What is the ultimate sensitivity of functional MRI: Does the whole brain activate?

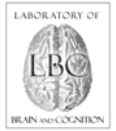
Javier Gonzalez Castillo[1], Ziad S. Saad[2], Daniel A. Handwerker[1], Souheil J. Inati[3], Noah Brenowitz[1], Peter A. Bandettini[1,3]

[1]Section on Functional Imaging Methods, Laboratory of Brain and Cognition, NIMH

[2]Scientific and Statistical Computing Core, NIMH

[3]Functional MRI Facility, NIMH

"Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis" PNAS (2012)



Declaration of Relevant Financial Interests or Relationships

Speaker Name: Javier Gonzalez-Castillo

I have no relevant financial interest or relationship to disclose with regard to the subject matter of this presentation.

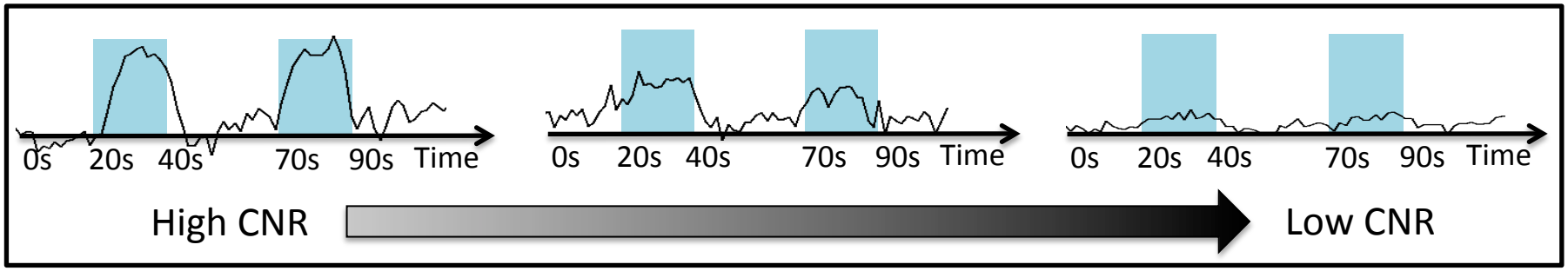
Introduction/Motivation

- **BOLD fMRI time-series are very noisy**

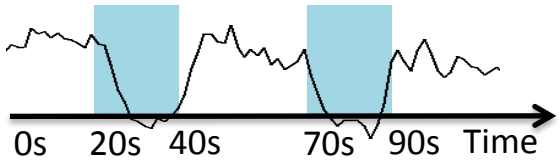
- Thermal Noise
- Signal Drift
- Intensity Inhomogeneity

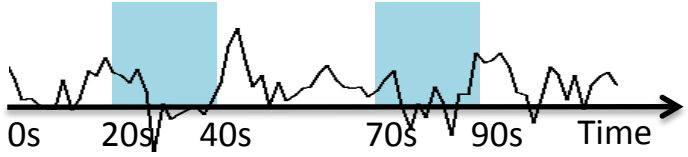
- Head Motion
- Physiological Noise
- Variable Compliance

- **BOLD responses are many times in the same order of magnitude as the noise**



- **BOLD responses vary regionally in shape and timing**

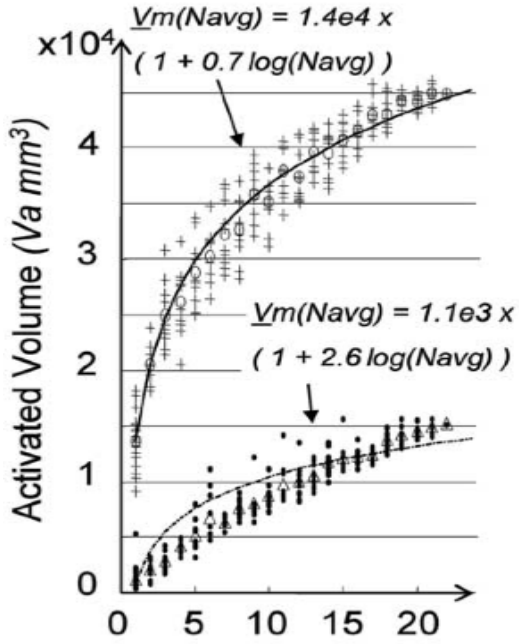




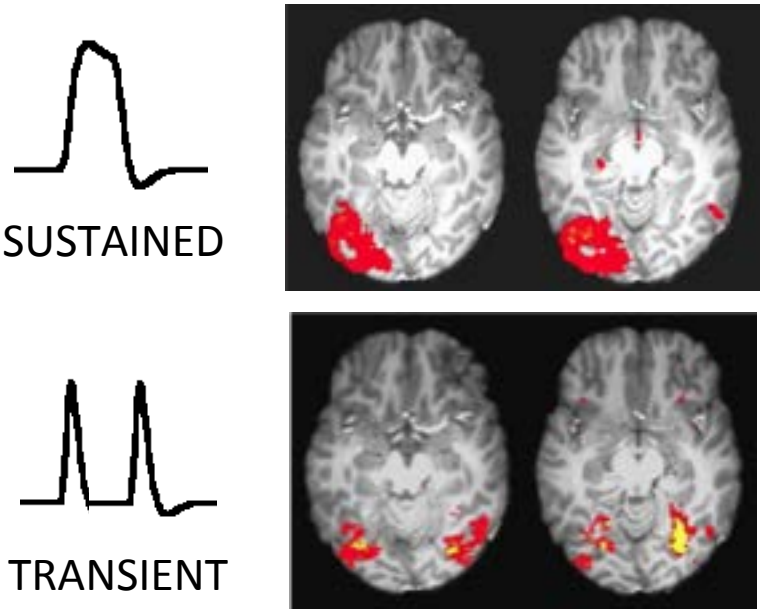
Introduction/Motivation (II)

fMRI Activation maps are highly dependent on:

- **Available Temporal Signal-to-Noise**
- **Assumptions on Response Shape and Timing**



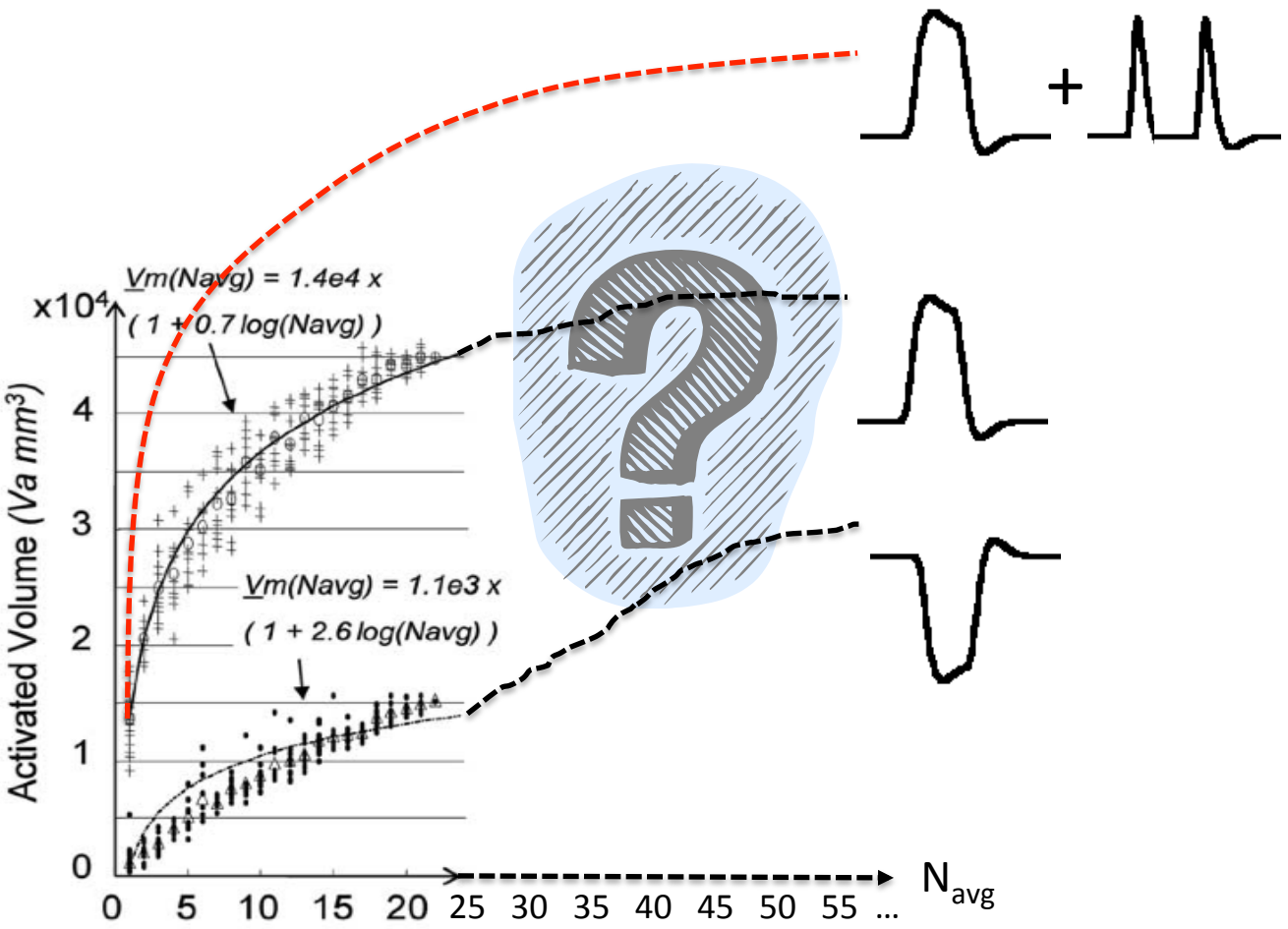
ACTIVATION VOLUME INCREASES LOGARITHMICALLY WITH NUMBER OF SCANS. [Saad et al. 2003]



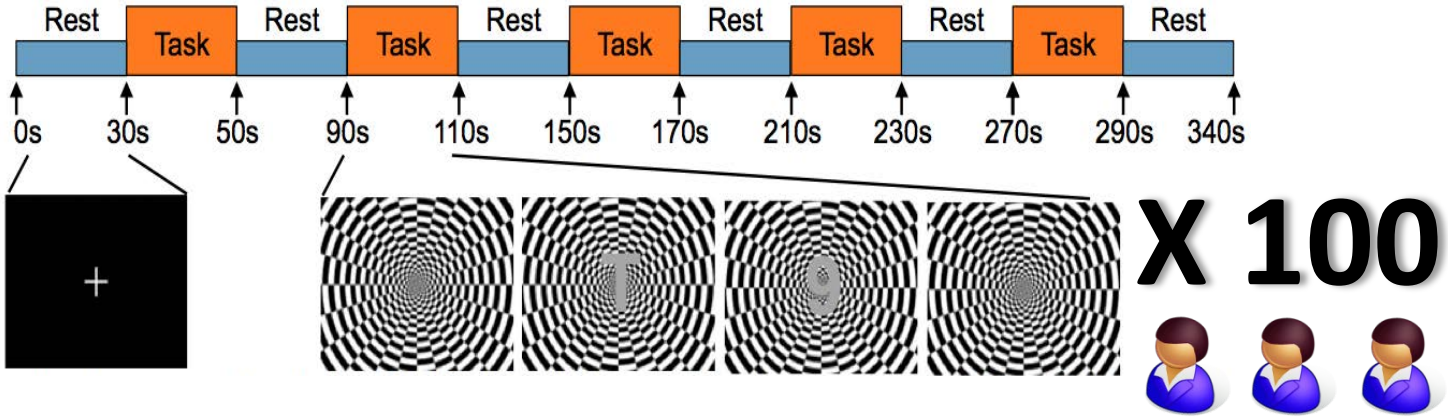
CONSIDERATION OF ADDITIONAL RESPONSE SHAPES ALLOW DETECTION OF NEW ACTIVATION SITES [Uludag et al. 2008]

Experimental Question 1

Is the sparseness of task-based fMRI activation maps real or a result of insufficient TSNR and/or analysis constrains?



Experimental Design / Methods



9 HOURS OF FUNCTIONAL DATA PER SUBJECT

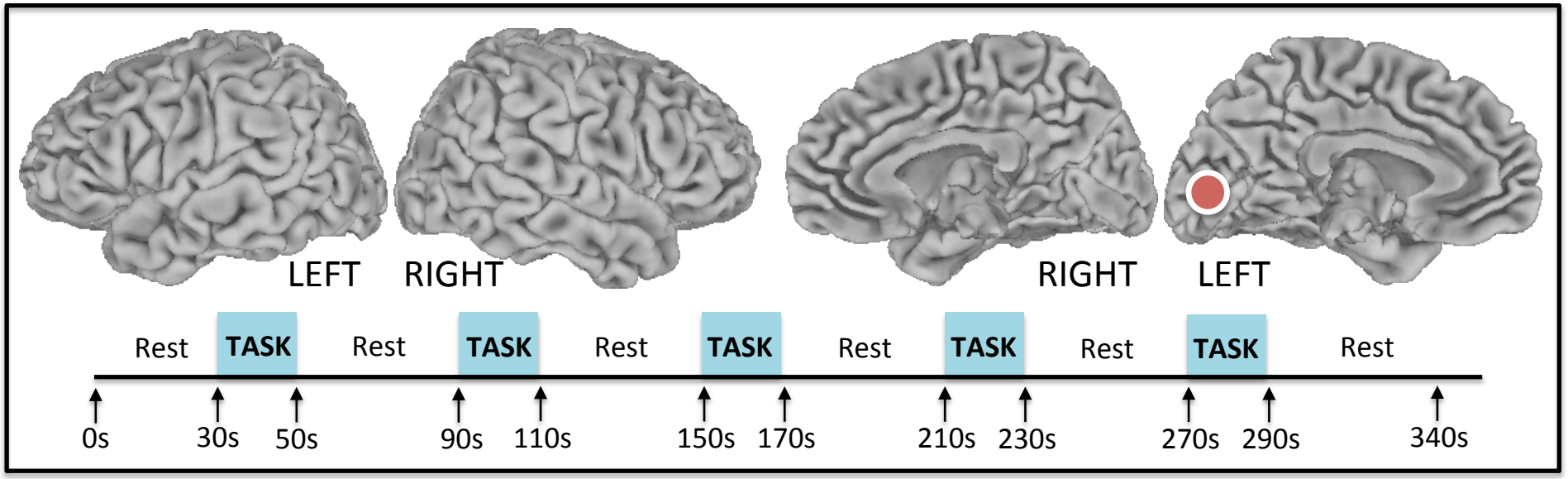
PRE-PROCESSING

1 DISCARD INITIAL VOLUMES
2 PHYSIO CORRECTION
3 SLICE TIMING CORRECTION
4 MOTION CORRECTION
5 ACROSS-SESSION ALIGNMENT
6 REGRESS MOTION & 1st DERIV.
7 INTENSITY NORMALIZATION

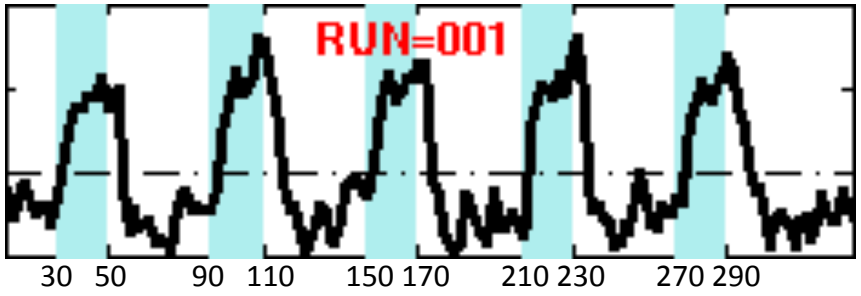
WITHIN-SUBJECT SCAN AVERAGING

- TO INCREASE TSNR
- N_{runs}=1 < -- > 100

Results: Primary Visual Cortex

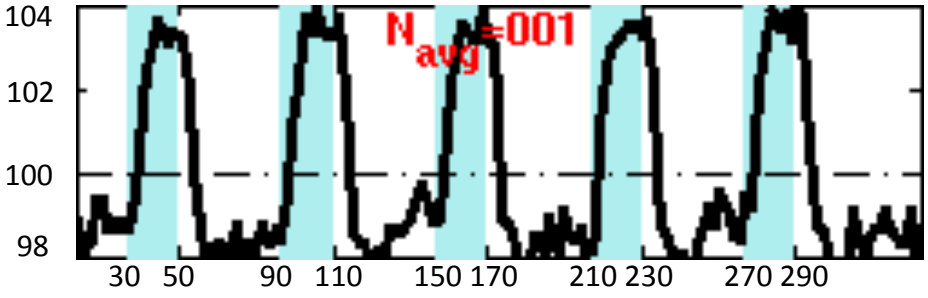


INDIVIDUAL RUNS



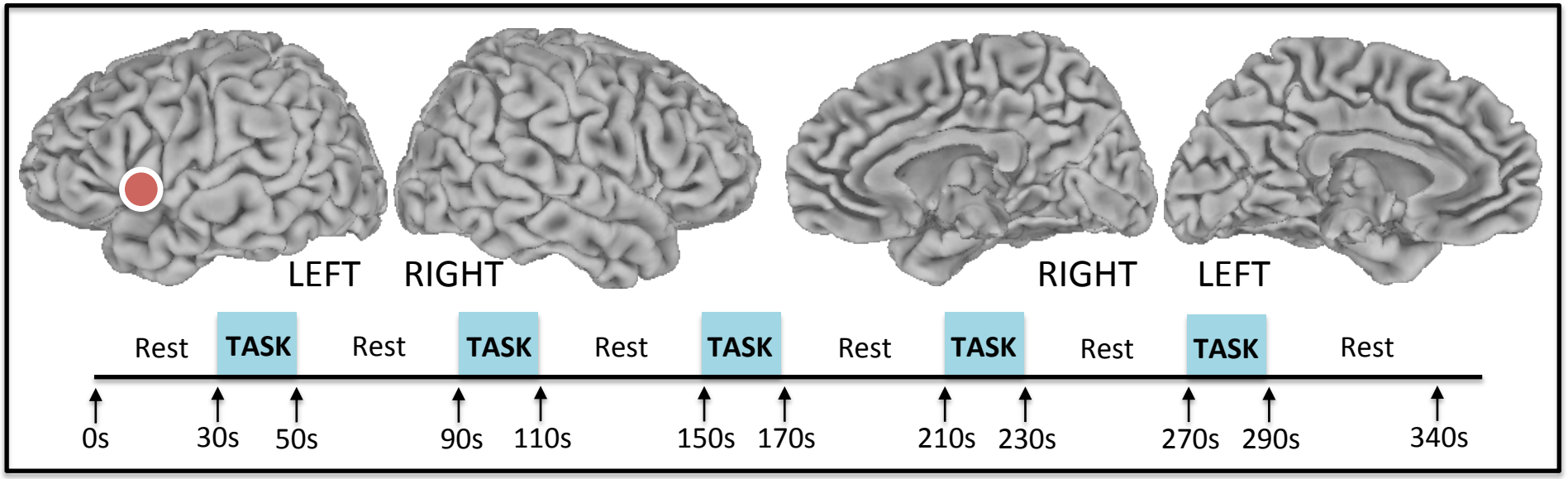
Time (s)

AVERAGING

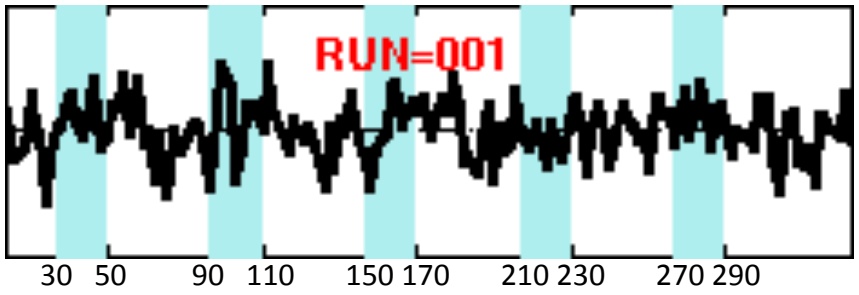


Time (s)

Results: Anterior Insular Cortex

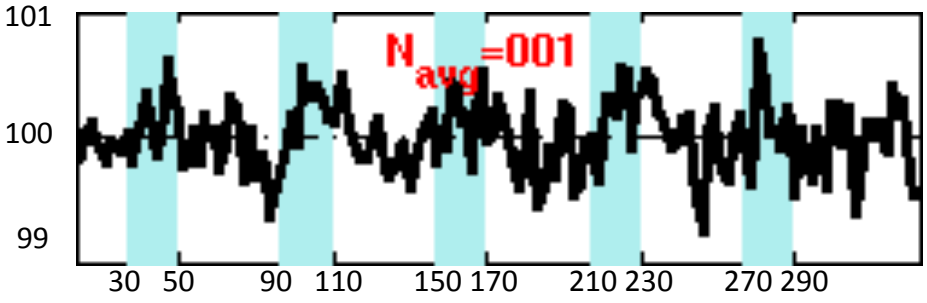


INDIVIDUAL RUNS



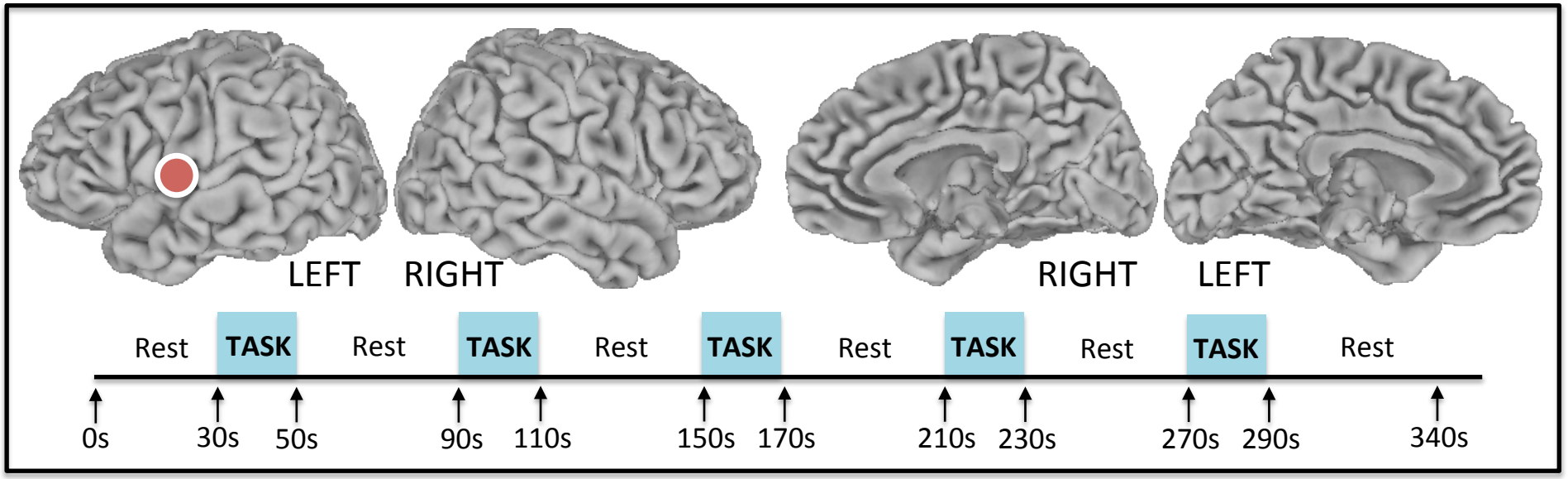
Time (s)

AVERAGING

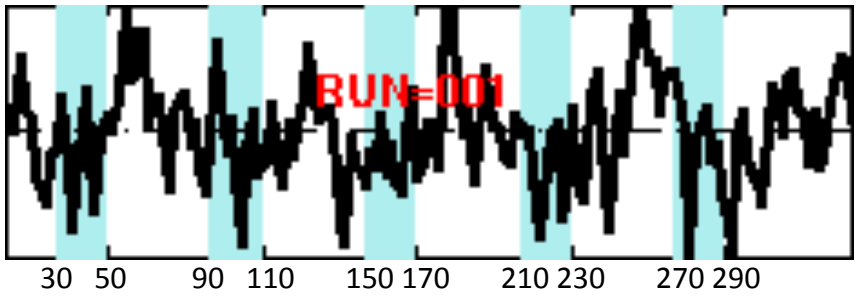


Time (s)

Results: Primary Auditory Cortex

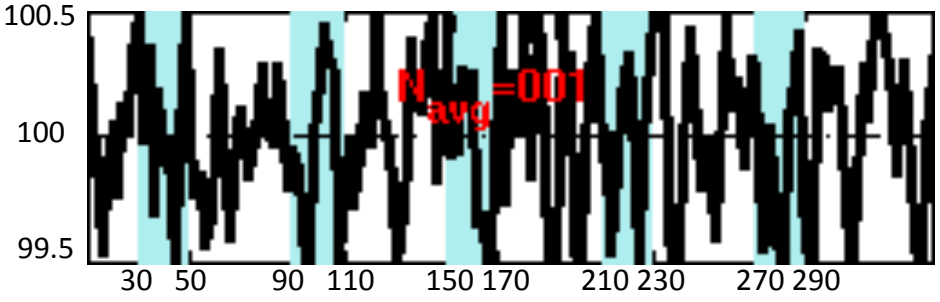


INDIVIDUAL RUNS



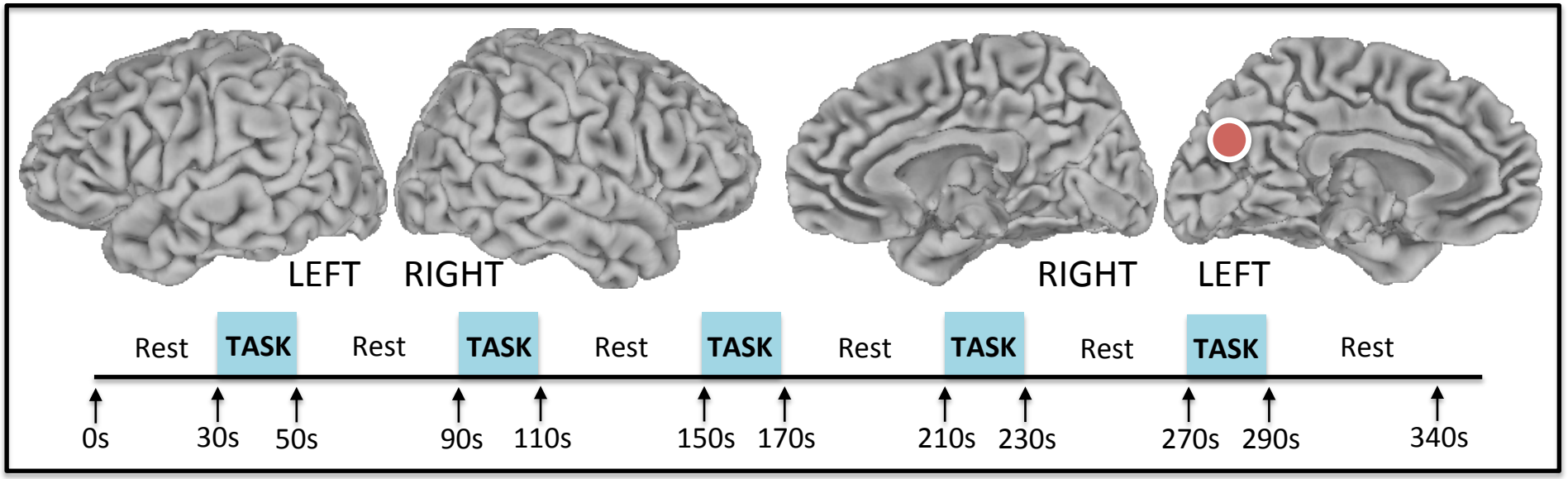
Time (s)

AVERAGING

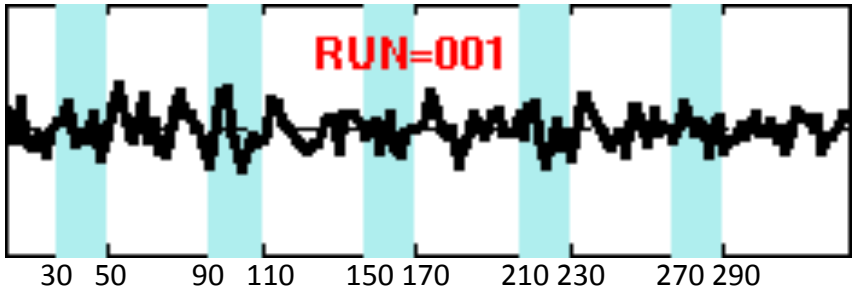


Time (s)

Results: Parieto-occipital Junction

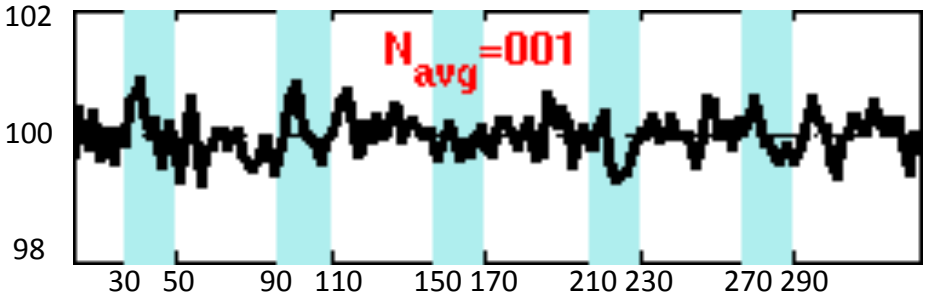


INDIVIDUAL RUNS



Time (s)

AVERAGING

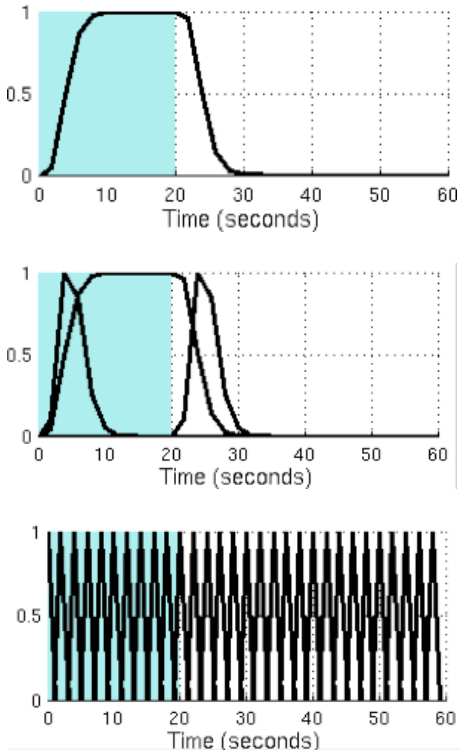


Time (s)

Experimental Question 2

How does this observation translates in terms of volume of activation?

VERSATILITY



SUSTAINED RESPONSE ONLY (SUS)

ONSET + SUSTAINED + OFFSET RESPONSE (SUS)

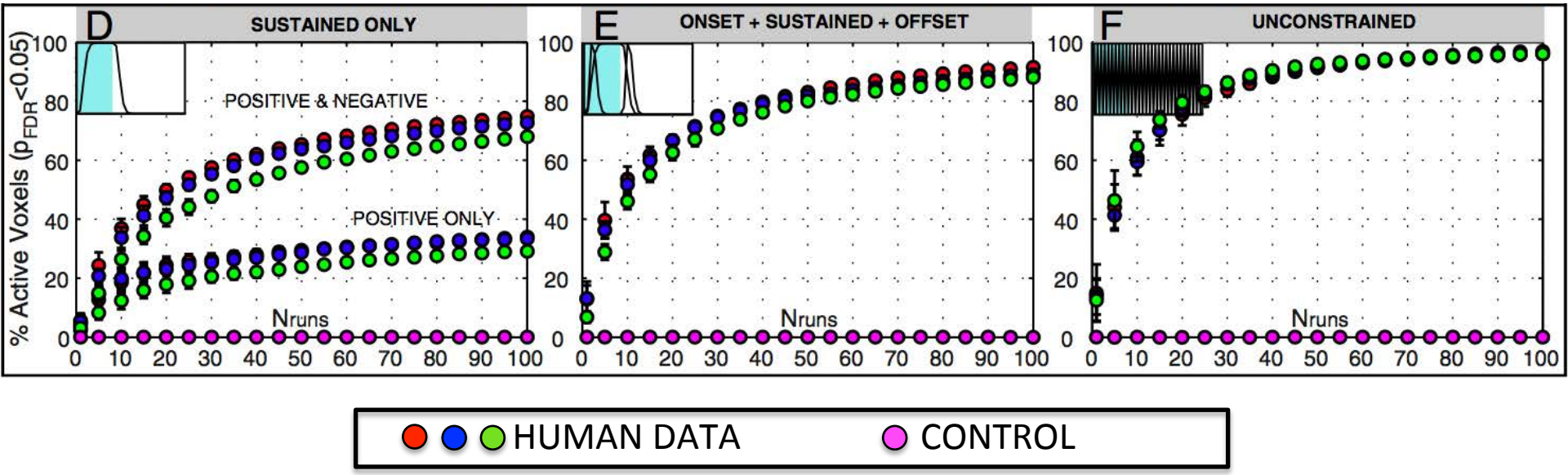
UNCONSTRAINED MODEL (UNC)

N_{runs} = 1, 5, 10, 15, 20, 25, 30, 35 … 100

[10 Permutations per N_{runs} level]

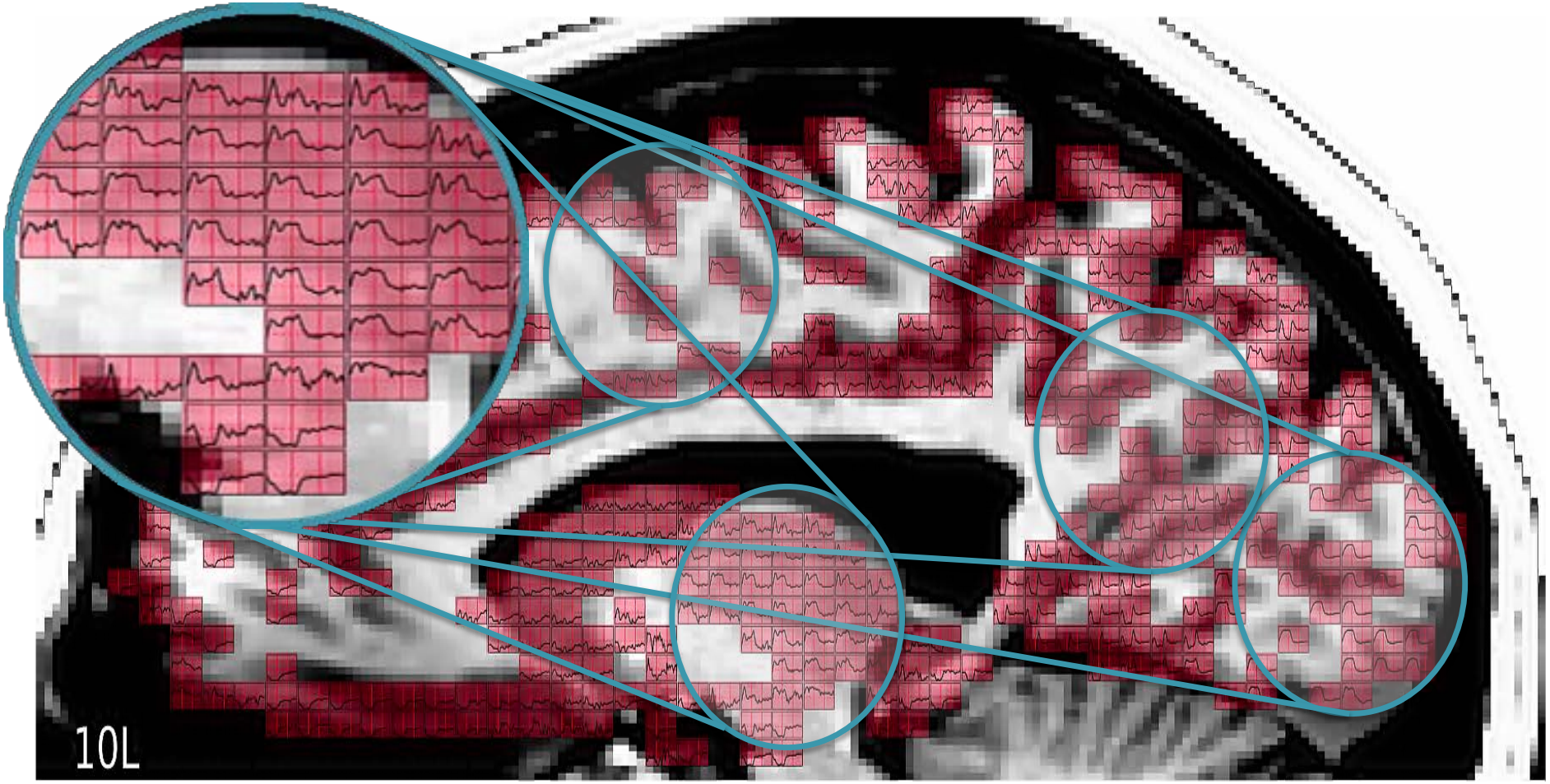
TSNR

Results: Activation Volume vs. Model & N_{runs}



- Activation Volume increases considerably between N_{runs}=5-10 and N_{runs}=100
- Activation Volume increases with versatility of expected response models
- For N_{runs}=100, Unconstrained Model & pFDR<0.05 ➔ Active Volume ≈ 95%

Experimental Question 3



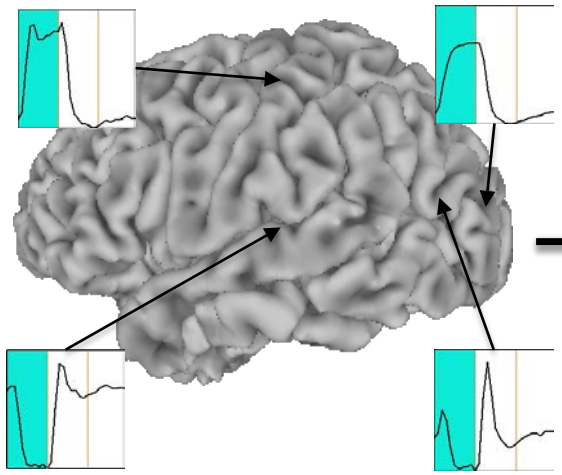
Are these additional responses that we detect biologically meaningful?

Are all these responses biologically meaningful?

ARE RESPONSE SHAPES RANDOMLY DISTRIBUTED ACROSS THE BRAIN

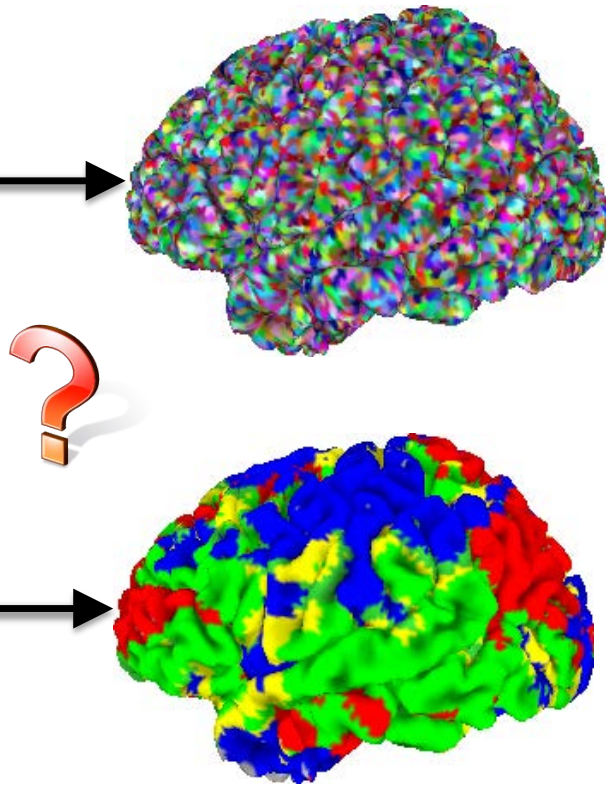
OR

DO THEY CLUSTER IN A FUNCTIONALLY/ANTOMICALLY MEANINGFUL MANNER?



WITHIN-SUBJECT AVERAGED RESPONSES ACROSS ALL RUNS AND TRIALS

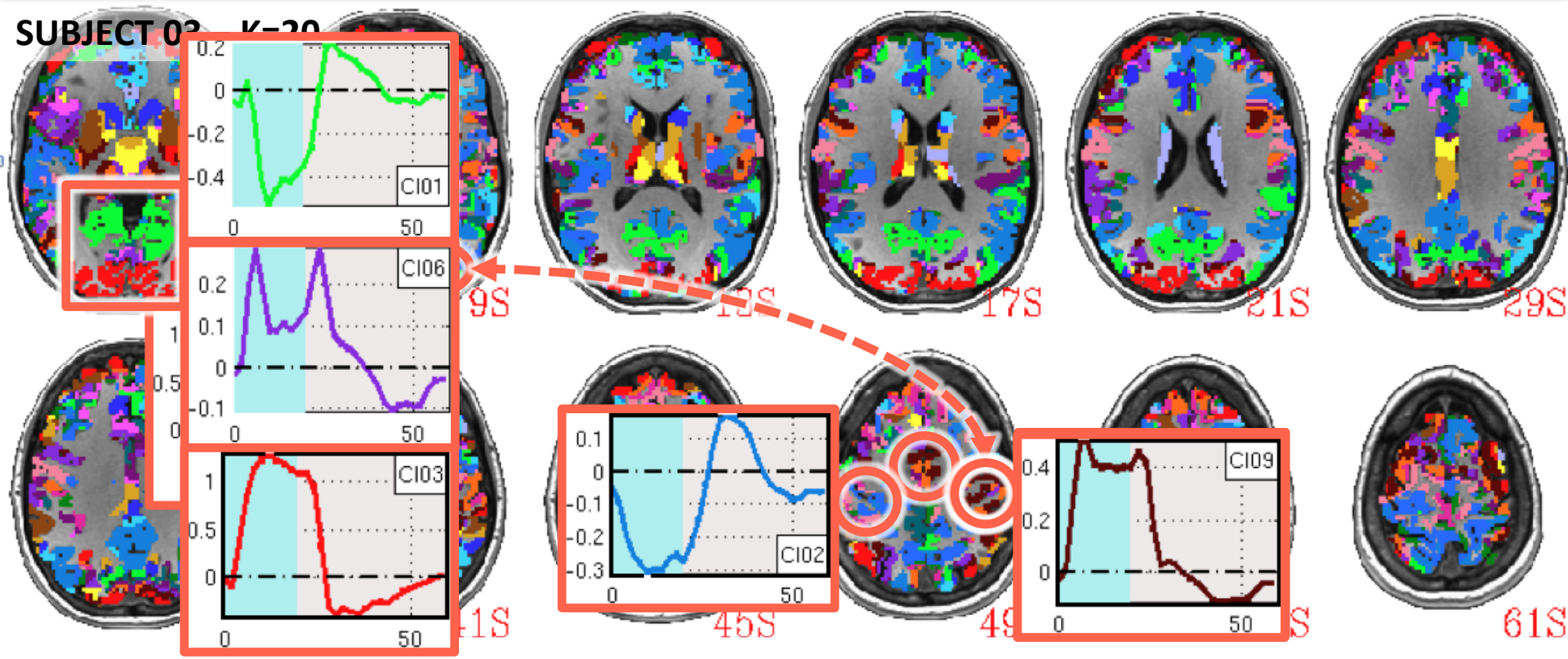
CLUSTERING



NIMH National Institute of Mental Health

Results: Clustering of Responses for N_{runs}=100

FIM fim.nimh.nih.gov



NOT RANDOMLY DISTRIBUTED IN SPACE

SYMETRICAL ACROSS HEMISPHERES

FUNCTIONALLY & ANATOMICALLY MEANINGFUL

REPRODUCIBLE PARCELLATION ACROSS SUBJECTS

Conclusions

- The sparseness of fMRI activation maps is partly a result of insufficient signal-to-noise and excessively strict response model assumptions during the analysis.
- Subtle and not-so-subtle inter-regional differences in BOLD response shape can be exploited to functionally parcellate the brain “in action”
- This data exemplifies the exquisite detail lying in fMRI signals beyond what it is normally examined.
- Need to understand how to discern between areas that are “essential” to task performance from those that are “accessory” or being inhibited.