Task Connectivity

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FC between regions varies depending on context

Resting-state/intrinsic FC

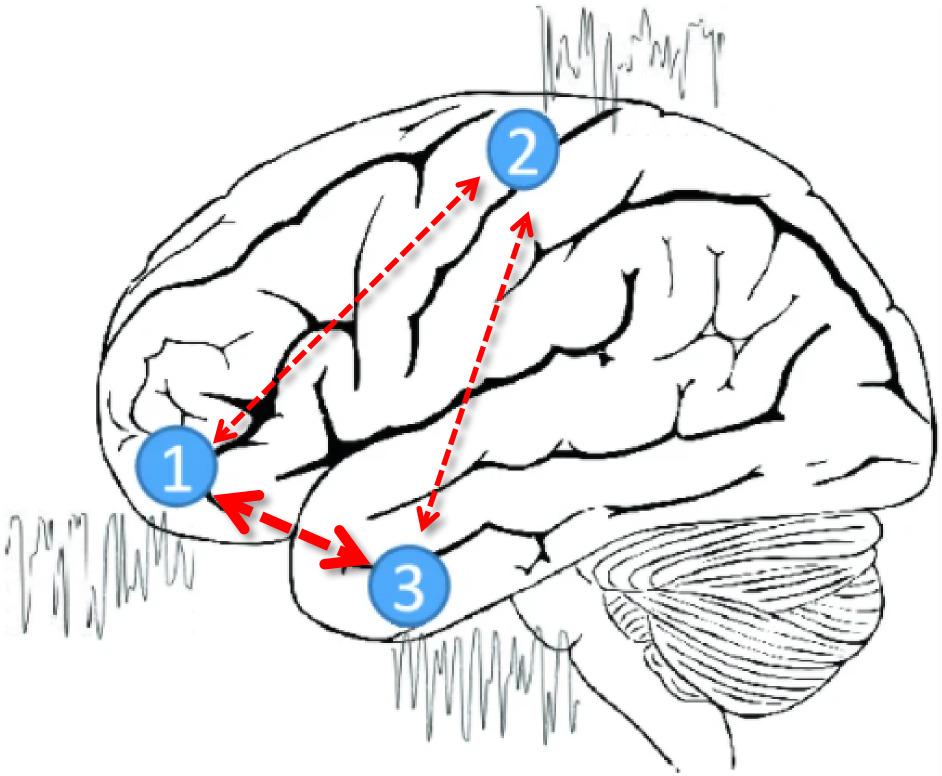
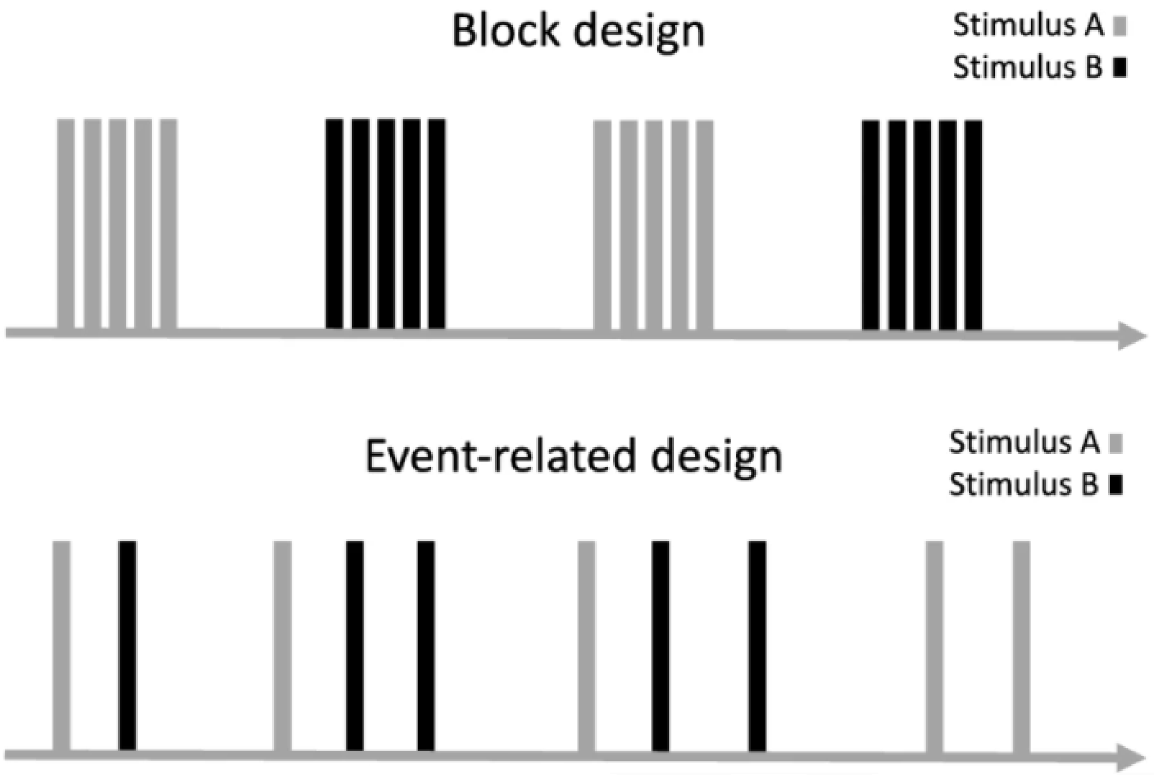


image: Sklerov et al., 2019

FC between regions varies depending on context

Task-evoked FC



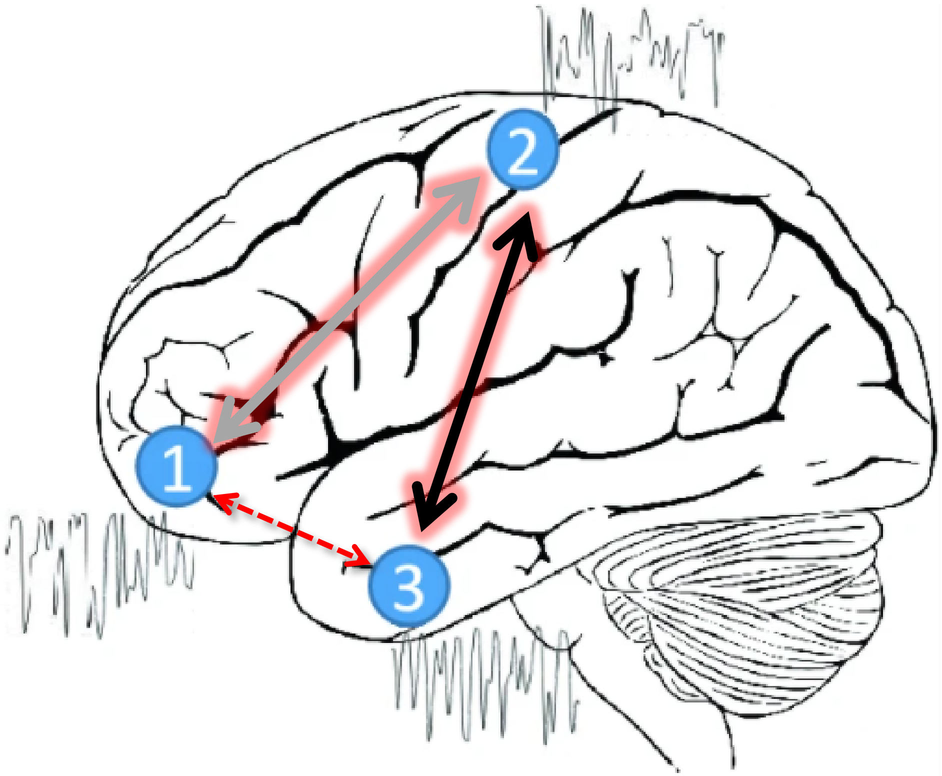


image: Sklerov et al., 2019

Common task FC approaches (exploratory)

- standard psychophysiological interaction (sPPI)
- generalized psychophysiological interaction (gPPI)
- correlational psychophysiological interaction (cPPI)
- beta-series correlation
- background/task-residual connectivity

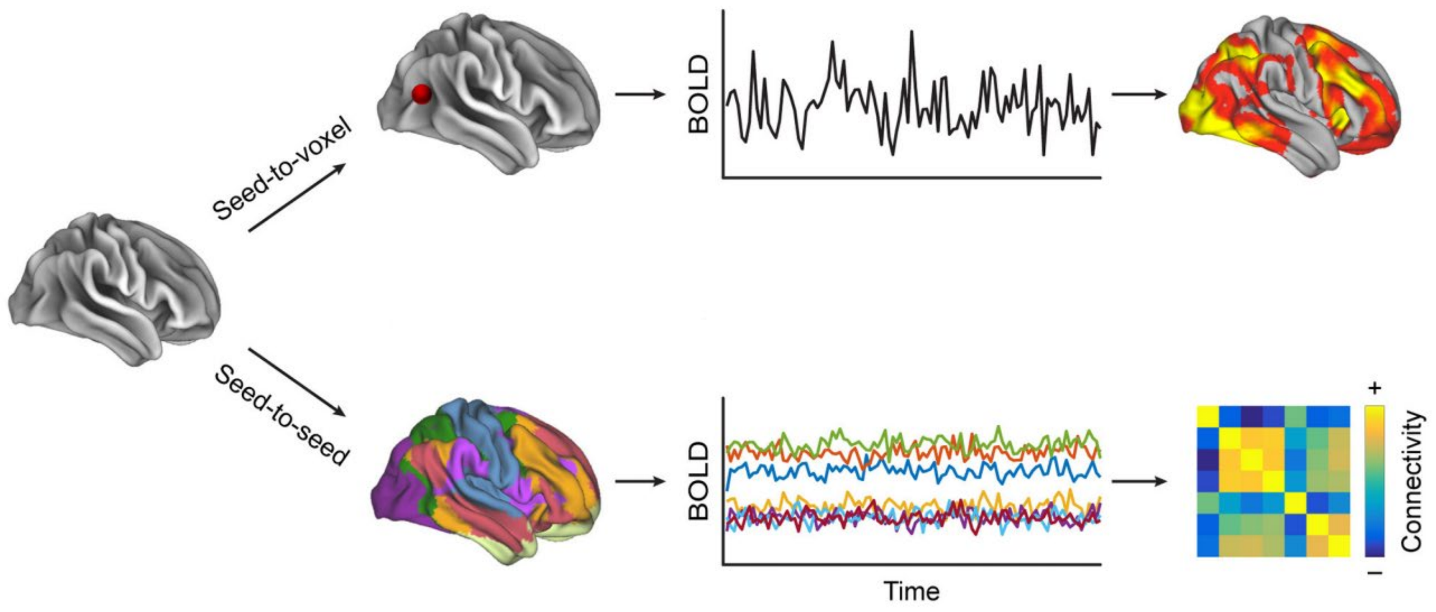
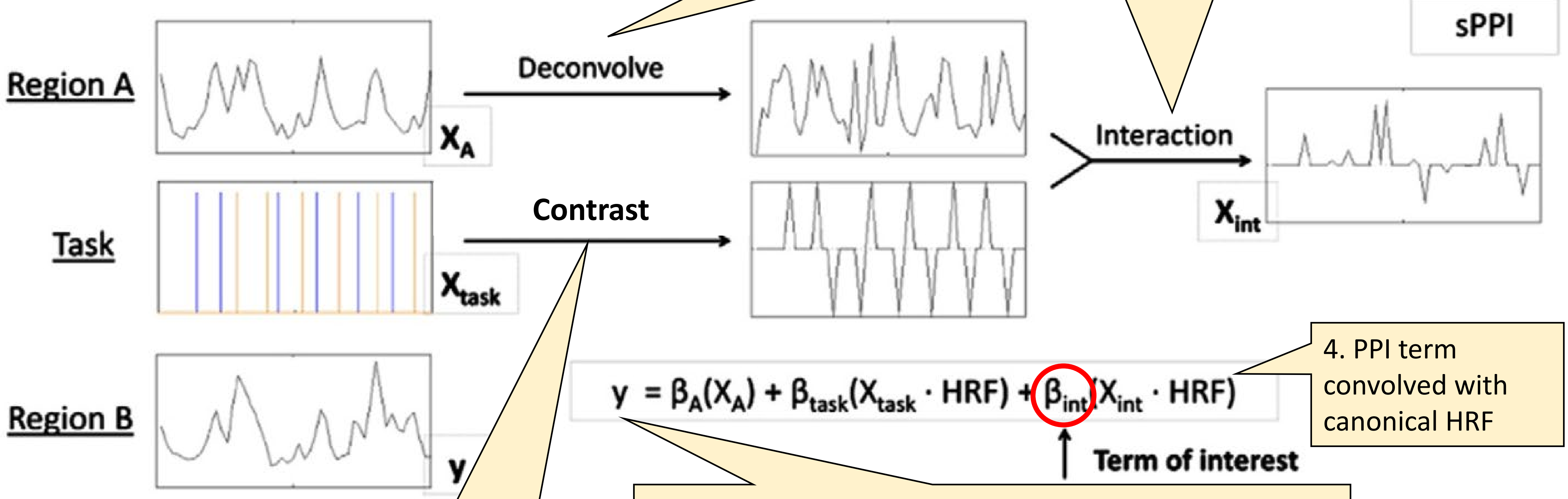


image: Tahedl et al., 2018

Standard PPI (sPPI)

2. BOLD data from region A (seed) deconvolved into est. of neural events

3. **PPI term** = mean-centered est. of neural events x contrast vector

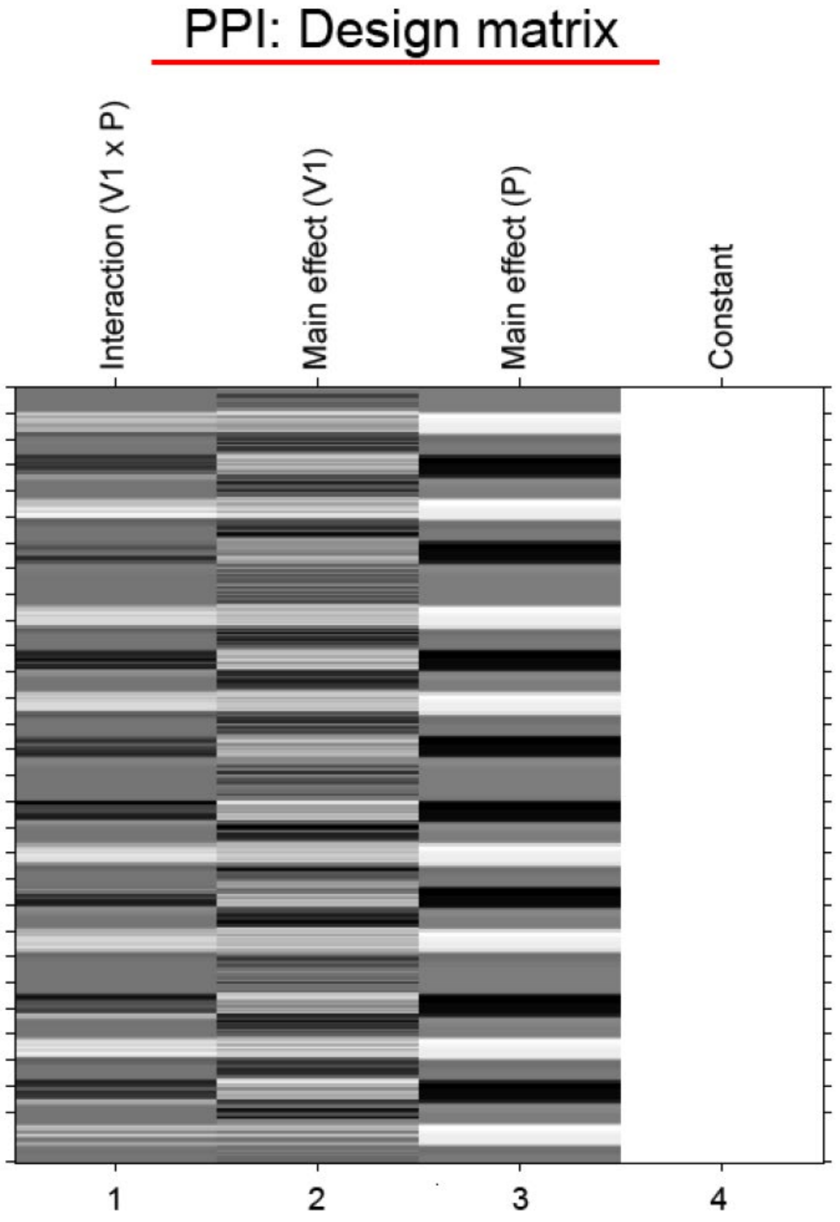


4. PPI term convolved with canonical HRF

1. Contrast vector created from experimental design (blue=1; yellow=-1)

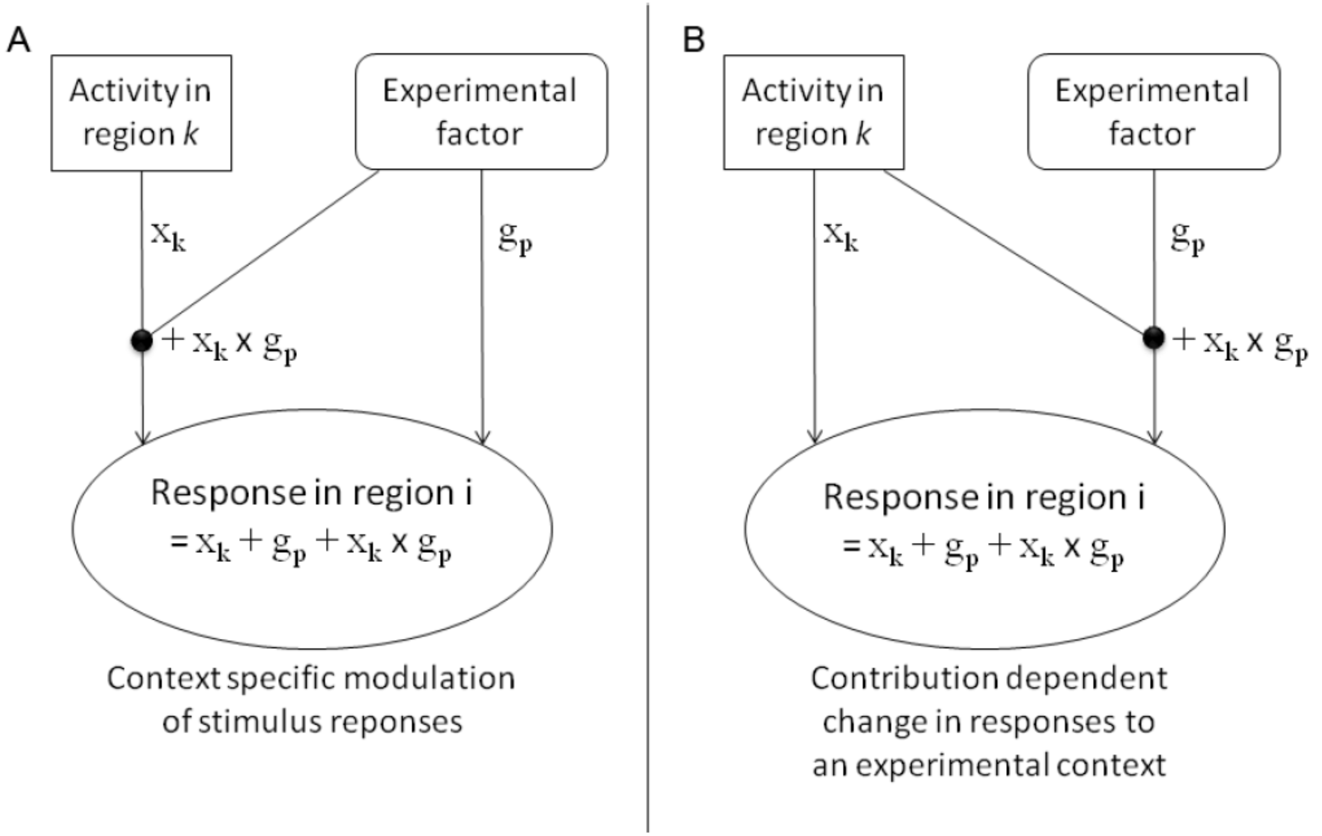
5. BOLD data from region B regressed on:
1) BOLD data from region A (main effect of region A)
2) convolved task predictor (main effect of task)
3) PPI term (interaction between task and region A)

Friston et al., 1997; Gitelman et al., 2003; Cisler et al., 2014



Inference -> interaction term
Contrast vector [1 0 0 0]

Two alternative interpretations of PPI effects (do not make causal claims)



Contribution of one area (k) to another (i) is altered by the experimental (psychological) context

The response of an area (i) to an experimental (psychological) context due to the contribution of region (k)

PPI in practice

- Mechanistically, a PPI analysis involves the following steps:
  1. Performing a standard GLM analysis.
  2. Extracting BOLD signal from a source region identified in the GLM analysis.
  3. Forming the interaction term (source signal x experimental treatment)
  4. Performing a second GLM analysis that includes
     - the interaction term
     - the source region's extracted signal
     - the experimental vector in the design

analogous to including the main effects in ANOVA to make an inference on the interaction

- Practical example for sPPI – SPM12 manual, p. 329.

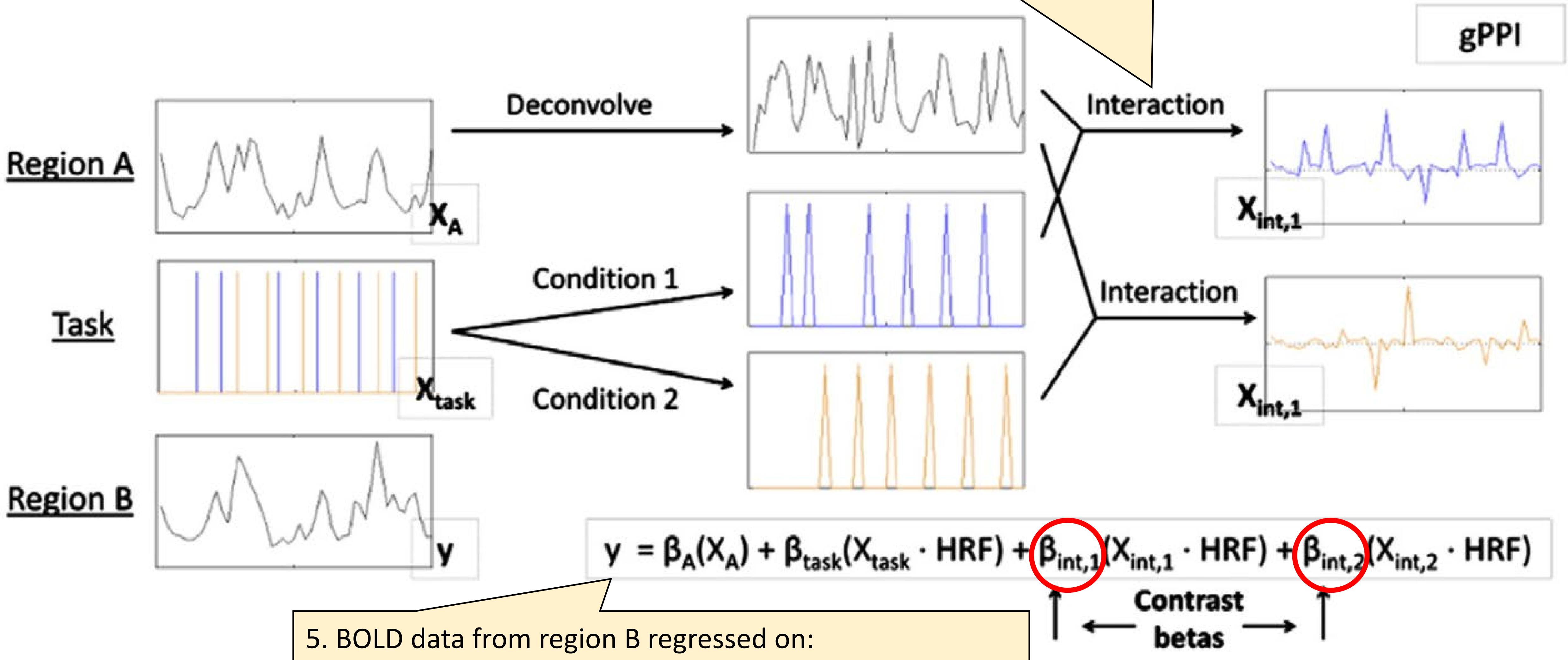
Pros and Cons of sPPI

- Pros
  - Model-based with an approximated neuronal input structure
  - Implemented in SPM

- Cons
  - New model for each seed
  - New model for each psychological contrast
  - Optimized for simple (e.g., 2-condition) designs, but may not be suitable for more complex designs (but see gPPI next)
  - Rudimentary “effective connectivity”, but still not much more than a simple correlation

Generalized PPI

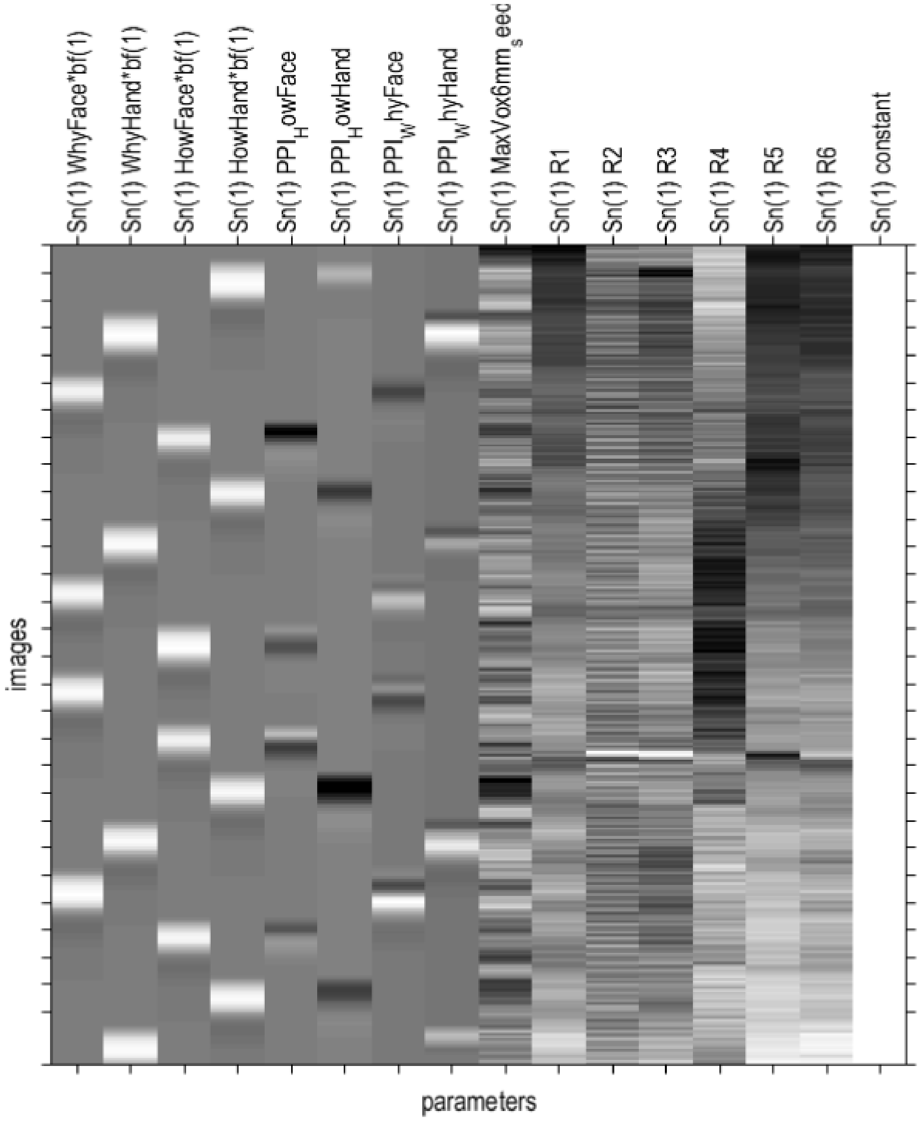
PPI terms: Each column of the design matrix (stimulus condition) is separately multiplied by the deconvolved neural est.



5. BOLD data from region B regressed on:
1) BOLD data from region A (main effect of region A)
2) convolved task predictors (main effect of task)
3) each convolved PPI term (task condition x neural est.)

McLaren et al., 2012; Cisler et al., 2014

gPPI: Design matrix



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Generalized PPI Toolbox

https://www.nitrc.org/projects/gppi/

gPPI Lab Topic – afternoon

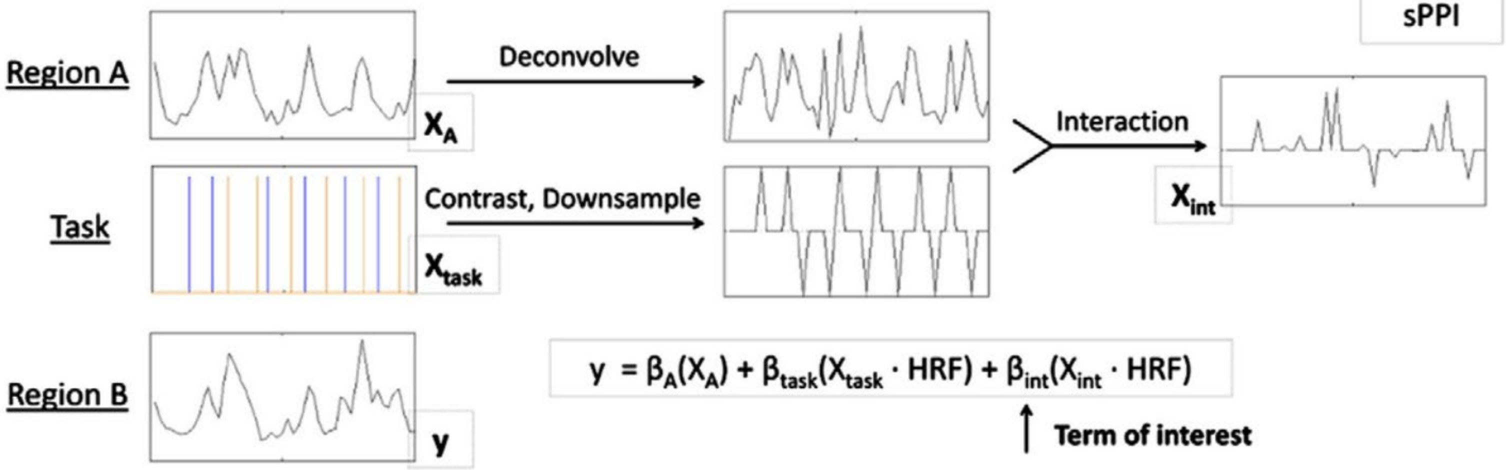
gPPI with CONN:

https://andysbrainbook.readthedocs.io/en/latest/FunctionalConnectivity/CONN_ShortCourse/CONN_11_Task_gPPI.html

JoVE video of gPPI analysis (Harrison et al., 2017):

https://www-jove-com.proxy.lib.umich.edu/v/55394/generalized-psychophysiological-interaction-ppi-analysis-memory

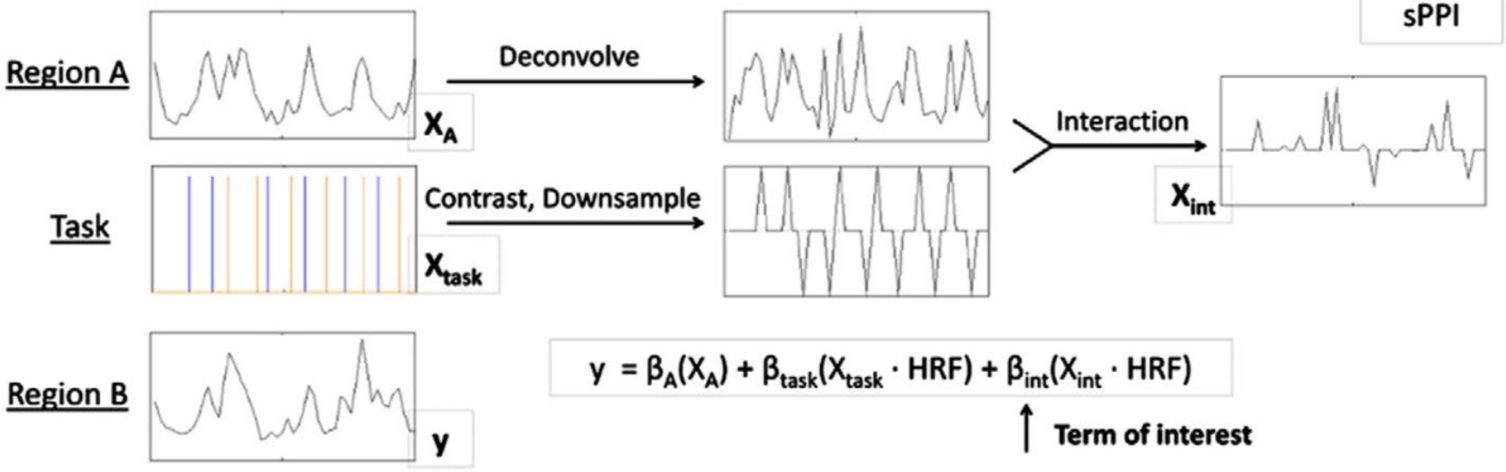
Correlational PPI



- PPI model is inherently directional
  - rudimentary "effective" connectivity: we assume activity in region A predicts activity in region B
- How about cases when this assumption cannot be made?
- We can use partial correlations to provide an undirected measure of inter-regional covariations in task-related activity modulations

Fornito et al., 2012

Correlational PPI



Procedure: for any two regions A and B:

- extract BOLD time series X_A and X_B
- compute the PPI interactions X_{intA} and X_{intB} (i.e., deconvolve each time series and multiply with task regressor like in standard PPI)
- convolve X_{intA} and X_{intB} with HRF, such that $I_A = X_{intA} \cdot HRF$ and $I_B = X_{intB} \cdot HRF$
- compute partial correlation $r_{I_A, I_B \cdot [X_A X_B X_{task} G]}$
  - i.e., correlation between the two PPI terms I_A and I_B while partialling covariance with the raw activity of the two regions X_A and X_B, the task regressor X_{task}, and any other potential confounds represented by G (e.g., motion).

Fornito et al., 2012

Correlational PPI

- Advantages over PPI:
  - avoids arbitrary directional assumptions
  - can be scaled to study pairwise functional interactions between many regions
- Note: as in standard PPI analysis, it works best when the task regressor defines a contrast between conditions

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cPPI Toolbox for fMRI

https://www.nitrc.org/projects/cppi_toolbox/

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Neural correlates of working memory training: Evidence for plasticity in older adults

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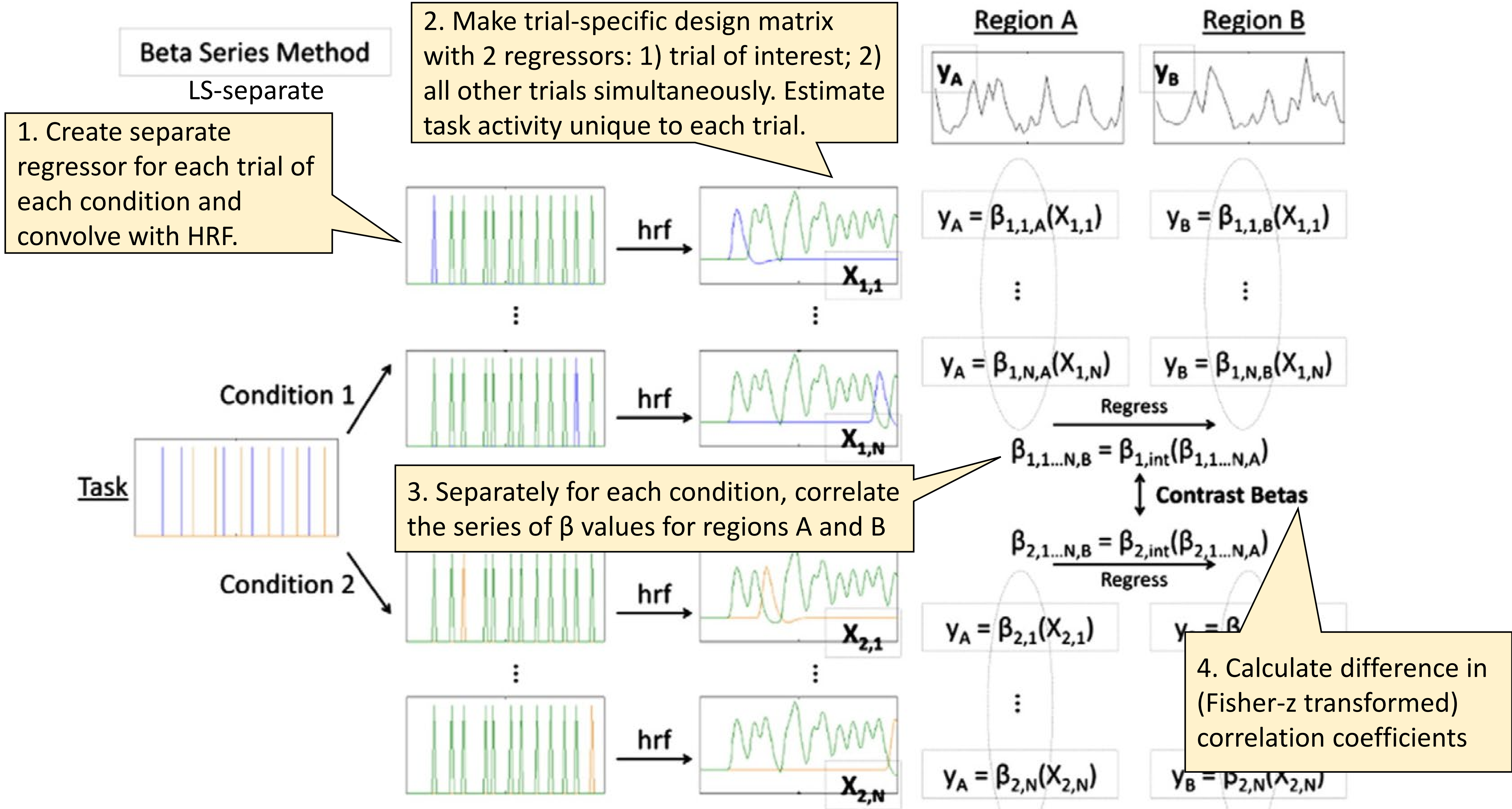
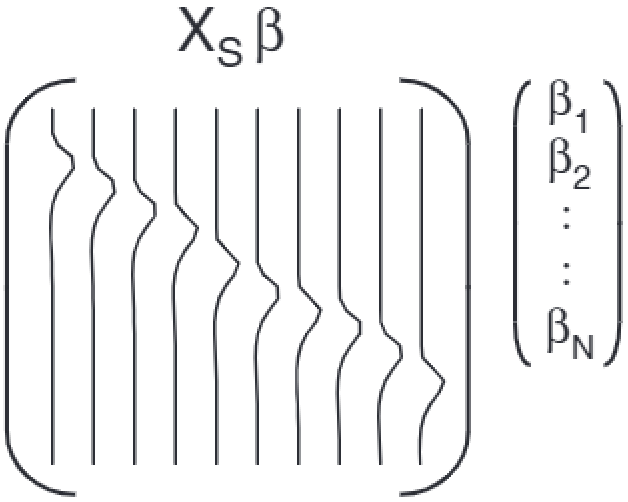


Rissman et al., 2004; Mumford et al., 2012; Cisler et al., 2014

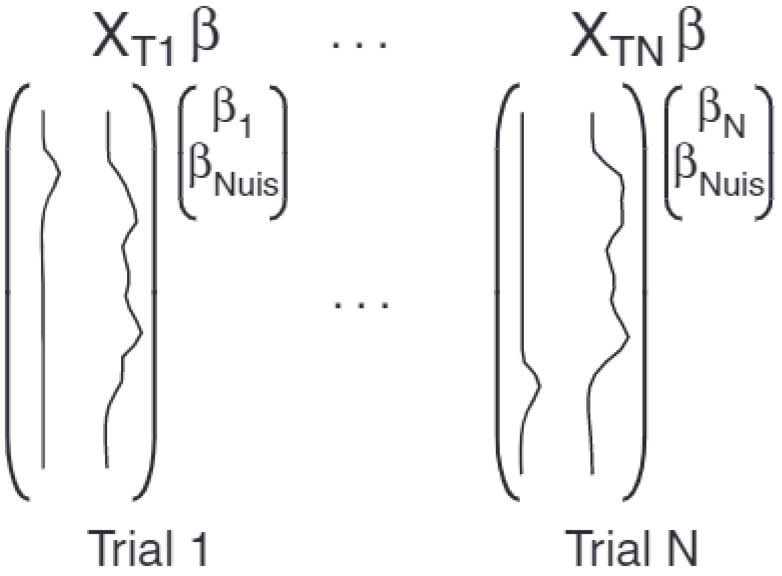
Beta-series estimation

Least Squares – All (LS-A)



Single model:
Doesn’t work very well in the presence of collinearity.

Least Squares – Separate (LS-S)



Runs a separate GLM for each trial:
the trial is modeled as the regressor of interest, and all other trials are combined into a nuisance regressor.

Mumford et al., 2012

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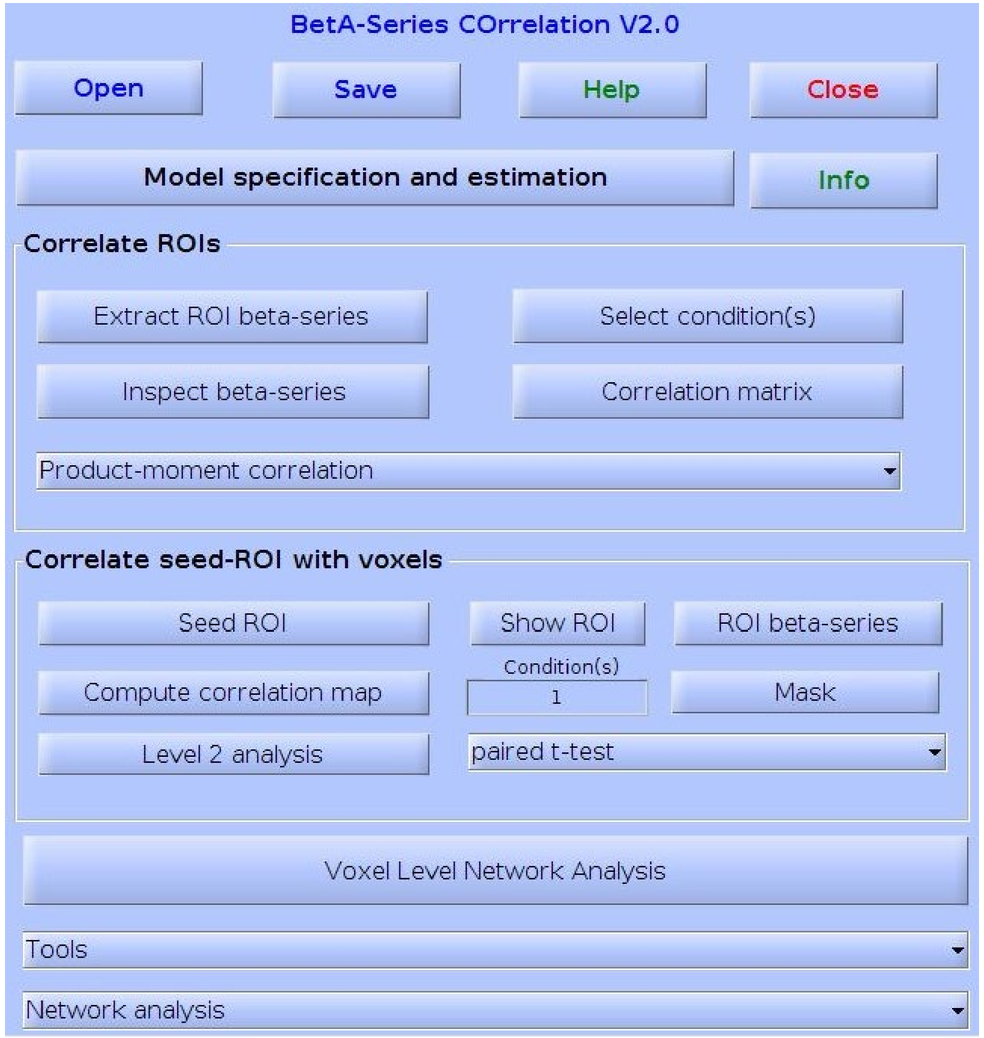
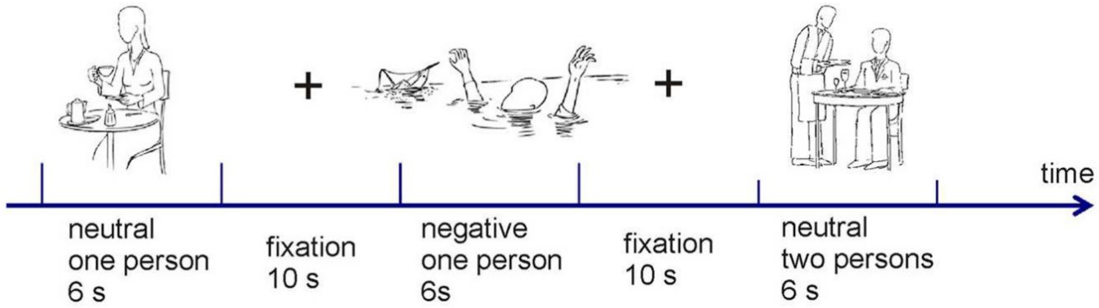
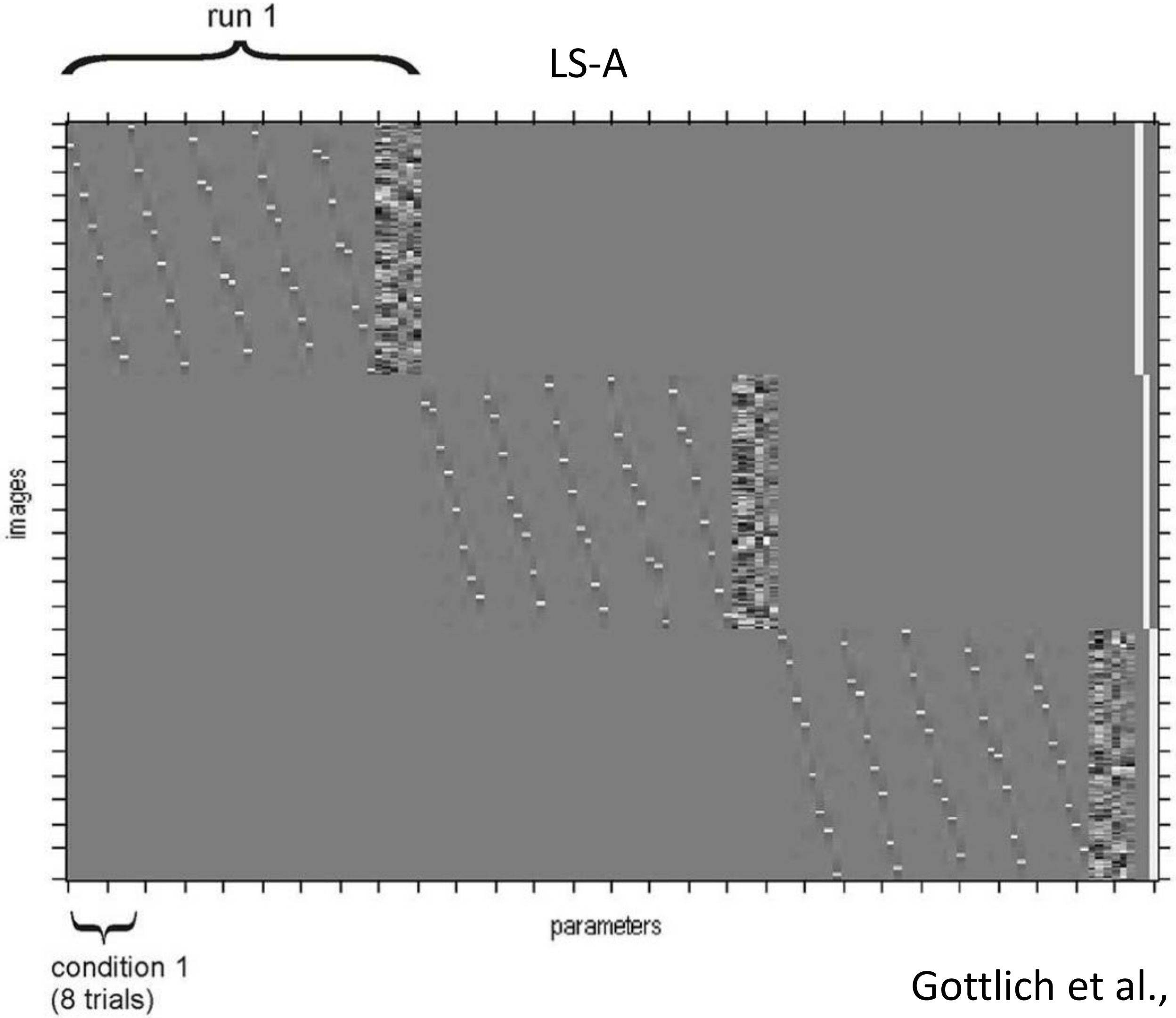
BetA-Series COrrelation

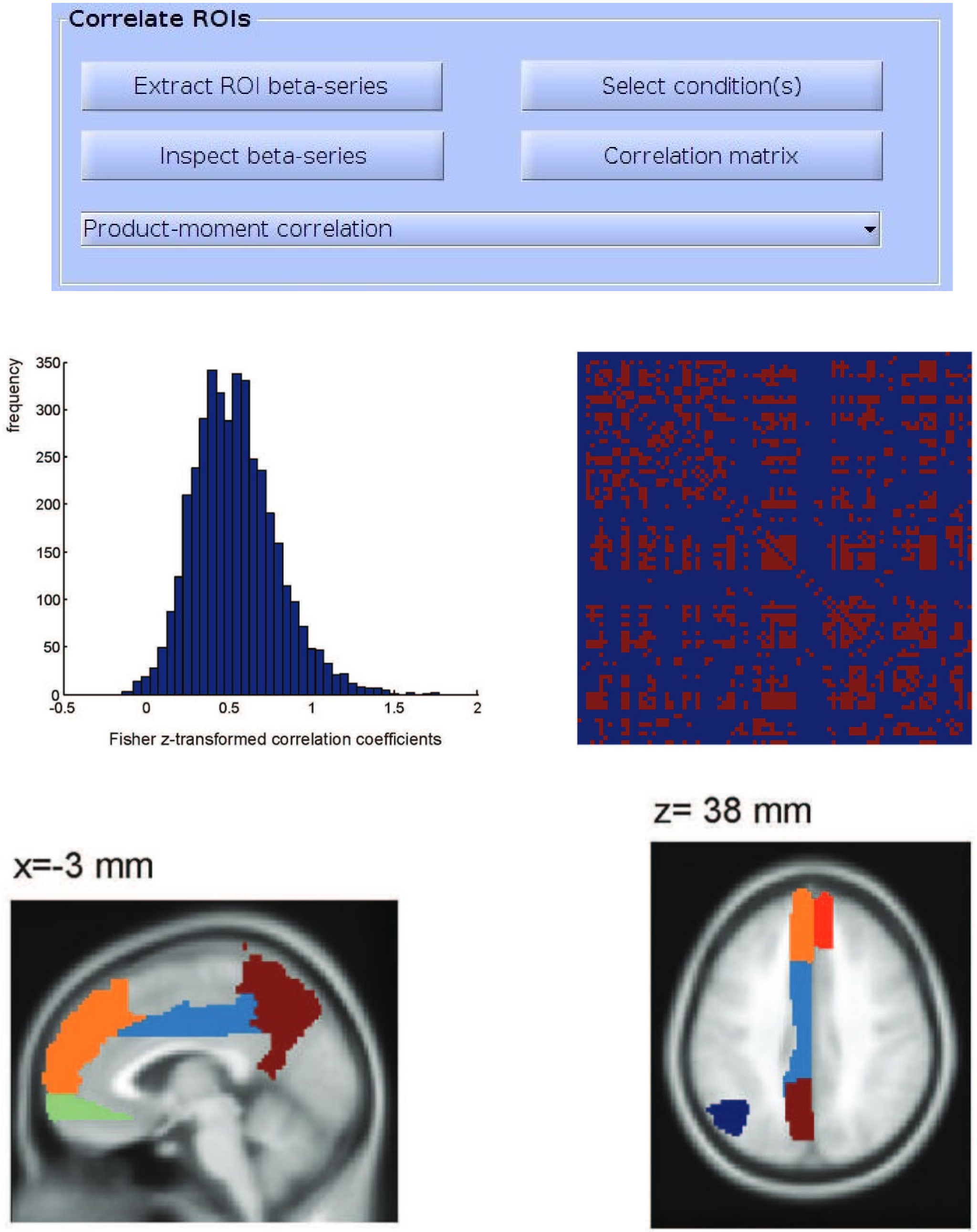
https://www.nitrc.org/projects/basco/

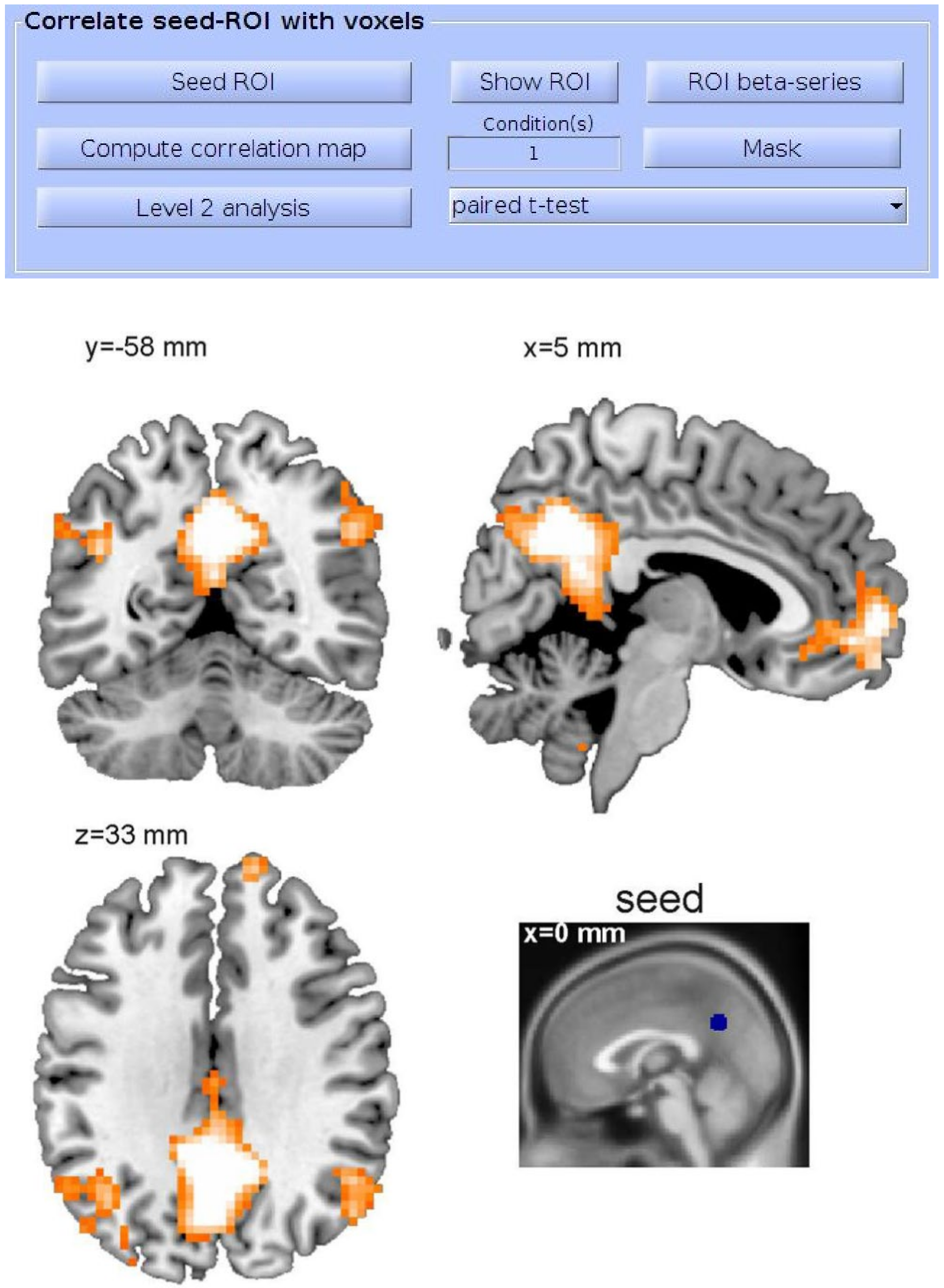






Gottlich et al., 2015





Gottlich et al., 2015

Pros and Cons of beta-series correlations

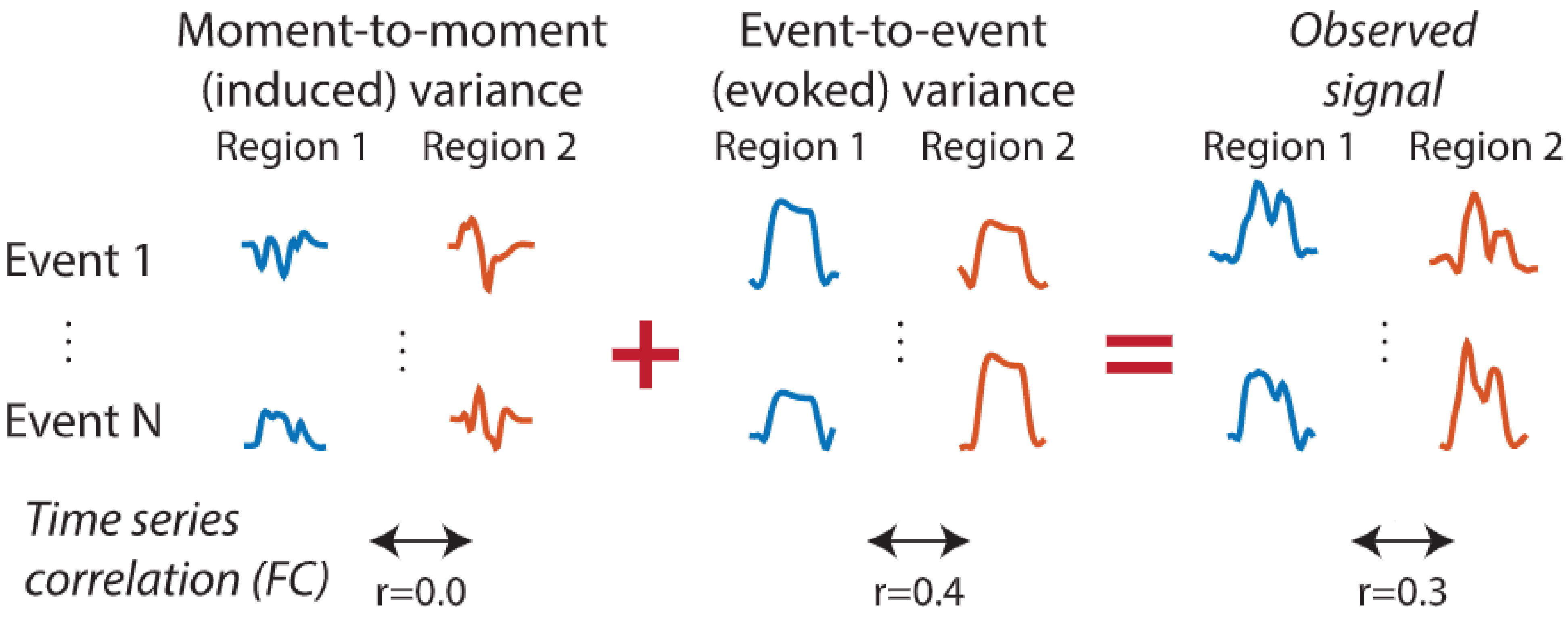
- Pros
  - Allows flexible modeling
    - Good for multi-event per trial designs
    - Tease apart sub-parts of psychological processes
  - After 1st level GLM is estimated, can repeat correlations on any number of seeds and conditions
  - Relatively more powerful for event-related designs
  - Retains power under conditions of HRF variability
- Cons
  - No directionality of inference (if you care)
  - Individual beta estimates are noisy (but LS-S better than LS-A)
  - Massive data output
  - Relatively less powerful for block designs (gPPI performs better)

PPI vs. beta-series correlation

- Fundamental difference
  - PPI measures a change in regression slope or parameter of a model of “effective connectivity” as a function of condition
    - Does more activation in region X predict more activation in region Y in condition A compared to condition B?
  - Beta-series correlation is “model-free” and measures changes correlation as a function of condition
    - Are regions X and Y more tightly coupled in condition A compared to condition B?
- Both methods measure phasic (stimulus-driven) responses. How about more tonic (intrinsic) states? (What is “true” FC?)

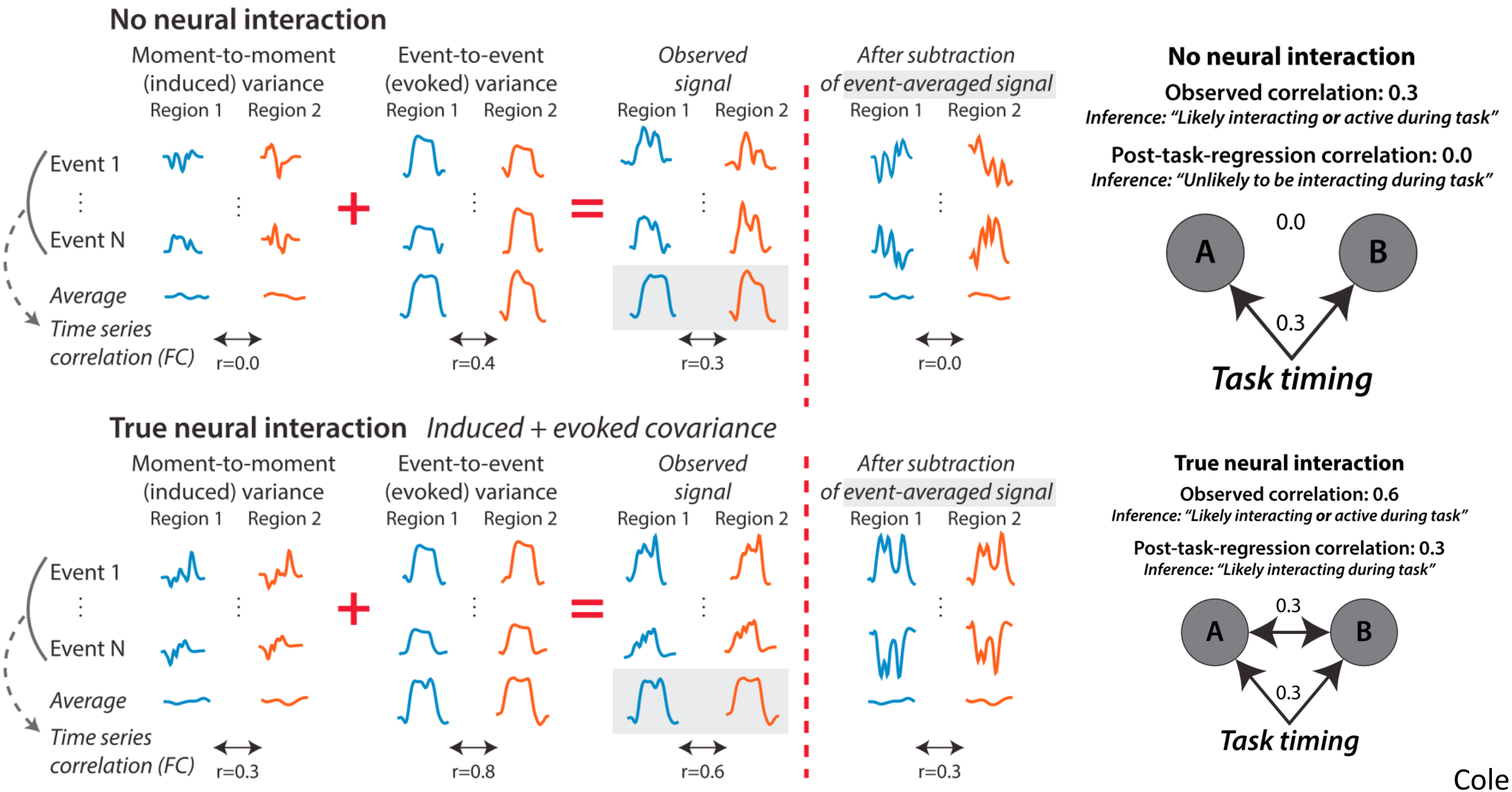
Cisler et al., 2014; Di et al., 2021

Task-evoked activations and task-state FC inferences



Cole et al., 2019

Background/task-residual connectivity = endogenous or "residual" FC between brain regions after accounting for variance related to evoked task activity



Cole et al., 2019

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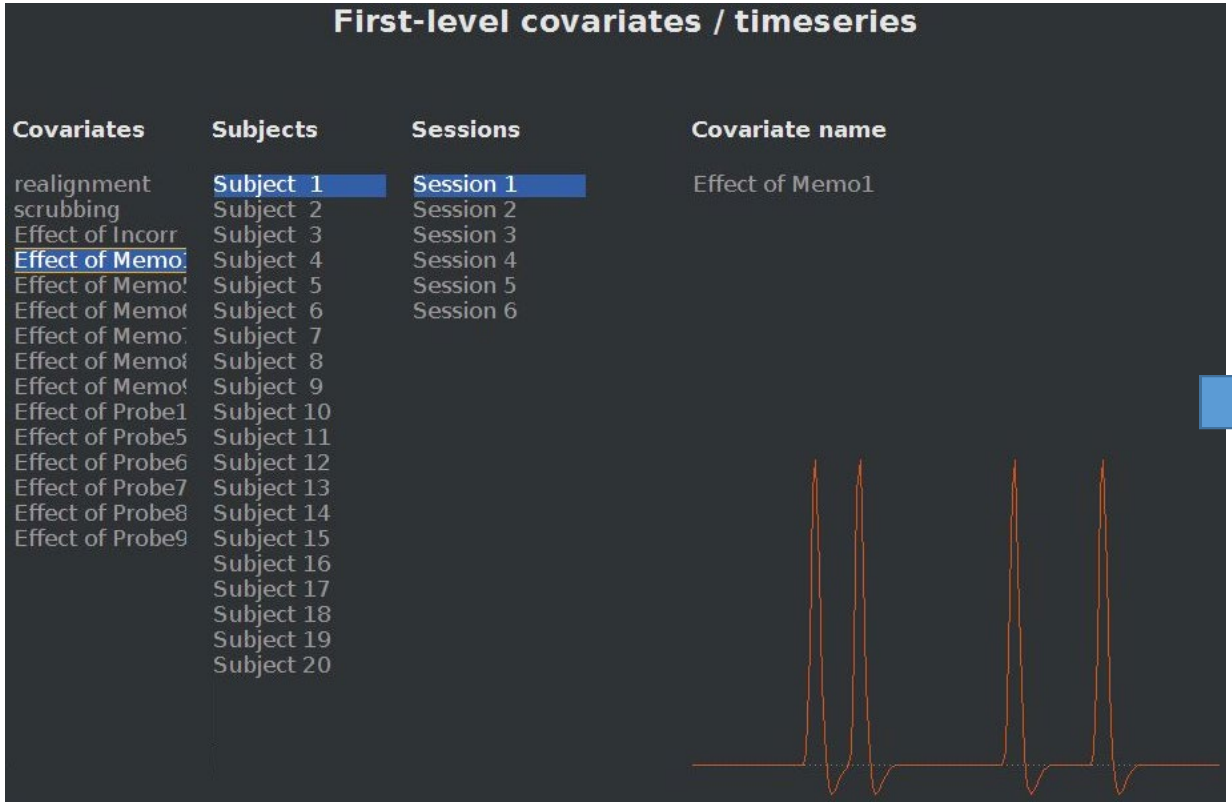
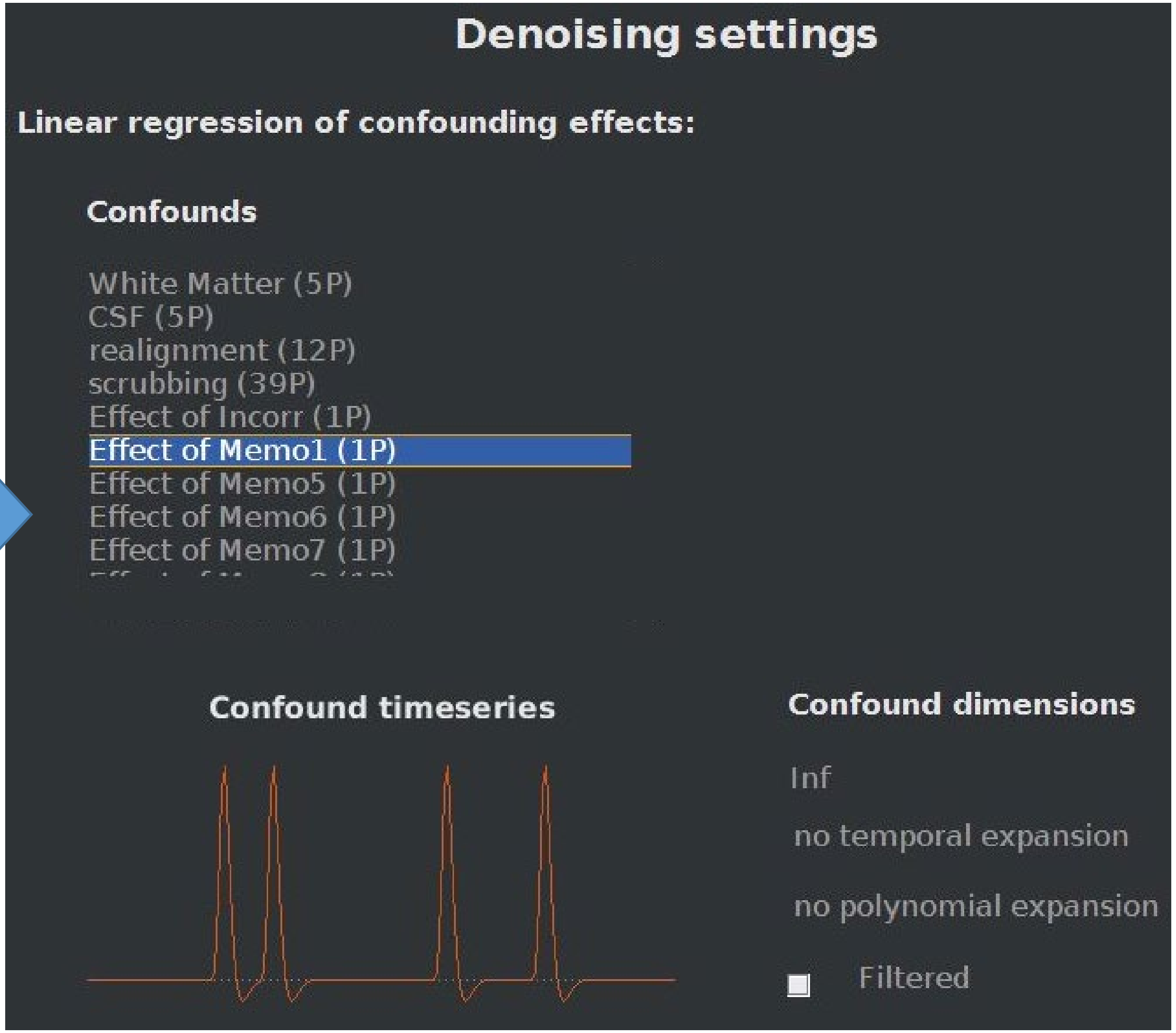
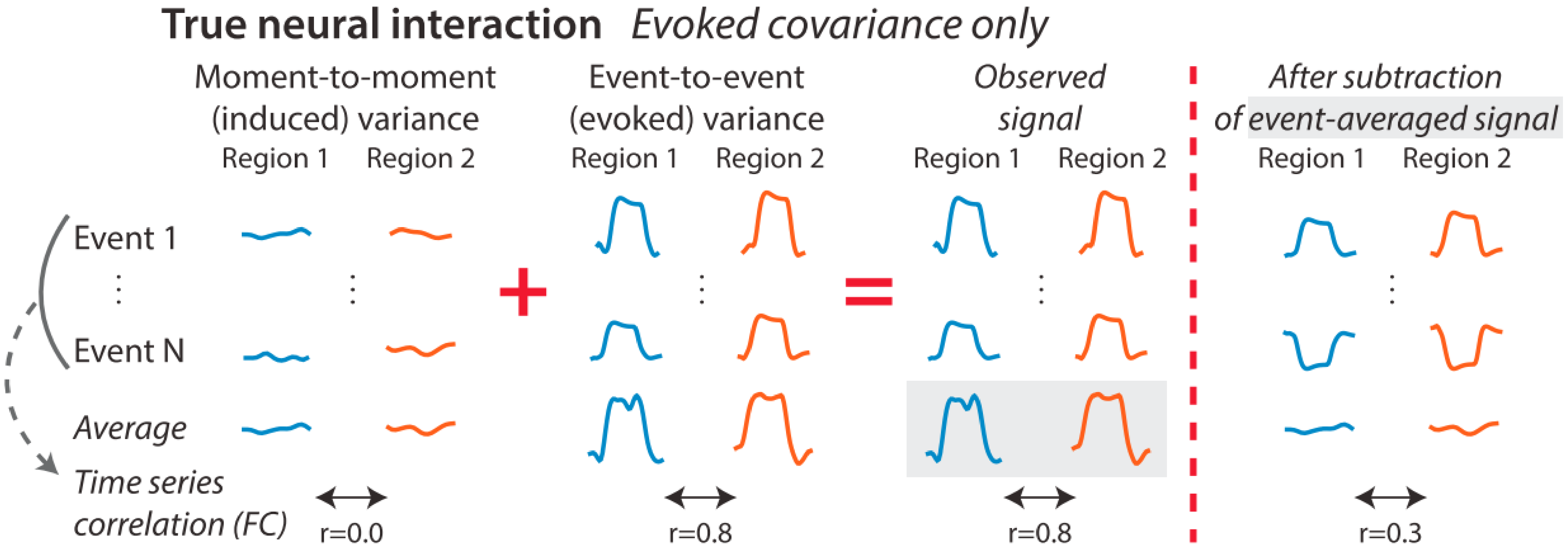
CONN : functional connectivity toolbox

https://www.nitrc.org/projects/conn/





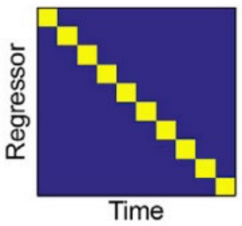
Note: Removing mean evoked responses doesn't remove all time-locked signals, but only those that are consistent in amplitude with the mean across task events.



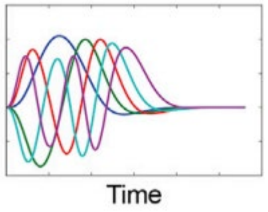
Cole et al., 2019

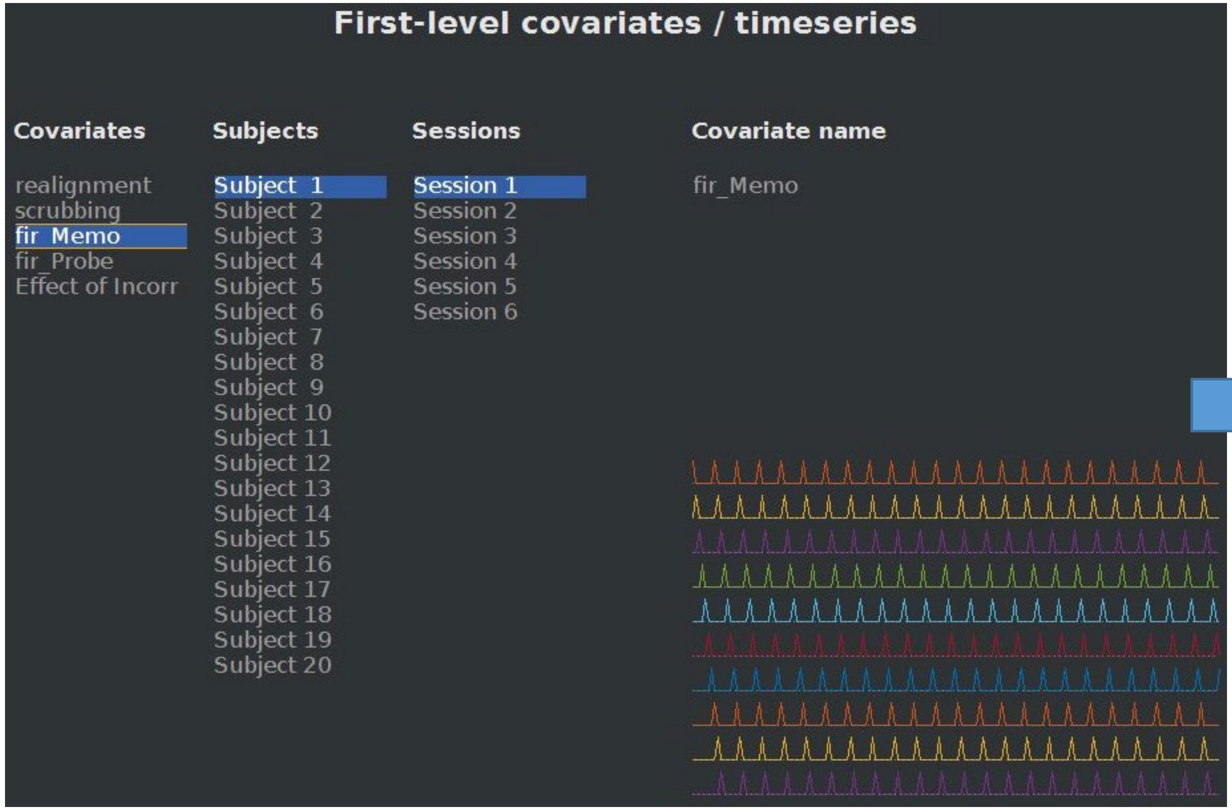
Alternatives:

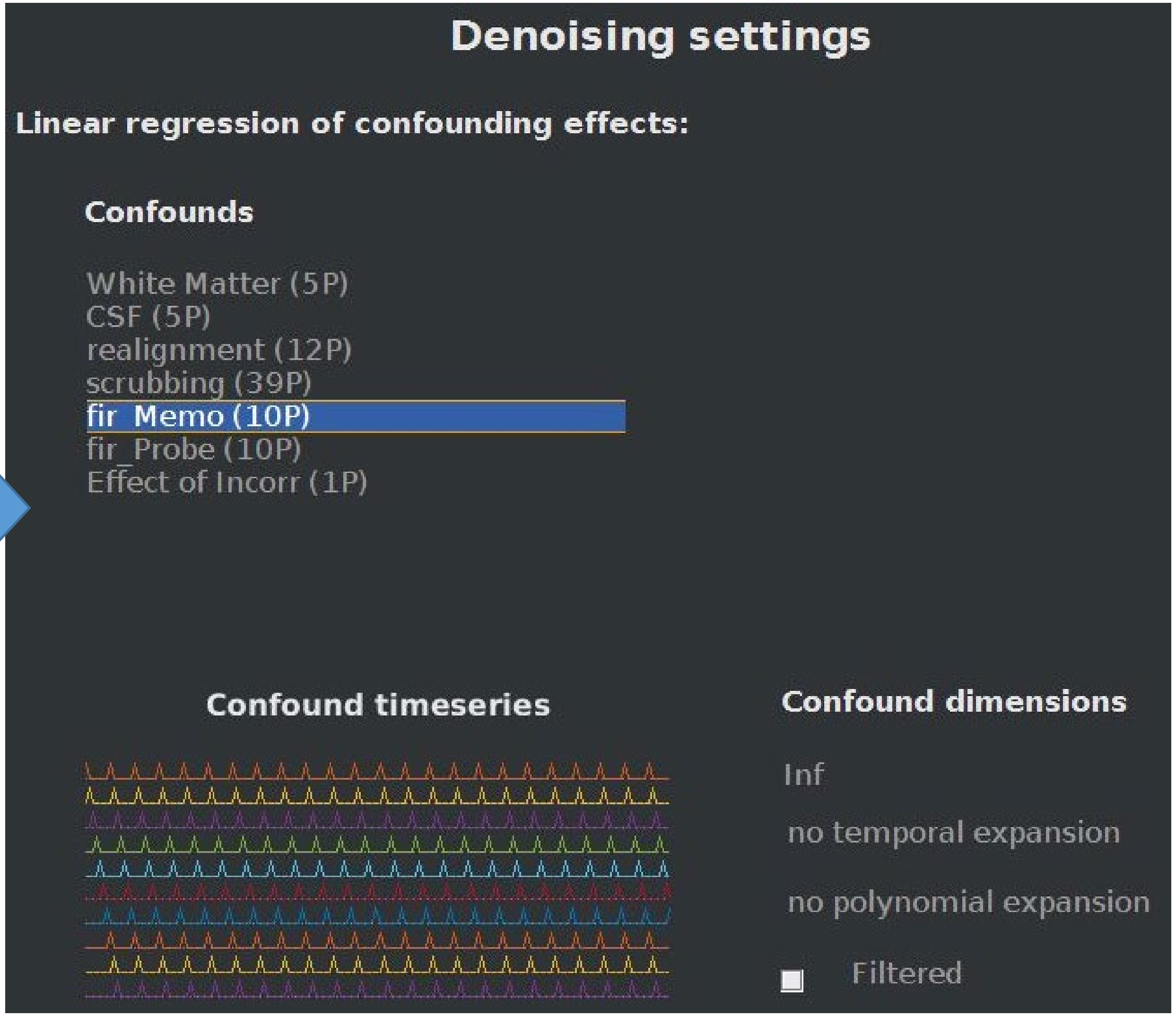
FIR modeling



Constrained basis set







However, keep an eye on the estimated remaining DoF!