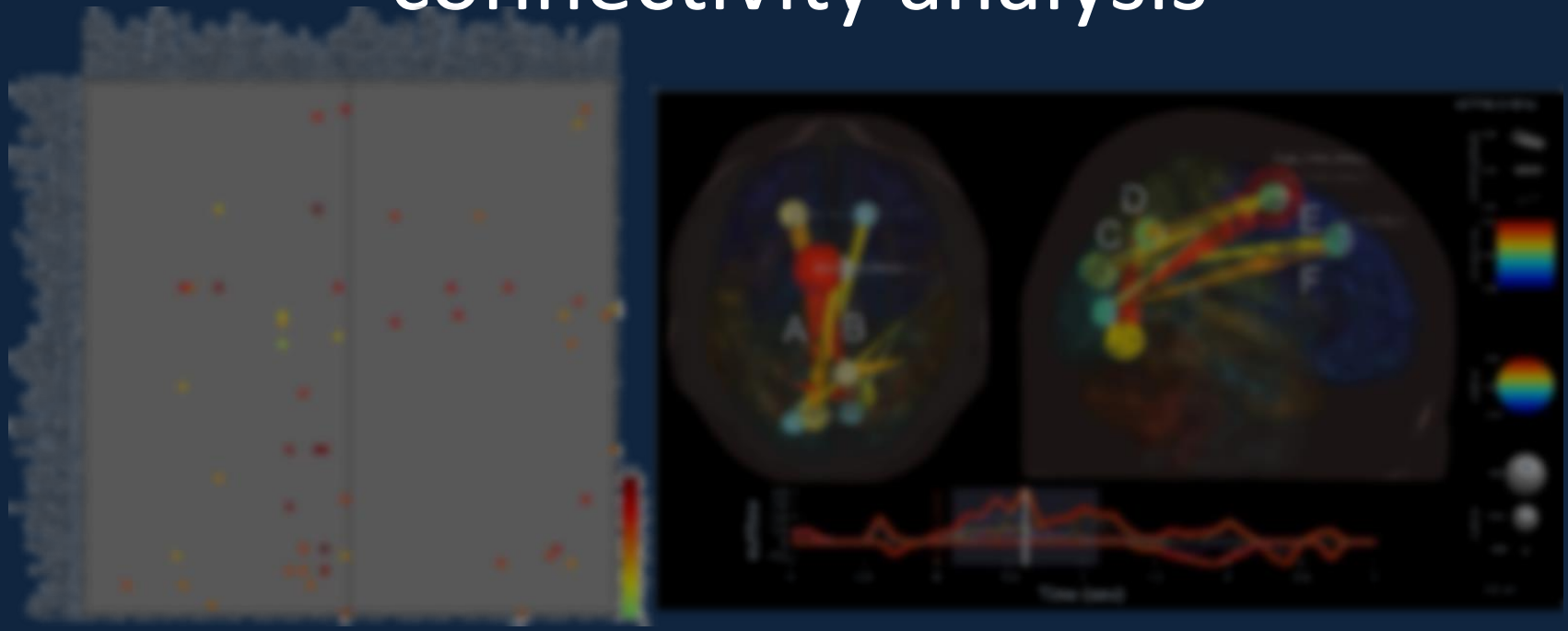
STUDY plugin for group level connectivity analysis



The 23rd EEGLAB Workshop

01/18/2017 Day 3, 15:30-16:00

Makoto Miyakoshi

Motive

- The problems of post-ICA process are:
  - Different numbers of ICs
  - Different locations of the ICs.

Subj 1

Subj 2

Subj 3

.....

Group mean

- This COMPLICATES Group-level statistics.
  - One of the reasons people don't use ICA!
- We don't want to go back to channel space.

Two approaches by two colleagues

- *Hierarchical Bayesian Modeling* by Tim Mullen and Wes Thompson.
  - Treats the inconsistency as missing values.
  - Complicated, taking years to develop.

- *Network Projection by* Nima Bigdely-Shamlo.
  - Allows inconsistency.
  - Simple, based on his publication.

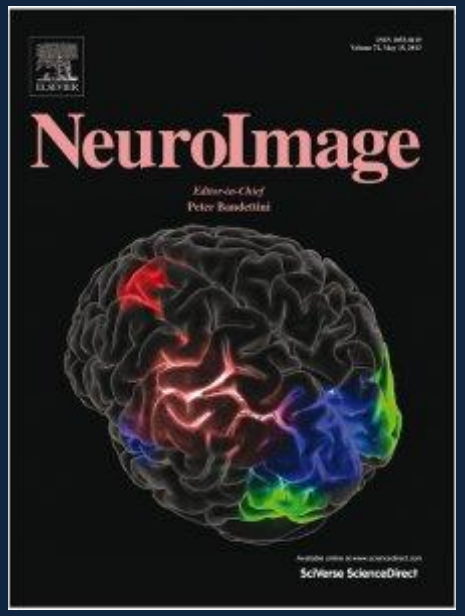
Two approaches by two colleagues

- *Hierarchical Bayesian Modeling* by Tim Mullen and Wes Thompson.
  - Treats the inconsistency as missing values.
  - Complicated, taking years to develop.
  - Often came in the lab in the late evening.

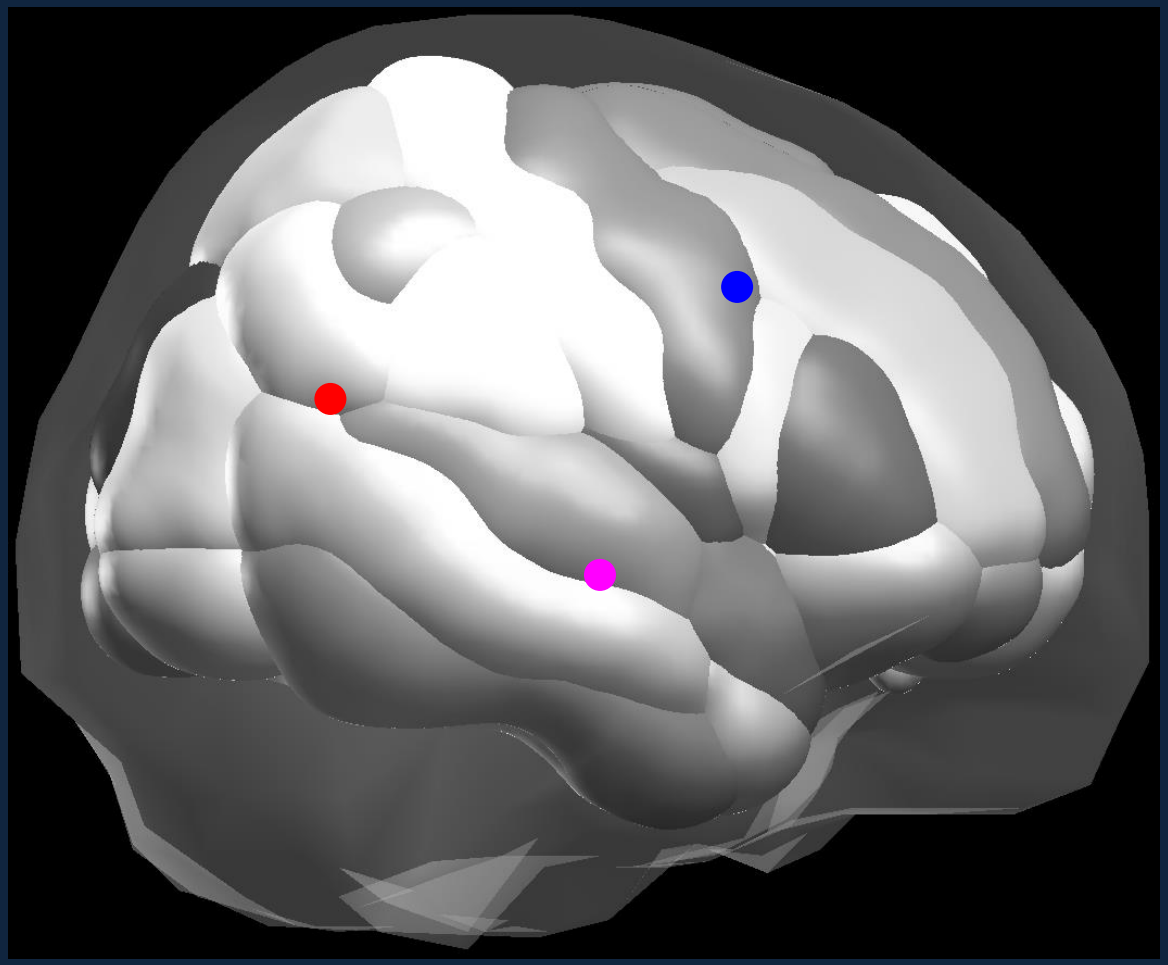
- *Network Projection by* Nima Bigdely-Shamlo.
  - Allows inconsistency.
  - Simple, based on his publication.
  - Always present in regular office hour.

Original ideas in Measure Projection

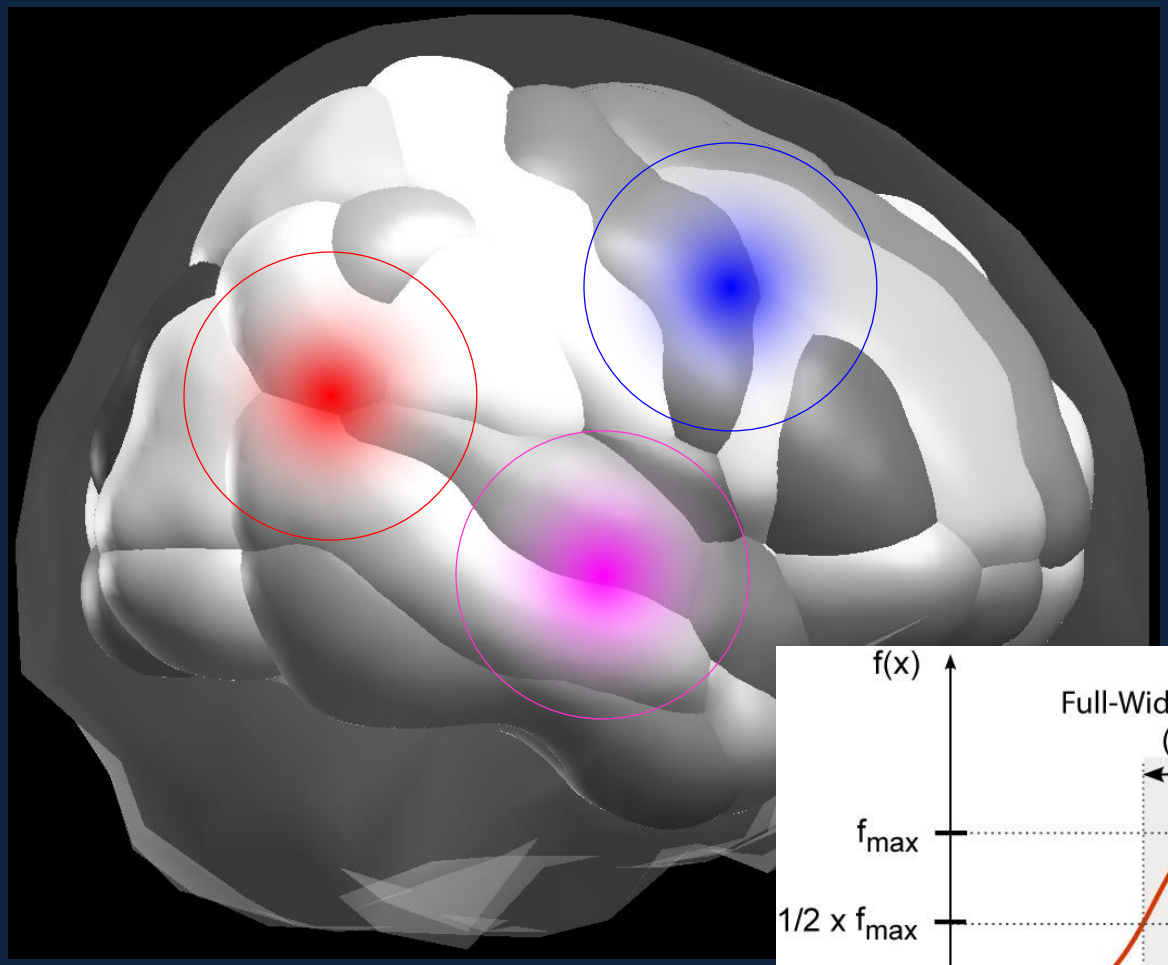
- Bigdely-Shamlo N, Mullen T, Kreutz-Delgado K, Makeig S. (2013). Measure projection analysis: a probabilistic approach to EEG source comparison and multi-subject inference. *Neuroimage.* 72:287-303.
- Apply 3-D Gaussian smoothing to dipole locations, weight them with measures (such as ERP), and cluster them using similarity measures at the group-level statistics.

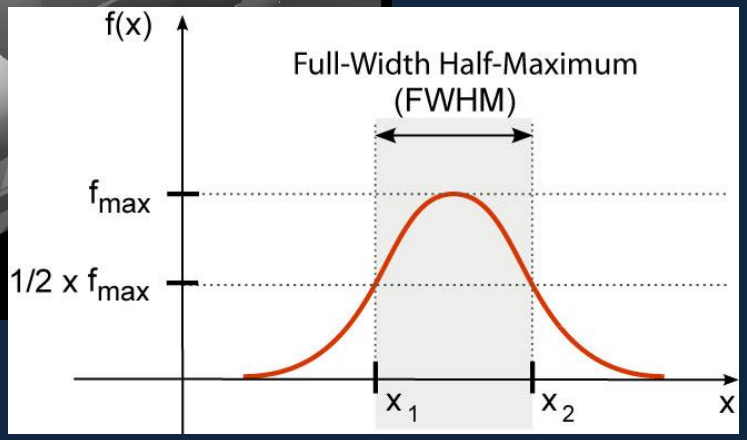


Dipole locations: Before smoothing



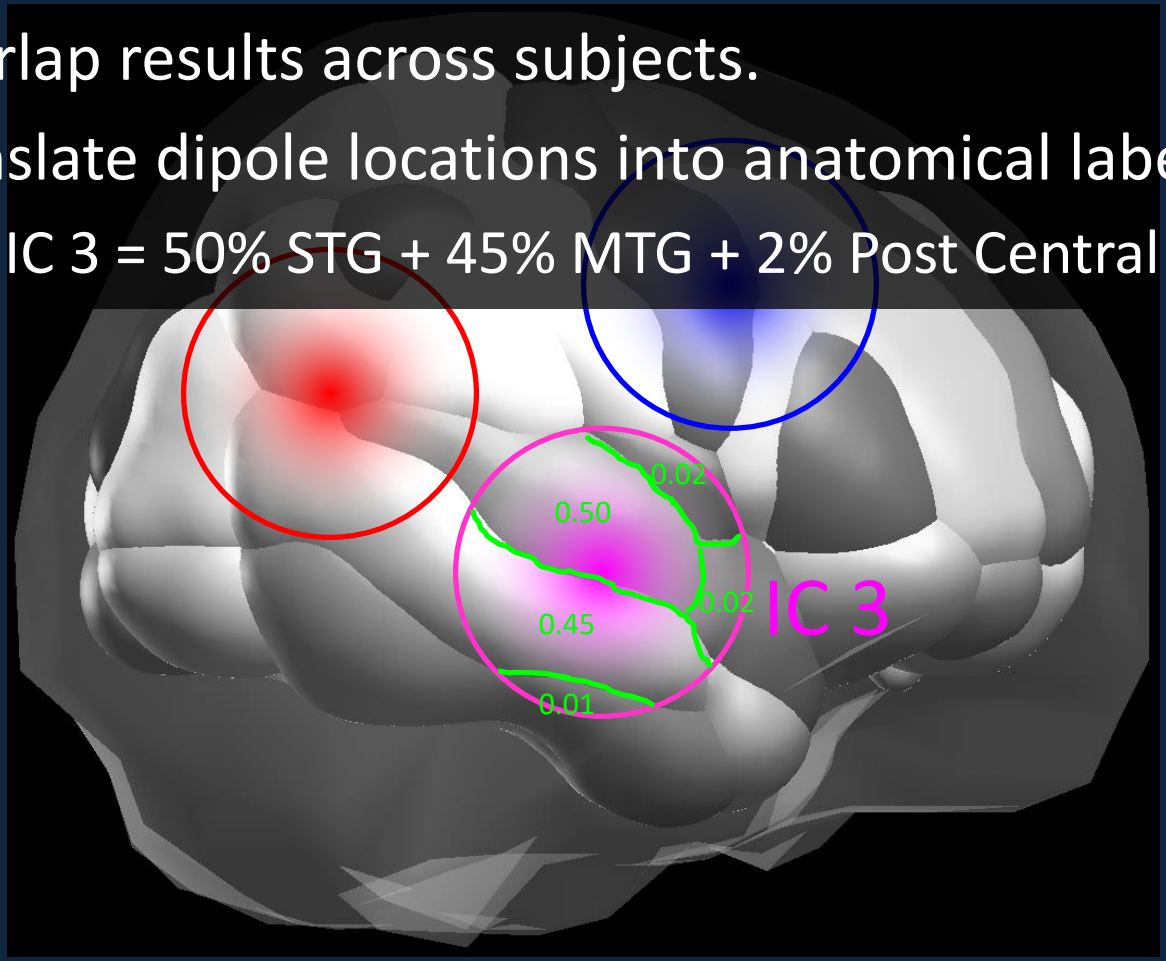
Dipole locations: After smoothing



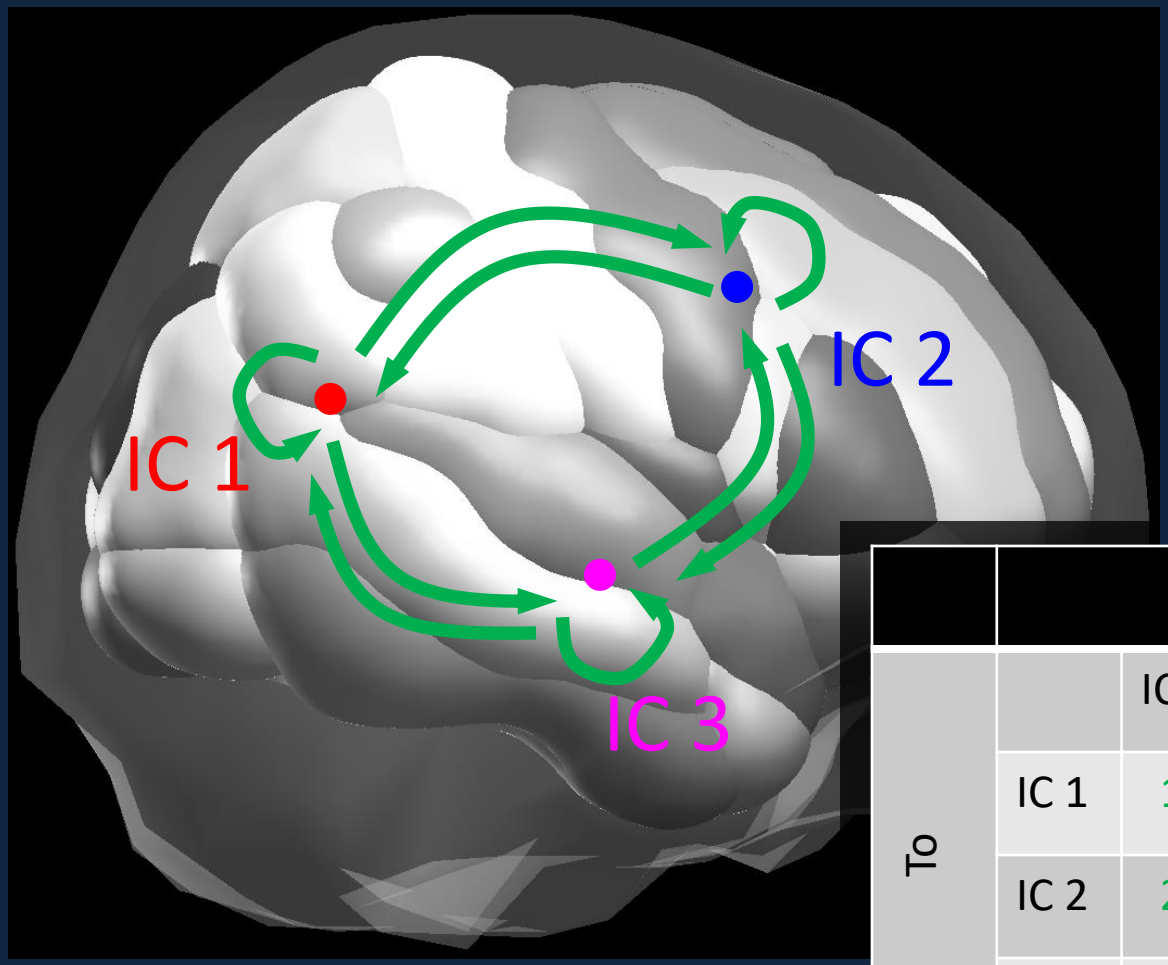


Why smoothing?

- To overlap results across subjects.
- To translate dipole locations into anatomical labels
  - e.g. IC 3 = 50% STG + 45% MTG + 2% Post Central Gyrus +…

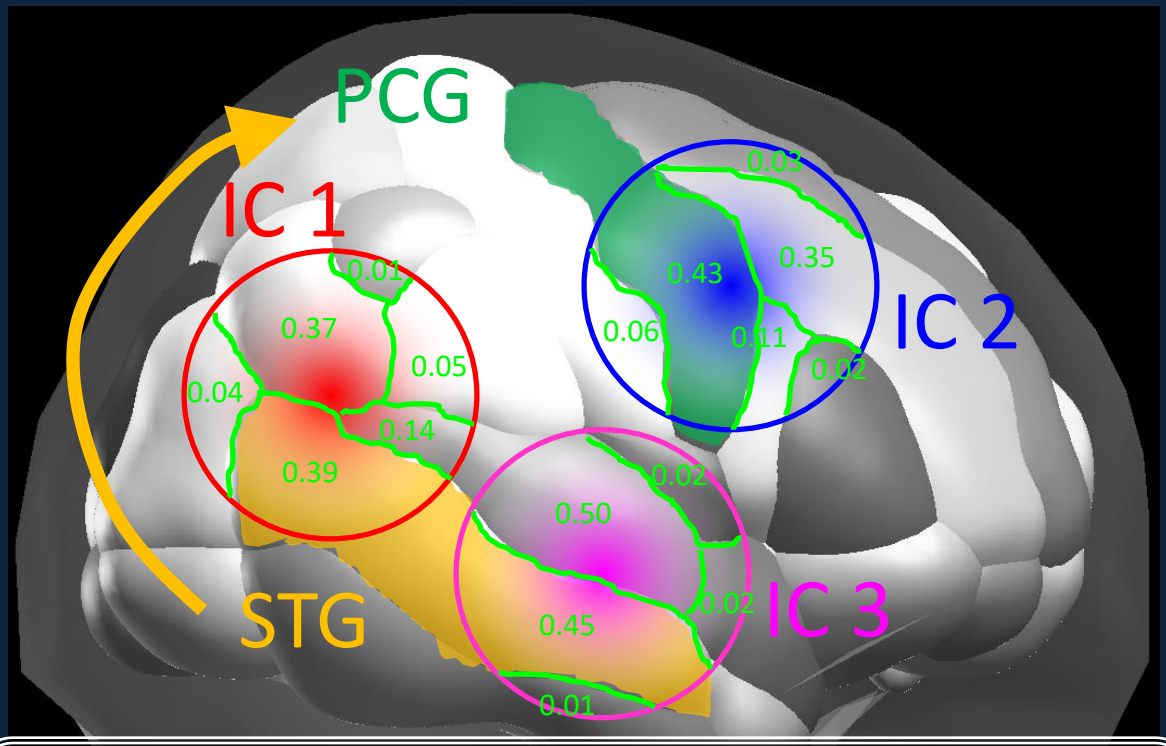


Pairwise dipole connectivity



		From		
		IC 1	IC 2	IC 3
To	IC 1	11	12	13
	IC 2	21	22	23
	IC 3	31	32	33

Pairwise dipole density connectivity



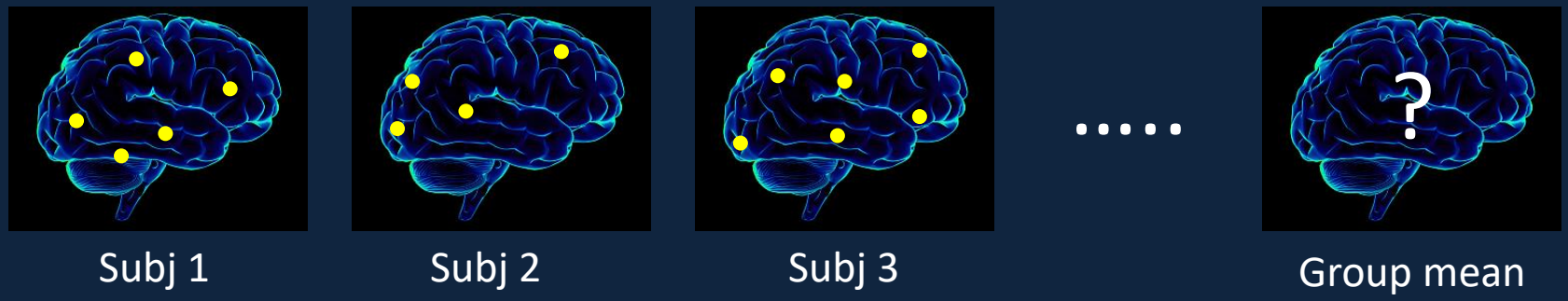
InfoFlow(STG->PCG) ==
InfoFlow(IC1->IC2)*(0.39*0.43)/(0.39*0.43+0.45*0.43) + …
InfoFlow(IC3->IC2)*(0.45*0.43)/(0.39*0.43+0.45*0.43)

Normalization term for dipole pair density.

Calculate this for all 76 x 76 = 5776 edges.

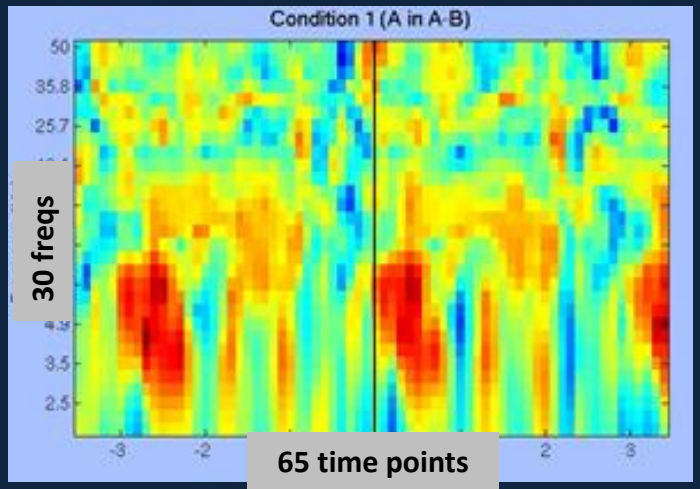
Core idea of this solution

- The problems of ICA are solved:
  - Inconsistent connectivity matrix sizes -> All 76 x 76.
  - Inconsistent locations -> Coregistered to anatomical ROIs.



Problem in multiple comparisons

- If there are 40 subjects, and the time-frequency effective connectivity measure has 30 frequencies and 65 time points, the final data matrix size will be 76 x 76 x 30 x 65 x 40.



- The group statistics has 76 x 76 x 30 x 65 = 11,263,200 pixels in total to be tested.
- If you correct everything with Bonferroni method, corrected $p < 0.05$ is equal to uncorrected $p < 0.00000005$.

Problem in the original Measure Projection

- Measure Projection attempts to use 'convergence statistics' to address this issue.
  - It computes similarity measures of whole time-frequency data across all edges.
- However, it is known to cause a problem of 'double dipping'
  - i.e. it inflates false positive rates by performing inferential statistics on data that are clustered by similarity.
- I do not recommend to use it.

applying this method. Because of this tendency, we sometimes observe apparent localization results within limbic, basal, and cerebellar regions, from which scalp-observable EEG signals are unlikely to be generated due to their citoarchitectures. Care needs to be taken to interpret these results, and the apparent deep-brain sources are, for now, better interpreted to be closer to the surface along with radial projection lines to the surface.

Another possible limitation of study is validity in one of the processes in MPA. MPA first uses ERP measure, in the case of current study, to create consistent domains, then test their differences across conditions. This way of using the same data twice is known to inflate a bias toward false positives, a problem known as 'double dipping' (Vul et al. 2009). Unfortunately, there is neither analytical nor empirical analysis to quantifying this bias in MPA, so it is hard to determine how much it influences the current result. However, there are at least two reasons why the use of it does not have to be excluded. One reason is that according to the principle of human functional brain mapping, ICs localized within a certain region should show naturally correlated activation patterns even without using constraint of similarity of measures. This is a different situation from what Vul and colleagues criticized in the social cognitive neuroscience studies, where sociocognitive scores were directly correlated to BOLD signal data. The other reason is that the number of ICs is much smaller than the number of voxels in fMRI: 100-1,000 ICs divided into 5-10 domains vs. whole-brain 200,000 voxels. From these comparisons, we believe that the situation in MPA is more benign than that of sociocognitive fMRI studies in question, and the estimated demerit of using MPA does not exclude the use of it.

Conclusions

CNP has the largest influence on ERP in a domain which includes the limbic system with no contribution from the sensory-motor cortex. In the domain including sensory-motor cortex MRCP of both patients groups is similar and delayed as compared to able bodied. Smaller differences exist in a domain which included visual cortex. Both pain and paralysis affect the reaferentation potential while CNP influences cognitive processes in a manner that depends on the area of the cortex.

List of Acronyms

CNP Central Neuropathic Pain, SCI Spinal Cord Injury, MI Motor Imagination, AB Able Bodied, PwP Patients with Pain, PnP Patients without Pain

Conflict of Interest

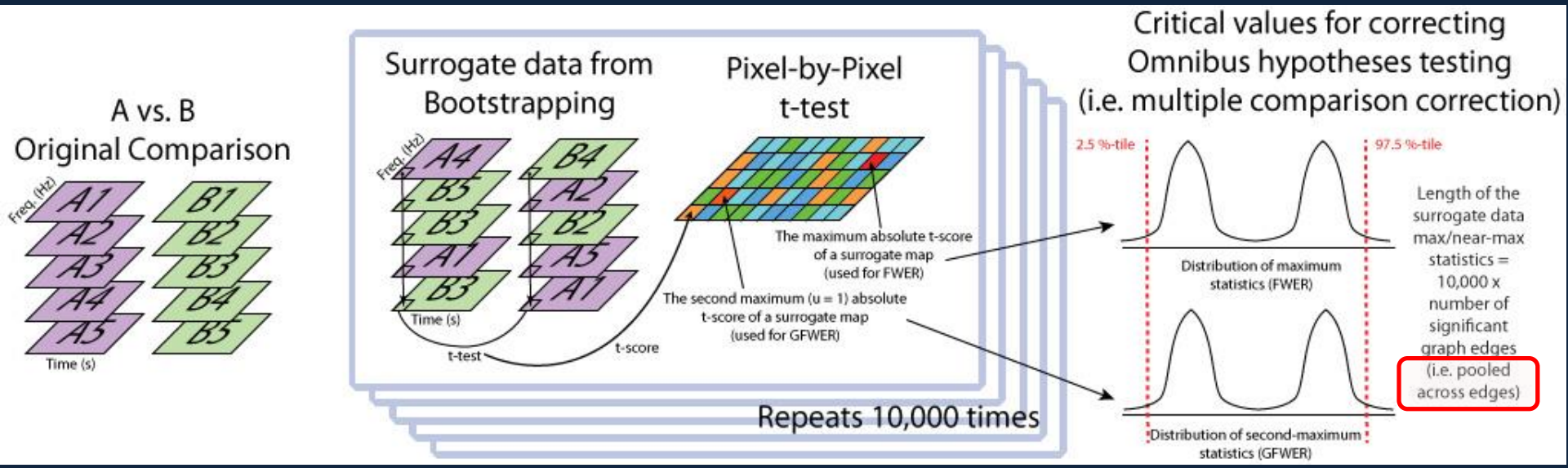
We report no conflict of interest

Author Contribution

AV Wrote the manuscript, provided interpretation of results, designed the experiment and contributed to data collection, MJ performed data analysis, MAH contributed to the design of experiment and collected data, MM contributed to data analysis and to writing of the manuscript, MF recruited patients and contributed to the design of the experiment

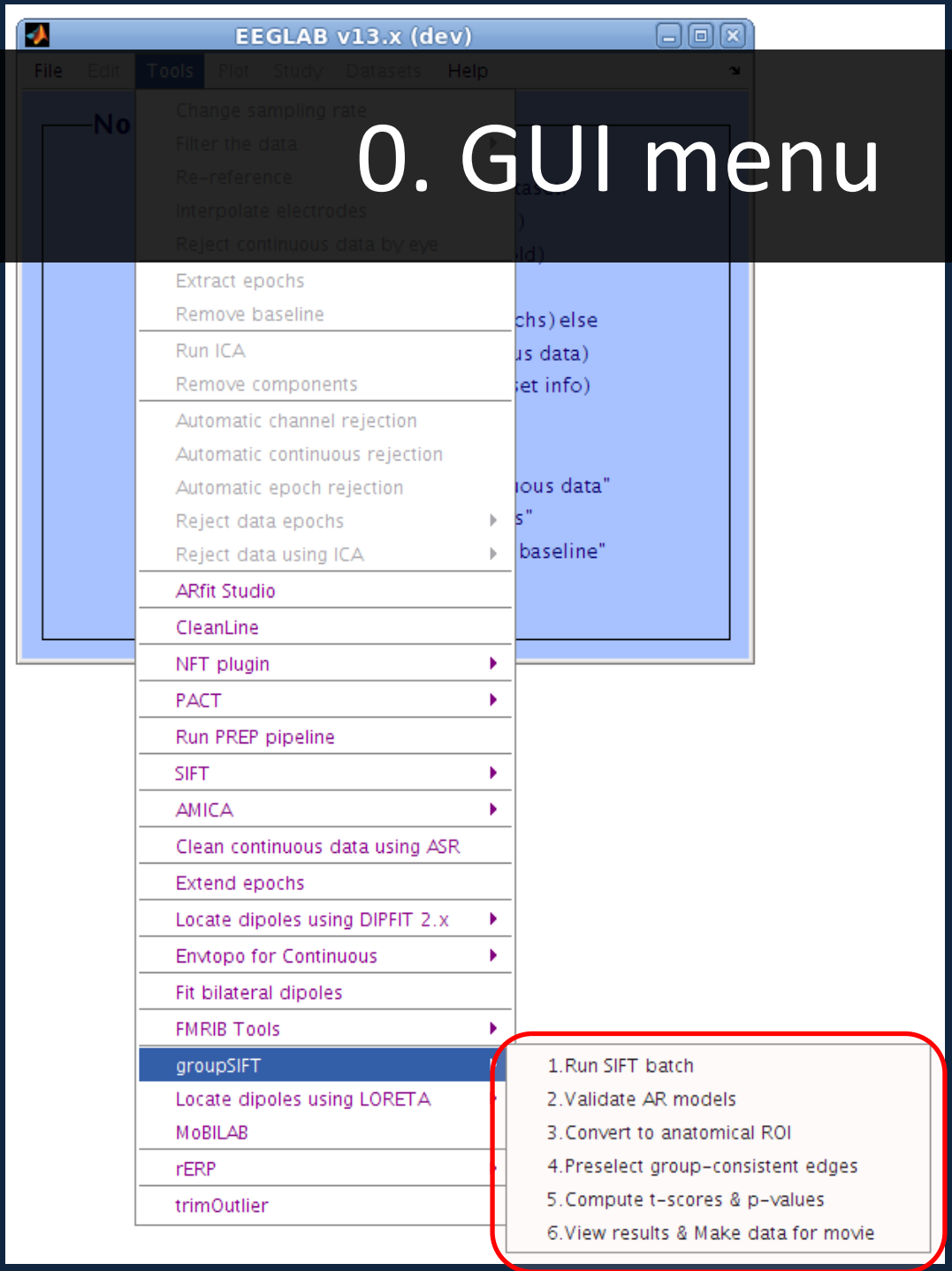
Funding

Multiple comparison correction across 76 x 76 (edges) x 30 (freqs) x 65 (time)



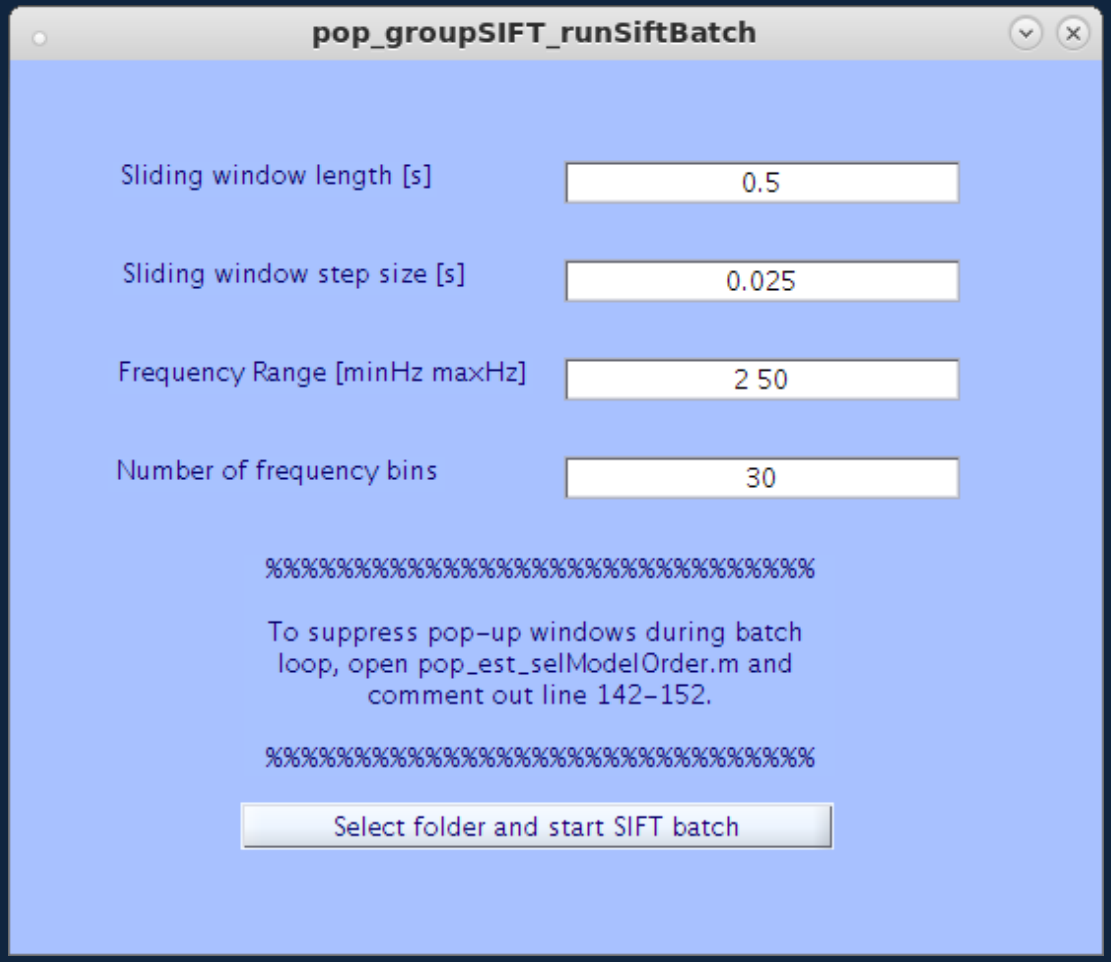
I would change it to a cluster-based method.

0. GUI menu



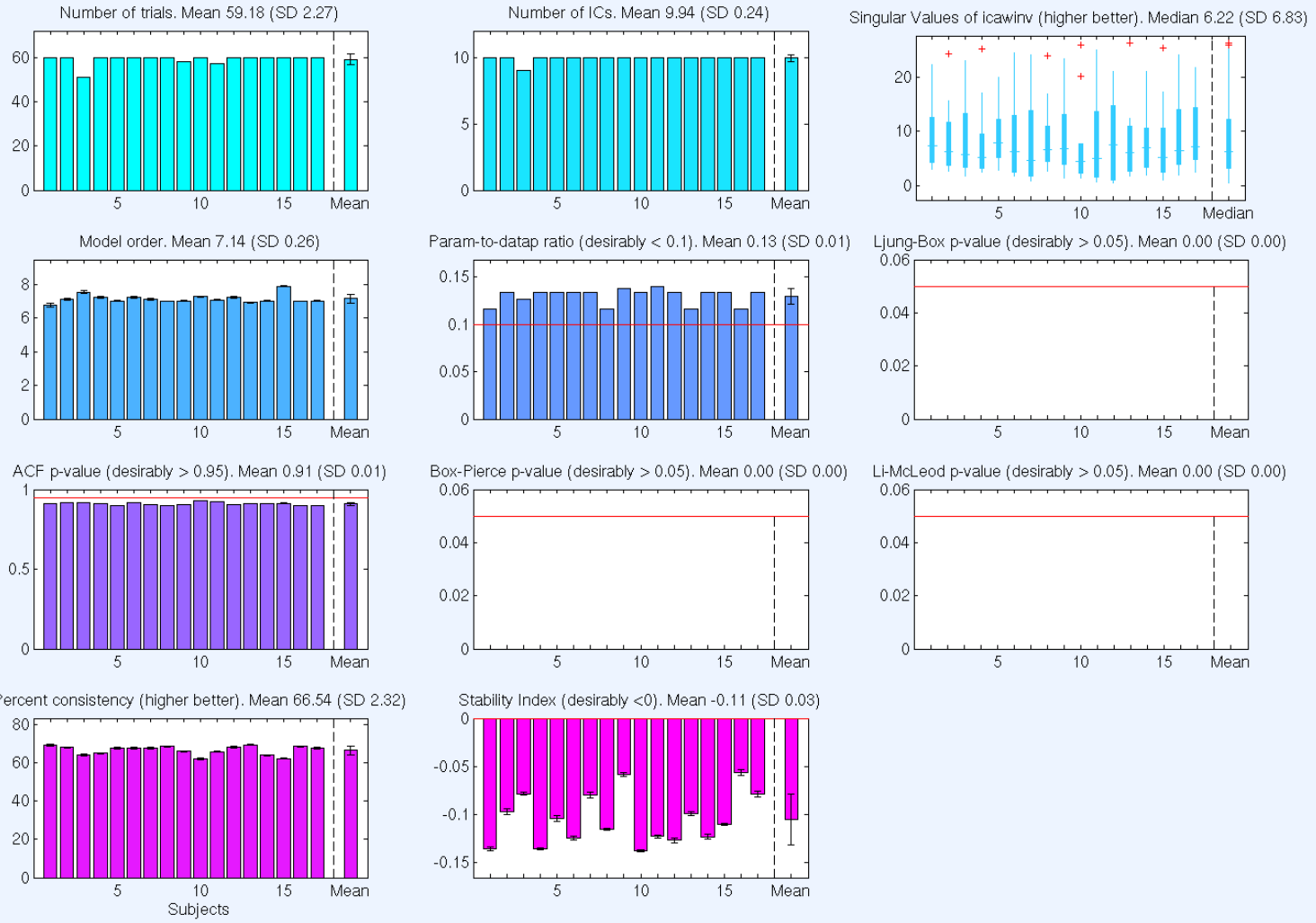
Preprocessing stages are numbered! (The revolution in the history of EEGLAB)

1. Run SIFT batch



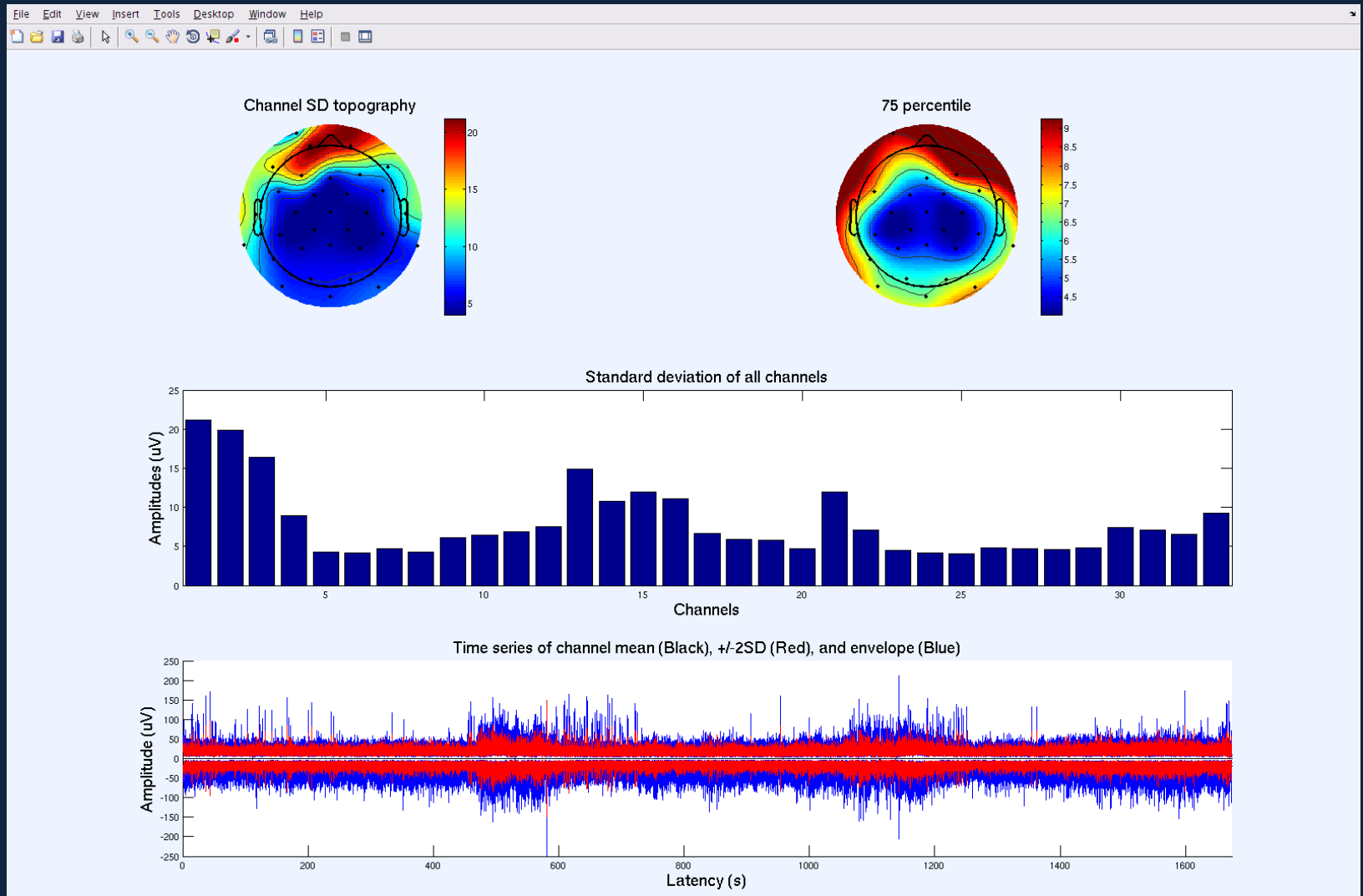
Good default preselected: selected measures are rPDC and dDTF; Model order automatically selected Hannan-Quin, etc.

2. Validate Models

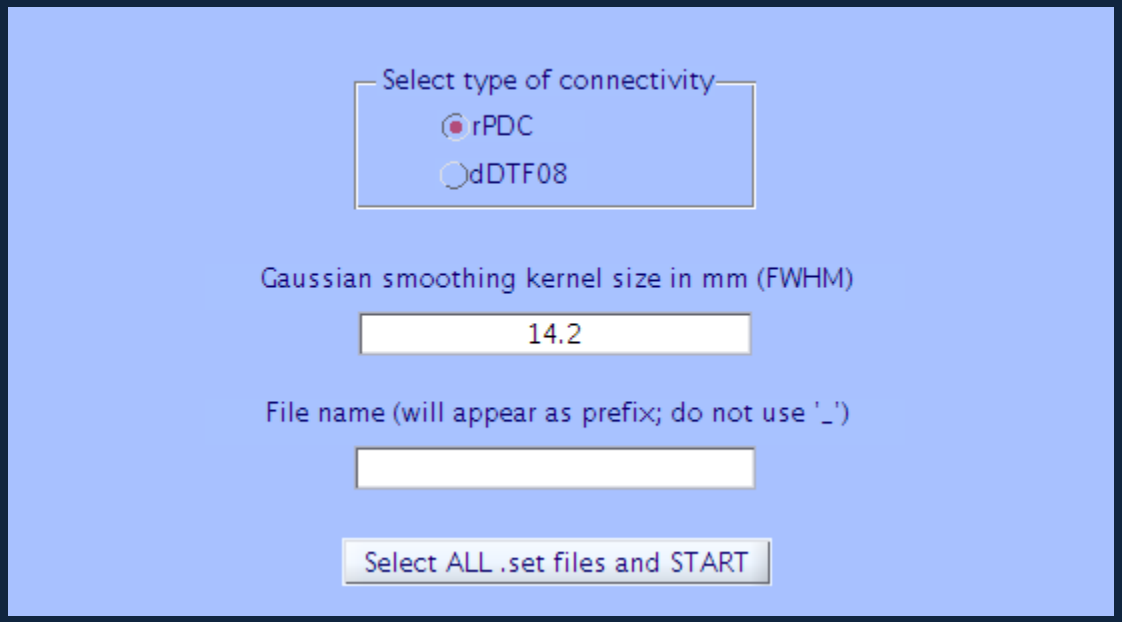


Ensures good surveyability across all important validations.

By way of speaking surveyability…

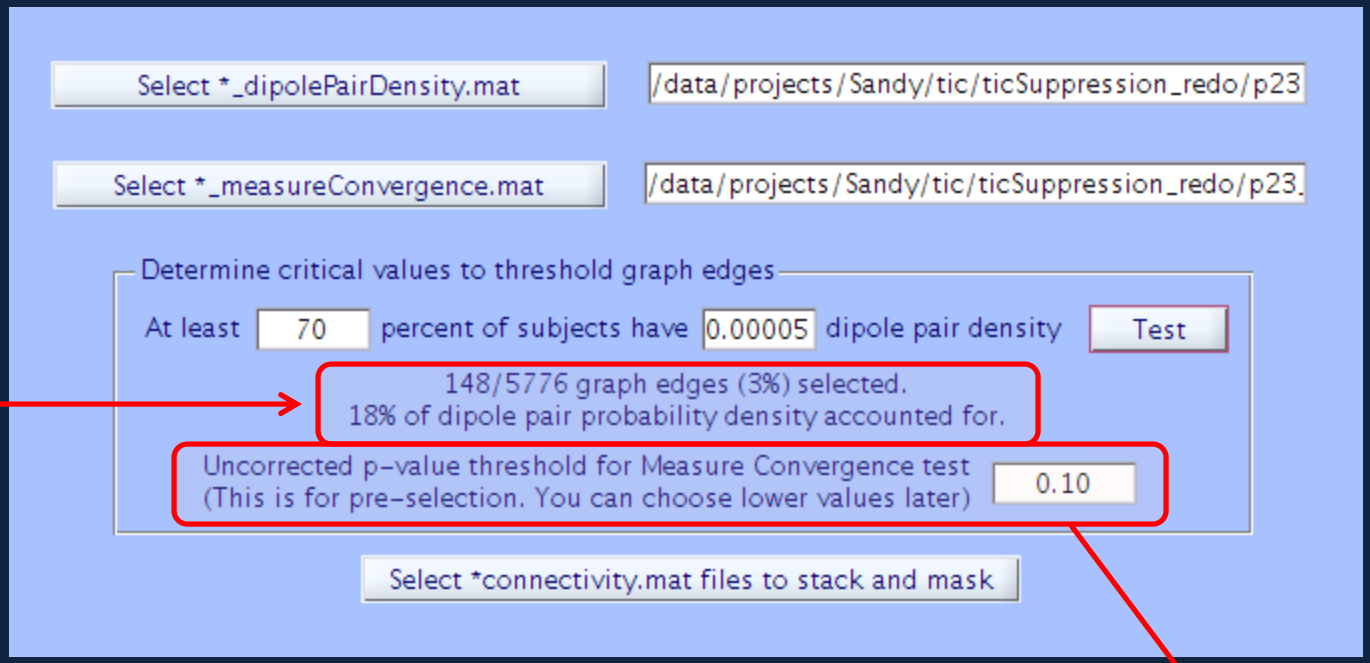


3. Convert to Anatomical ROI



FWHM of 14.2mm achieves SD = 9.6mm that is average dipole fitting error across whole brain with no MRI, according to Zeynep Akalin Acar.

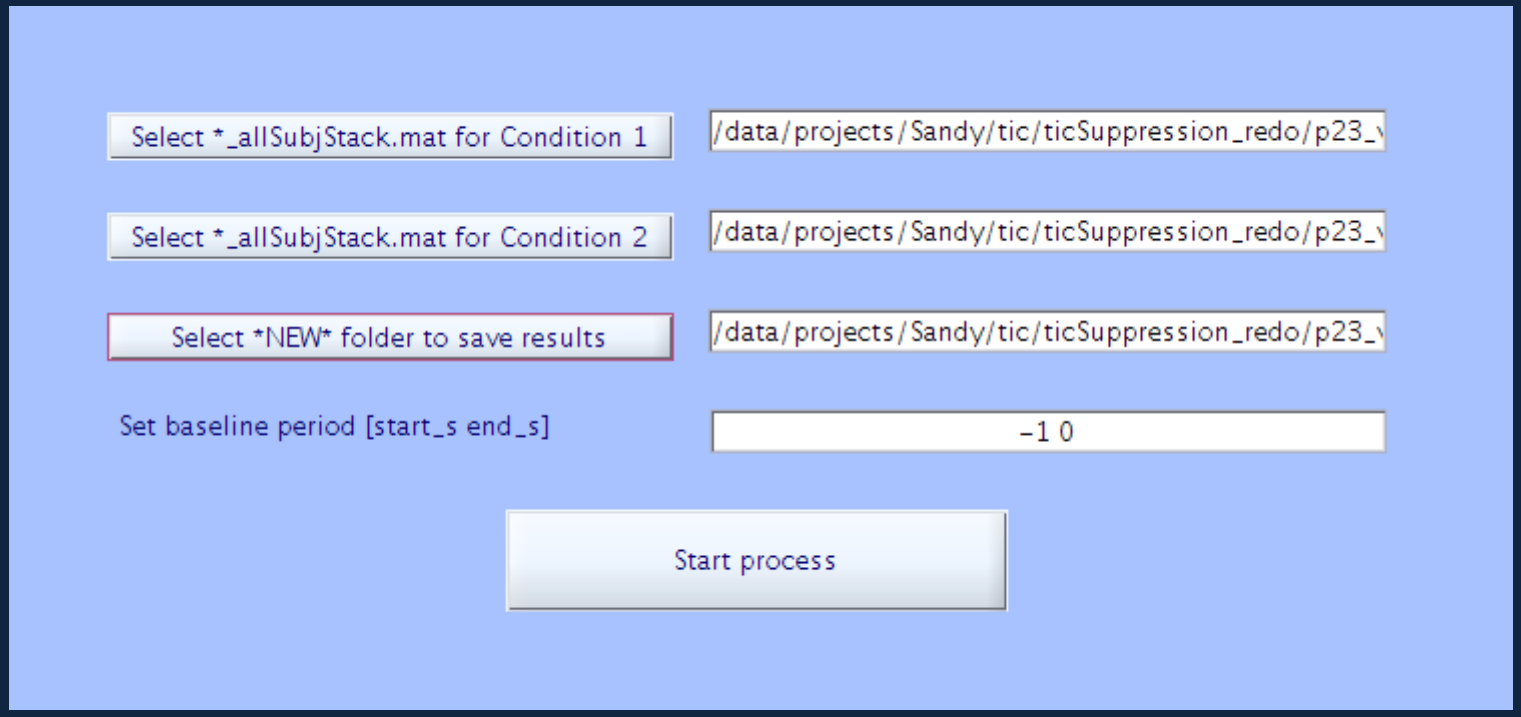
4. Preselect group-consistent edges



Interactively and iteratively test to determine the final amount of edges.

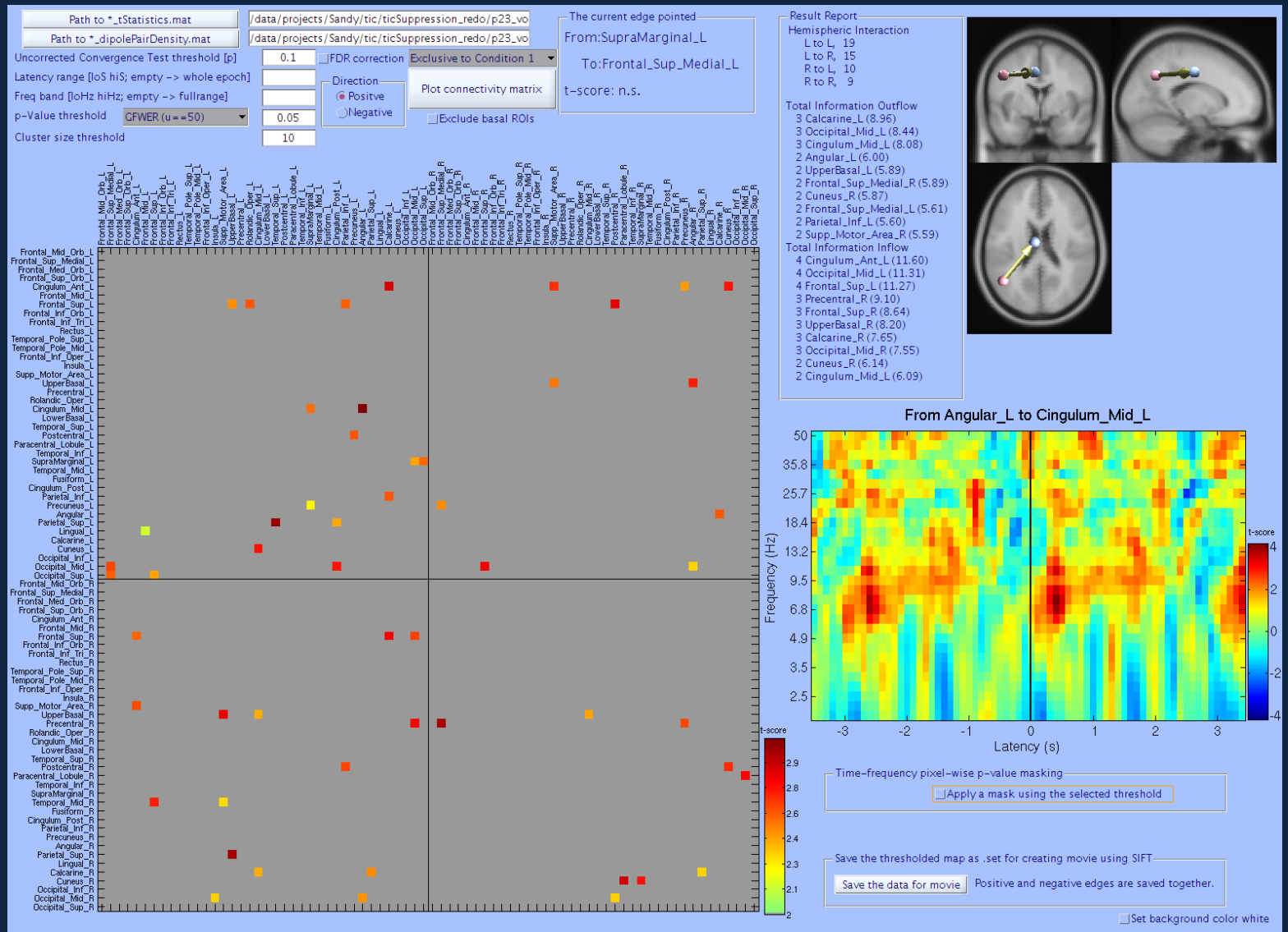
Optional (Not recommended; potential double dipping issue).

5. Compute t-scores and p-values

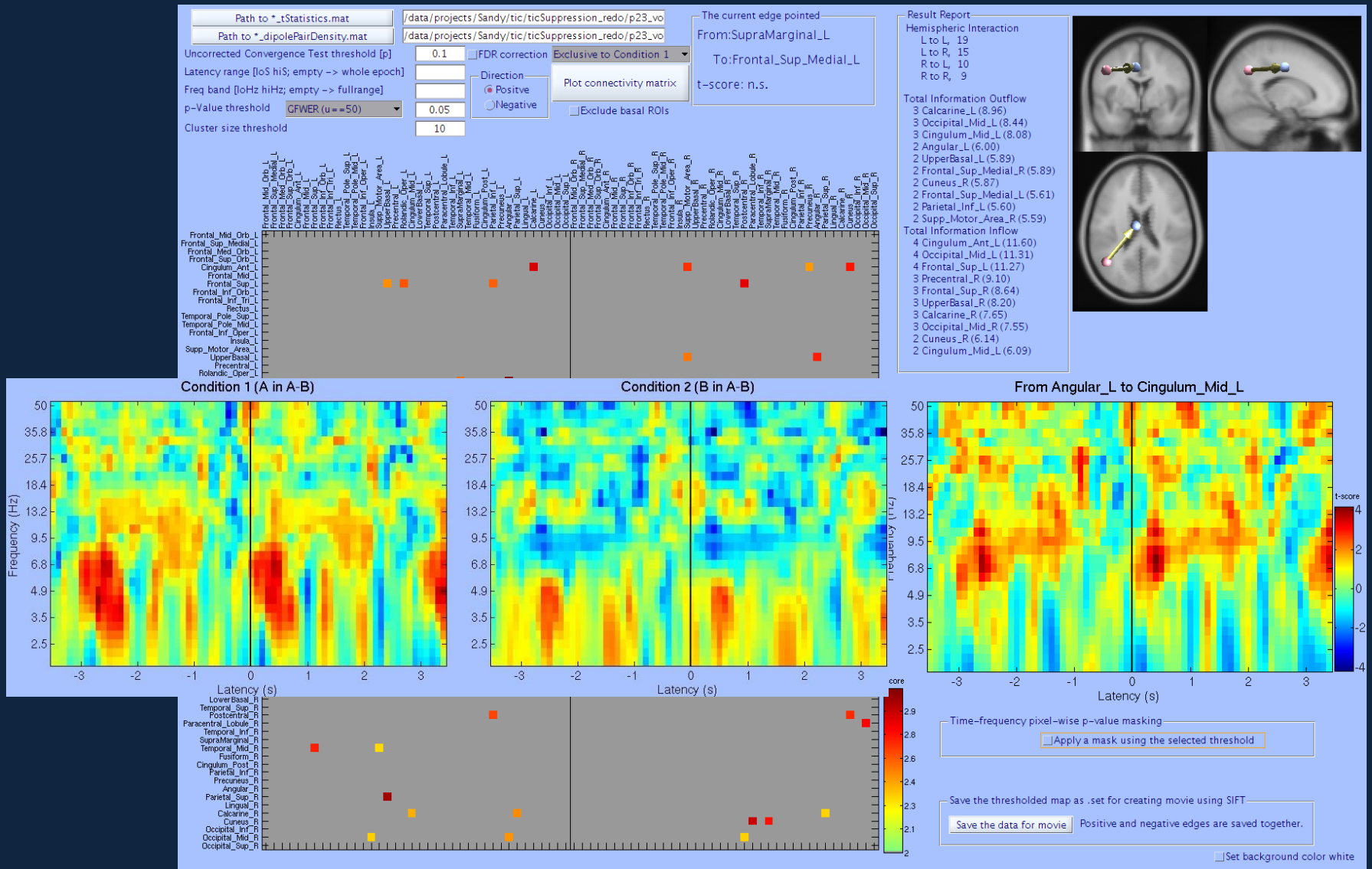


- T-test across 76 x 76 (anatomical ROI) 30 (freqs) x 65 (time points) x 40 (subjects) x 2 (conditions), for example.

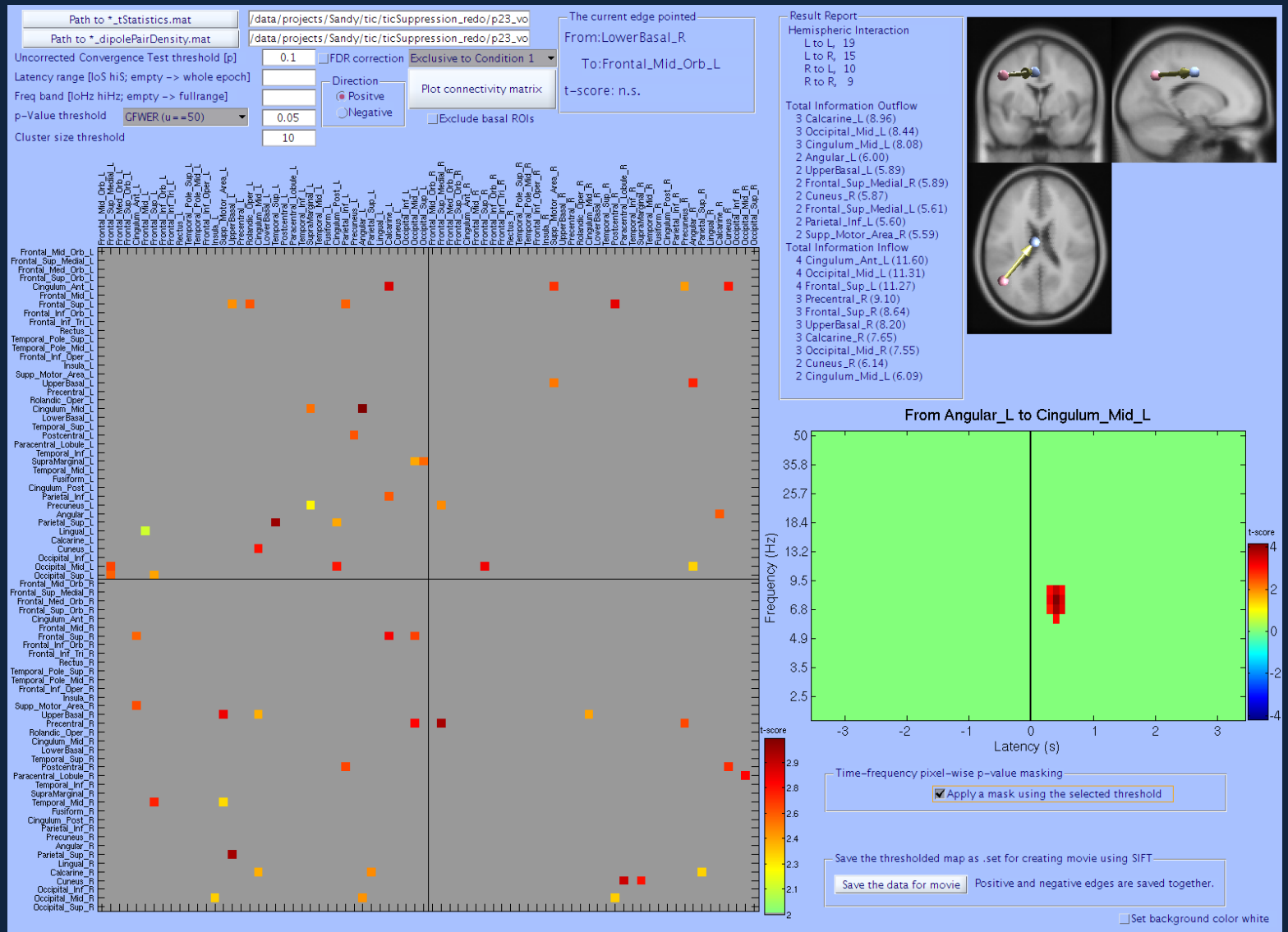
6. View Results and make data for movie



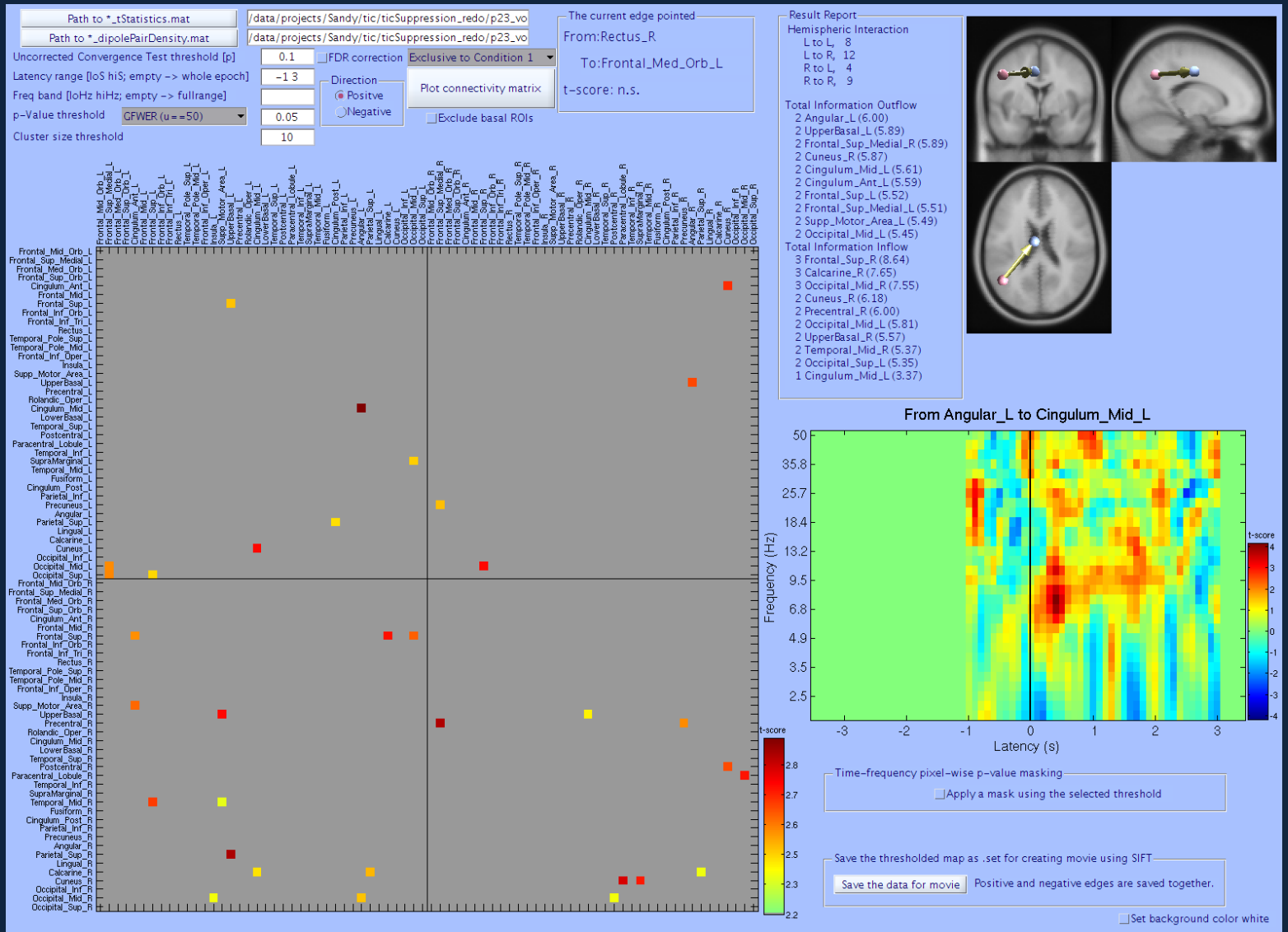
Showing both conditions before subtraction



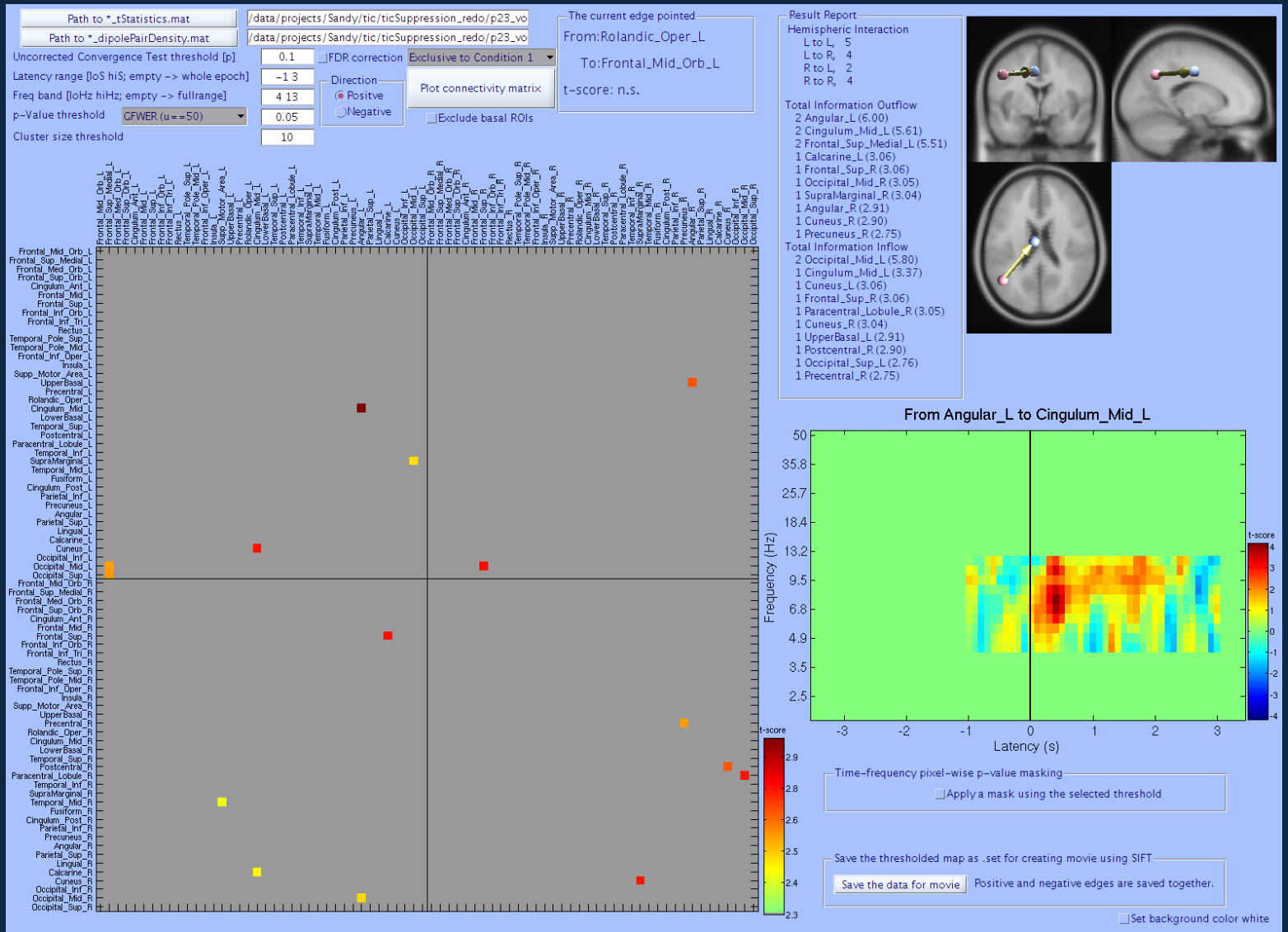
Applying (generalized) family-wise error correction for time-frequency data



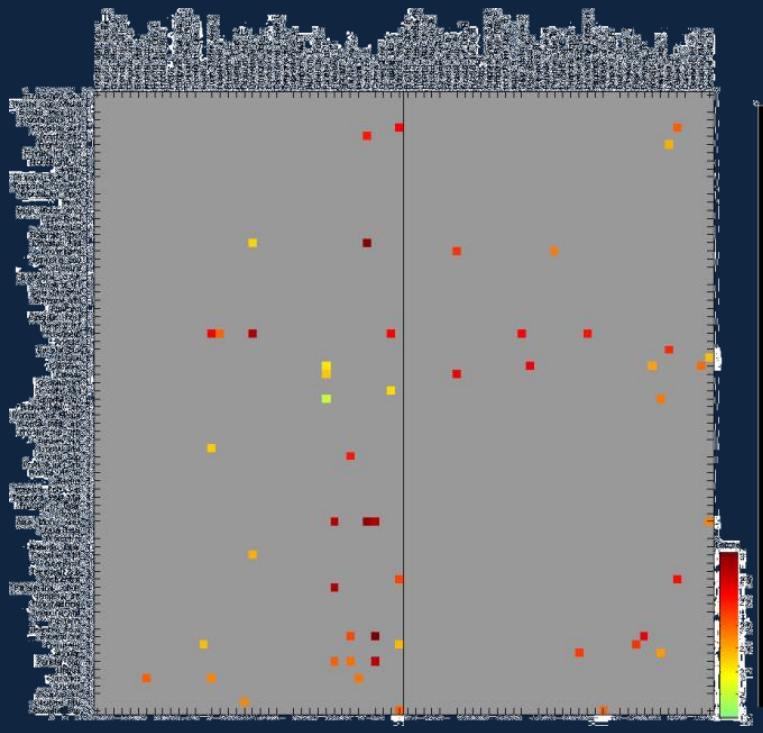
Selecting edges with specified time window

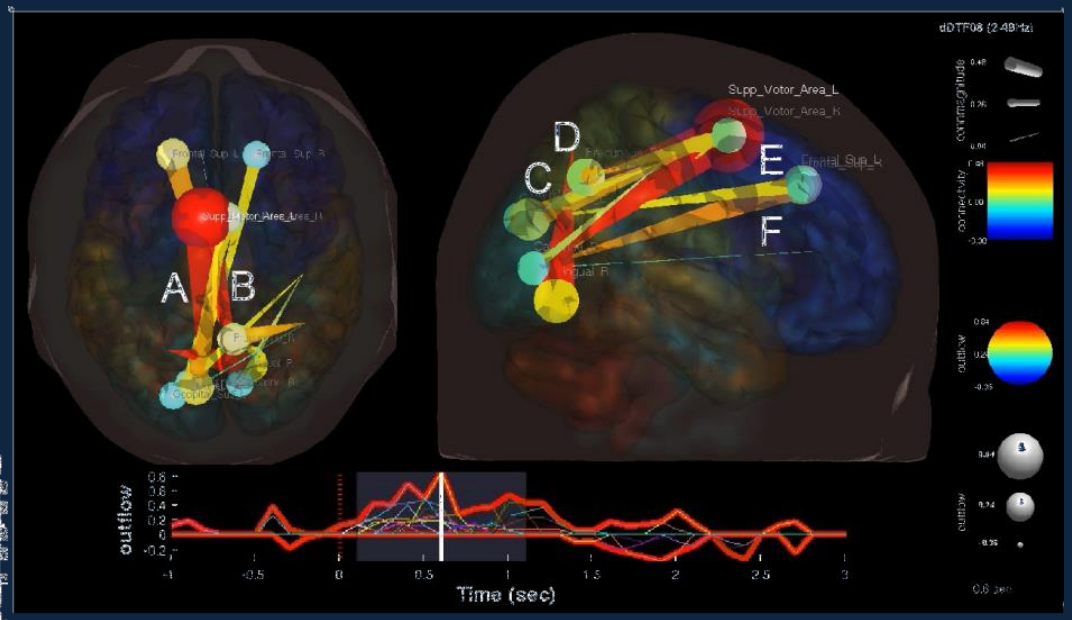


Selecting edges with specified time and frequency window



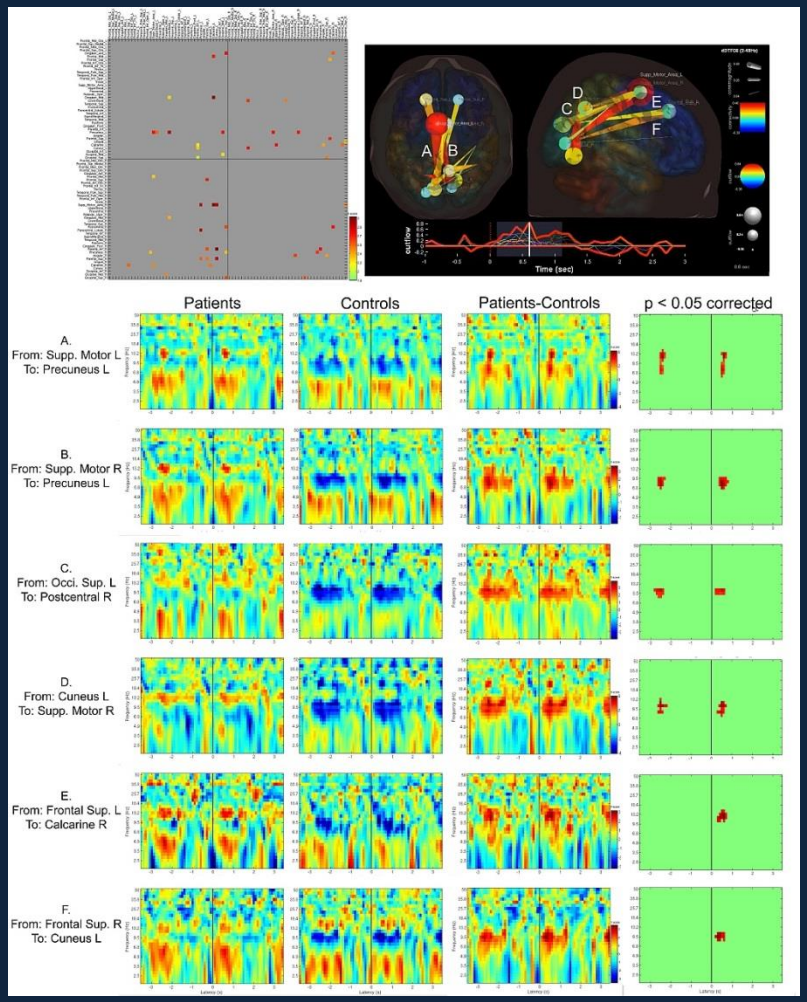
Making a movie using SIFT



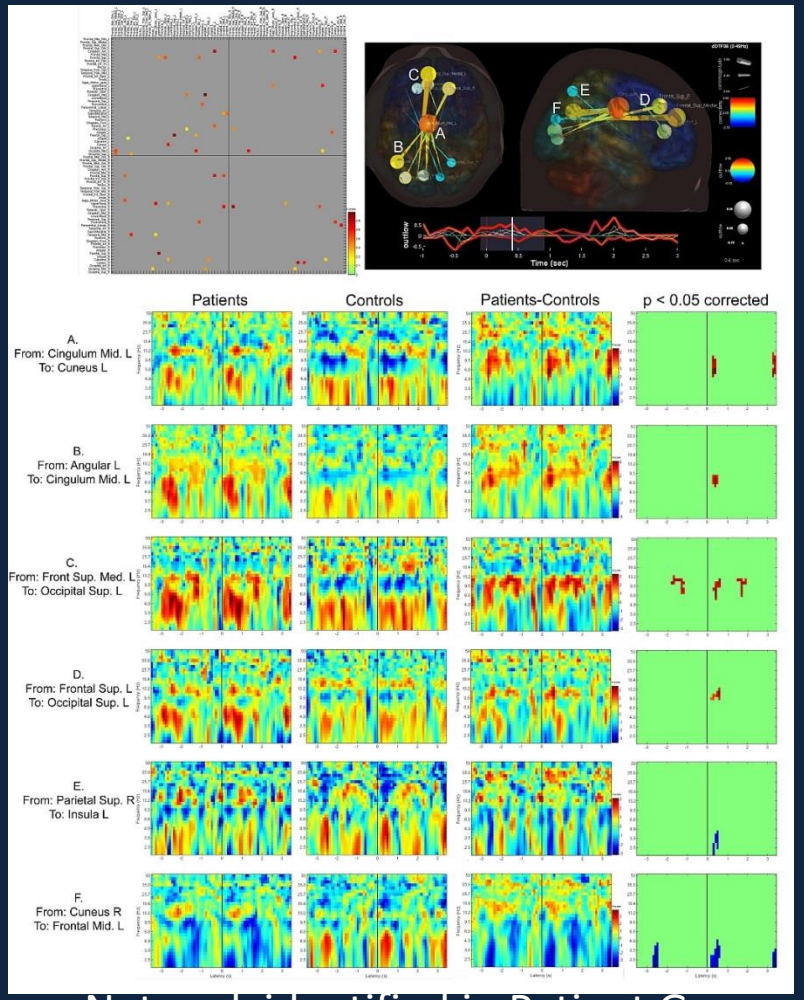


- It uses SIFT's GUI to make the movie by feeding single subject dataset replaced with group-mean data.

Manuscript being prepared
UCLA Tourette study (PI: Sandy Loo)



Network identified in Control Group
Patient - Control



Network identified in Patient Group
Patient - Control

Conclusion

- The proposed method allows to use ICA results for the group-level connectivity analysis.
  - Accepts individual differences in number of ICs and their locations.
  - The same idea can be applied for other measures such as ERP, ERSP, spectrum, etc… the idea is the same as performing Measure Projection without creating domains defined by similarity but anatomical ROIs.
- Designed to be simple, intuitive, and interactive.
  - Intended to be a blackbox tool for psychologists and clinicians.
- Recommended for ICA purist.
- The final statistics can be improved
  - I will try a cluster-based method.
- Further dimension reduction is desirable
  - 76 x 76 = 5776 edges are too many dimensions.
  - I will try PARAFAC, Non-negative matrix factorization, etc.