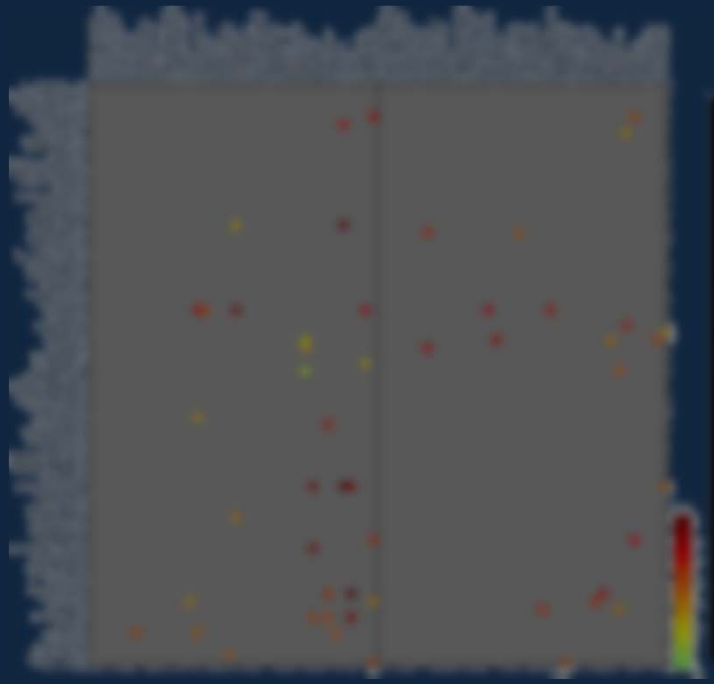
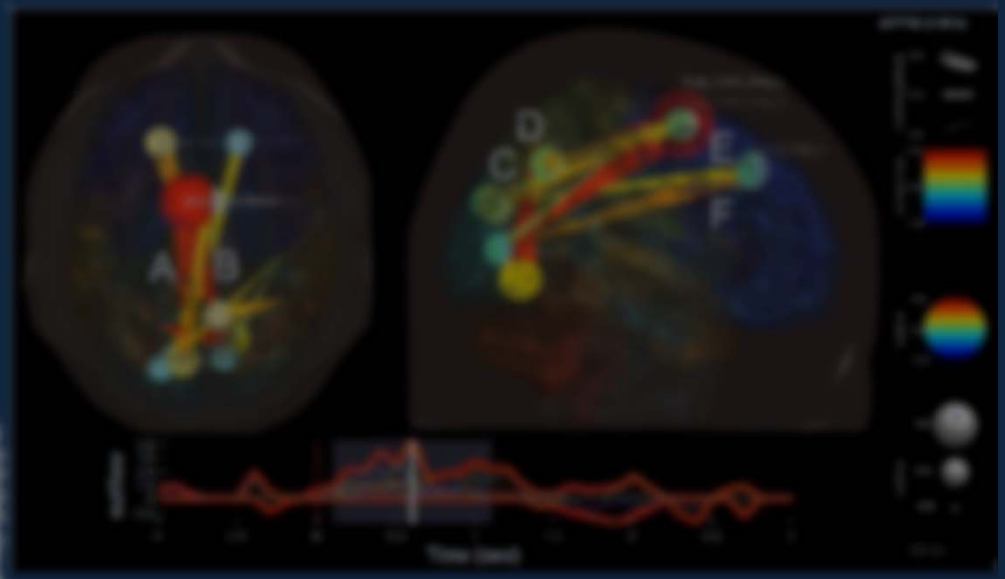
Group-Level Connectivity (ver. 2.0)





Makoto Miyakoshi

9/29/2017

The 25th EEGLAB Workshop in Tokyo

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.

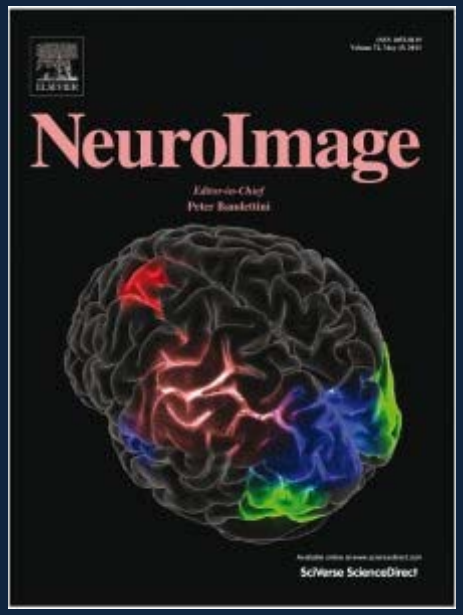
Two approaches by two colleagues

- *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.

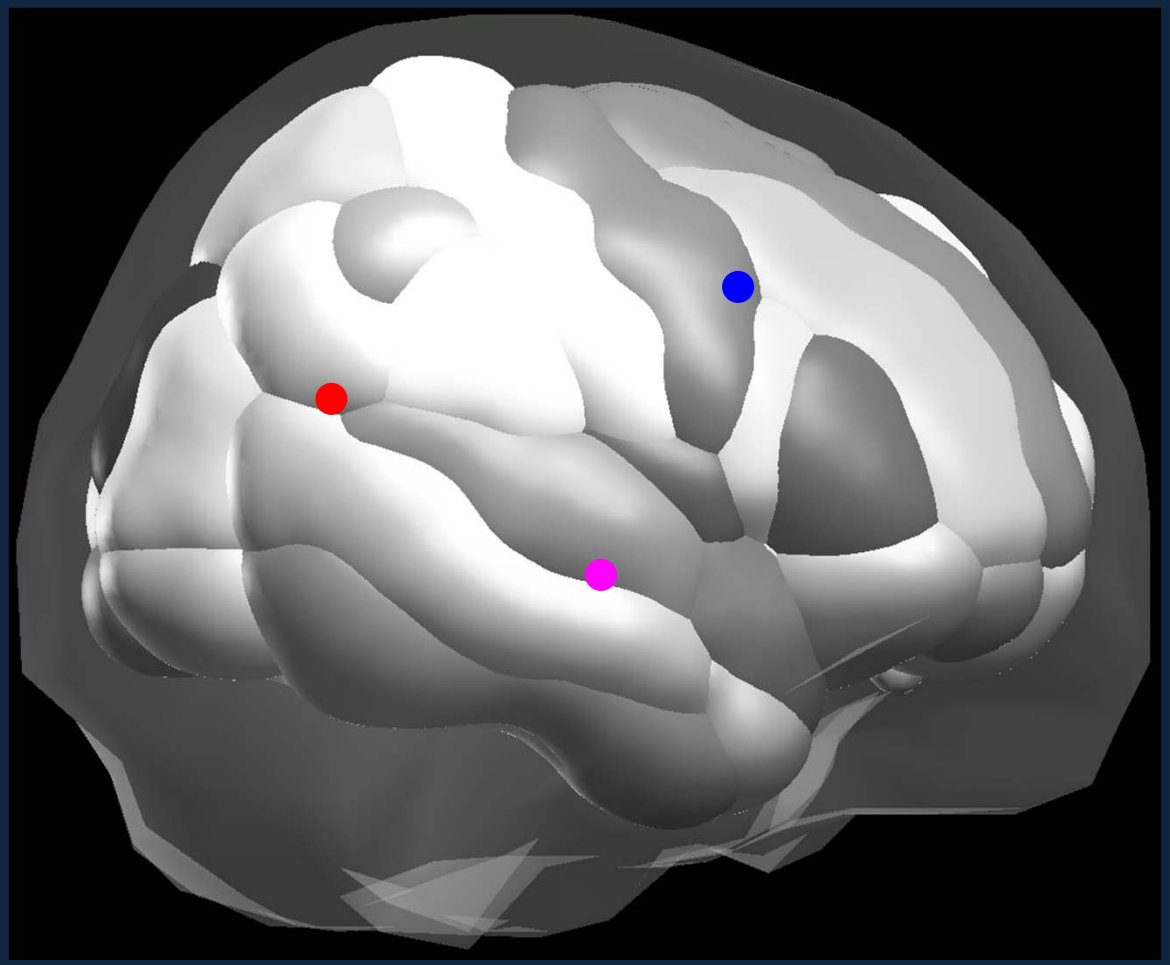
- *Network Projection by* Nima Bigdely-Shamlo.
  - Allows inconsistency.
  - Simple, based on his publication.
  - Always present in regular office hour.

Original ideas in Measure Projection

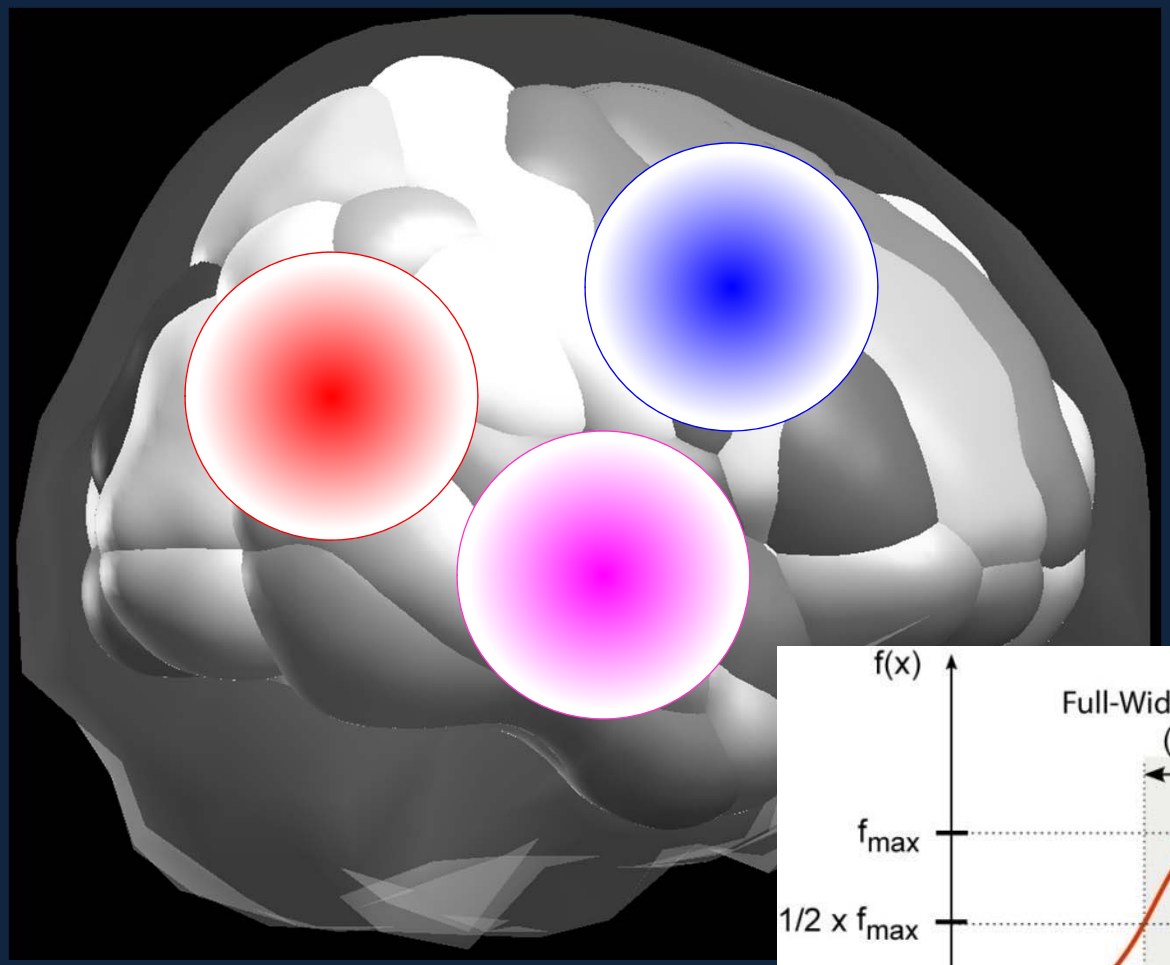
- Bigdely-Shamlo N, Mullen T, Kreutz-Delgado K, Makeig S. (2013). Measure projection analysis: a probabilistic approach to EEG source comparison and multi-subject inference. *Neuroimage.* 72:287-303.
- Apply 3-D Gaussian smoothing to dipole locations, weight them with measures (such as ERP), and cluster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

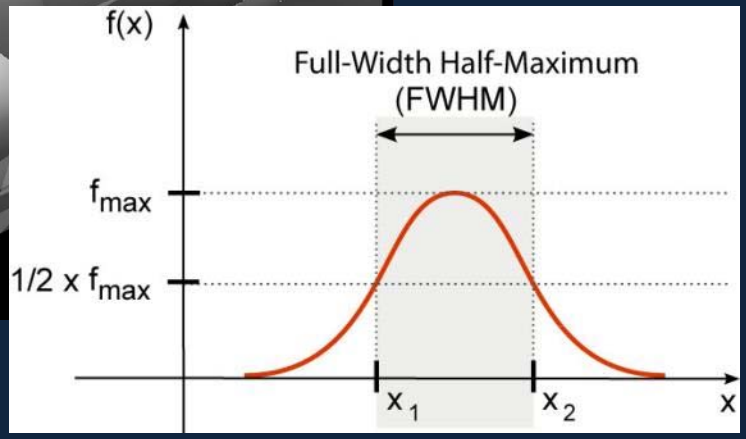


Dipole locations: Before smoothing



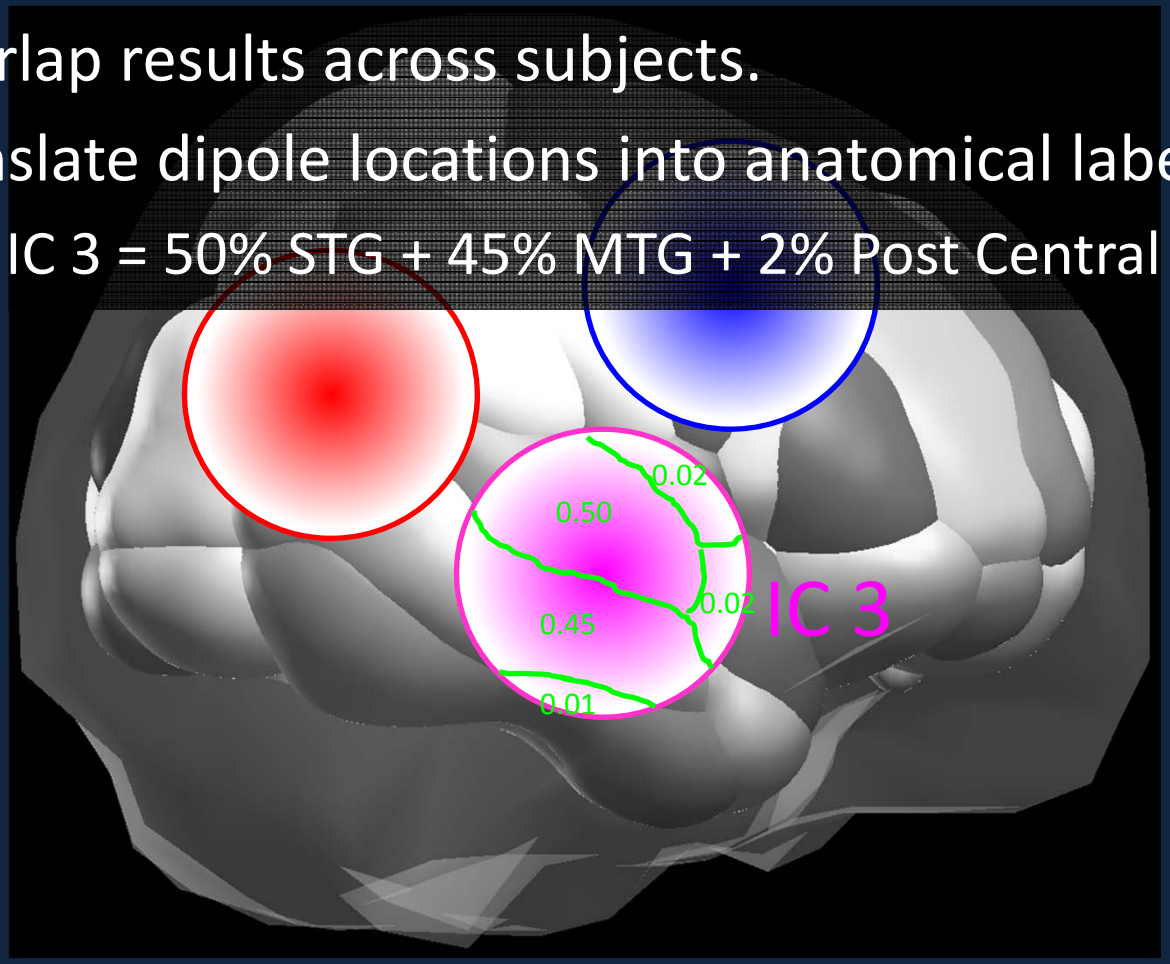
Dipole locations: After smoothing



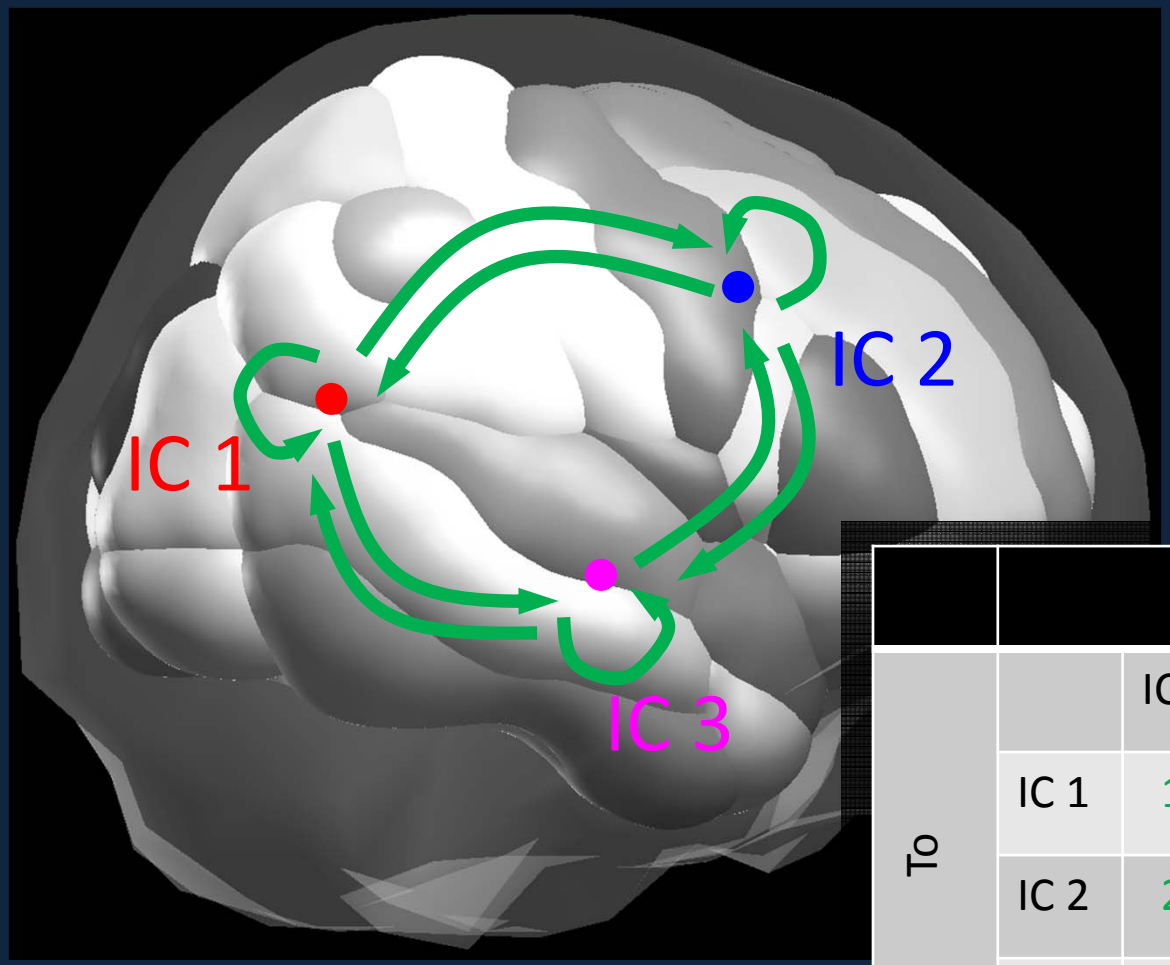


Why smoothing?

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



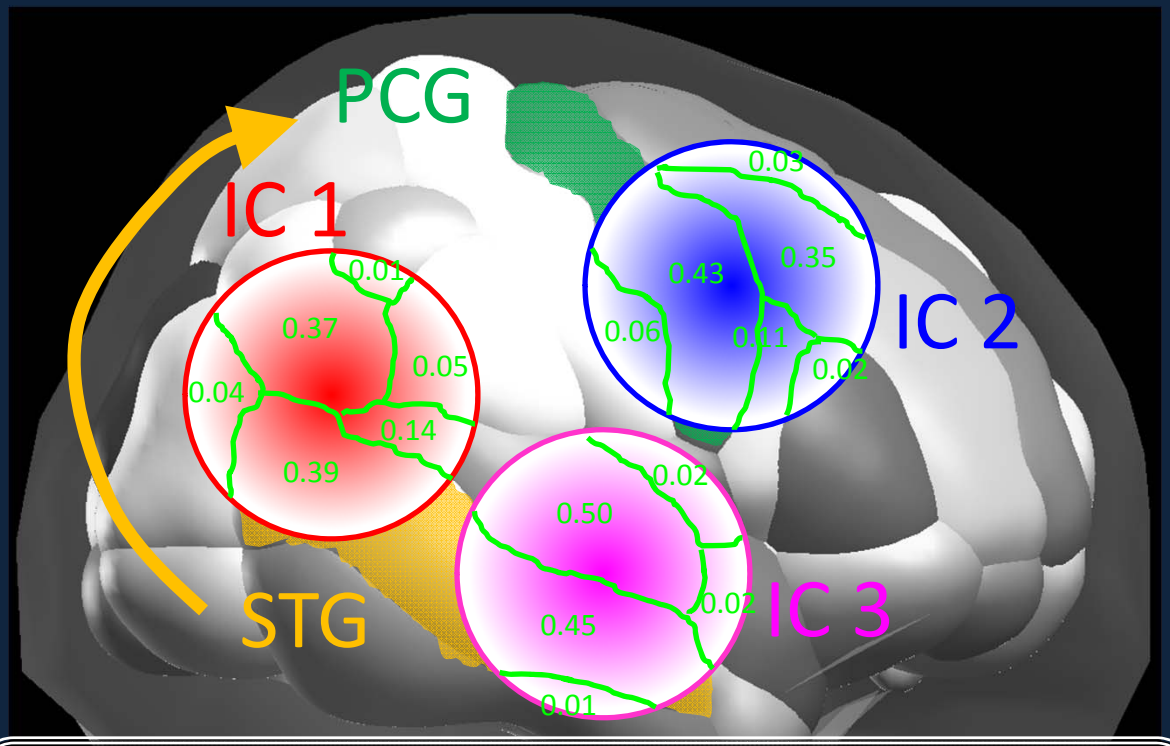
Pairwise dipole connectivity



3 x 3 ICs

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

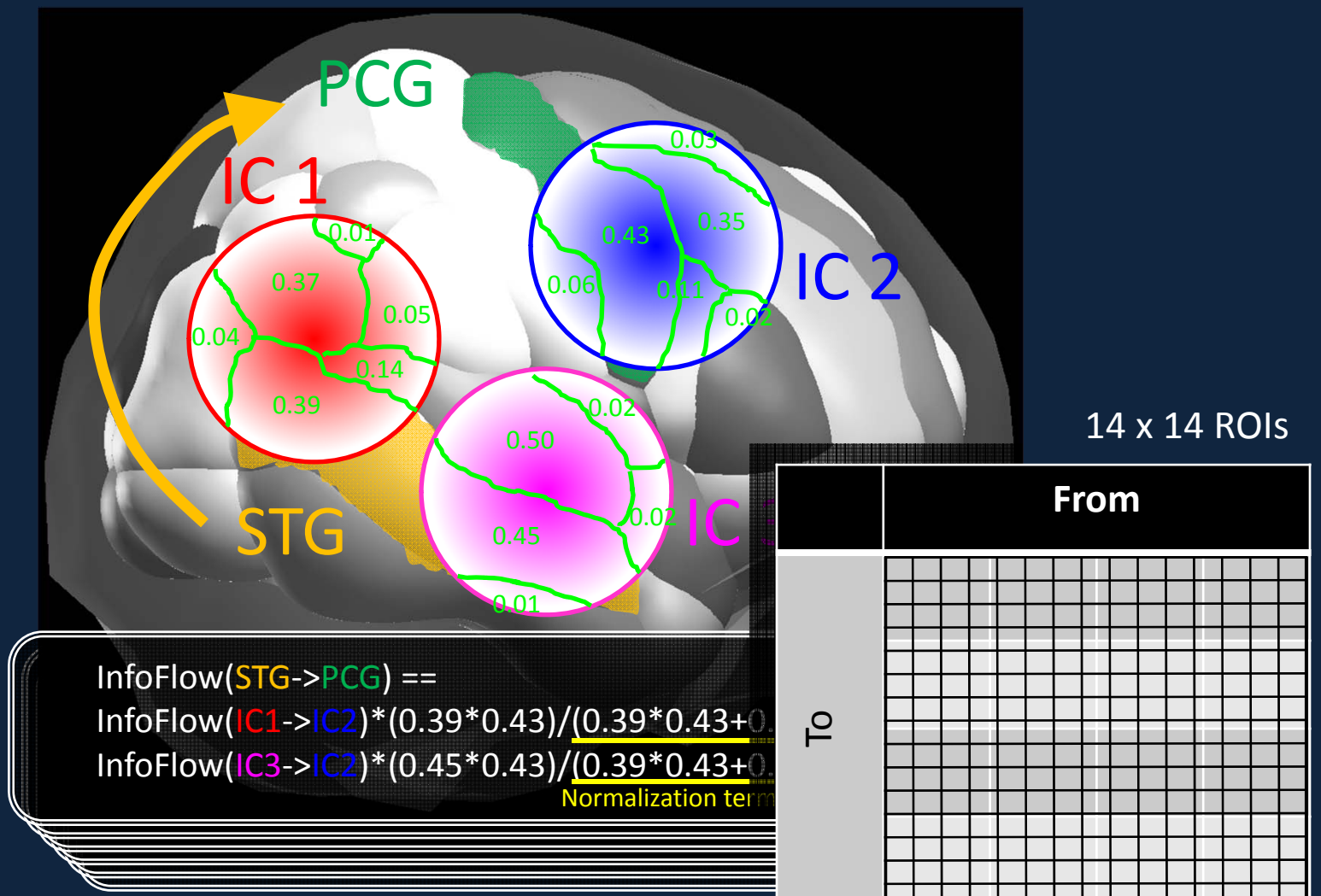
Pairwise dipole density connectivity



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.

Pairwise dipole density connectivity

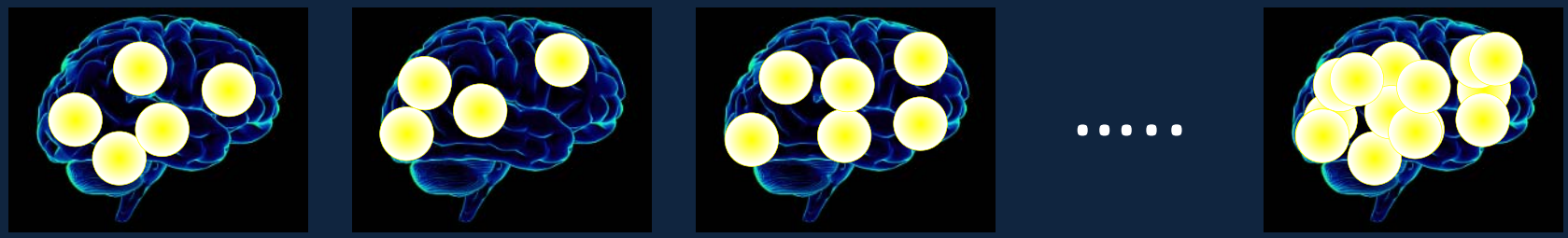


There are total of 76 ROIs x 76 ROIs = 5776 edges.

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.

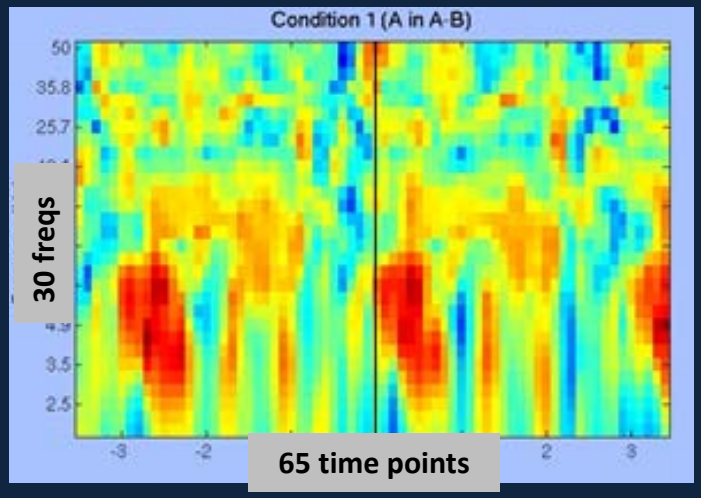
Subj 1 Subj 2 Subj 3 ..... Group mean



Subj 1 Subj 2 Subj 3 ..... Group sum

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 uses ‘convergence statistics’ to cluster similar data first.
- But turned out to cause a problem known as ‘double dipping’.
  - i.e. it inflates Type I error (false positives) rate.
- This groupSIFT avoids to use ‘convergence statistics’.
  - fMRI researchers knows about 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

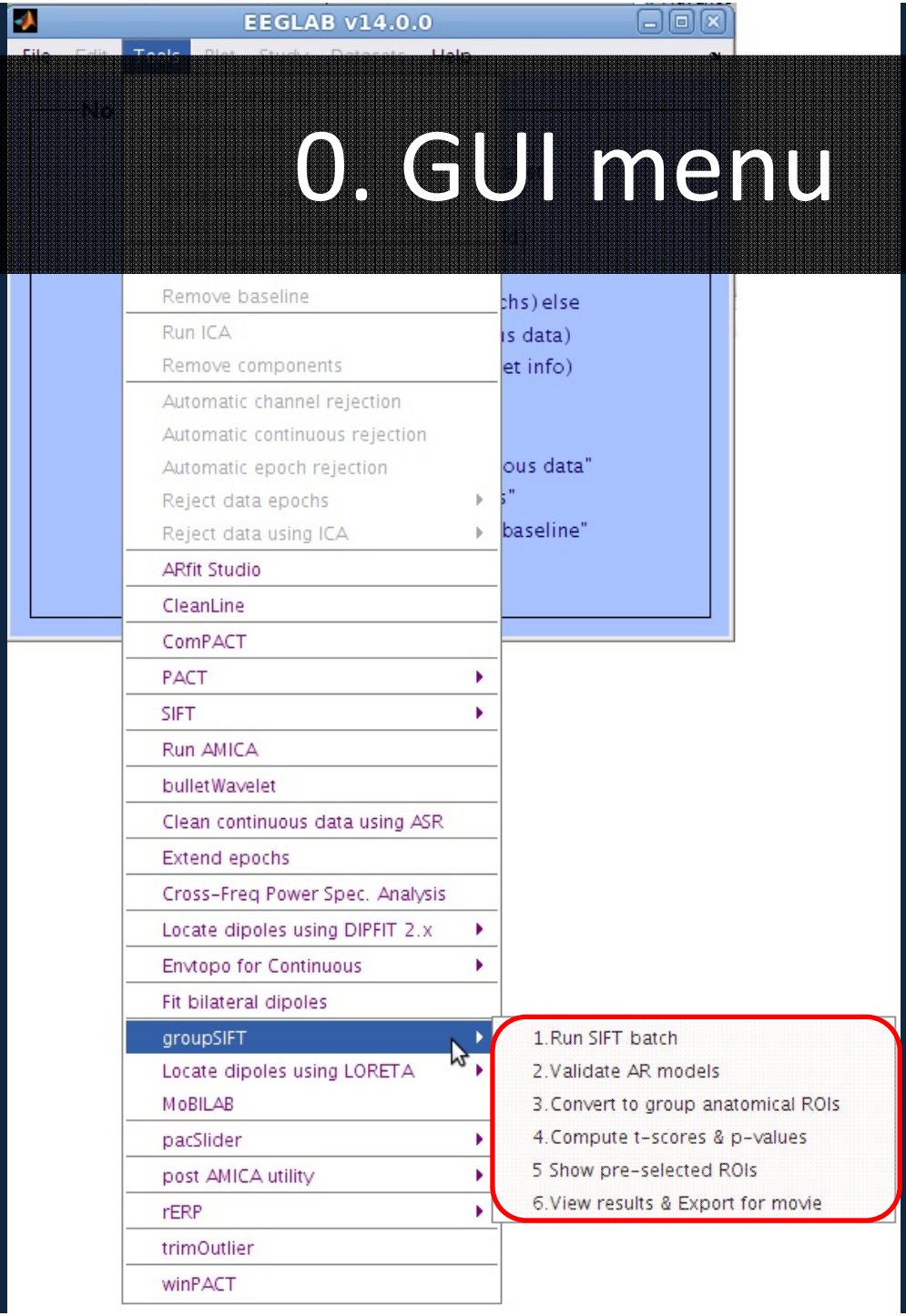
Funding

Cluster-level correction as a weak Family-wise Error Rate (FWER) correction

1. Compute the true difference between conditions and *mass of clusters*: the sum of t-scores within a cluster ('blob') of significant pixels.
2. Do the same with condition permutation for 10,000 times to build surrogate distribution of *mass of clsuters*.
3. Identify 95%-tile of the surrogate distribution as a critical value, and use it for single-step omnibus hypothesis correction.
4. In short, *the largest blob survives first*.

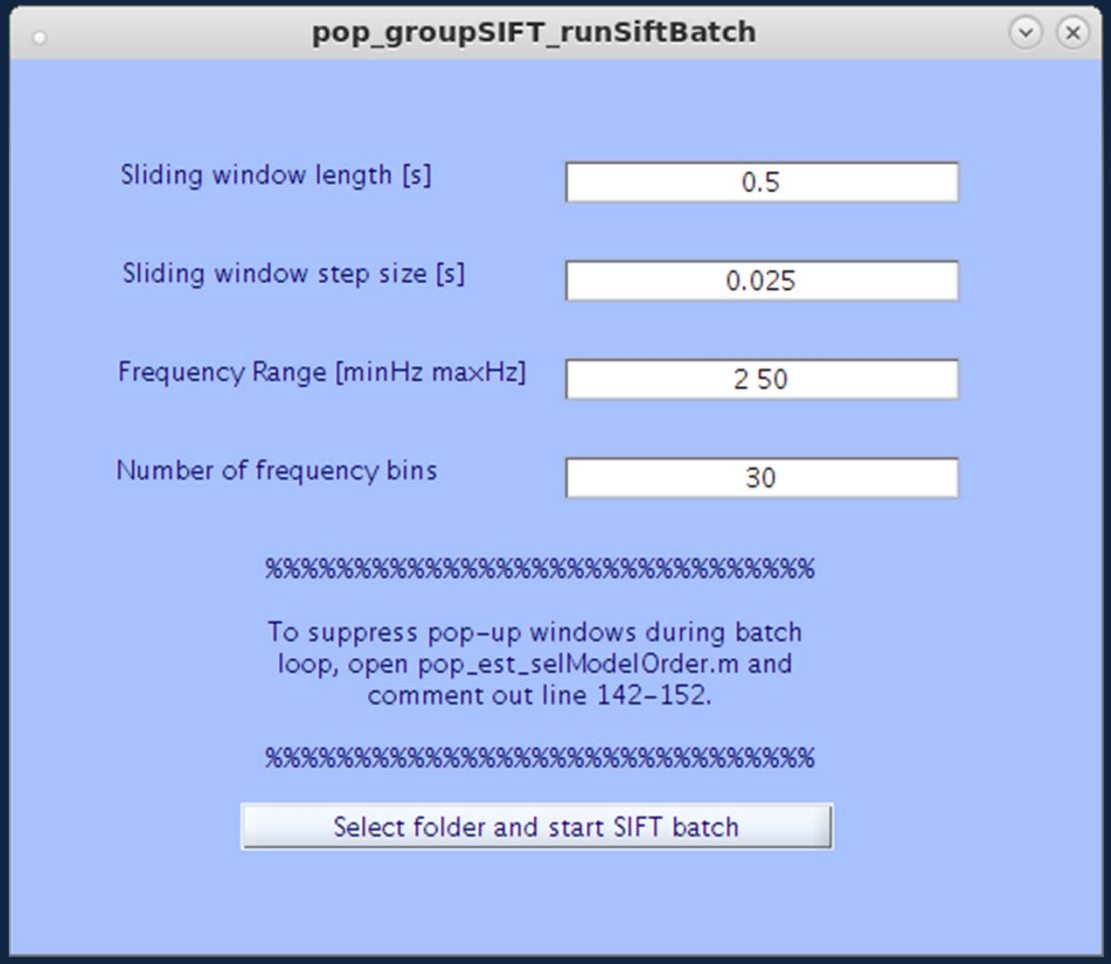
Tour guide (no tutorial!)

0. GUI menu



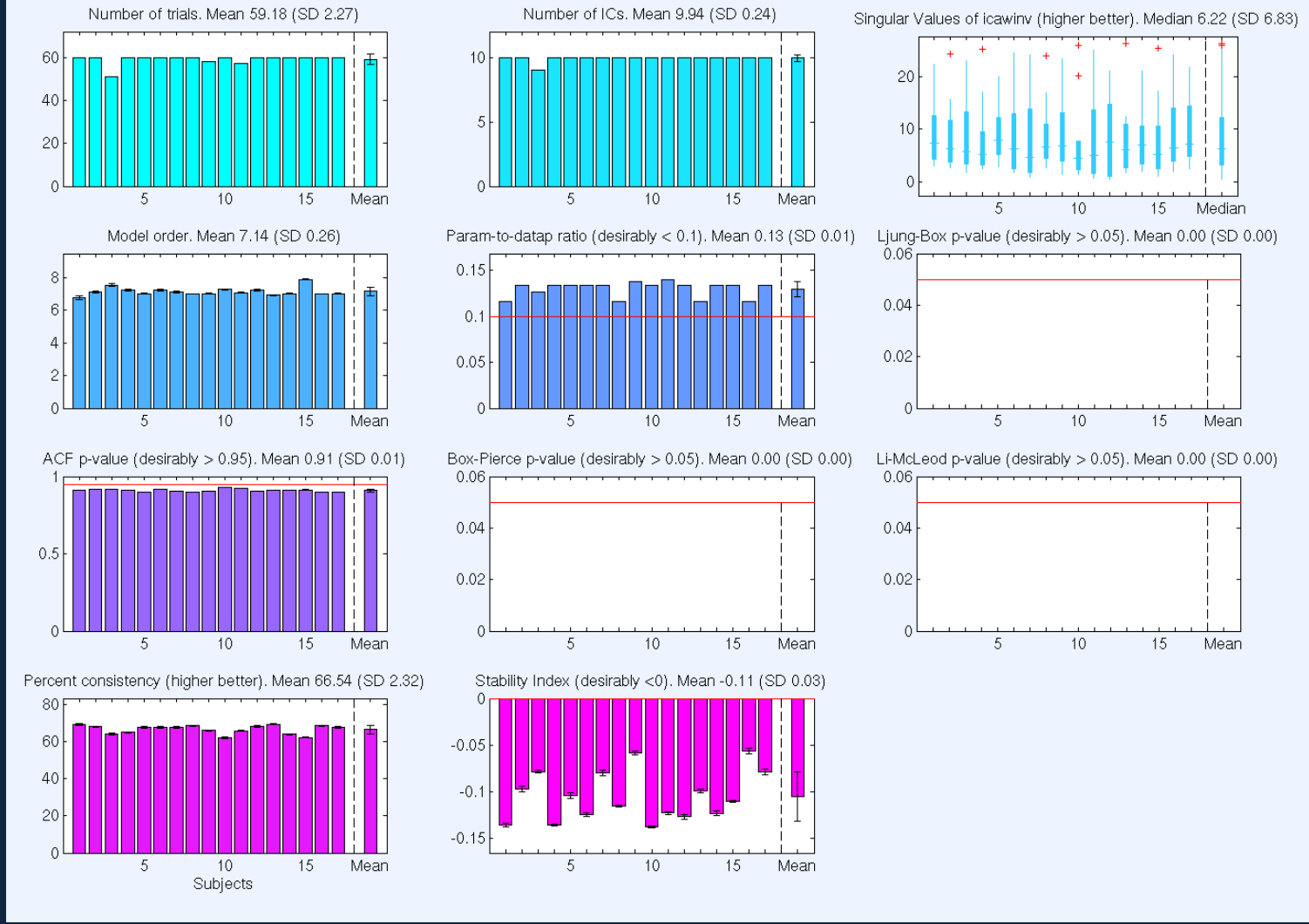
Preprocessing stages are numbered! (The revolution in the history of EEGLAB)

1. Run SIFT batch



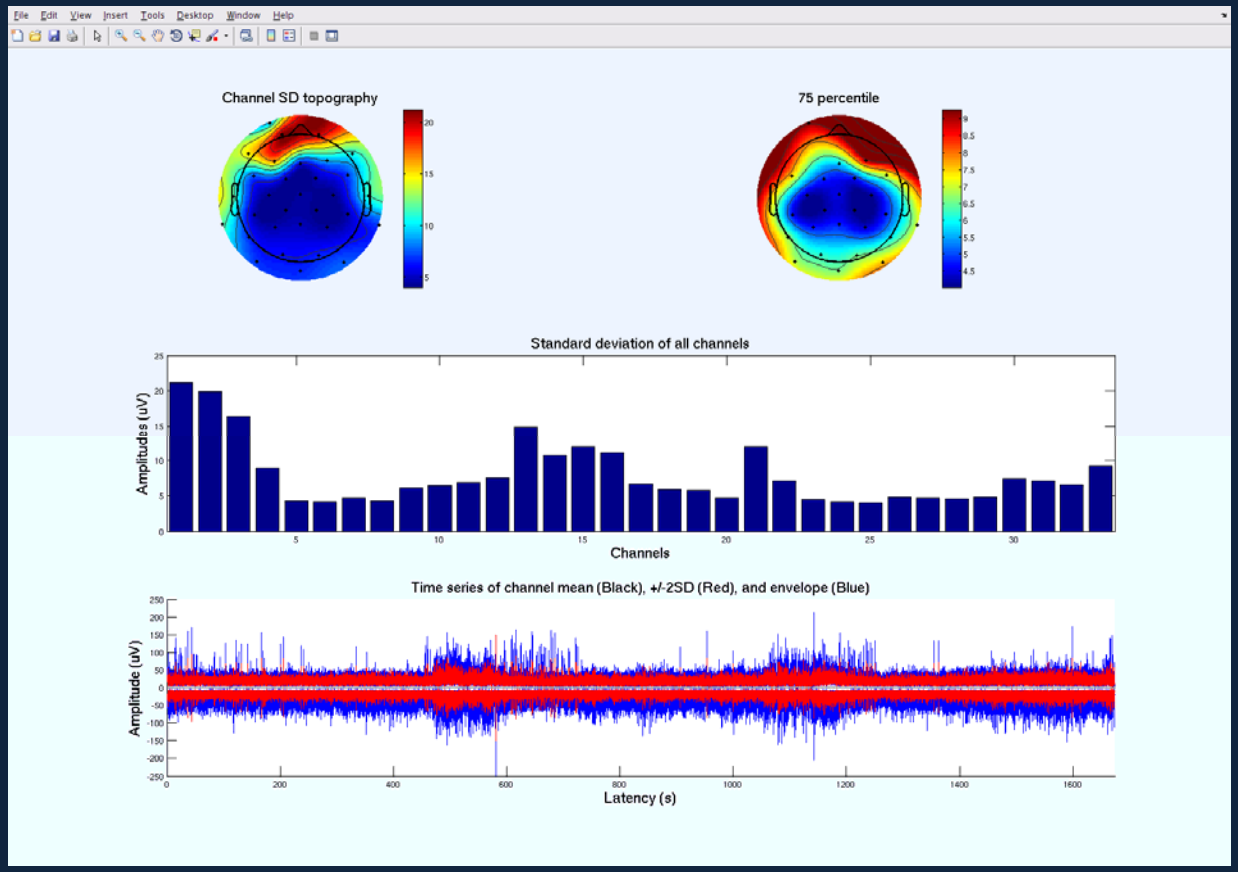
Good default preselected: selected measures are rPDC and dDTF; Model order automatically selected Hannan-Quin, etc.

2. Validate Models



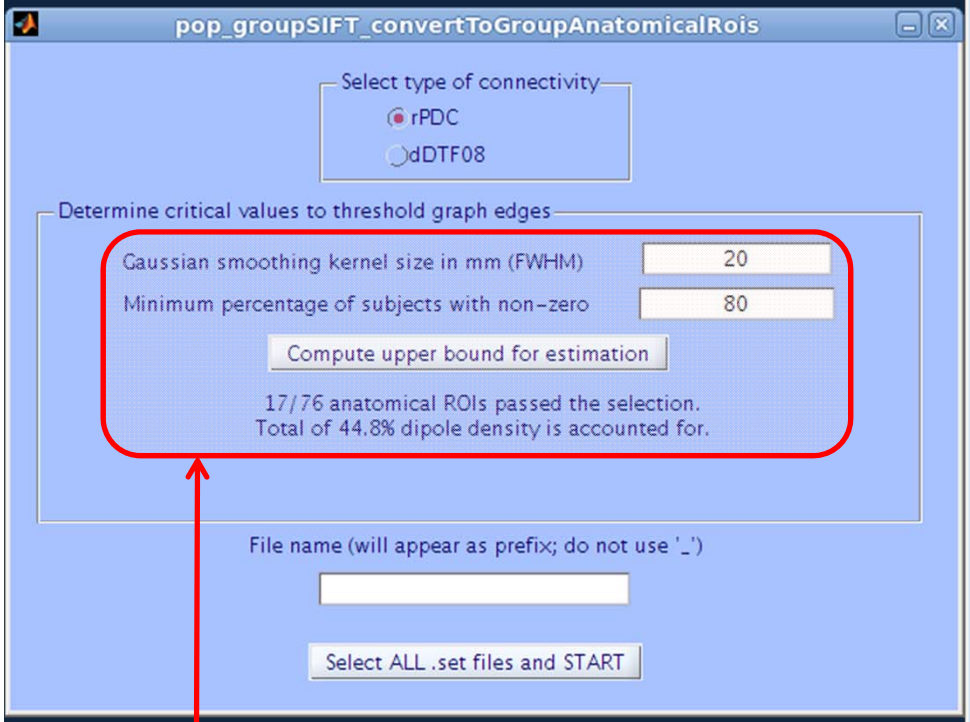
Ensures good *surveyability* across all important validations.

Talking about *surveyability*…

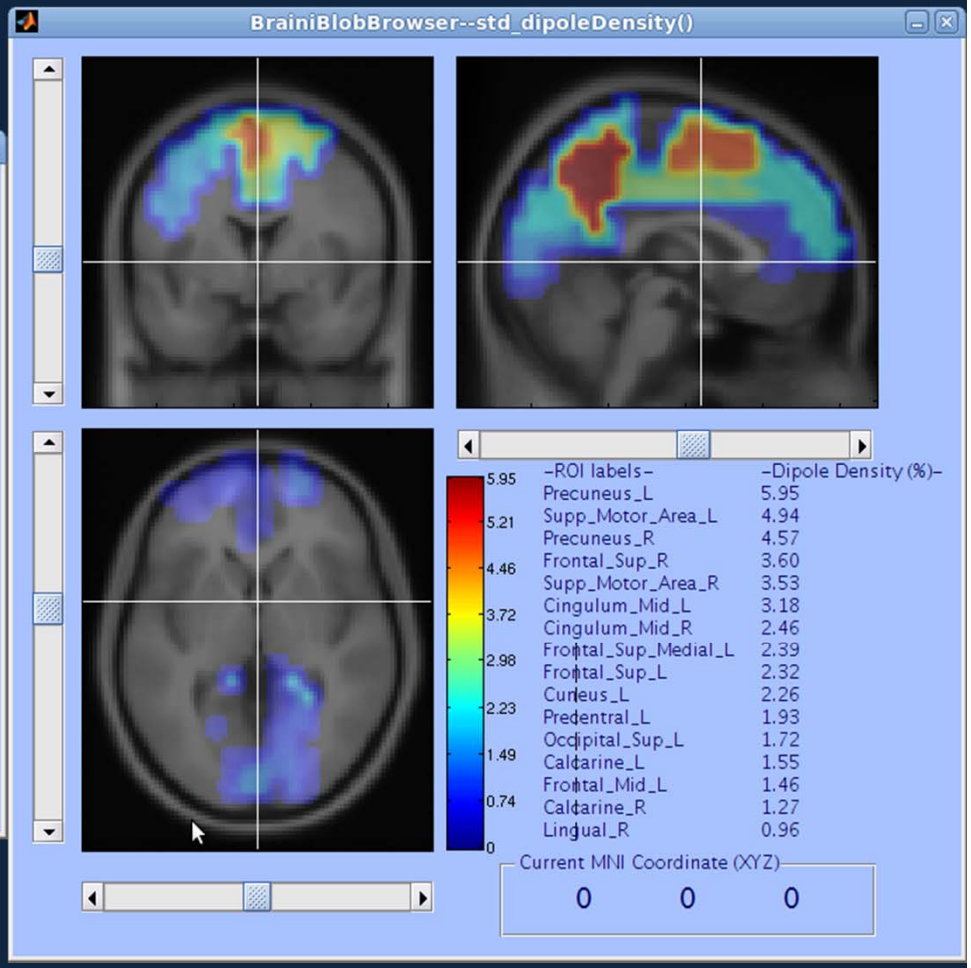


My EEGLAB plugin *trinOutlier()* provides good *surveyability*: it is the only solution to see *all channels* and *all time points* at a glance! Check out https://sccn.ucsd.edu/wiki/TrimOutlier

3. Convert to group anatomical ROI

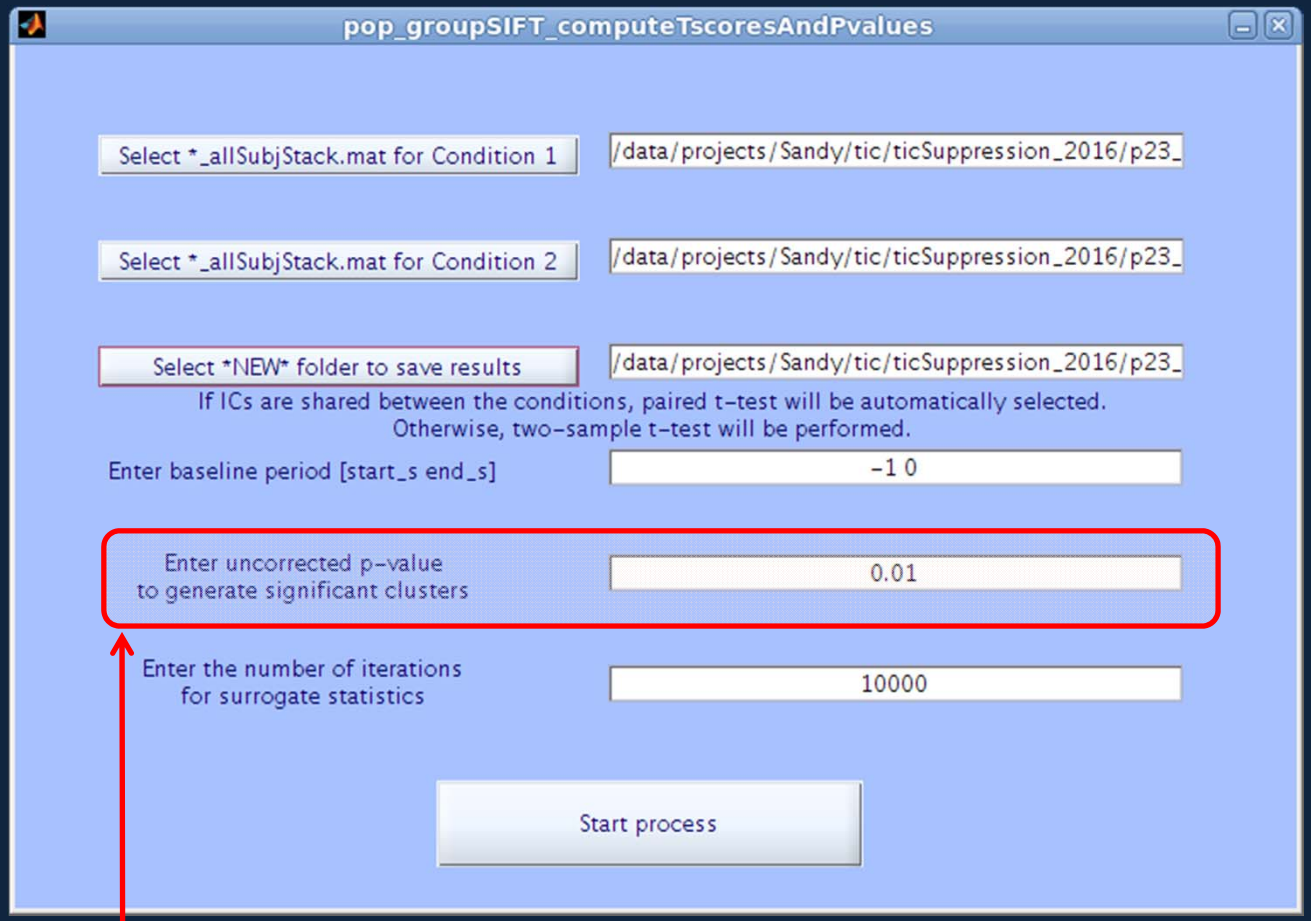


Interactively and iteratively test to determine the final number of edges.



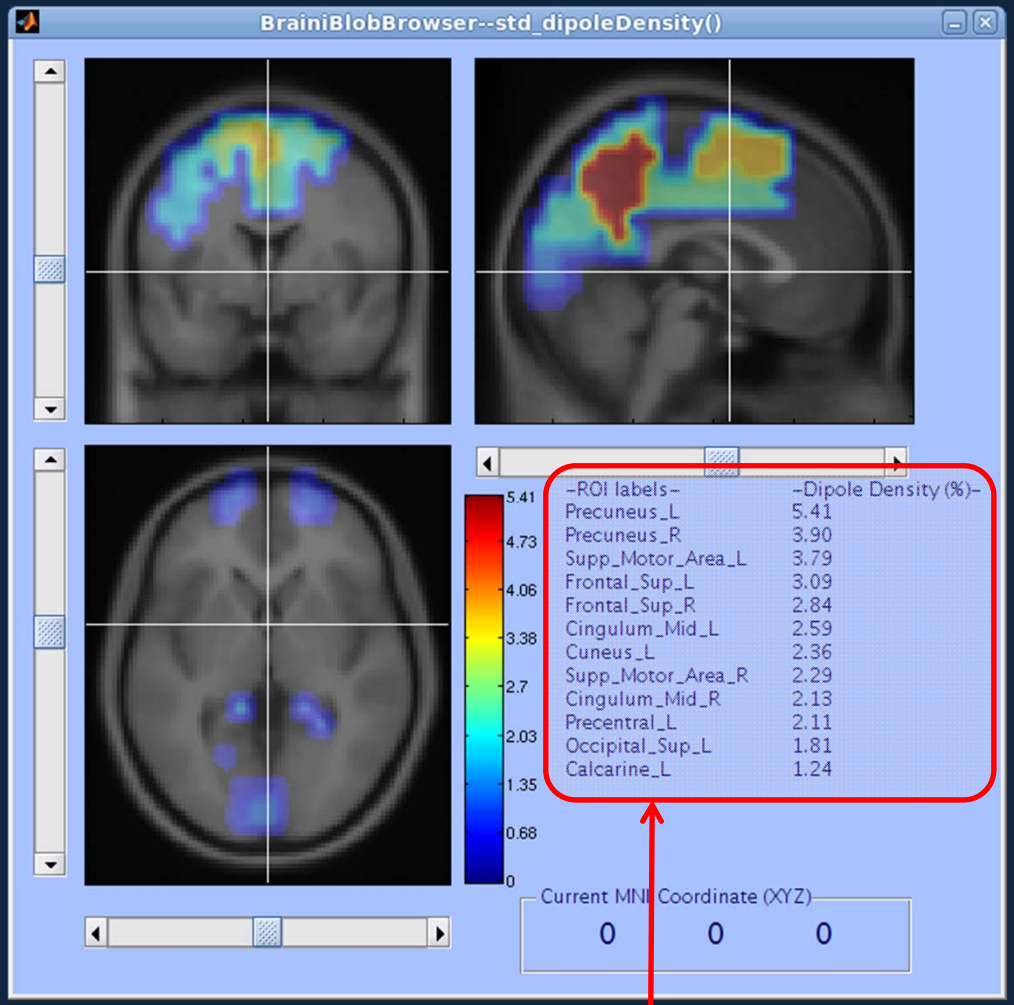
Distribution of dipole density segmented into anatomical ROIs. If a ROI receives no dipole density, no network node there.

4. Compute t-scores and p-values



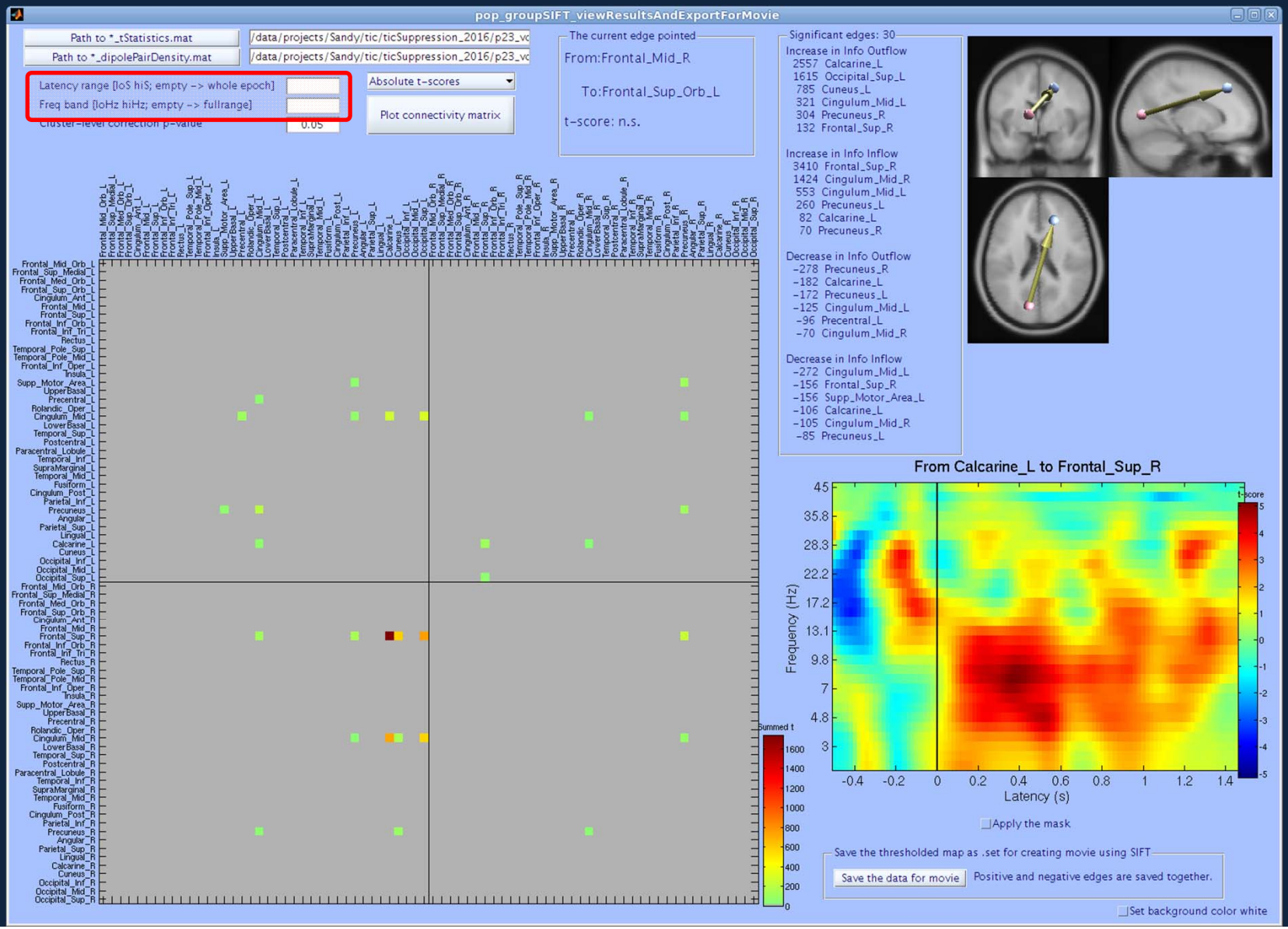
This determines the size of the blobs.

5. Show preselected ROIs

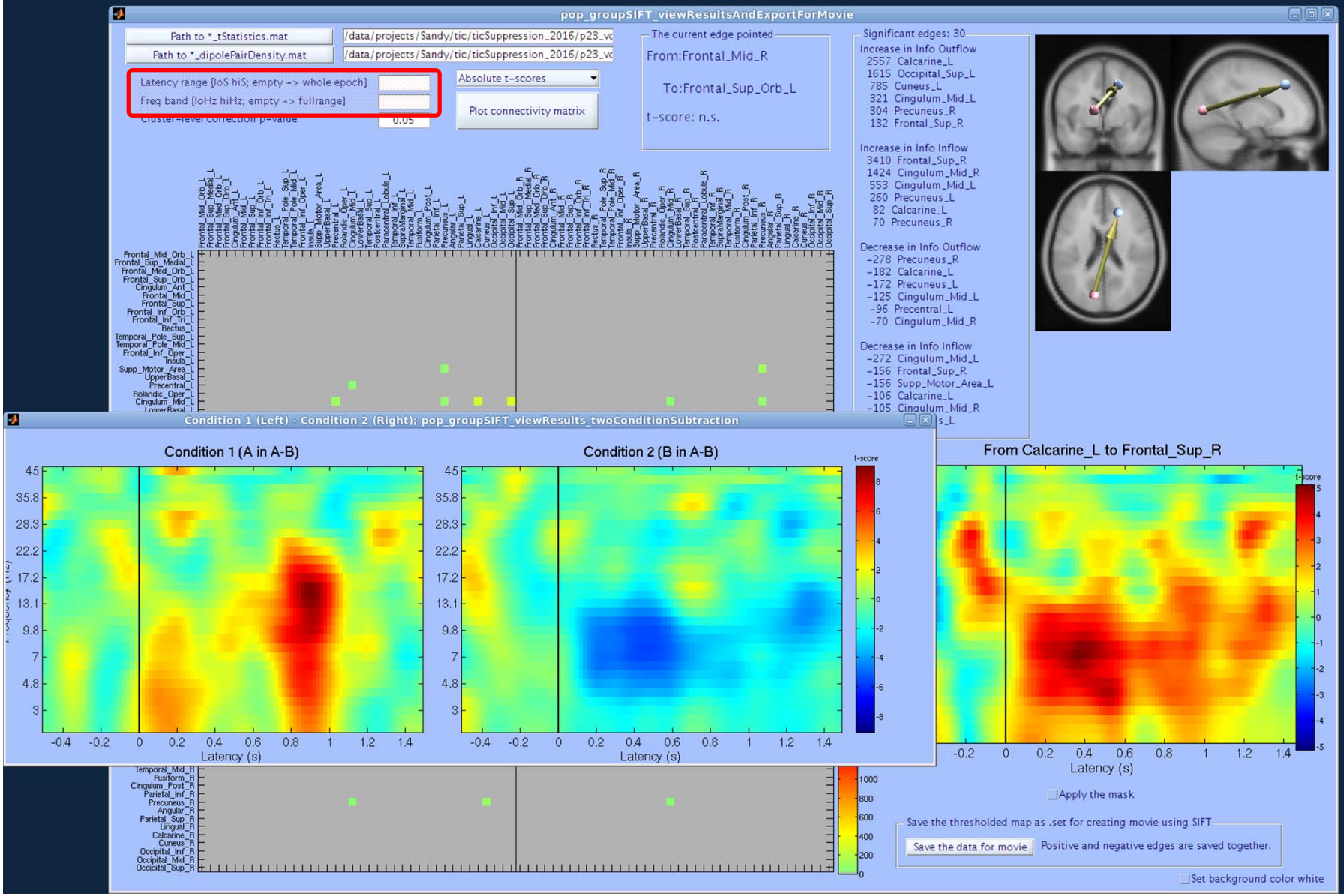


This shows the common ROIs between the two conditions compared.

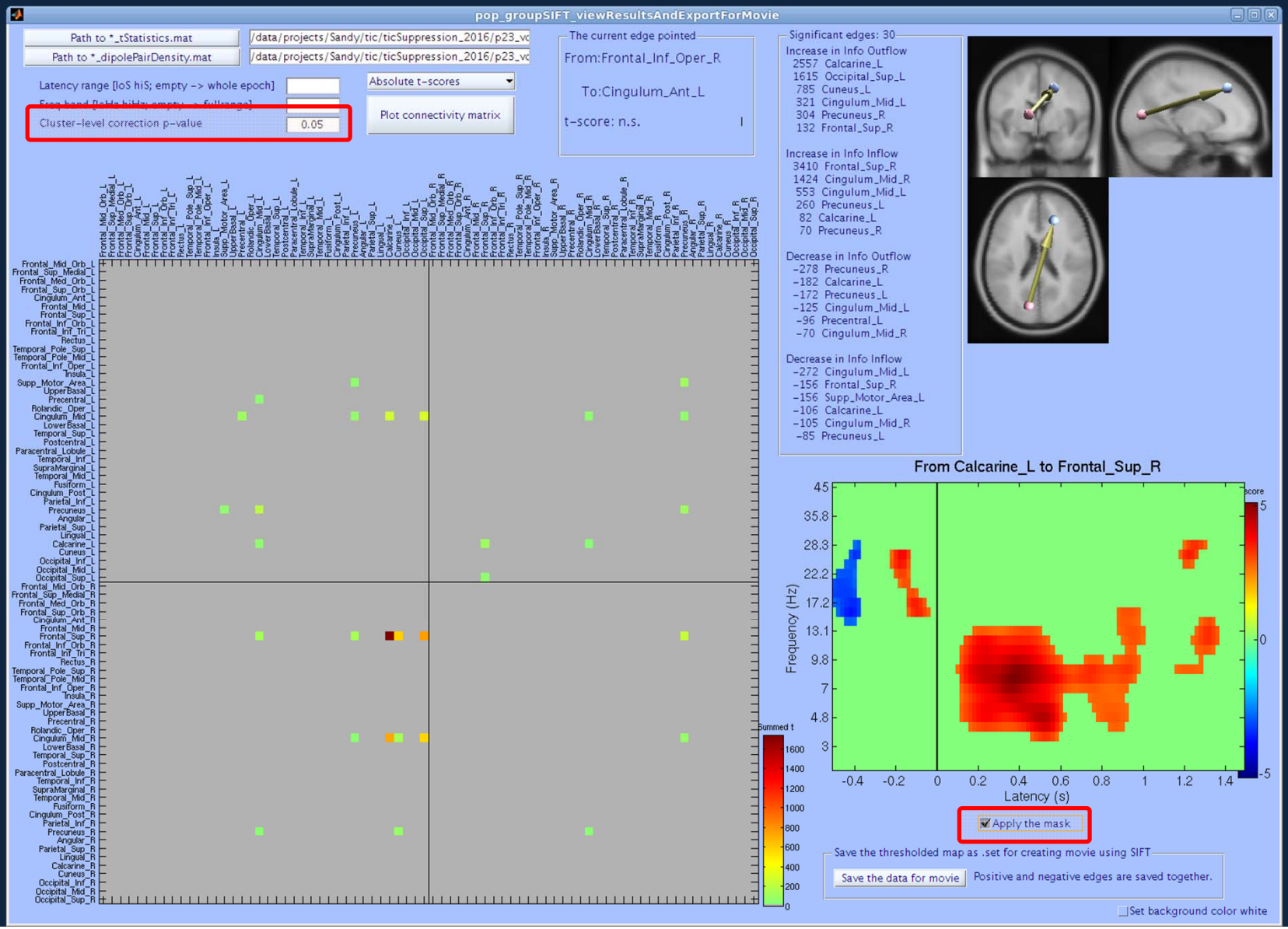
6. View Results and make data for movie



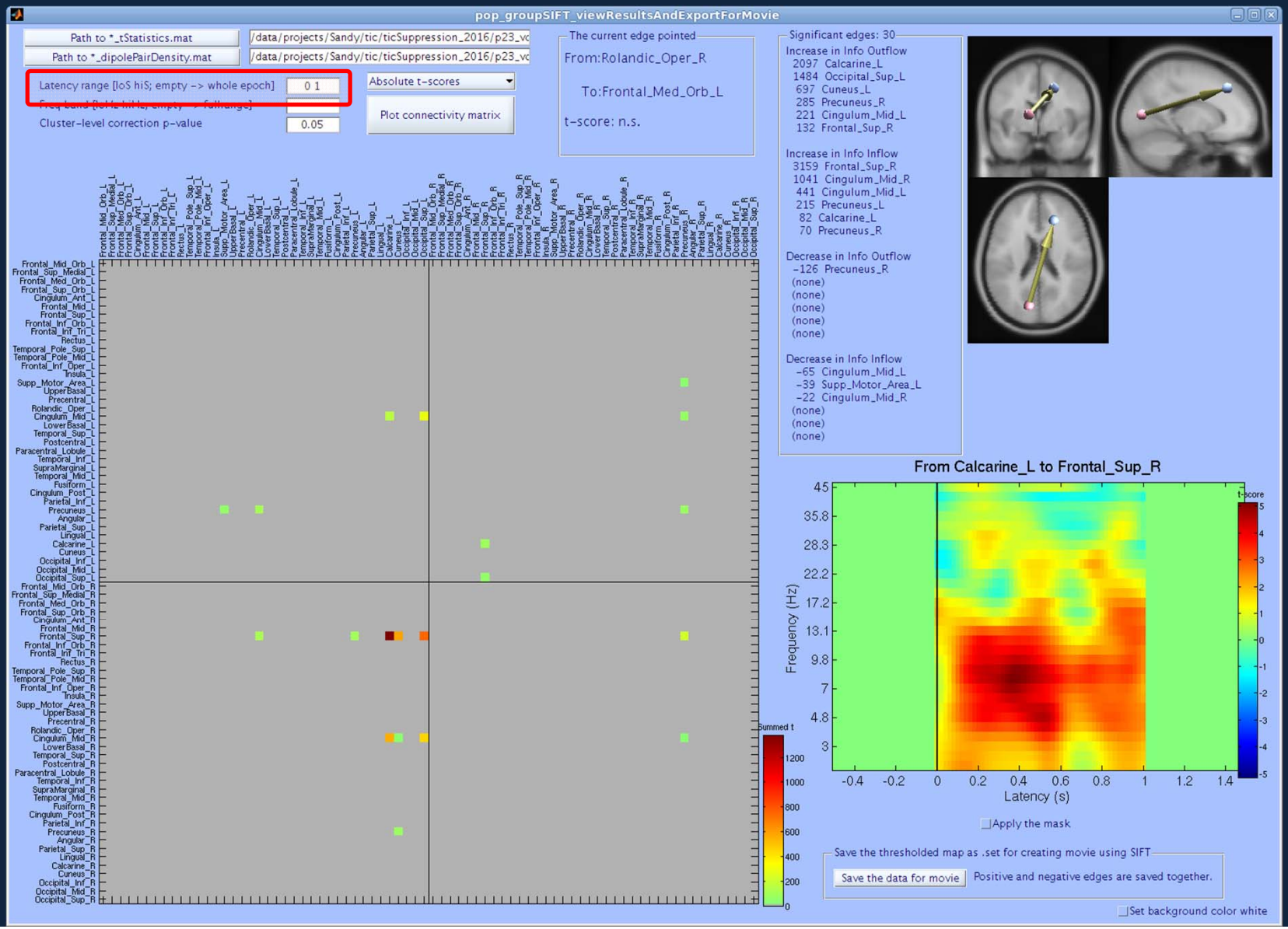
Showing data before subtraction



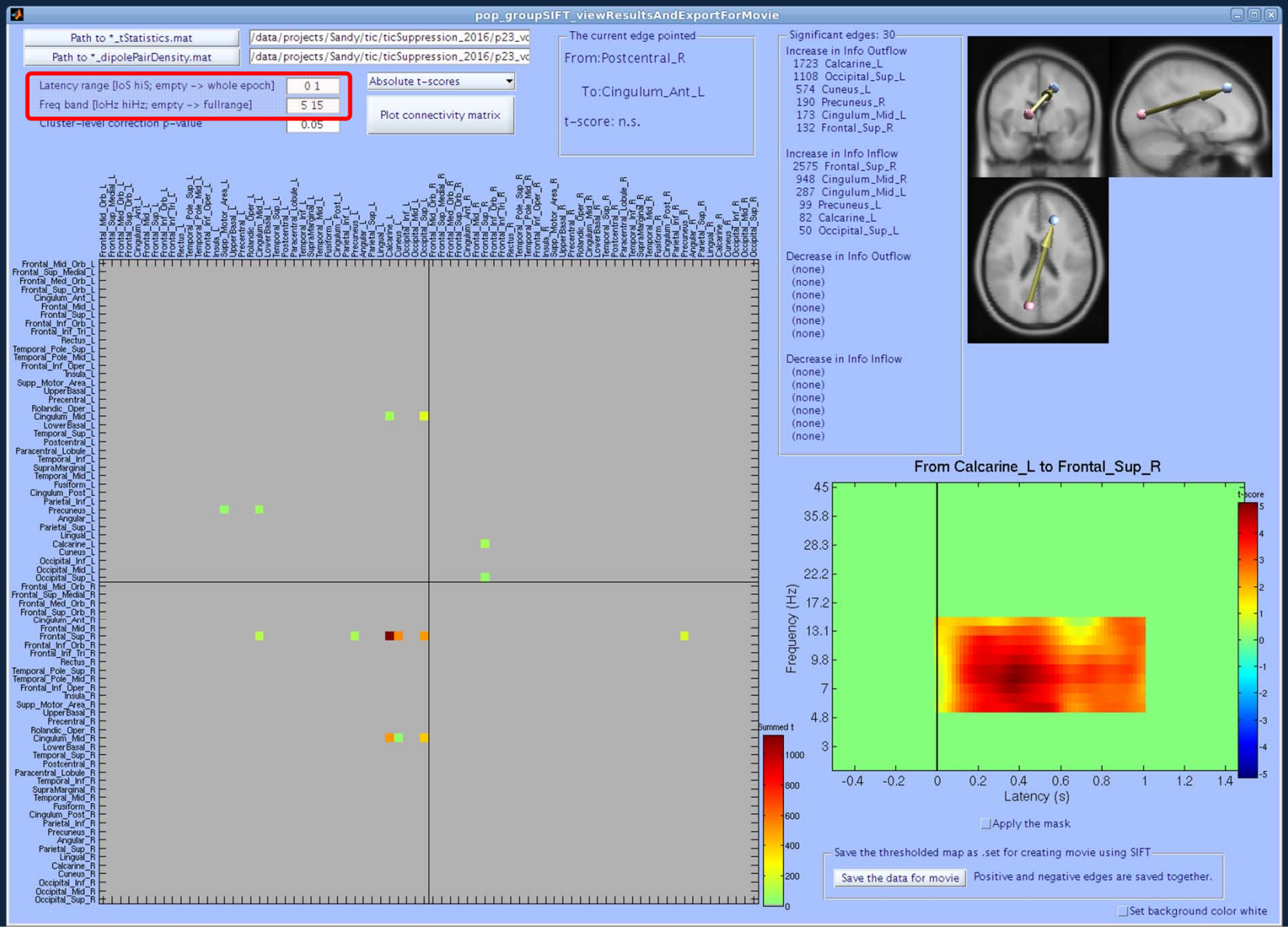
Applying a mask (Cluster-level p < 0.05)



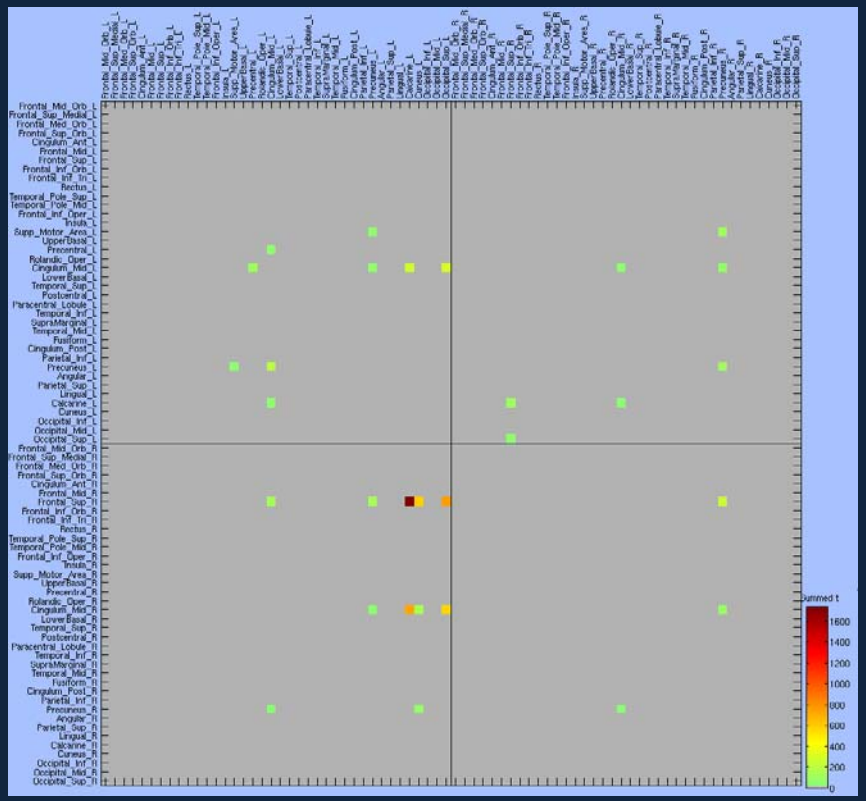
Selecting a time window

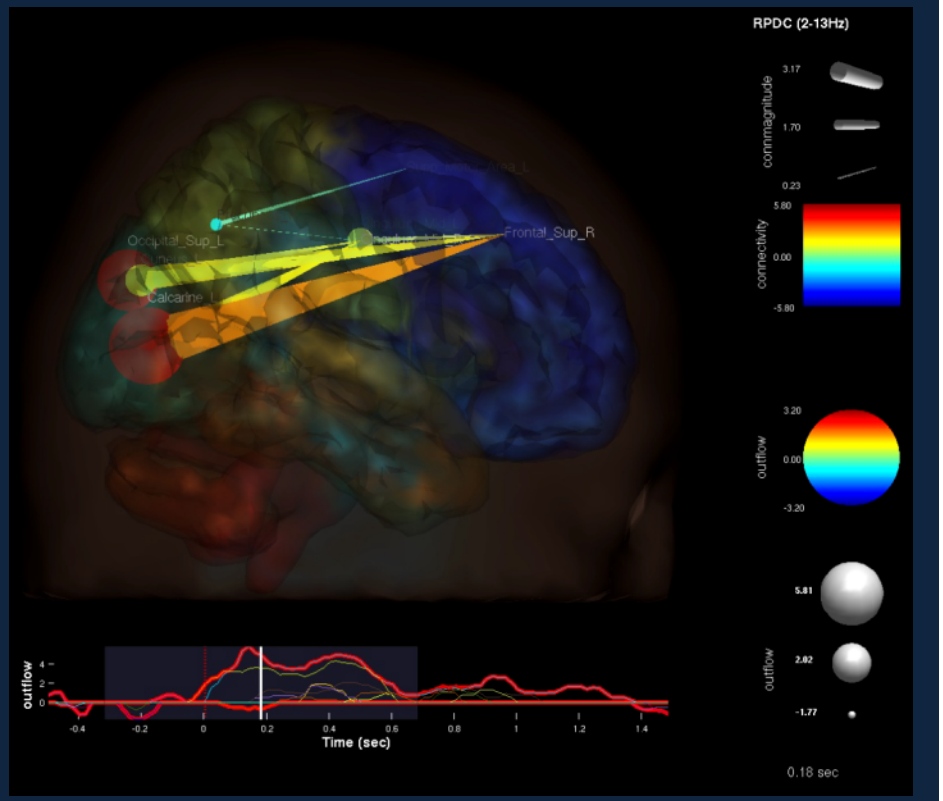


Selecting time and frequency window



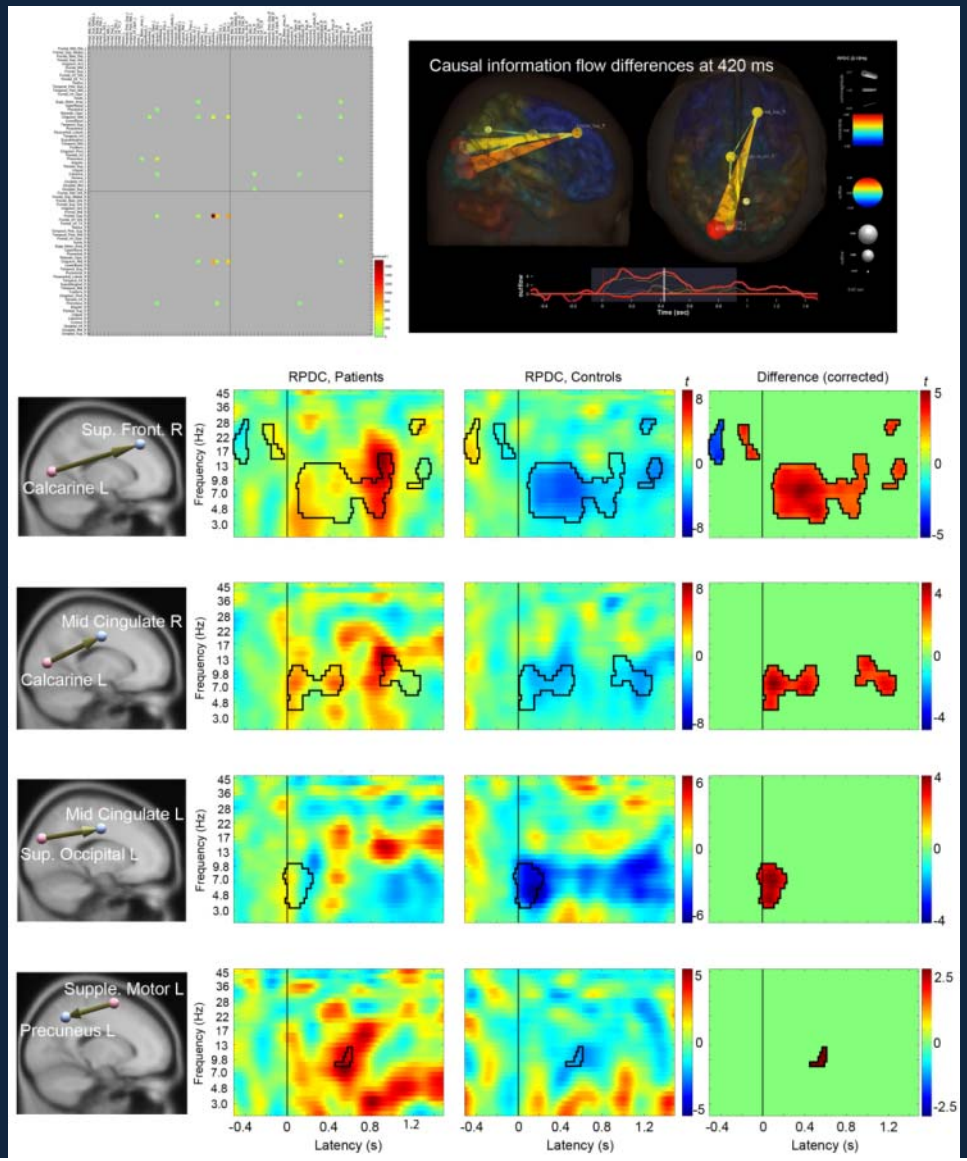
Making a movie using SIFT





- It uses SIFT's GUI to make the movie by feeding single subject dataset replaced with group-mean data.
- Tim coded this BEAUTIFUL visualization. Good job Tim!

Pathological information flow during voluntary blink task revealed in tic patients (PI: Sandy Loo in UCLA, in prep)



Conclusion

- The proposed method works as post-SIFT group-level statistics solution with fully corrected results.
- It is one of the solutions to address post-ICA problems of inconsistent number of ICs as well as their locations across subjects.
- This is ICA purist's solution, typical SCCN work.
- It is not published yet!