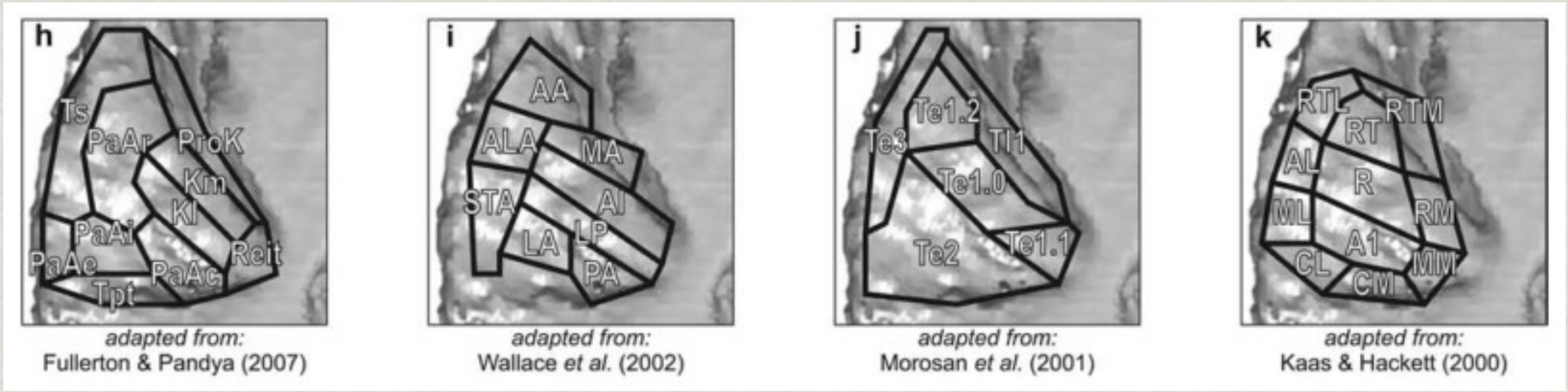
NO SOUND CONSENSUS

- No consensus on how to parcellate auditory cortex beyond A1



LANGERS ET AL, 2011

- Why is this different from vision?

  (1) Fewer researchers?

  (2) Smaller regions/greater individual variability?

  (3) Intrinsically less modular, perhaps due to the statistics of sensory signals

No sound consensus

Aims

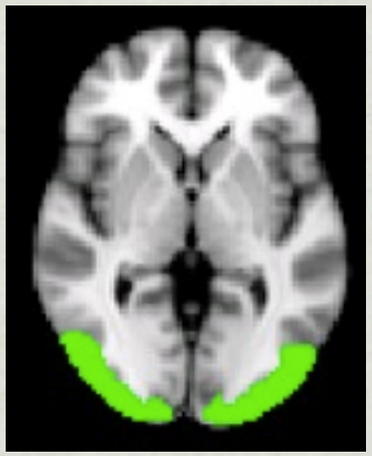
1. Quantify modularity in auditory and visual cortex
2. If appropriate, produce the best possible parcellation of auditory cortex and characterize the resulting modules

Our approach

- Build team to fuse multiple data sources (*Human Connectome Project, Allen Brain Atlas, fc1000, Neurosynth)*
- Cluster on Amazon EC2 used to perform all analyses
- Integration of tools from multiple software packages *(FSL, SPM, Freesurfer, NiPy, NiBabel)* and programming languages *(Bash, Python, C, Matlab, Javascript, JQuery, d3)*

No sound consensus

Methods

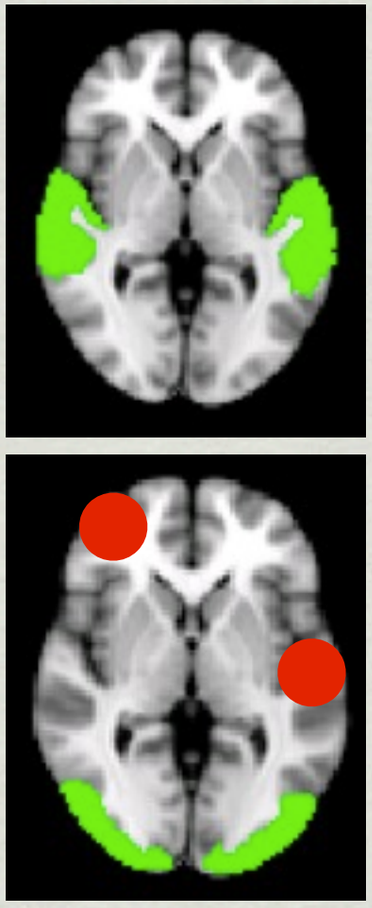


- Seed ROIs in auditory and visual cortex from Neurosynth
- 120 target ROIs spanning brain (from Craddock et al, 2011)
- Diffusion tractography and resting state to calculate connectivity of each seed voxel to each target ROI
- Cluster seed voxels by their signature of connectivity and calculate a modularity score, Q

Awesome datasets from HCP Q1: dMRI has 90 directions of 3 b-values, 168x144x111 voxels; rsfMRI 4800 scans of 104x90x72 voxels

No sound consensus

Methods



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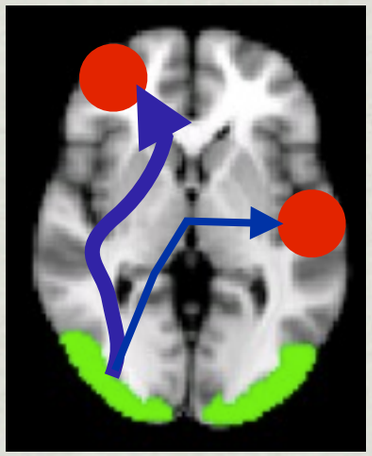

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No sound consensus

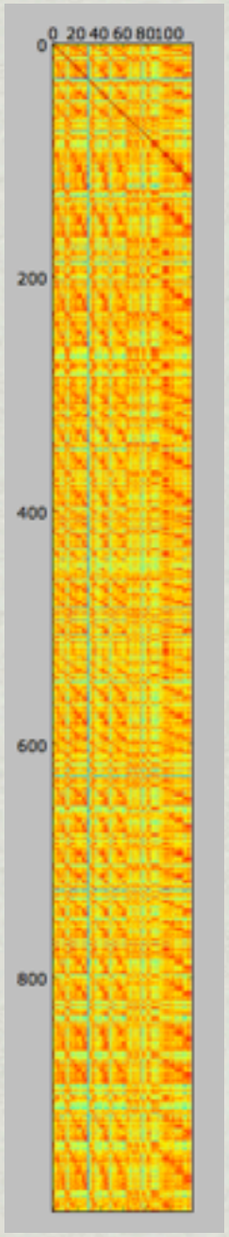
Analysis

- Diffusion tractography
  - Warp seeds to individual space
  - bedpostx (~6 days per subject on Sandy Bridge E core)
  - probtrackx (~14 days per subject)
  - Warp results to MNI-152 and then Conte 69 surface space
- Resting state
  - Temporal bandpass filtering
  - Data scrubbing by modeling out movement (Volterra kernel expansion method), white and CSF signal

No sound consensus

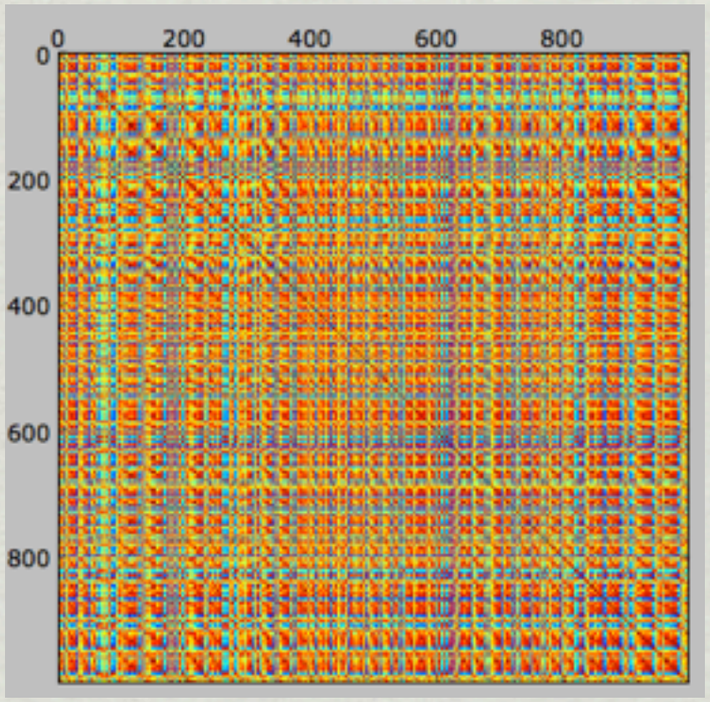
Form graph, calculate modularity

TARGETS



SEEDS

Pairwise Pearson product-moment coefficient



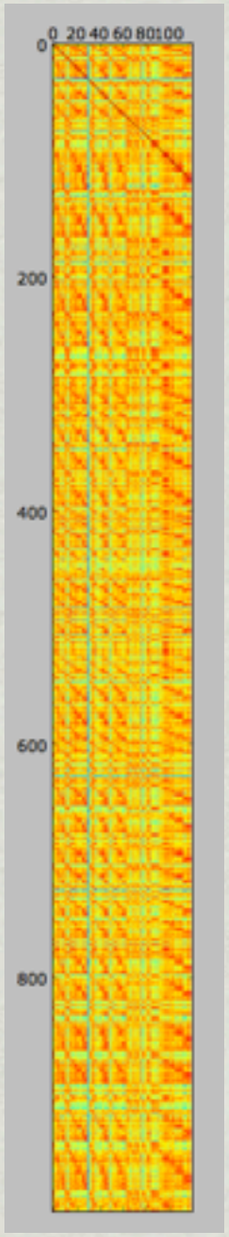
Tells us the *local story*.

“Is *this* voxel ‘similar to’ *that* voxel?”

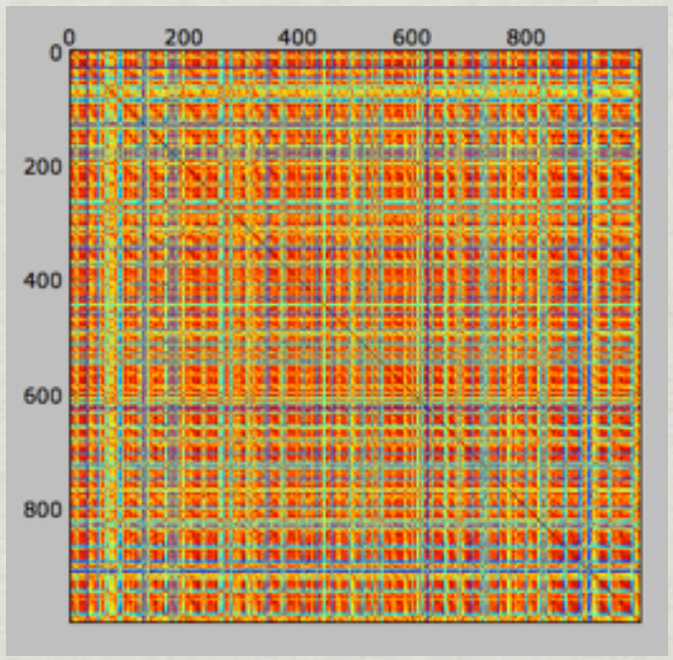
No sound consensus

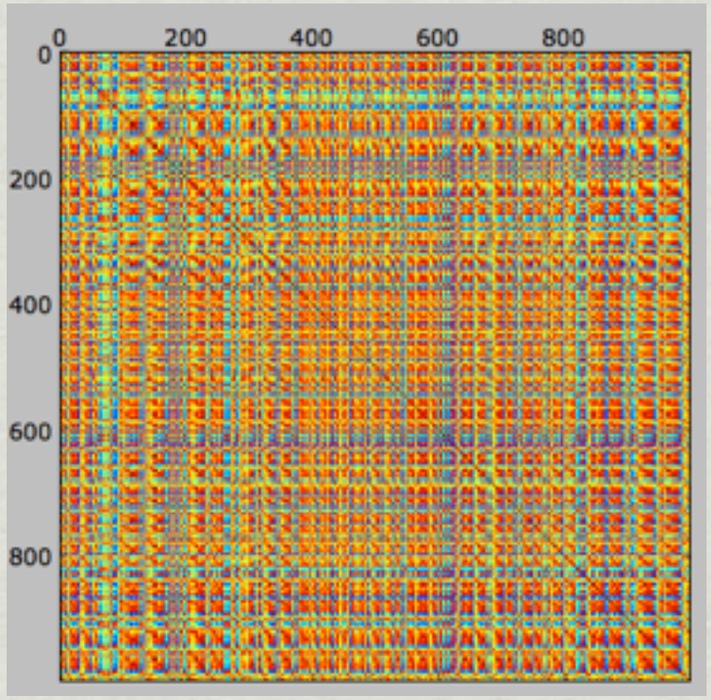
Form graph, calculate modularity

TARGETS



SEEDS





mean

$$\mathrm{eta}^2 = 1 - \frac{\sum_{i=1}^{n}\left[(a_i - m_i)^2 + (b_i - m_i)^2\right]}{\sum_{i=1}^{n}\left[(a_i - \bar{M})^2 + (b_i - \bar{M})^2\right]}$$

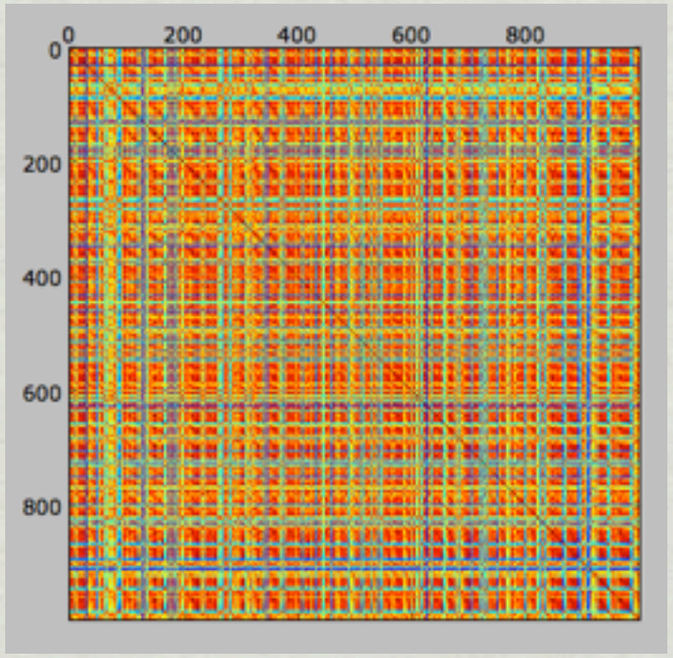
value

grand mean

This tells the *global story*. "How much does the global connectivity pattern of *this* look like the global connectivity pattern of *that*?

No sound consensus

Form graph, calculate modularity

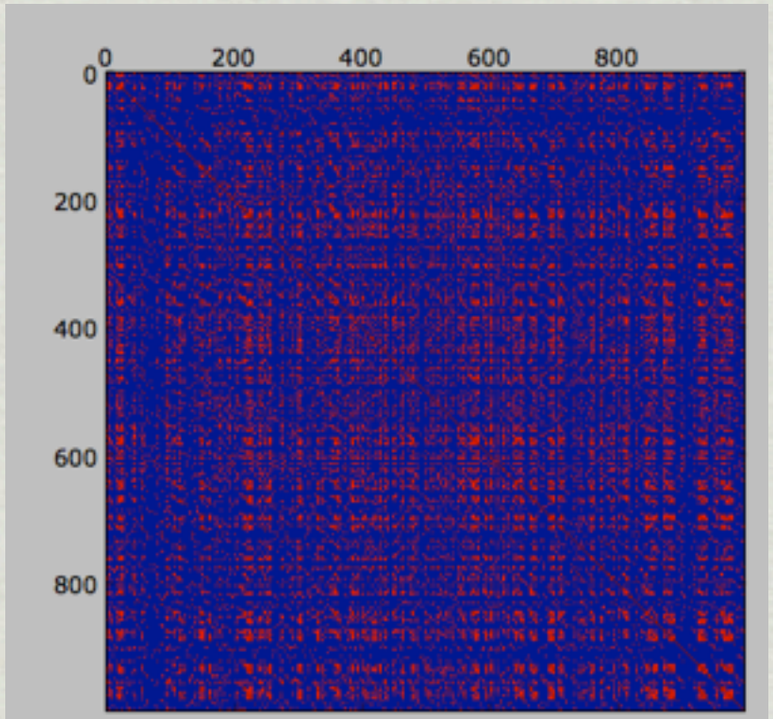


Threshold, S=2.0

$$S = \log|V| / \log K$$

vertices

avg degree



Reinterpret as adjacency matrix for a graph

No sound consensus

You need a cluster to cluster

- File server & development
  - cc2.8xlarge (32 cores, 61 GB RAM, 10Gb connect, 88 ECUs)
  - Ubuntu 12.04, NFS, 6 x 1TB EBS drives stitched together using LVM
  - Condor to manage queue. Matlab components compiled.
- Compute nodes
  - Either cc2.8xlarge or cr1.8xlarge (244 GB RAM)
  - Custom memory monitor to EC2 console.

```
          LINUX      X86_64 Claimed   Busy     1.000  1872  0+00:04:36
          LINUX      X86_64 Claimed   Busy     1.000  1872  0+00:03:40
          LINUX      X86_64 Claimed   Busy     1.000  1872  0+00:27:13
            Total Owner Claimed Unclaimed Matched Preempting Backfill

X86_64/LINUX   294     0     285         9       0          0        0

       Total   294     0     285         9       0          0        0
```

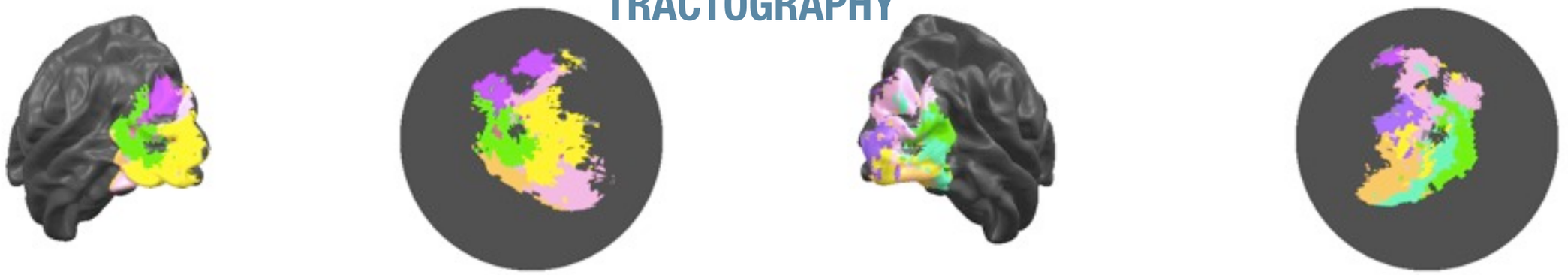
No sound consensus

Louvain modularity

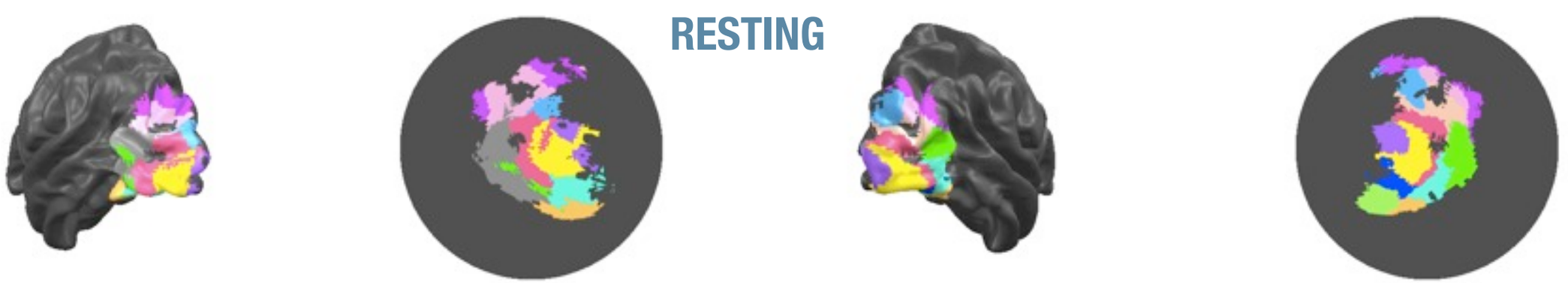
- Tractography
  - Visual (Q=0.76) higher ($p<0.02$) than auditory cortex (Q=0.69), but modular in both regions
- rs-fMRI
  - Visual (Q=0.66) and auditory cortex (Q=0.66) similar
- **First conclusion**
  - Auditory cortex is modular, although not quite to the same degree as visual cortex

No sound consensus

TRACTOGRAPHY

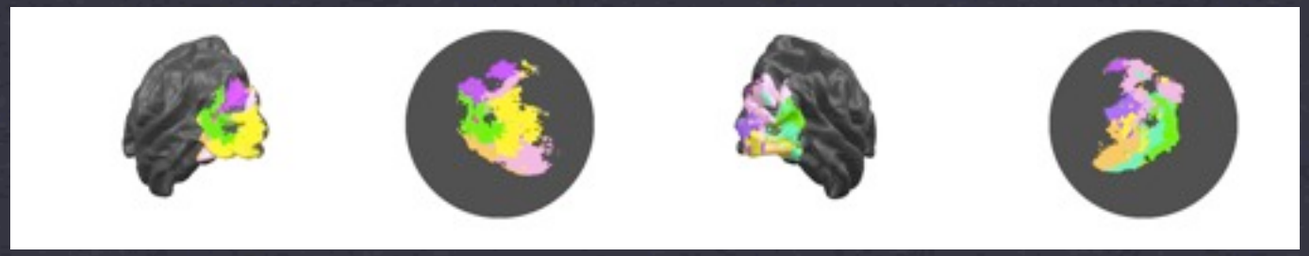


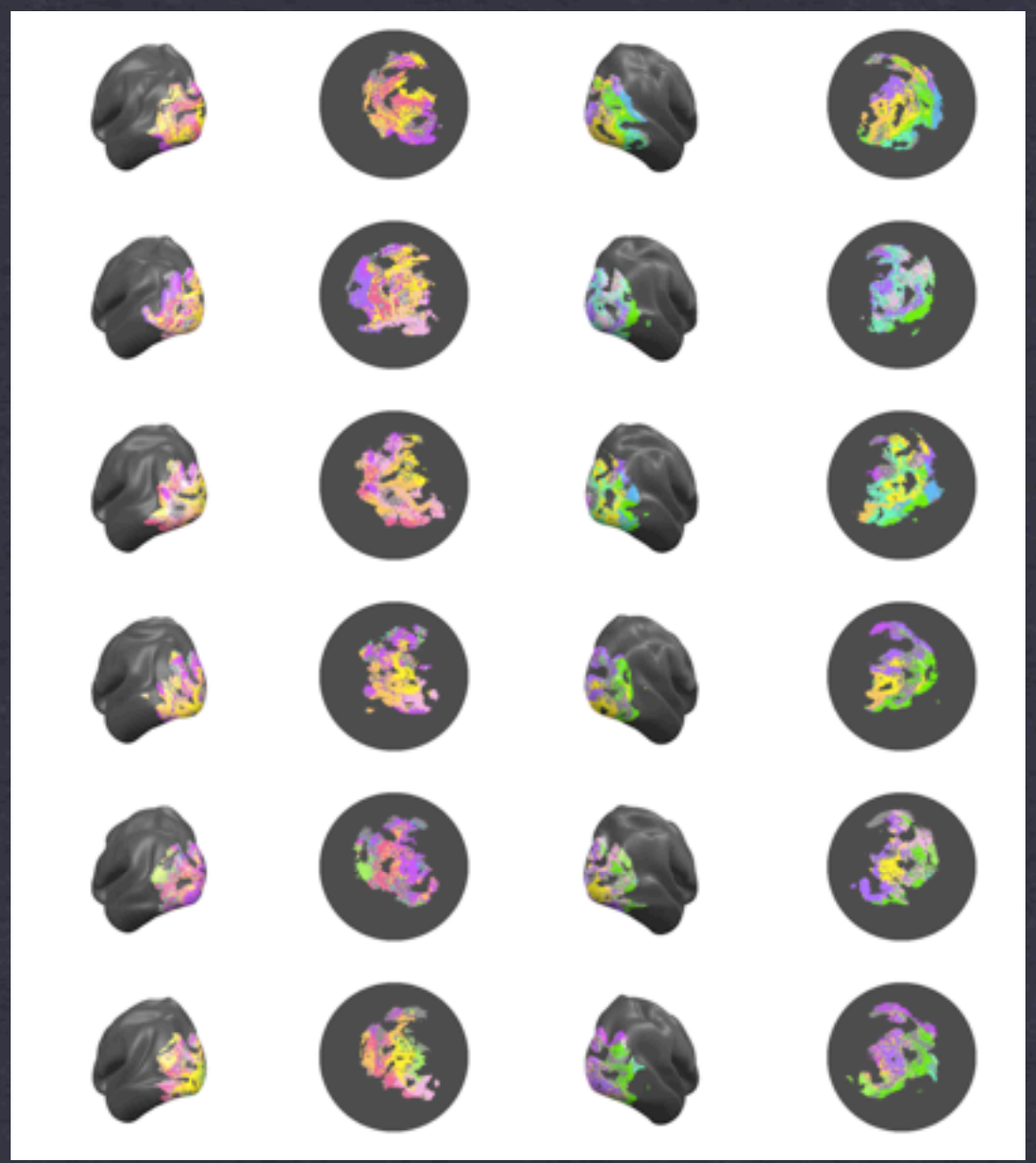
RESTING

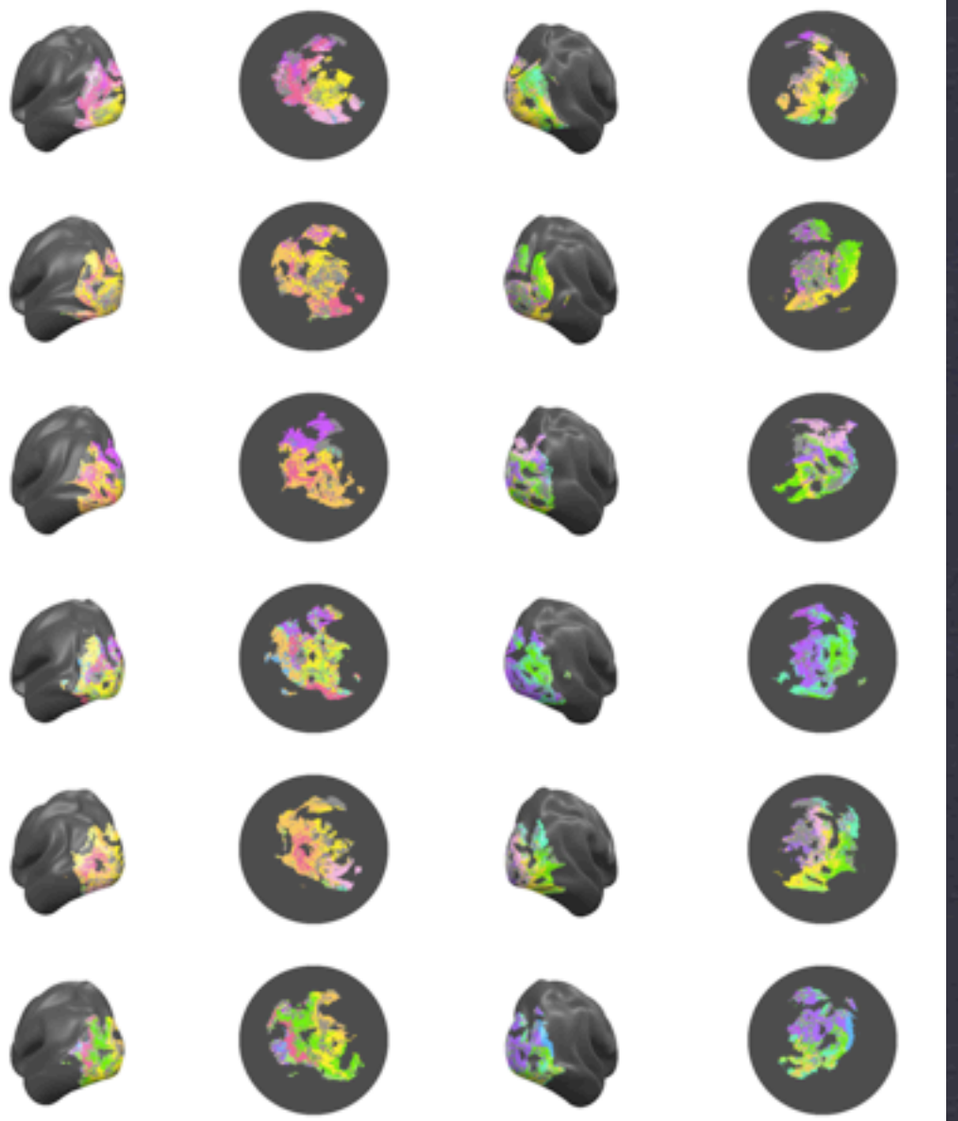


GROUP DATA - VISUAL

No sound consensus

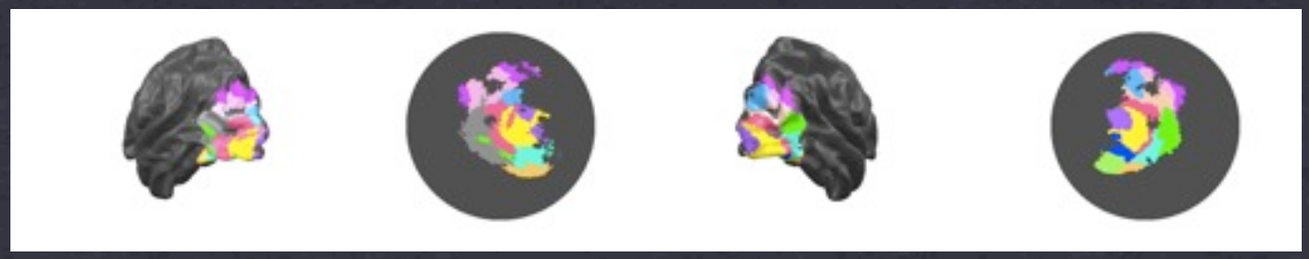


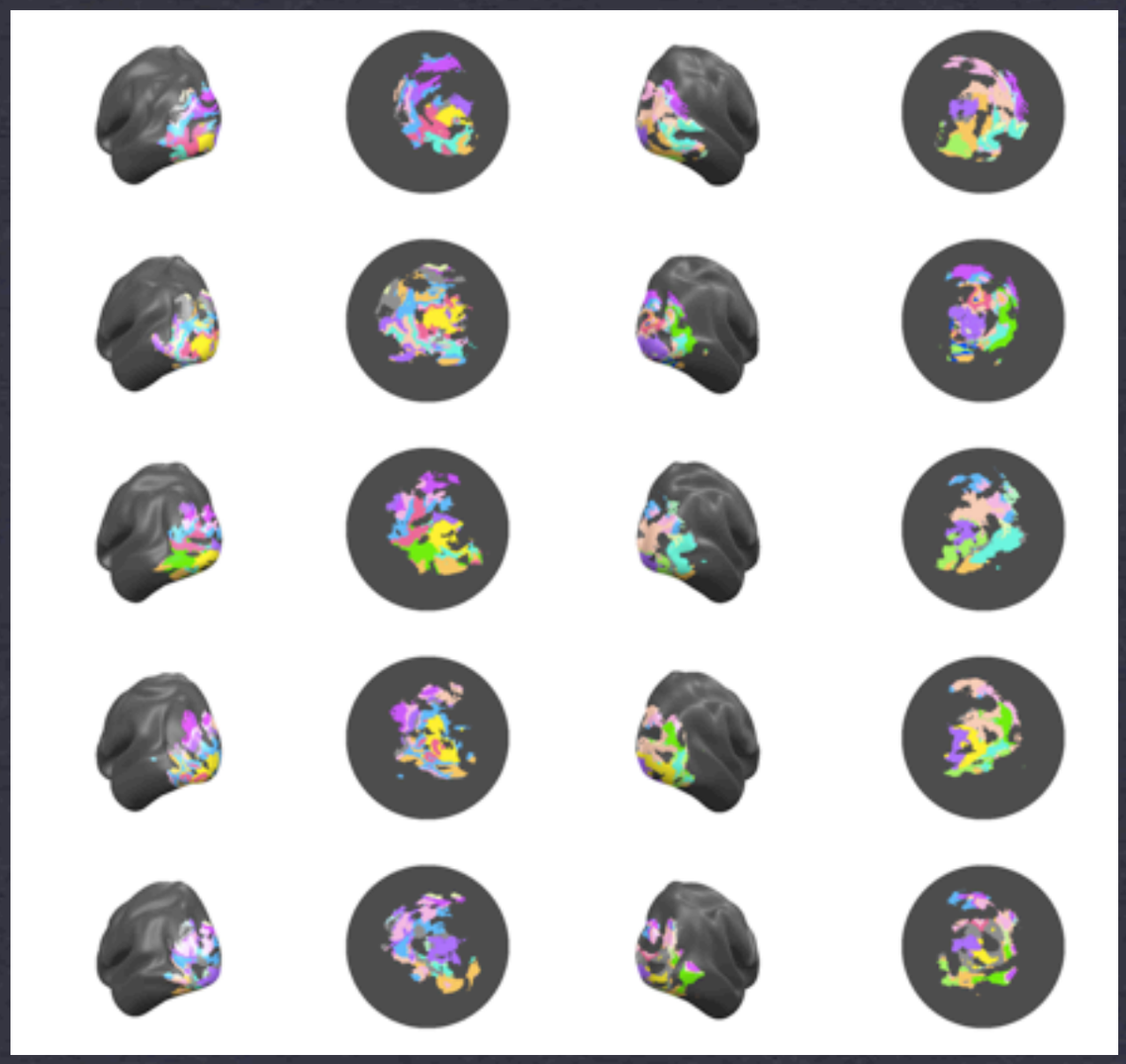


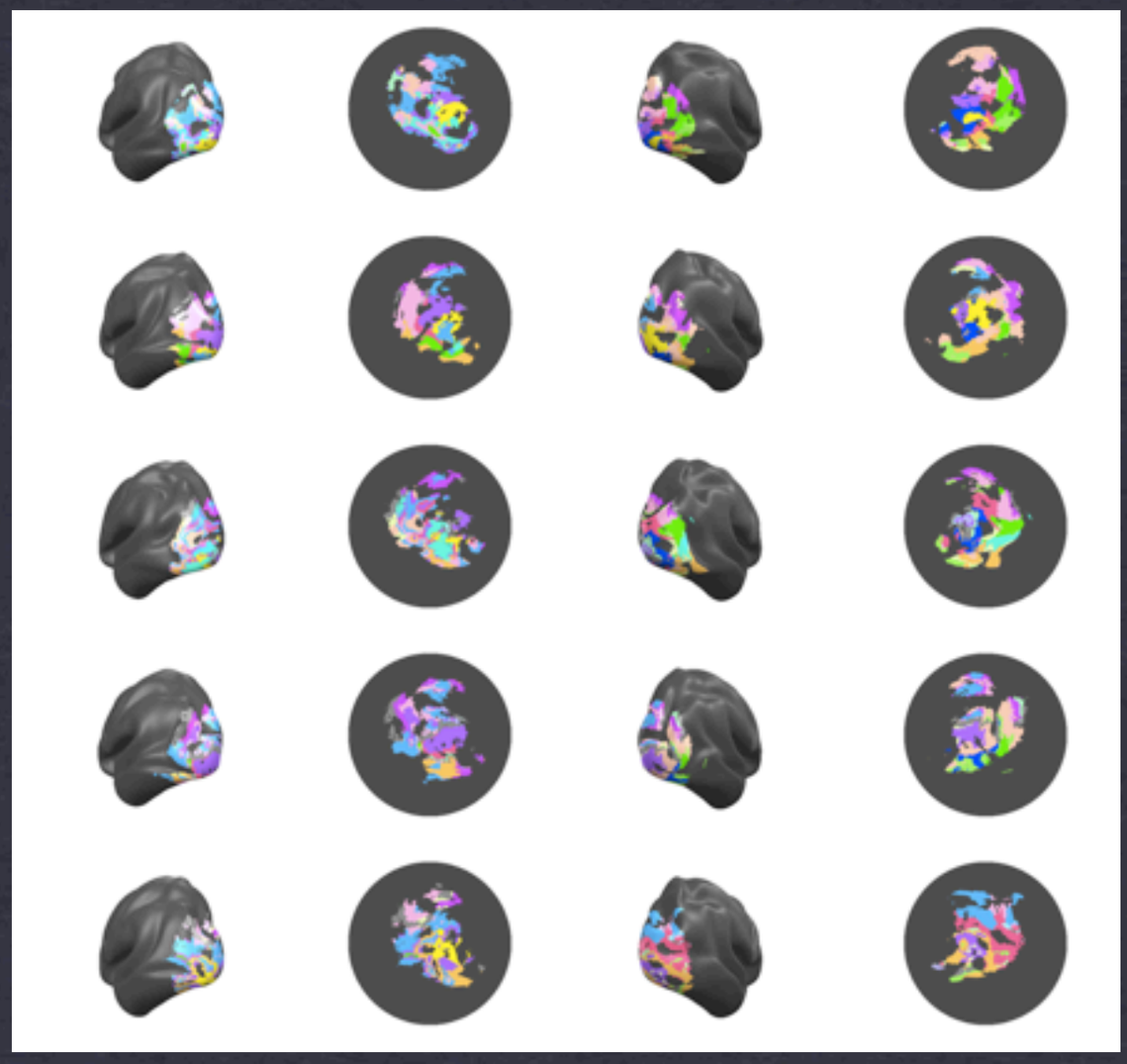


VISUAL - TRACTOGRAPHY - INDIVIDUALS

No sound consensus



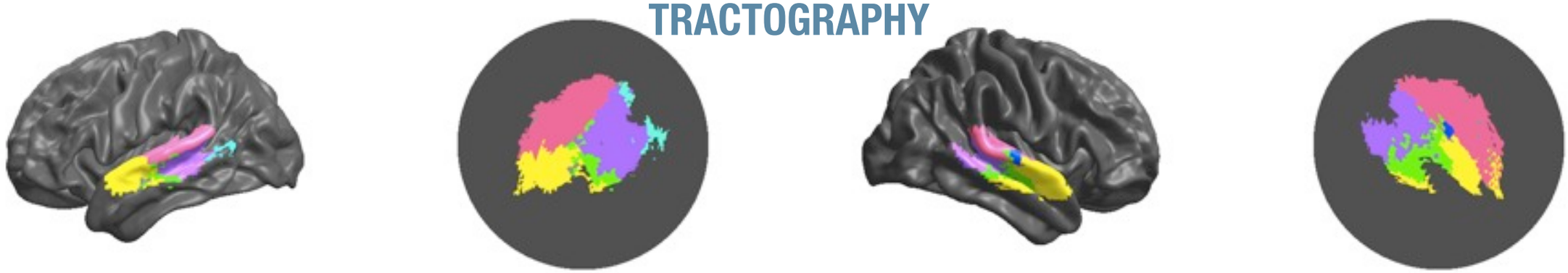




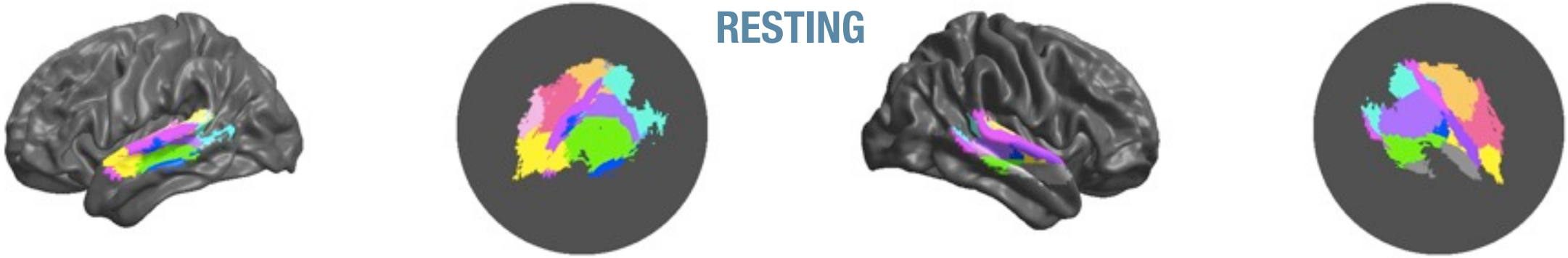
VISUAL - RESTING - INDIVIDUALS

No sound consensus

TRACTOGRAPHY

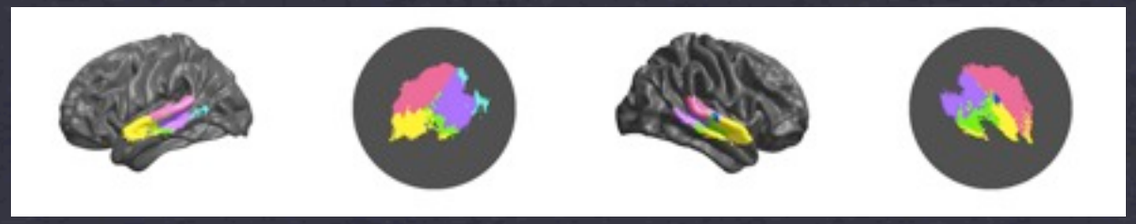


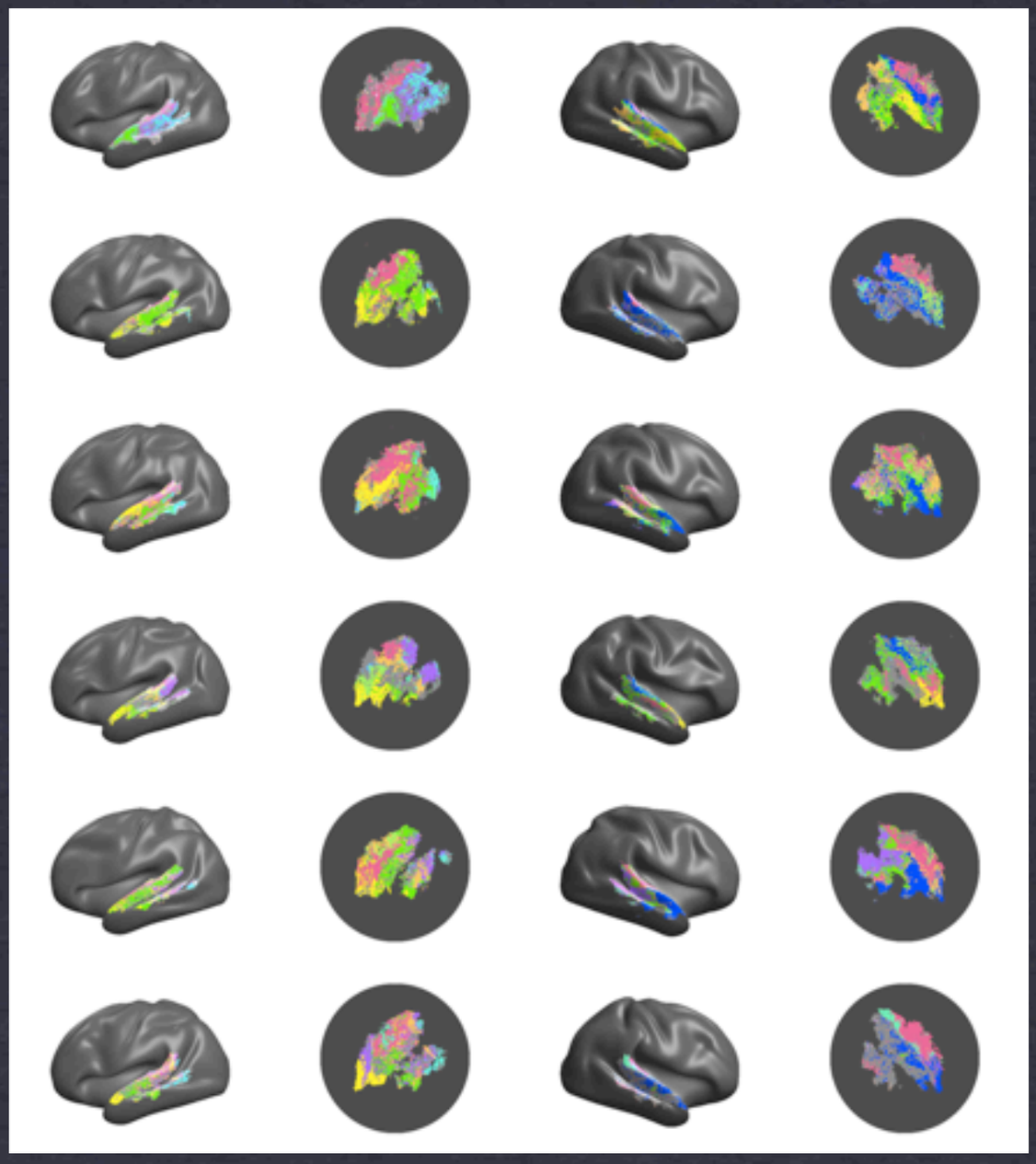
RESTING

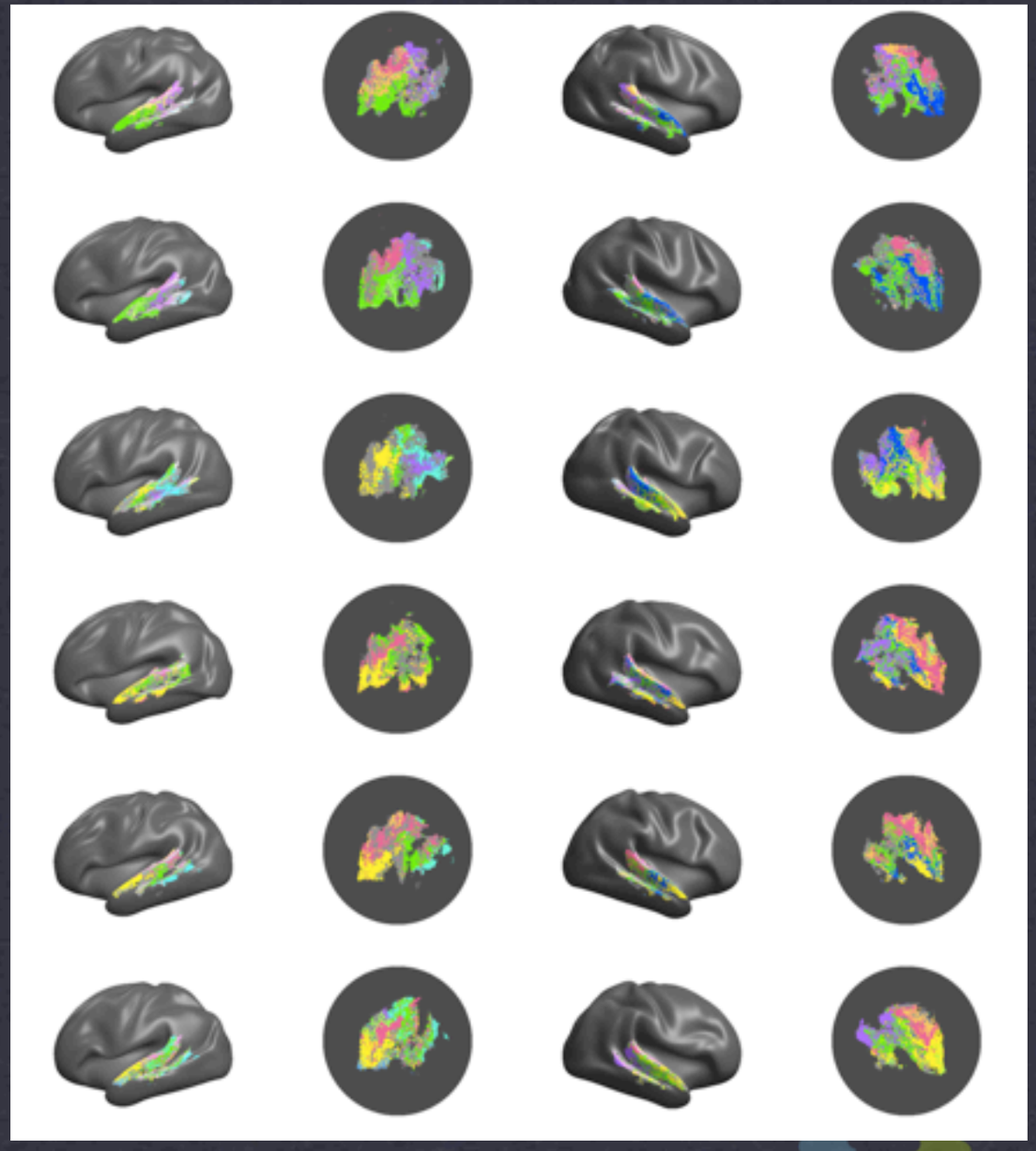


AUDITORY - GROUP

No sound consensus

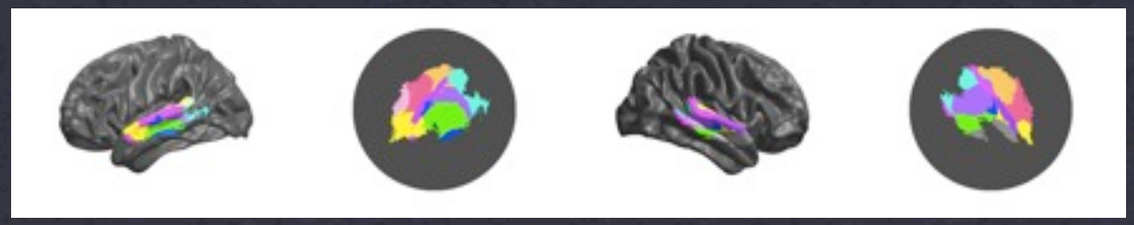


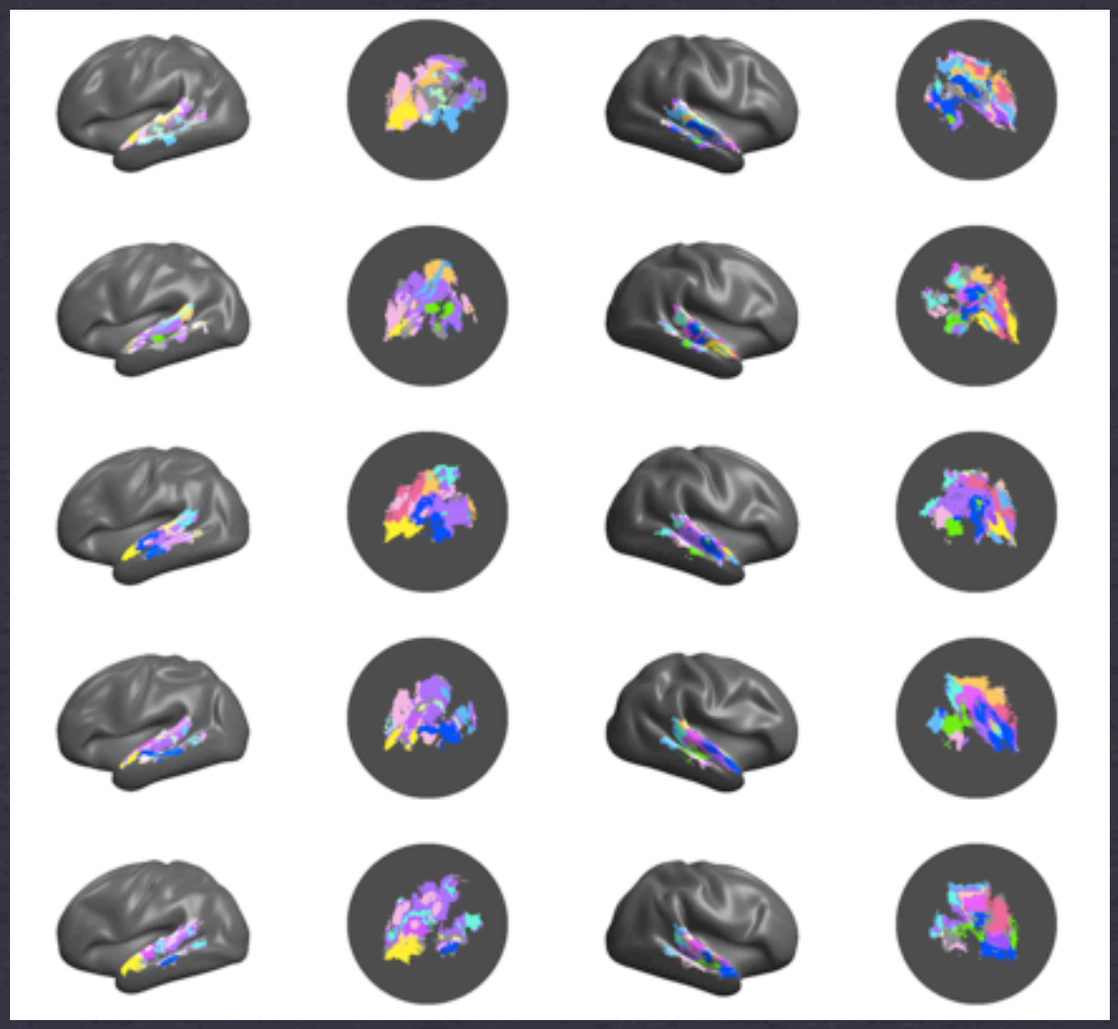


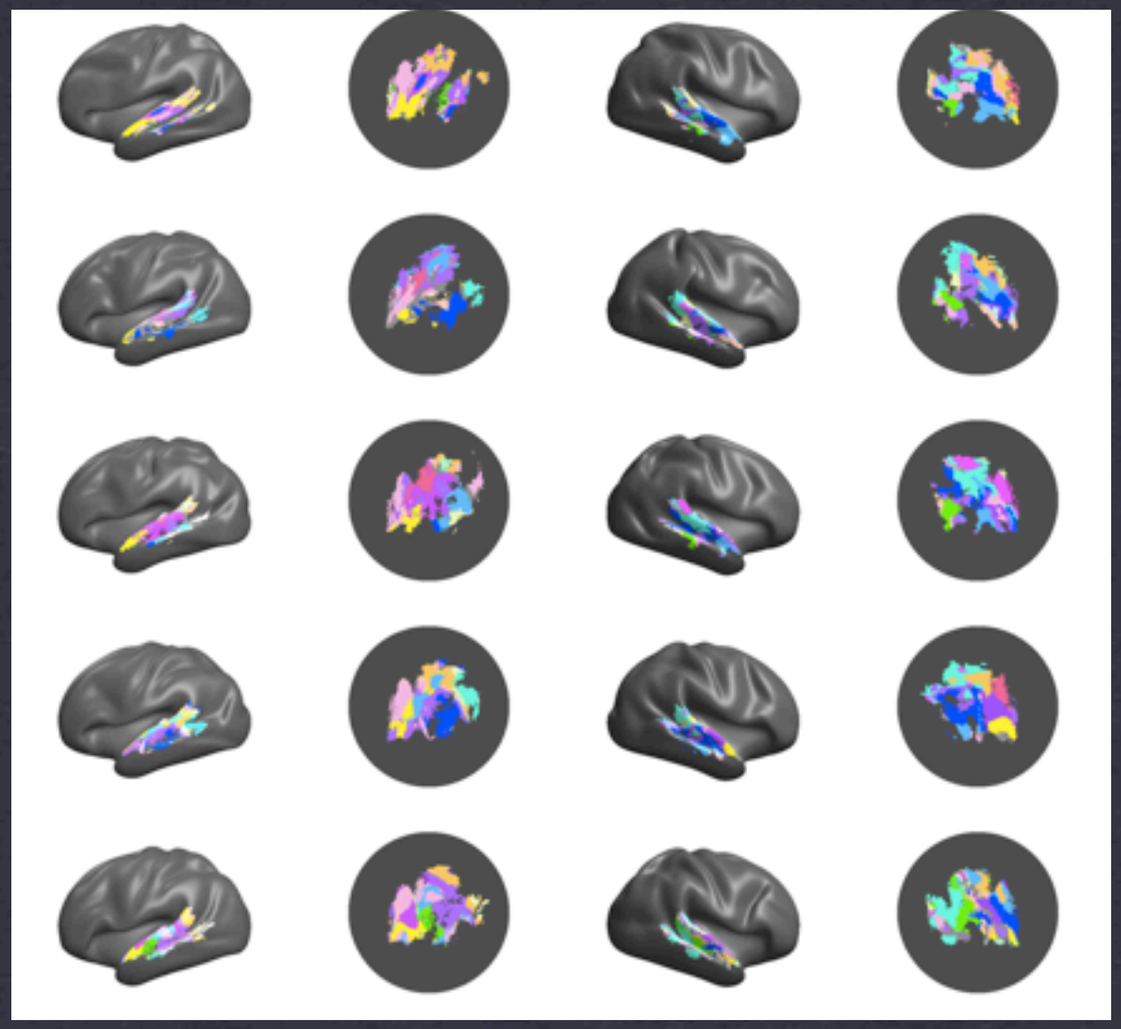


AUDITORY - TRACTOGRAPHY - INDIVIDUALS

No sound consensus





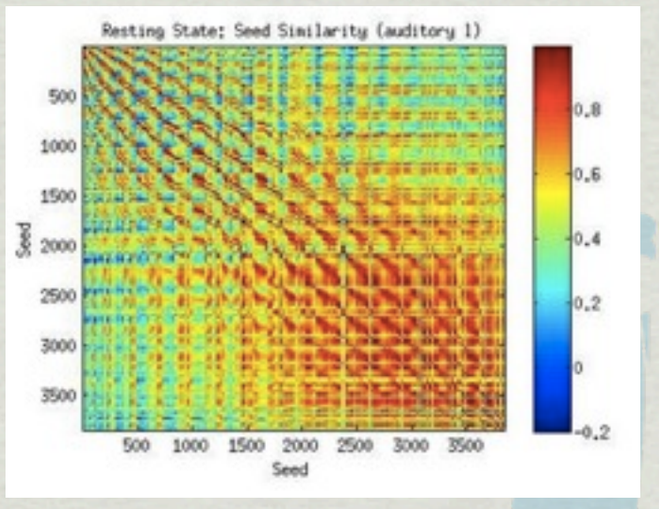


AUDITORY - RESTING - INDIVIDUALS

No sound consensus

Comparison of tractography & resting

- Seed-target connectivity patterns (2nd order RSA)
  - Auditory (r=0.03, 0.15 for L, R, each p<0.0001)
  - Visual (r=0.11, 0.01 for L, R each p<0.0001)
- Seed-seed similarity (3rd order RSA)
  - Auditory (r=0.29, 0.35 for L, R, each p<0.0001)
  - Visual (r=0.26, 0.30 for L,R each p<0.0001)

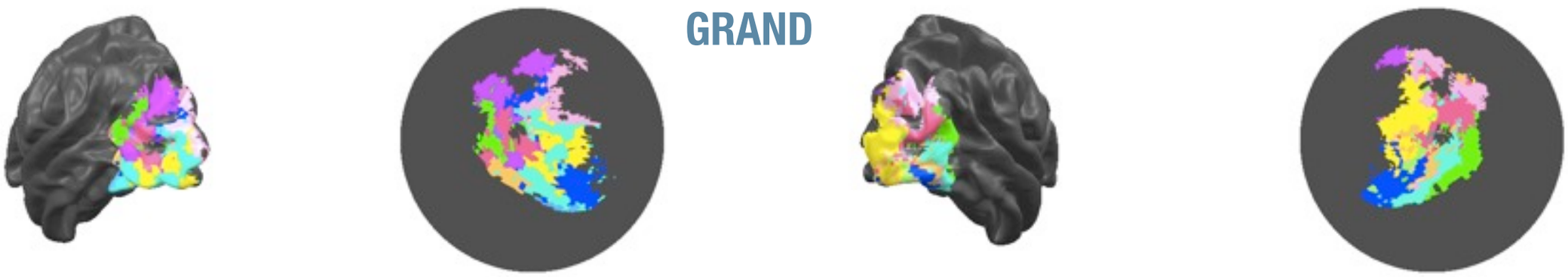


No sound consensus

DIFF

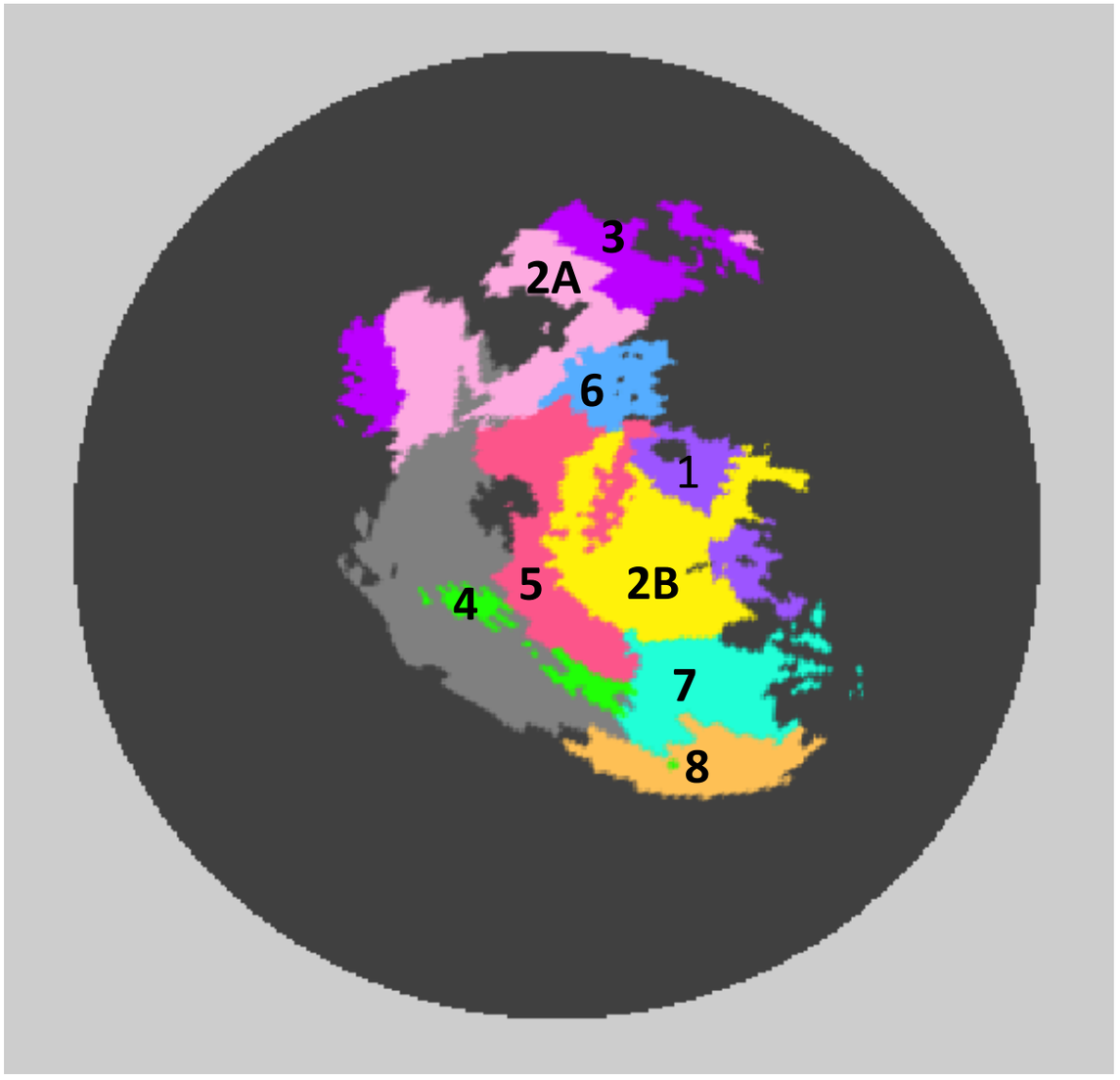
RESTING

GRAND

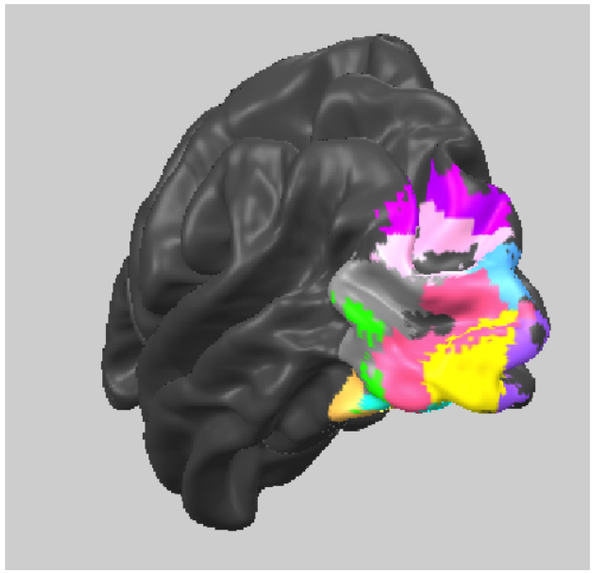


GRAND PARCELLATION - VISUAL

No sound consensus

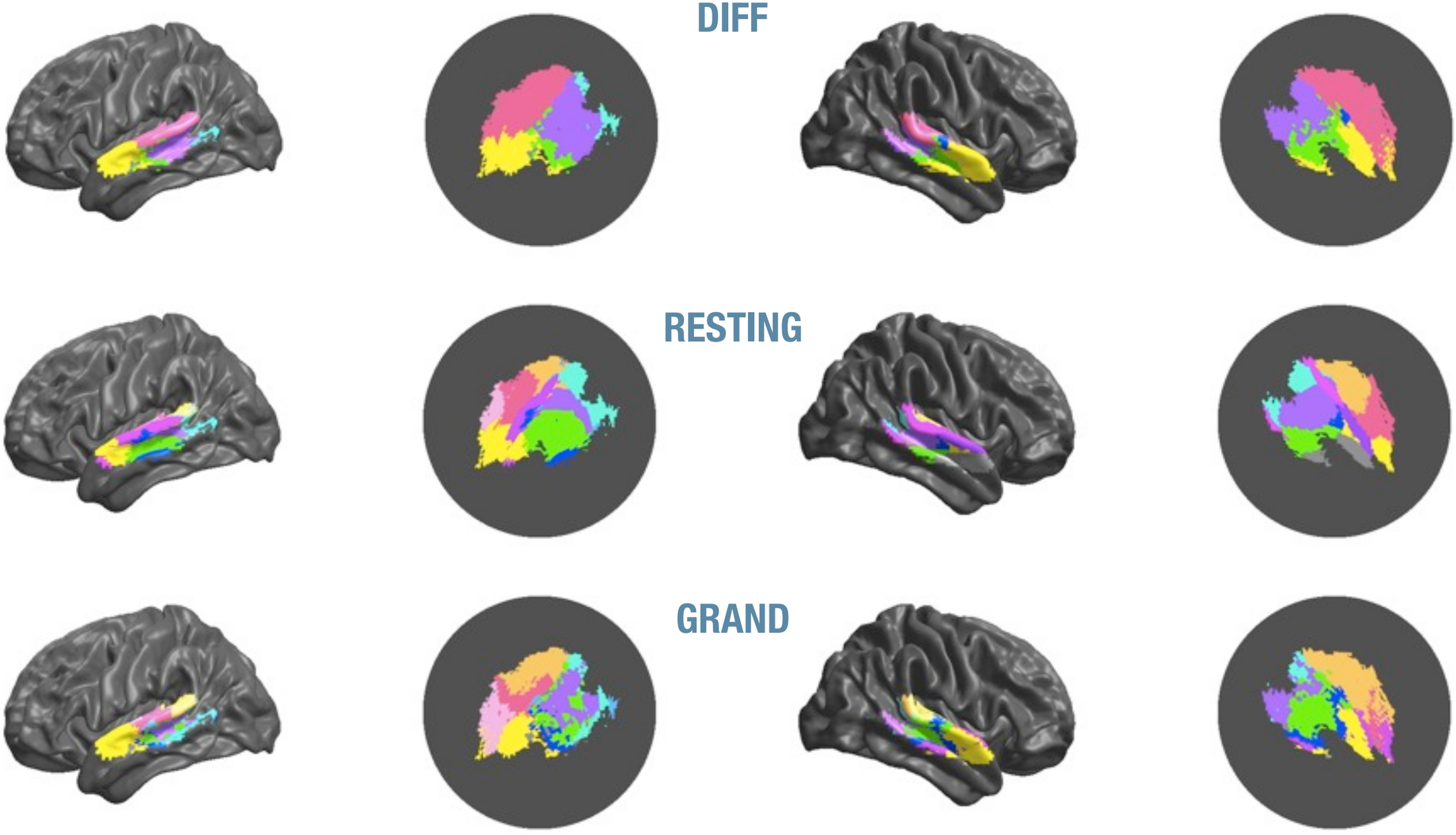


Resting_L_Visual



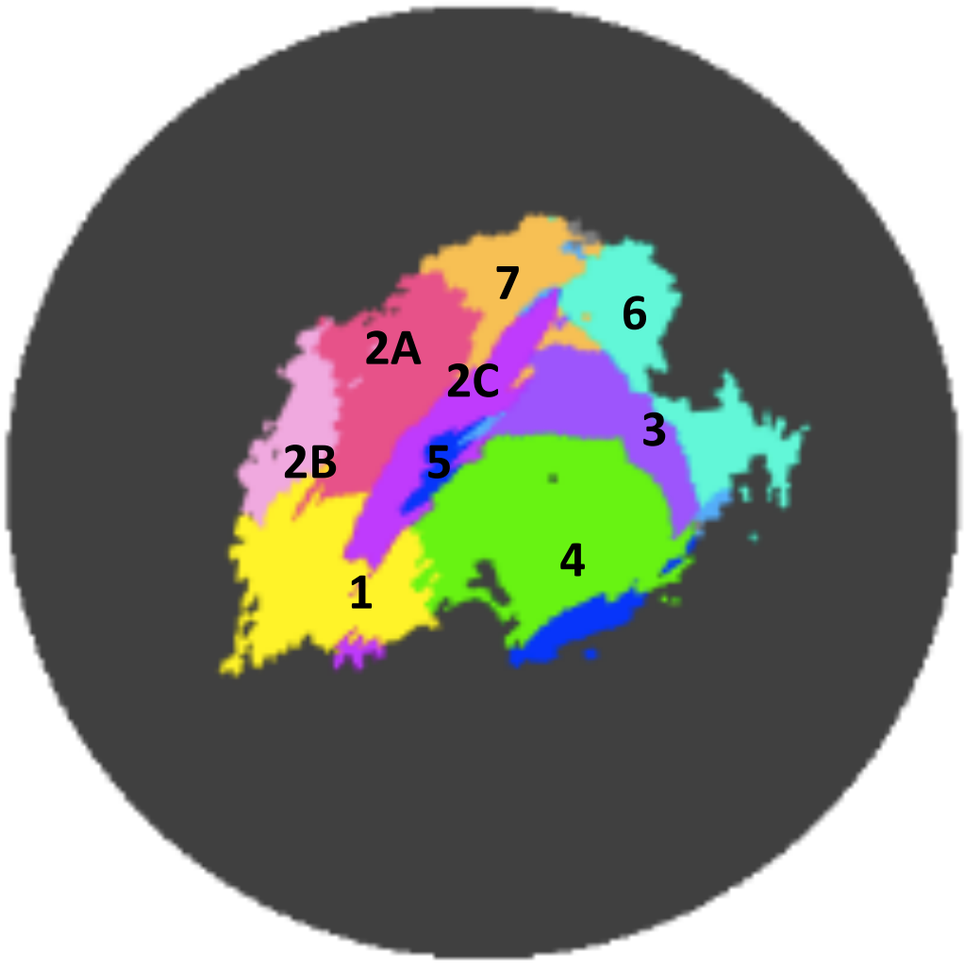
Module #	Surface
1	V1/V2
2A	V3b (more lateral) V4/LO superior
2B	V2/V3
3	V4/LO superior
4	V5/MT
5	V3/V4
6	V3a
7	V4/LO inferior
8	LO inferior/Fusiform gyrus

No sound consensus

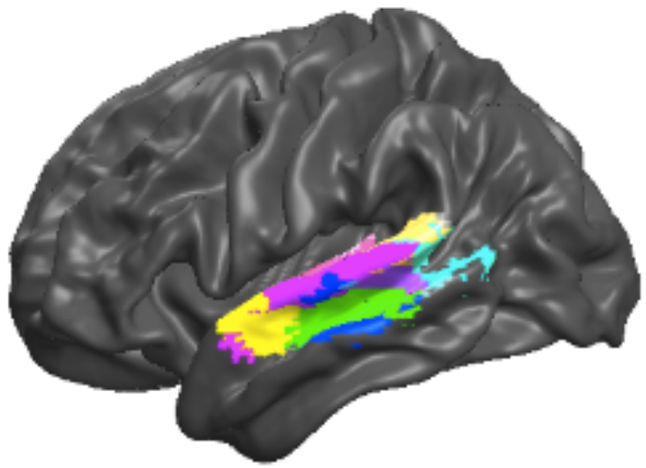


GRAND PARCELLATION - AUDITORY

No sound consensus



Resting_L_Auditory



Module #	Surface
1	Temporal pole Anterior STG (lower bank) and MTG
2	2A: planum polare/STG (upper bank)/ Heschl's gyrus 2B: planum polare 2C: Heschl's gyrus *Juelich atlas: A1 TE 1.0/1.1/1.2*
3	MTG posterior(BA 21)/STG (lower bank)
4	MTG anterior (BA 21)/STG (lower bank)
5	MTG upper bank *Juelich atlas: A1 TE 1.0*
6	MTG posterior(upper bank)/STG posterior part (lower bank)
7	STG posterior (upper bank)

No sound consensus

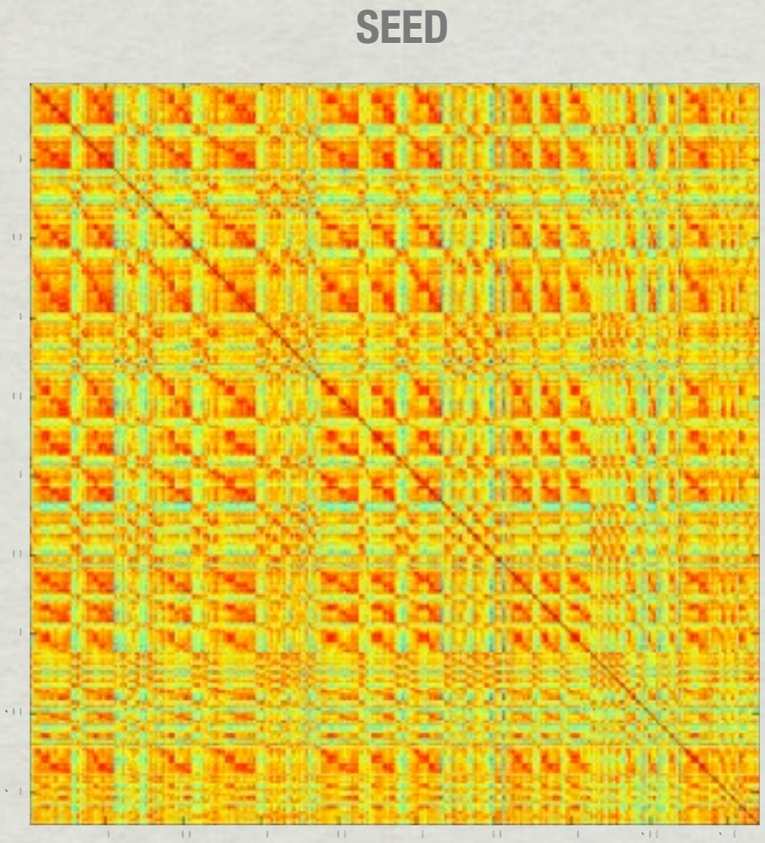
Gene expression from Allen Brain Atlas

- Merge six subjects, select cortex, sort by lobe (frontal, parietal, temporal, occipital, limbic, insula, cortical nuclei)
- ~58000 genes per structure probe
- Cortical distribution of points, denser sampling on left:

542 frontal
290 parietal
470 temporal
212 occipital
389 limbic
44 insula
342 cortical nuclei

No sound consensus

Unexpected structure in similarity matrix

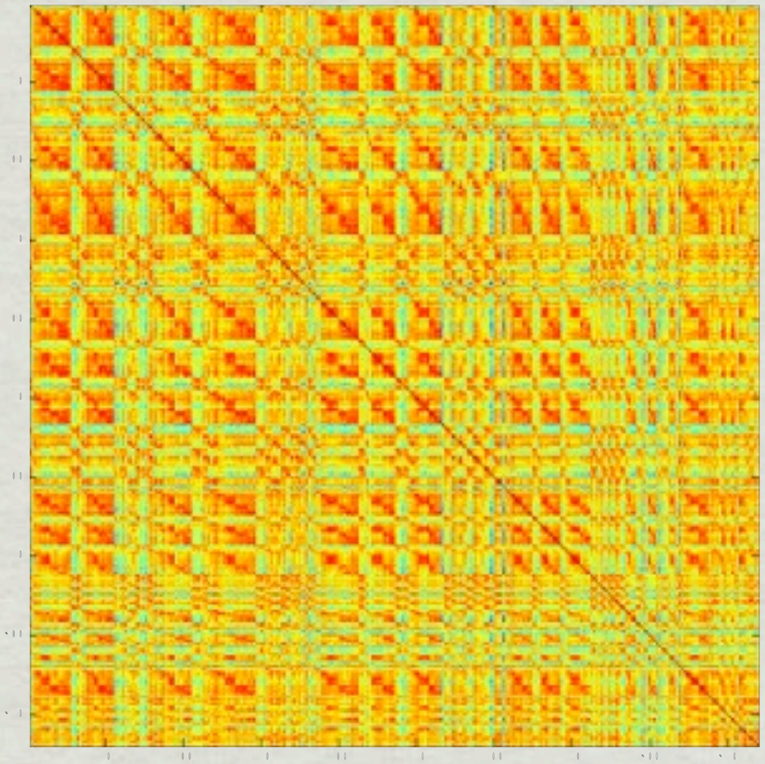


TEMPORAL LOBE

No sound consensus

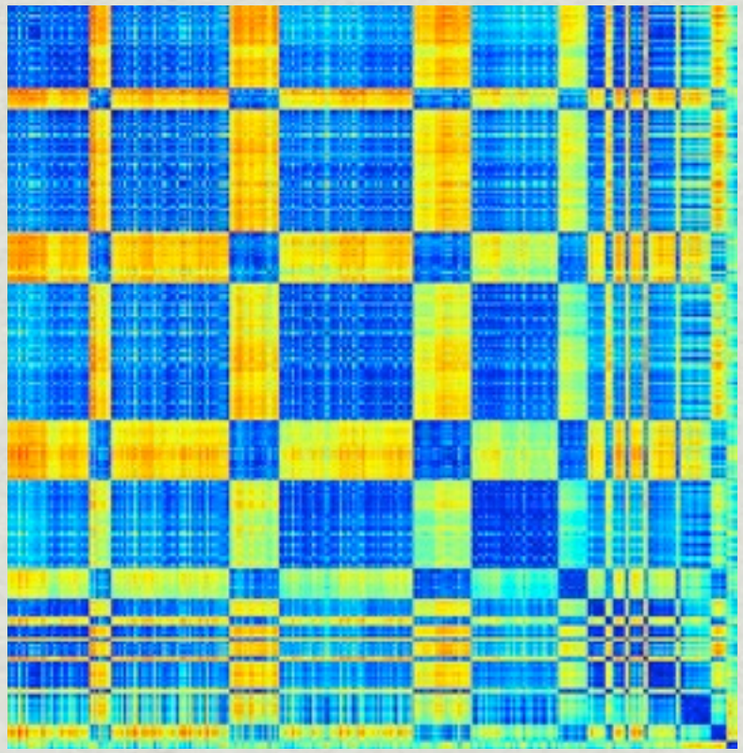
Unexpected structure in similarity matrix

SEED



SEED

CONFOUND 1: DISTANCE

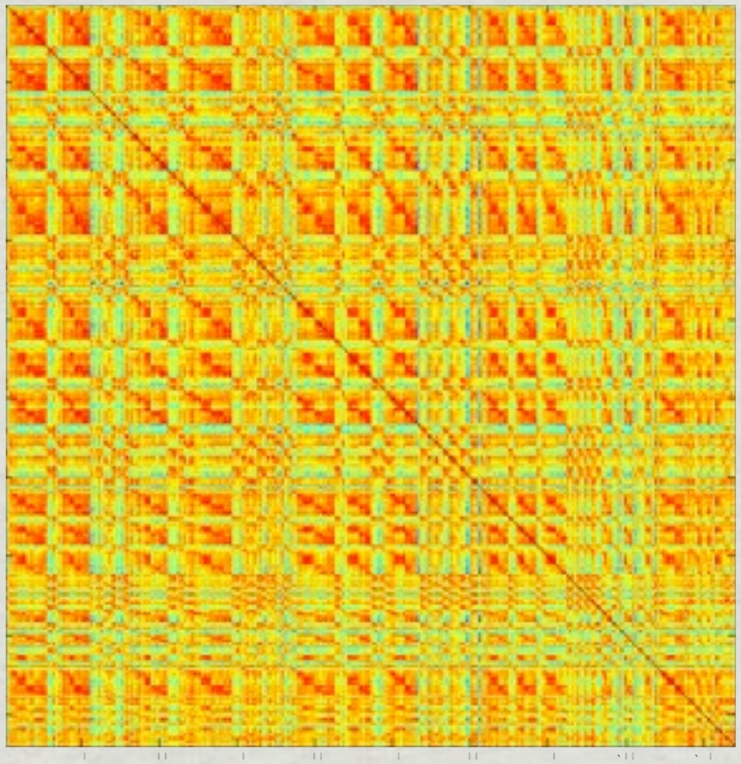


TEMPORAL LOBE

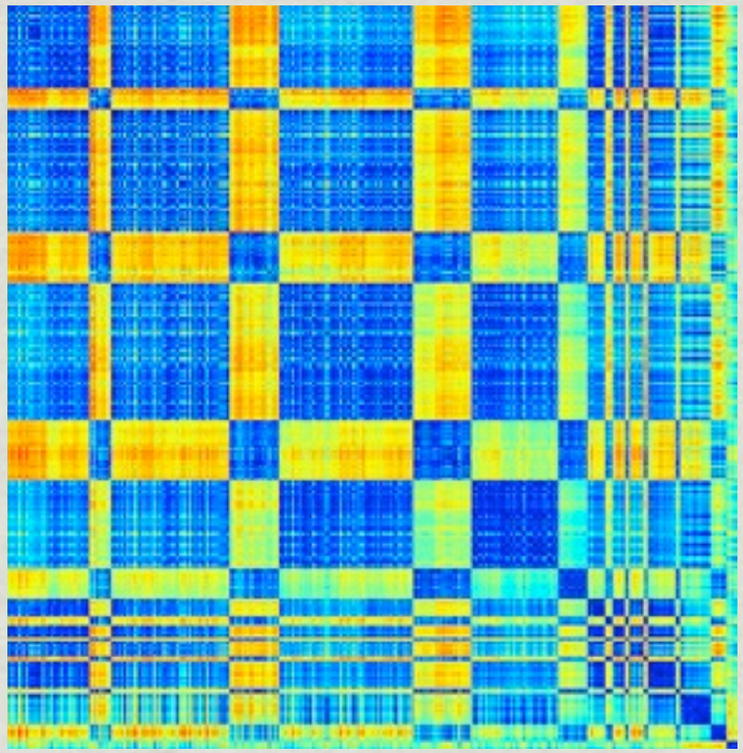
No sound consensus

Unexpected structure in similarity matrix

SEED



SEED



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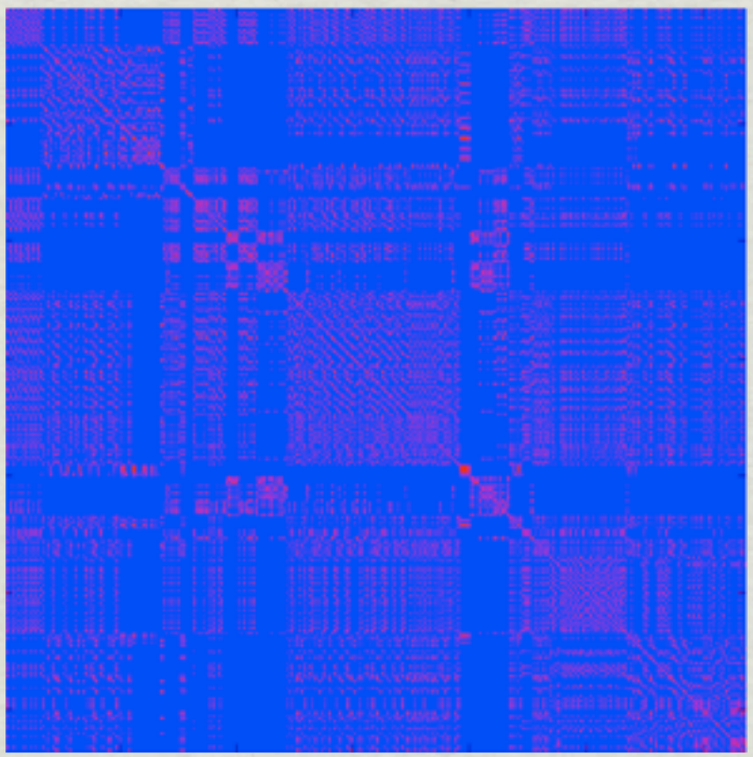


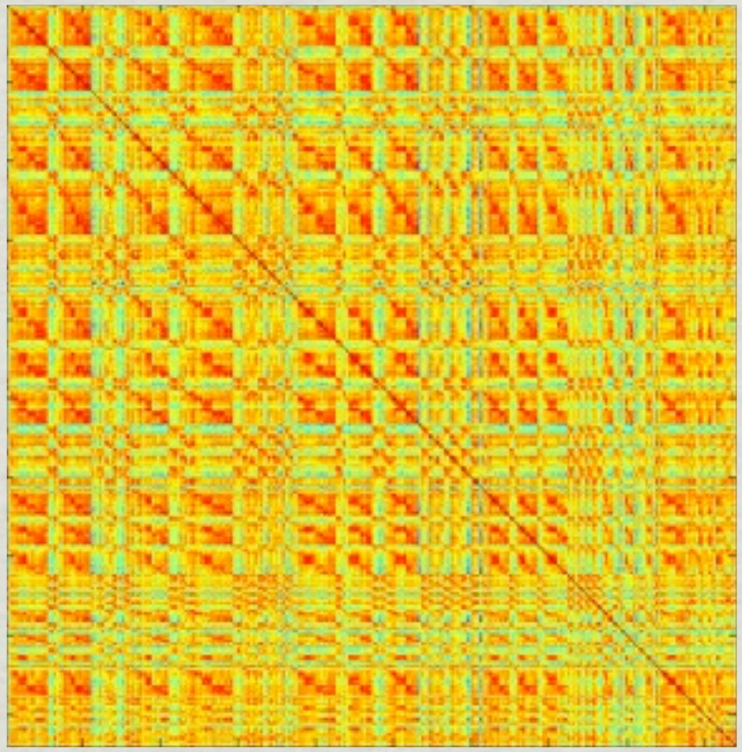
CONFOUND 2: SLAB NUMBER

TEMPORAL LOBE

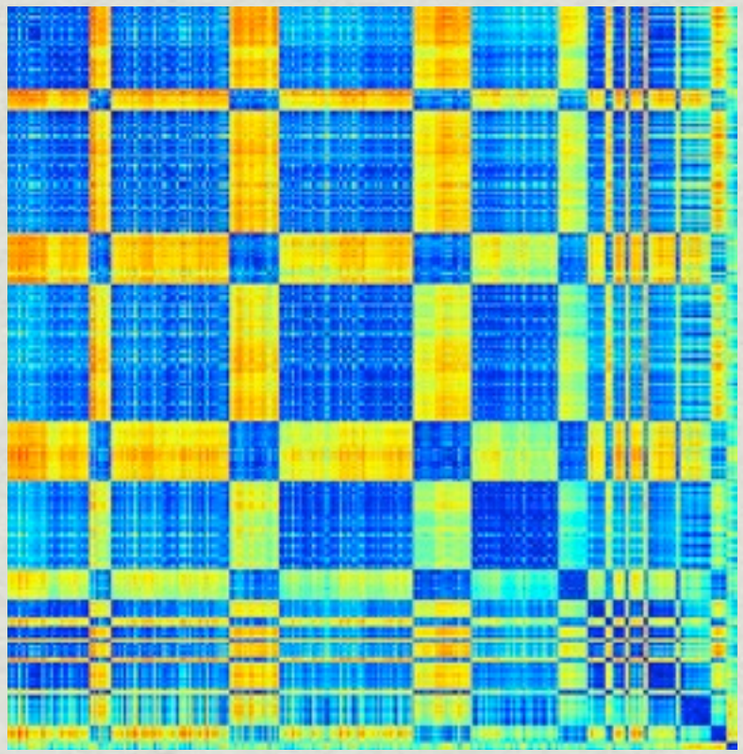
No sound consensus

Unexpected structure in similarity matrix

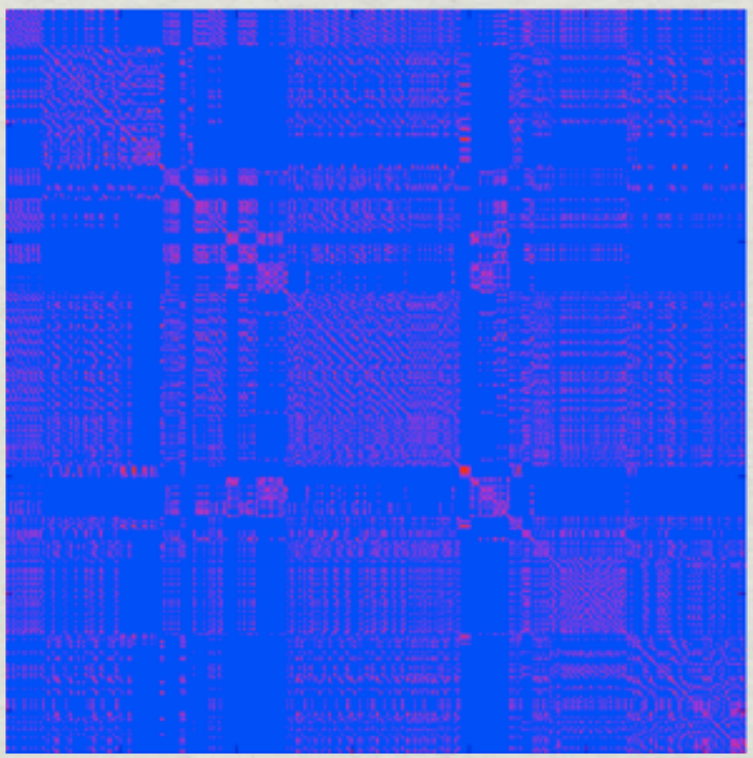
SEED



CONFOUND 1: DISTANCE



CONFOUND 2: SLAB NUMBER

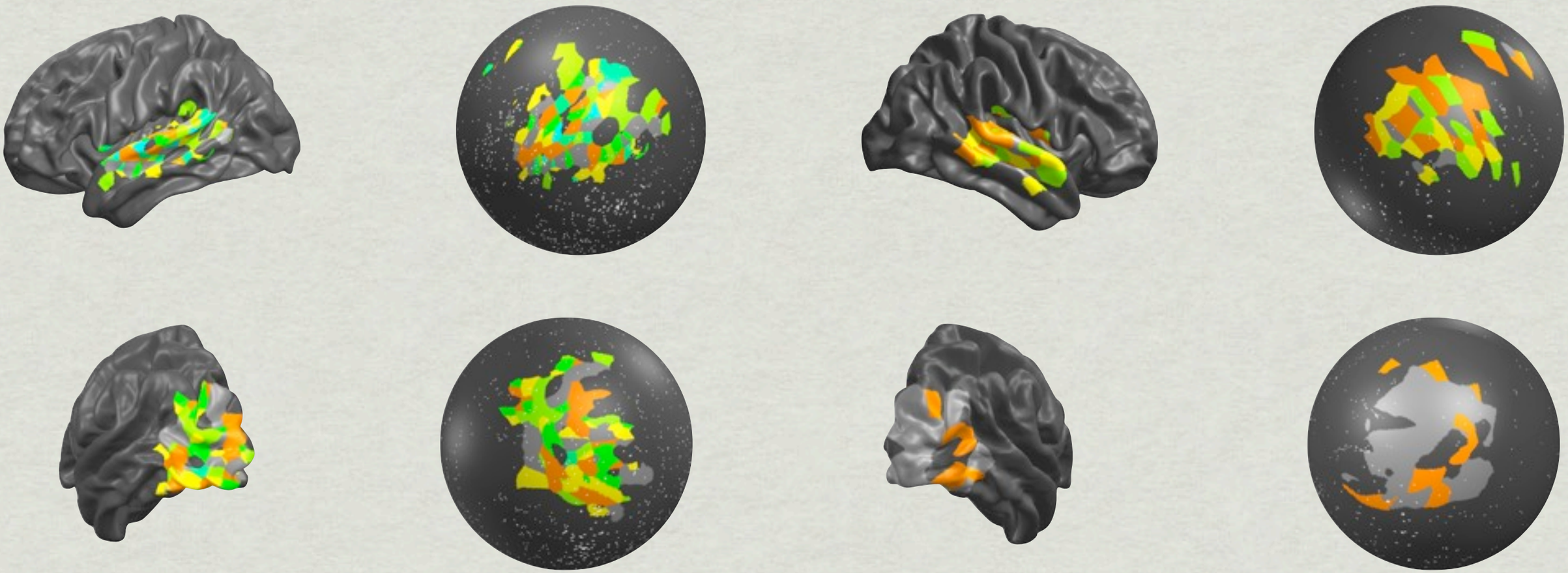


- Regress out confounds
- Cluster

TEMPORAL LOBE

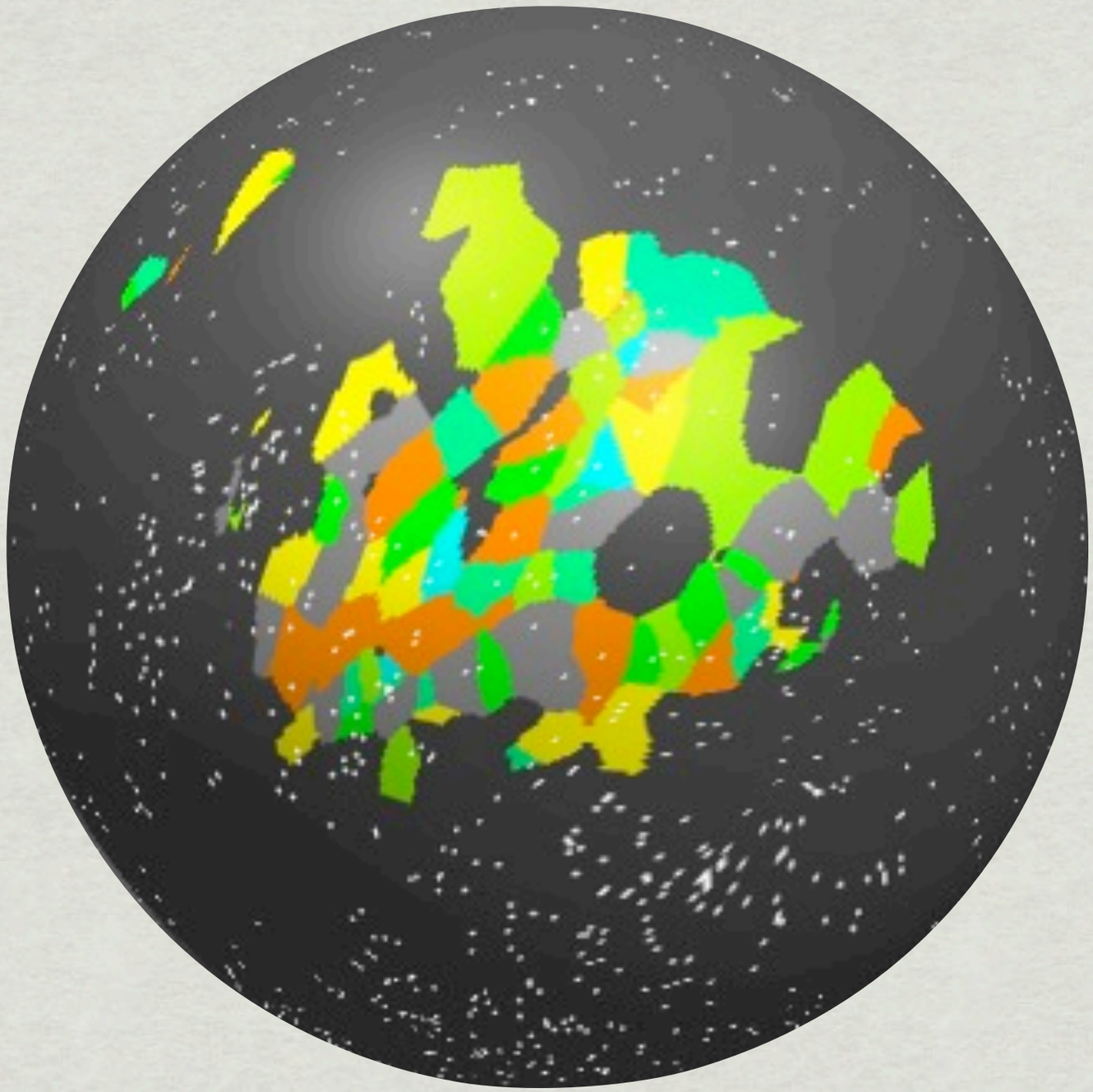
No sound consensus

Clustering by gene-ex



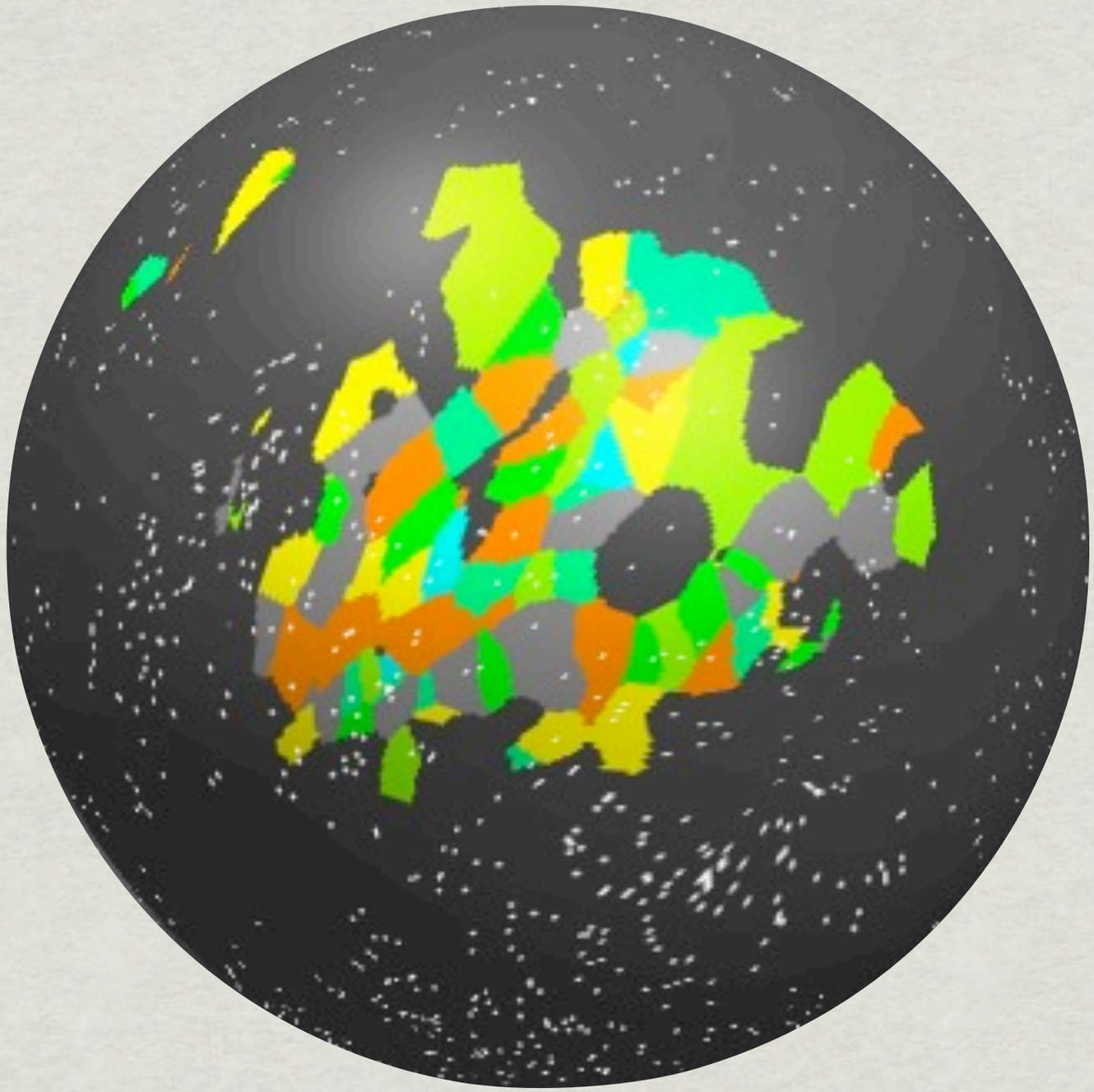
No sound consensus

Clustering by gene-ex



No sound consensus

Clustering by gene-ex



- Clustering not improved by: PCA dimension reduction; filtering by gene variablity; change of clustering method (k-means with 5 modules)

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Is gene expression more similar within modules?

- Calculate within & across module similarity scores
- Use permutation testing
- Gene-ex more similar within visual modules than across
  - Visual L: $r=0.07$, $p<0.00001$
  - Visual R: $r=0.16$, $p<0.00001$
- In auditory cortex, N.S. in right and low negative $r=-0.04$ in left

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Conclusions

- Tractography and resting data showed good modularity for both visual and auditory cortices
- However, stronger modularity in gene expression found in visual cortex
- Broadly consistent parcellations found across hemispheres and modalities

Future work

- Evaluate effect of retinotopic/tonotopic representation
- Mash with task-based fMRI
- Compare gene-ex in HG & neighboring regions
- Expand to developmental datasets

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Once the digital dust had settled...

- Hours of Skype & Hangout, *many* late nights
- Produced 4.5 TB of output, followed 3.2 billion diffusion streamlines, 1 trillion voxel steps
- 250 days of Sandy Bridge E core. Cluster of three machine configurations, up to 295 simultaneous cores, 1.7 TB RAM, 10 Gb interconnect
- We were nearly called: *Mödüüläär Füsiön; (mod n); if (size(data) > size(storage)), problems += 1; ctrl+alt+deskFlip; The Connectome Canaries (we died in the DTI mine, so you don't have to!)*

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