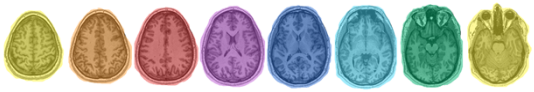
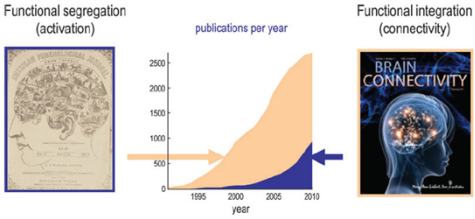
EGNER LAB



Functional Connectivity: Psychophysiological Interaction (PPI) and Residual Correlation Analyses

Functional Connectivity: PPI and Residuals



Friston (2011), *Brain Connectivity*

Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

- **Intrinsic Functional connectivity**
  Unconstrained ("resting-state") activity correlations, interpreted as reflecting intrinsic functional connectivity.

Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

- **Intrinsic Functional connectivity**
  Unconstrained ("resting-state") activity correlations, interpreted as reflecting intrinsic functional connectivity.
- **Context-dependent Functional connectivity**
  Physiological correlation as modulated by psychological variable(s), interpreted as reflecting context-dependent changes in connectivity.

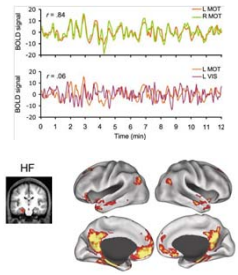
Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

- **Intrinsic Functional connectivity**
  Unconstrained ("resting-state") activity correlations, interpreted as reflecting intrinsic functional connectivity.
- **Context-dependent Functional connectivity**
  Physiological correlation as modulated by psychological variable(s), interpreted as reflecting context-dependent changes in connectivity.
  - **PPI**: Incorporates model of task-/event-driven activations. (Presently very commonly used in event-related designs)
  - **Residuals**: Removes task-/event-driven activations. (Typically used to gauge state-related effects in block designs)

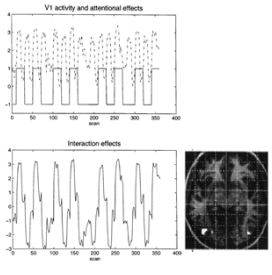
Functional Connectivity: PPI and Residuals

Intrinsic Functional connectivity



E.g. Vincent et al. (2008), *J Neurophysiol*

Context-dependent Functional connectivity



Friston et al. (1997), *Neuroimage*

Functional Connectivity: PPI and Residuals

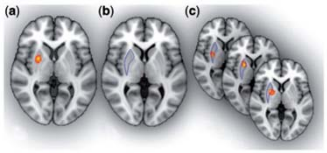
PPI Basics

- Friston et al. (1997) developed the basic analysis (now in SPM, FSL, and AFNI):
- (1) extract representative activation time course data from a *seed region of interest* (usually based on task activations) = **physiological variable**

Functional Connectivity: PPI and Residuals

PPI Basics

- Friston et al. (1997) developed the basic analysis (now in SPM, FSL, and AFNI):
- (1) extract representative activation time course data from a *seed region of interest* (usually based on task activations) = **physiological variable**



Both the seed regions and target search space can also be defined in various ways (e.g., anatomical ROI, functionally defined ROI, conjunction, etc.).

Functional Connectivity: PPI and Residuals

PPI Basics

- Friston et al. (1997) developed the basic analysis (now in SPM, FSL, and AFNI):
- (1) extract representative activation time course data from a seed region (usually based on task activations) = **physiological variable**
- (2) create a psychological vector/contrast of interest (e.g., "main effect of attention") = **psychological variable**

Functional Connectivity: PPI and Residuals

PPI Basics

- Friston et al. (1997) developed the basic analysis (now in SPM, FSL, and AFNI):
- (1) extract representative activation time course data from a seed region (usually based on task activations) = **physiological variable**
- (2) create a psychological vector/contrast of interest (e.g., "main effect of attention") = **psychological variable**
- (3) calculate element-by-element product between the physiological and psychological time courses = **psychophysiological interaction (PPI) variable**

Functional Connectivity: PPI and Residuals

PPI Basics

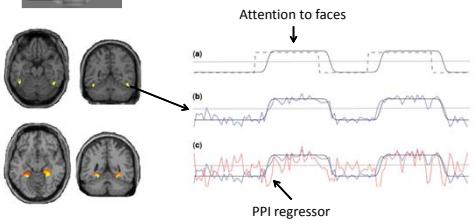
- Friston et al. (1997) developed the basic analysis (now in SPM, FSL, and AFNI):
- (1) extract representative activation time course data from a seed region (usually based on task activations) = **physiological variable**
- (2) create a psychological vector/contrast of interest (e.g., "main effect of attention") = **psychological variable**
- (3) calculate element-by-element product between the physiological and psychological time courses = **psychophysiological interaction (PPI) variable**
- (4) Build a new model to search for voxels whose time courses are reliably correlated with the PPI regressor.

Functional Connectivity: PPI and Residuals

	Attend Face	Attend Scene

Functional Connectivity: PPI and Residuals

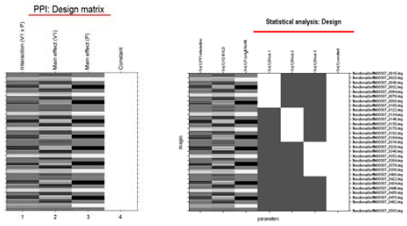
	Attend Face	Attend Scene
	FFA ↑ PPA ↓	FFA ↓ PPA ↑



Functional Connectivity: PPI and Residuals

PPI Basics

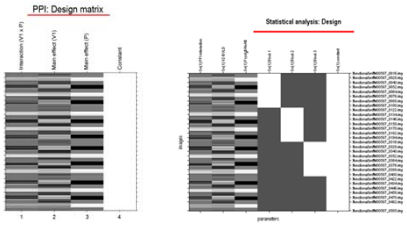
- Key considerations (1): In addition to the PPI regressor, **always** include both the original physiological and psychological variables in the PPI model! We are interested in variance explained by the PPI *above and beyond* that explained by the task effect and the seed region time course. (This guards against spurious findings but also results in relatively low power).



Functional Connectivity: PPI and Residuals

PPI Basics

- While traditional PPI models entail only these 3 regressors, it is now widely recommended to include any other additional regressors that model known variance in the data (like other conditions, motion parameters, etc.).



Functional Connectivity: PPI and Residuals

PPI Basics

- Key considerations (2): Friston et al.'s (1997) original application was based on block-designs. When extending PPIs to event-related designs, an additional issue became more apparent: the psychological context is measured in "real time" but its consequence on the BOLD response is delayed by ≈6s.

Functional Connectivity: PPI and Residuals

PPI Basics

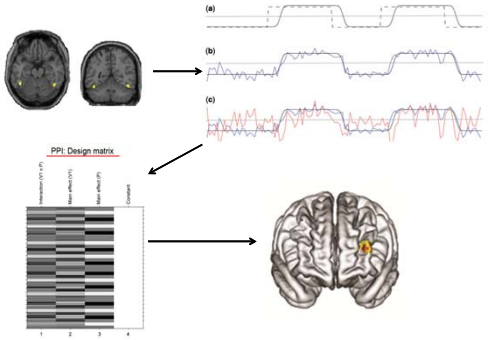
- Key considerations (2): Friston et al.'s (1997) original application was based on block-designs. When extending PPIs to event-related designs, an additional issue became more apparent: the psychological context is measured in "real time" but its consequence on the BOLD response is delayed by ≈6s.
- To solve this issue, Gitelman et al. (2003) developed a method to *deconvolve* the physiological time course, trying to translate BOLD signals back to an estimated "neuronal" time-course. This time-course is then used to compute the PPI term, after which all 3 terms get convolved with an HRF.

Functional Connectivity: PPI and Residuals

PPI Basics

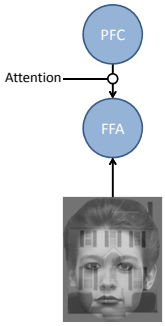
- Key considerations (2): Friston et al.'s (1997) original application was based on block-designs. When extending PPIs to event-related designs, an additional issue became more apparent: the psychological context is measured in "real time" but its consequence on the BOLD response is delayed by ≈6s.
- To solve this issue, Gitelman et al. (2003) developed a method to *deconvolve* the physiological time course, trying to translate BOLD signals back to an estimated "neuronal" time-course. This time-course is then used to compute the PPI term, after which all 3 terms get convolved with an HRF.
- While the PPI utility in SPM employs deconvolution of the BOLD time-course to "match" neural and psychological events, FSL instead convolves the psychological time series with the HRF to achieve the same goal.

Functional Connectivity: PPI and Residuals



Functional Connectivity: PPI and Residuals

Functional Connectivity: PPI and Residuals



Functional Connectivity: PPI and Residuals

	Attend Face	Attend Scene

Functional Connectivity: PPI and Residuals

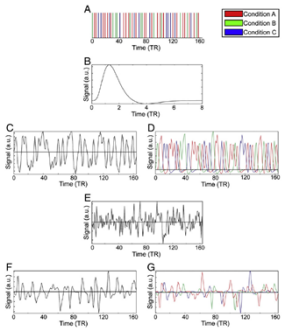
	Attend Face	Attend Scene
Task Repetition		
Task Switch		

Limitation of traditional PPI: using only single PPI regressor can be tricky in more complicated designs, often ignores parts of the "task space" and does not allow us to flexibly compare connectivity across more than two conditions.

This shortcoming is addressed in a "generalized PPI" (gPPI) Toolbox (http://www.nitrc.org/projects/gppi/) that facilitates the simultaneous modeling of multiple PPI vectors.

McLaren et al. (2012), *Neuroimage*

Functional Connectivity: PPI and Residuals



Here, in addition to the seed region time-course, PPI (and task) regressors for all conditions get included in the PPI design matrix.

"Connectivity contrasts" can then be carried out between any conditions of interest (and estimated for single conditions).

McLaren et al. (2012), *Neuroimage*

Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

- **Intrinsic Functional connectivity**
  Unconstrained ("resting-state") activity correlations, interpreted as reflecting intrinsic functional connectivity.
- **Context-dependent Functional connectivity**
  Physiological correlation as modulated by psychological variable(s), interpreted as reflecting context-dependent changes in connectivity.
  - **PPI**: Incorporates model of task-/event-driven activations. (Presently very commonly used in event-related designs)
  - **Residuals**: Removes task-/event-driven activations. (Typically used to gauge state-related effects in block designs)

Functional Connectivity: PPI and Residuals

Why correlate residuals across brain regions?

- The motivation behind the use of residuals is partly that brain function is characterized both by phasic, stimulus-driven responses as well as (and in interaction with) more tonic, endogenous brain states, and that the latter might "set the stage" for much of the former.
- Using residuals (after removing all task-related effects from the data) may also be the safest way to avoid spurious connectivity results (e.g., stimulus-driven correlations). Even though we model task-related factors in PPI analyses, it is likely that some (un-modelled) task-driven variance remains (e.g., components that might not be captured by canonical HRF).

Functional Connectivity: PPI and Residuals

OPEN ACCESS Freely available online PLoS BIOLOGY

Neocortical Connectivity during Episodic Memory Formation

Christopher Summerfield[1]*, Matthew Greene[1], Tor Wager[1], Tobias Egner[2], Joy Hirsch[2], Jennifer Mangels[1]

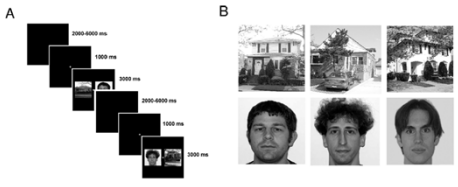
1 Department of Psychology, Columbia University, New York, New York, United States of America, 2 Functional MRI Research Center, Department of Radiology, Columbia University, New York, New York, United States of America

During the formation of new episodic memories, a rich array of perceptual information is bound together for long-term storage. However, the brain mechanisms by which sensory representations (such as colors, objects, or individuals) are selected for episodic encoding are currently unknown. We describe a functional magnetic resonance imaging experiment in which participants encoded the association between two classes of visual stimuli that elicit selective responses in the extrastriate visual cortex (faces and houses). Using connectivity analyses, we show that correlation in the hemodynamic signal between face- and place-sensitive voxels and the left dorsolateral prefrontal cortex is a reliable predictor of successful face–house binding. These data support the view that during episodic encoding, "top-down" control signals originating in the prefrontal cortex help determine which perceptual information is fated to be bound into the new episodic memory trace.

Citation: Summerfield C, Greene M, Wager T, Egner T, Hirsch J, et al. (2006) Neocortical connectivity during episodic memory formation. PLoS Biol 4(5): e128. DOI: 10.1371/journal.pbio.0040128

Summerfield et al. (2006), *PLoS Biology*

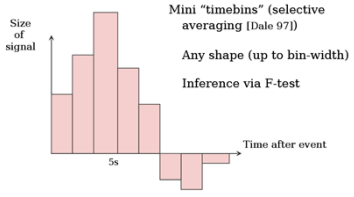
Functional Connectivity: PPI and Residuals



Subjects encoded face-house pairs in 20 blocks of 7 trials. We later used block-wise residuals in FFA/PPA to locate frontal regions whose "background connectivity" with these regions varied with encoding success (block-wise ROC), reflective of a "cognitive set" that facilitates encoding. To remove all stimulus-evoked responses from FFA/PPA time-series, we modeled events with **finite impulse response (FIR)** basis functions and then used the remaining ''residual'' hemodynamic activity for connectivity analyses.

Summerfield et al. (2006), *PLoS Biology*

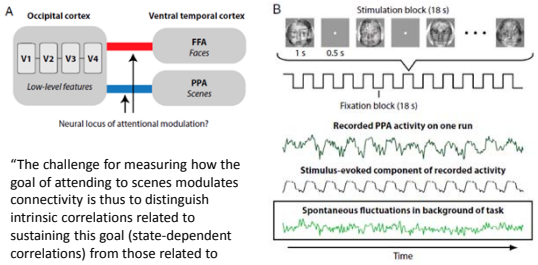
Functional Connectivity: PPI and Residuals



Subjects encoded face-house pairs in 20 blocks of 7 trials. We later used block-wise residuals in FFA/PPA to locate frontal regions whose "background connectivity" with these regions varied with encoding success (block-wise ROC), reflective of a "cognitive set" that facilitates encoding. To remove all stimulus-evoked responses from FFA/PPA time-series, we modeled events with **finite impulse response (FIR)** basis functions and then used the remaining ''residual'' hemodynamic activity for connectivity analyses.

Summerfield et al. (2006), *PLoS Biology*

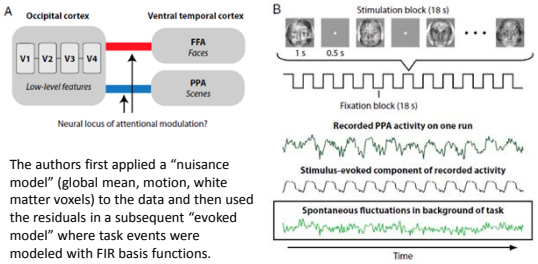
Functional Connectivity: PPI and Residuals



"The challenge for measuring how the goal of attending to scenes modulates connectivity is thus to distinguish intrinsic correlations related to sustaining this goal (state-dependent correlations) from those related to synchronized stimulus-evoked responses (stimulus-driven correlations)."

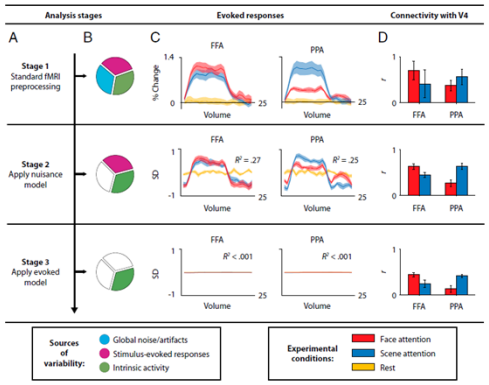
Al-Aidroos et al. (2012), *PNAS*

Functional Connectivity: PPI and Residuals



The authors first applied a "nuisance model" (global mean, motion, white matter voxels) to the data and then used the residuals in a subsequent "evoked model" where task events were modeled with FIR basis functions. Residuals from the evoked model were then employed for the correlation ("background connectivity") analysis.

Al-Aidroos et al. (2012), *PNAS*



Al-Aidroos et al. (2012), *PNAS*

Functional Connectivity: PPI and Residuals

Different types of activity time-course ***correlations***:

- **Intrinsic Functional connectivity**
  Unconstrained ("resting-state") activity correlations, interpreted as reflecting intrinsic functional connectivity.
- **Context-dependent Functional connectivity**
  Physiological correlation as modulated by psychological variable(s), interpreted as reflecting context-dependent changes in connectivity.
  - **PPI**: Incorporates model of task-/event-driven activations. (Presently very commonly used in event-related designs)
  - **Residuals**: Removes task-/event-driven activations. (Typically used to gauge state-related effects in block designs)