



University of
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Swiss Federal Institute of Technology Zurich



Translational Neuromodeling Unit

Methods & Models for fMRI Analysis 2019

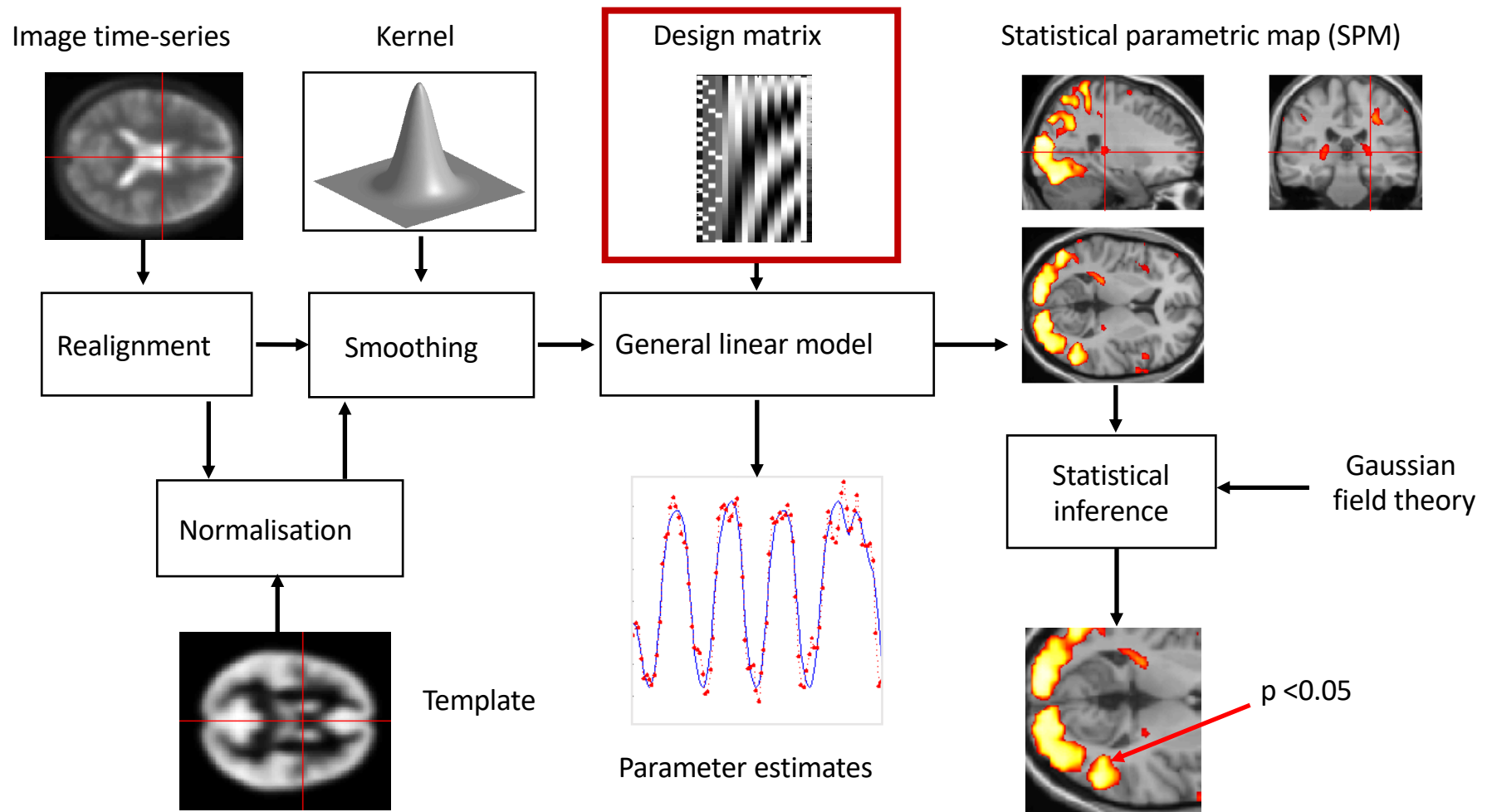
Experimental design of fMRI studies

Sara Tomiello

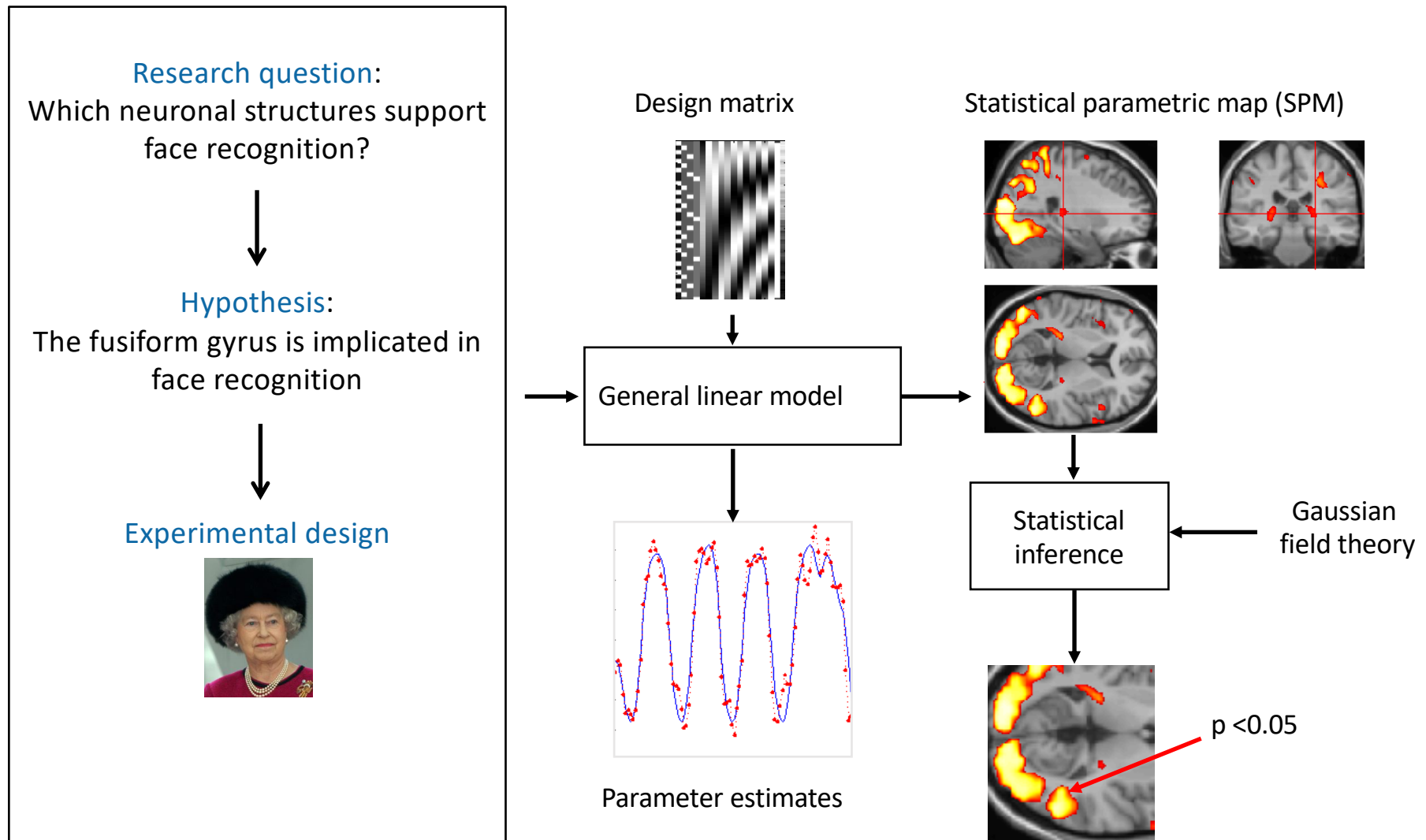
With many thanks for slides & images to:

Sandra Iglesias,
Klaas Enno Stephan,
FIL Methods group,
Christian Ruff

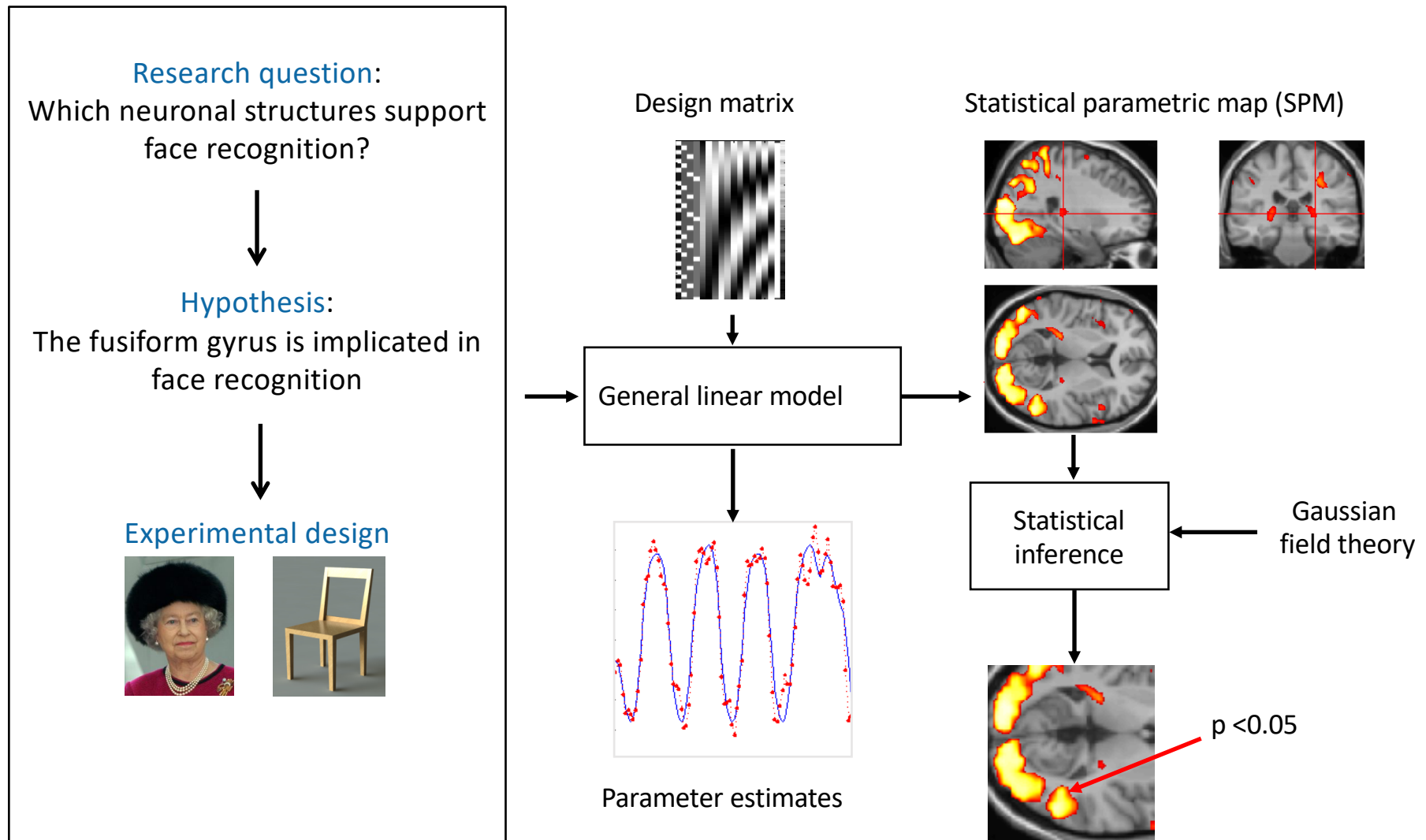
Overview of SPM



Overview of SPM



Overview of SPM



Overview Experimental Designs

- Categorical designs

- | | |
|-------------|---------------------------------------------------|
| Subtraction | - Pure insertion, evoked / differential responses |
| Conjunction | - Testing multiple hypotheses |

- Parametric designs

- | | |
|-----------|------------------------------------------------|
| Linear | - Adaptation, cognitive dimensions |
| Nonlinear | - Polynomial expansions, neurometric functions |

- Factorial designs

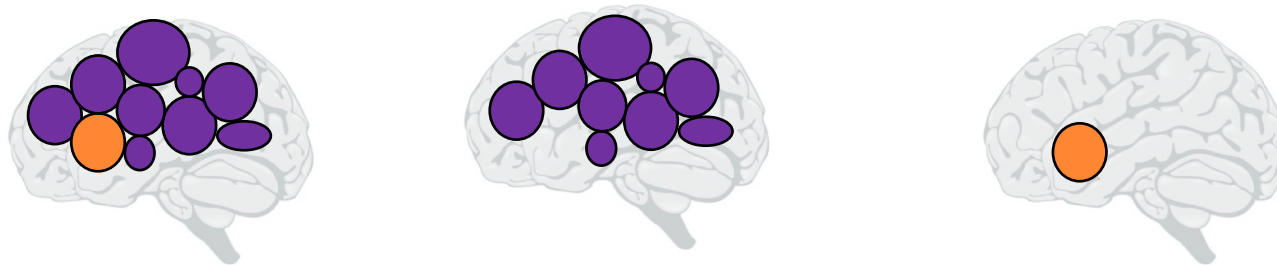
- | | |
|-------------|-------------------------------------|
| Categorical | - Interactions and pure insertion |
| Parametric | - Linear and nonlinear interactions |
| | - Psychophysiological interactions |

Categorical Designs

Subtraction

- Aim: Find neuronal structures underlying a *single* process P
- Procedure:

$$[\text{task with } P] - [\text{control task without } P] = P$$



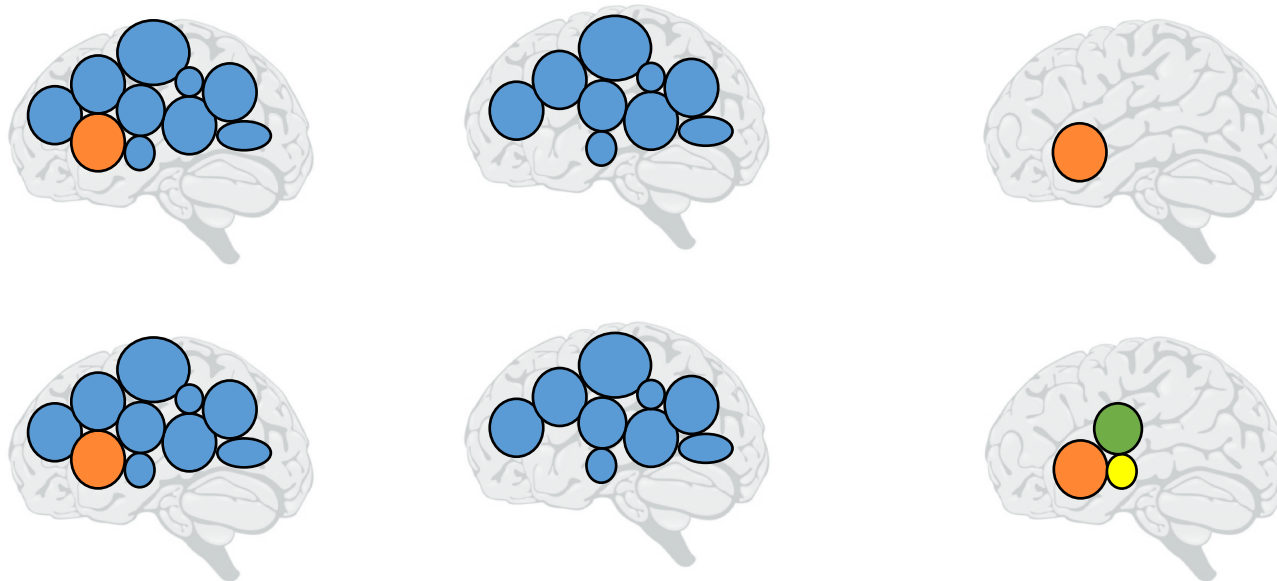
Under the critical assumption of „pure insertion“

Categorical Designs

Subtraction

- Aim: Find neuronal structures underlying a *single* process P
- Procedure: Under the critical assumption of „pure insertion“

$$[\text{task with } P] - [\text{control task without } P] = P$$



Categorical Designs

Subtraction, Example

Cognitive subtraction originated with reaction time experiments (F. C. Donders).

Measure the time for a process to occur by comparing two reaction times, one which has the same components as the other + the process of interest.

Example:

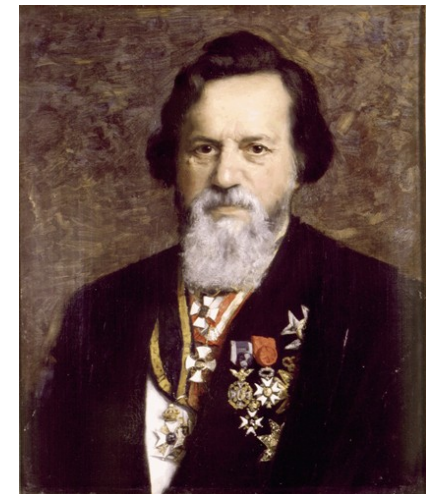
T1: Hit a button when you see a light

T2: Hit a button when the light is green but not red

T3: Hit the left button when the light is green and the right button when the light is red

$T2 - T1$ = time to make discrimination between light color

$T3 - T2$ = time to make a decision



F.C. Donders 1868

Assumption of pure insertion:

You can insert a component process into a task without disrupting the other components.

Categorical Designs

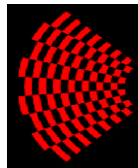
Subtraction: Baseline problem

Which neuronal structures support face recognition ?

- „Distant“ stimuli



-



→ Several components differ

- „Related“ stimuli



-



„Queen!“

„Aunt Jenny?“

→ Additional processes in control condition (?)

- Same stimuli, different task



-



Name Person!

Name Gender!

→ Interaction of task and stimuli (specificity for naming)
(i.e. do task differences depend on stimuli chosen (?))

Categorical Designs

Subtraction, Example

Experimental design

Face viewing: F

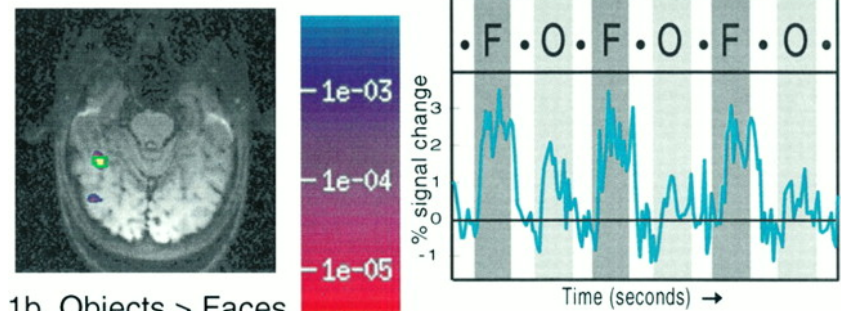
Object viewing: O

F - O = Face recognition

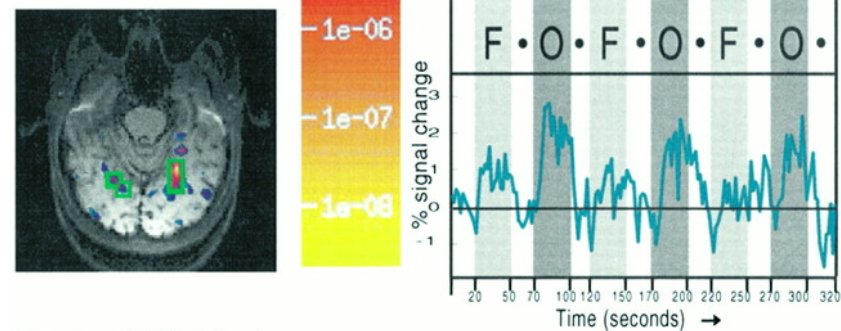
O - F = Object recognition

...under assumption of pure insertion

1a. Faces > Objects



1b. Objects > Faces



Categorical Designs

Subtraction, Example SPM

The SPM contrast manager dialog box is titled "define contrast...". It contains the following fields and controls:

- name:** A1-A2
- type:** ☒ t-contrast, ☐ F-contrast
- contrast:** A text area containing the contrast weights vector: 1 -1 1 -1 1 -1 1 -1. Below this is a ". submit" button.
- Design matrix:** A large matrix visualization showing the relationship between tasks and sessions. It is labeled "Design matrix" and "parameter estimability".
- contrast(s):** A small matrix visualization at the top right, labeled "contrast(s)".
- parameter estimability:** A row of 10 small squares at the bottom right, labeled "parameter estimability".
- Buttons:** "Reset", "Cancel", and "OK" at the bottom left.
- Status bar:** "name defined, contrast defined" and a "?" icon.

Annotations on the right side of the image point to specific parts of the Design matrix:

- Task 1:** Points to the first column of the Design matrix.
- Task 2:** Points to the second column of the Design matrix.
- Session:** Points to the first row of the Design matrix.

Subtraction - Pure insertion, evoked / differential responses

- Linear and nonlinear interactions
- Psychophysiological interactions

Categorical Designs

Conjunction

- One way to minimize 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.
- Note: the contrasts entering a conjunction must be **orthogonal**

Categorical Designs

Conjunction, Example

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

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

Visual Processing:

Object Recognition:

Phonological Retrieval:

V

R

P

Categorical Designs

Conjunction, Example

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

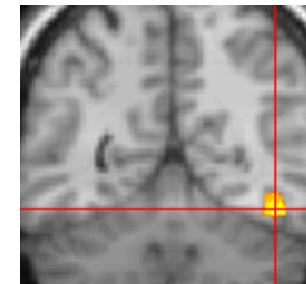
		Task (1/2)	
		Viewing	Naming
Stimuli (A/B)	Colours	A1 Visual Processing V	A2 Visual Processing V Phonological Retrieval P
	Objects	B1 Visual Processing V Object Recognition R	B2 Visual Processing V Phonological Retrieval P Object Recognition R

(Object - Colour viewing) [B1 - A1]

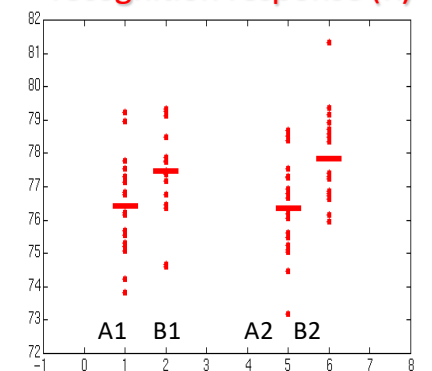
&

(Object - Colour naming) [B2 - A2]

[V,R - V] & [P,V,R - P,V] = R & R = **R**



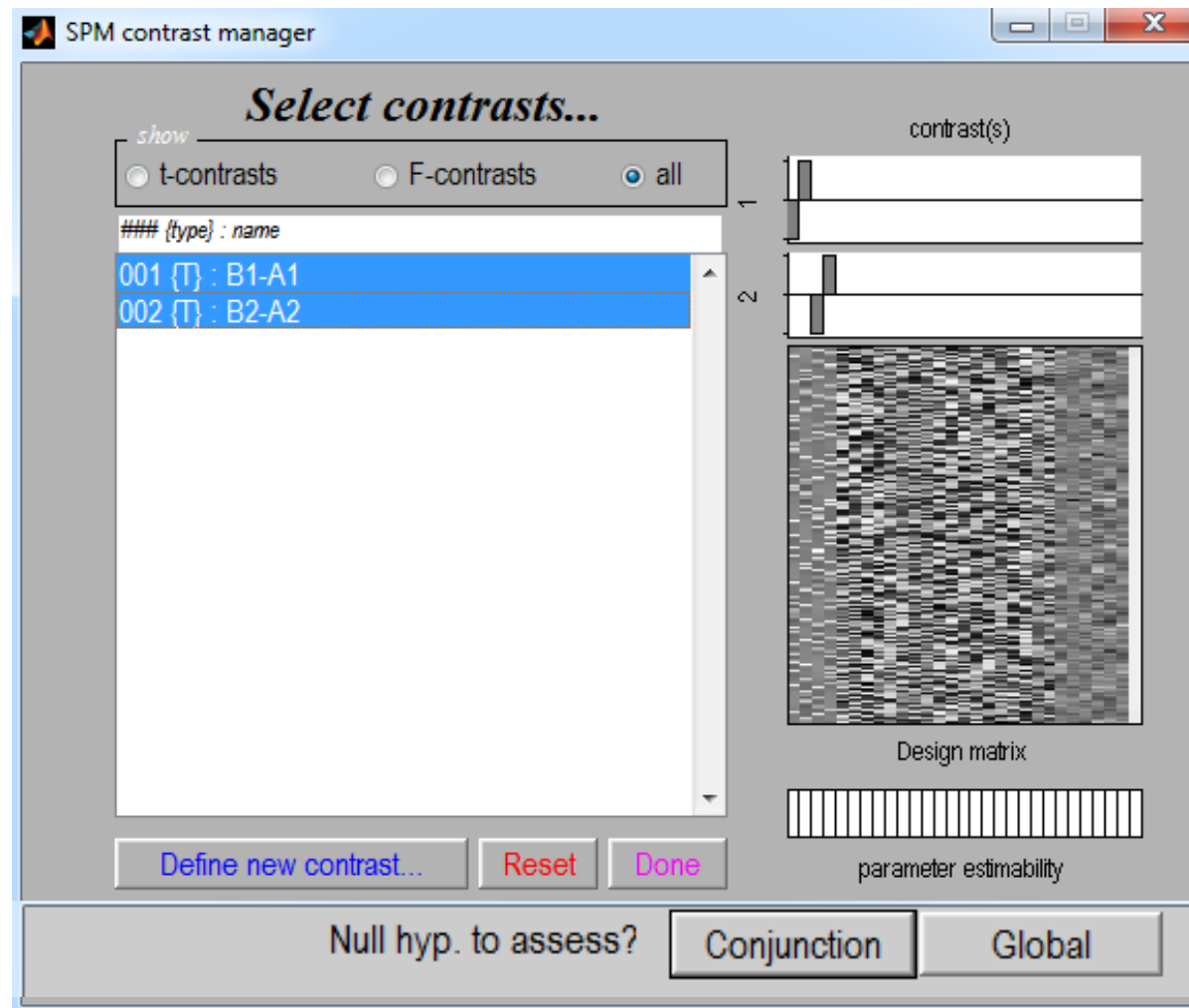
Common object recognition response (R)



Price et al. 1997, NeuroImage

Categorical Designs

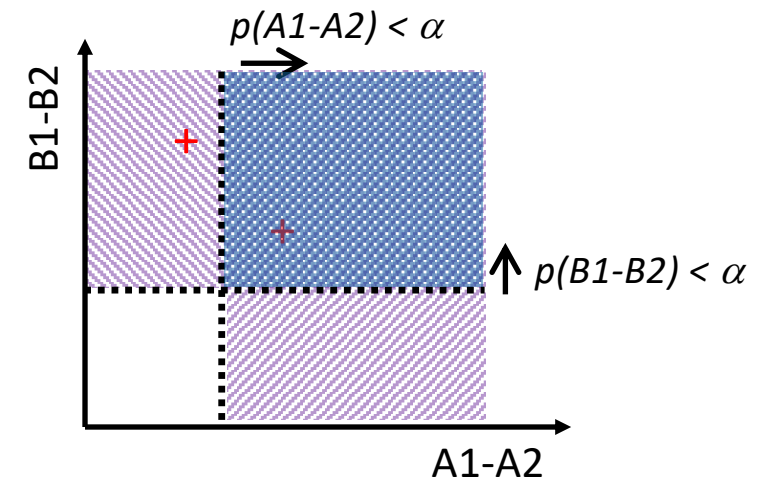
Conjunction, Example SPM



Categorical Designs

Types of Conjunctions

- Test of **conjunction global null hypothesis**:
Significant set of consistent effect
 - ➔ “Which voxels show effects of similar direction (but not necessarily individual significance) across contrasts?”
 - ➔ $H_1: k > 0$
 - ➔ H_0 : No contrast is significant: $k = 0$
 - ➔ Does **not** correspond to a logical AND !
- Test of **conjunction null hypothesis**:
Set of consistently significant effects
 - ➔ “Which voxels show, for each specified contrast, significant effects?”
 - ➔ $H_1: k = n$
 - ➔ H_0 : Not all contrasts are significant: $k < n$
 - ➔ Corresponds to a logical AND



k = effects
 n = contrasts

Friston et al., 2005, NeuroImage
 Nichols et al., 2005, NeuroImage

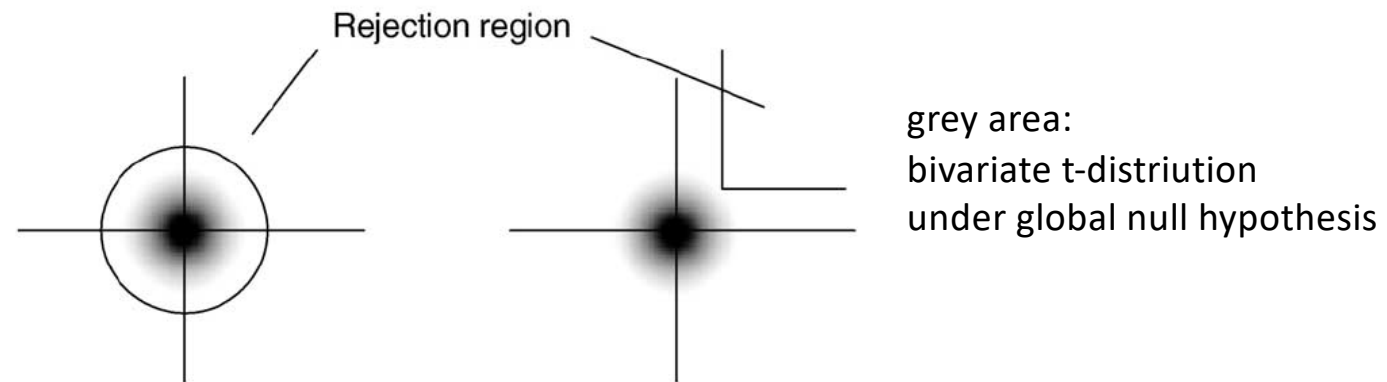
Categorical Designs

Conjunction Global Null Hypothesis

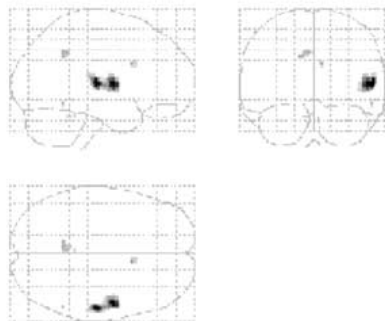
- Based on the "minimum t statistic":
 - imagine a voxel where contrast A gives $t=1$ and contrast B gives $t=1.4$
 - neither t-value is significant alone, but the fact that **both** values are **larger than zero** suggests that there may be a real effect (= all consistent)
- Test: compare the observed minimum t value to the null distribution of minimal t-values for a given set of contrasts
 - one can find **uncorrected and corrected thresholds** for a minimum of two or more t-values (Worsley & Friston, Stat. Probab. Lett., 2000, 47 (2), 135–140)
 - but the contrasts have to be orthogonal (= independent)!

Categorical Designs

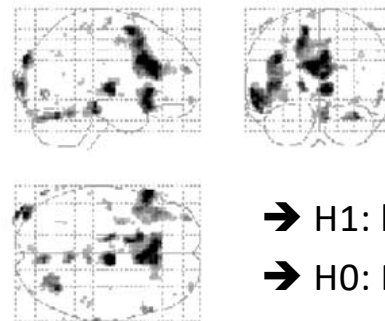
F-test vs. Conjunction Global Null



F-test



Conjunction



→ $H_1: k > 0$

→ H_0 : No contrast is significant: $k = 0$

Overview Experimental Designs

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- **Parametric designs**

- | | |
|-----------|------------------------------------------------|
| Linear | - Adaptation, cognitive dimensions |
| Nonlinear | - Polynomial expansions, neurometric functions |

- Factorial designs

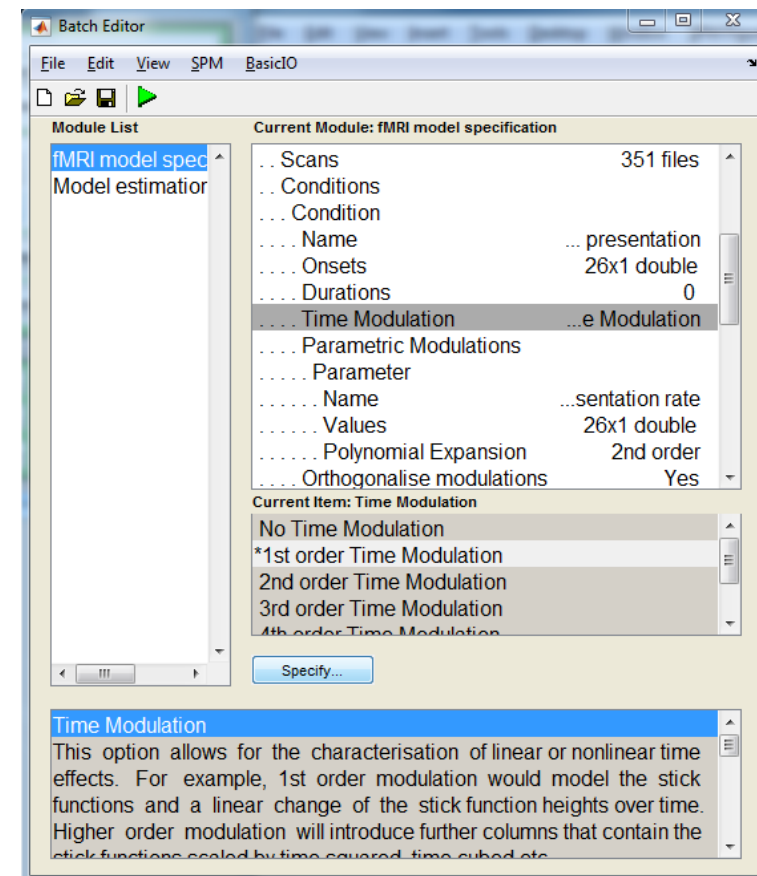
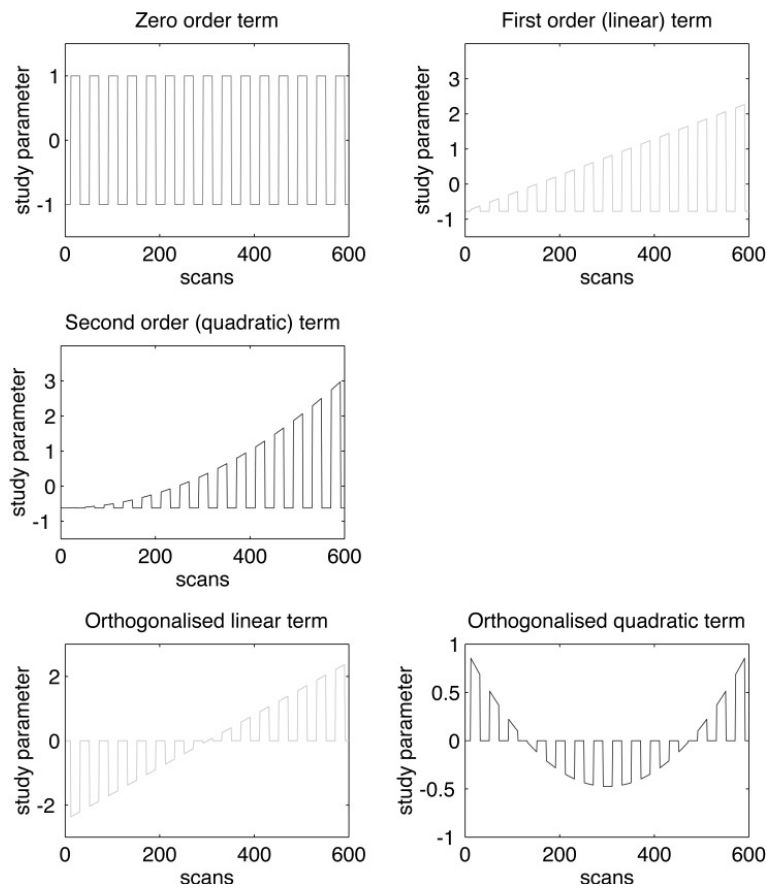
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Parametric Designs

- Parametric designs approach the baseline problem by:
 - varying the stimulus-parameter of interest on a **continuum, in multiple ($n > 2$) steps...**
 - ... and relating measured BOLD signal to this parameter
- Possible tests for such relations are manifold:
 - Linear
 - Nonlinear: Quadratic/cubic/etc. (polynomial expansion)
 - Model-based (e.g. predictions from learning models)

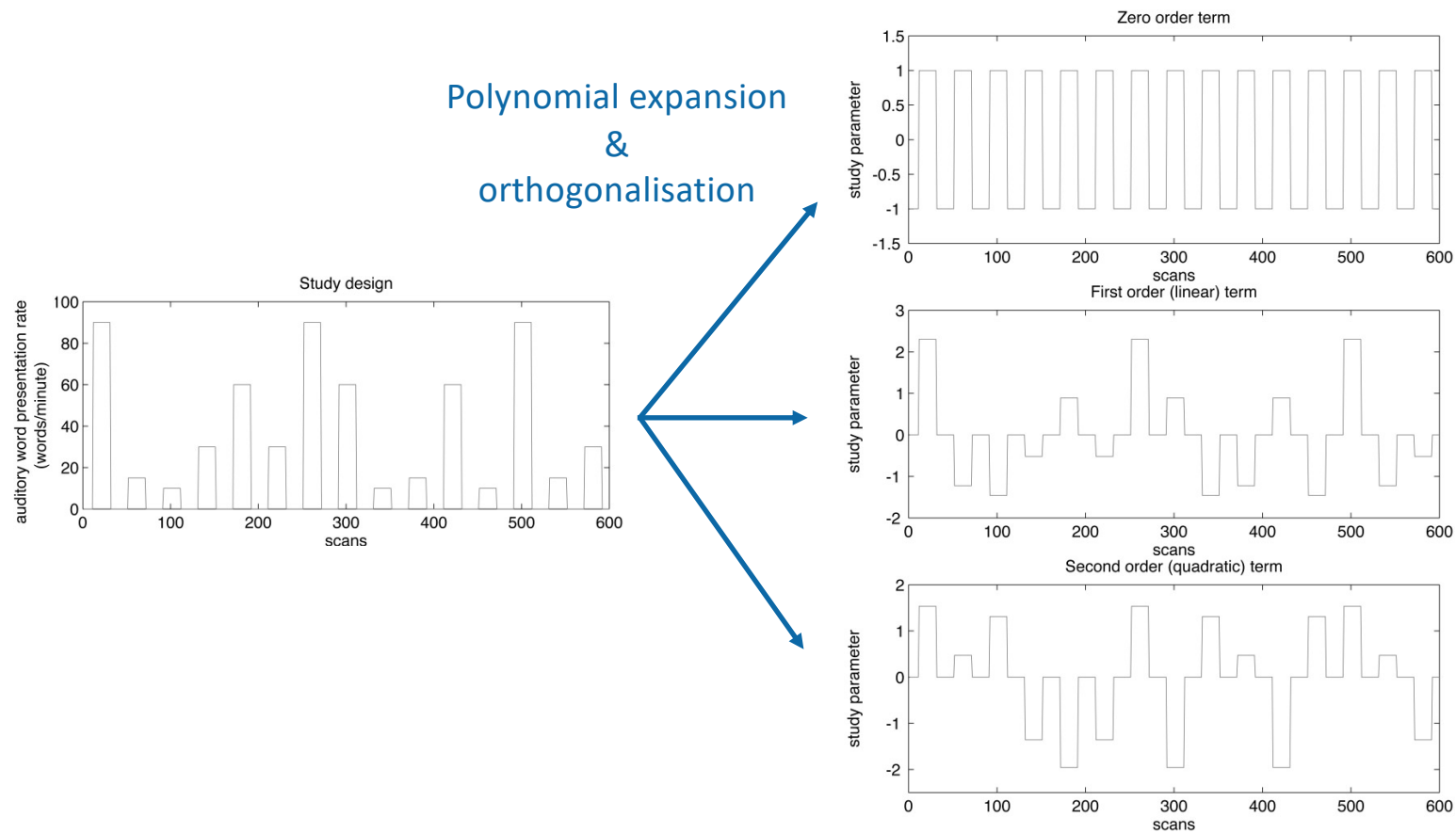
Parametric Designs

Parametric modulation of regressors by time



Parametric Designs

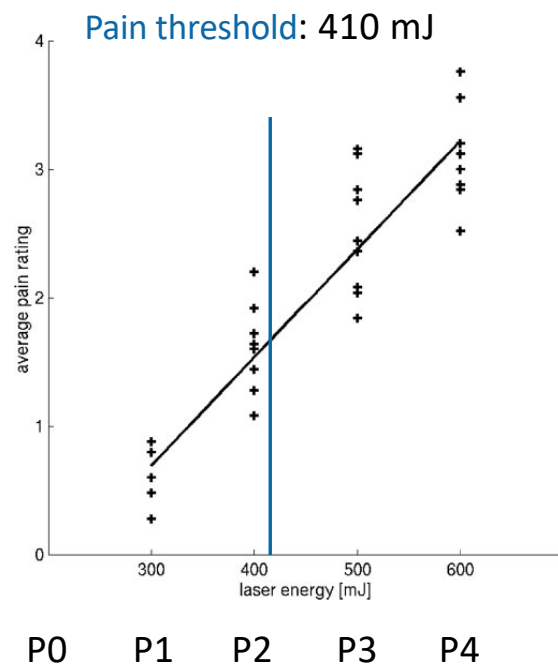
Parametric modulation of regressors



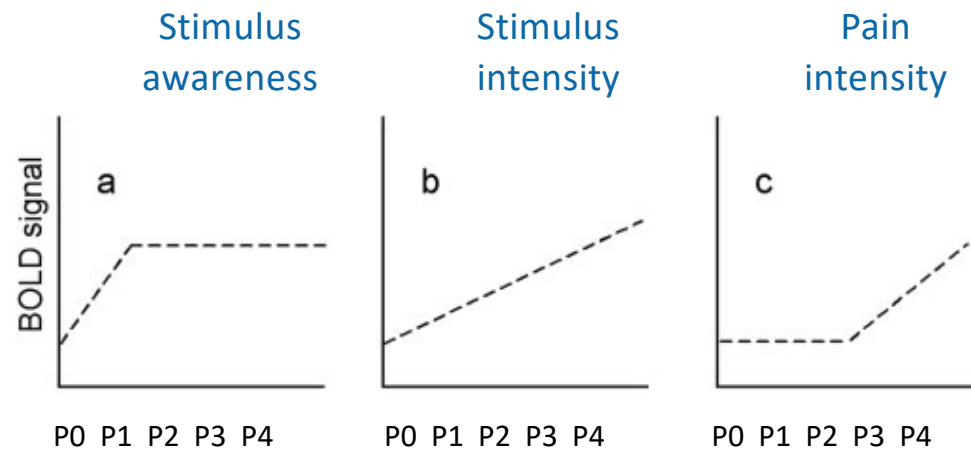
Büchel et al., 1998, NeuroImage

Parametric Designs

Investigating neurometric functions

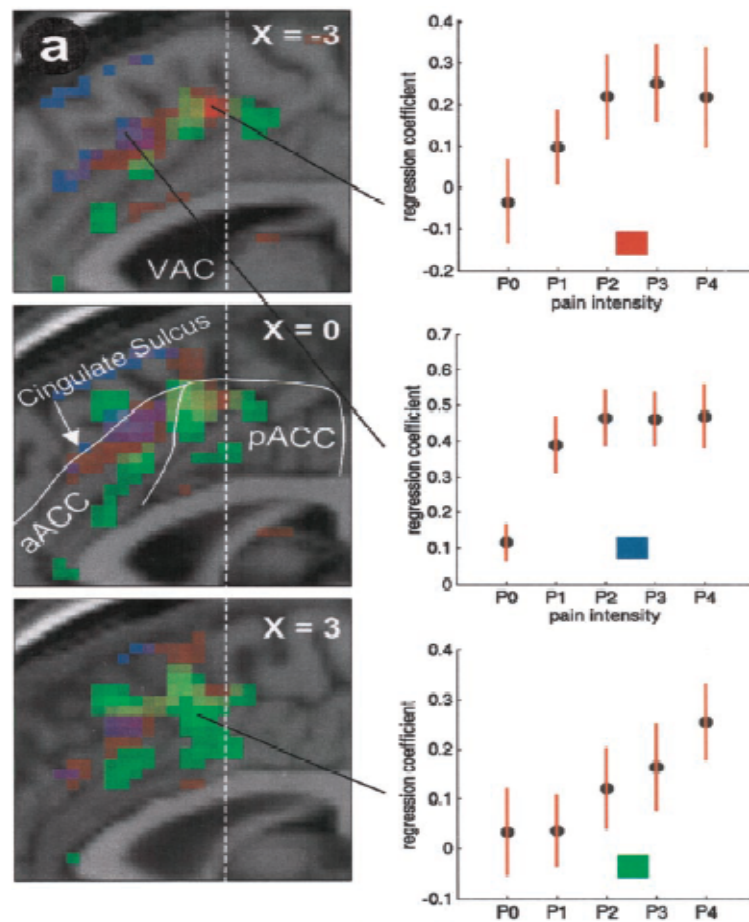


P0-P4: Variation of intensity of a laser stimulus applied to the right hand (0, 300, 400, 500, and 600 mJ)



Parametric Designs

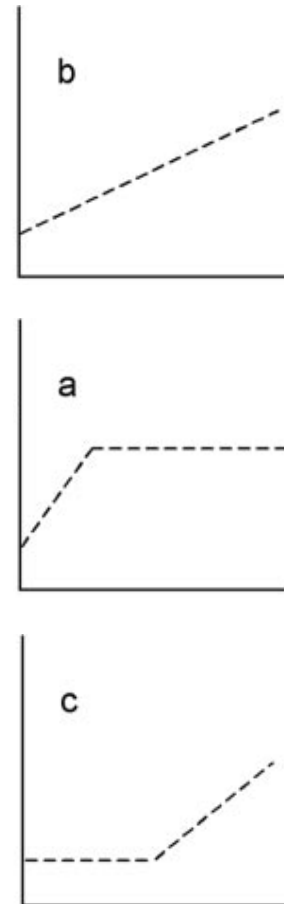
Investigating neurometric functions



→ Stimulus intensity
dorsal pACC

→ Stimulus awareness
cingulate sulcus aACC

→ Pain intensity
ventral pACC



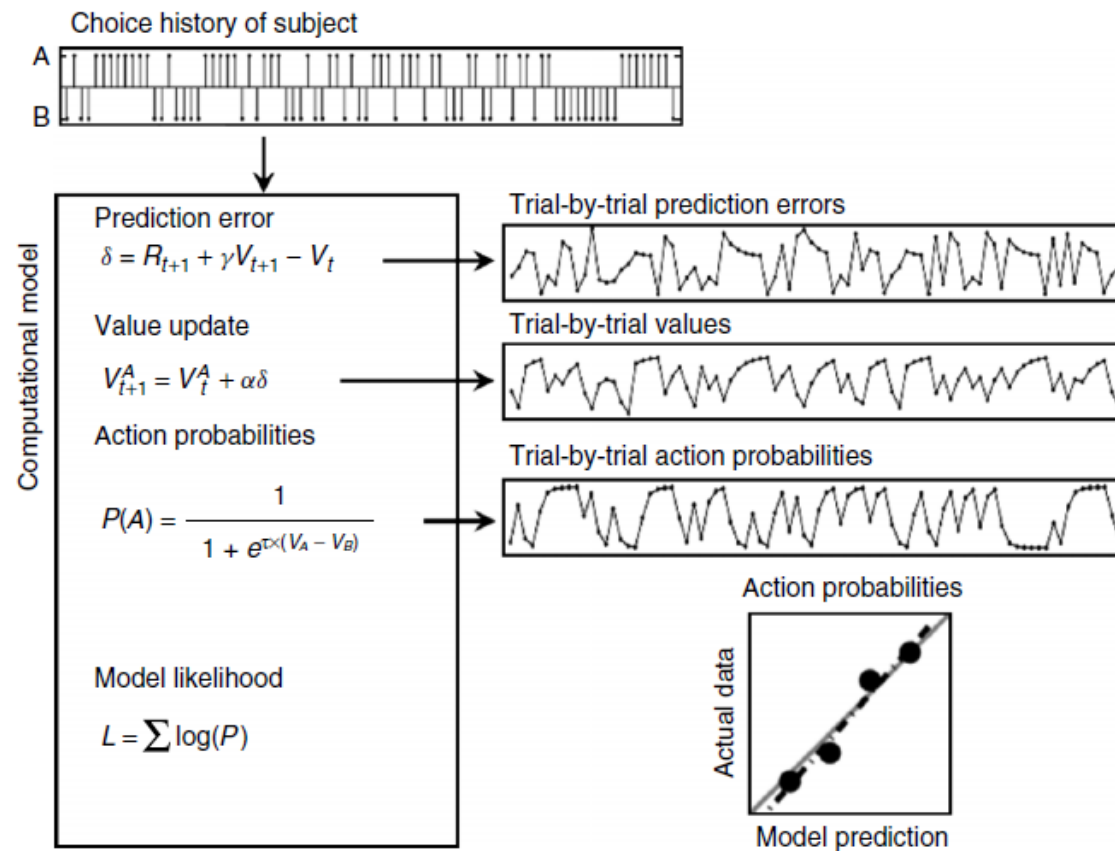
Parametric Designs

Model-based regressors

- General idea:
generate predictions from a **computational model**, e.g. of learning or decision-making
- Commonly used models:
 - Rescorla-Wagner learning model
 - Temporal difference (TD) learning model
 - Bayesian models
- **Predictions used to define regressors**
- Inclusion of these regressors in a GLM and testing for significant correlations with voxel-wise BOLD responses

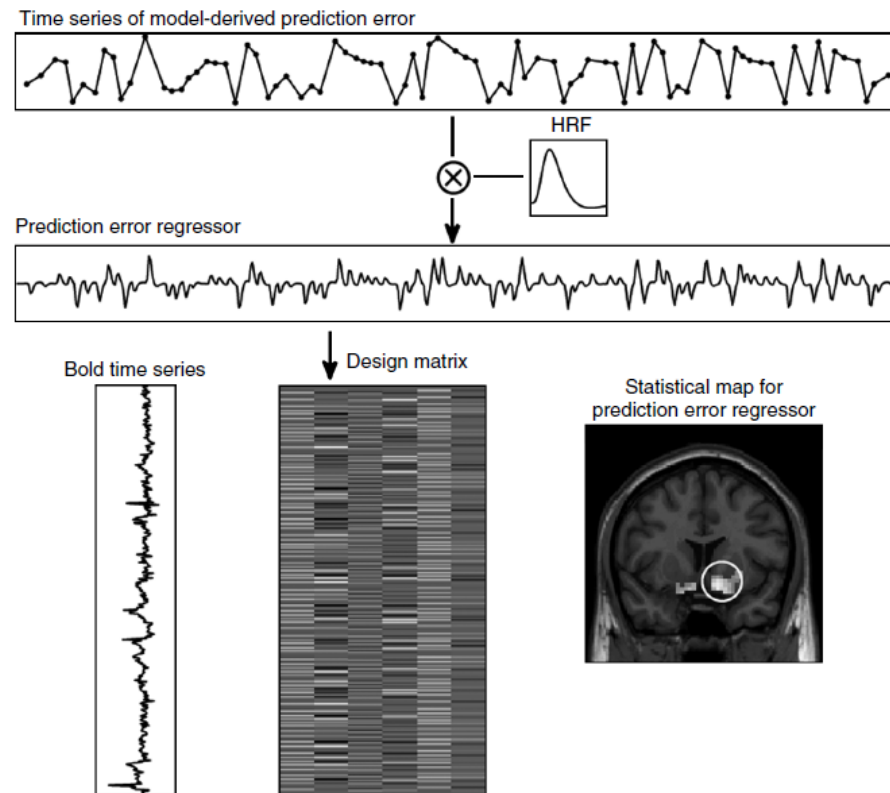
Parametric Designs

Model-based fMRI analysis, Example



Parametric Designs

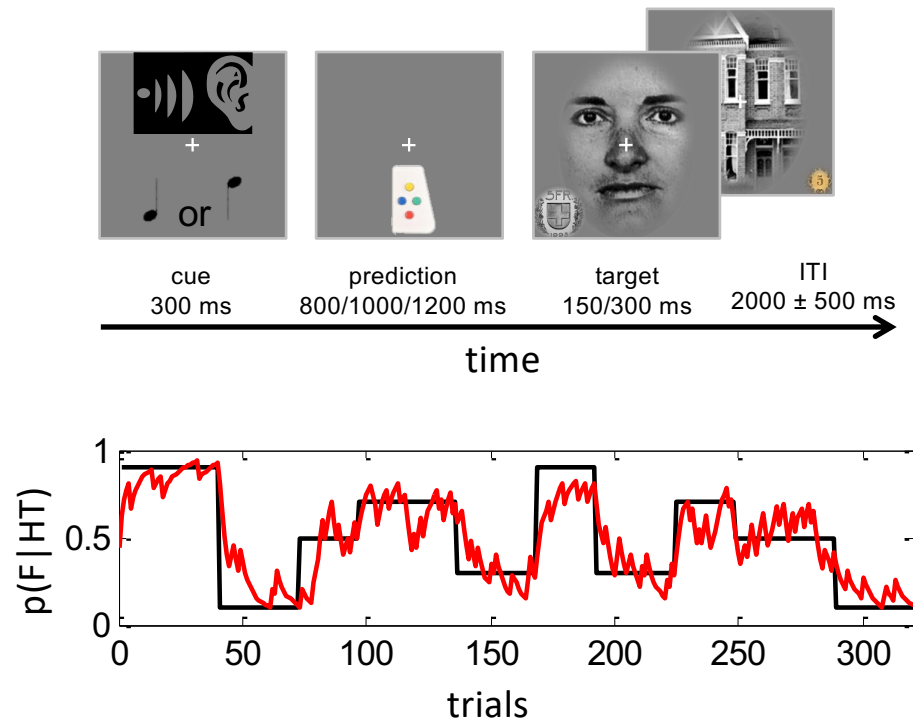
Model-based fMRI analysis, Example



Parametric Designs

Model-based fMRI analysis, Example

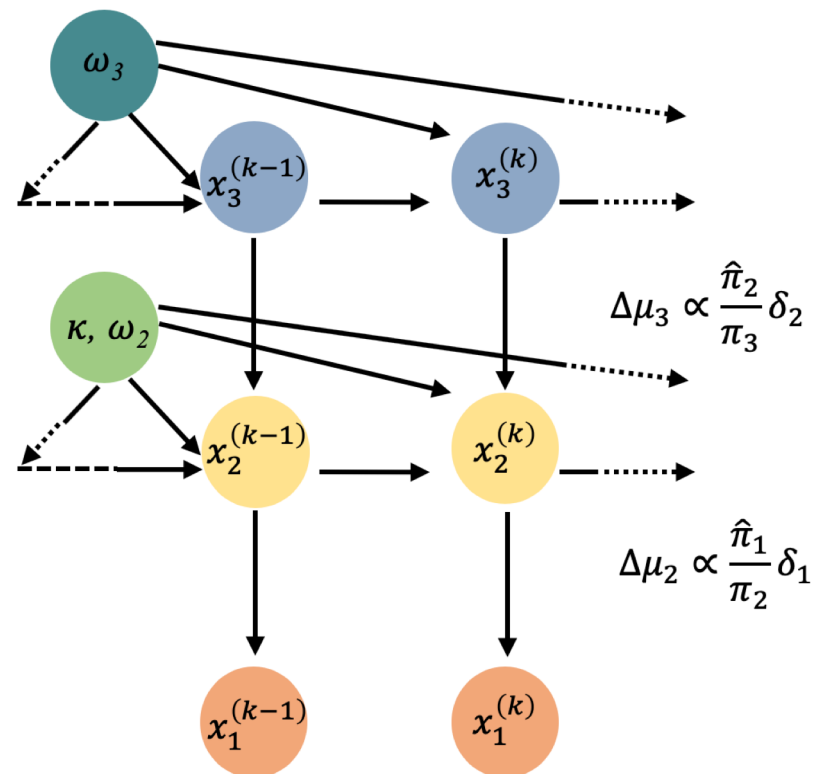
Hierarchical prediction errors
about sensory outcome and its probability



Parametric Designs

Model-based fMRI analysis, Example

The Hierarchical Gaussian Filter (HGF)



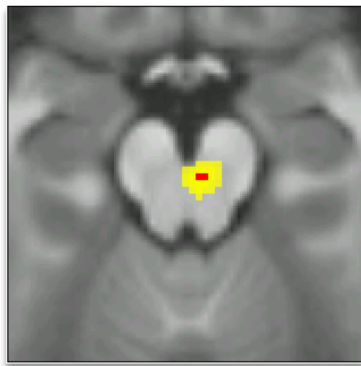
$$\Delta\mu_i \propto \frac{\hat{\pi}_{i-1}}{\pi_i} PE_{i-1}$$

Parametric Designs

Model-based fMRI analysis, Example

Hierarchical prediction errors
about sensory outcome and its probability

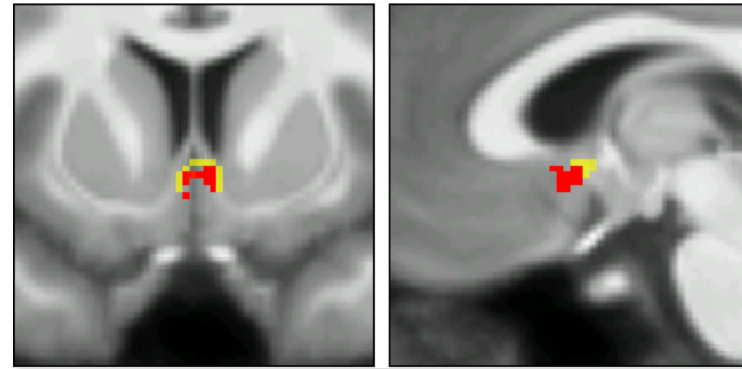
ε_2 in midbrain (N=45)



$$\varepsilon_2 = \sigma_2^{(k)} \delta_1^{(k)}$$

p<0.05, whole brain FWE corrected
p<0.05, SVC FWE corrected

ε_3 in basal forebrain (N=45)



$$\varepsilon_3 \propto \sigma_3^{(k)} \delta_2^{(k)}$$

p<0.05, SVC FWE corrected
p<0.001, uncorrected

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Factorial Designs

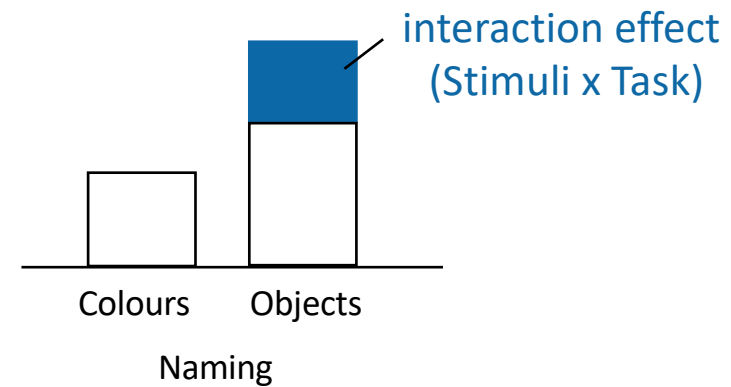
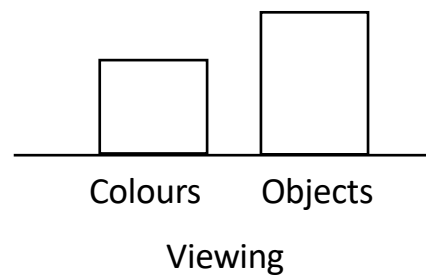
Main effects and Interactions

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

- Main effect of task: $(A1 + B1) - (A2 + B2)$
- Main effect of stimuli: $(A1 + A2) - (B1 + B2)$
- Interaction of task and stimuli:
Can show a failure of pure insertion

$$(A1 - B1) - (A2 - B2)$$

Is the inferotemporal region implicated in phonological retrieval during object naming?



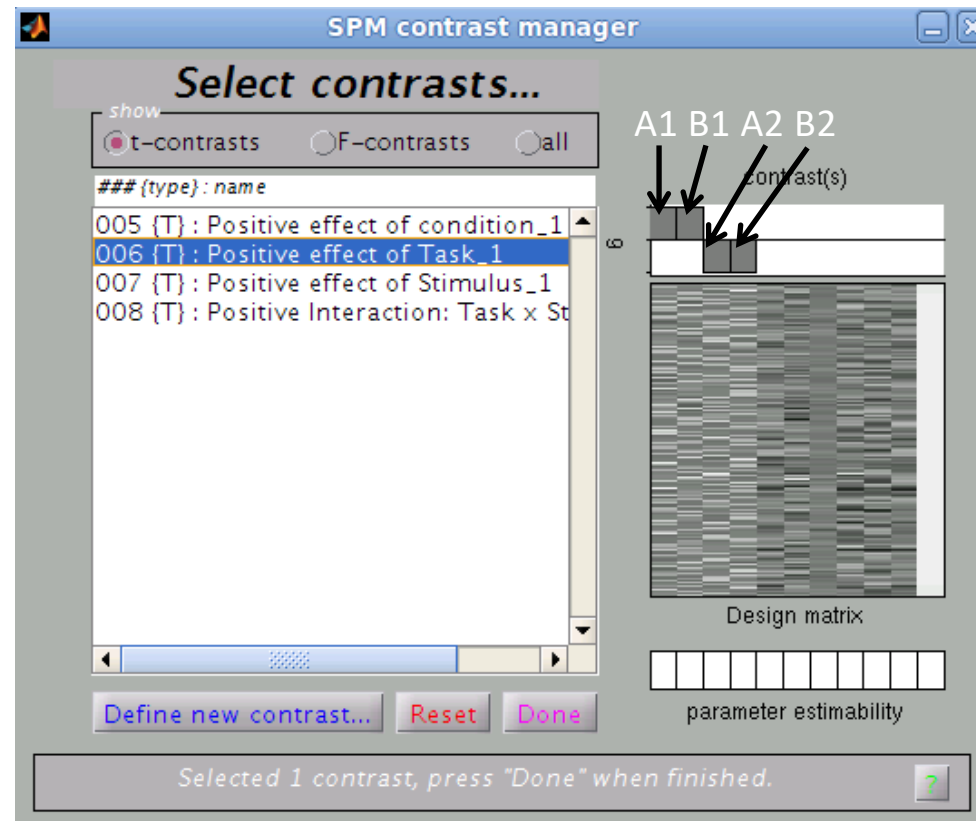
Factorial Designs

Main effect, Example SPM

Task (1/2)	
Viewing	Naming
A1	A2
B1	B2

Stimuli (A/B)
Objects Colours

Main effect of task:
 $(A1 + B1) - (A2 + B2)$



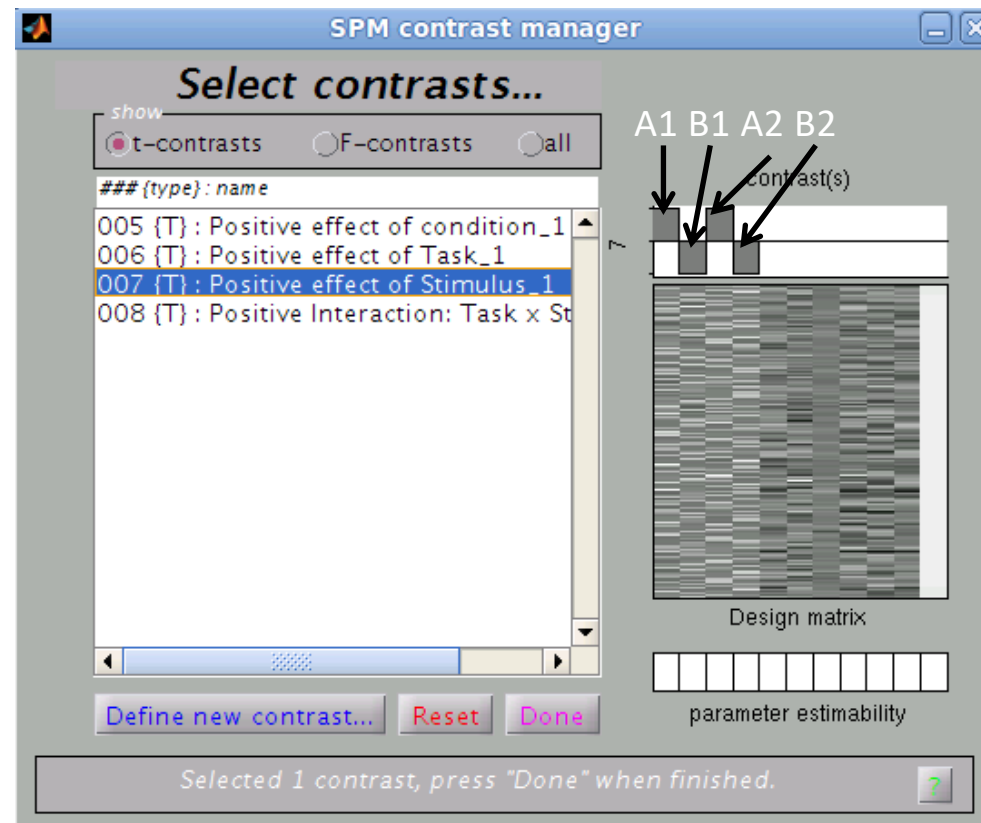
Factorial Designs

Main effect, Example SPM

Task (1/2)	
Viewing	Naming
A1	A2
B1	B2

Stimuli (A/B)
Objects Colours

Main effect of stimuli:
 $(A1 + A2) - (B1 + B2)$



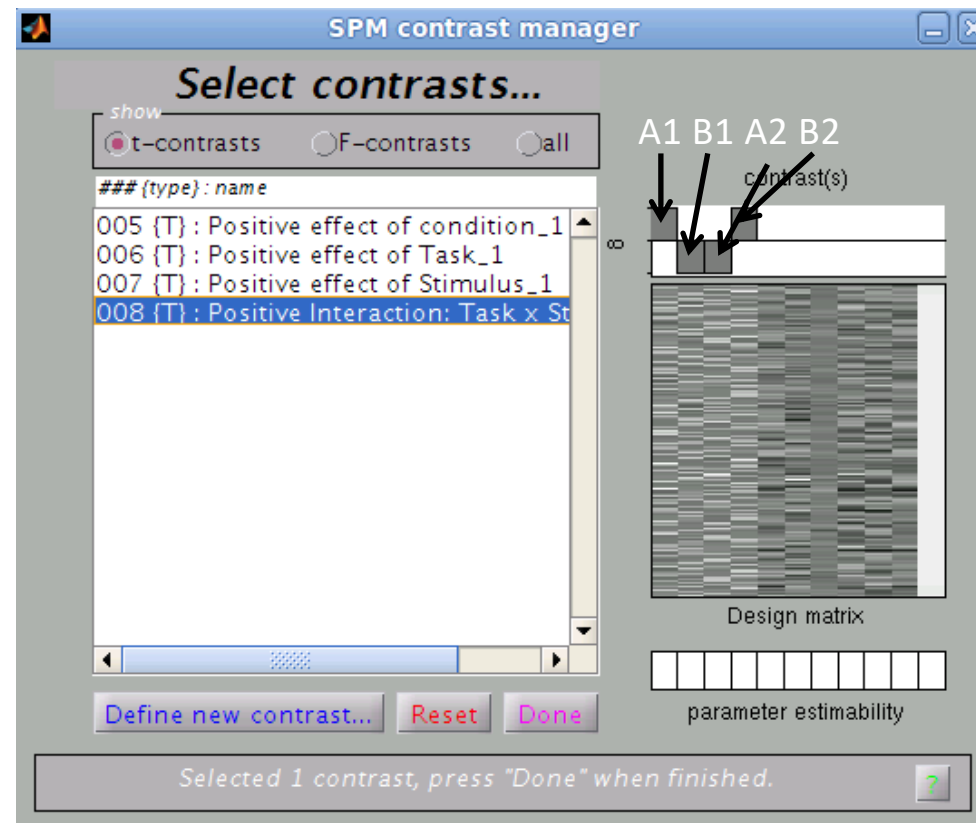
Factorial Designs

Interaction, Example SPM

Task (1/2)	
Viewing	Naming
A1	A2
B1	B2

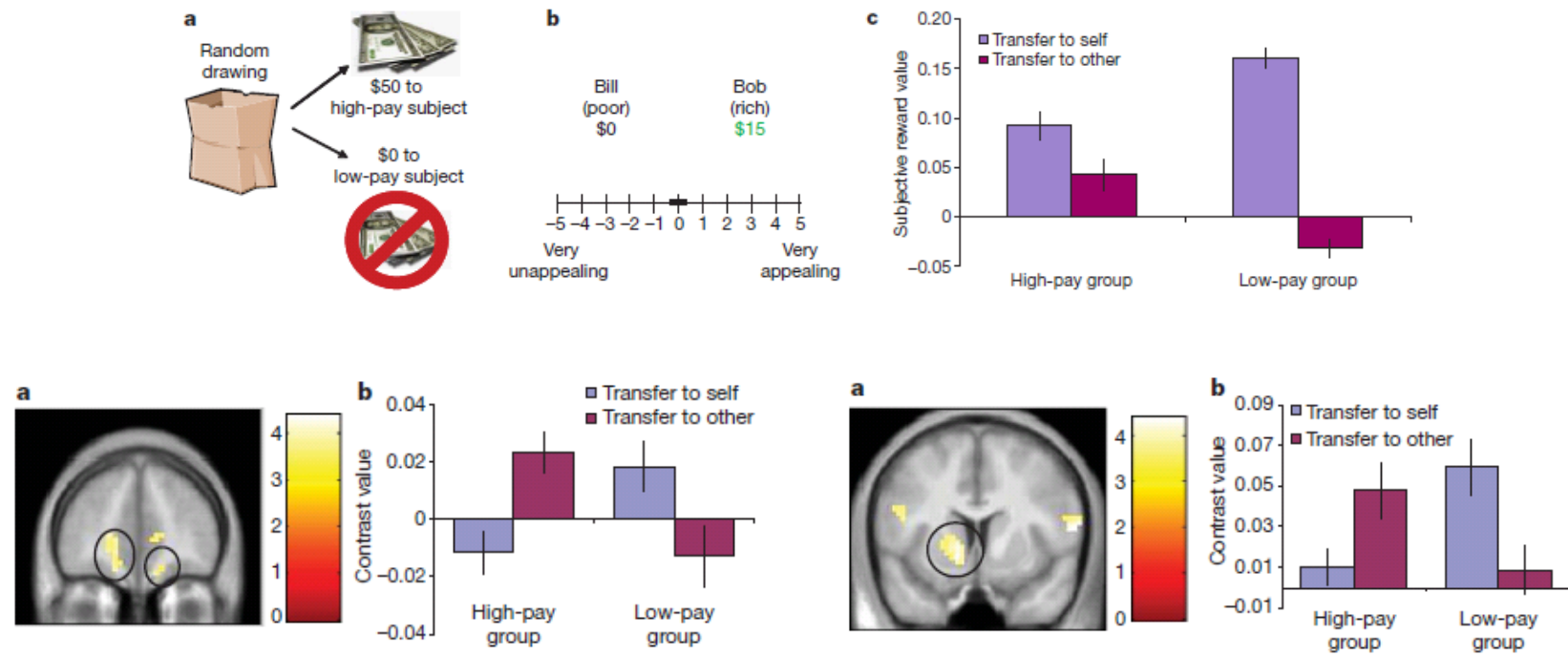
Stimuli (A/B)
Objects Colours

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



Factorial Designs

Example



Factorial Designs

Psycho-Physiological Interactions (PPIs)

		Task factor	
		Task A	Task B
Stimulus factor	Stim 1	T_A/S_1	T_B/S_1
	Stim 2	T_A/S_2	T_B/S_2

GLM of a 2x2 factorial design:

$$y = (T_A - T_B) \beta_1 + (S_1 - S_2) \beta_2 + (T_A - T_B)(S_1 - S_2) \beta_3 + e$$

← main effect of task
 ← main effect of stim. type
 interaction

We can replace one main effect in the GLM by the time series of an area that shows this main effect.

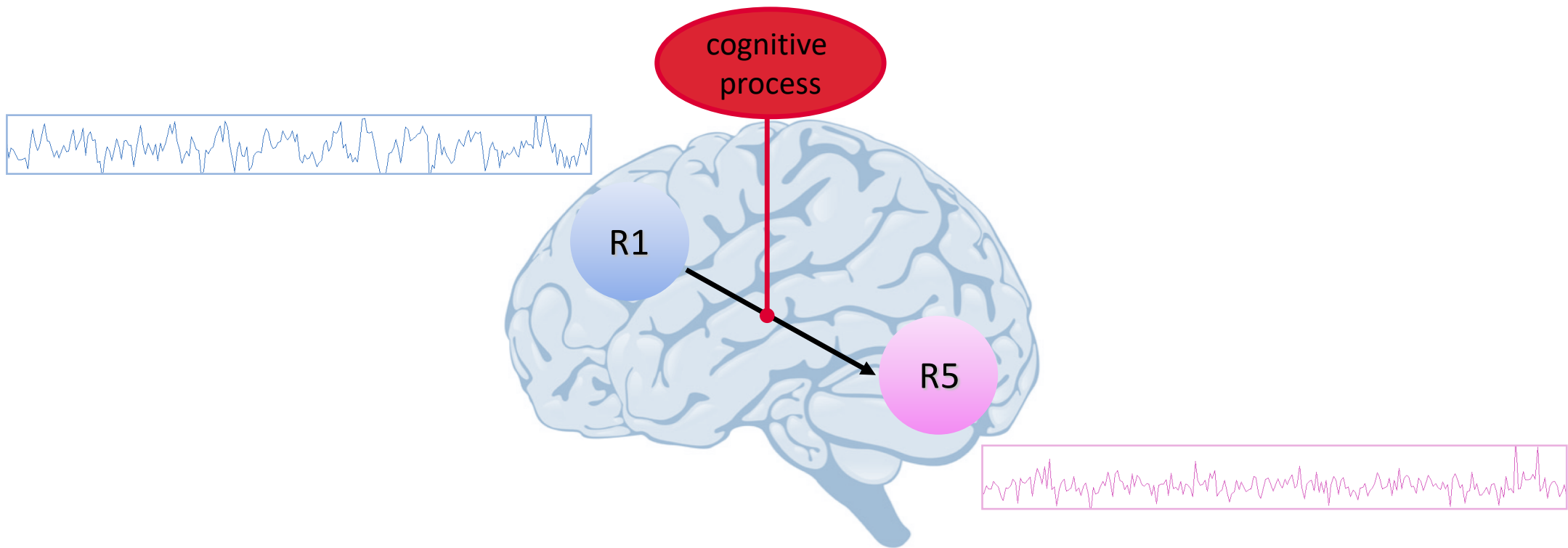
E.g. let's replace the main effect of stimulus type by the time series of area V1.

$$y = (T_A - T_B) \beta_1 + V1 \beta_2 + (T_A - T_B) V1 \beta_3 + e$$

← main effect of task
 ← V1 time series \approx main effect of stim. type
 PPI

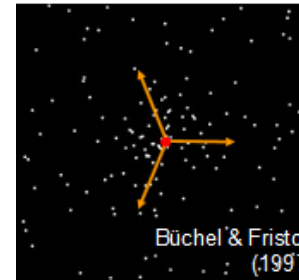
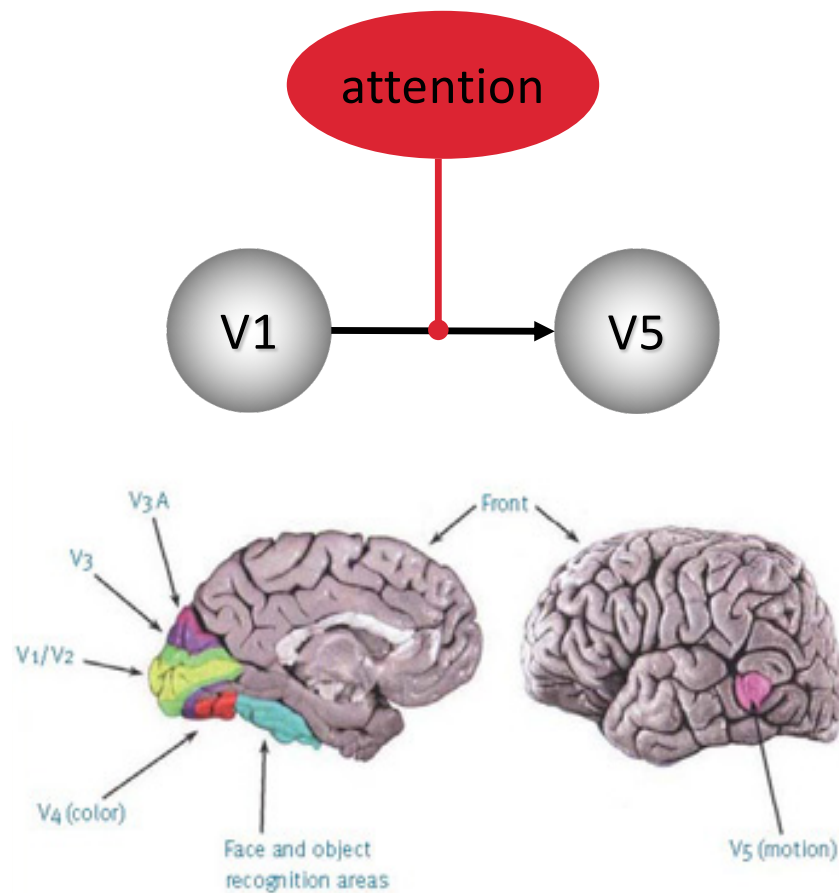
Factorial Designs

Psycho-Physiological Interactions (PPIs)



Factorial Designs

PPI, Example



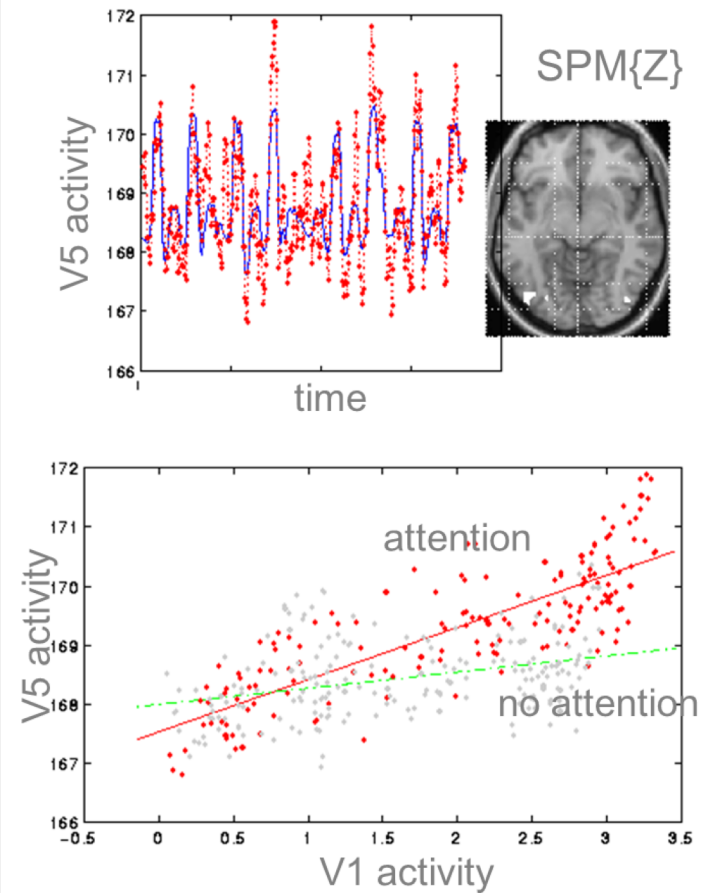
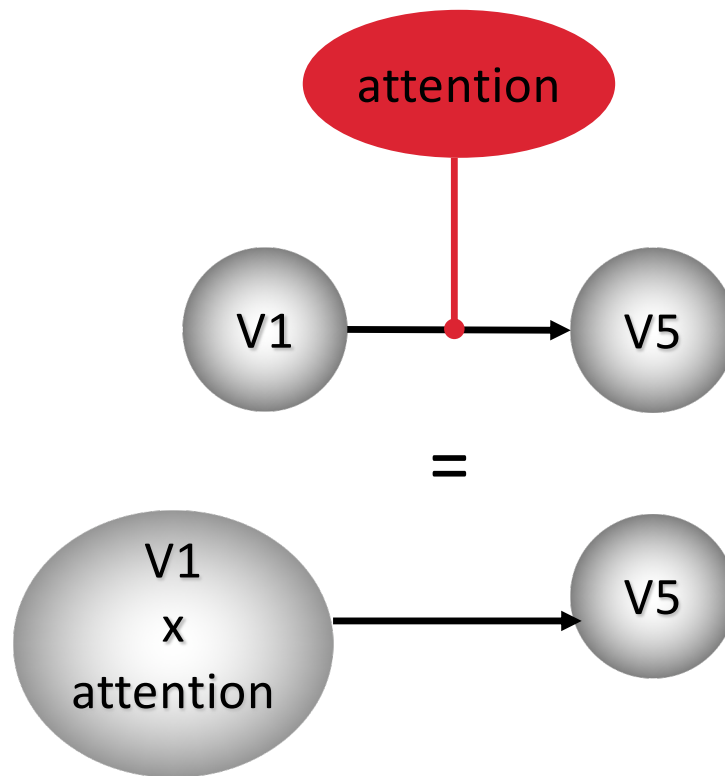
Radially moving dots

Conditions:

- Stationary
- Motion and attention ("detect changes")
- Motion without attention

Factorial Designs

PPI, Example



Friston et al. 1997, NeuroImage

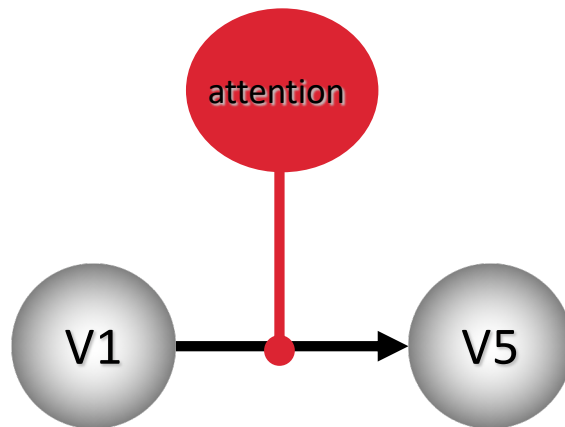
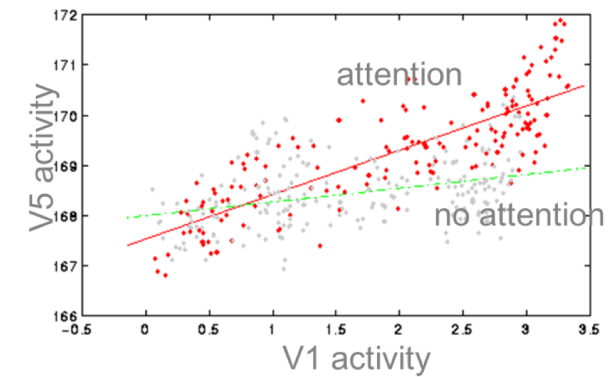
Büchel & Friston, 1997, Cereb. Cortex

Factorial Designs

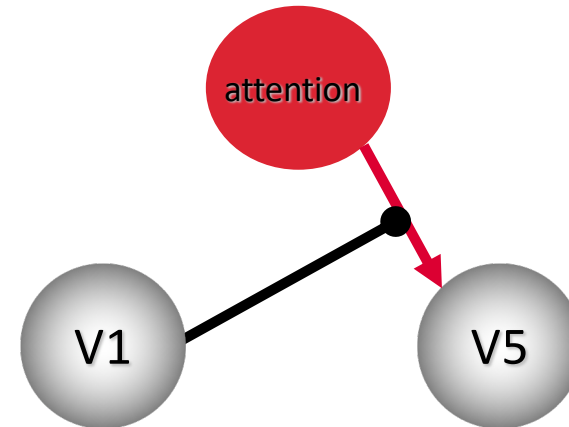
PPI, Example

$$y = (T_A - T_B) \beta_1 + V1 \beta_2 + (T_A - T_B) V1 \beta_3 + e$$

Two possible interpretations of the PPI term



Modulation of V1 → V5 by attention



Modulation of attention → V5 by V1

Questions?

- Categorical designs

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