Mapping Functional Networks: The ICA and Dual Regression Approach

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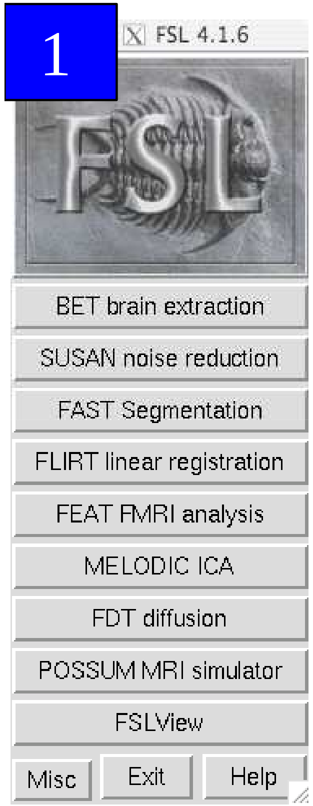
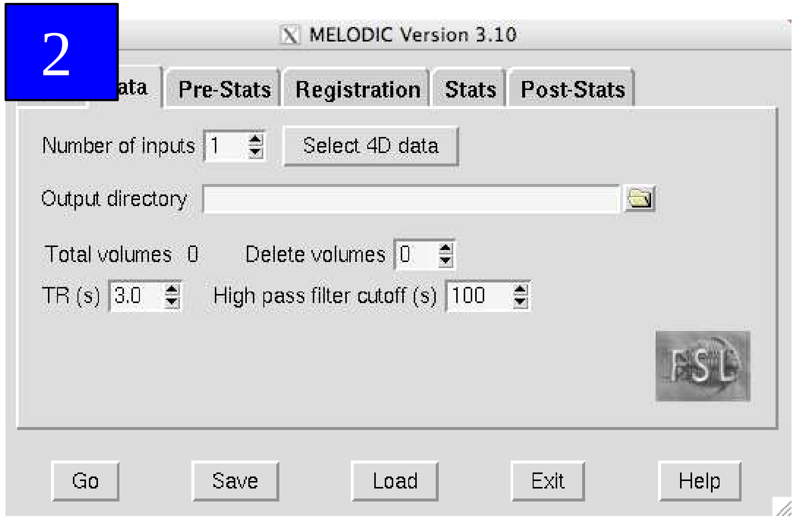
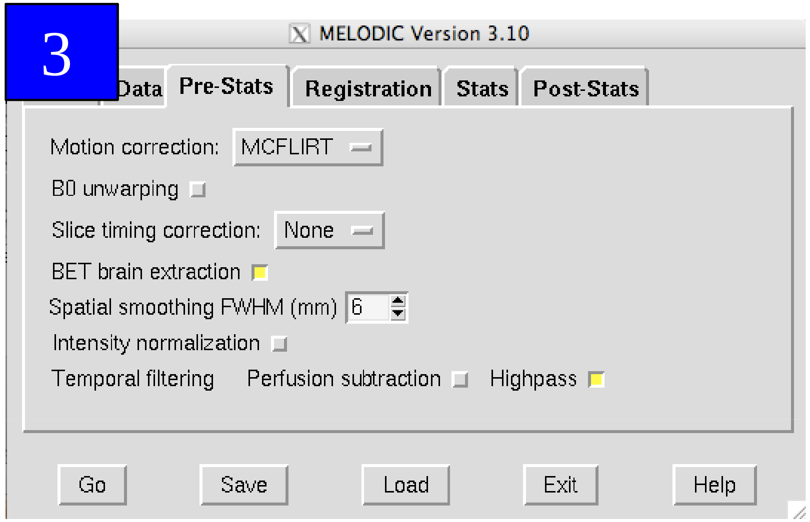
Independent Component Analysis (ICA)

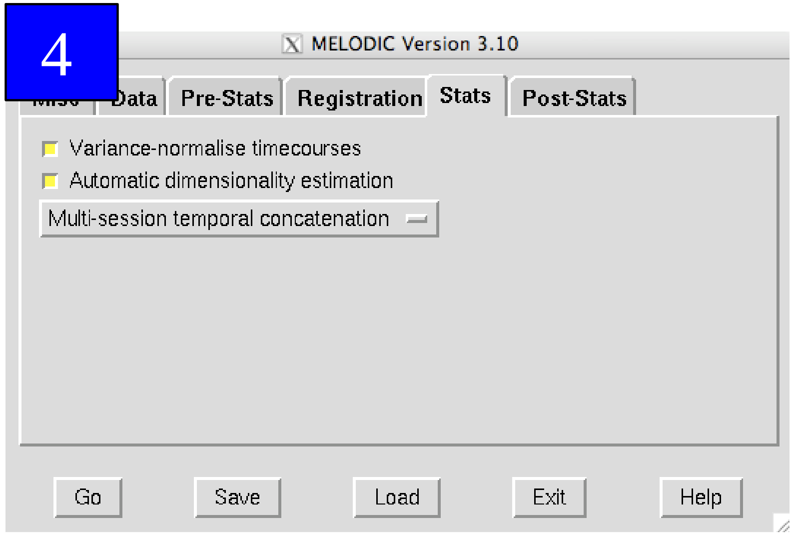
- Explores spatial-temporal properties of resting state fMRI
- A multivariate, data-driven approach that doesn't require a priori knowledge
- Able to extract structured noise (e.g. physiological) and interacting networks → macro-seed regions

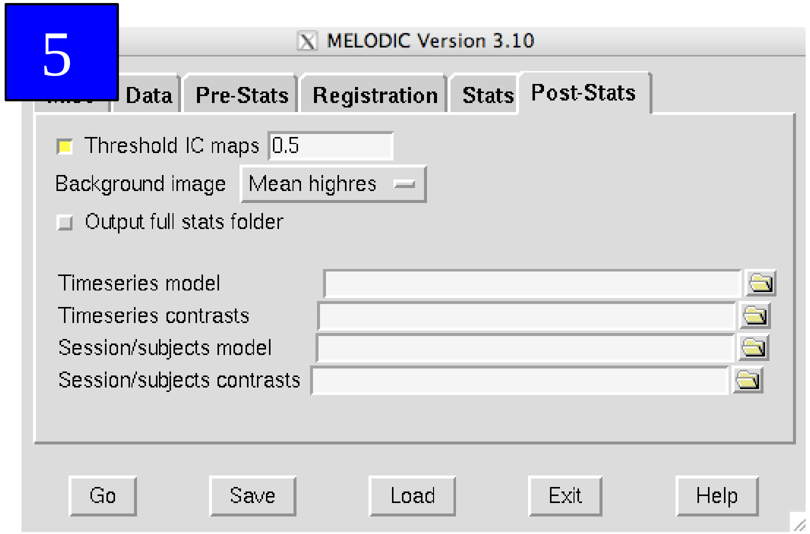
MELODIC is the ICA tool in FSL



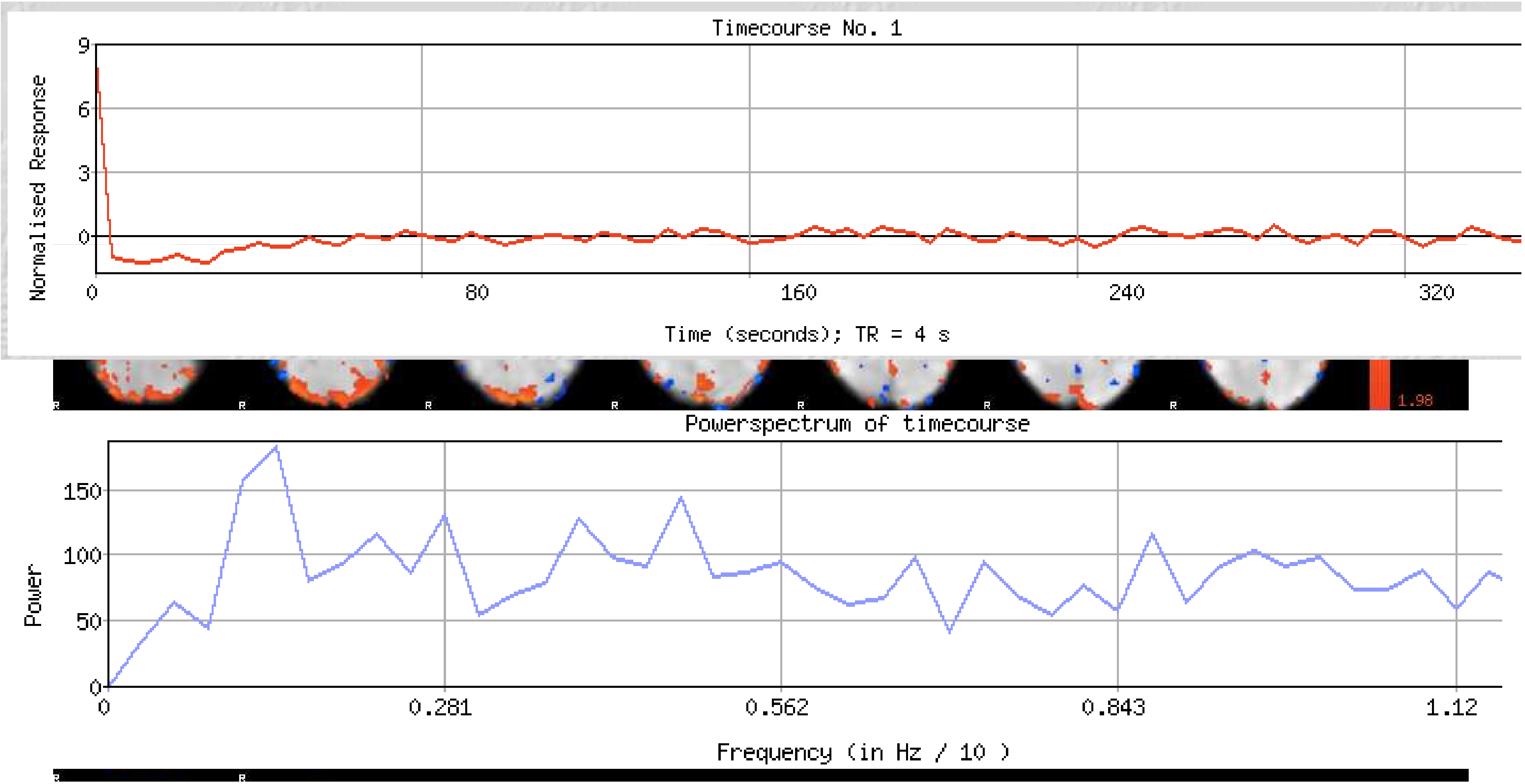








Single-session ICA is useful for denoising fMRI data



Commandline for Denoising

fsl_regfilt –i filtered_func_4D.nii.gz –o denoised_4D.nii.gz –d folder.ica/melodic_mix –f “2,3,10”

Key:

filtered_func_4D.nii.gz: preprocessed fMRI data

denoised_4D.nii.gz: denoised fMRI data output file

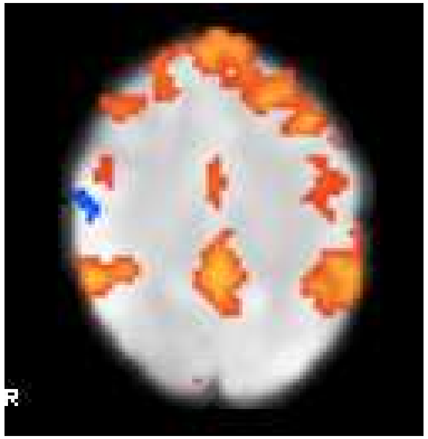
melodic_mix: design matrix with components

-f “2,3,10”: f stands for filter; the number refer to noisy comp’s

Problem: How do you compare components between subjects following session ICA?

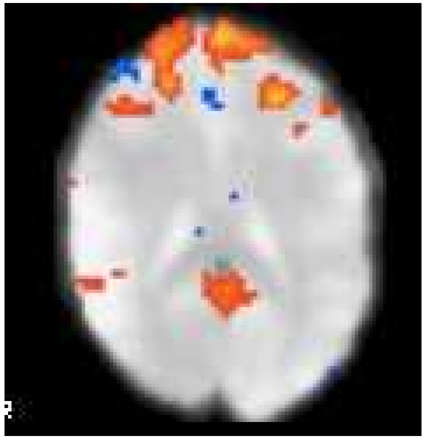
Subject 1

- 20 components
- “DMN” component is 5th component



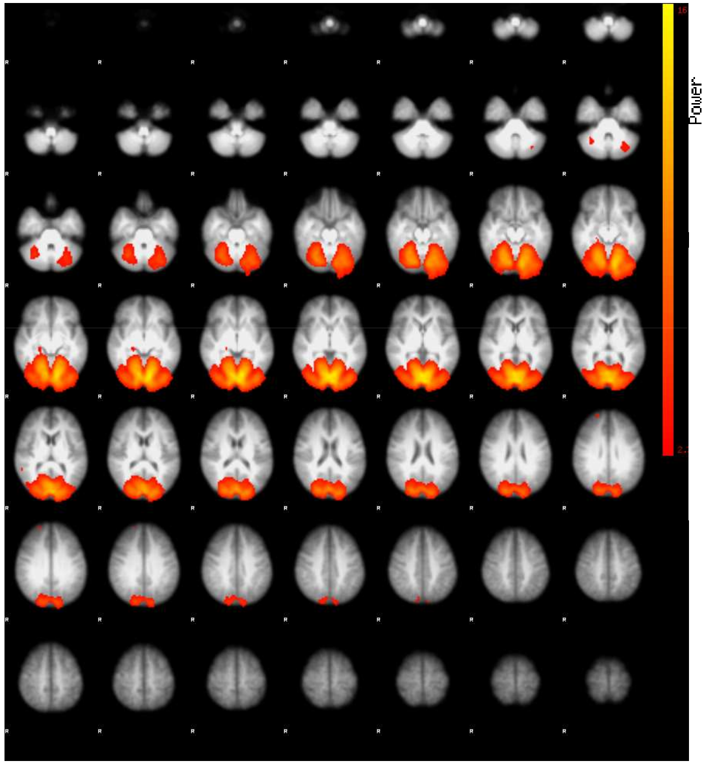
Subject 2

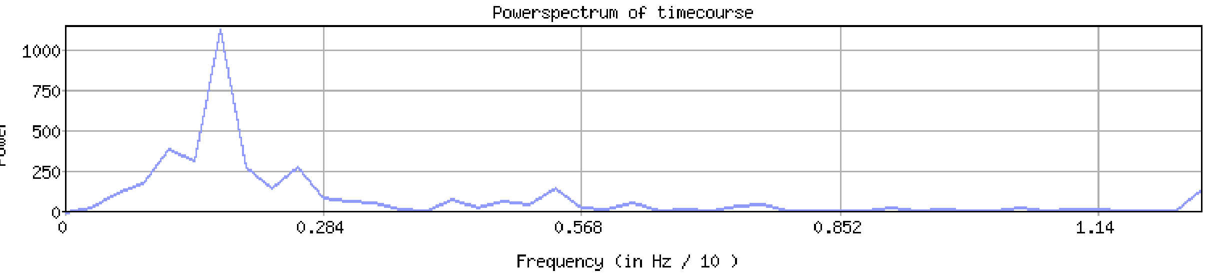
- 13 components
- “DMN” component is 10th component

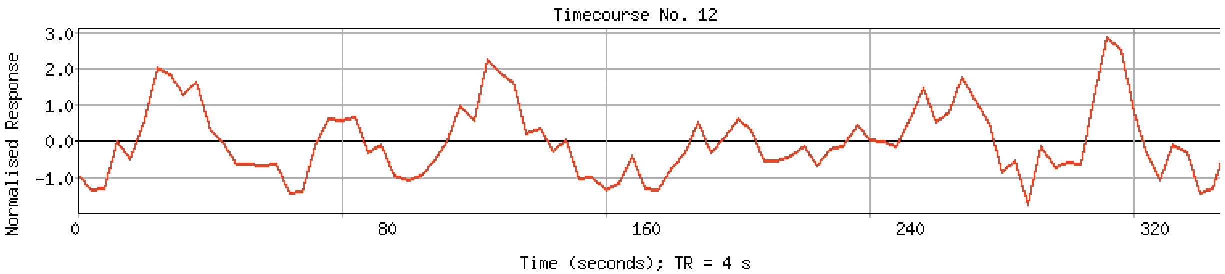


Solution: Run TICA on group to acquire robust group components

Group components allow you to identify RSN's of interest







GLM β's	*F-test on full model fit*	*Contrasts*
PE(1): 0.30 PE(2): 0.15 PE(3): 0.28 PE(4): 3.42 PE(5): 0.91 PE(6): 0.37 PE(7): -0.18 PE(8): 1.71 PE(9): -1.42 PE(10): 1.23 PE(11): -0.80 PE(12): 0.68 PE(13): -0.24 PE(14): 1.09 PE(15): 0.33 PE(16): -0.48 PE(17): -1.45 PE(18): 0.63	F = 0.60 dof1 = 18; dof2 = 15 p < 0.85347 (uncorrected for #comp.)	COPE(1): z = 0.77 ; p < 0.21959 COPE(2): z = -0.77 ; p < 0.78041

Questions

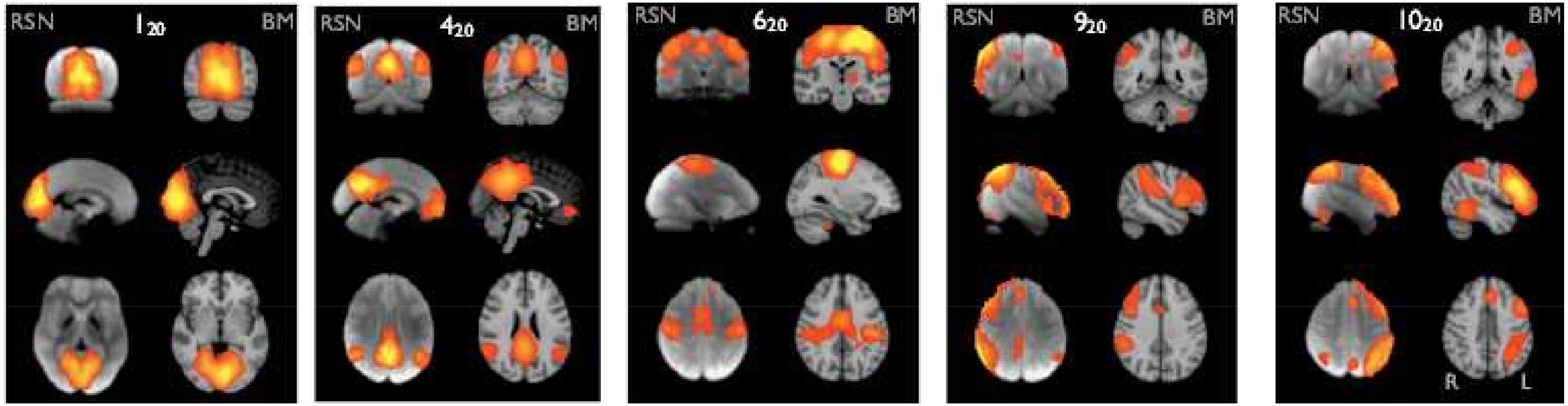
Q: Why standardize into Z-maps?

A: Measures SNR (accounts for background noise)

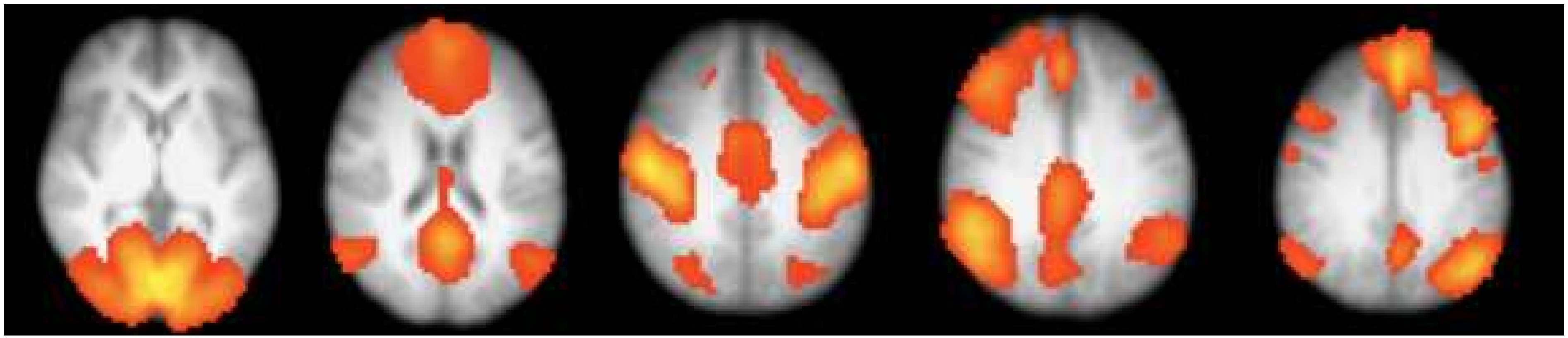
Q: How to apply stricter control for false positives?

A: Increase threshold level (e.g. 0.5→0.66)

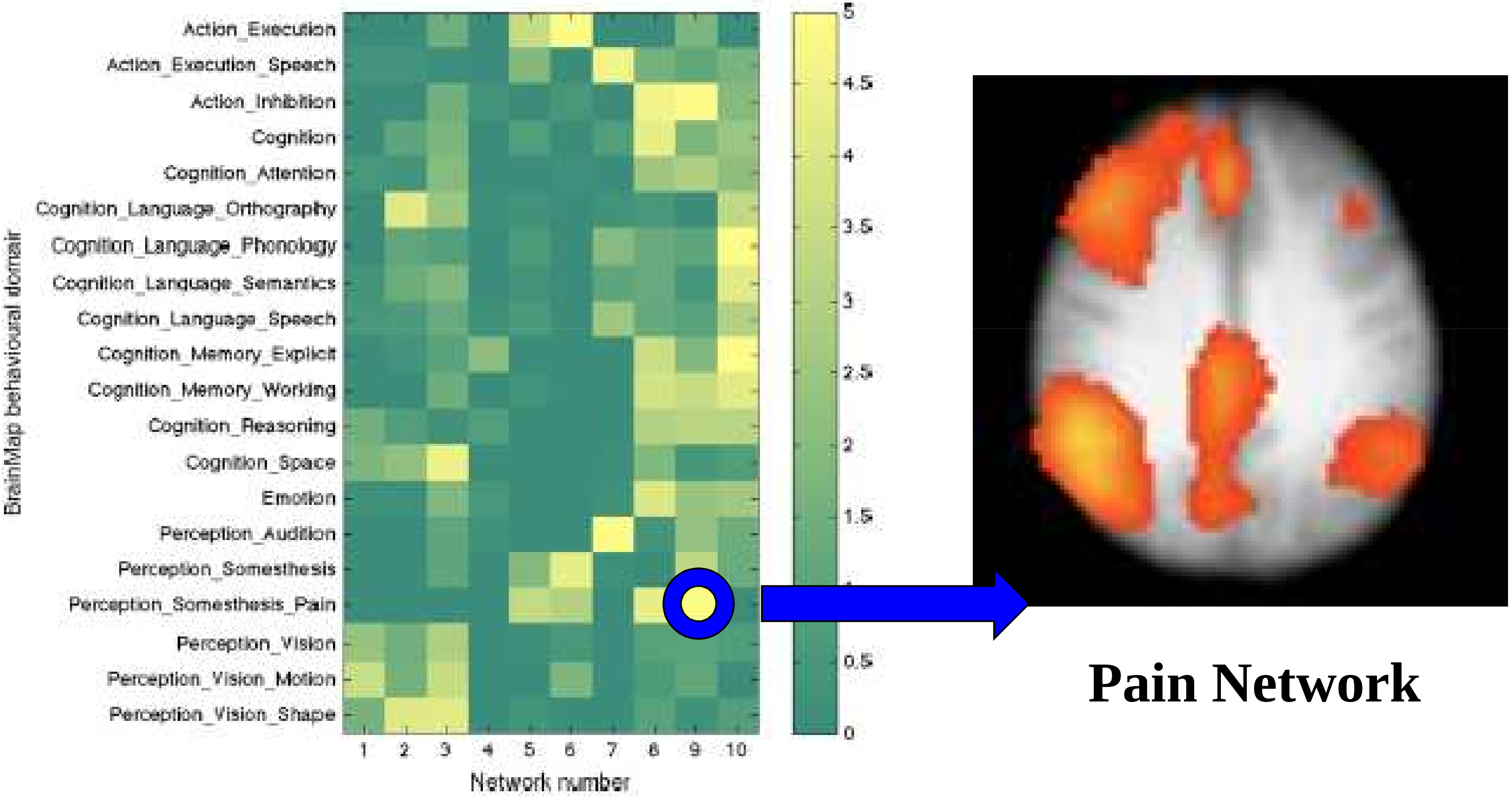
Match ICA group components with previously identified RSN's, such as Smith et al. 2009



Visual DMN Sensorimotor Pain Language



High correspondence between functional networks during task and at rest



Pain Network

Next, use dual regression to assess network differences by group and/or condition

- **Goal:** Derive subject-specific networks corresponding to ICA group components
- Two steps:
  1) Spatial regression → obtain sub. timeseries
  2) Temporal regression → obtain sub. spatial maps

The Dual Regression

- 2 groups: smokers and control

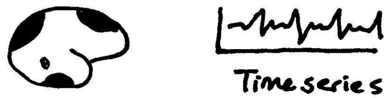
Multi-concat ICA

↓ • temporally concatenates all subs

Components

↓ • Post Hoc regression will reveal significant components

Significant component



↓

Dual Regression

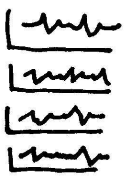
① Spatial Regression

- unthresholded component map is linearly regressed against preprocessed functional data

⇒

Output: Subject timecourses of signal fluctuation corresponding to component

Sub 1:
Sub 2:
Sub 3:
Sub 4:

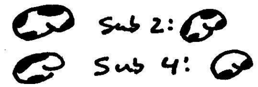


② Temporal Regression

- Within-subject time courses are variance-normalized and regressed against fMRI data, converting each timeseries to a spatial map of component

Output: Subject spatial maps for component

Sub 1: Sub 2:
Sub 3: Sub 4:

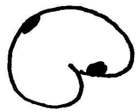


⇓

③ Randomise

- Spatial maps probed voxel-wise via multiple regression

Output: Group difference in co-activity



Smokers v. control

Commandline

dual_regression groupICA.gica/groupmelodic.ica/melodic_IC 1 design.mat design.con 500 output `cat groupICA.gica/.filelist`

KEY:

melodic_IC: 4D file with ICA group components (can split)

design files: your design matrix for cross-subject modelling

ouput: the name of your output directory

.filelist: filepaths where preprocessed, standard space 4D files are stored

DR Output Files

1) **dr_stage1_sub#:** timeseries per subject w/ separate column for each component
2) **dr_stage2_sub#:** spatial maps for each subject with separate 3D image per component
3) **dr_stage2_subZ:** normalized spatial maps
4) **dr_stage2_ic{#}:** 4D file of group component, each 3D image is one subject
5) **dr_stage3_ic{#}:** cross-subject statistics based on your design matrix (randomise)

Brief synopsis of third-level analysis:

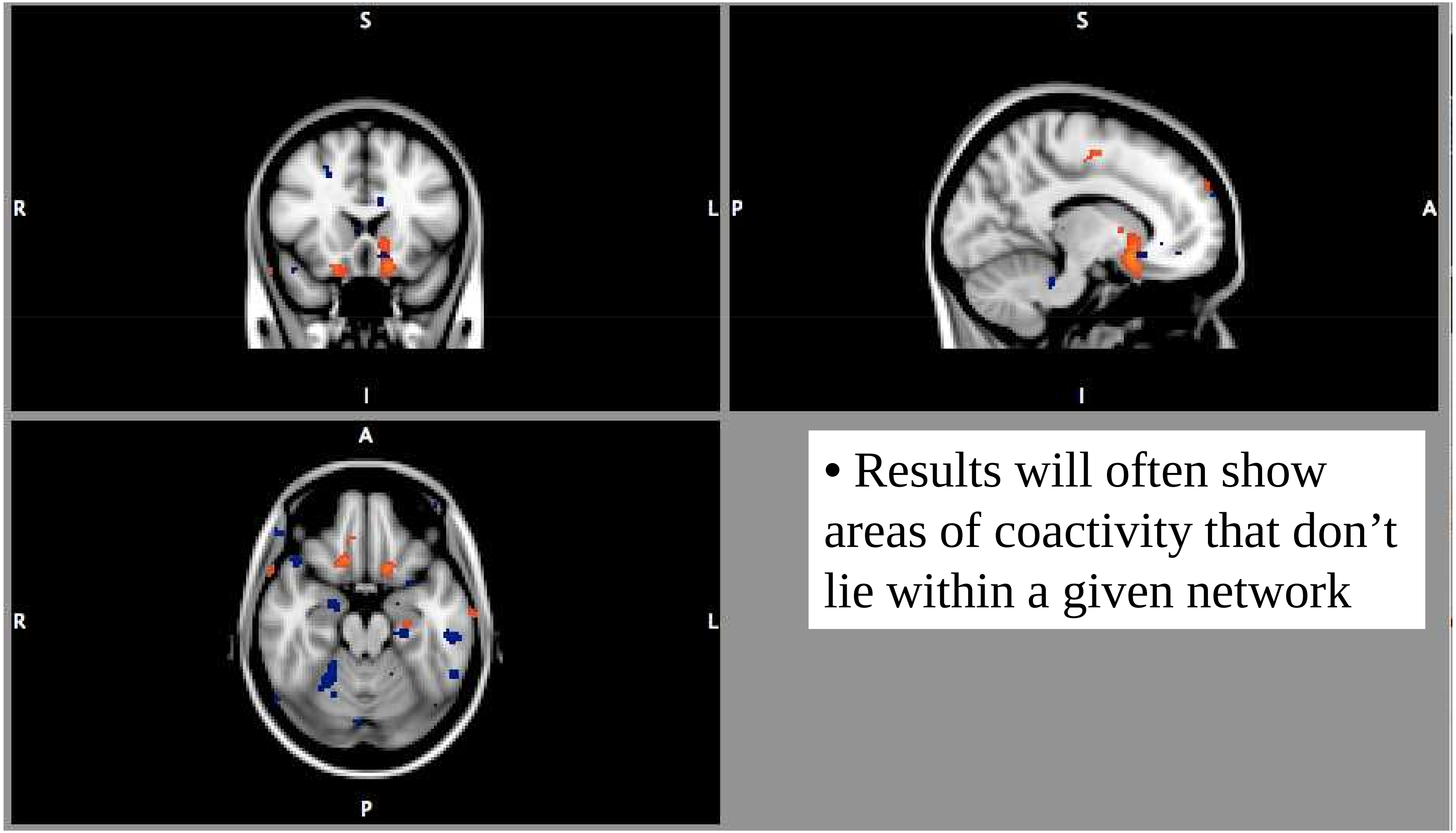
- Experiment with 2 sessions per subject:

- 1) Run the **TICA** to get group components by adding all subjects/sessions as input. Order the inputs so that the two sessions are next to each other (e.g. subject one's session 1 and 2 are inputs 1 and 2; subject two's session 1 and session 2 are inputs 3 and 4 ...etc.). This will make averaging easier later on.
- 2) For your component of interest, say IC8, run **Dual Regression** with a *fixed effects matrix.

- **I'm pretty sure the matrix you enter in here is mostly irrelevant though, since your main interest is in getting subject-level IC8 maps (meaning you can ignore the dr_stage3 output, which the matrix is for)

- 3) Use **fslsplit** on the dr_stage2_IC8.nii.gz file. This is a 4D image file where the subjects' IC8 maps are stacked. Now the split volumes will be numbered in the same order as your inputs.
- 4) **fslmerge -t** each subject's two session maps to get a single subject 4D file, then use **fslmaths -Tmean** on that file to get the subject's average.
- 5) Finally, **fslmerge -t** ALL of the averaged subject files to create an IC8 4D file. The file is stacked so that each 3D image represents a single averaged subject.
- 6) Feed this IC8 file into randomise with your design matrix of choice.

Dual regression helps determine how components differ by condition



- Results will often show areas of coactivity that don’t lie within a given network

Possible Analyses

1) Examine differences in functional networks by condition or subject populations → randomise

   Example: How does the DMN of smokers differ from non-smokers?

   Debate over control-only group components

2) Use a priori knowledge to examine changes in network *inter-activity* → correlate component timeseries in stage1 output

   Example: In smokers, how is the anti-correlation between the DMN and ECN affected by nicotine withdrawal?

3) Perform covariate analysis by constructing appropriate matrix for randomise → randomise w/ demeaned behavioral variable

   Example: How does network activity vary with cortisol level?