Experimental design

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With thanks to the FIL methods group, in particular Rik Henson

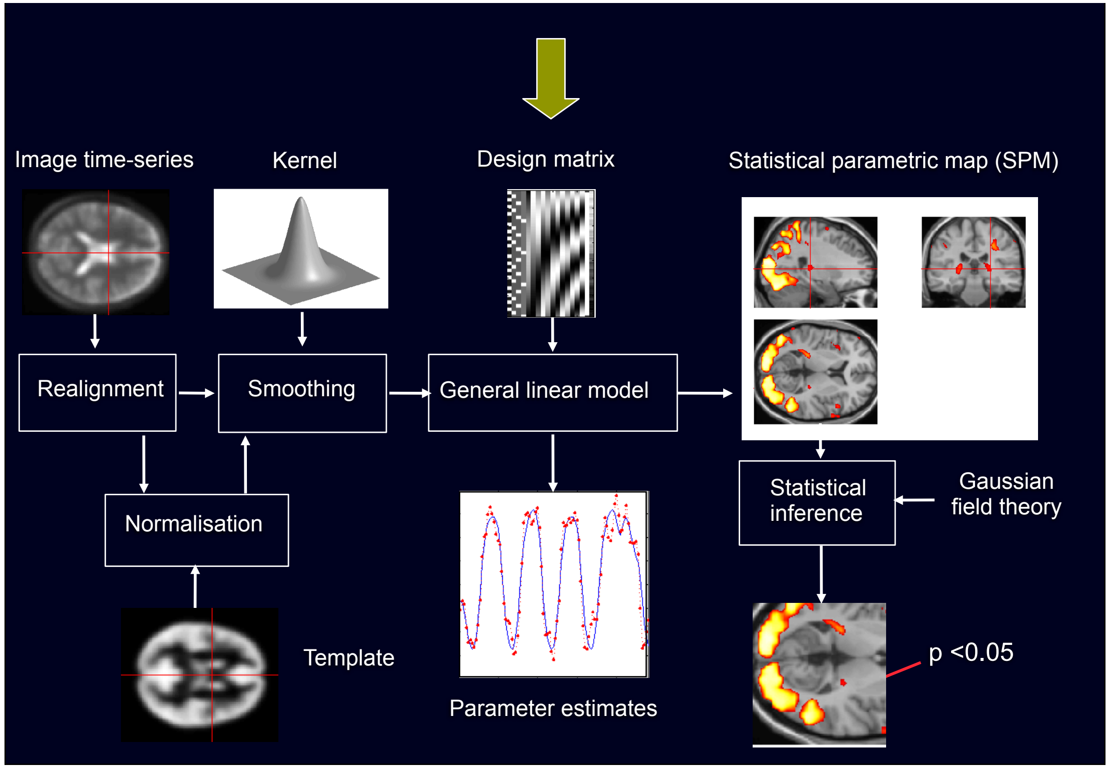


Image time-series
Kernel
Design matrix
Statistical parametric map (SPM)
Realignment
Smoothing
General linear model
Normalisation
Template
Parameter estimates
Statistical inference
Gaussian field theory
p <0.05

Overview

- Categorical designs
  - Subtraction - pure insertion, baseline problems
  - Conjunction - testing multiple hypotheses
- Parametric designs
  - Linear - adaptation, cognitive dimensions
  - Nonlinear - polynomial expansion
  - Model-based - algorithmic definition
- Factorial designs
  - Categorical - Main effects and Interactions
  - Parametric - Psychophysiological interactions

Subtraction designs

- Question:
  – Brain activity supporting process *P*?

- Procedure:
  – Contrast: [Task with *P*] – [control task without *P*] = *P*

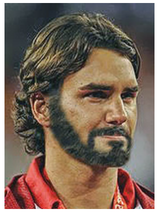
- The critical assumption of “pure insertion”:
  – Cognitive (and neural) processes can be added to others without changing them
  – Changed behavior (and brain activity) reflects only added process

Subtraction designs

- Question:
  - Brain activity supporting process *P*?

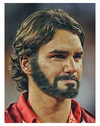
- Procedure:
  - Contrast: [Task with *P*] – [control task without *P*] = *P*

- Example: Brain activity involved in face recognition?

 –  = face recognition (?)

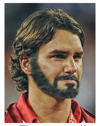
Subtraction designs: Baseline problems

- „Distant“ stimuli

 - 

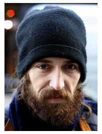
➔ Several components differ !

- „Related“ stimuli



„Roger“

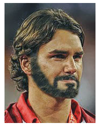
\-



„My yoga teacher?“

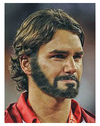
➔ Implicit processes in control condition ?

- Same stimuli, different task



Name Person!

\-

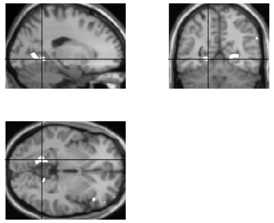


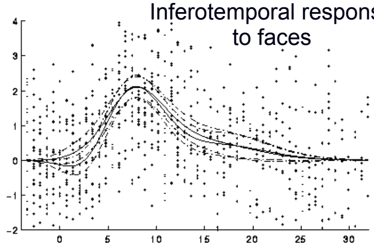
Name Gender!

➔ Interaction of process and task ?

Rest baseline: Evoked responses

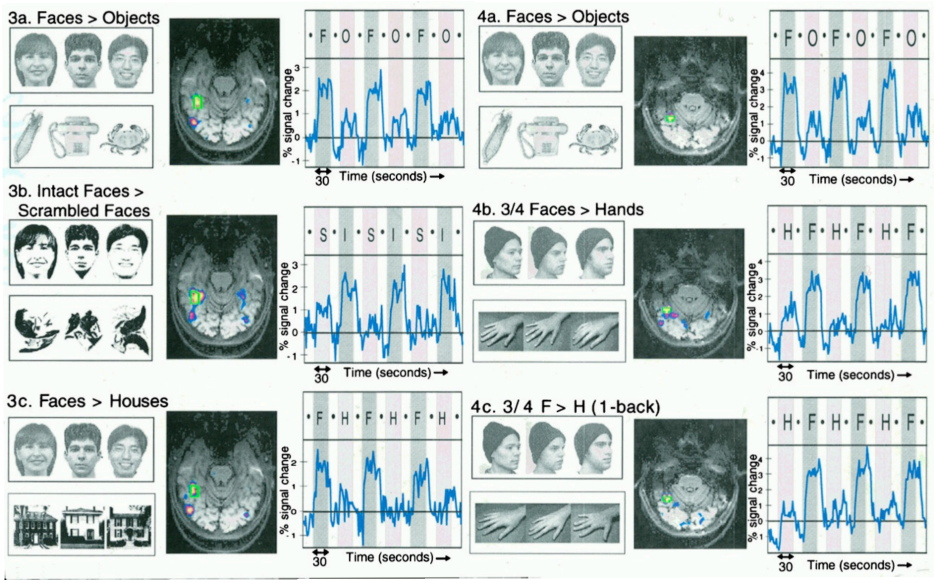
SPM{F} testing for evoked responses





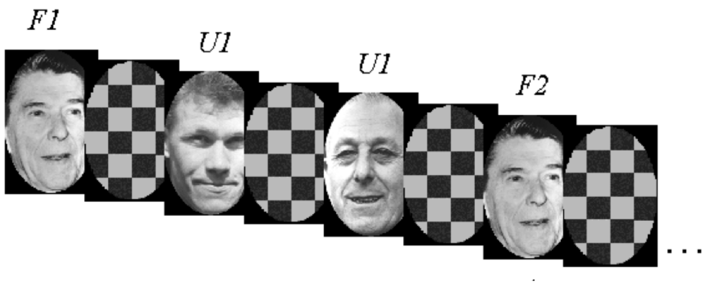
- "Baseline" here corresponds to session mean, and thus processing during "rest"
- Problems:
  - Null events or long SOAs essential for estimation
  - "Cognitive" interpretation hardly possible, as cognitive processes during rest unclear, but useful to define regions involved in task

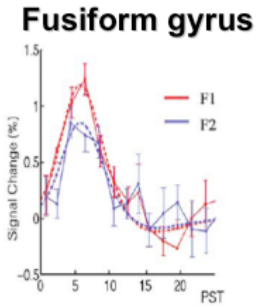
Example I: Face selectivity in fusiform gyrus



Kanwisher, McDermott, Chun (1997) JNeurosci

Example II: Repetition suppression





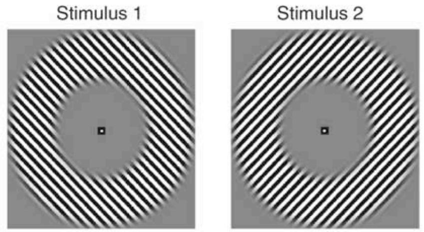
- Repeated viewing of the same face elicits lower BOLD activity in face-selective regions

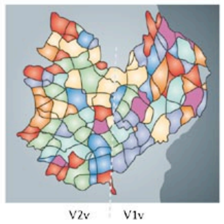
- Repetition suppression / adaptation designs:
  BOLD decreases for repetition used to infer functional specialization for this task/stimulus

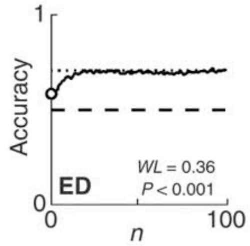
Henson, Dolan, Shallice (2000) Science

Henson et al (2002) Cereb Cortex

Example III: MVPA







- Focus on multivariate activity patterns across voxels (rather than univariate signal in each voxel)
- Many MVPA designs involve categorical comparisons between 2 types of stimuli (and hence all associated baseline/pure insertion problems)

Haynes & Rees (2004) Nat Neurosci

Kamitani & Tong (2004) Nat Neurosci

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  - Parametric - Linear and nonlinear interactions

Conjunctions

- One way to minimise the baseline/pure insertion problem is to isolate the same process by two or more separate comparisons, and inspect the resulting simple effects for commonalities

- A test for such activation common to several independent contrasts is called "Conjunction"

- Conjunctions can be conducted across a whole variety of different contexts:
  - Tasks
  - Stimuli
  - Senses (vision, audition)
  - etc.

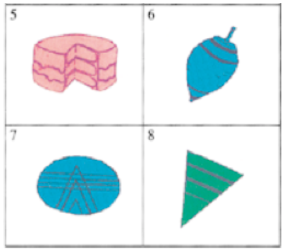
- But the contrasts entering a conjunction have to be truly independent!

Conjunctions

Example:
Which neural structures support object recognition, independent of task (naming vs viewing)?

Task (1/2)

Stimuli (A/B)	Naming	Viewing
Objects	A1	A2
Colours	B1	B2



Price & Friston (1997) Neuroimage

Conjunctions

Example:
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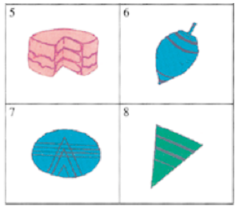

Task (1/2)

Stimuli (A/B)		Naming	Viewing
	Objects	Vis Rec Word	Vis Rec
	Colours	Vis Word	Vis

Visual Processing (Vis)
Object Recognition (Rec)
Word Retrieval (Word)

Object Naming		Colour Naming		Object Viewing		Colour Viewing		
(Vis) (Rec) (Word)	-	(Vis) (Word)	&	(Vis) (Rec)	-	(Vis)	=	**(Rec)**

Price & Friston (1997) Neuroimage

Conjunctions

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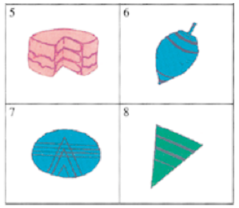
Which neural structures support object recognition, independent of task (naming vs viewing)?



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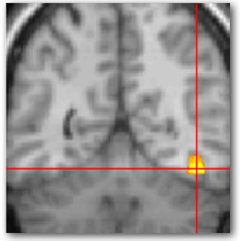
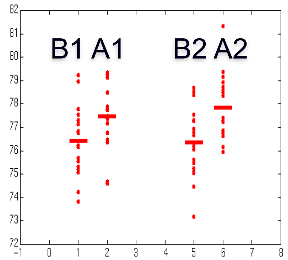
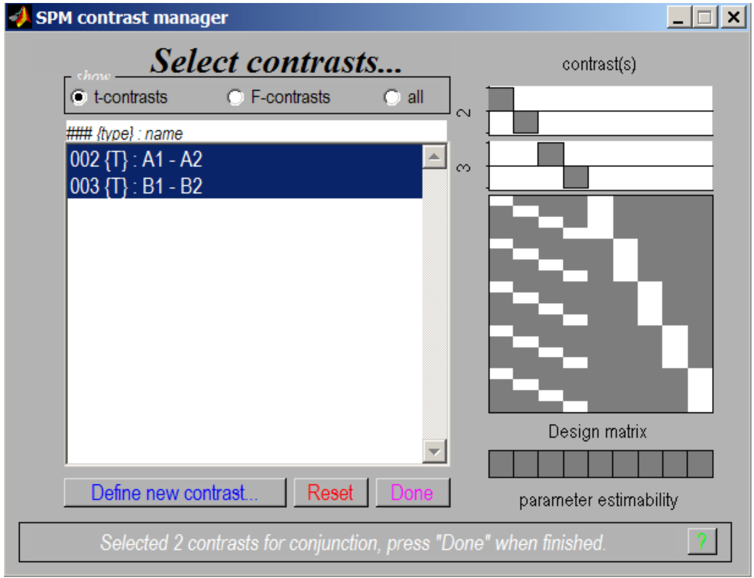


Common object recognition response (Rec)



Price & Friston (1997) Neuroimage

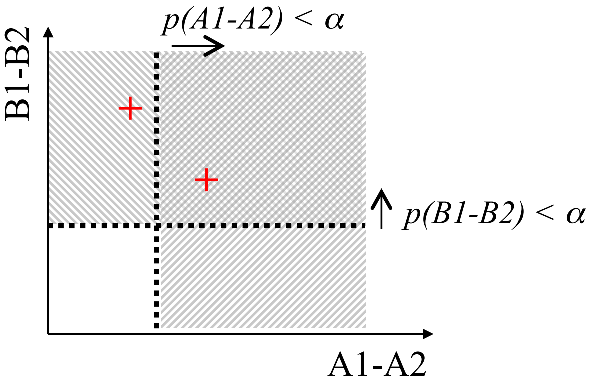
Conjunctions



Two flavours of inference about conjunctions

- Test of global null hypothesis:
  Significant set of consistent effects
  - *"which voxels show effects of similar direction across contrasts?"*
  - *does not correspond to logical AND*

- Test of conjunction null hypothesis:
  Set of consistently significant effects
  - *"which voxels show for each contrast effects > threshold?"*
  - *corresponds to logical AND*



- Choice of test depends on hypothesis and congruence of contrasts; the global null test is more sensitive

Friston et al. (2005) Neuroimage

Nichols et al (2005) Neuroimage

Overview

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- **Parametric designs**
  - Linear - adaptation, cognitive dimensions
  - Nonlinear - polynomial expansion
  - Model-based - algorithmic definition
- Factorial designs
  - Categorical - Main effects and Interactions
  - Parametric - Psychophysiological interactions

Parametric designs

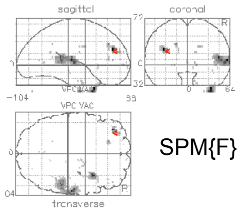
- Parametric designs approach the baseline problem by:
  - Varying an experimental parameter on a continuum, in multiple (n>2) steps...
  - ... and relating blood-flow to this parameter
  - No limit on the number steps (continuous scale)

- Such parameters can reflect many things:
  - Stimulus and task properties (e.g., color intensity, item difficulty, rated attractiveness)
  - Experimental contexts (e.g., time since last presentation of same stimulus)
  - Participant performance (e.g., reaction time, degree of certainty)

- Flexible choice of tests for BOLD-parameter relations:
  - „Data-driven“ (e.g., neurometric functions for limited number of steps)
  - Linear
  - Nonlinear: Quadratic/cubic/etc.
  - Model-based

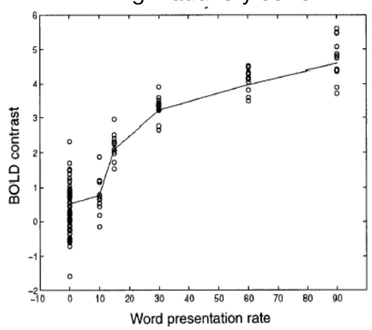
Parametric designs: Linear and nonlinear effects

- Example: Varying word presentation rate

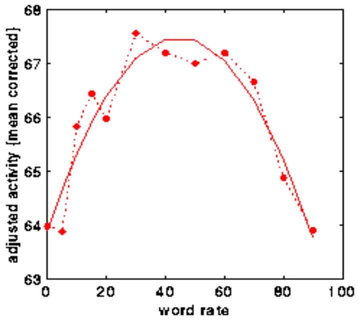


SPM{F}

Right auditory cortex



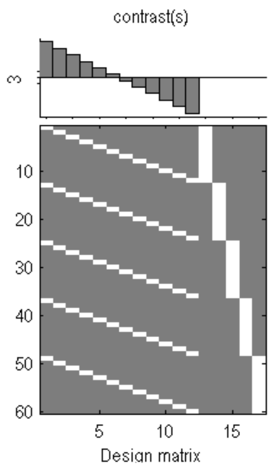
Left DLPFC



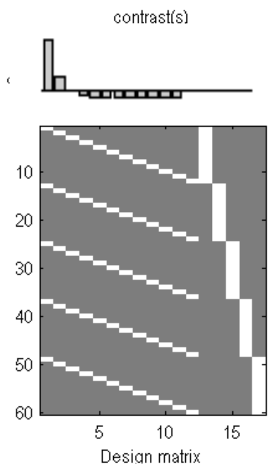
Rees et al (1997) Neuroimage

Model I: Separate regressors

Linear contrast:



Nonlinear contrast:

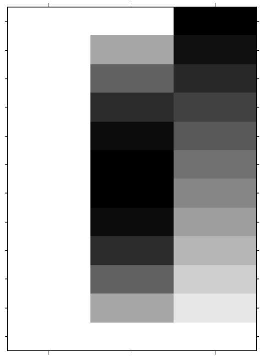


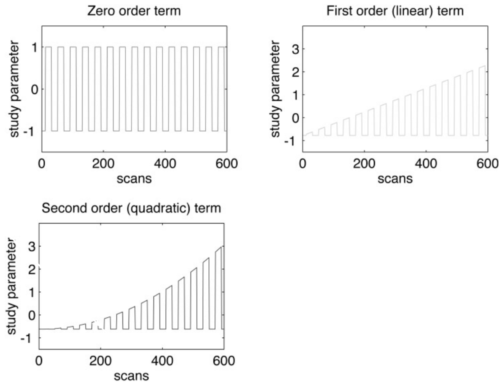
- Advantage:
  - Data-driven characterisation of BOLD-parameter relation
- Disadvantages:
  - only possible for small number of parameter steps
  - reduced statistical power (less df)
  - contrasts often hard to define
  - linear and non-linear components not properly separated

Model 2: Parametric modulation

Polynomial expansion:
$f(x) \sim b_0 + b_1 x + b_2 x^2 + \ldots$

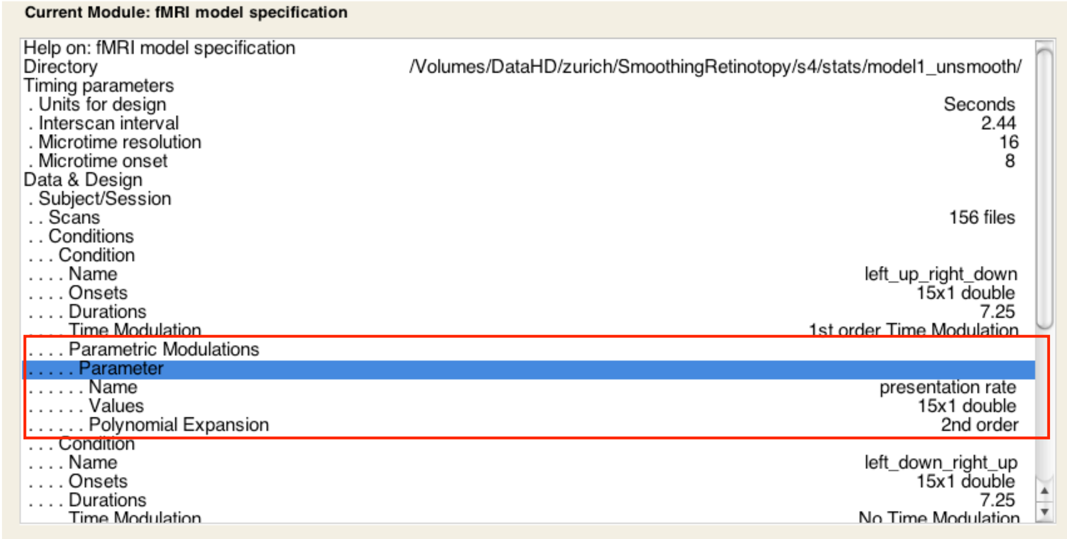
…up to (N-1)th order for N levels



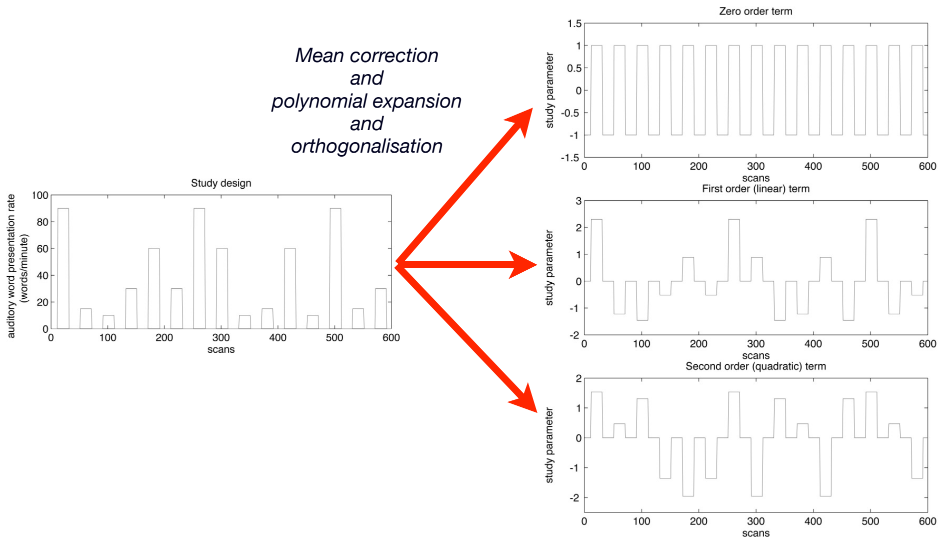


Buechel et al (1998) Neuroimage

Polynomial expansion in SPM



Polynomial expansion in SPM

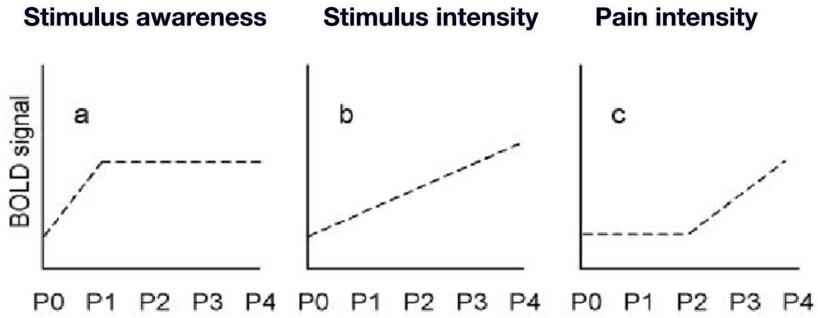


- Separation of linear and non-linear effects on different regressors
- F-test on nonlinear regressor controls for linear and mean effects

Buechel et al (1998) Neuroimage

Parametric Designs: Neurometric functions

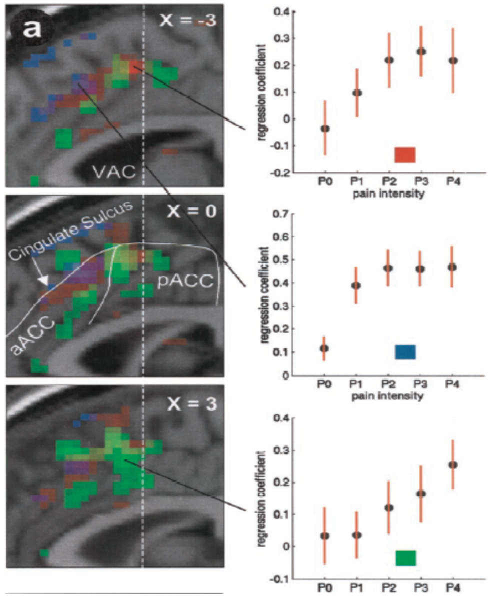
– **Neural coding of different aspects of tactile perception?**



– P0-P4: Variation of intensity of a laser stimulus applied to the right hand (0, 300, 400, 500, 600 mJ)

Buechel et al (2002) JNeurosci

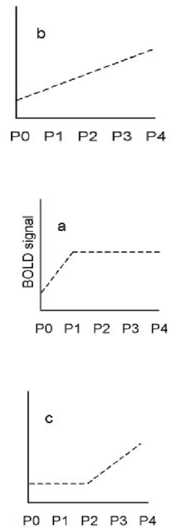
Parametric Designs: Neurometric functions



→ Stimulus intensity

→ Stimulus presence

→ Pain intensity



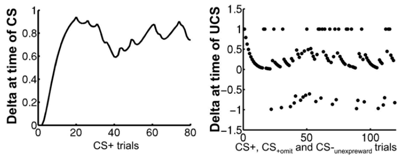
Buechel et al (2002) JNeurosci

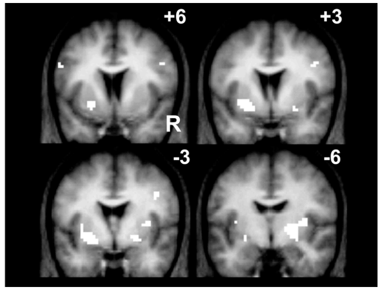
Parametric Designs: Model-based regressors

- Parameters can be derived from computational model that specifies a neural mechanism, based on individual experimental context
- These “model-based” parameters can be included in the design matrix like any other parameter, and related to BOLD activity

- Example: VS correlates with TD prediction error during appetitive conditioning

$$V(t+1) = V(t) + \alpha\left[R(t) + \gamma V(t+1) - V(t)\right]$$





O’Doherty et al (2003) Neuron

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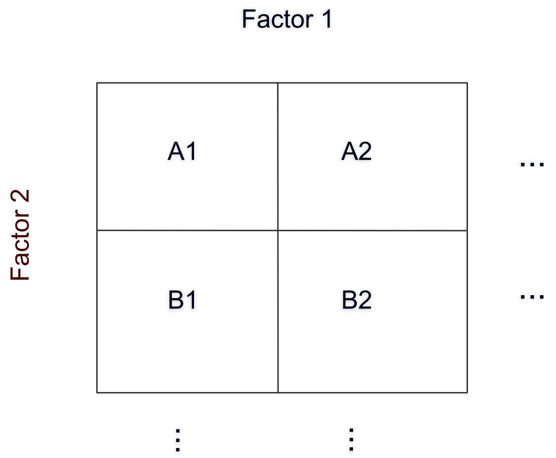
Factorial designs: General principle



- Combining n>2 factors (categorical and/or parametric)
- Fully balanced: Each factor step is paired with each step of the other factor, ideally with the same number of events
- Balanced factorial designs allow you to address the maximum number of questions with equal sensitivity

Factorial designs: Main effects and Interactions

Stimuli (A/B)	Task (1/2)	Naming	Viewing
	Objects	A1	A2
	Colours	B1	B2

Factorial designs: Main effects and Interactions

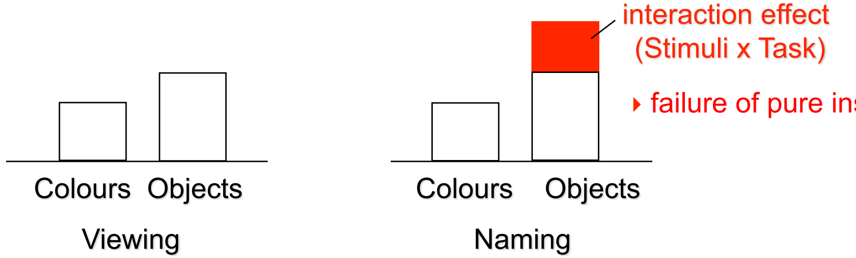
Task (1/2)

Stimuli (A/B)		Naming	Viewing
	Objects	A1	A2
	Colours	B1	B2

Main effect (and conjunction) of task:
(A1 + B1) – (A2 + B2)

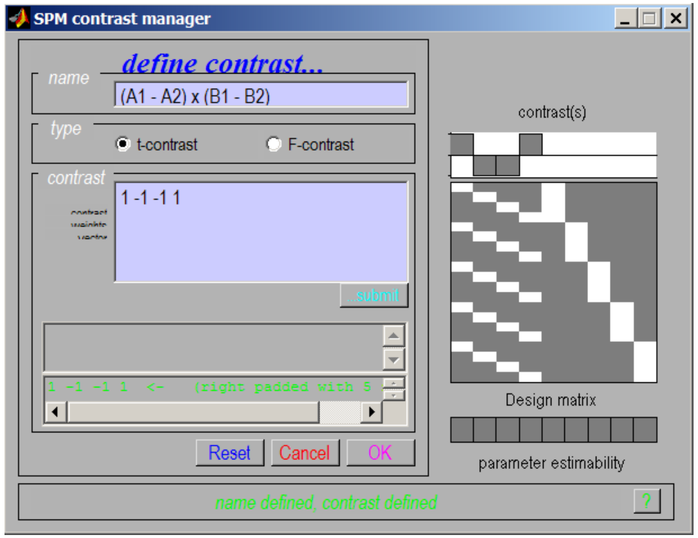
Main effect (and conjunction) of stimuli:
(A1 + A2) – (B1 + B2)

Interaction of task and stimuli:
(A1 – B1) – (A2 – B2)



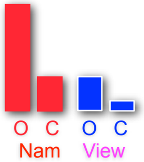
- failure of pure insertion

Interactions and pure insertion



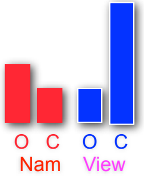
Interactions:

simple



and

cross-over



We can selectively inspect our data for one or the other by masking during inference

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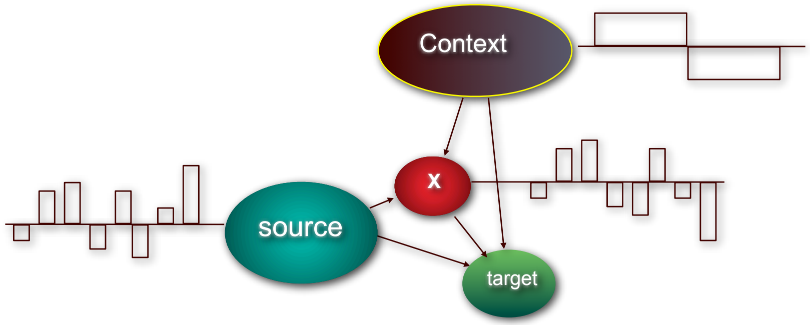
Psycho-physiological interactions (PPIs)

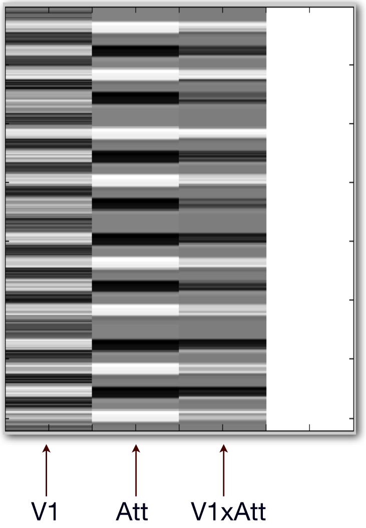
Parametric factorial design in which one factor is a psychological context …

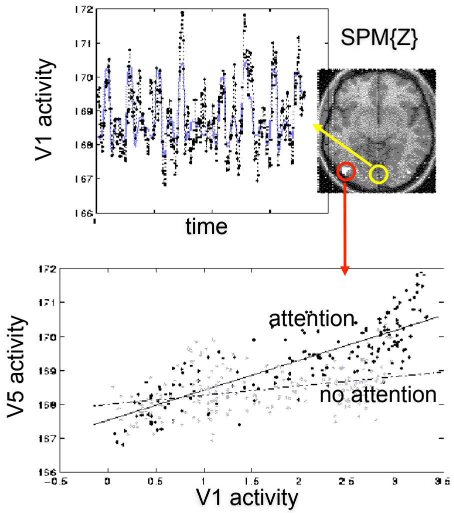
...and the other is a physiological source *(activity extracted from a brain region of interest)*



PPIs: Example

Changes in connectivity of V1 with attention to motion?

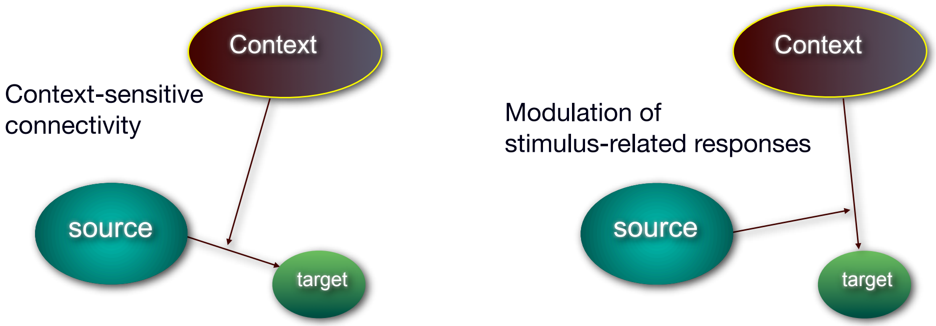




Friston et al (1997) Neuroimage

PPIs: Two possible interpretations

Knowledge about neurobiological plausibility of both interpretations often necessary for interpreting PPI results



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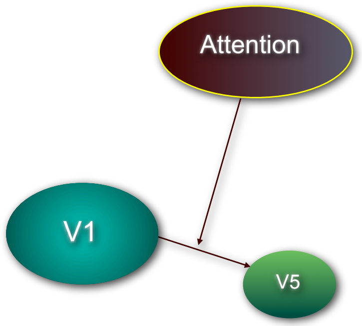
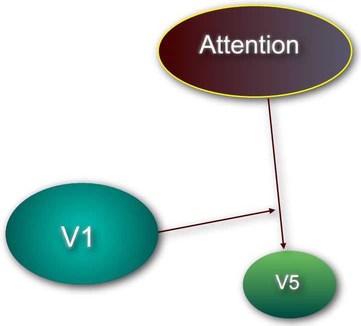
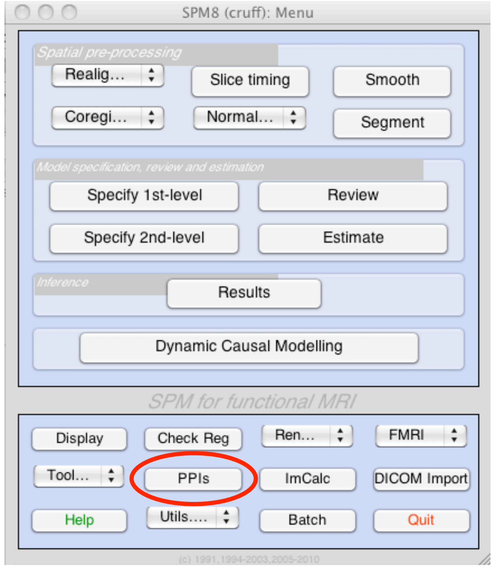
Attention modulates V1- V5 connectivity



V1 modulates impact of attention on V5



PPI: Regressor construction



- PPI tested by a GLM with form:
  $\mathbf{y} = (\mathbf{V1xA}).b_1 + \mathbf{V1}.b_2 + \mathbf{A}.b_3 + \mathbf{e}$
- SPM provides routines that construct PPI regressors based on region timeseries and existing SPM.mat
- For interaction term (V1xA), we are interested in the interaction at the neural level, before convolution with HRF
- SPM thus deconvolves timeseries (V1) before producing interaction term (V1xA) and reconvolving with HRF