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Seed analysis and PPI

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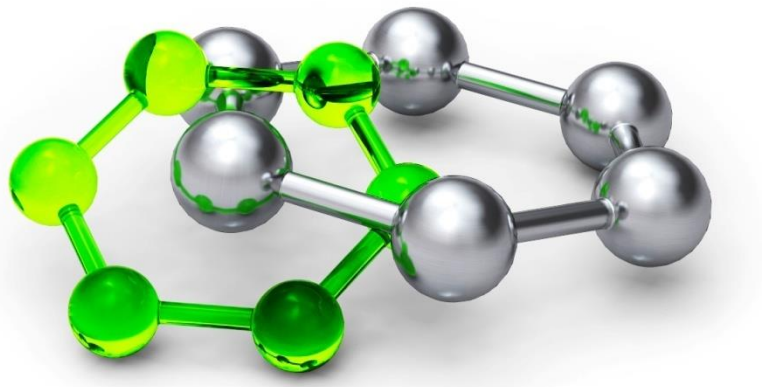

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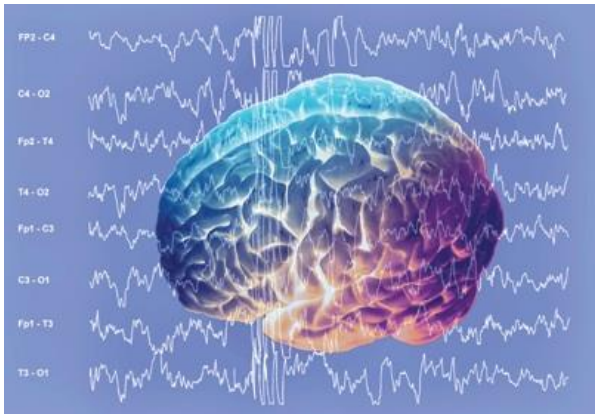
OP Research and Development for Innovation

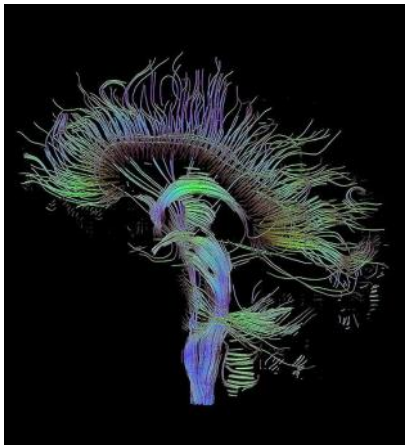
Connectivity

- Functional – observed statistical dependencies between time series from particular brain regions



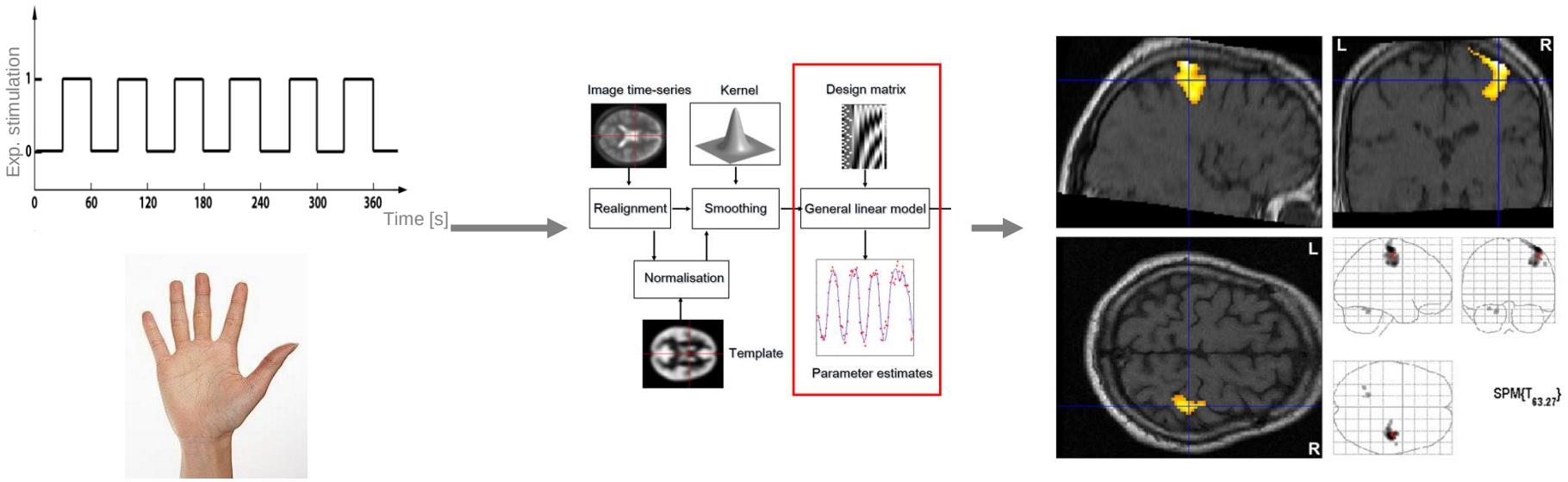
- Effective – causal effect of influence that exerts one neuronal system over another (**PPI**, DCM)

- Anatomical – real connections between neuronal populations, presence of axonal connections



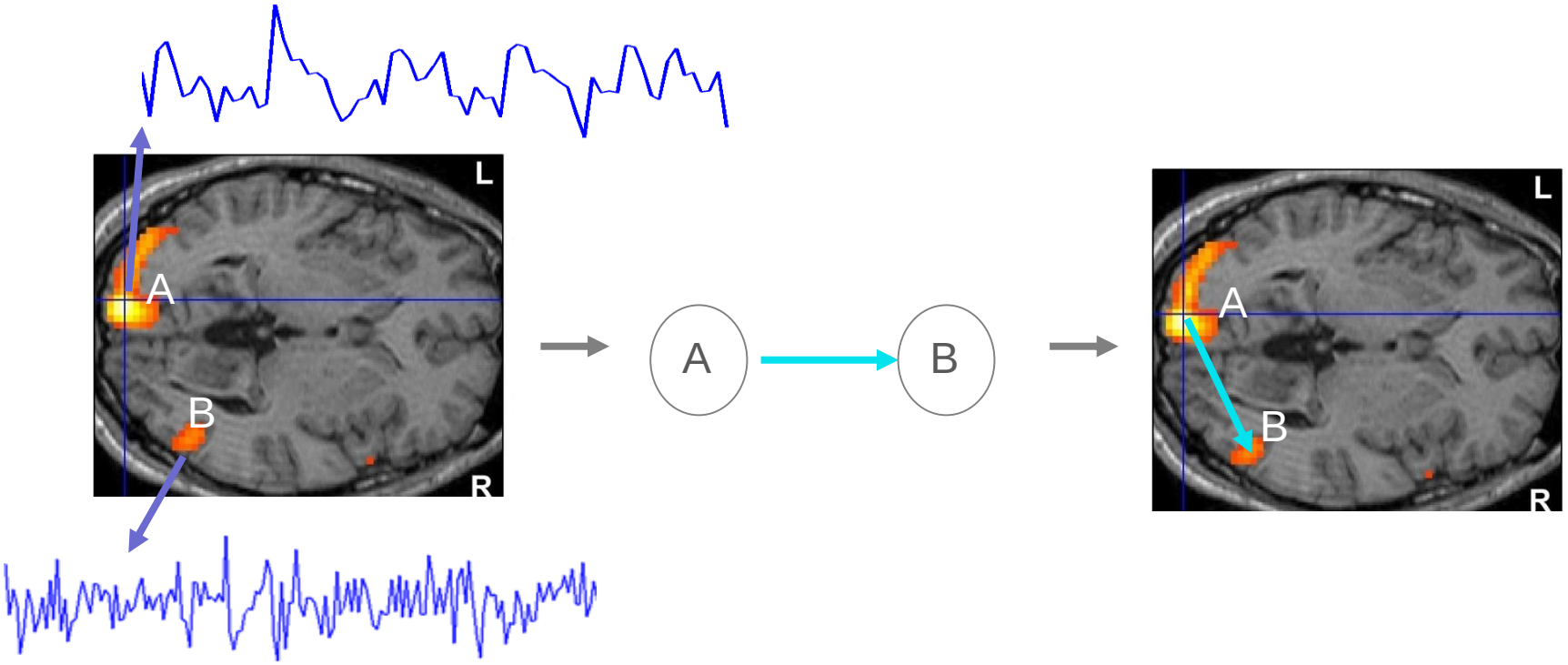
Functional specialization

- Cortical area belonging to a part of perceptual or motor processing
- Example – localization of motor center for right hand



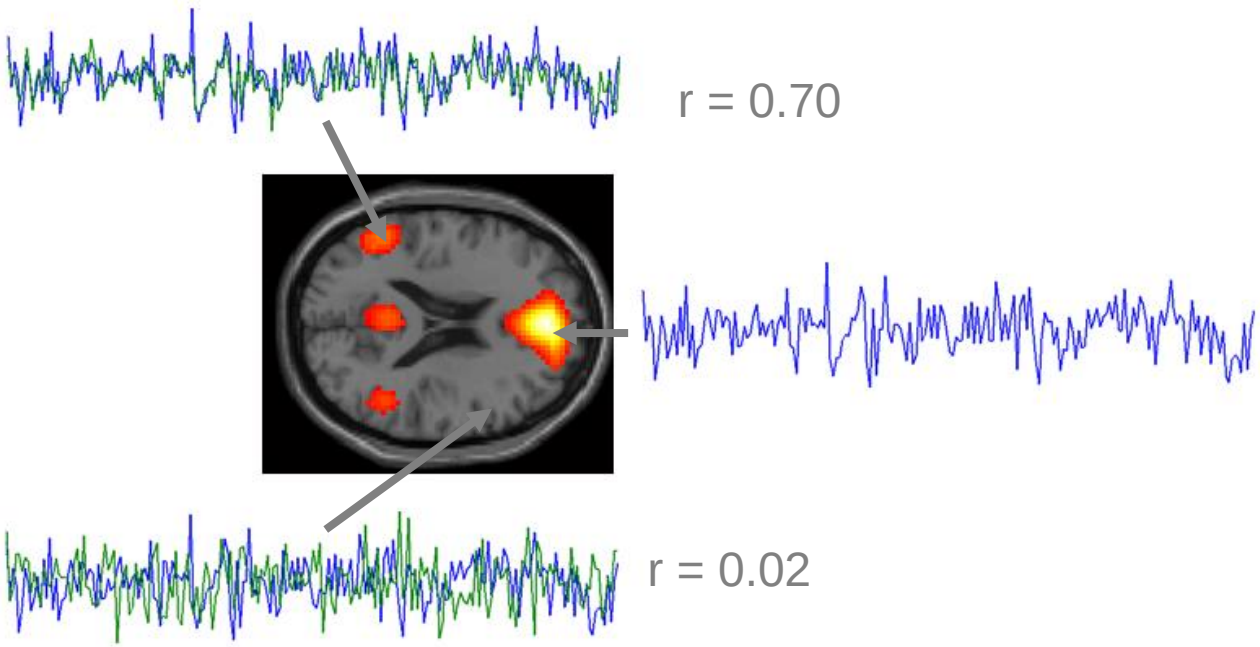
Functional integration

- Mutual connection of several reasonable areas for execution of specific function



Introduction to seed analysis

- the most simple, basic variant of FUNCTIONAL CONNECTIVITY
- observing of „correlations“ between BOLD signals from seed and other brain voxels



SEED

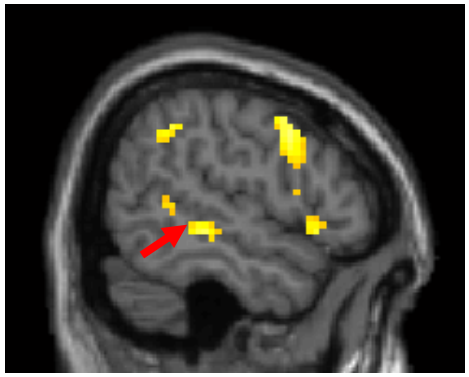
SEED selection

based on *a priori* hypothesis

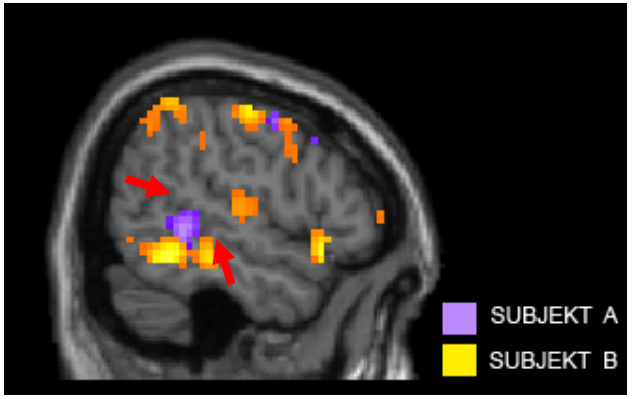
based on the group analysis

group coordinates

individual coordinates



!CIRCULARITY!



SEED – typically first PCA component of signsls from spherical region centered on coordinate

APLICATION of GLM

- we can use the same way (GLM approach like in the case of task) for correlation analysis
- design matrix contains seed signal
- testing of the seed signal effect is analogical for correlation coefficient computation

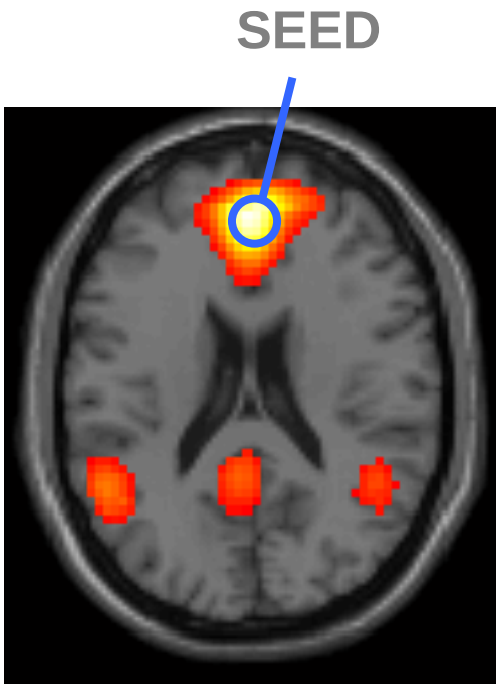
$$T \sim r$$

INTERPRETATION

- functional connectivity between SEEDand other regions of brain

- in the case of dataset with task, we can interpret it as “background” functional connectivity
- in such a situation, the FC can be independent of external stimulation

- typical usage: RESTING STATE networks

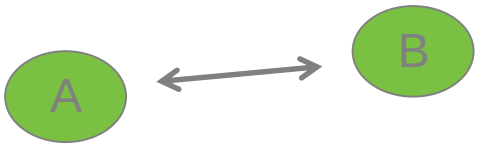


Default Mode Network

PPI INTRODUCTION

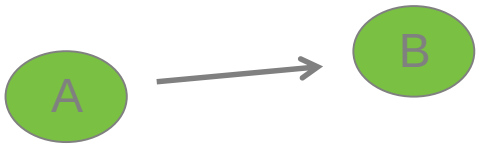
- variant of effective connectivity

SEED analysis



CORRELATION

PPI analysis



CHANGE IN CORRELATION CAUSED BY EXTERNAL STIMULATION

- observing of the influence of external stimulation on linkage between SEED and other brain regions
- PPI asses the link in the direction from SEED to (connected) region

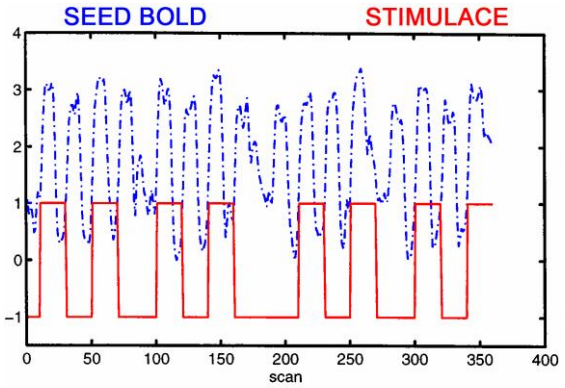
SEED at PPI analysis

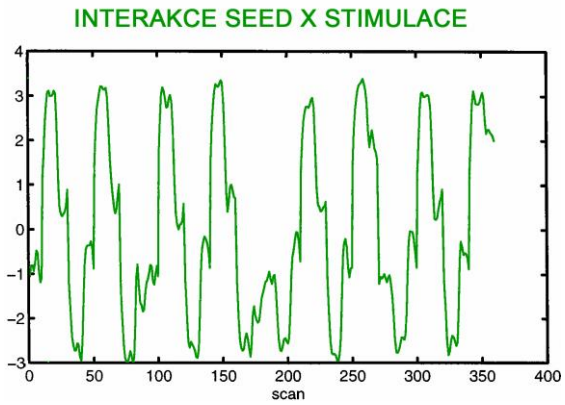
- the same problems as in SEED correlation analysis

- hypothesis vs. fMRI data-driven approach
- group vs. individual coordinates

PPI a GLM

- PPI Design Matrix contains three regressors:
  - SEED BOLD signal - statistical correlation with SEED
  - modeled task-based BOLD signal
  - interaction of stimulation function and the SEED BOLD signal
    - dynamic response to stimulation from seed





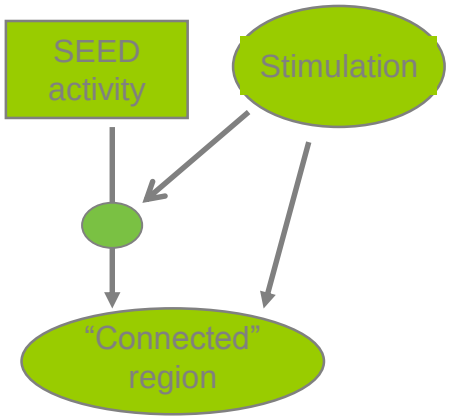
- GLM: $$x_i = x_{SEED} \times g_P \cdot \beta_i + \left[x_{SEED} g_P\right] \cdot \beta_G + \varepsilon_i$$

x_i .. BOLD signal in “connected” region
x_{SEED} .. SEED BOLD signal
g_P .. stimulation
b_i .. efect of interakce
e_i .. residuals in “connected” region

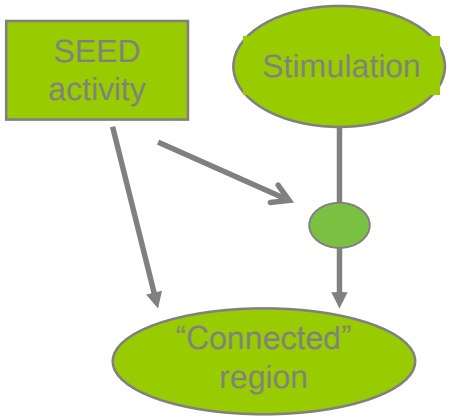
- interactions can be computed on different level (SPM vs. FSL)

INTERPRETATION

- effective connectivity between SEEDem aand other brain regions
- two possible views during interpretation



Modulation of linkage as a cause of stimulation



Activity of the seed modulates sensitivity (for response to stimulation) of different region

Friston et al. 1997

Overview

SEED CORRELATION ANALYSIS

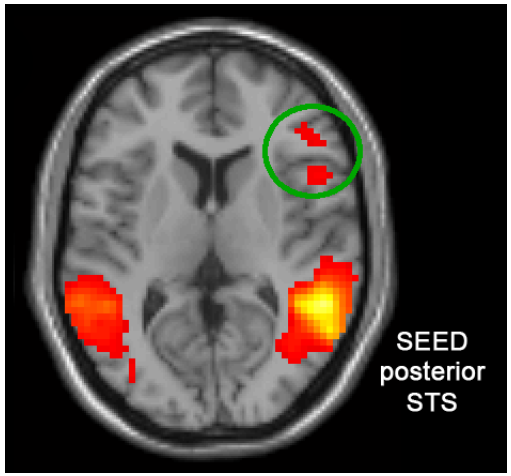
functional connectivity

simple correlation between SEED signal and signals from other regions

PPI

effective connectivity

change in correlation of BOLD signals from seed and other regions

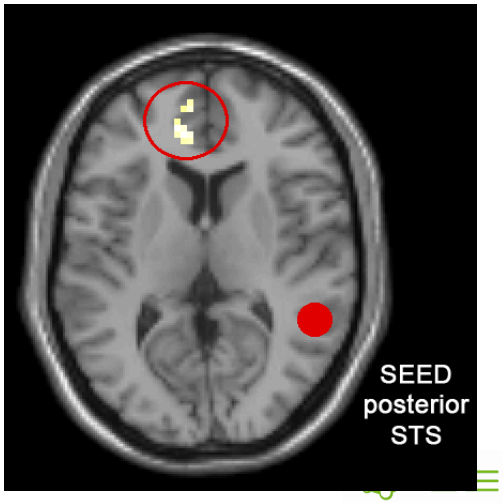


Visual ODDBALL

6% targets

XXXX vs OOOO

20 healthy subjects

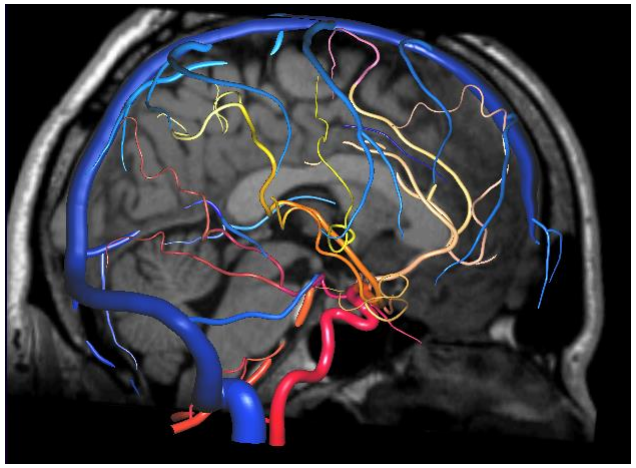


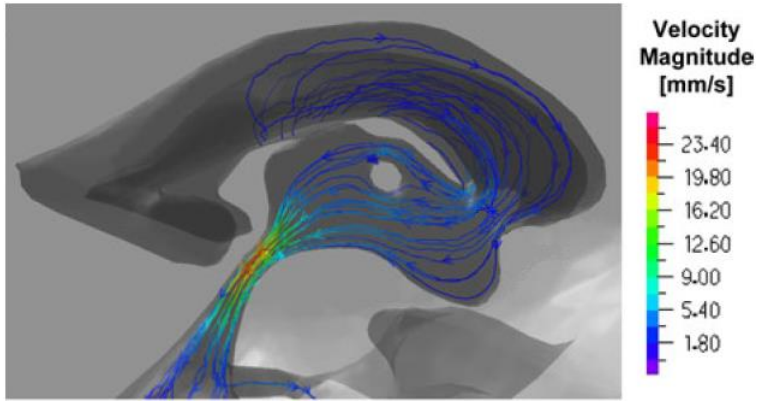
Connectivity
…sources of (anti-) correlations

- fMRI data contains a great amount of irrelevant information/relationships
- Sources:
  - Scanner hardware
  - Head motion
  - Heartbeat, breathing
- Correction
  - Filtering of global signal / (very) low frequency fluctuations
  - Involvement of motion parameters estimates in analysis
  - Filtering with modeled signals reflecting different pulse / breathing processes
  - Involvement of white matter / liquor signals

Sources of pulse artifact in fMRI data

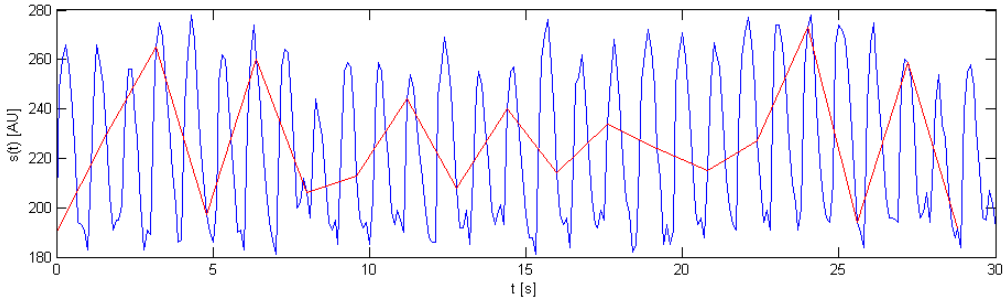
Areas (and proximity) with large vessels, areas with liquor pulsation (mainly III. ventricle, aqueduct, IV. ventricle, …)





SWEETMAN, B., LINNINGER A. A.,Cerebrospinal Fluid Flow Dynamics in the Central Nervous System, 2010

Example (TR=0.1 s; TR=1.6 s):



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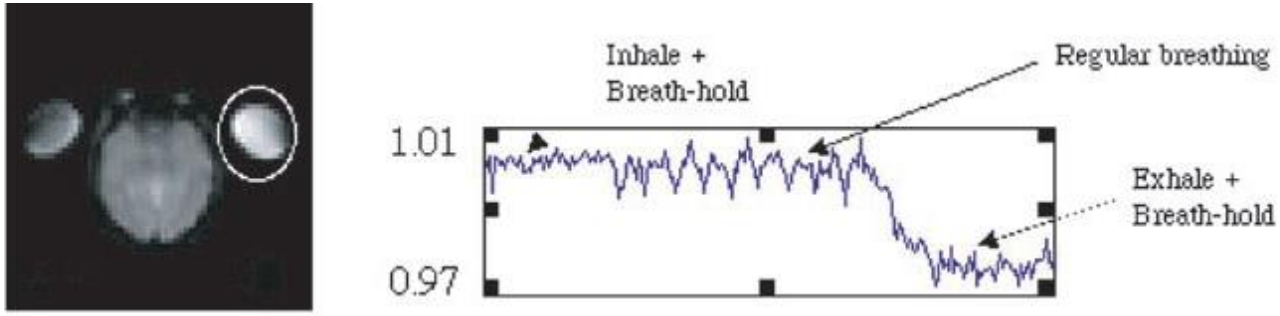
Physiological artifacts, breathing

- Breathing
  - changes in location, compressing of scanned structures
  - changes in B0 homogenity in the rhytm of motion and bulk changes of chest

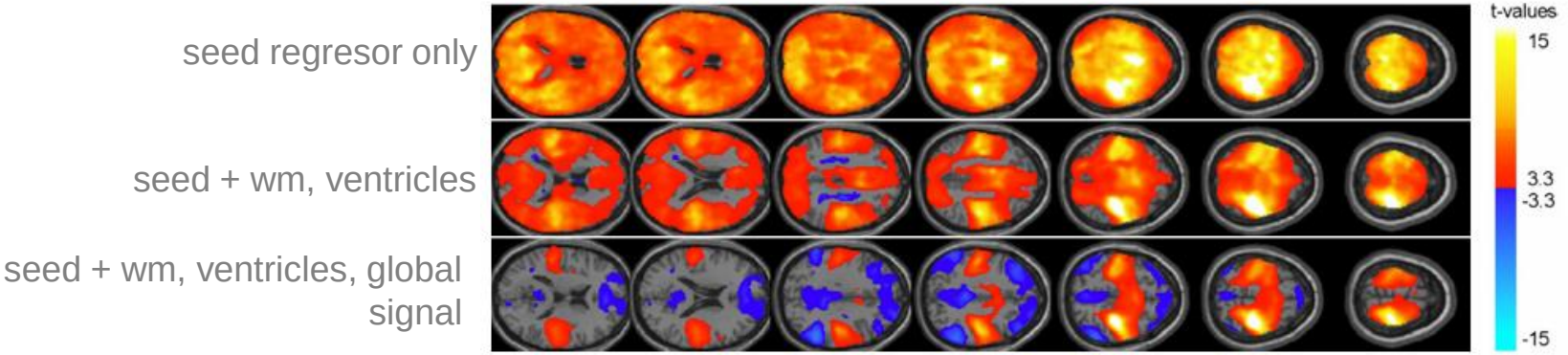


Raj D et al. (2001) Respiratory effects in human functional magnetic resonance imaging due to bulk susceptibility changes. Physics in Medicine and Biology 46:3331.

ARTIFICIAL CORRELATION

- false positive (and false negative too) results due to artificial signals
  - physiological noise (heartbeat, breathing)
  - motion artifacts

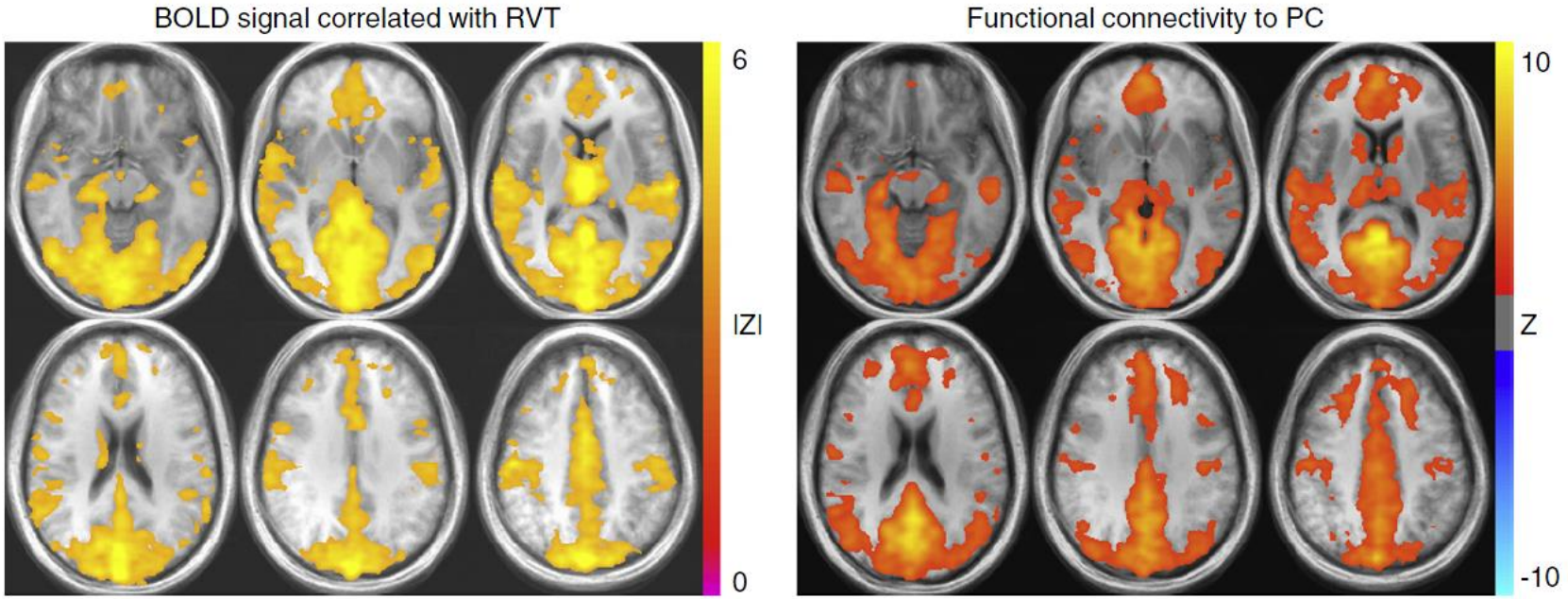
- solution – addition of regressor(s) modeling artificial signal(s)
- (they can explain part of variability caused by artifacts)



Weissenbacher et al., 2009

Changes in heartrate, breathing frequency and volume – causes and consequences

- Changes in sympathetic tone -> physiological changes in breathing and cardiac action ->
  - a) artifact in data
  - b) changes in neuronal activity (and BOLD signal)



PPI and filtering

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Basic neuroscience

Sensitivity of PPI analysis to differences in noise reduction strategies

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HIGHLIGHTS

- We found that dealing with noise in PPI is not consistent in papers from 2013.
- We tested RETROICOR and data-driven filtering on real and simulated data.
- Differing of results due to different filtering in real data was observed.
- Simulation study was done to estimate significant filtering factors.
- Usage of RETROICOR and suitable data driven signals for filtering are suggested.

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ABSTRACT

Background: In some fields of fMRI data analysis, using correct methods for dealing with noise is crucial for achieving meaningful results. This paper provides a quantitative assessment of the effects of different preprocessing and noise filtering strategies on psychophysiological interactions (PPI) methods for analyzing fMRI data where noise management has not yet been established.
Methods: Both real and simulated fMRI data were used to assess these effects. Four regions of interest (ROIs) were chosen for the PPI analysis on the basis of their engagement during two tasks. PPI analysis was performed for 32 different preprocessing and analysis settings, which included data filtering with RETROICOR or no such filtering; different filtering of the ROI "seed" signal with a nuisance data-driven time series; and the involvement of these data-driven time series in the subsequent PPI GLM analysis. The extent of the statistically significant results was quantified at the group level using simple descriptive statistics. Simulated data were generated to assess statistical improvement of different filtering strategies.
Results: We observed that different approaches for dealing with noise in PPI analysis yield differing results in real data. In simulated data, we found RETROICOR, seed signal filtering and the addition of data-driven covariates to the PPI design matrix significantly improves results.
Conclusions: We recommend the use of RETROICOR, and data-driven filtering of the whole data, or alternatively, seed signal filtering with data-driven signals and the addition of data-driven covariates to the PPI design matrix.

Conclusion

- Seed correlation analysis
  - Seed selection -> observing of correlation
  - Artificial signals!, filtering

- PPI
  - Seed selection -> computation of interaction with the change of contextual condition, observing of correlation
  - Artificial signals!, filtering

Thank you for your attention

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