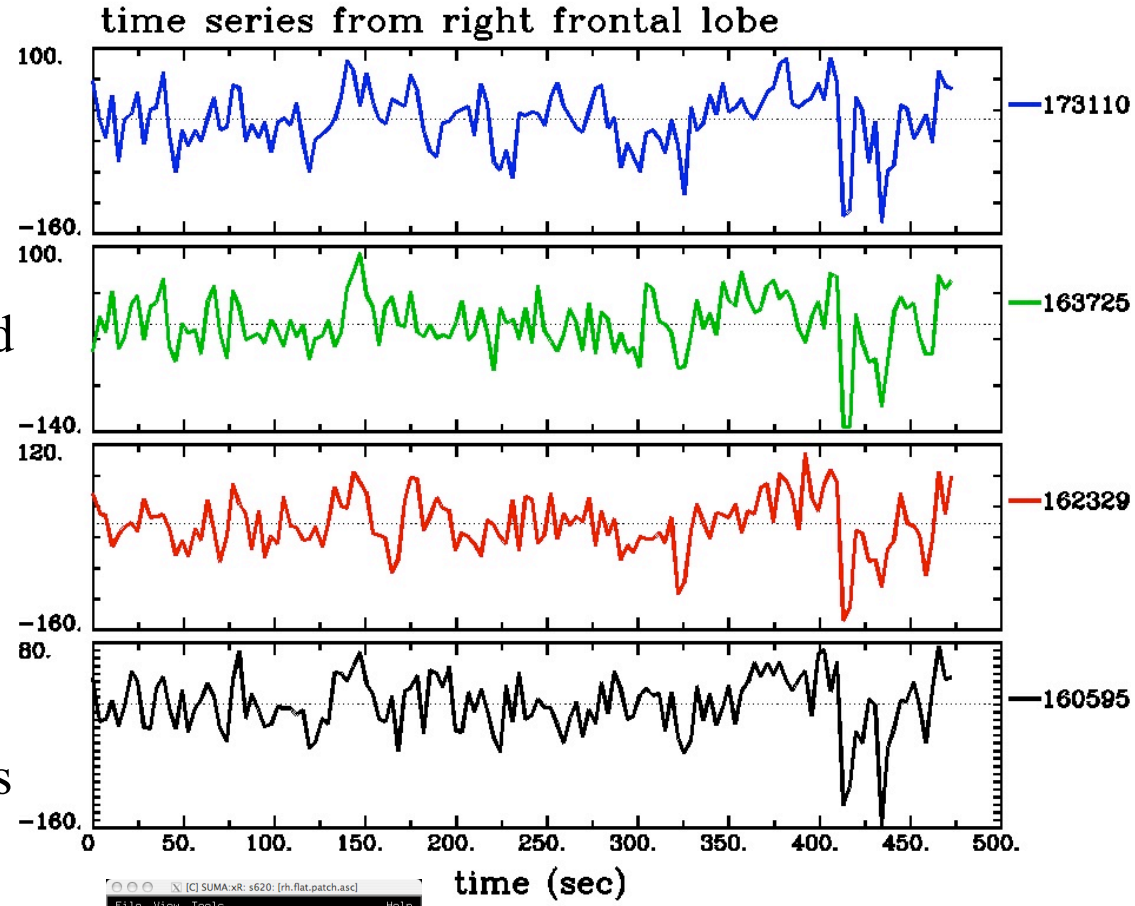


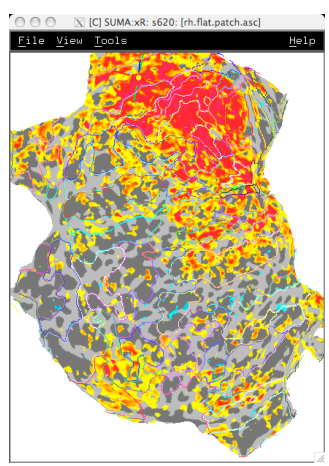
Using ‘g’key

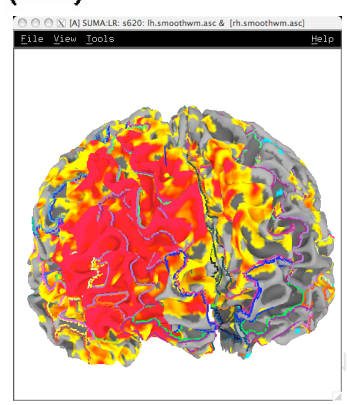


That looks promising, now for some weird stuff

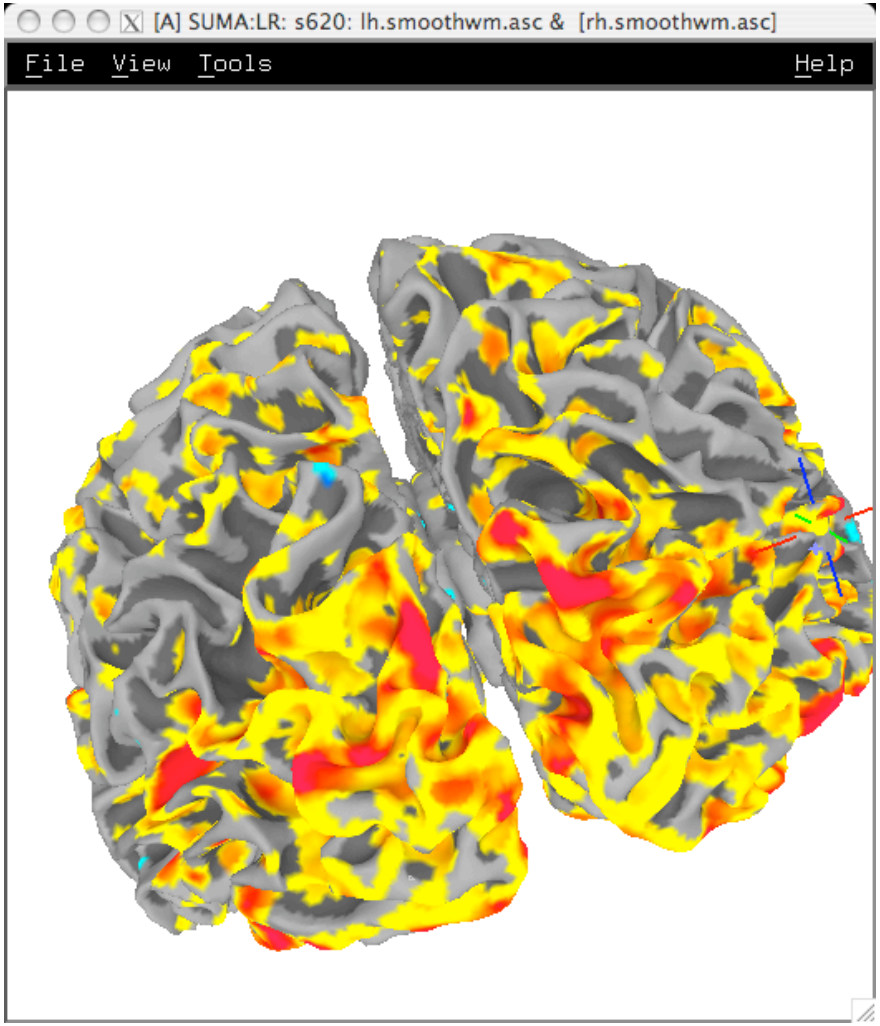
- Time series from multiple slices
- Note correlated dips towards end
- Absence of contralateral effect
- Not sure what caused this yet
    - Can seriously affect results
-

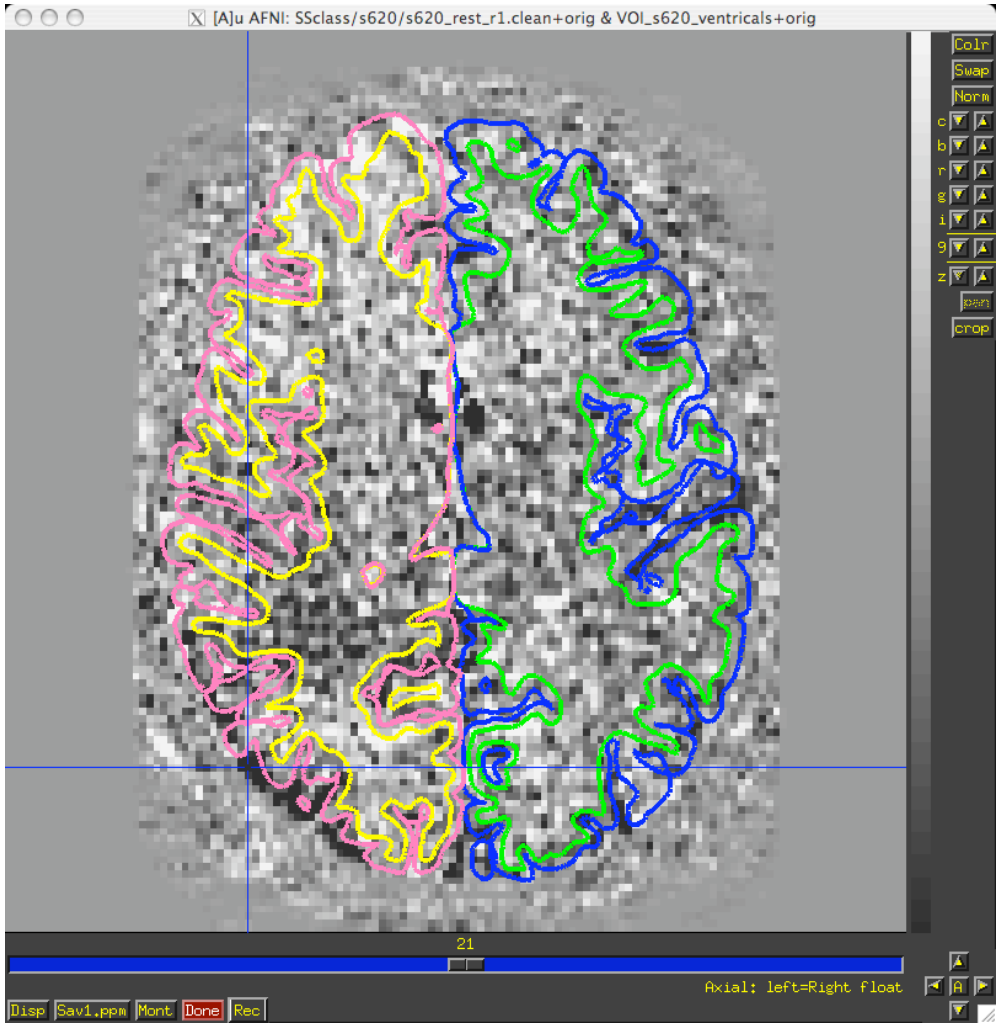






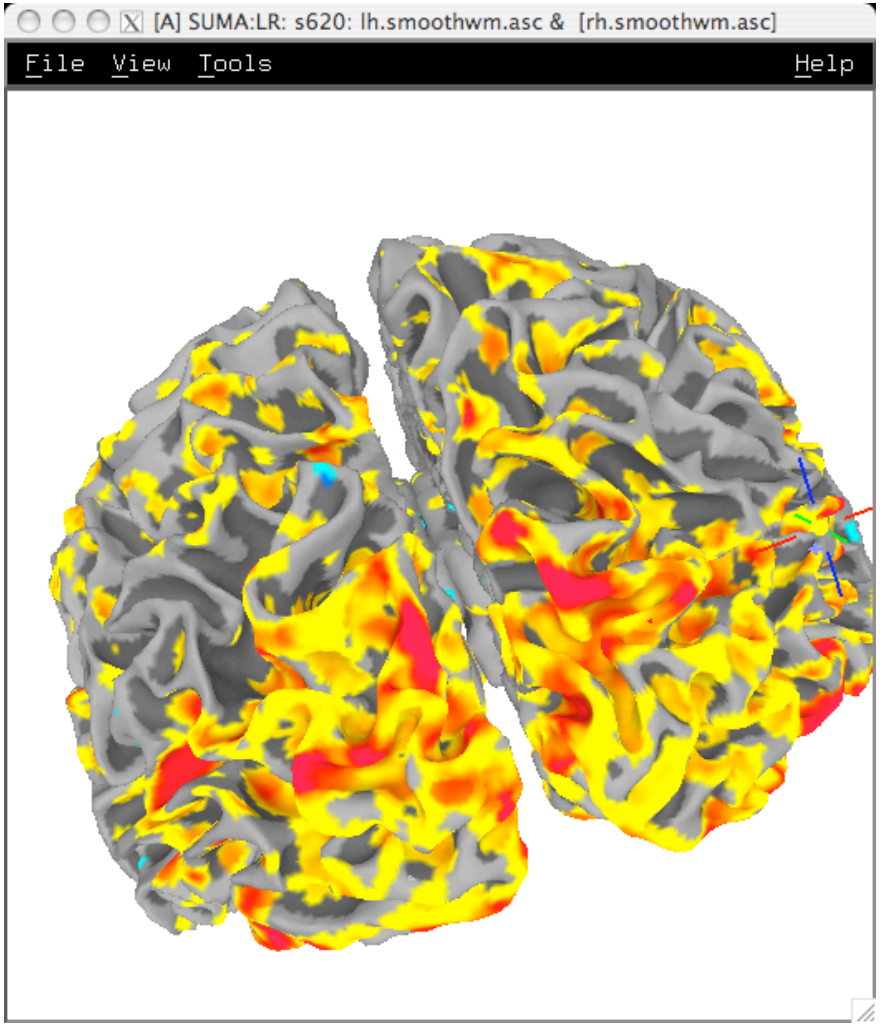
InstaCorr on the Surface with Time Series from the Volumes

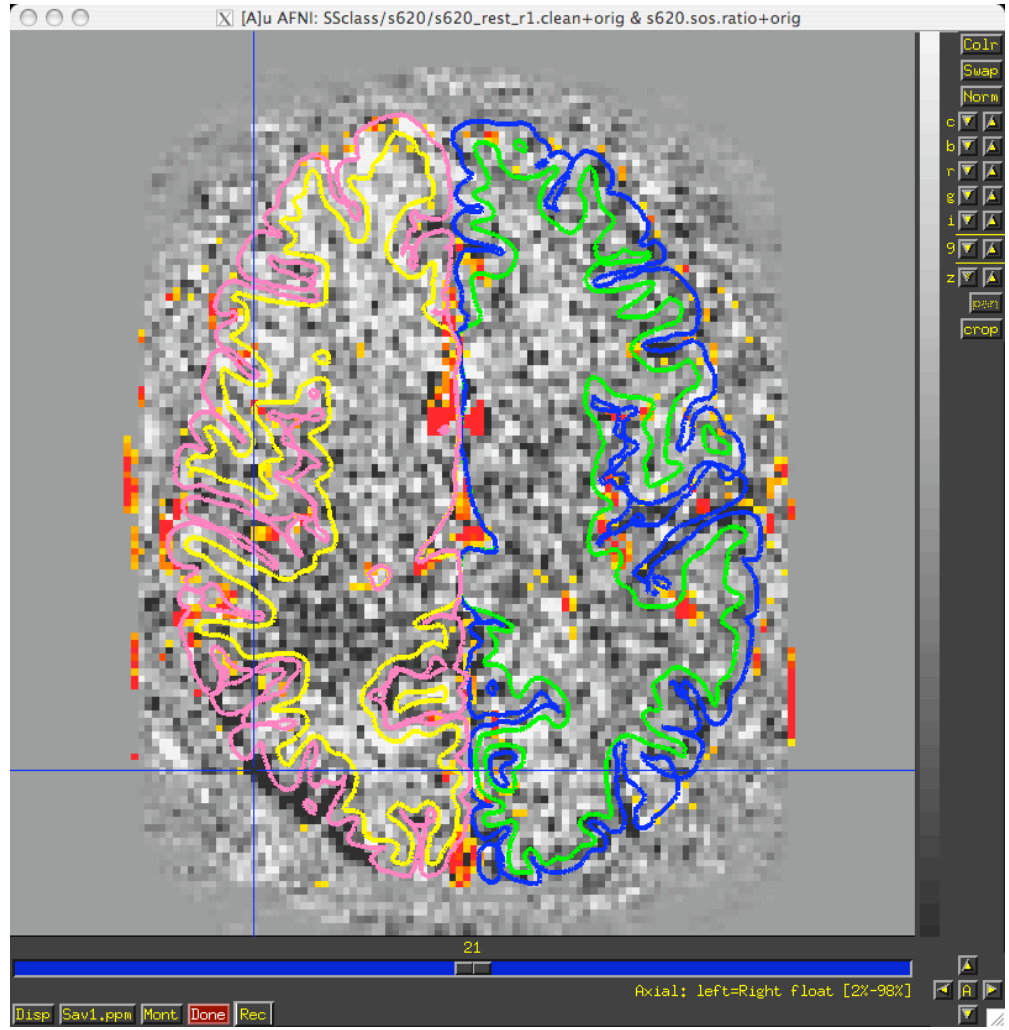




Even after pre-processing, likely large veins correlate with data from cortex only.

InstaCorr on the Surface with Time Series from the Volumes

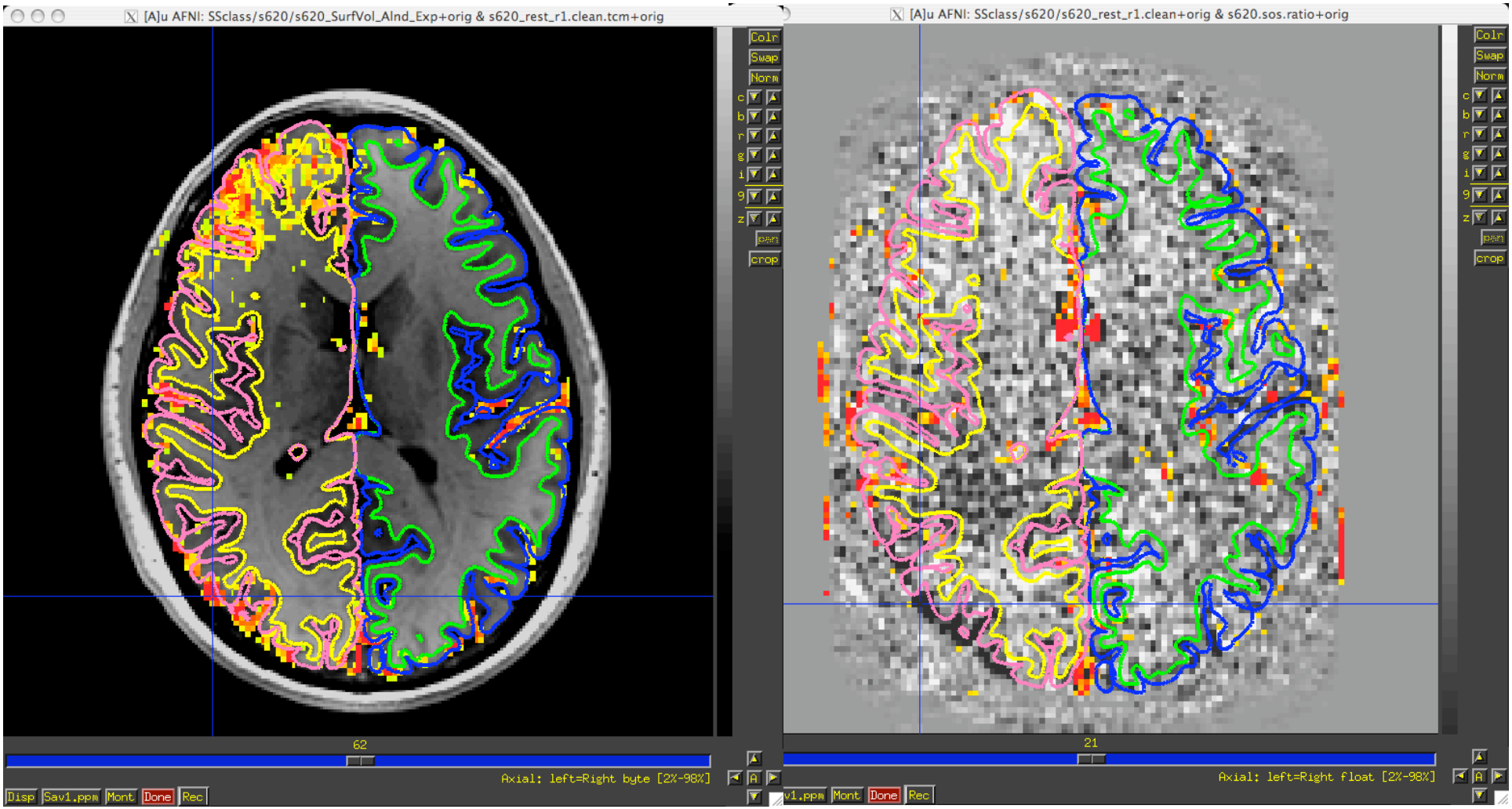




Even after pre-processing, likely large veins correlate with data from cortex only.

But this vein did not fit RETROICOR signals well

Regions Of Interest: The most popular voxels



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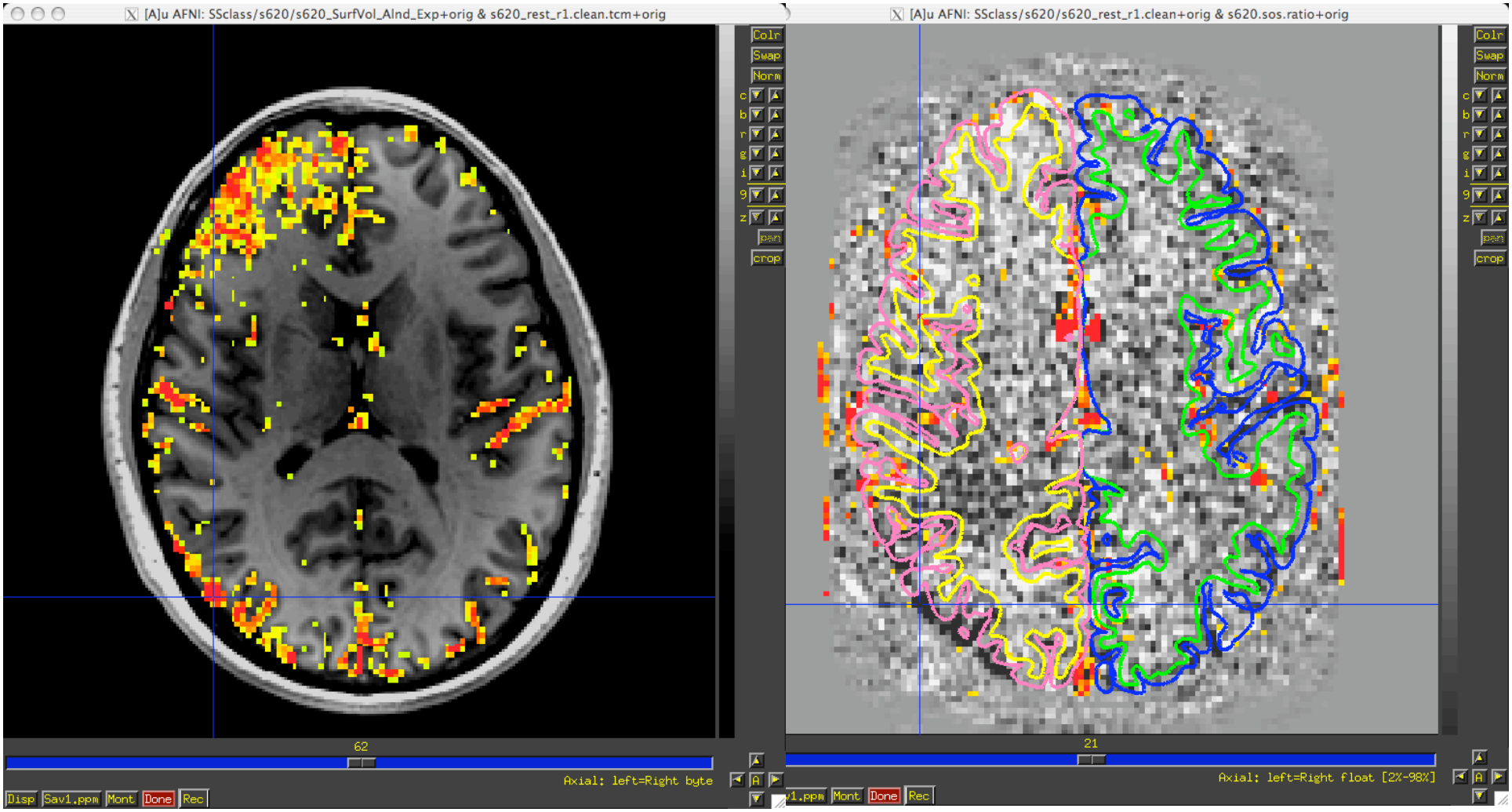
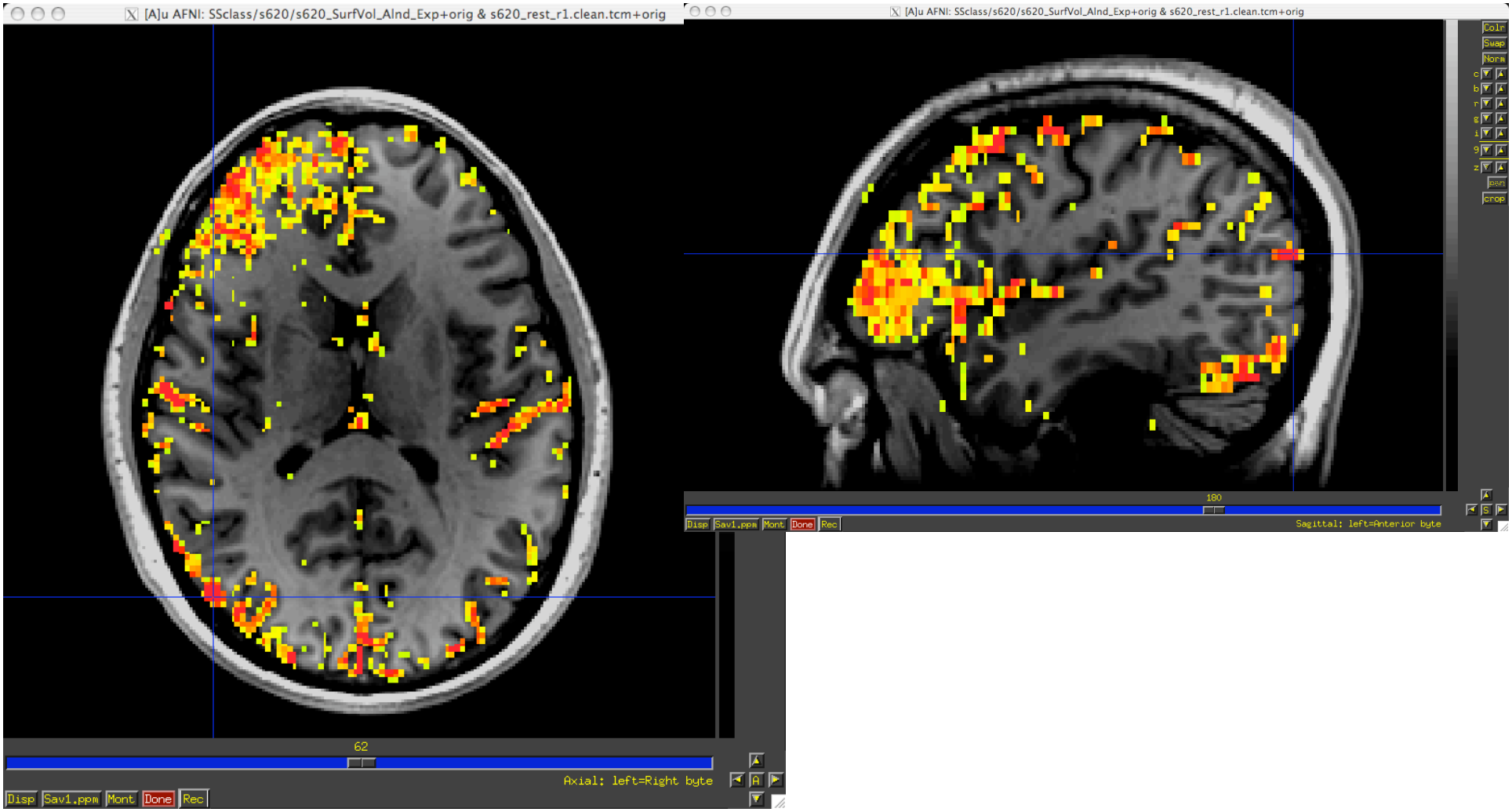
Regions Of Interest: The most popular voxels



A map of popular voxels obtained with 3dTcorrMap

See @run_3dTcorrMap

Regions Of Interest: The most popular voxels



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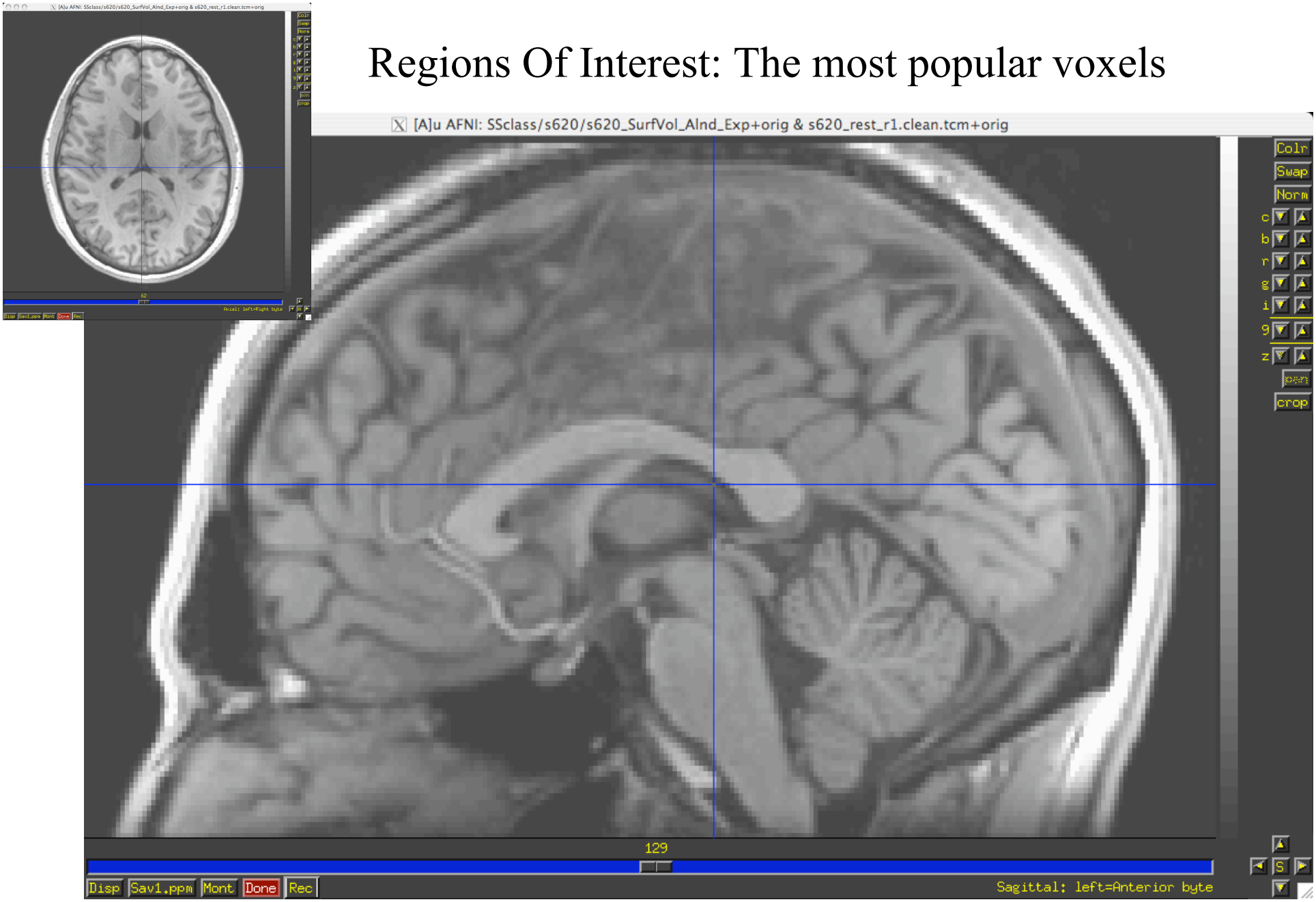
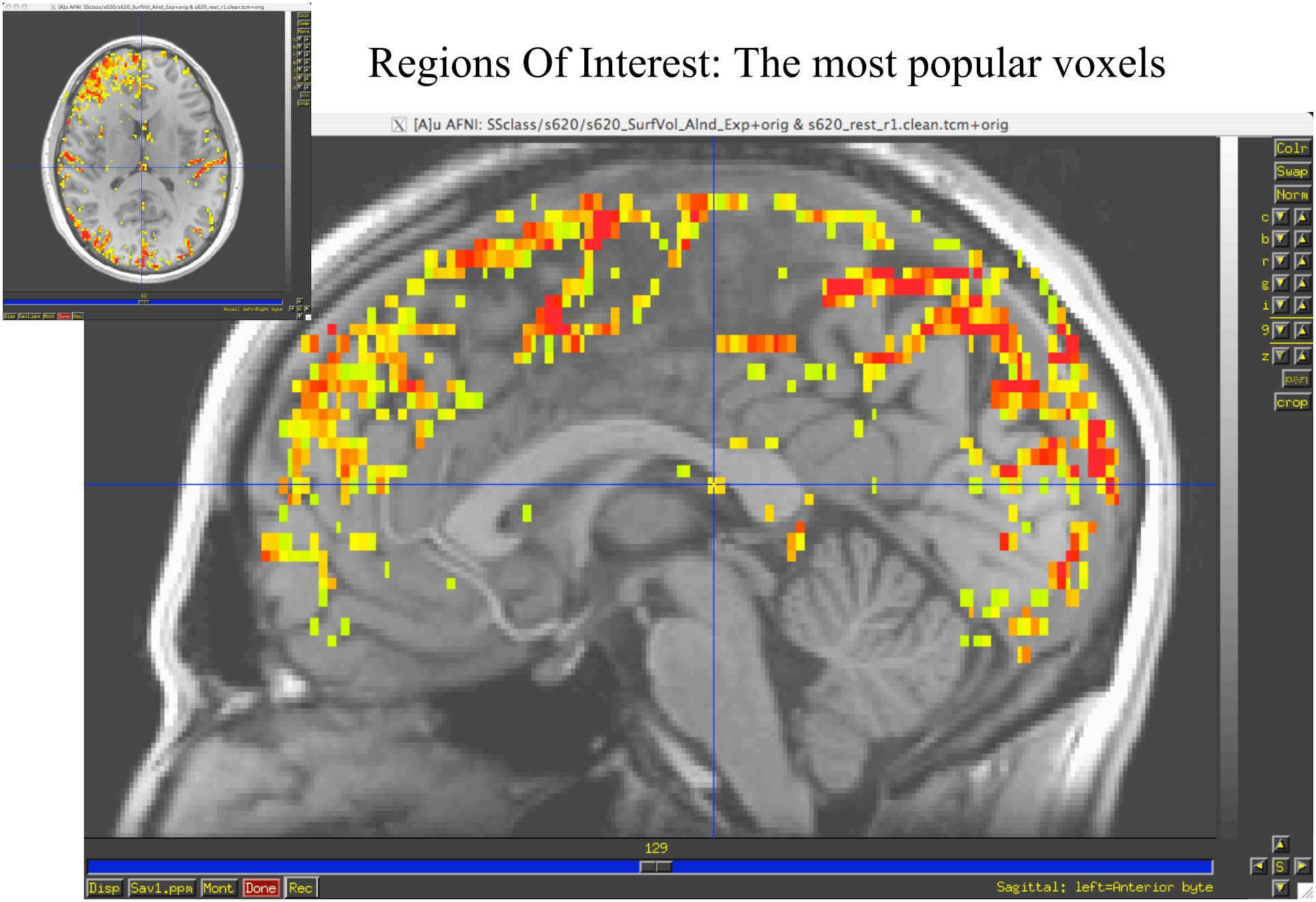


Regions Of Interest: The most popular voxels

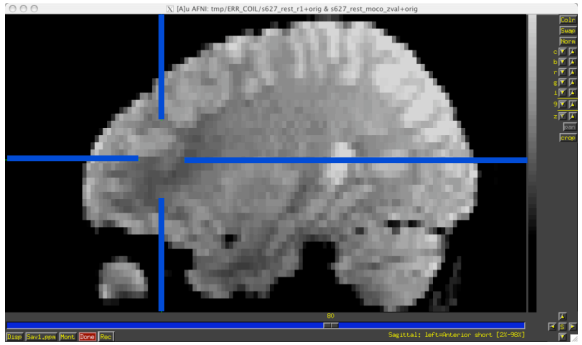


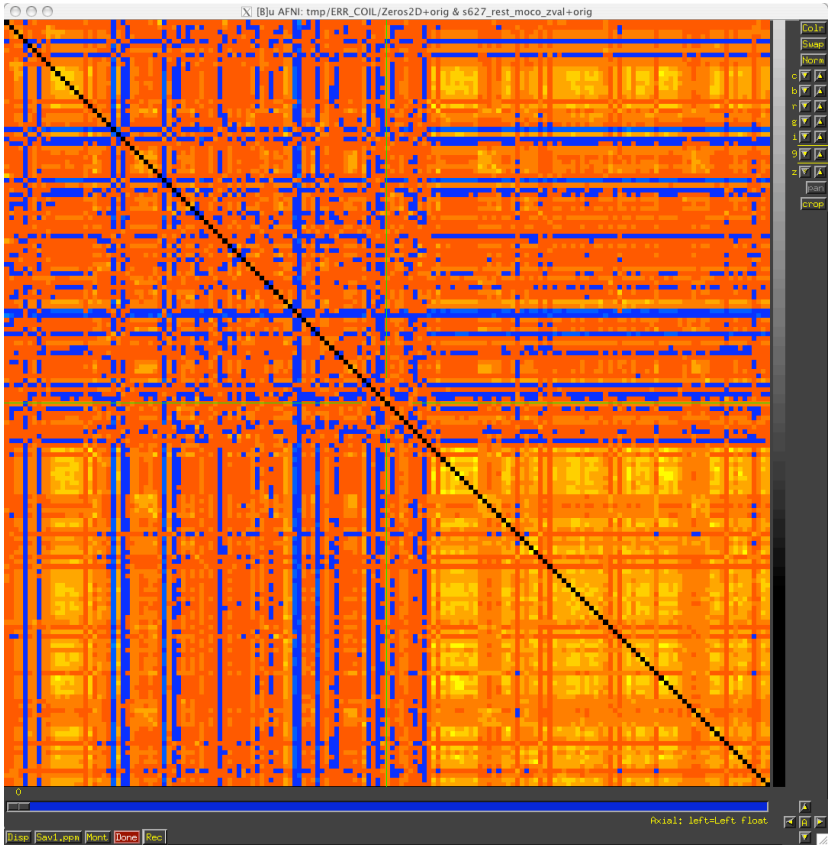
A Correlation Matrix As Your Friend

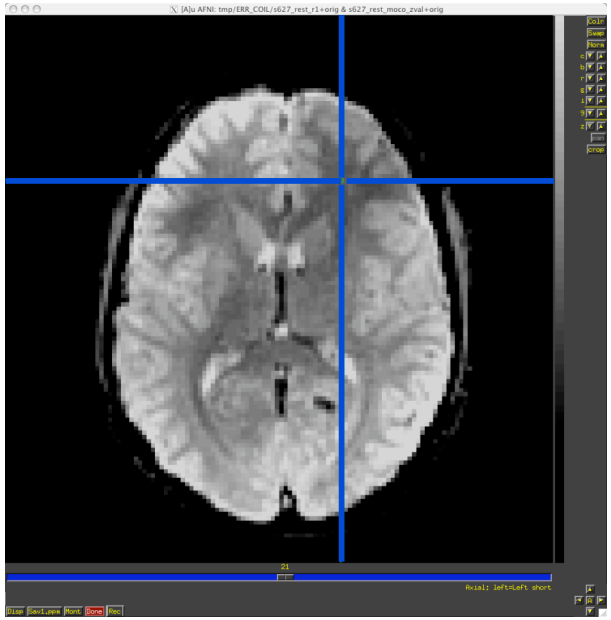
- When you're down, and troubled, and you need a helping hand
  - **`@ROI_Corr_Mat`**
  - See **@run_ROI_Corr_Mat** for demo

```
@ROI_Corr_Mat  -roi     SUMA/aparc.a2005s+aseg.nii    \
               -ts      s${subj}_rest_r1+orig    \
               -prefix  s${subj}.Zmatrix
```

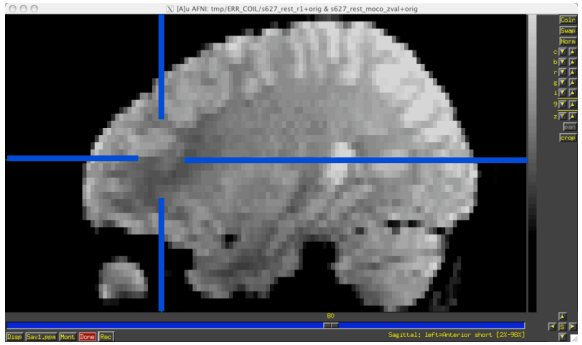
Scanner Glitch - 2

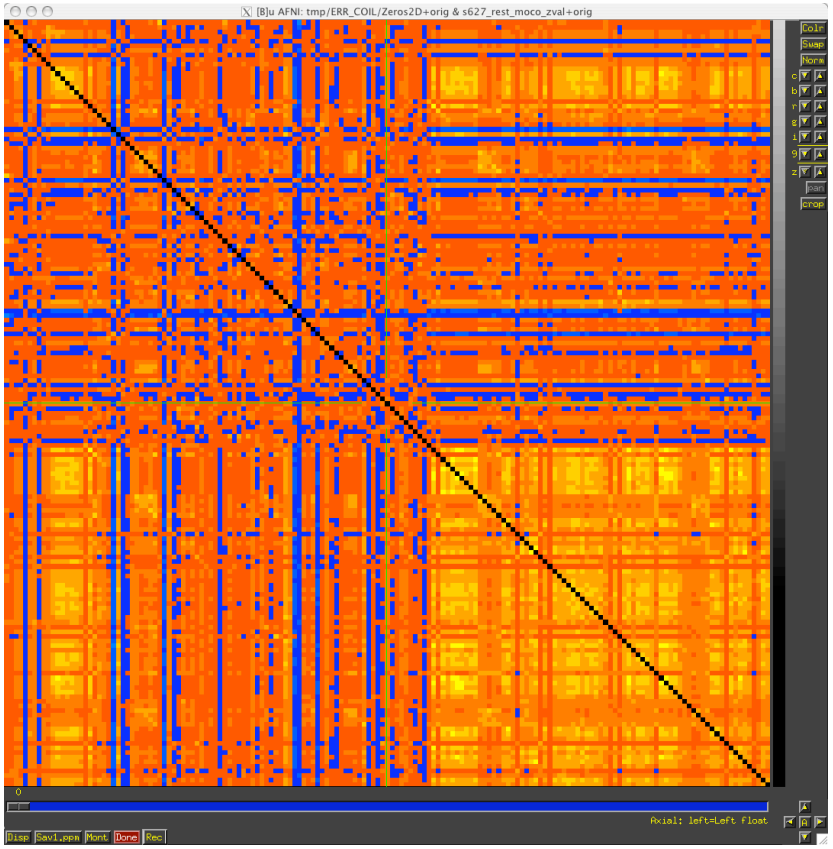


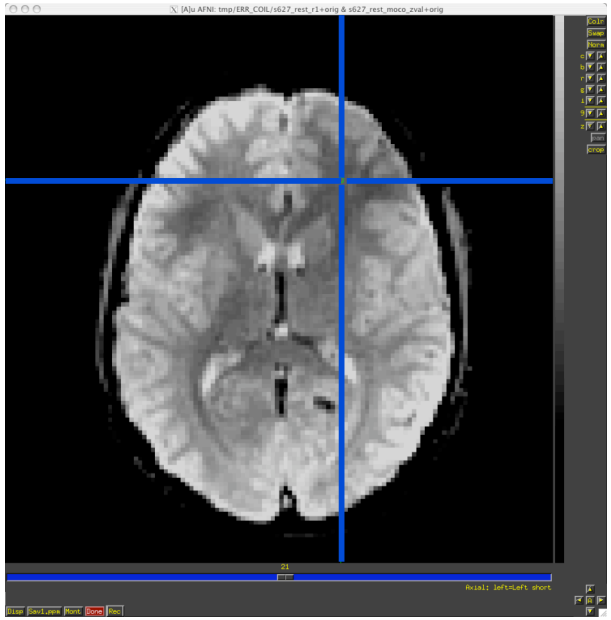


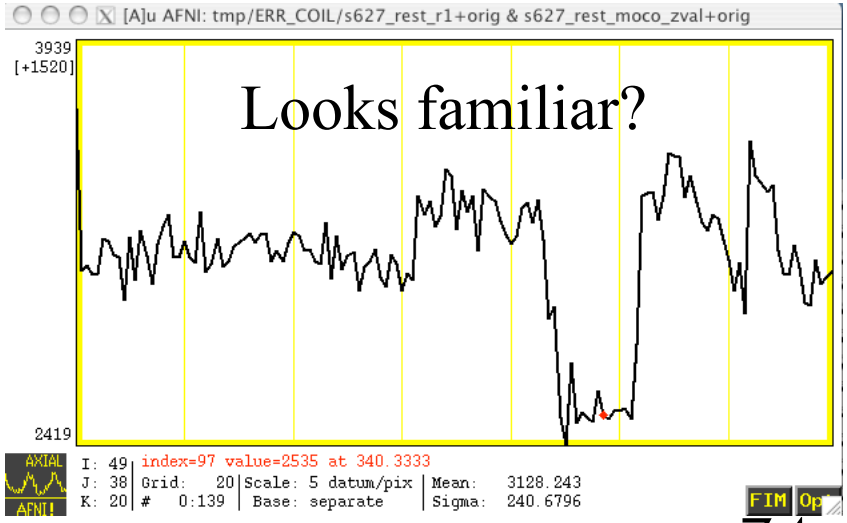


Scanner Glitch - 2

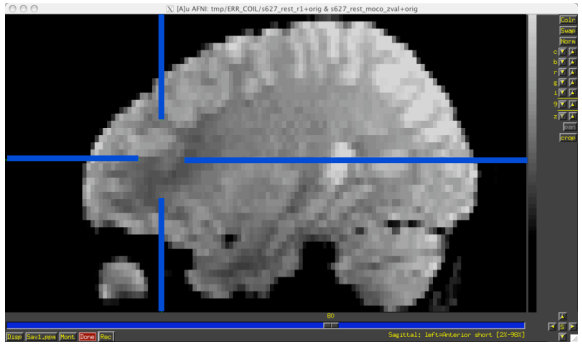


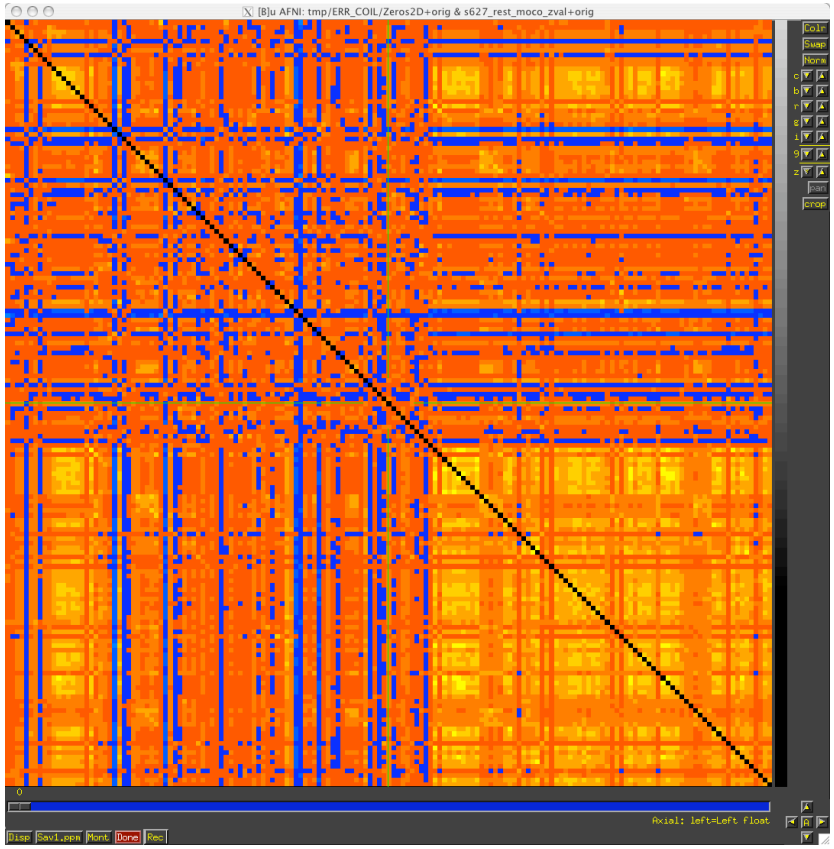


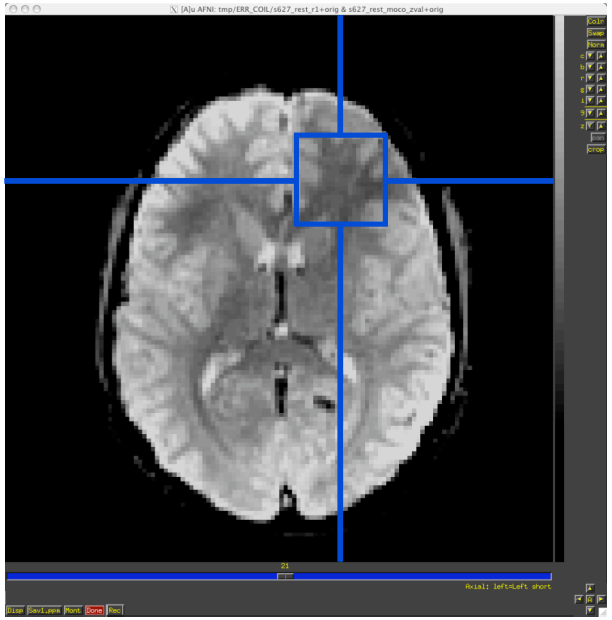


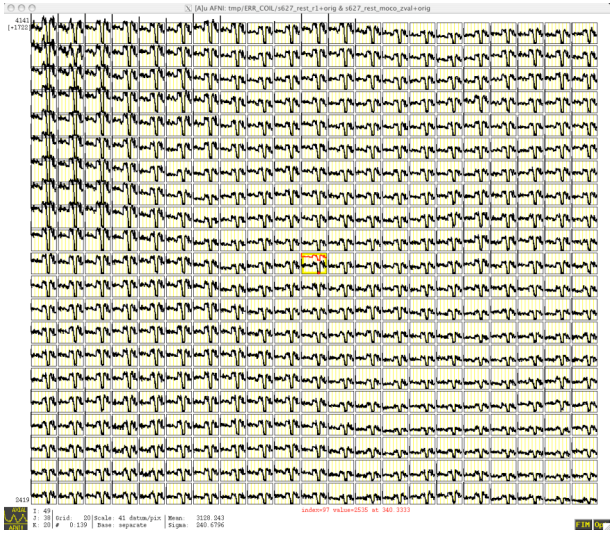


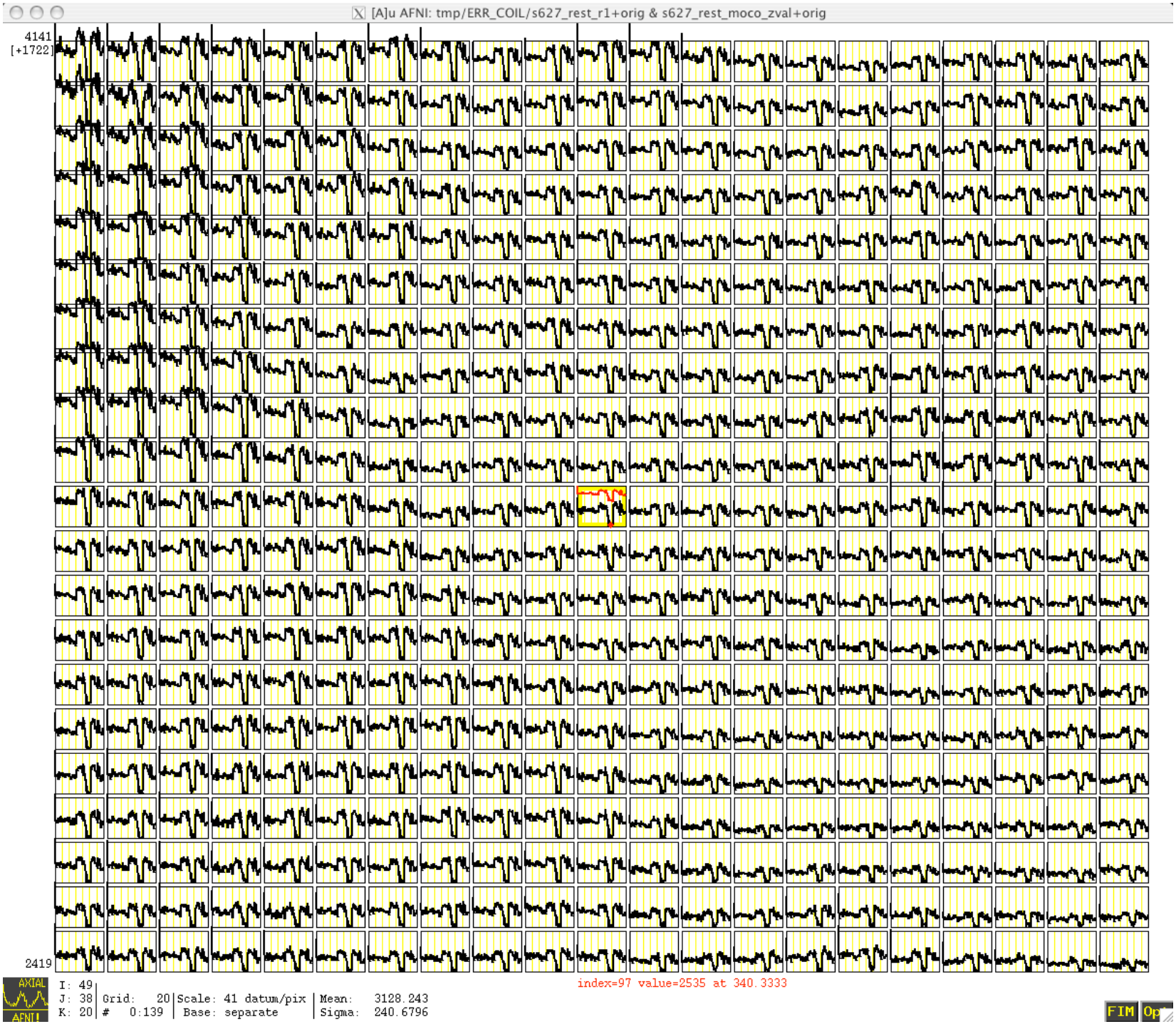
Scanner Glitch - 2

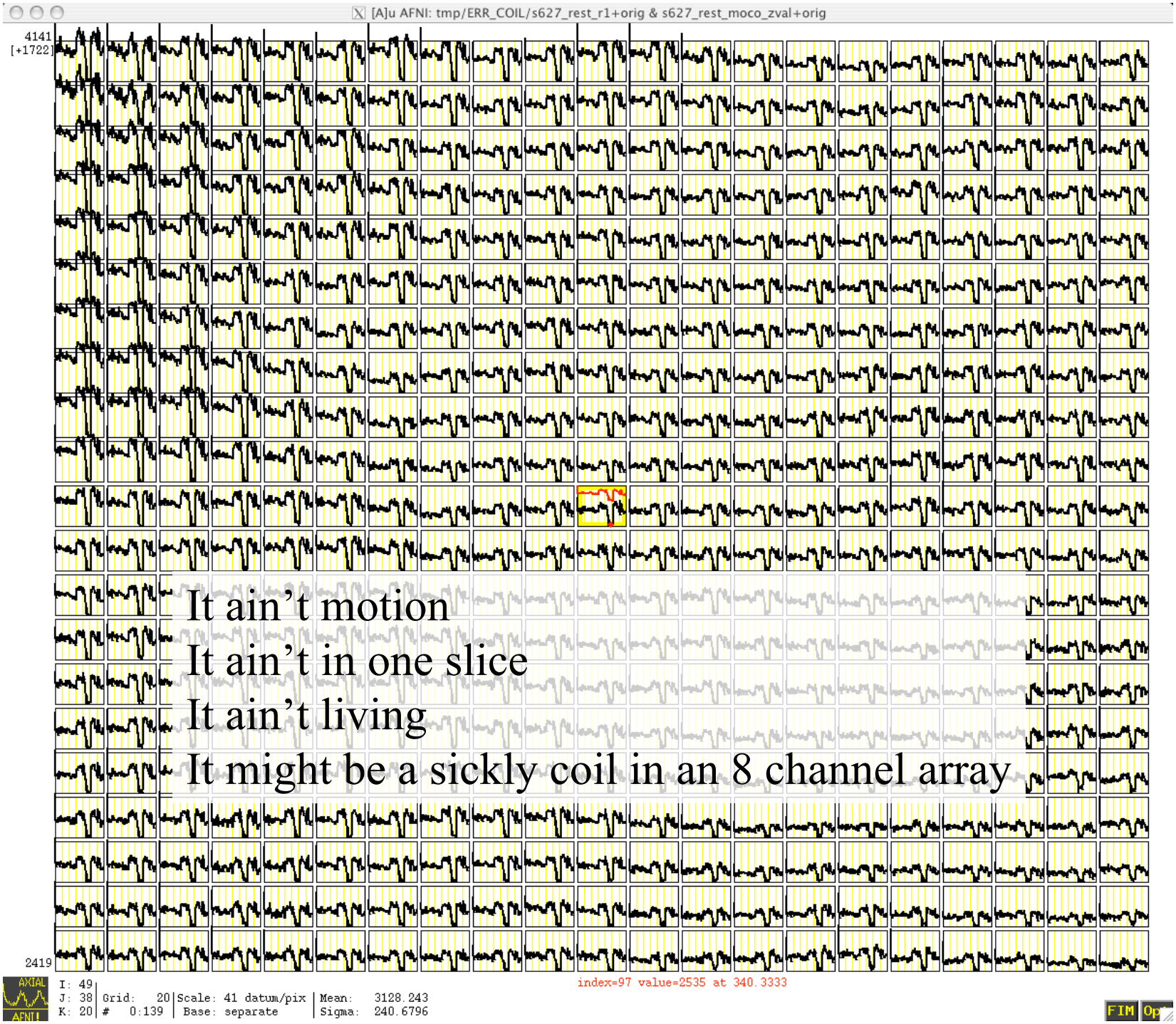


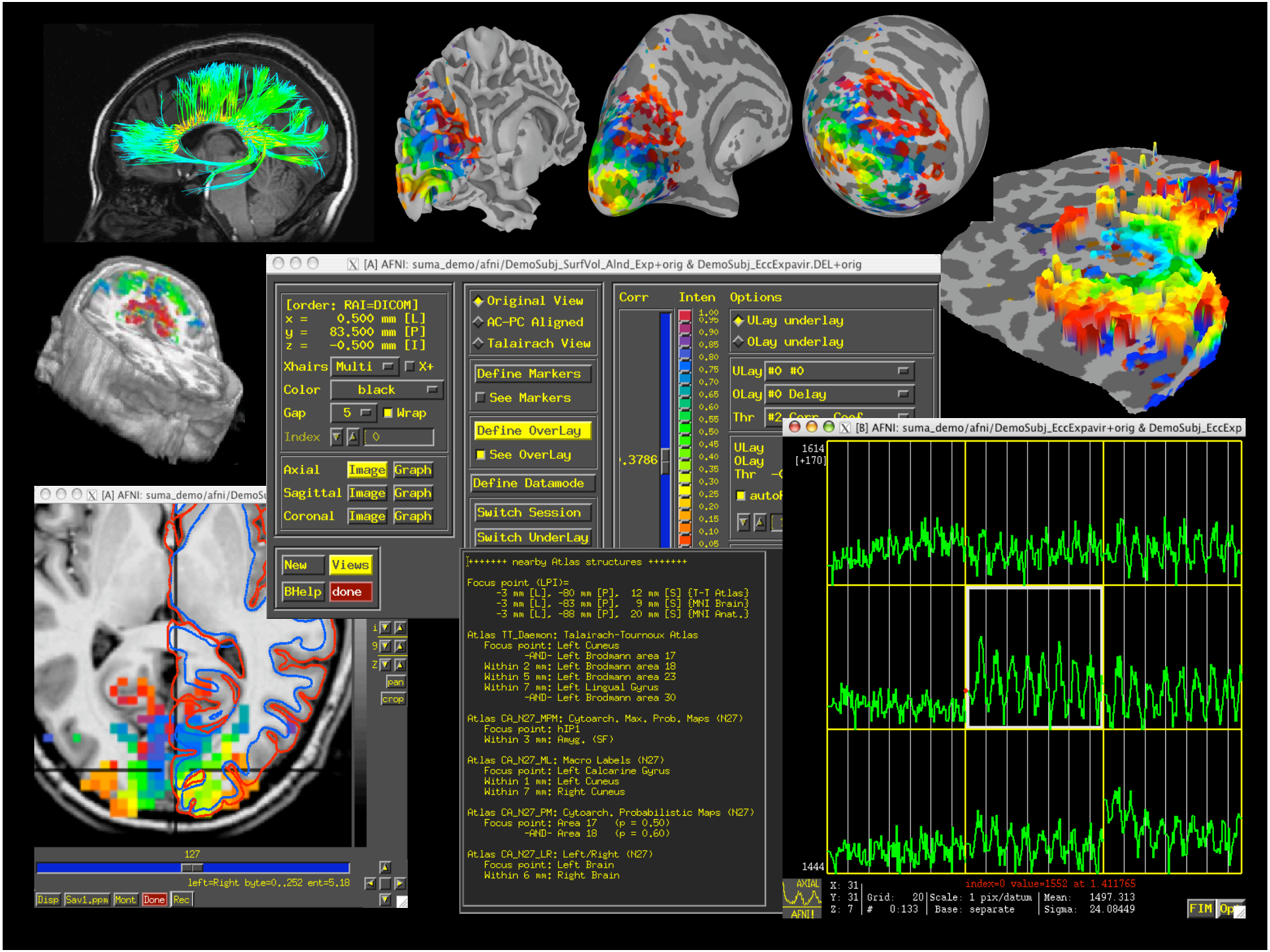







[A]u AFNI: tmp/ERR_COIL/s627_rest_r1+orig & s627_rest_moco_zval+orig
4141
[+1722]
2419
index=97 value=2535 at 340.3333
AXIAL
AFNI
I: 49
J: 38
K: 20
Grid: 20
0:139
Scale: 41 datum/pix
Base: separate
Mean: 3128.243
Sigma: 240.6796
FIM
Op


[A]u AFNI: tmp/ERR_COIL/s627_rest_r1+orig & s627_rest_moco_zval+orig
4141
[+1722]
2419
It ain't motion
It ain't in one slice
It ain't living
It might be a sickly coil in an 8 channel array
AXIAL
AFNI
I: 49
J: 38
K: 20
Grid: 20
0:139
Scale: 41 datum/pix
Base: separate
Mean: 3128.243
Sigma: 240.6796
index=97 value=2535 at 340.3333
FIM


[A] AFNI: suma_demo/afni/DemoSubj_SurfVol_Alnd_Exp+orig & DemoSubj_EccExpavir.DEL+orig
[order: RAI=DICOM]
x = 0.500 mm [L]
y = 83.500 mm [P]
z = -0.500 mm [I]
Xhairs Multi X+
Color black
Gap 5 Wrap
Index 0
Axial Image Graph
Sagittal Image Graph
Coronal Image Graph
New Views
BHelp done
Original View
AC-PC Aligned
Talairach View
Define Markers
See Markers
Define OverLay
See OverLay
Define Datamode
Switch Session
Switch UnderLay
Corr Inten Options
ULay underlay
OLay underlay
ULay #0 #0
OLay #0 Delay
Thr #2 Corr Coef
.3786
[A] AFNI: suma_demo/afni/DemoSu
127
left=Right byte=0..252 ent=5.18
Disp Sav1.ppm Mont Done Rec
pan
crop
+++++++ nearby Atlas structures +++++++
Focus point (LPI)=
-3 mm [L], -80 mm [P], 12 mm [S] {T-T Atlas}
-3 mm [L], -83 mm [P], 9 mm [S] {MNI Brain}
-3 mm [L], -88 mm [P], 20 mm [S] {MNI Anat.}
Atlas TT_Daemon: Talairach-Tournoux Atlas
Focus point: Left Cuneus
-AND- Left Brodmann area 17
Within 2 mm: Left Brodmann area 18
Within 5 mm: Left Brodmann area 23
Within 7 mm: Left Lingual Gyrus
-AND- Left Brodmann area 30
Atlas CA_N27_MPM: Cytoarch. Max. Prob. Maps (N27)
Focus point: hIP1
Within 3 mm: Amyg. (SF)
Atlas CA_N27_ML: Macro Labels (N27)
Focus point: Left Calcarine Gyrus
Within 1 mm: Left Cuneus
Within 7 mm: Right Cuneus
Atlas CA_N27_PM: Cytoarch. Probabilistic Maps (N27)
Focus point: Area 17 (p = 0.50)
-AND- Area 18 (p = 0.60)
Atlas CA_N27_LR: Left/Right (N27)
Focus point: Left Brain
Within 6 mm: Right Brain
[B] AFNI: suma_demo/afni/DemoSubj_EccExpavir+orig & DemoSubj_EccExp
1614
[+170]
1444
index=0 value=1552 at 1.411765
X: 31
Y: 31
Z: 7
Grid: 20
0:133
Scale: 1 pix/datum
Base: separate
Mean: 1497.313
Sigma: 24.08449
FIM