Granger Causality in fMRI connectivity analysis

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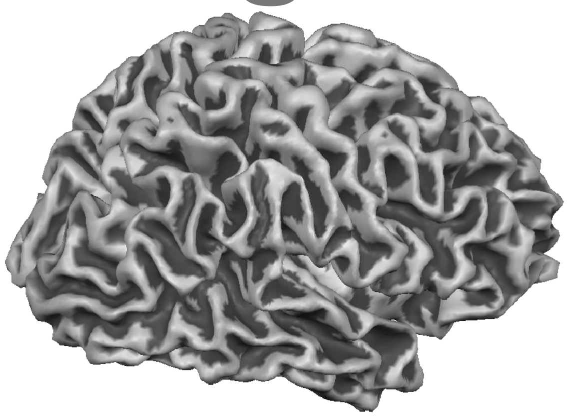
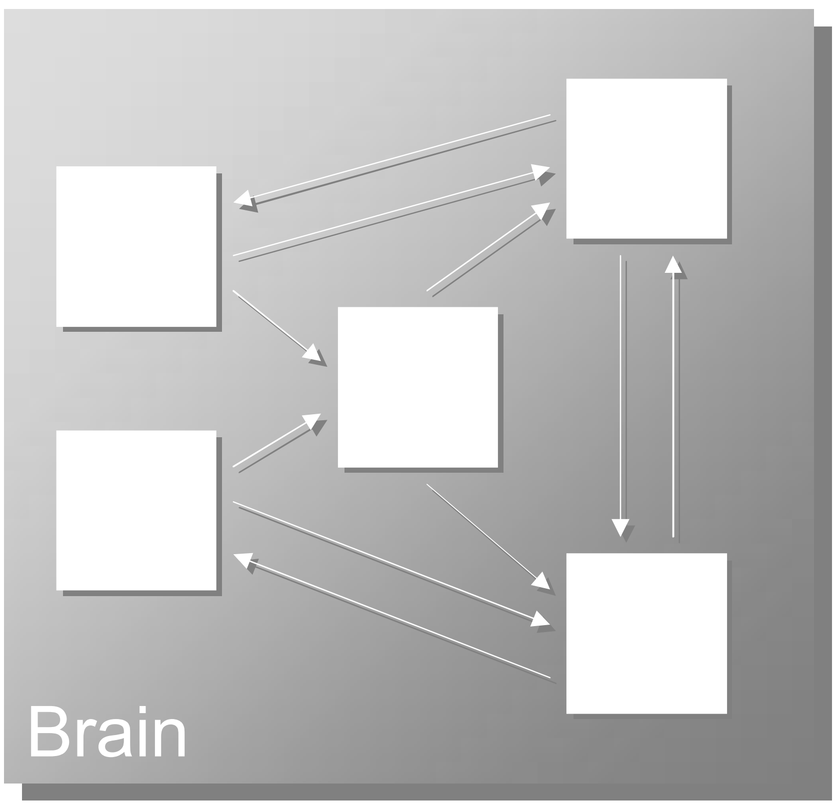
Overview

- **fMRI signal & connectivity**
- **Functional & Effective connectivity**
- **Structural model & Dynamical model**
  - Identification & model selection
- **Granger causality & fMRI**
  - Granger causality and its variants
  - Granger causality mapping
- **Issues with variable hemodynamics**
  - Hemodynamic deconvolution

Integration and connectivity

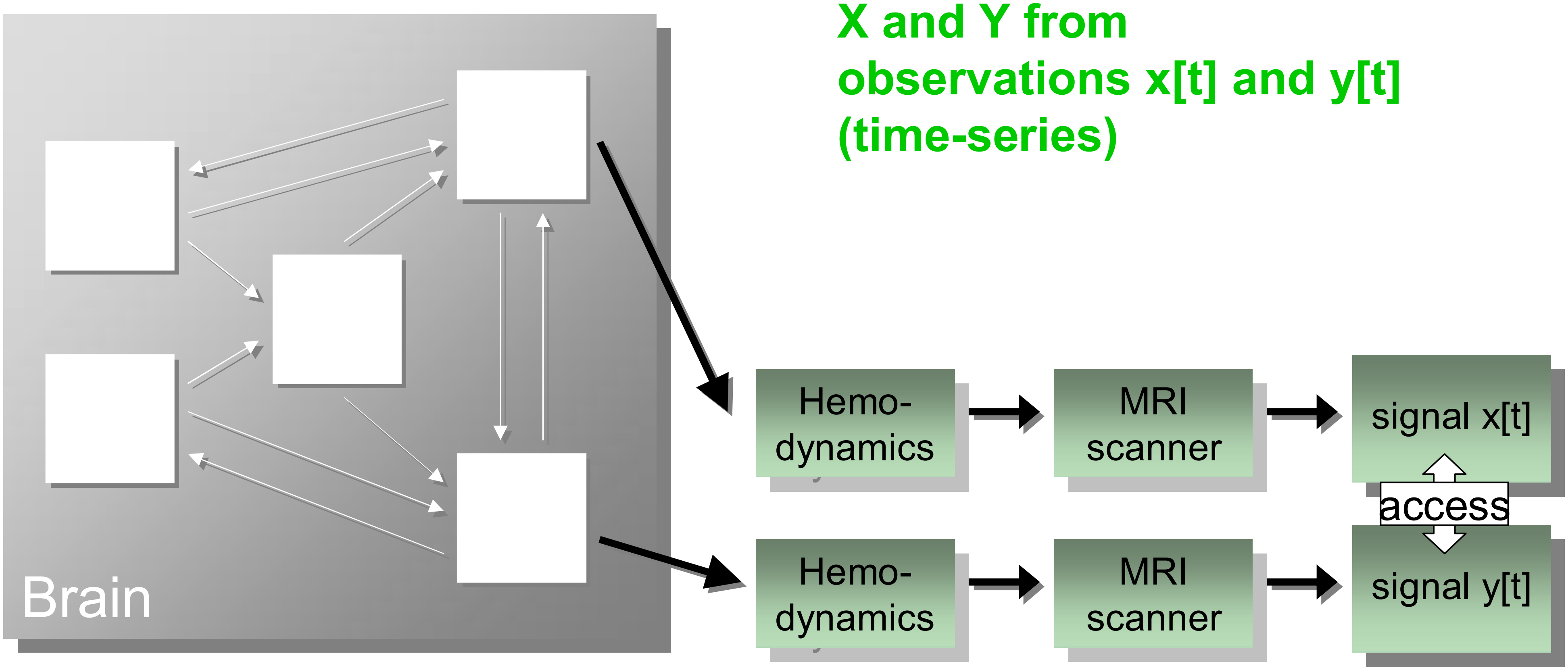




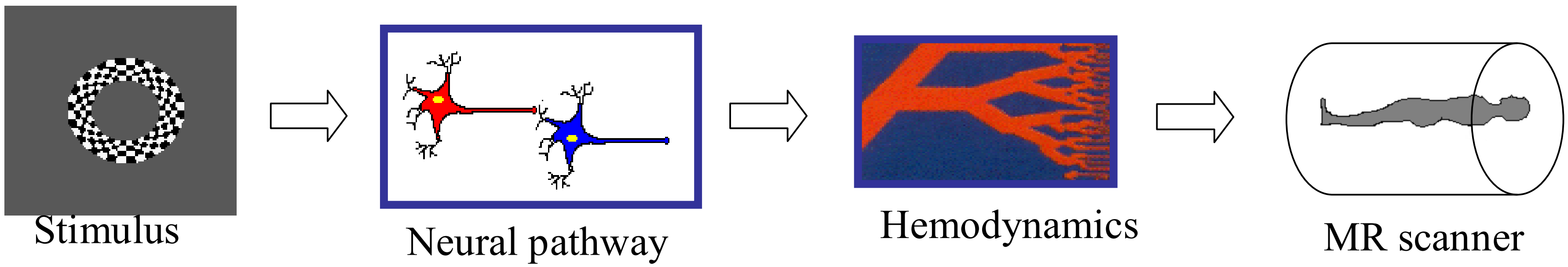
- **Performance of complex tasks requires interaction of specialized brain systems (functional integration)**
- **Interaction of specialized areas requires connectivity**
- **Investigation of complex tasks requires connectivity analysis**

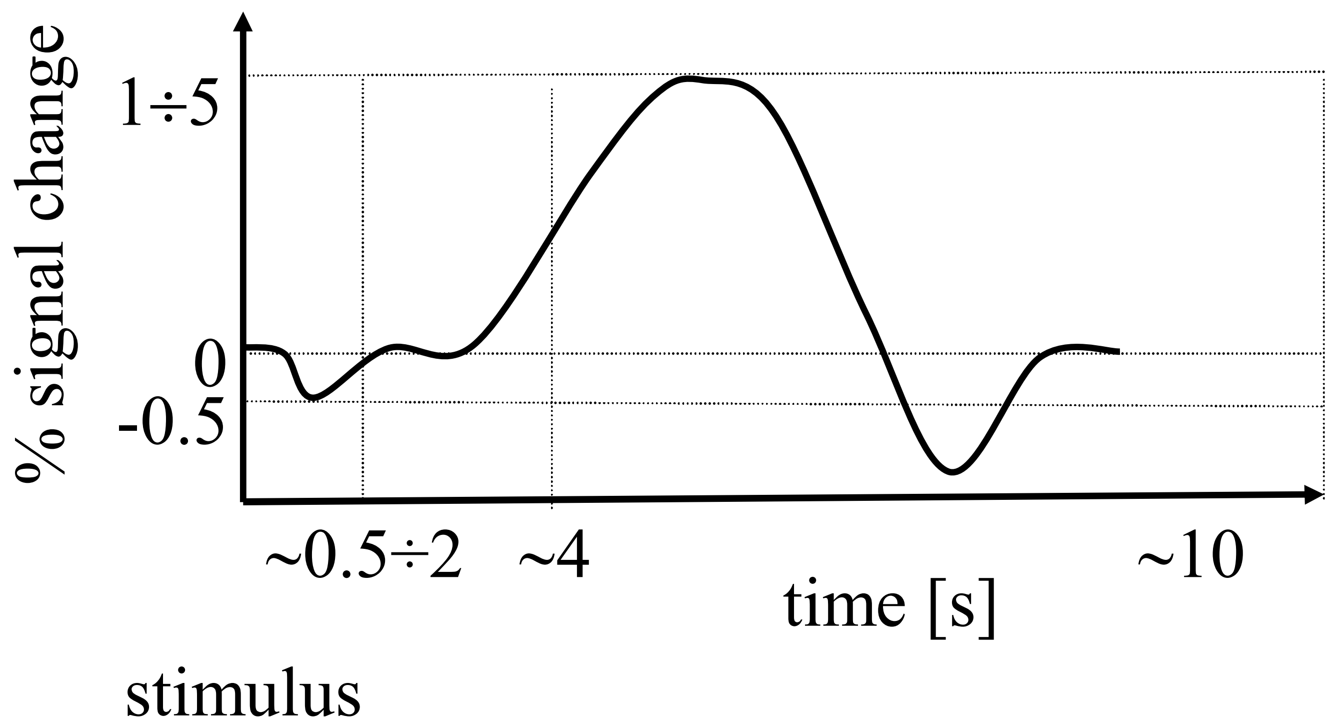
A problem for fMRI connectivity

- **In fMRI our access to the neural activity is *indirect***
- **We want to infer interaction between Area X and Y from observations x[t] and y[t] (time-series)**



fMRI: The BOLD signal





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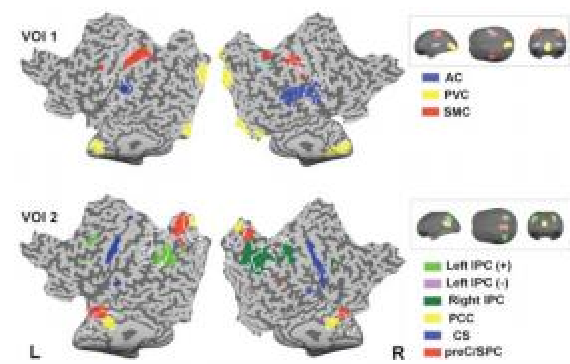
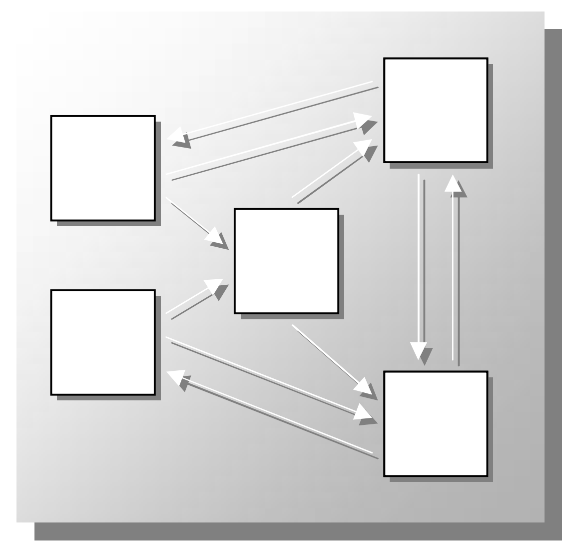
Functional & Effective Connectivity

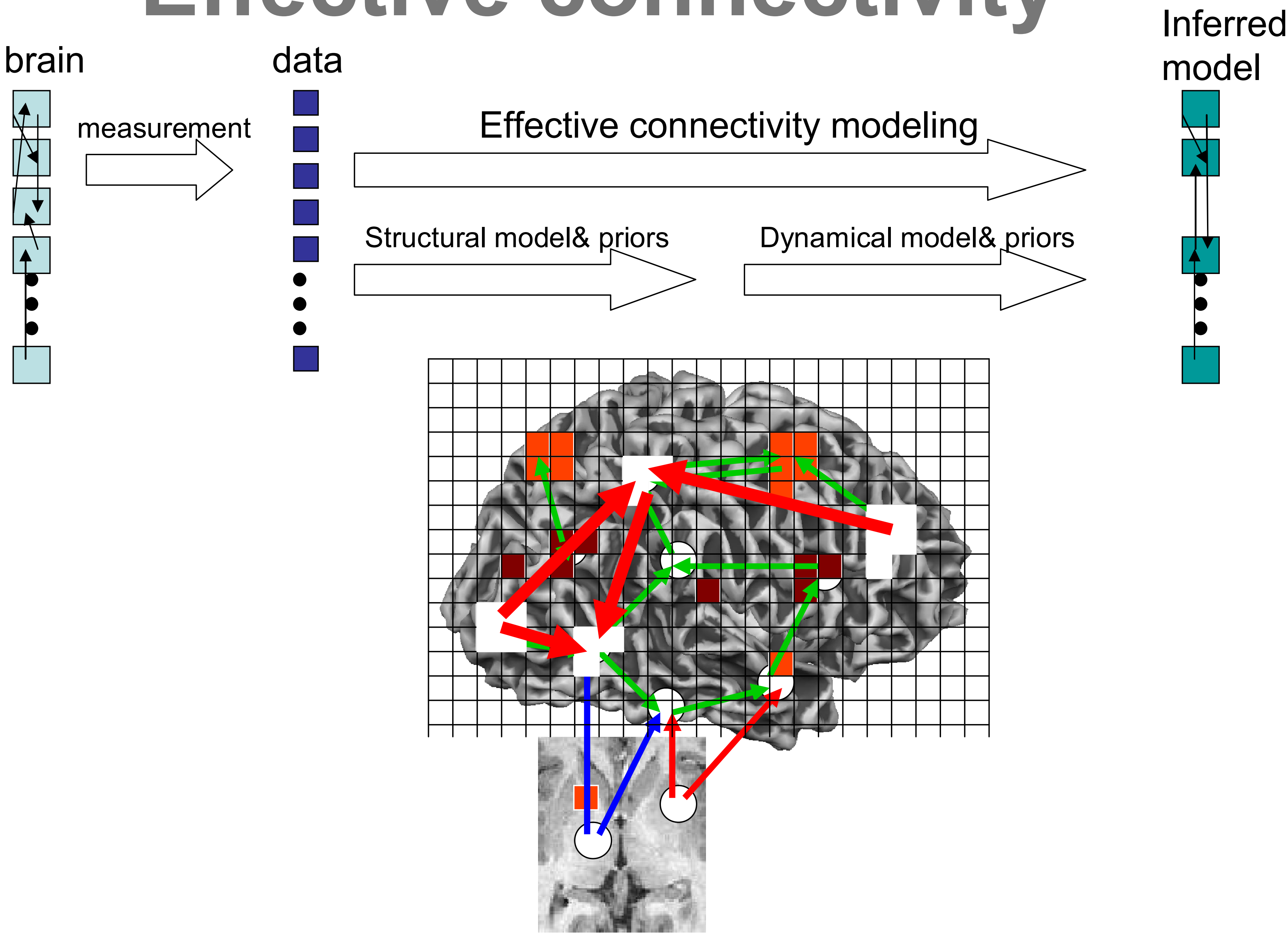
- **Functional connectivity**
  - Association (mutual information)
  - Localization of whole networks



- **Effective connectivity**
  - Uncover network mechanisms (causal influence)
  - Directed vs. undirected
  - Direct vs. indirect



Effective connectivity

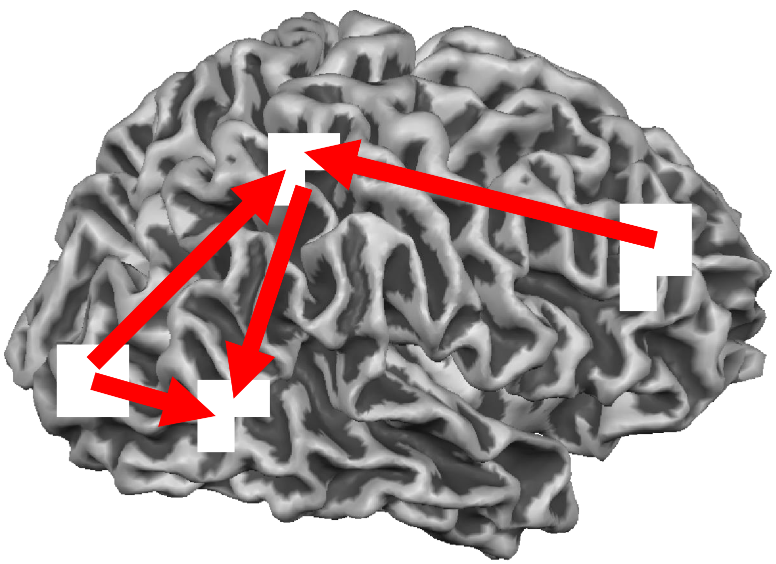


Effective connectivity

Structural model& priors

Dynamical model& priors

- **ROI selection**
- **Graph selection**



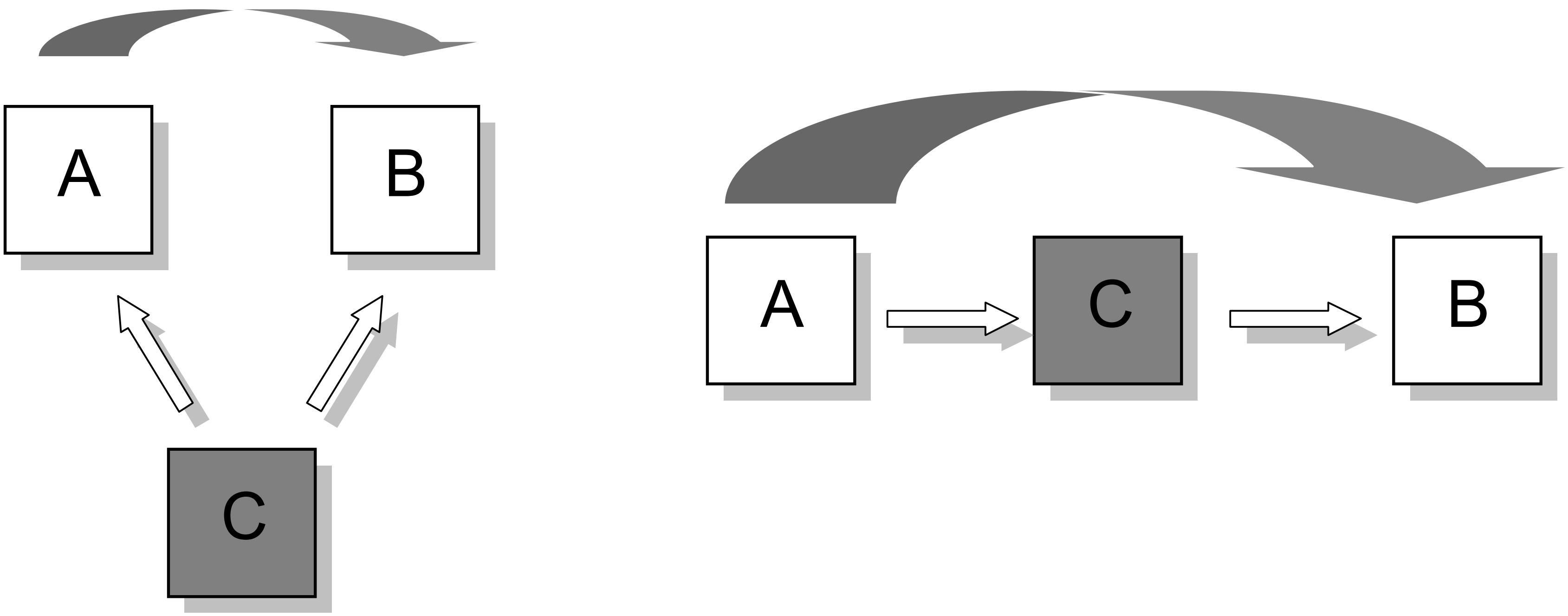
What interacts

- **Deterministic vs. stochastic models**
- **Linear vs. non-linear**
- **Forward observation models**

$$\begin{pmatrix} x[t] \\ y[t] \end{pmatrix} = \sum_{i=1}^{p} \mathbf{A}_i \begin{pmatrix} x[t-i] \\ y[t-i] \end{pmatrix} + \begin{pmatrix} e_{x|y} \\ e_{y|x} \end{pmatrix} \quad \mathrm{cov}\begin{pmatrix} e_{x|y} \\ e_{y|x} \end{pmatrix} = \begin{pmatrix} \sigma_{x|y}^2 & \sigma_{xy} \\ \sigma_{xy} & \sigma_{y|x}^2 \end{pmatrix} = \Sigma$$

How does it interact: signal model

Problem: spurious influence



- Danger of strong structural models:
- When important regions are 'left out' (of the anatomical model), ANY correct method will give 'wrong' answers

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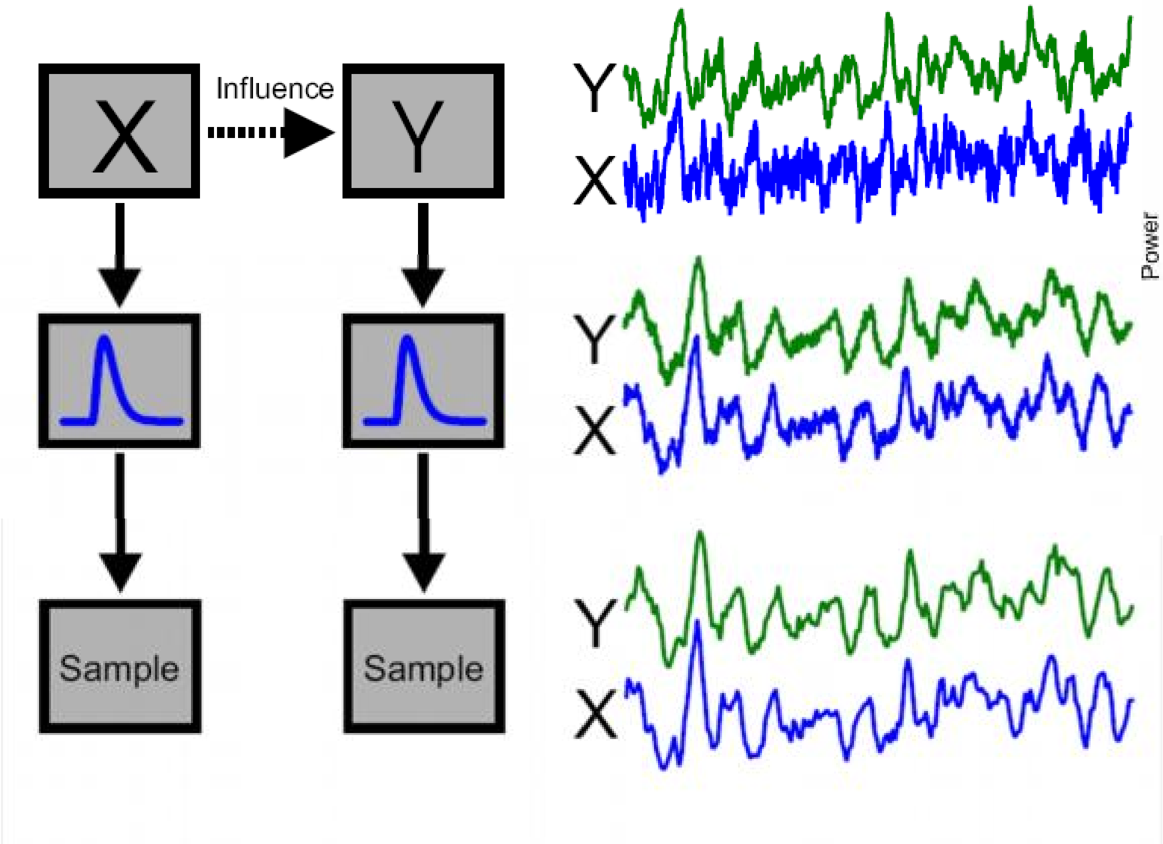
Granger causality (G-causality)

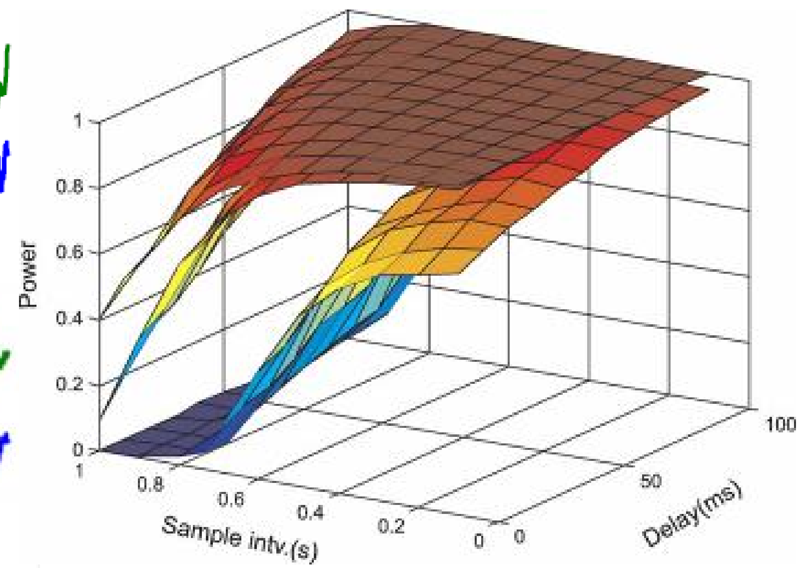
$$\begin{pmatrix} x[t] \\ y[t] \end{pmatrix} = \sum_{i=1}^{p} \mathbf{A}_i \begin{pmatrix} x[t-i] \\ y[t-i] \end{pmatrix} + \begin{pmatrix} e_{x|y} \\ e_{y|x} \end{pmatrix} \qquad \operatorname{cov}\begin{pmatrix} e_{x|y} \\ e_{y|x} \end{pmatrix} = \begin{pmatrix} \sigma_{x|y}^2 & \sigma_{xy} \\ \sigma_{xy} & \sigma_{y|x}^2 \end{pmatrix} = \Sigma$$

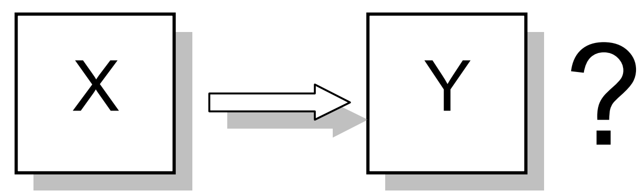
- **Predictions are quantified with a linear multivariate autoregressive (AR) model**
  - Though not necessarily: non-linear AR or nonparametric (e.g. Dhamala et al., NI, 2008)
- **AR Transfer function form gives frequency distribution**
- **Various normalizations**
  - Geweke's decomposition (Geweke, 1982; Roebroeck, NI, 2005)
  - Directed transfer function (DTF; Blinowska, PhysRevE, 2004; Deshpande, NI, 2008)
  - Partial directed coherence (PDC; Sameshima, JNeuSciMeth, 1999; Sato, HBM, 2009)

Sampling & Hemodynamics



Granger causality analysis



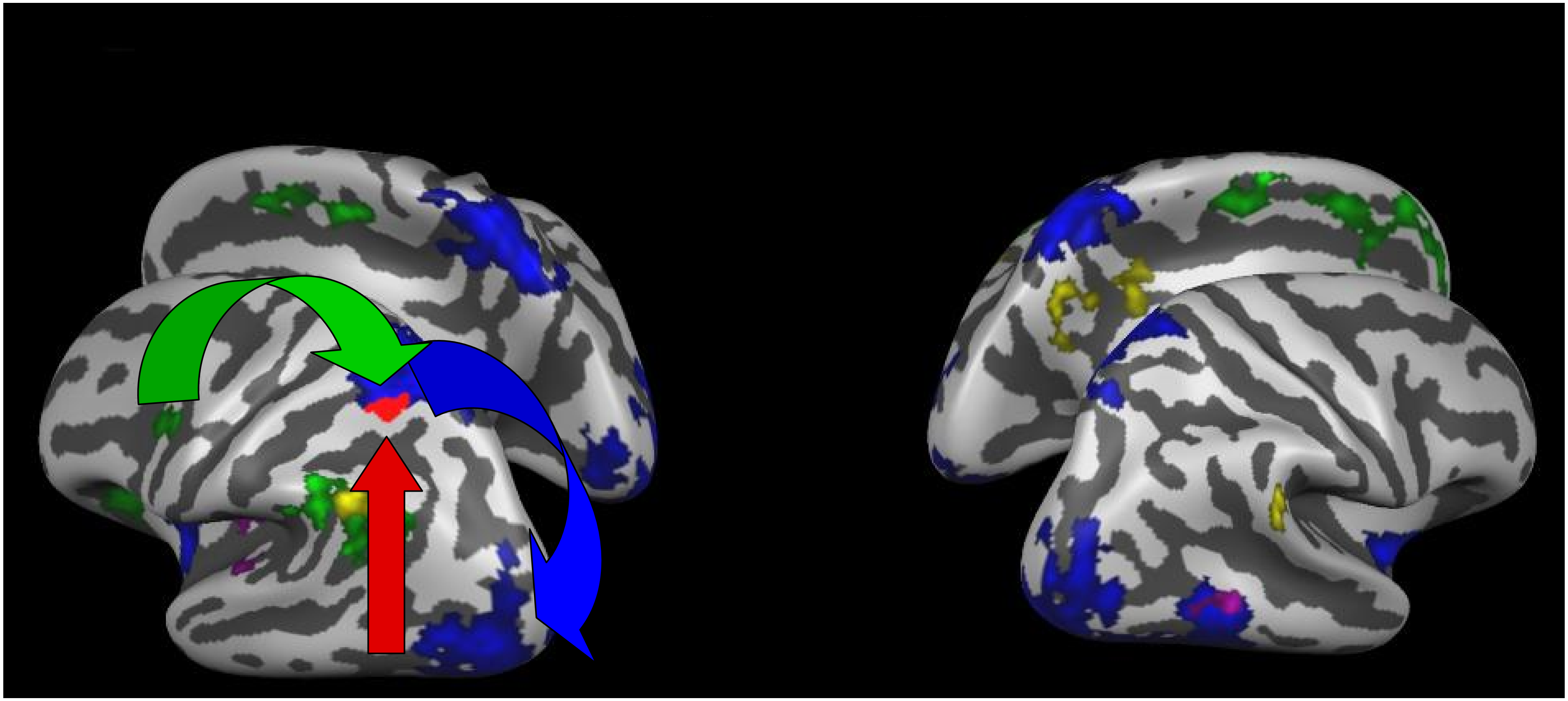


Roebroeck, NI 2005

Structural model for GC

- **ROI-based as in SEM, DCM**
  - E.g. Stilla, 2007; Sridharan, 2008; Udaphay, 2008; Deshpande, 2008
- **Massively multivariate based on parcelation of the cortex**
  - Valdes Sosa, 2004, 2005
- **Granger causality mapping**
  - Massively bivariate without prior anatomical asumptions

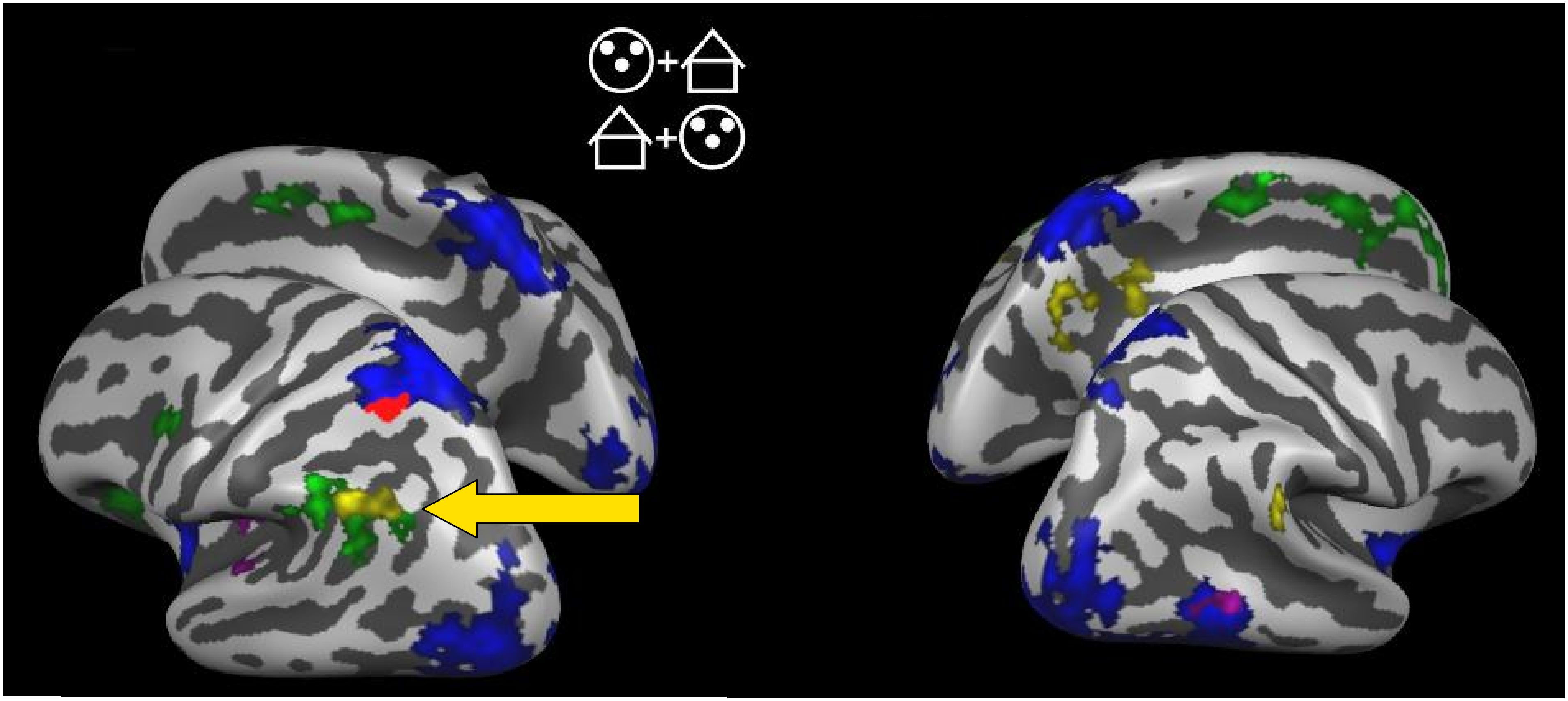
Granger causality mapping (GCM)

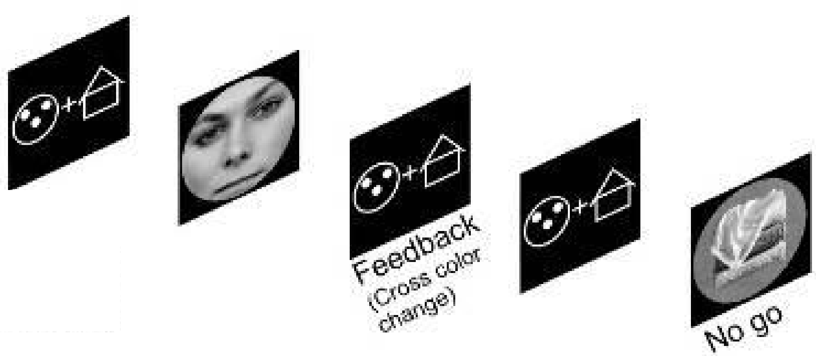


Random effects level GCMs

Roebroeck, NI 2005; Goebel, MRI 2004

Granger causality mapping (GCM)





Experimental modulation:

- Functional assignment
- Avoid HRF confound

Roebroeck, NI 2005; Goebel, MRI 2004

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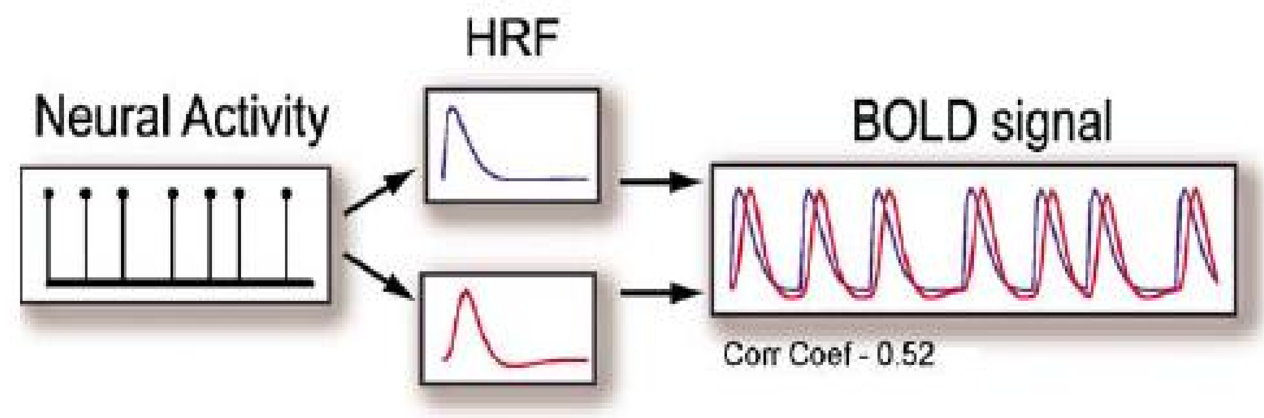
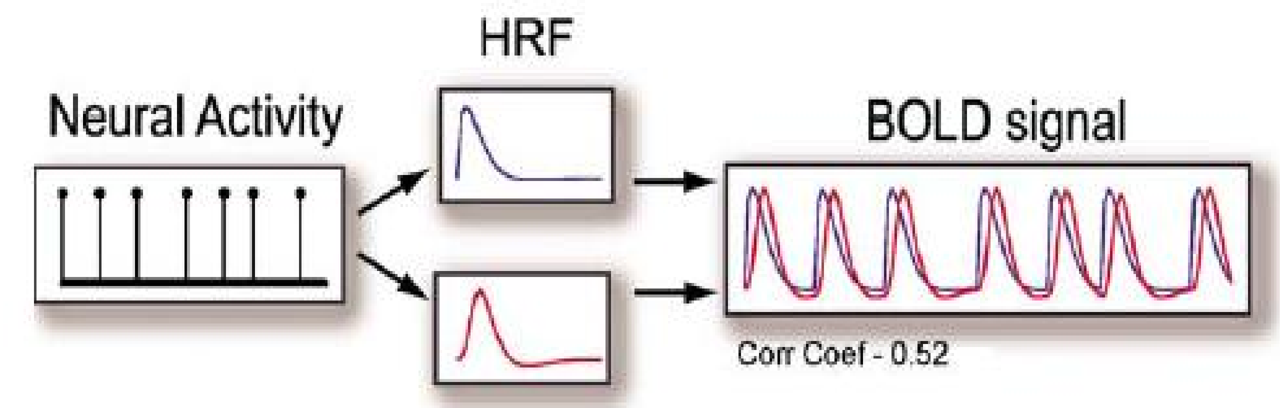
Hemodynamics & GC



- GC could be due purely to differences in hemodynamic latencies in different parts of the brain
- Which are estimated to be in the order of 100's - 1000's ms (Aguirre, NI, 1998; Saad, HBM, 2001)

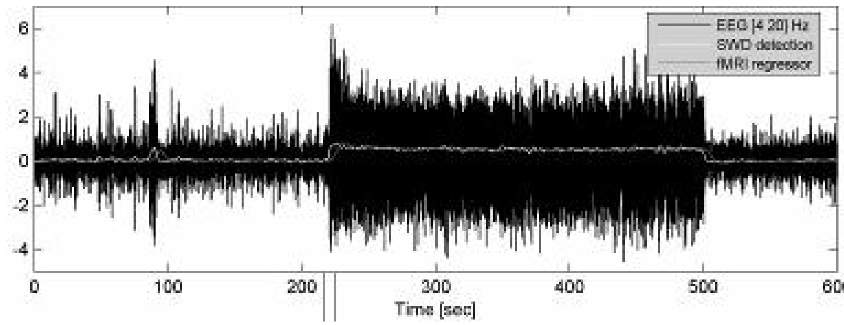
Hemodynamics & GC

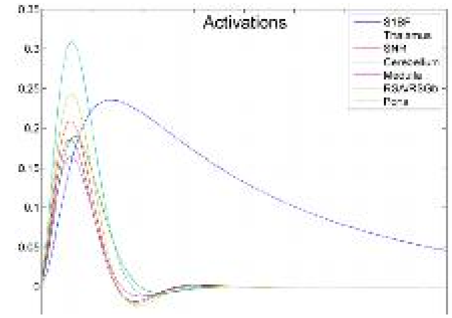


- **Caution needed in applying and interpreting temporal precedence**
- **Tools:**
  - Finding experimental modulation of GC
  - Studying temporally integrated signals for slow processes (e.g. fatigue; Deshpande, HBM, 2009)
  - Combining fMRI with EEG or MEG
  - Hemodynamic deconvolution

Hemodynamic deconvolution

m(t) = s(t) ⊗ h(t)

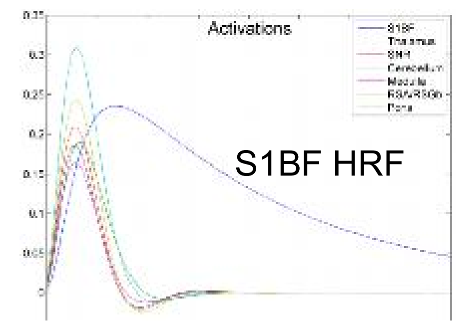
fMRI signal = 

⊗ 

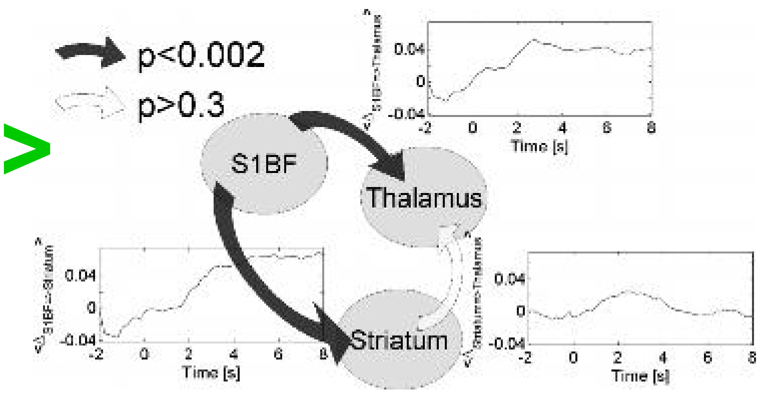
- **Deconvolve neuronal source signal s(t) and hemodynamic response h(t) from fMRI signal**
  - E.g. by wiener deconvolution (Glover, NI, 1999)
- **Only possible if:**
  - Strong **constraints on s(t)** are assumed (e.g. DCM: stimulus functions), **or**
  - An **independent measure of s(t)** is available (e.g. simultaneous EEG) and EEG/fMRI coupling can be assumed

Hemodynamic deconvolution

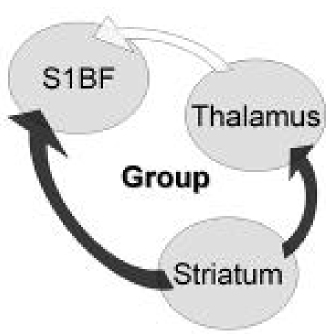
- Rat study of epilepsy
- Simultaneous fMRI/EEG



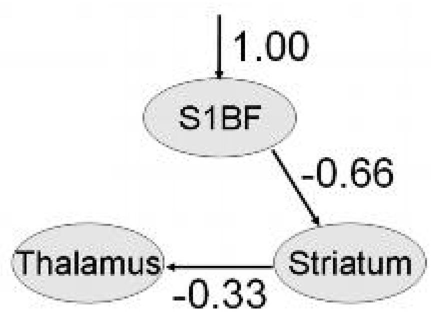
- Gold standard model =>



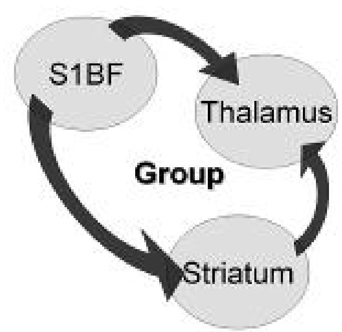
Granger without deconvolution



DCM



Granger using deconvolution



David, PLoS Biology, 2008

Summary

- G-causality and AR models are powerful tools in fMRI effective connectivity analysis
- GC is ideal for massive exploration of the structural model
- Caution is needed with GC in the face of variable hemodynamics