



Task Connectivity

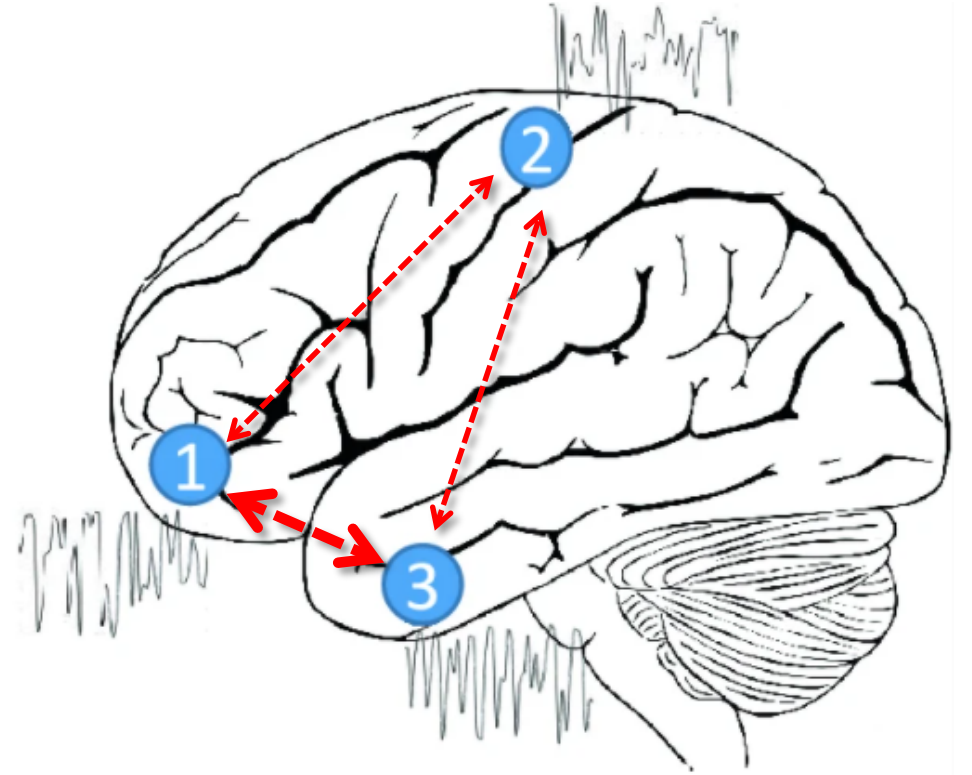
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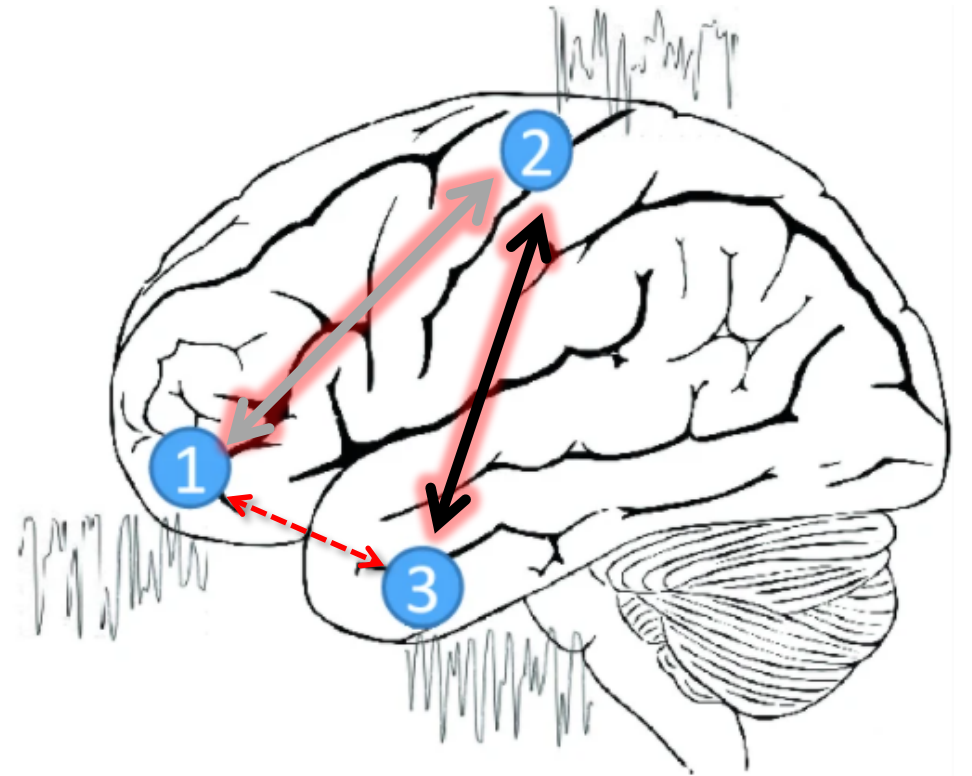
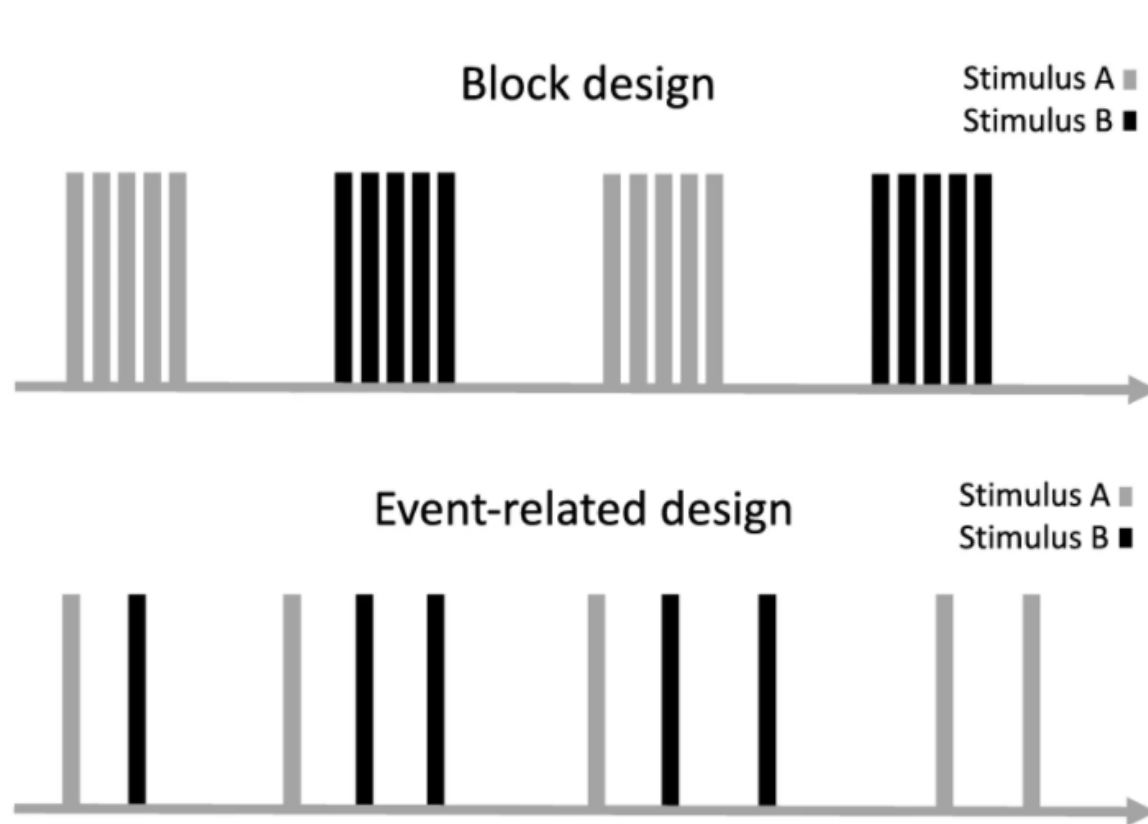
FC between regions varies depending on context

Resting-state/intrinsic FC



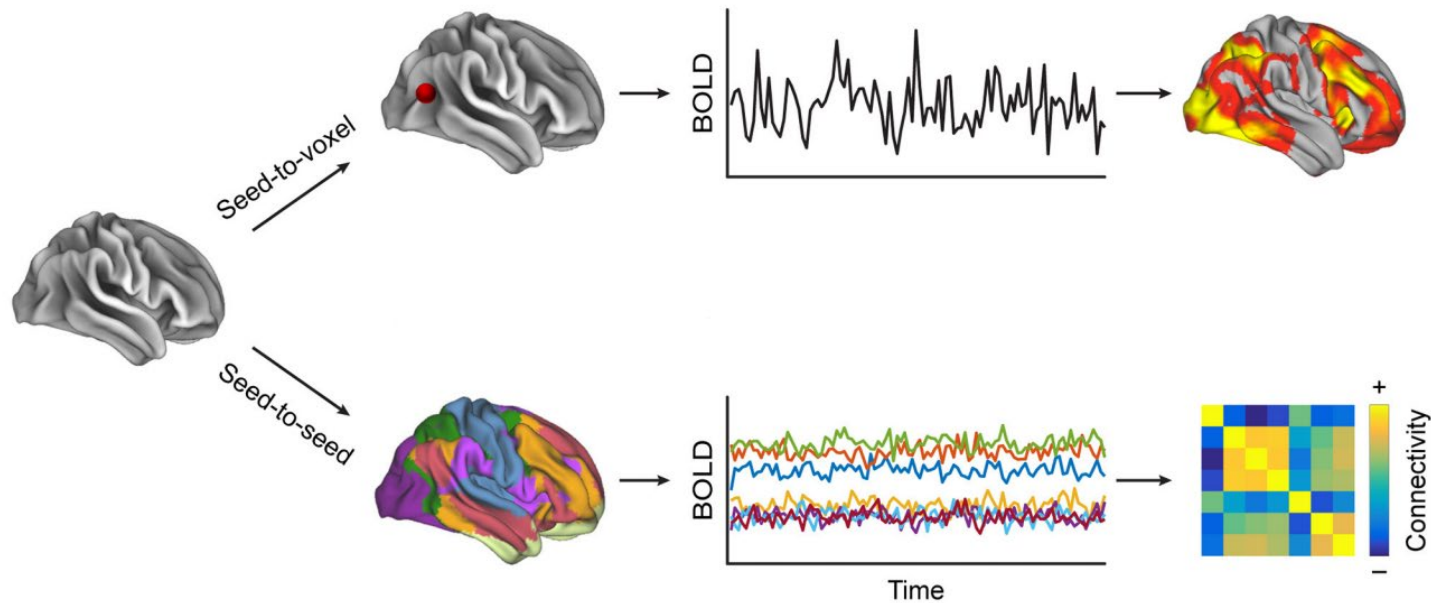
FC between regions varies depending on context

Task-evoked FC

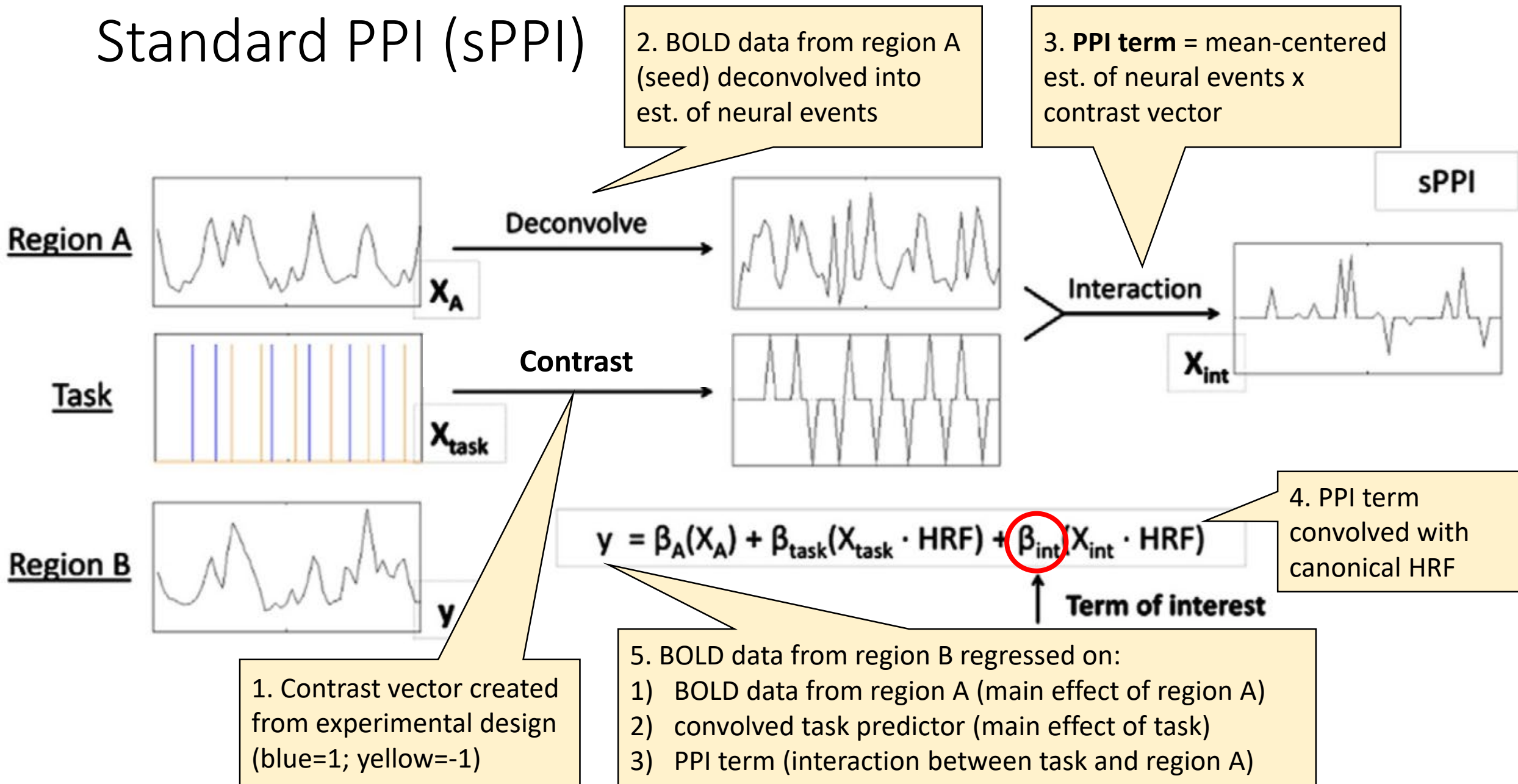


Common task FC approaches (exploratory)

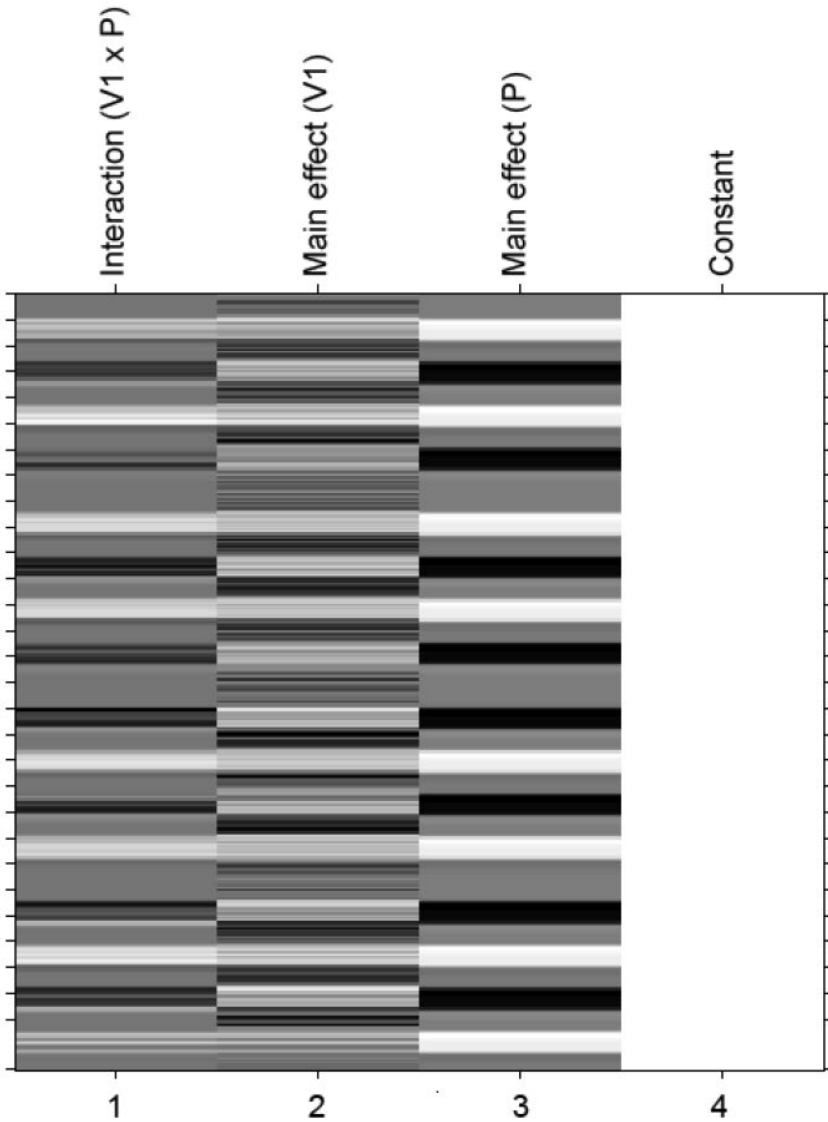
- standard psychophysiological interaction (sPPI)
- generalized psychophysiological interaction (gPPI)
- correlational psychophysiological interaction (cPPI)
- beta-series correlation
- background/task-residual connectivity



Standard PPI (sPPI)

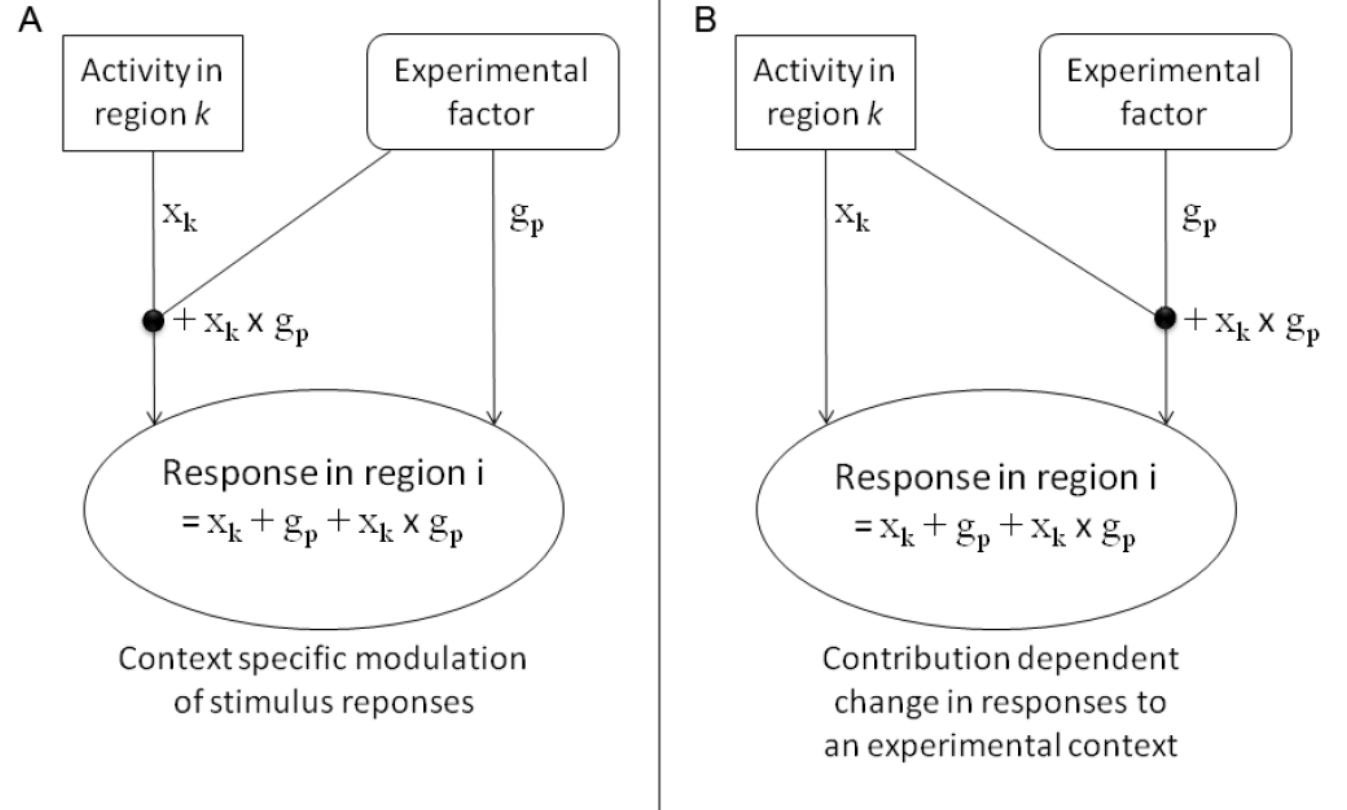


PPI: Design matrix



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

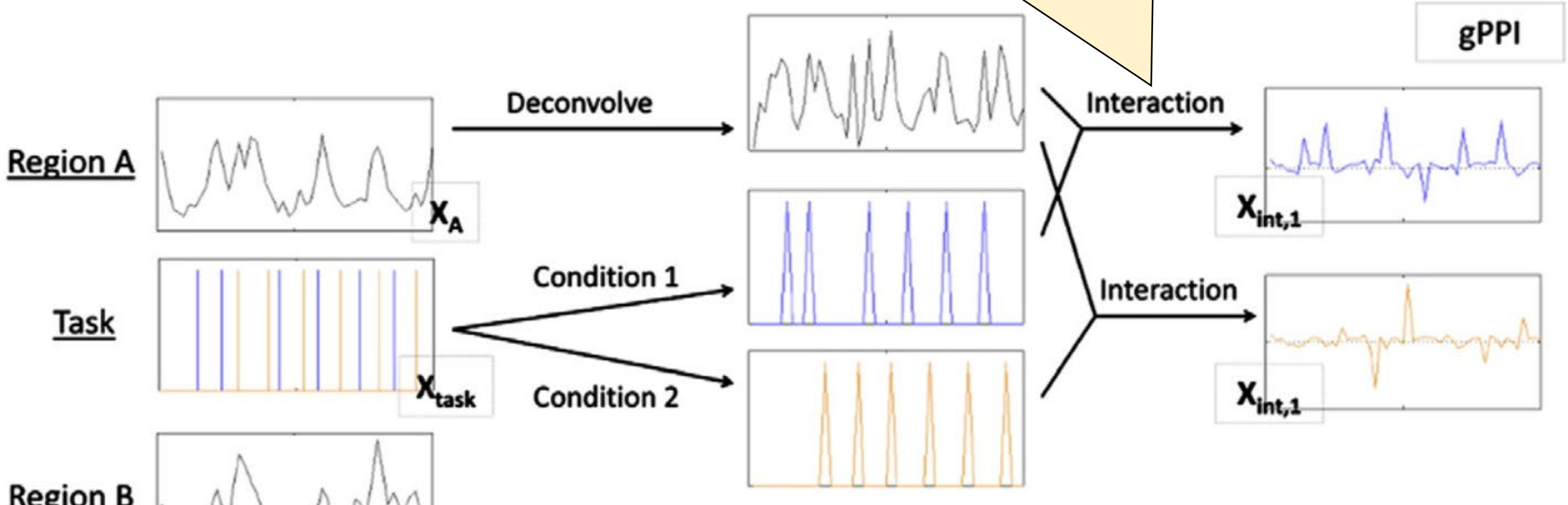
- Model-based with an approximated neuronal input structure
- Implemented in SPM

- 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.



$$y = \beta_A(X_A) + \beta_{task}(X_{task} \cdot HRF) + \beta_{int,1}(X_{int,1} \cdot HRF) + \beta_{int,2}(X_{int,2} \cdot HRF)$$

Contrast betas

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.)

gPPI: Design matrix



Generalized PPI Toolbox

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



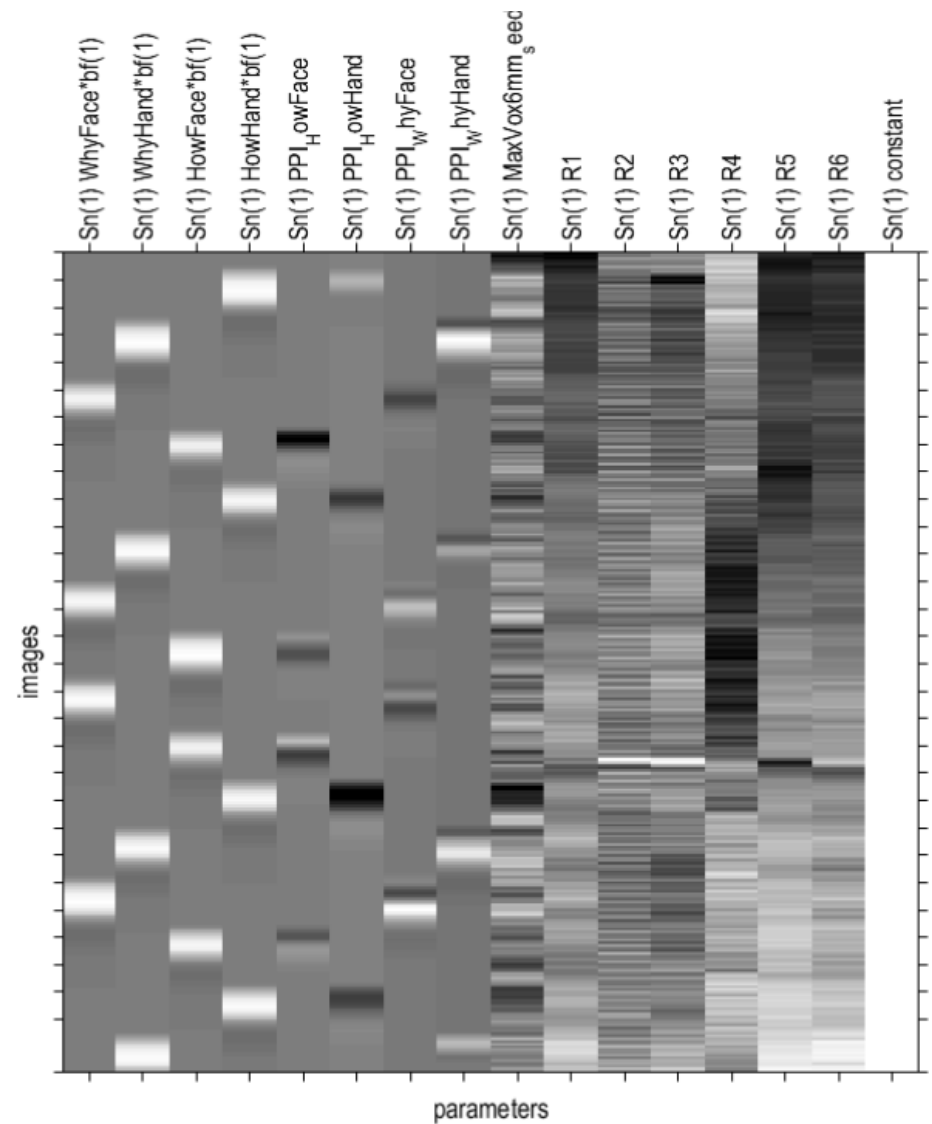
gPPI Lab Topic – afternoon

gPPI with CONN:

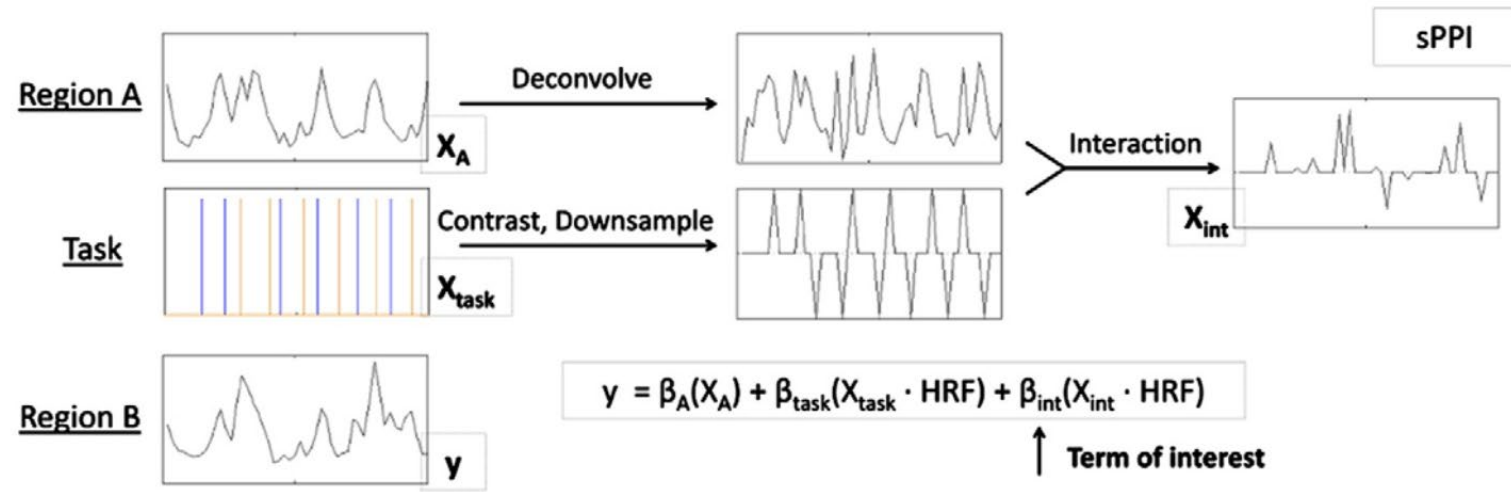
https://andysbrainbook.readthedocs.io/en/latest/FunctionalConnectivity/CONN_ShortCourse/CONN_11_Task_gPPI.html

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>

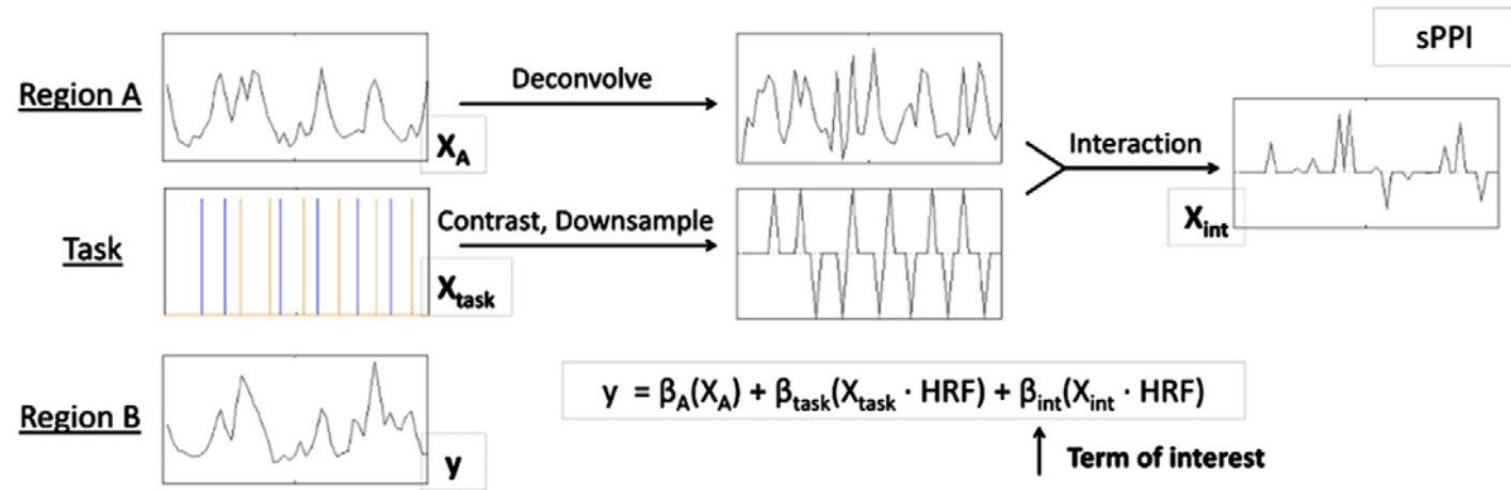


Correlational PPI



- 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

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).

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



cPPI Toolbox for fMRI

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

NeuroImage 217 (2020) 116887



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



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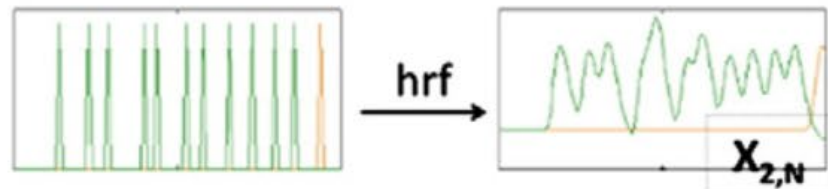
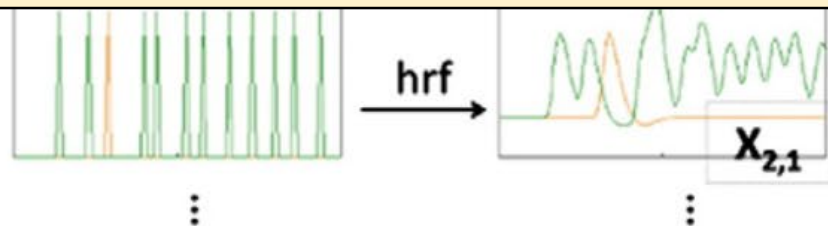
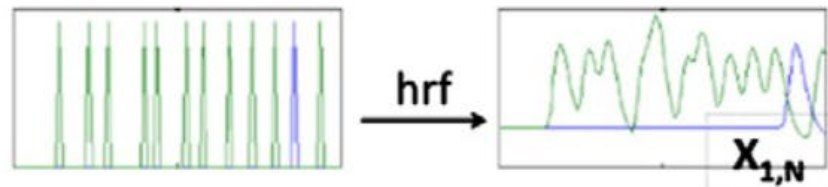
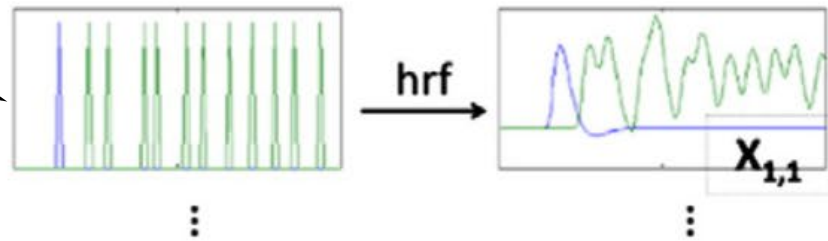
^f Functional MRI Laboratory, Department of Biomedical Engineering, University of Michigan, 2360 Bonisteel Blvd, Ann Arbor, MI, 48109, United States

Beta Series Method

LS-separate

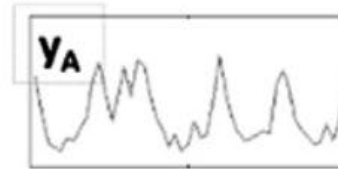
1. Create separate regressor for each trial of each condition and convolve with HRF.

2. Make trial-specific design matrix with 2 regressors: 1) trial of interest; 2) all other trials simultaneously. Estimate task activity unique to each trial.



3. Separately for each condition, correlate the series of β values for regions A and B

Region A



$$y_A = \beta_{1,1,A}(X_{1,1})$$

$$\vdots$$

$$y_A = \beta_{1,N,A}(X_{1,N})$$

$$\beta_{1,1\dots N,B} = \beta_{1,int}(\beta_{1,1\dots N,A})$$

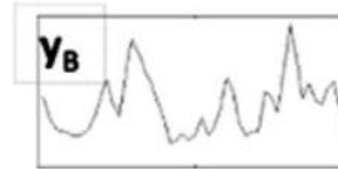
$$\beta_{2,1\dots N,B} = \beta_{2,int}(\beta_{2,1\dots N,A})$$

$$y_A = \beta_{2,1}(X_{2,1})$$

$$\vdots$$

$$y_A = \beta_{2,N}(X_{2,N})$$

Region B



$$y_B = \beta_{1,1,B}(X_{1,1})$$

$$\vdots$$

$$y_B = \beta_{1,N,B}(X_{1,N})$$

Contrast Betas

4. Calculate difference in (Fisher-z transformed) correlation coefficients

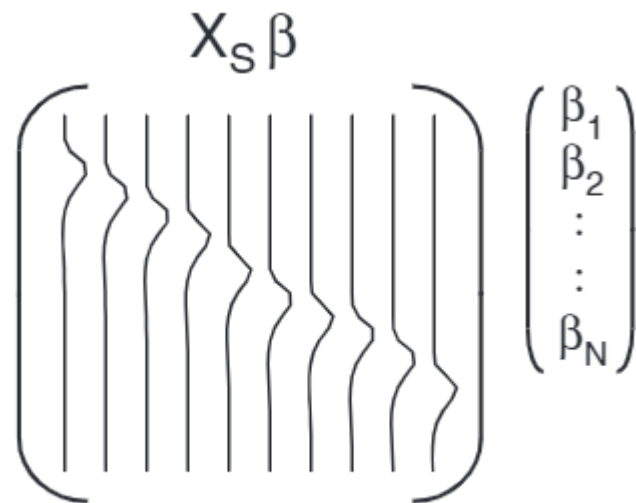
Task

Condition 1

Condition 2

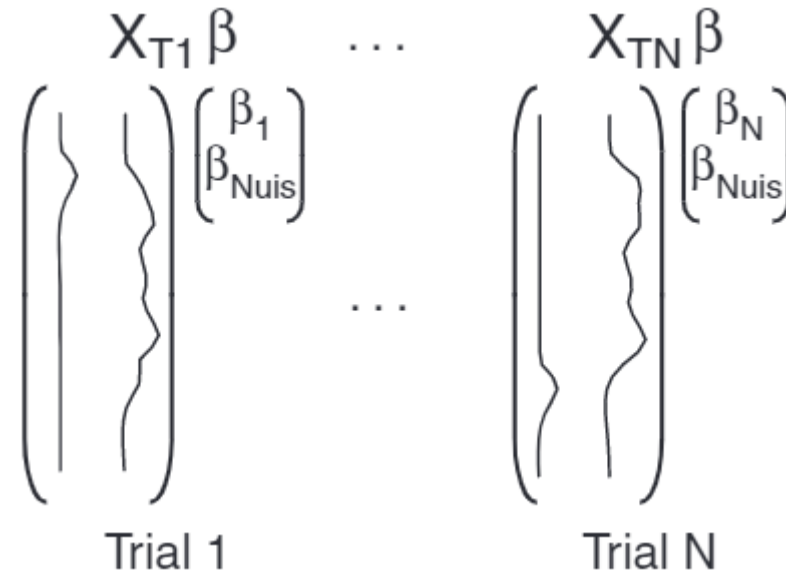
Beta-series estimation

Least Squares – All (LS-A)



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

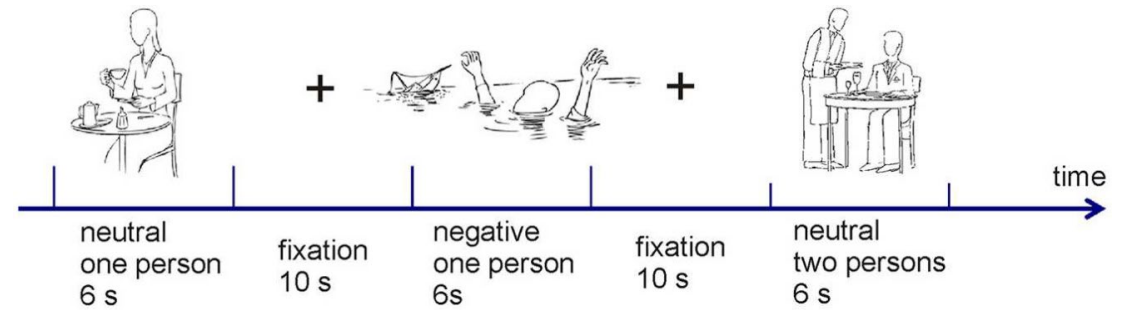
Least Squares – Separate (LS-S)



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.

Beta-Series COrrrelation

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



Beta-Series COrrrelation V2.0

Open Save Help Close

Model specification and estimation Info

Correlate ROIs

Extract ROI beta-series Select condition(s)

Inspect beta-series Correlation matrix

Product-moment correlation

Correlate seed-ROI with voxels

Seed ROI Show ROI ROI beta-series

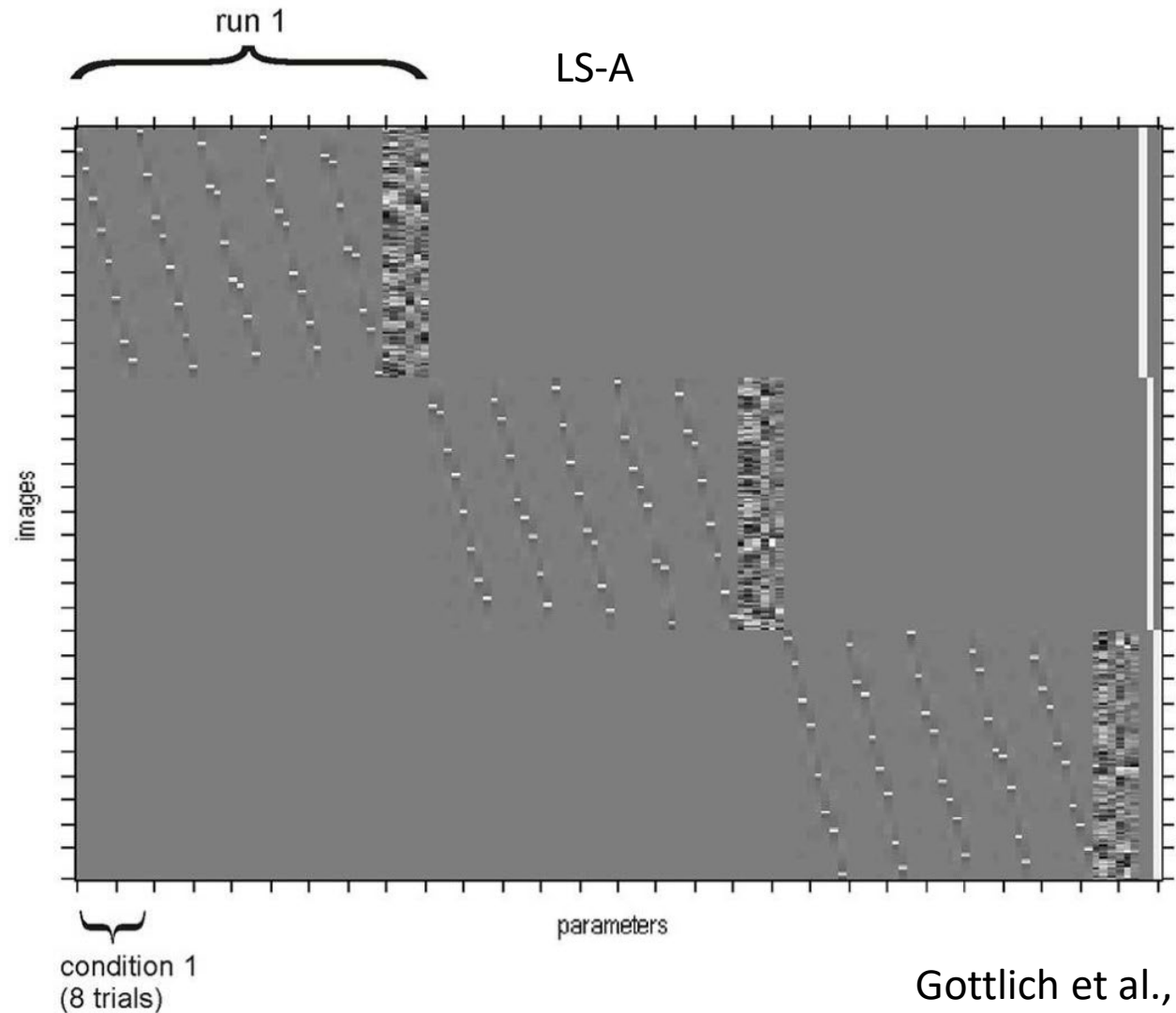
Compute correlation map Condition(s) 1 Mask

Level 2 analysis paired t-test

Voxel Level Network Analysis

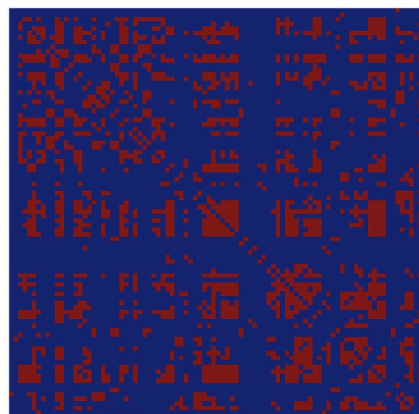
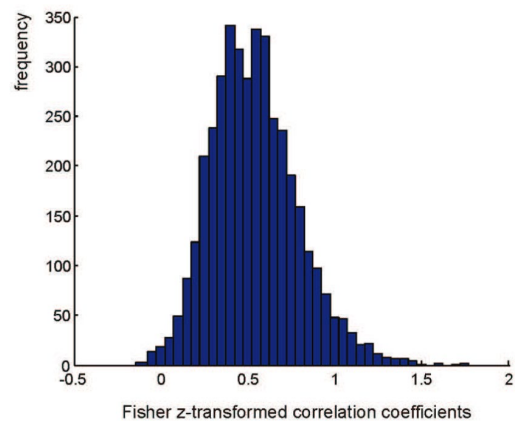
Tools

Network analysis

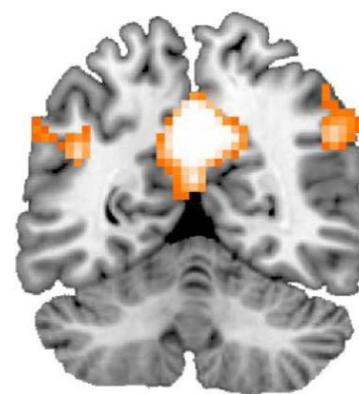


Correlate ROIs

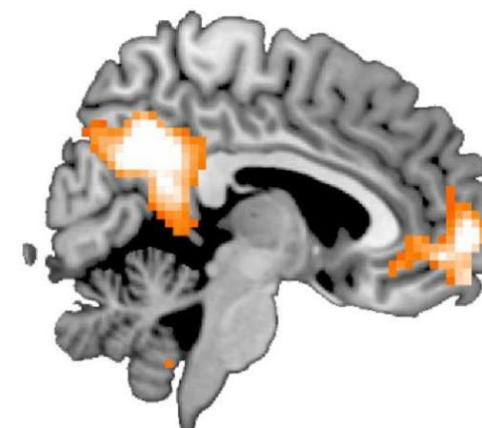
Correlate seed-ROI with voxels



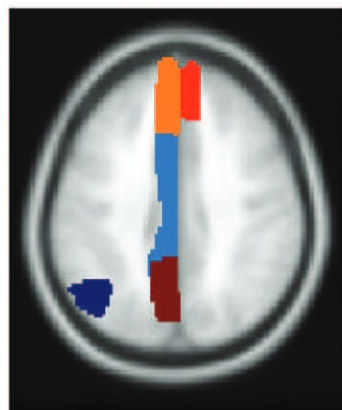
y=-58 mm



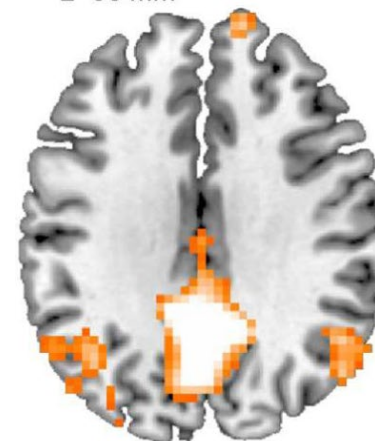
x=5 mm



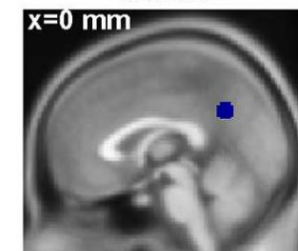
z= 38 mm



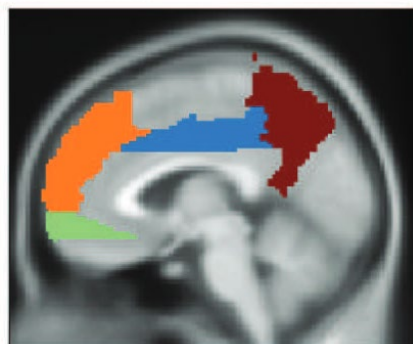
z=33 mm



seed



x=-3 mm



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

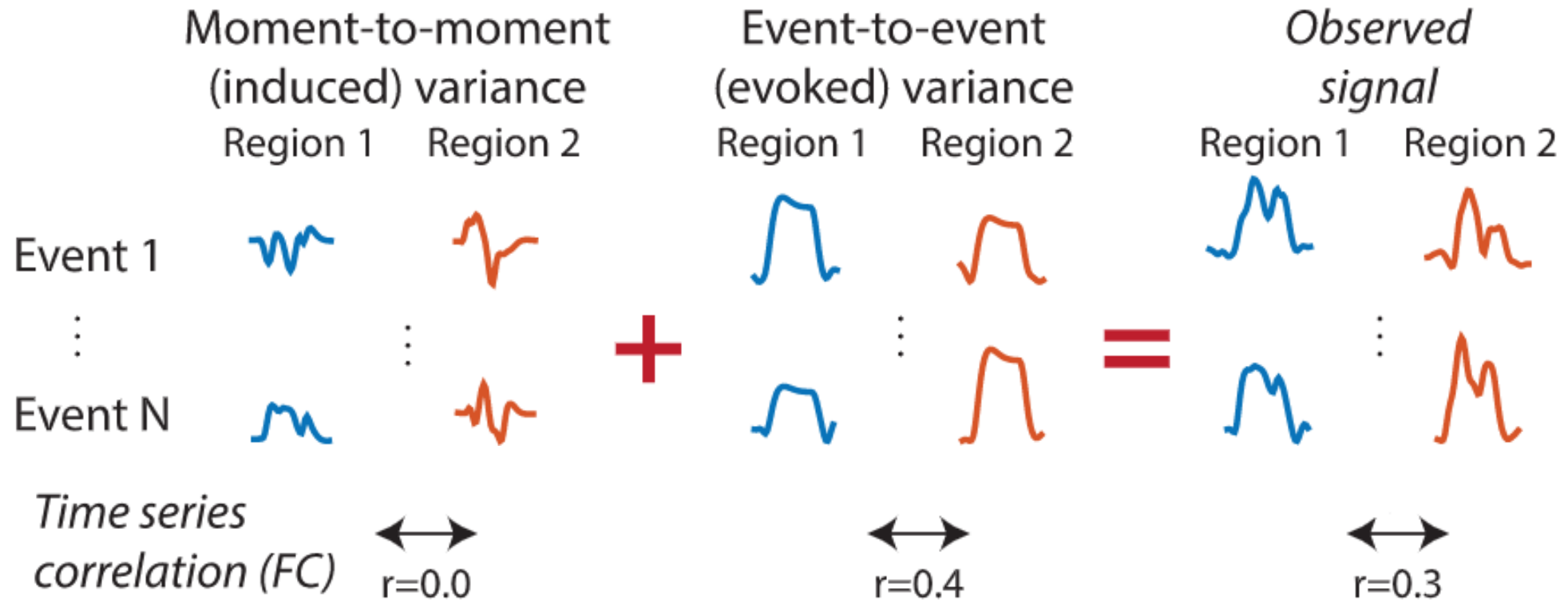
- Cons

- 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

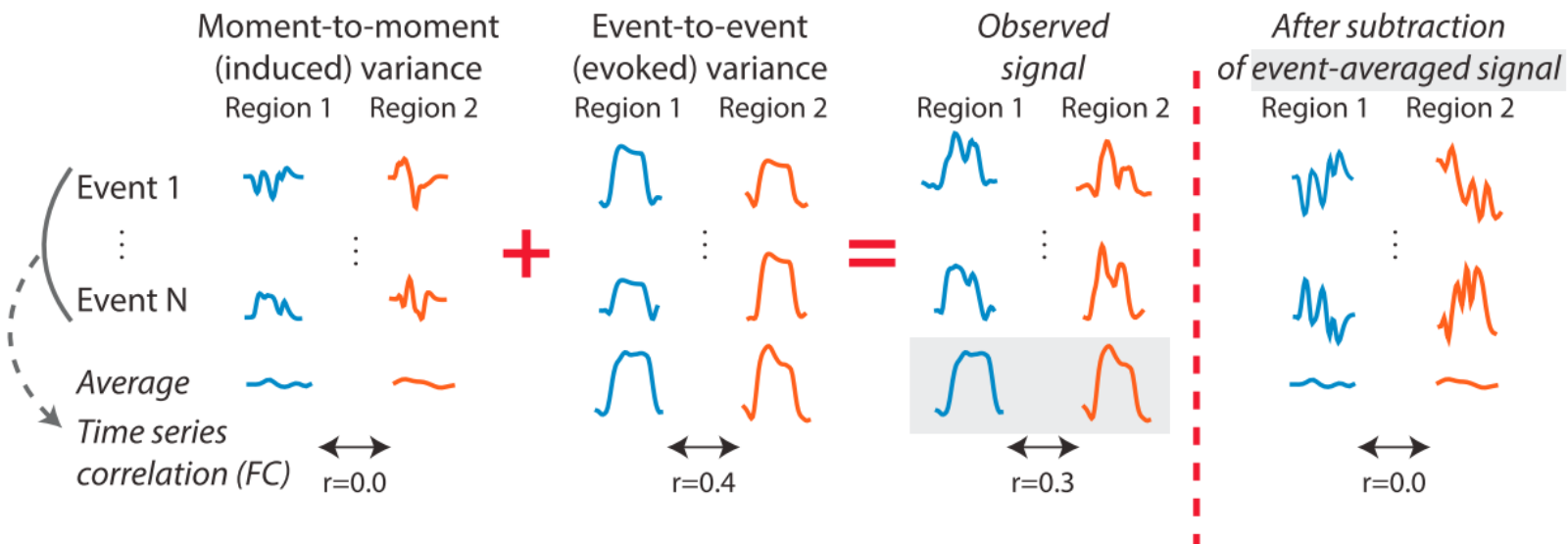
- Fundamental difference
 - PPI measures a change in regression slope or parameter of a model of “effective connectivity” as a function of condition
 - Does more activation in region X predict more activation in region Y in condition A compared to condition B?
 - Beta-series correlation is “model-free” 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?)

Task-evoked activations and task-state FC inferences



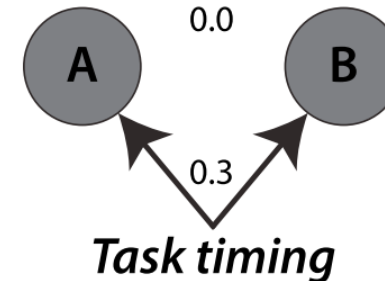
Background/task-residual connectivity = endogenous or “residual” FC between brain regions after accounting for variance related to evoked task activity

No neural interaction

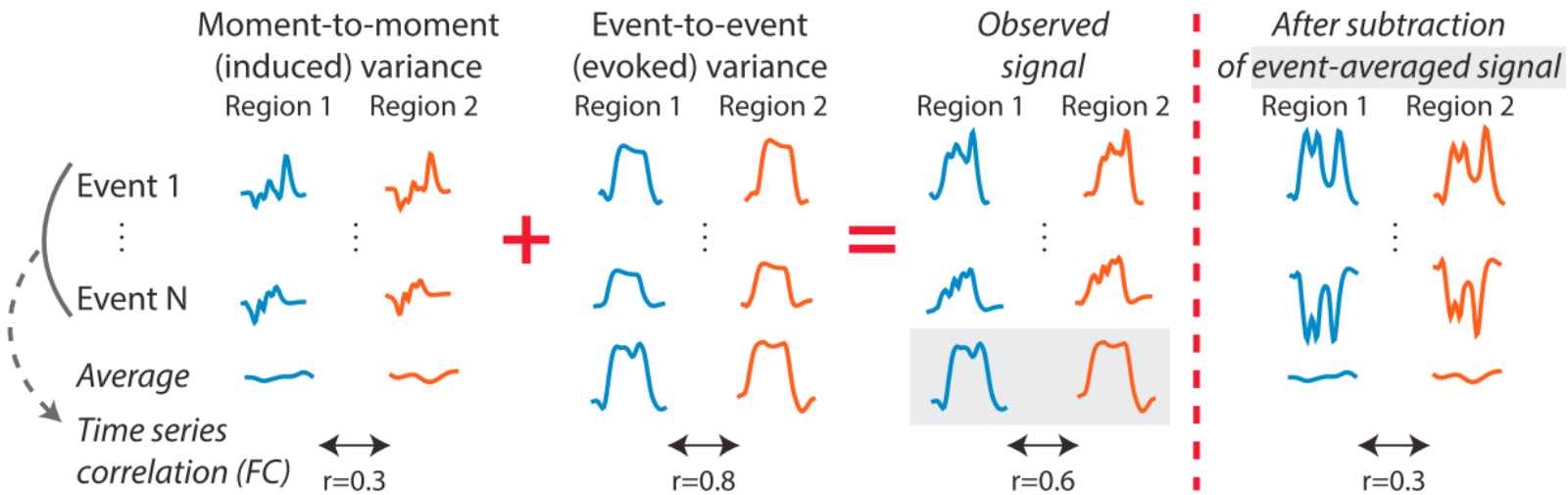


No neural interaction
Observed correlation: 0.3
Inference: “Likely interacting or active during task”

Post-task-regression correlation: 0.0
Inference: “Unlikely to be interacting during task”

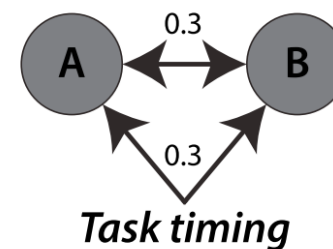


True neural interaction *Induced + evoked covariance*



True neural interaction
Observed correlation: 0.6
Inference: “Likely interacting or active during task”

Post-task-regression correlation: 0.3
Inference: “Likely interacting during task”




CONN : functional connectivity toolbox

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

First-level covariates / timeseries

Covariates	Subjects	Sessions	Covariate name
realignment	Subject 1	Session 1	Effect of Memo1
scrubbing	Subject 2	Session 2	
Effect of Incorr.	Subject 3	Session 3	
<u>Effect of Memo1</u>	Subject 4	Session 4	
Effect of Memo1	Subject 5	Session 5	
Effect of Memo1	Subject 6	Session 6	
Effect of Memo1	Subject 7		
Effect of Memo1	Subject 8		
Effect of Memo1	Subject 9		
Effect of Probe1	Subject 10		
Effect of Probe5	Subject 11		
Effect of Probe6	Subject 12		
Effect of Probe7	Subject 13		
Effect of Probe8	Subject 14		
Effect of Probe9	Subject 15		
	Subject 16		
	Subject 17		
	Subject 18		
	Subject 19		
	Subject 20		




Denoising settings

Linear regression of confounding effects:

Confounds

- White Matter (5P)
- CSF (5P)
- realignment (12P)
- scrubbing (39P)
- Effect of Incorr (1P)
- Effect of Memo1 (1P)**
- Effect of Memo5 (1P)
- Effect of Memo6 (1P)
- Effect of Memo7 (1P)

Confound timeseries



Confound dimensions

- Inf
- no temporal expansion
- no polynomial expansion
- Filtered

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.

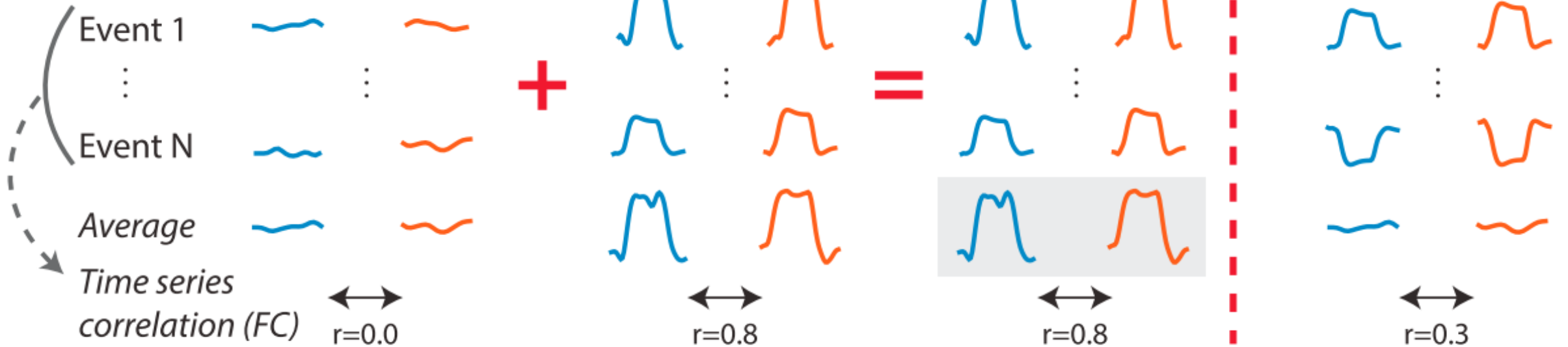
True neural interaction *Evoked covariance only*

Moment-to-moment
(induced) variance
Region 1 Region 2

Event-to-event
(evoked) variance
Region 1 Region 2

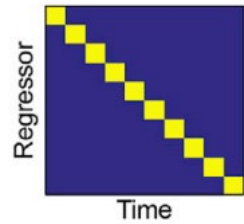
Observed
signal
Region 1 Region 2

After subtraction
of event-averaged signal
Region 1 Region 2

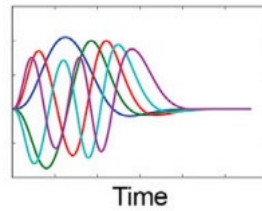


Alternatives:

FIR modeling



Constrained basis set



First-level covariates / timeseries

Covariates	Subjects	Sessions	Covariate name
realignment	Subject 1	Session 1	fir_Memo
scrubbing	Subject 2	Session 2	
fir Memo	Subject 3	Session 3	
fir Probe	Subject 4	Session 4	
Effect of Incorr	Subject 5	Session 5	
	Subject 6	Session 6	
	Subject 7		
	Subject 8		
	Subject 9		
	Subject 10		
	Subject 11		
	Subject 12		
	Subject 13		
	Subject 14		
	Subject 15		
	Subject 16		
	Subject 17		
	Subject 18		
	Subject 19		
	Subject 20		



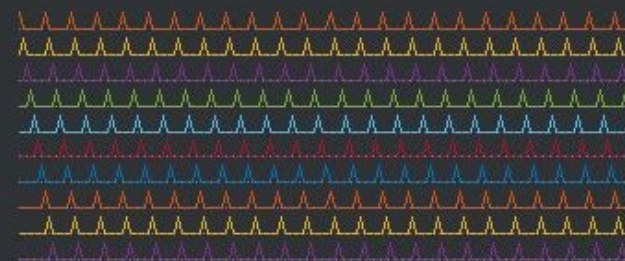
Denoising settings

Linear regression of confounding effects:

Confounds

- White Matter (5P)
- CSF (5P)
- realignment (12P)
- scrubbing (39P)
- fir Memo (10P)**
- fir Probe (10P)
- Effect of Incorr (1P)

Confound timeseries



Confound dimensions

- Inf
- no temporal expansion
- no polynomial expansion

■ Filtered

However, keep an eye on the estimated remaining DoF!