

# Experimental design of fMRI studies

Kerstin Preuschoff

Computational Neuroscience Lab, EPFL  
LREN

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With many thanks for slides & images to:

Rik Henson  
Christian Ruff  
Sandra Iglesias

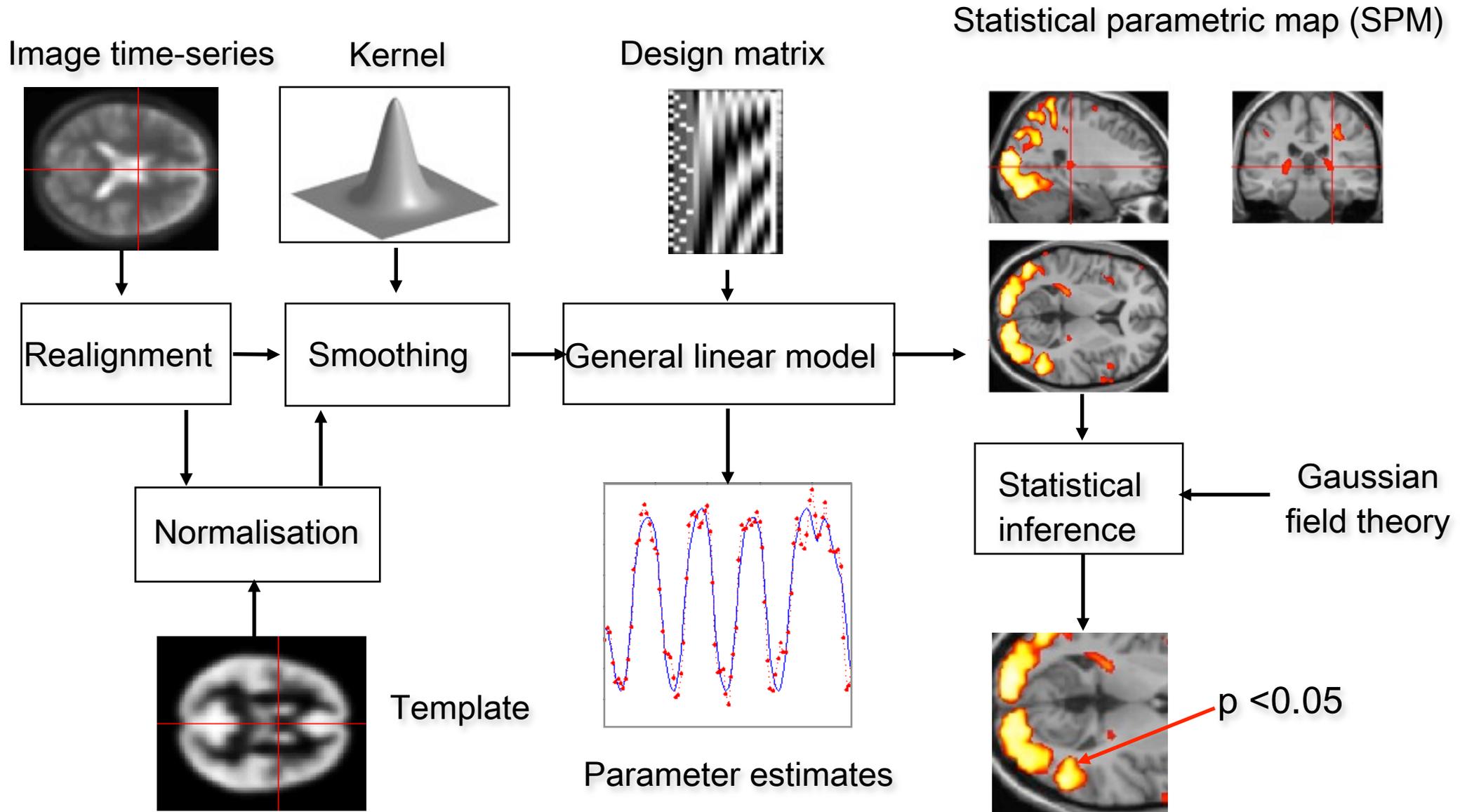
# Essential reading

*Henson, R. N. (2007). Efficient experimental design for fMRI. Statistical parametric mapping: the analysis of functional brain images (pp. 193-210). Academic Press.*

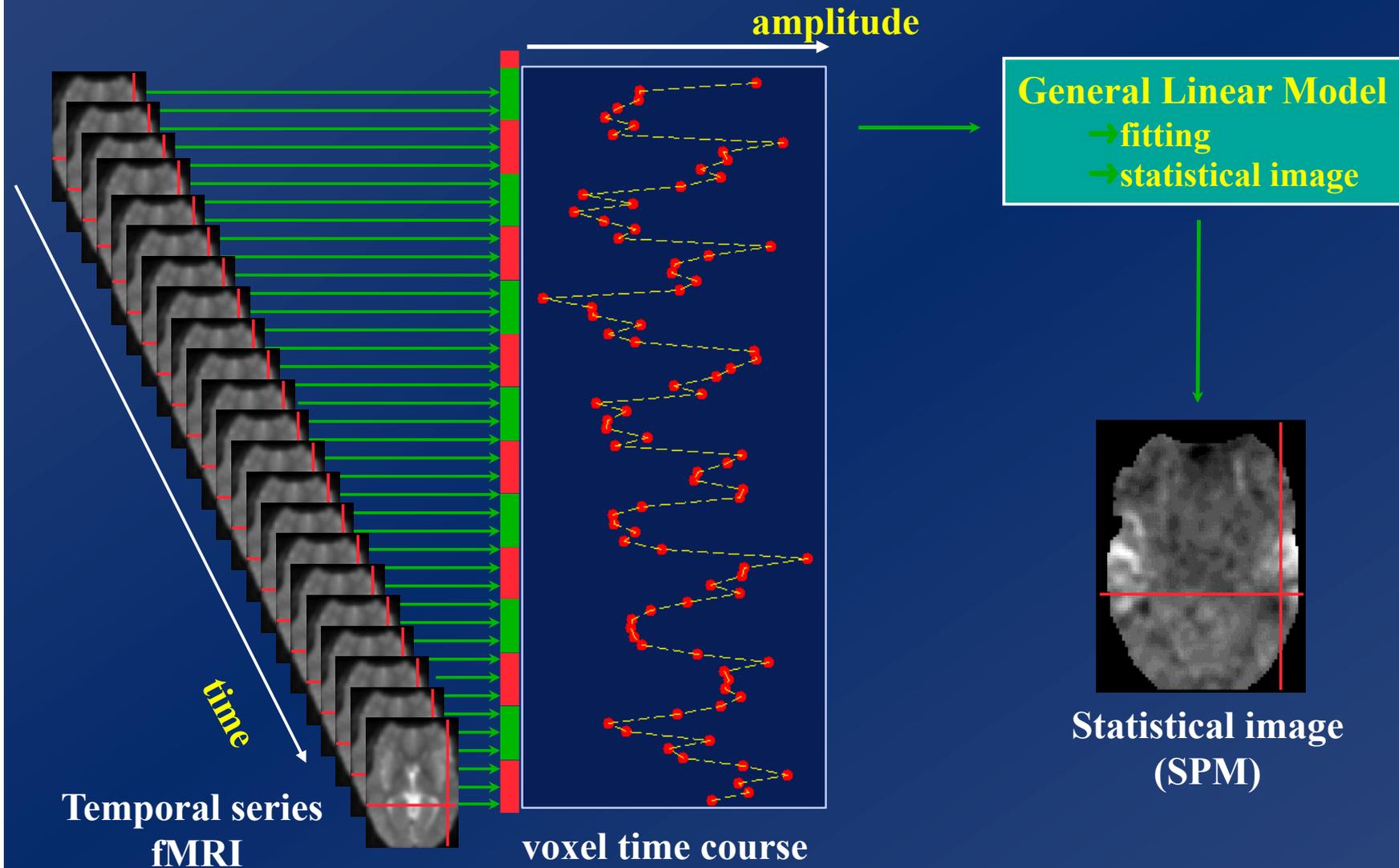
This book chapter covers the most common experimental designs along with how to efficiently design your experiments such that you maximize your chances of obtaining significant results.

Note the answers to ‘common questions’ at the end of this chapter.

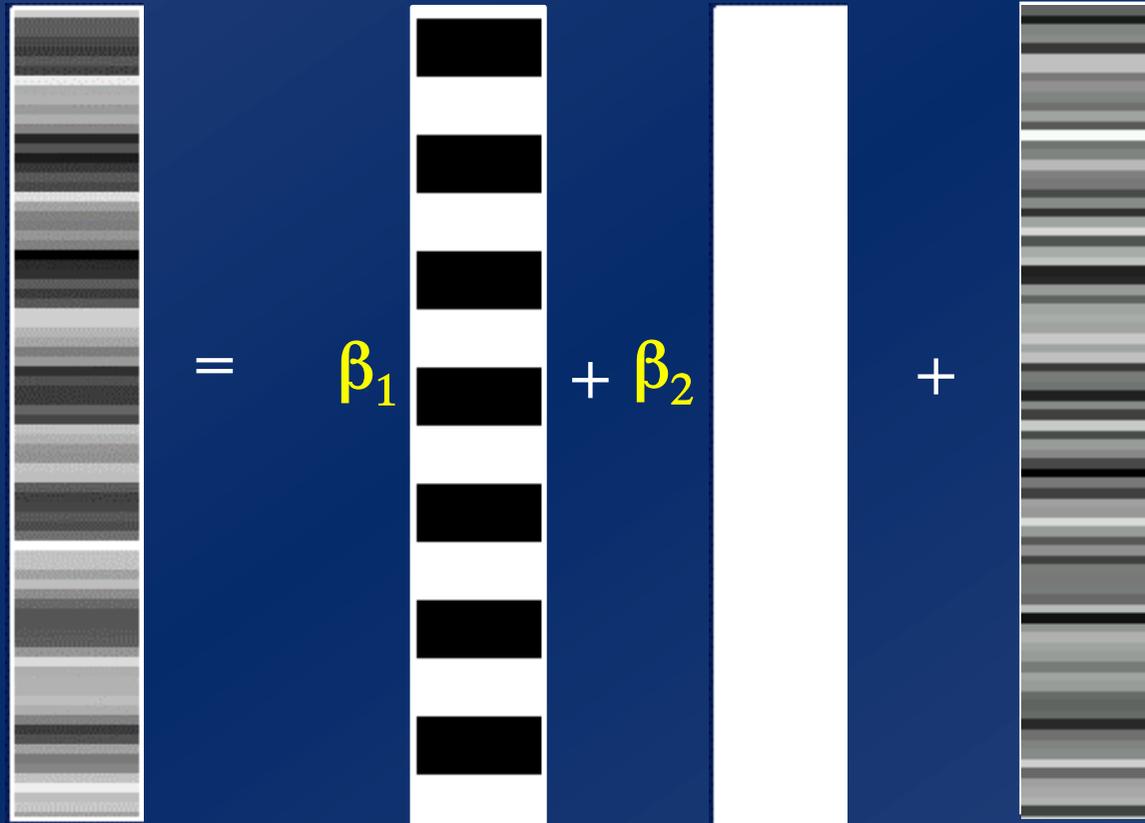
# Overview of SPM



# One voxel = One test (t, F, ...)

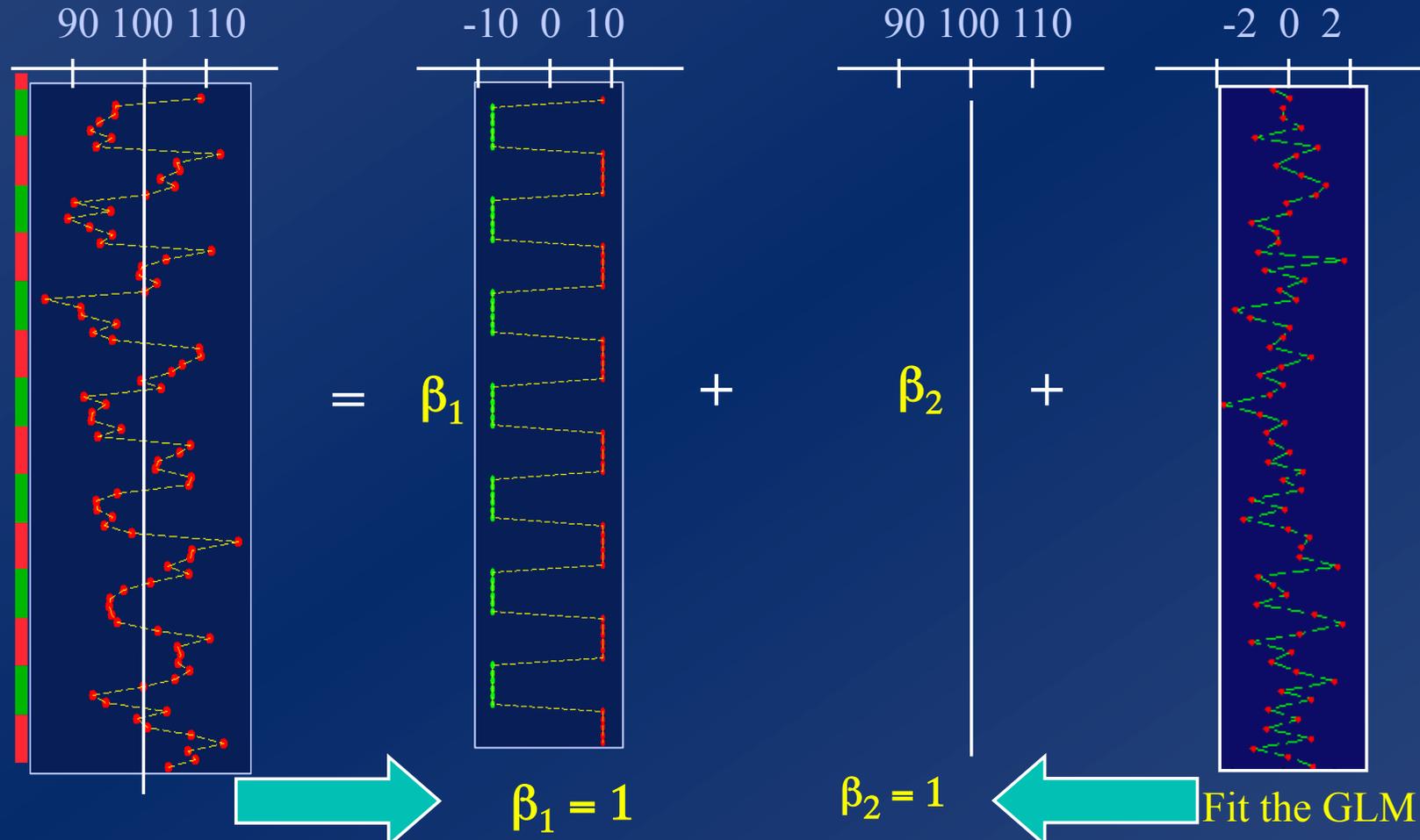


# ...revisited : matrix form



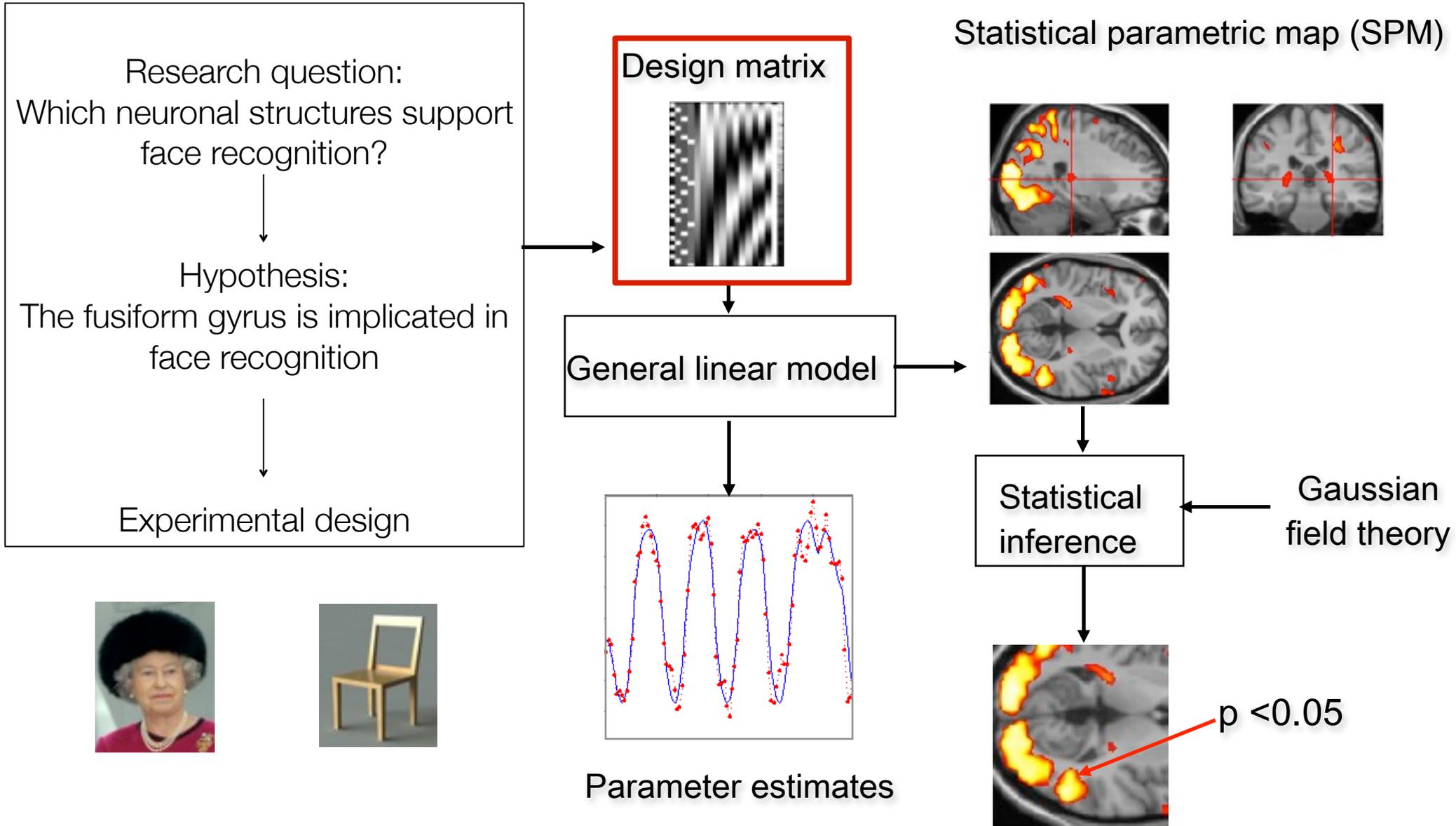
$$Y = \beta_1 \times f(t) + \beta_2 \times 1 + \epsilon$$

# Regression example...



voxel time series    **box-car reference function**    Mean value

# Overview of SPM



# Overview

- Categorical designs

  - Subtraction

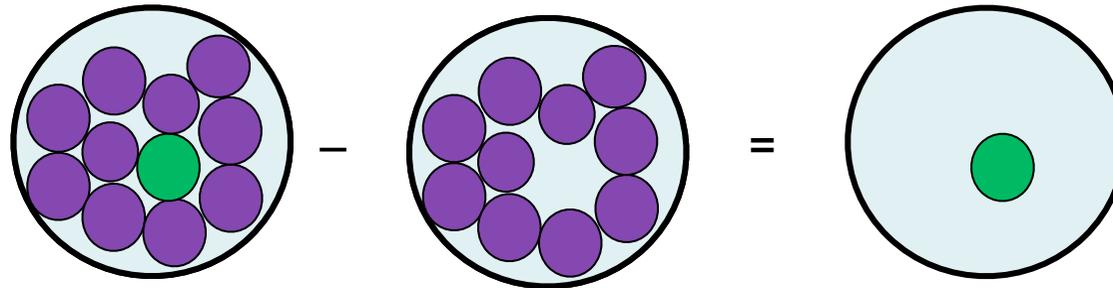
    - Pure insertion, evoked / differential responses

  - Conjunction

    - Testing multiple hypotheses

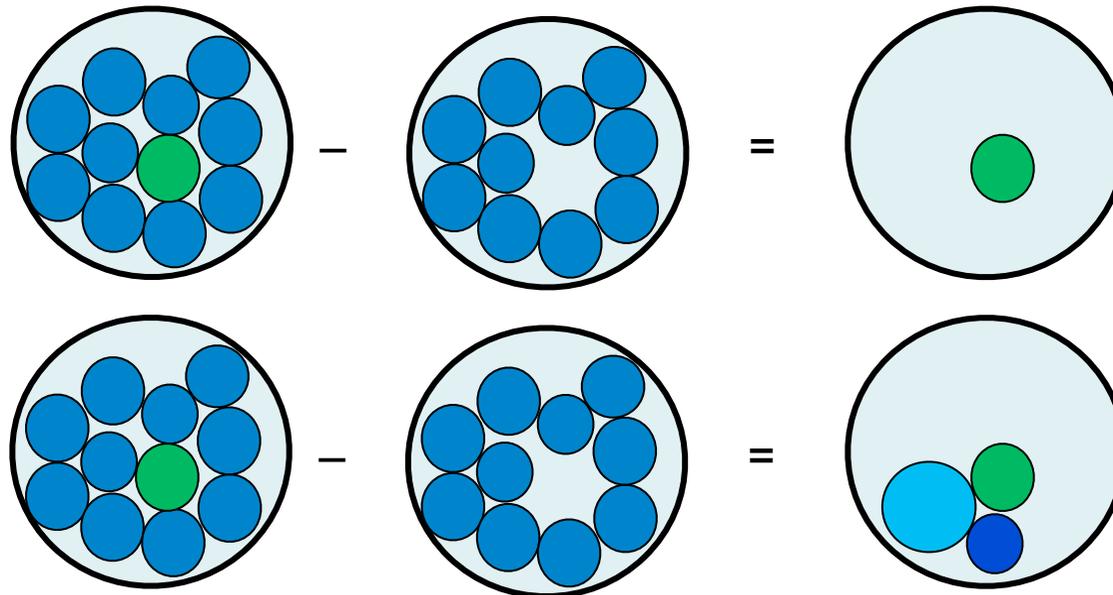
# Cognitive subtraction

- Aim:
  - Neuronal structures underlying a single process P (e.g., face recognition)?
- Procedure:
  - Contrast: [Task with P] – [control task without P] = P
  - the critical assumption of „pure insertion“
- Example: [Task with P] – [task without P] = P



# Cognitive subtraction

- Aim:
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  - the critical assumption of „pure insertion“
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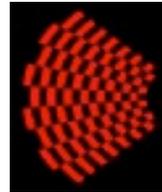
# Cognitive subtraction: Baseline problems

Which neuronal structures support face recognition ?

- „Distant“ stimuli



-



→ Several components differ!

- „Related“ stimuli



-



„Queen!“

„Aunt Jenny?“

→ P implicit in control condition?

- Same stimuli, different task



-



Name Person!

Name Gender!

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

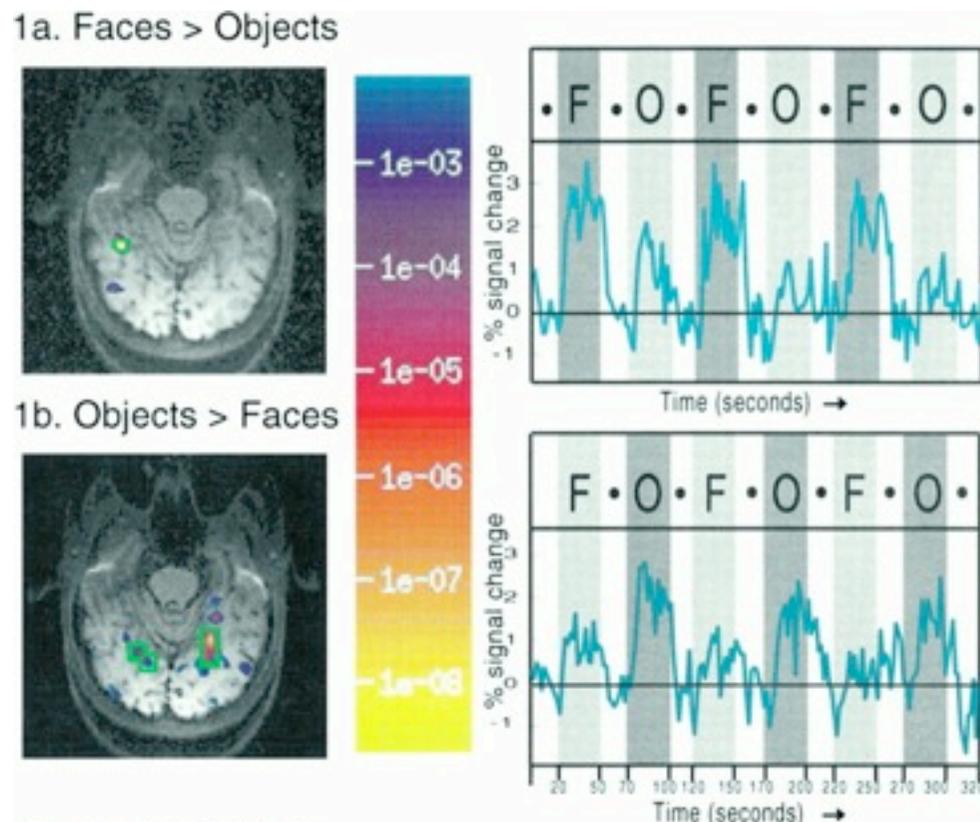
# A categorical analysis

## Experimental design

Face viewing                    F  
Object viewing                O

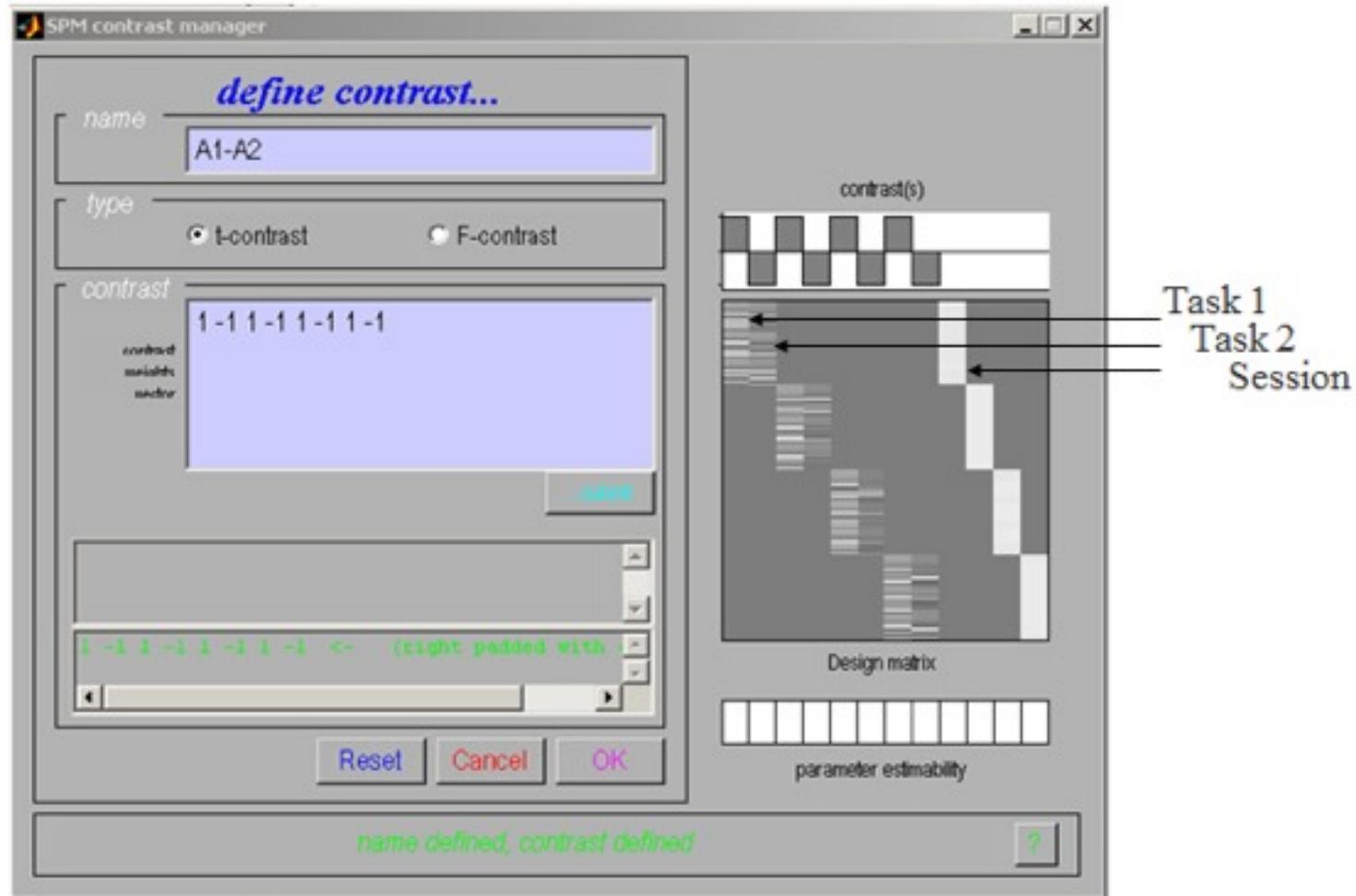
F - O = Face recognition  
O - F = Object recognition

...under assumption of pure insertion



Kanwisher N et al. J. Neurosci. 1997;

# Categorical design



# Overview

- Categorical designs

  - Subtraction

  - Conjunction

    - Pure insertion, evoked / differential responses

    - Testing multiple hypotheses

- Parametric designs

  - Linear

  - Nonlinear

    - Adaptation, cognitive dimensions

    - Polynomial expansions, neurometric functions

- Factorial designs

  - Categorical

  - Parametric

    - Interactions and pure insertion

    - Linear and nonlinear interactions

    - Psychophysiological Interactions

# Conjunctions

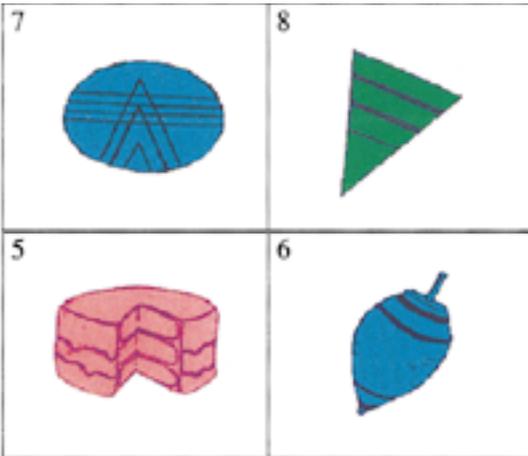
- One way to minimize the baseline/pure insertion problem is to isolate the same process by two or more separate comparisons, and inspect the resulting simple effects for commonalities
- A test for such activation common to several independent contrasts is called “conjunction”
- Conjunctions can be conducted across a whole variety of different contexts:
  - tasks
  - stimuli
  - senses (vision, audition)
  - etc.
- Note: the contrasts entering a conjunction must be orthogonal (this is ensured automatically by SPM)

# Conjunctions

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

Task (1/2)

	Viewing	Naming
Stimuli (A/B)	7	8
Objects	5	6
Colours		



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

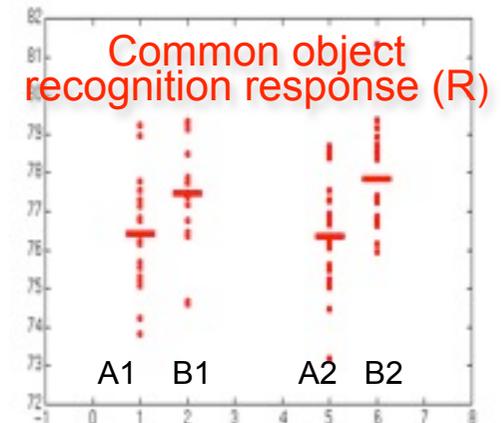
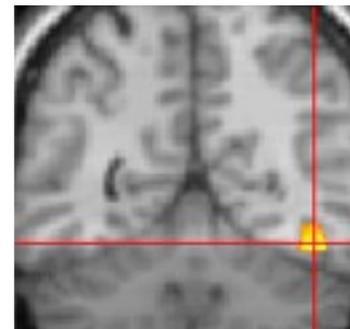
Which neural structures support object recognition?

(Object - Colour viewing) [B1 - A1]  
&

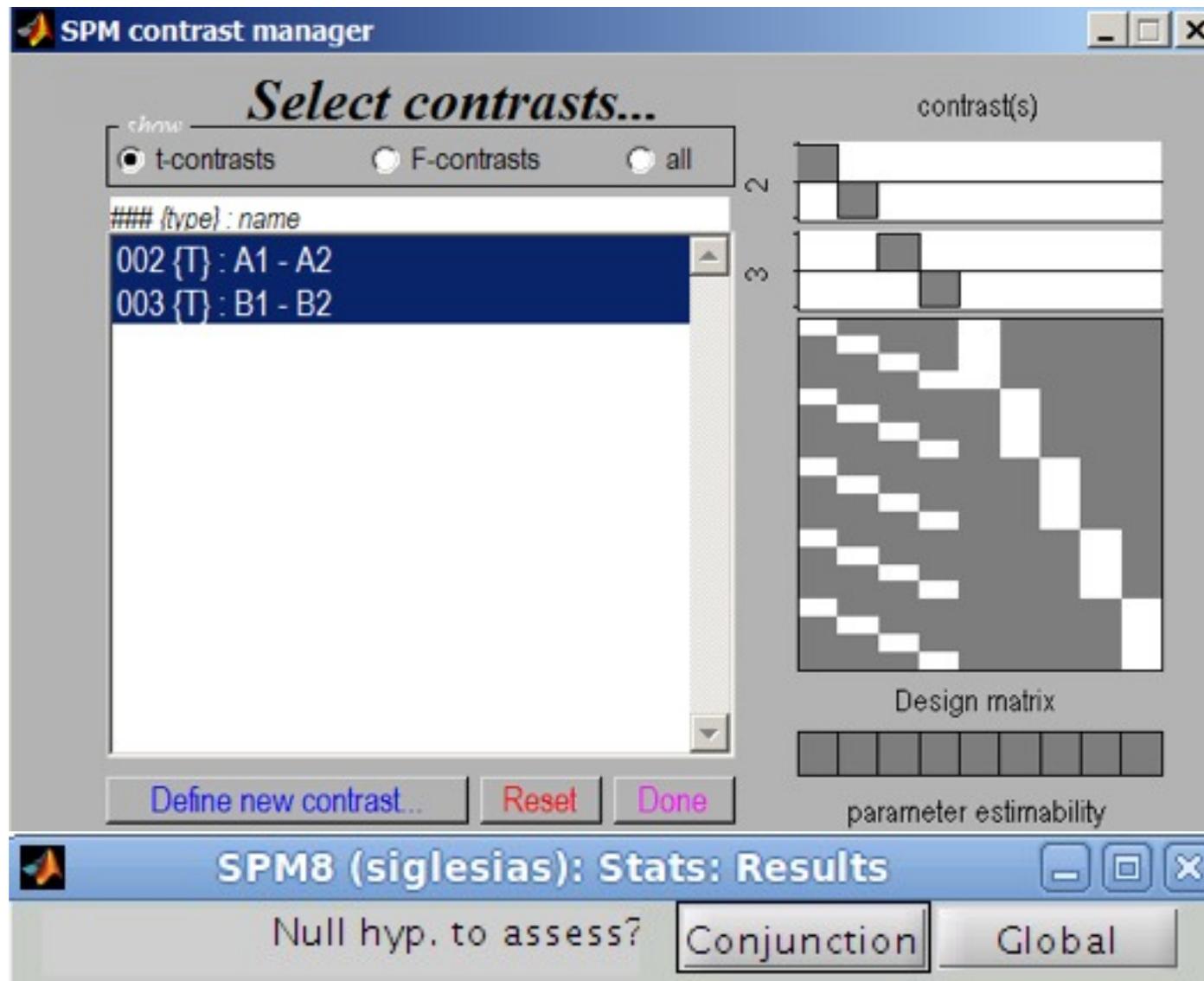
(Object - Colour naming) [B2 - A2]

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

Price et al. 1997

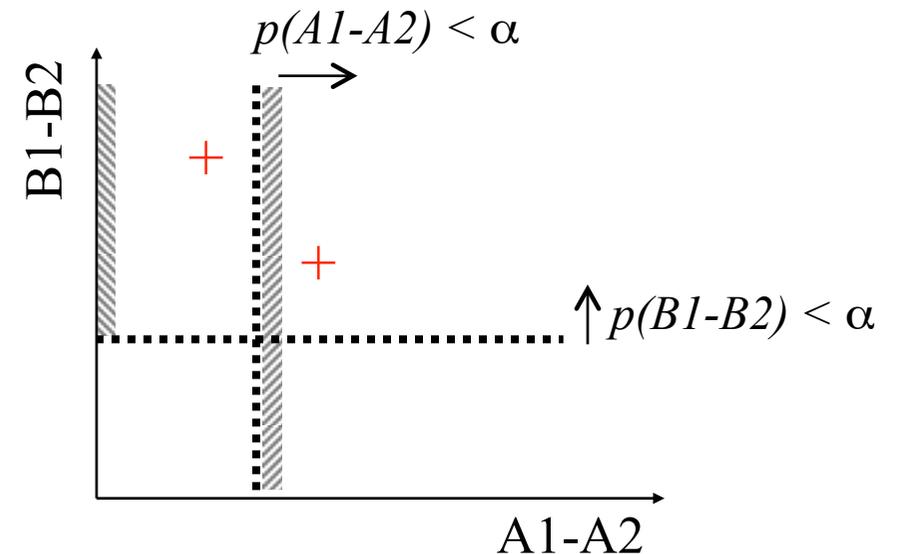


# Conjunctions



# Two types of conjunctions

- Test of **global null hypothesis**:  
Significant set of consistent effects
  - “Which voxels show effects of similar direction (but not necessarily individual significance) across contrasts?”
  - Null hypothesis: No contrast is significant:  $k = 0$
  - does not correspond to a logical AND !



Friston et al. (2005). *Neuroimage*, 25:661-667.

Nichols et al. (2005). *Neuroimage*, 25:653-660.

# Overview

- 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

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

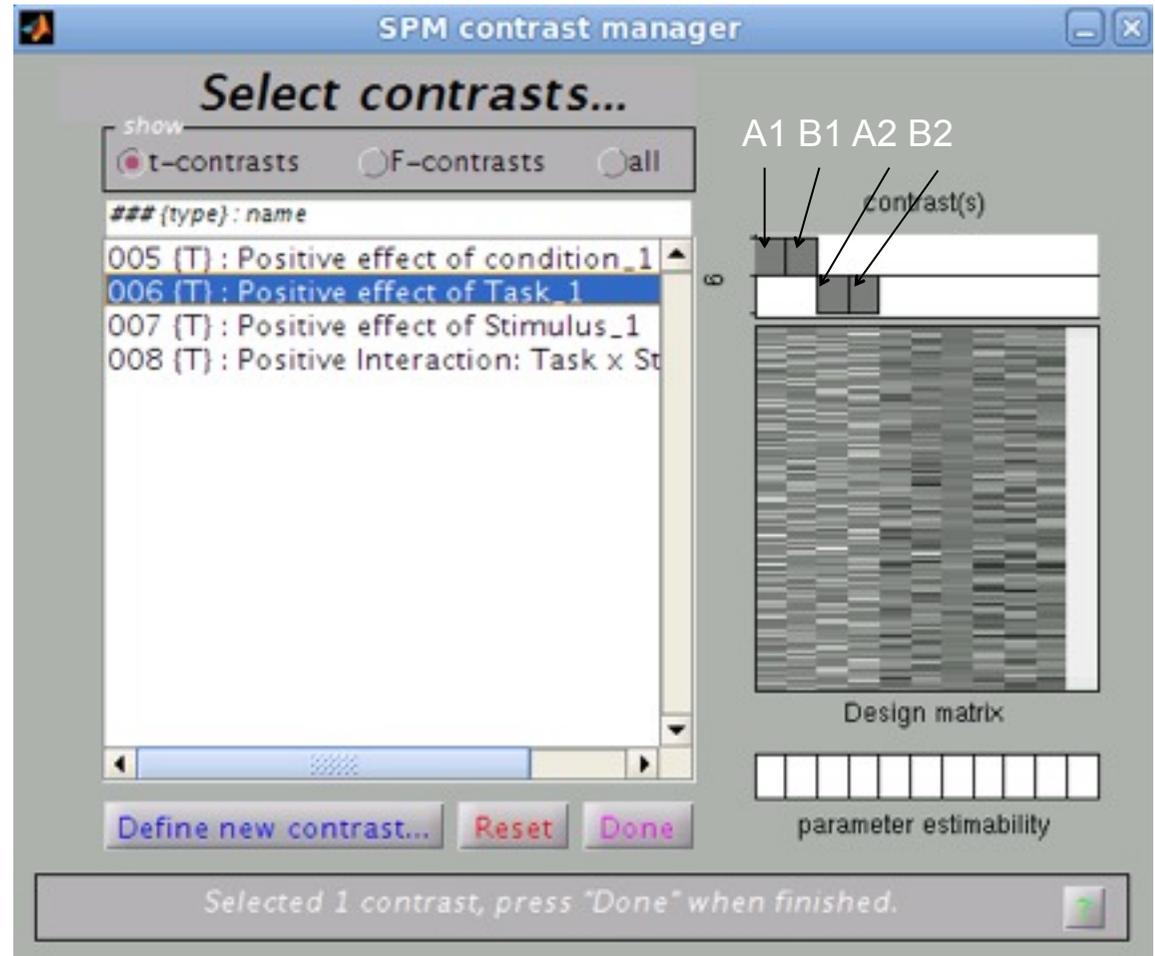
# Factorial design

Stimuli (A/B)

Objects Colours

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

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



# Factorial design

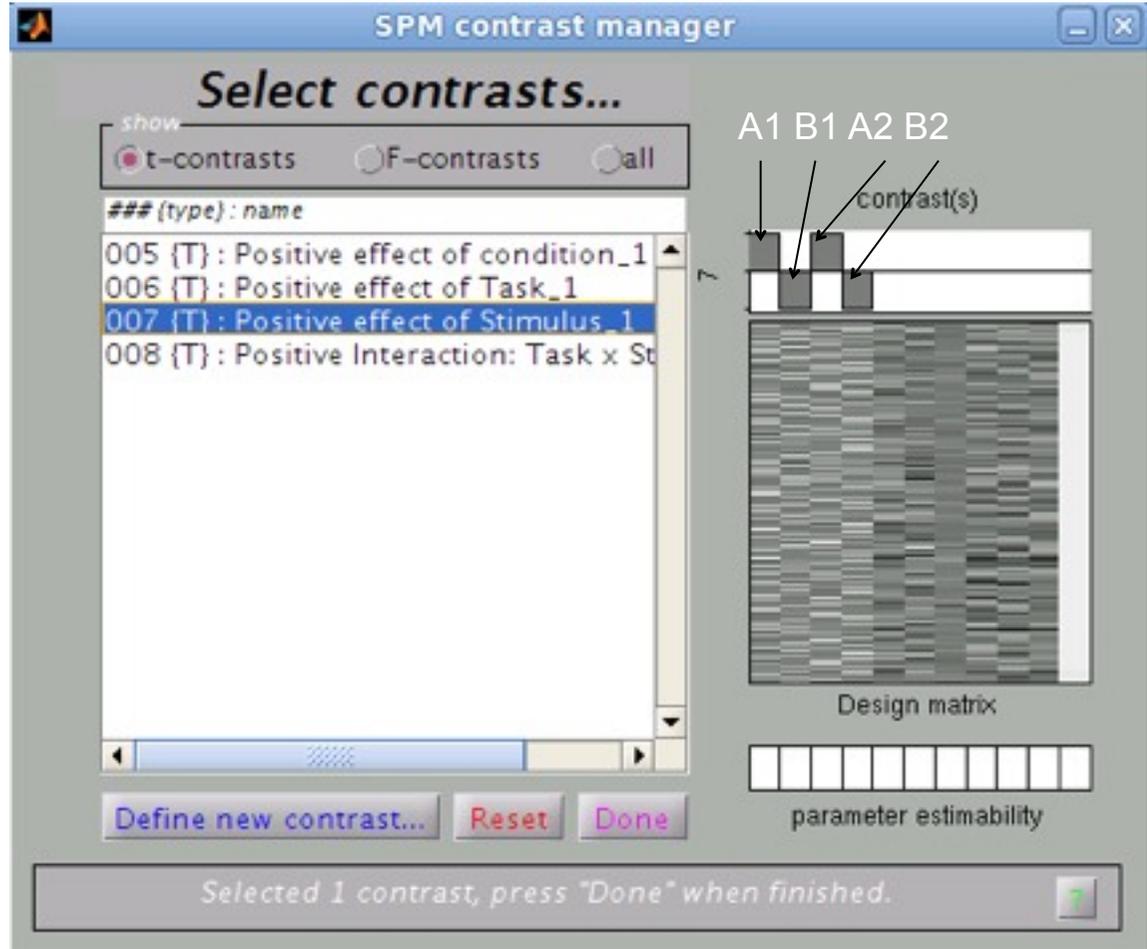
Stimuli (A/B)

Objects Colours

Task (1/2)  
Viewing Naming

A1	A2
B1	B2

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



# Factorial design

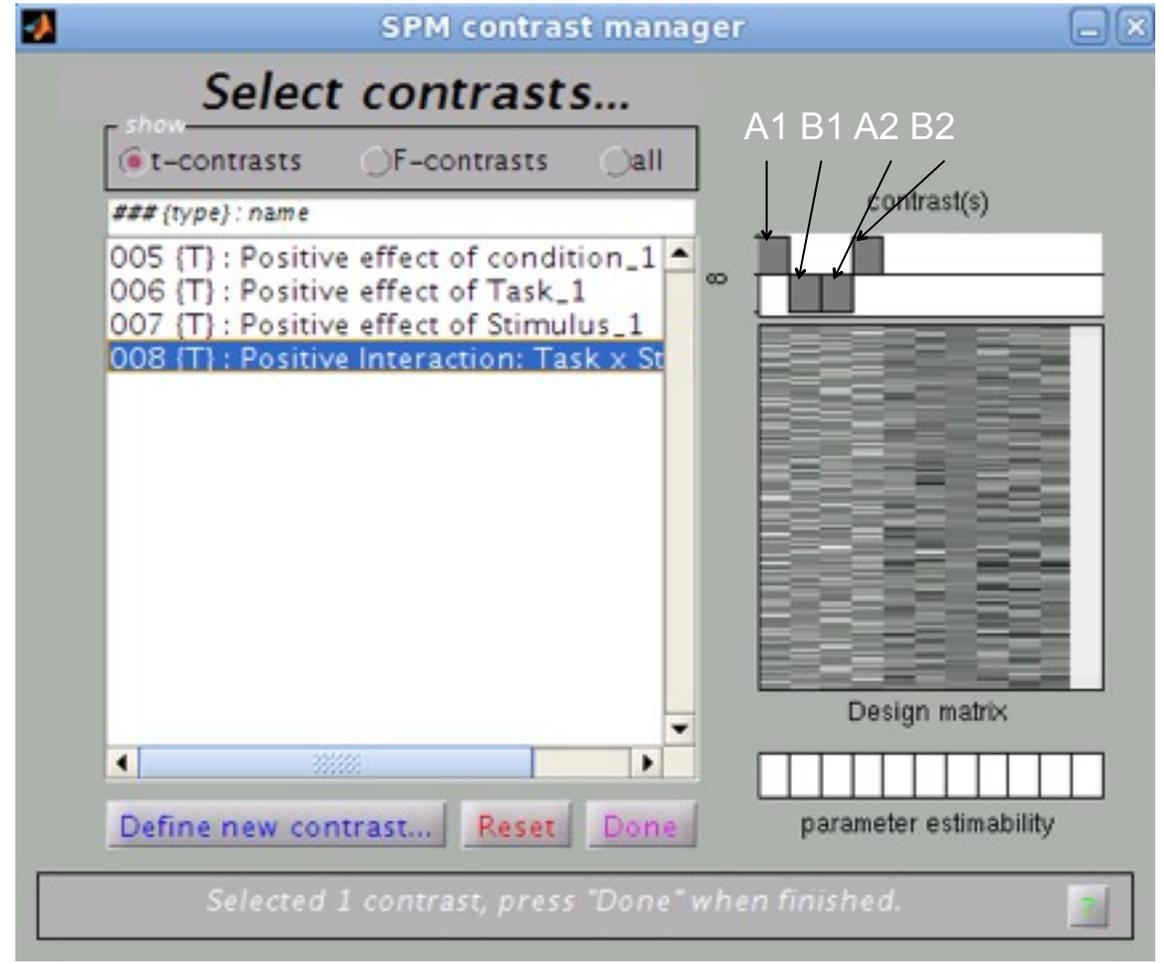
Stimuli (A/B)

Objects Colours

Task (1/2)  
Viewing Naming

A1	A2
B1	B2

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



# Main effects and interactions

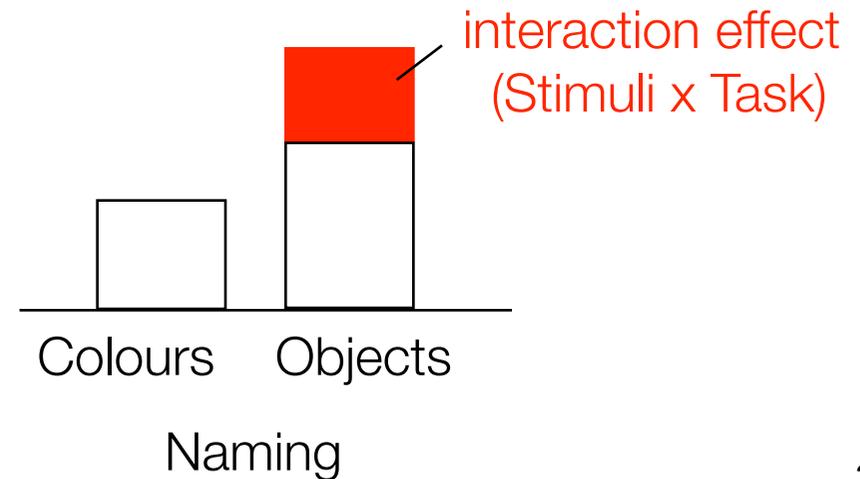
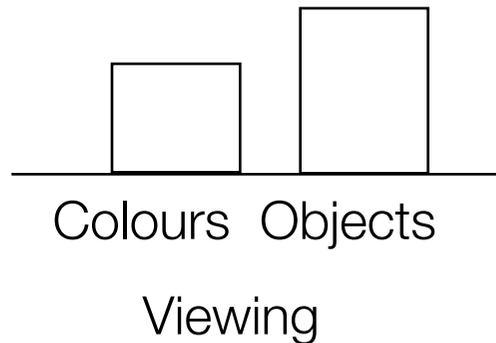
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Can show a failure of pure insertion

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

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



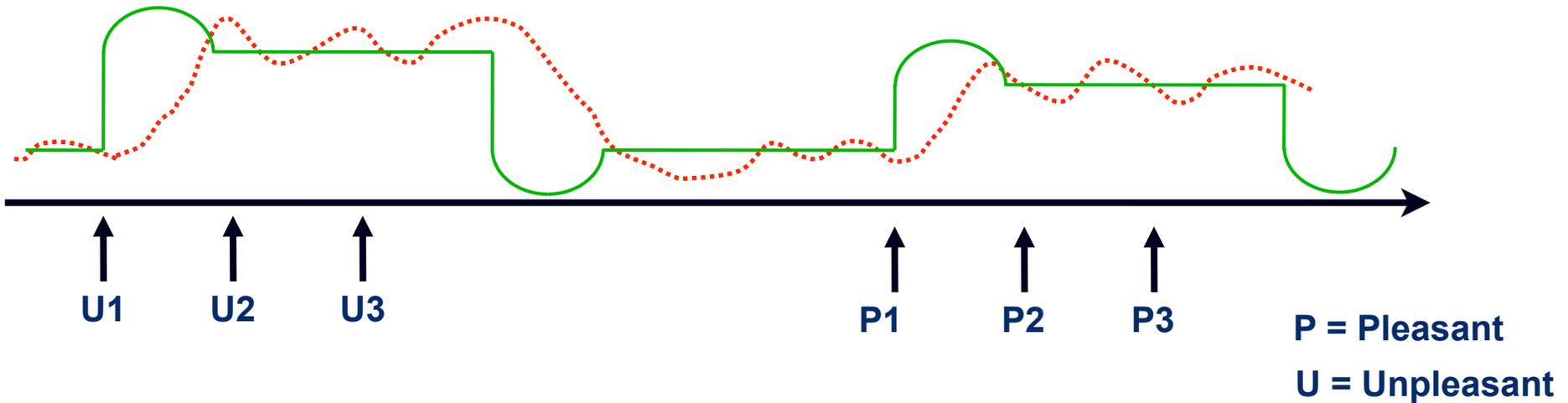
# Event-related fMRI

# Overview

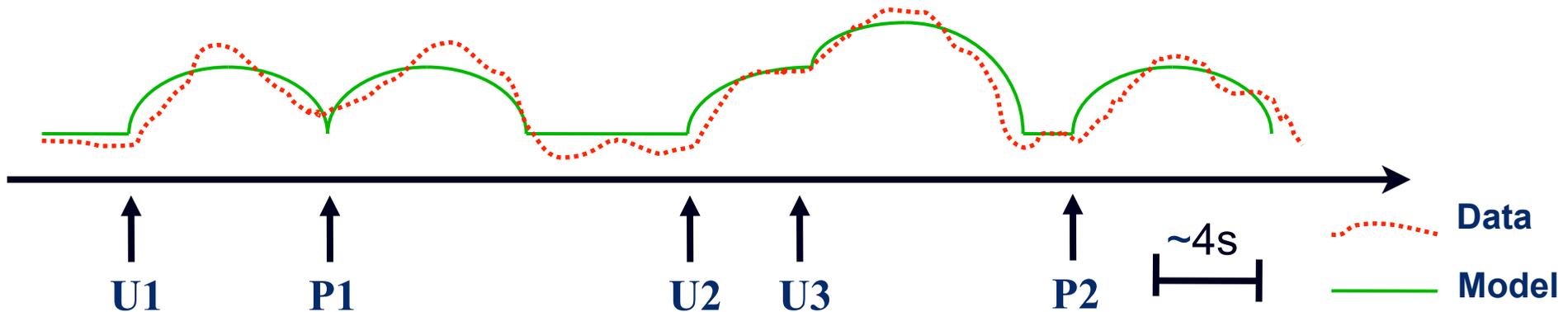
1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”

# Block/epoch designs vs event-related designs

Block/epoch designs examine responses to series of similar stimuli



Event-related designs account for response to each single stimulus

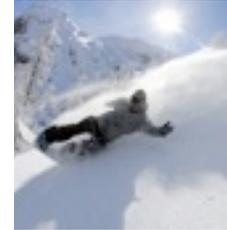


# Advantages of event-related fMRI

1. Randomised trial order

# efMRI: Randomised trial order

Blocked designs may trigger expectations and cognitive sets



Unpleasant (U)

Pleasant (P)

Intermixed designs can minimise this by stimulus randomisation



Pleasant (P)

Unpleasant (U)

Unpleasant (U)

Pleasant (P)

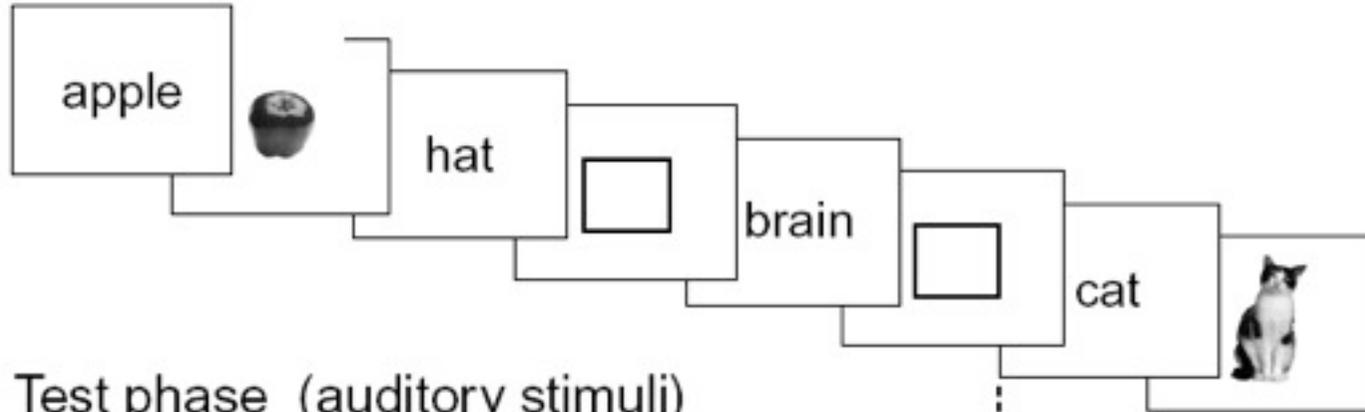
Unpleasant (U)

# Advantages of event-related fMRI

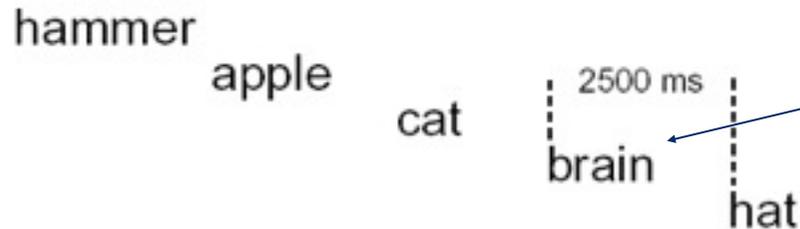
1. Randomised trial order
2. Post-hoc subjective classification of trials

# efMRI: Post-hoc classification of trials

Study phase (visual stimuli)



Test phase (auditory stimuli)



Participant response:  
„was *not* shown as picture“

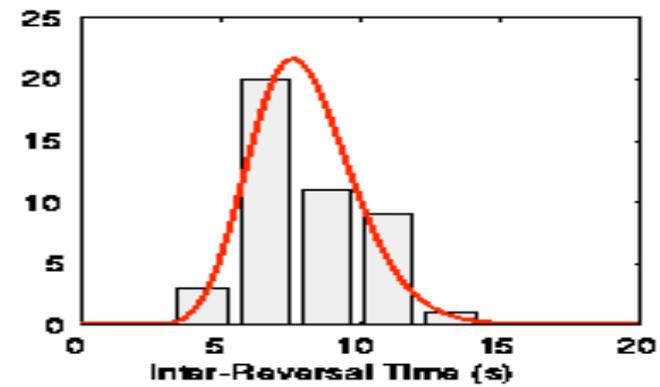
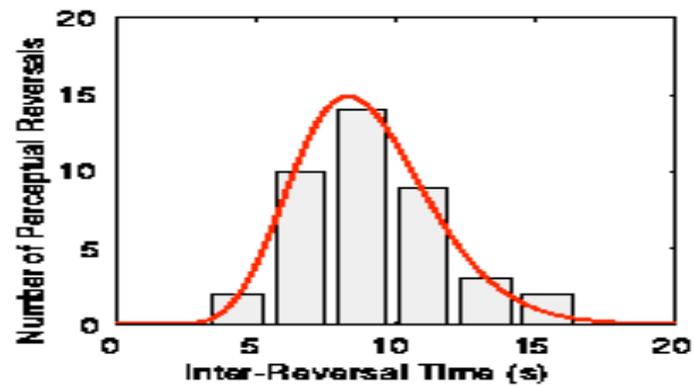
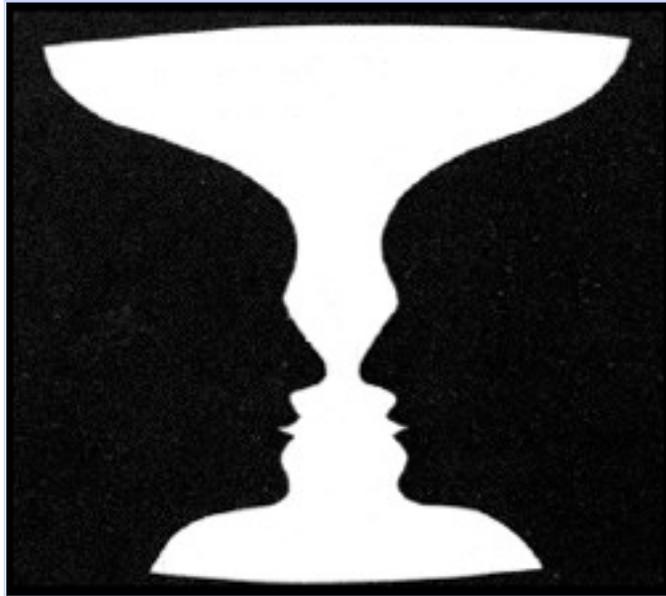
„was shown as picture“

Items with wrong memory of picture („hat“) were associated with more occipital activity *at encoding* than items with correct rejection („brain“)

# Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant

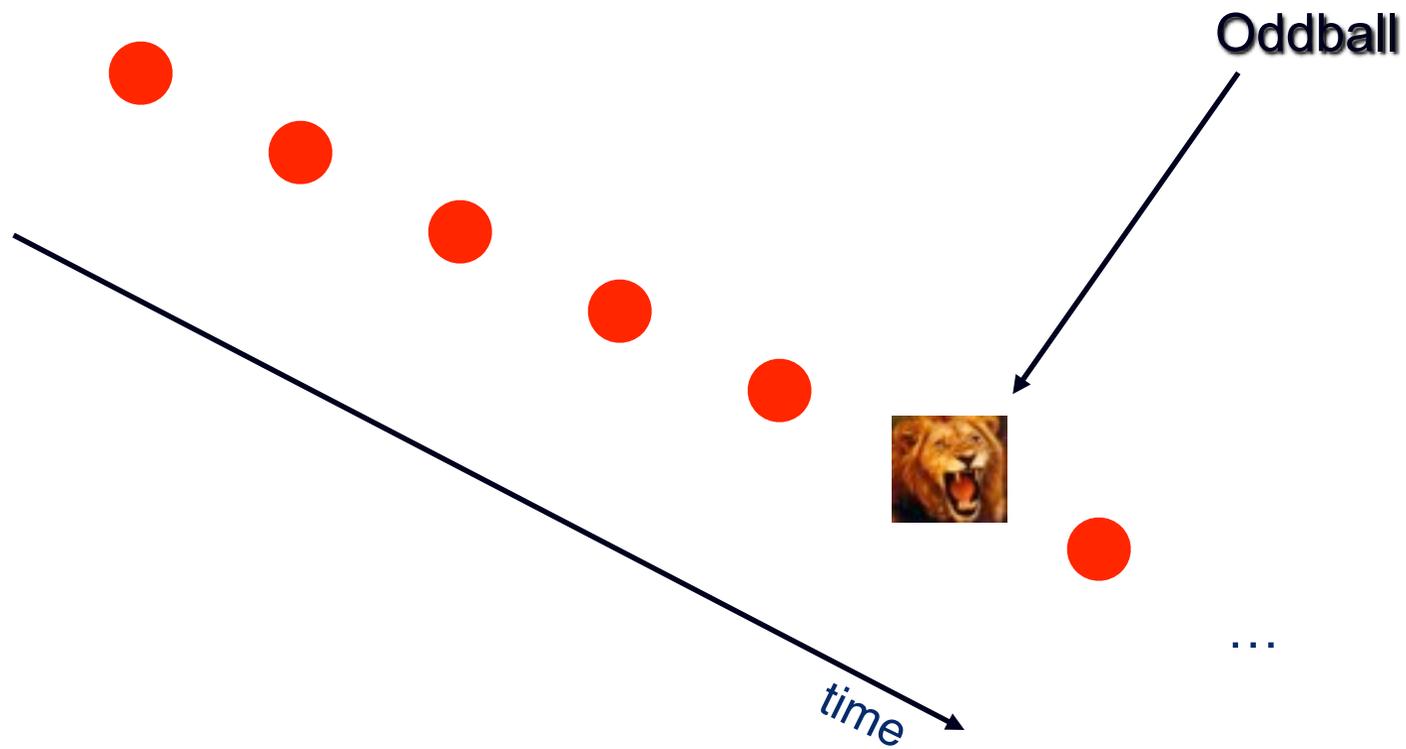
# efMRI: Online event definition



# Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context

# efMRI: Stimulus context

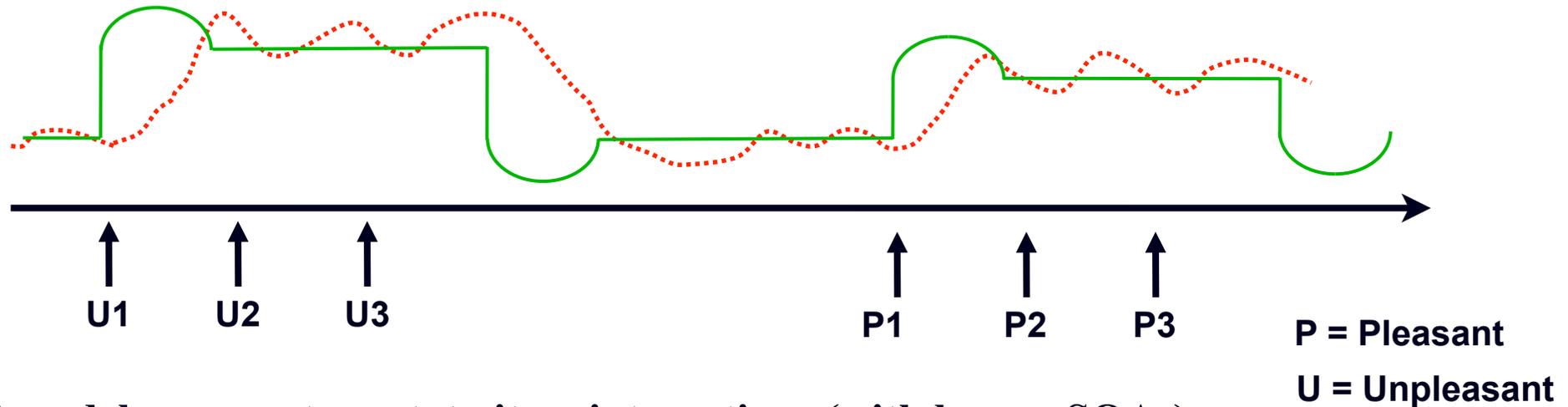


# Advantages of event-related fMRI

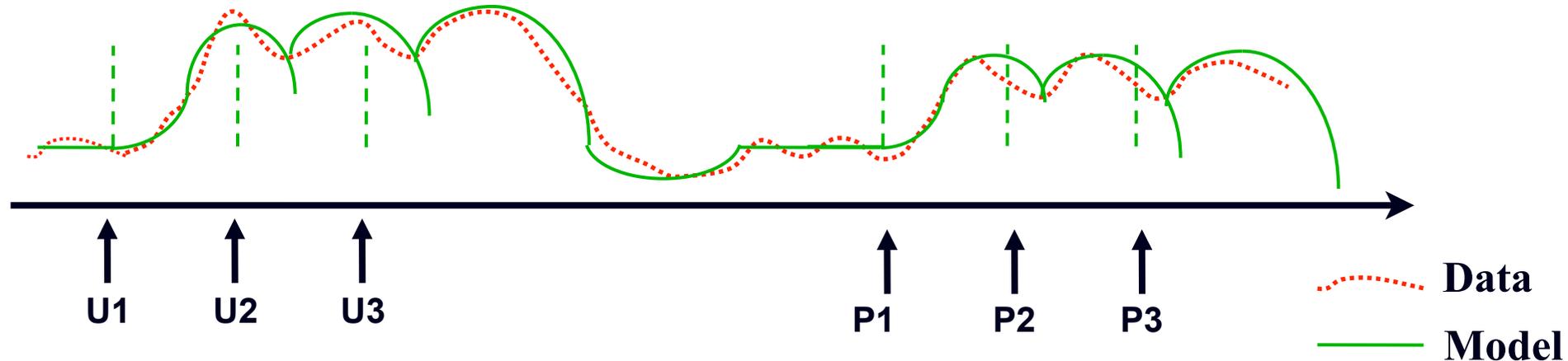
1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context
5. More accurate model even for epoch/block designs?

# “Event” model of block design

“Epoch” model assumes constant neural processes throughout block

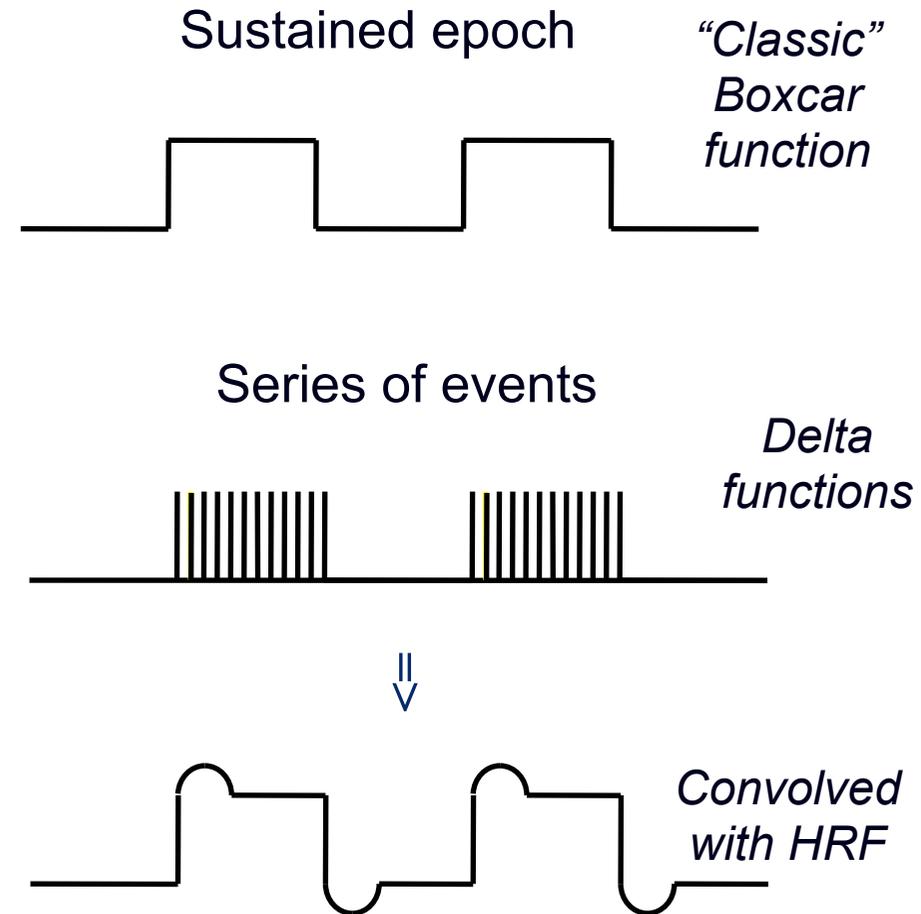


“Event” model may capture state-item interactions (with longer SOAs)



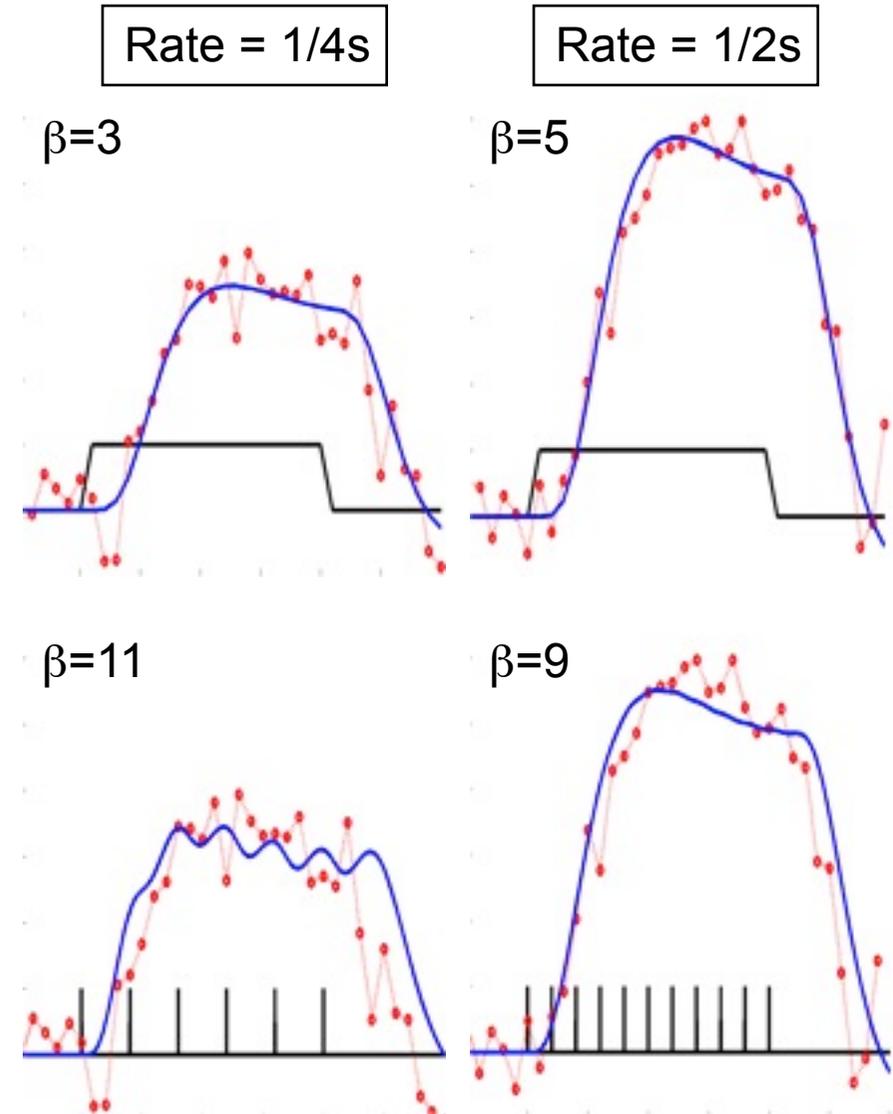
# Modeling block designs: Epochs vs events

- Designs can be blocked or intermixed, BUT models for blocked designs can be epoch- or event-related
- Epochs are periods of sustained stimulation (e.g, box-car functions); Events are impulses (delta-functions)
- Near-identical regressors can be created by 1) sustained epochs, 2) rapid series of events (SOAs <  $\sim 3$ s)
- In SPM12, all conditions are specified in terms of their 1) onsets and 2) durations
  - ... epochs: variable or constant duration
  - ... events: zero duration



# Modeling block designs: Epochs vs events

- Blocks of trials can be modeled as boxcars or runs of events
- BUT: interpretation of the parameter estimates may differ
- Consider an experiment presenting words at different rates in different blocks:
  - An “epoch” model will estimate parameter that increases with rate, because the parameter reflects response per block
  - An “event” model may estimate parameter that decreases with rate, because the parameter reflects response per word

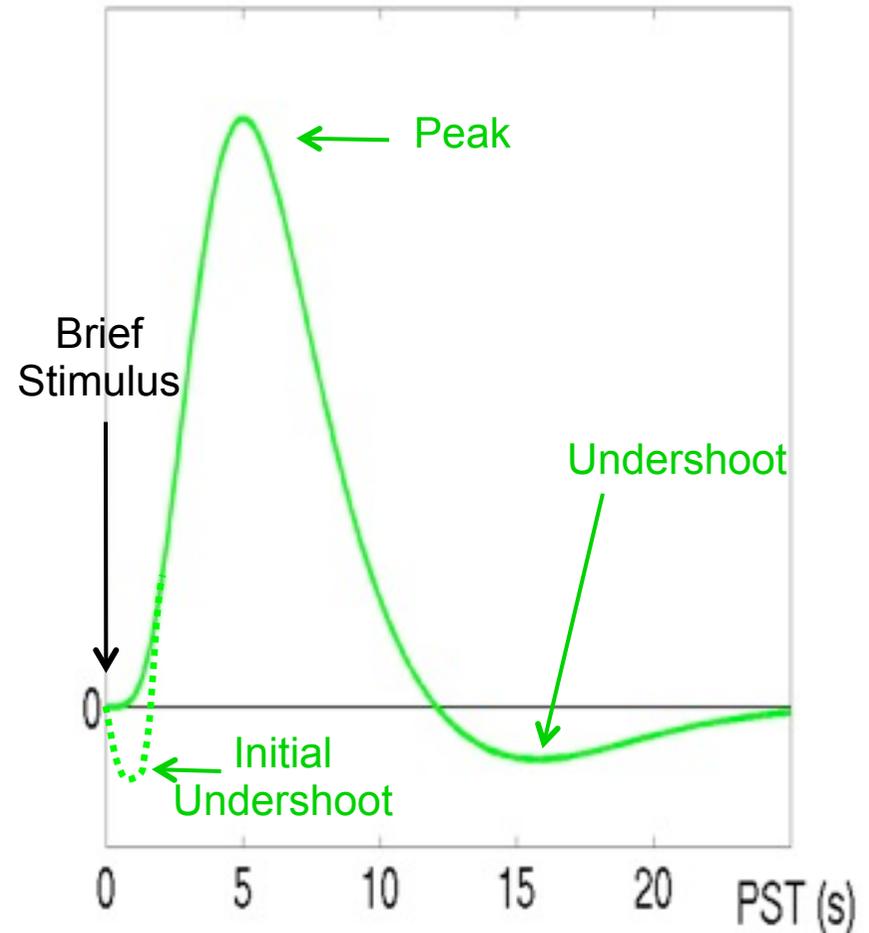


# Disadvantages of intermixed designs

1. Less efficient for detecting effects than blocked designs
2. Some psychological processes have to/may be better blocked (e.g., if difficult to switch between states, or to reduce surprise effects)

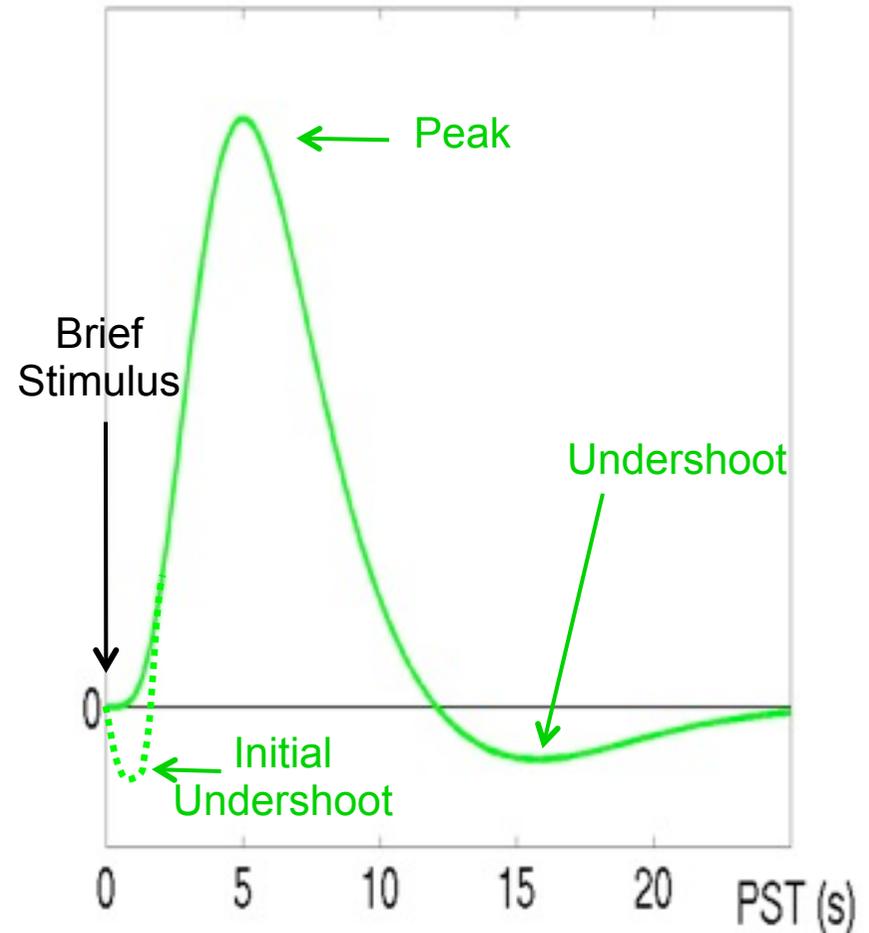
# BOLD impulse response

- Function of blood oxygenation, flow, volume
- Peak (max. oxygenation) 4-6s poststimulus; baseline after 20-30s
- Initial undershoot can be observed
- Similar across V1, A1, S1...
- ... but possible differences across:
  - other regions
  - individuals



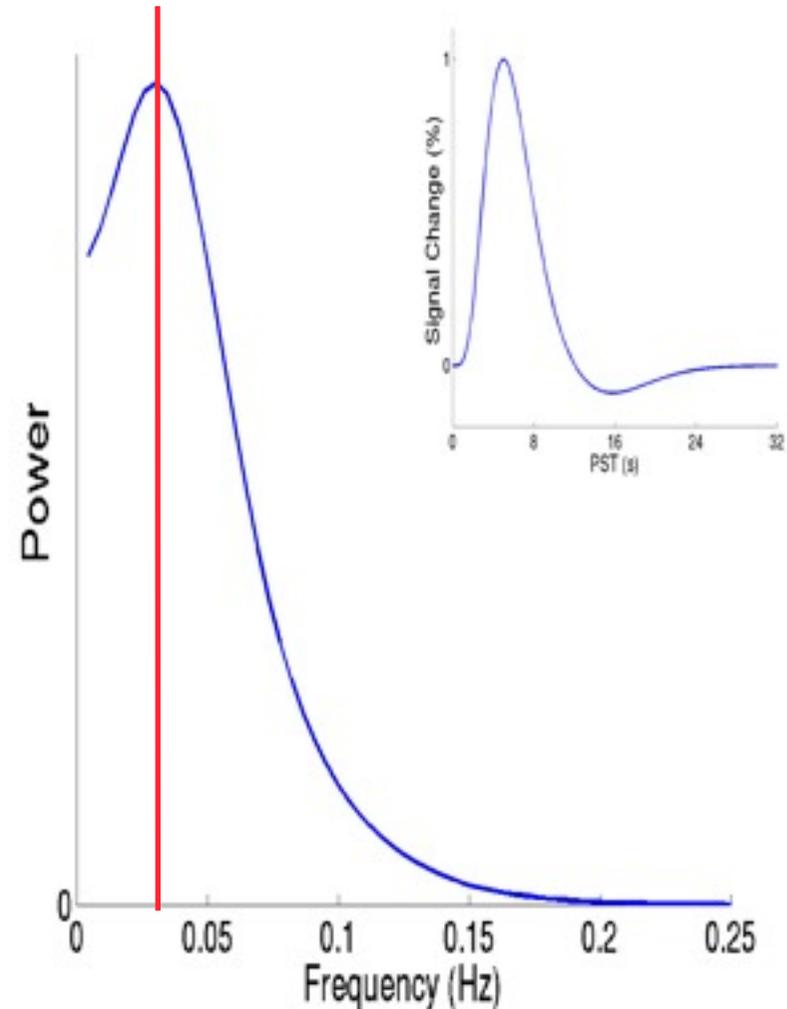
# BOLD impulse response

- Early event-related fMRI studies used a long Stimulus Onset Asynchrony (SOA) to allow BOLD response to return to baseline
- However, overlap between successive responses at short SOAs can be accommodated if the BOLD response is explicitly modeled, particularly if responses are assumed to superpose linearly
- Short SOAs are more sensitive; see later



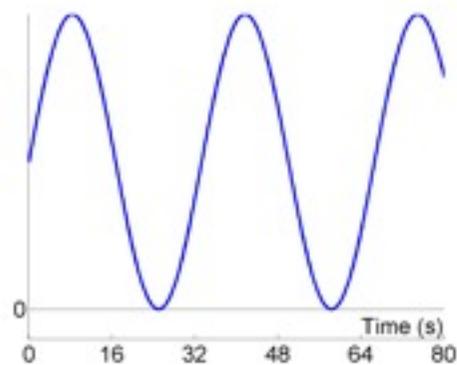
# Design efficiency

- HRF can be viewed as a filter (Josephs & Henson, 1999)
  - We want to maximise the signal passed by this filter
  - Dominant frequency of canonical HRF is  $\sim 0.04$  Hz
- ➔ The most efficient design is a sinusoidal modulation of neural activity with period  $\sim 24$ s (e.g., boxcar with 12s on/ 12s off)

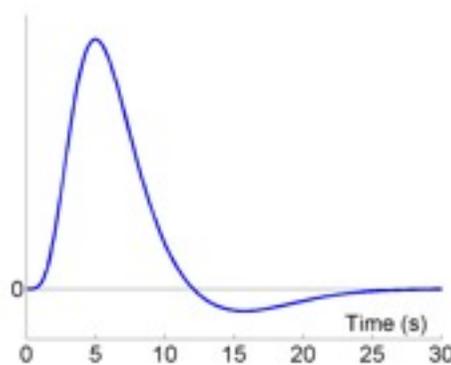


# Sinusoidal modulation, $f = 1/33$

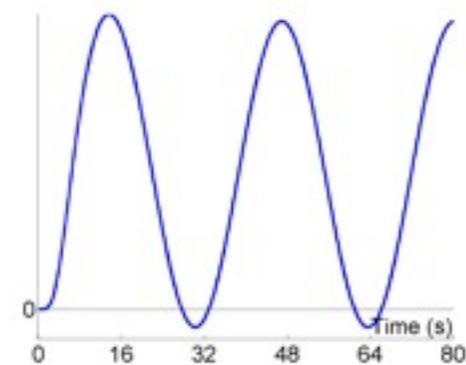
Stimulus ("Neural")



HRF

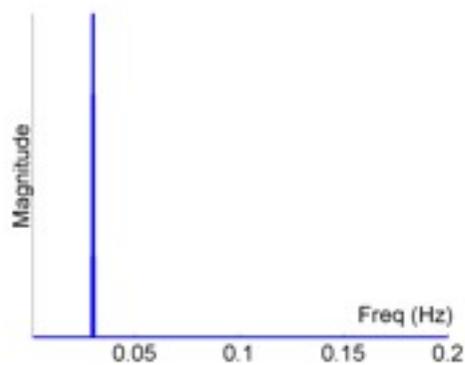


Predicted Data



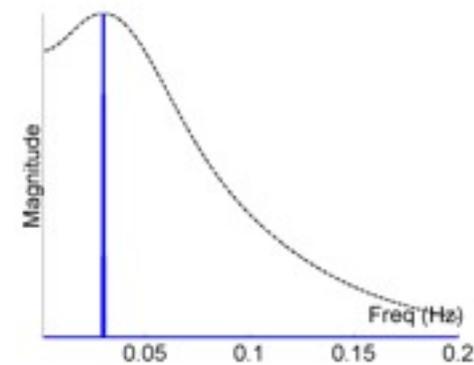
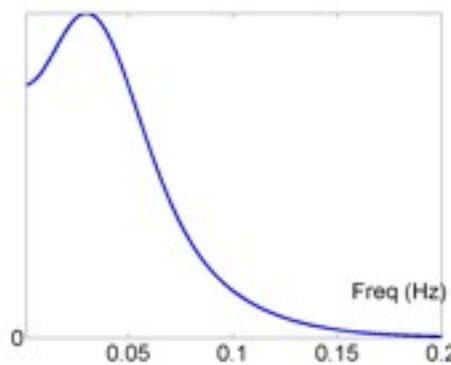
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$\times$

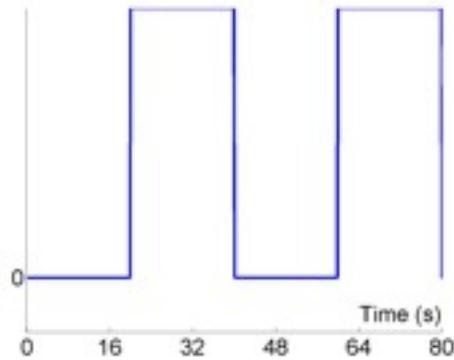
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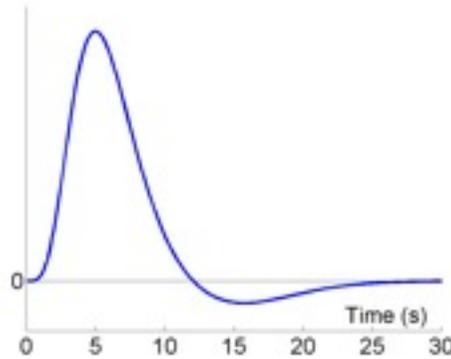
A very "efficient" design!

# Blocked, epoch = 20 sec

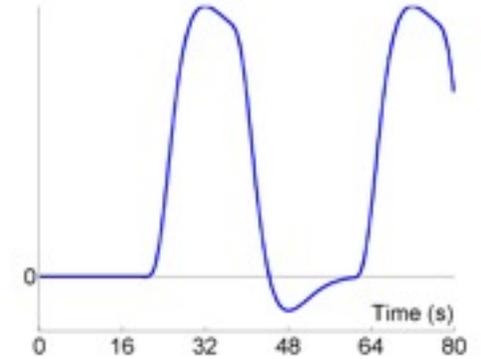
Stimulus ("Neural")



HRF

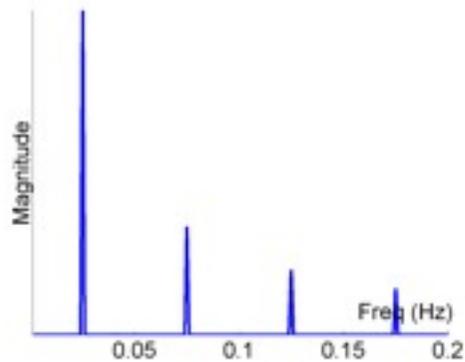


Predicted Data



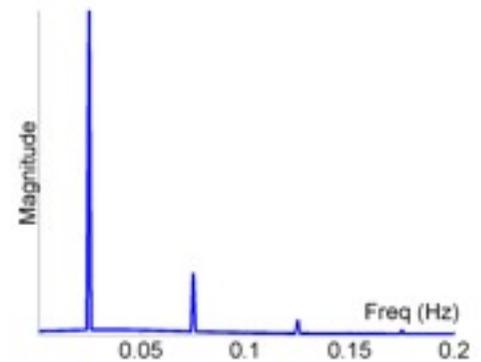
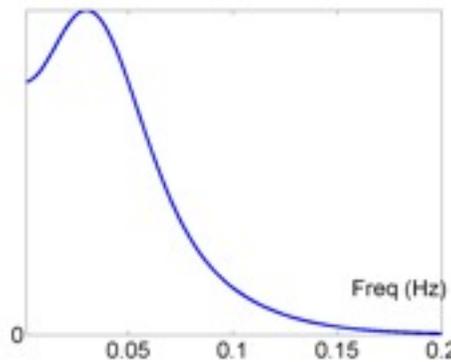
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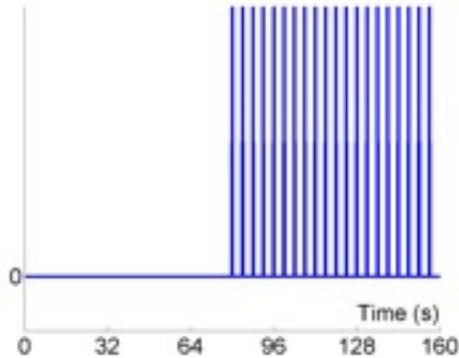
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Blocked-epoch (with small SOA) quite "efficient"

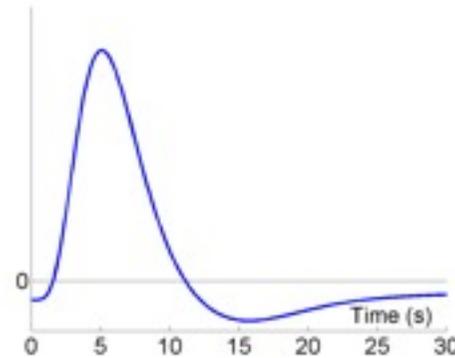
# Blocked (80s), SOAmin=4s, highpass filter = 1/120s

Stimulus ("Neural")



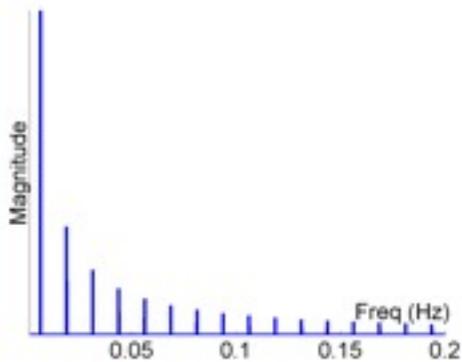
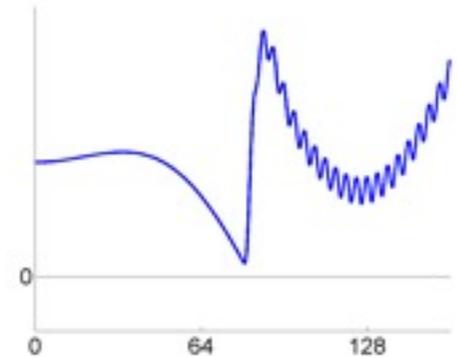
⊗

HRF

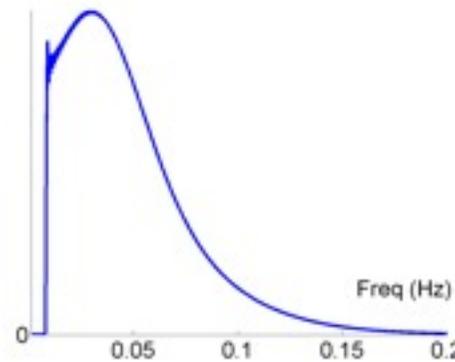


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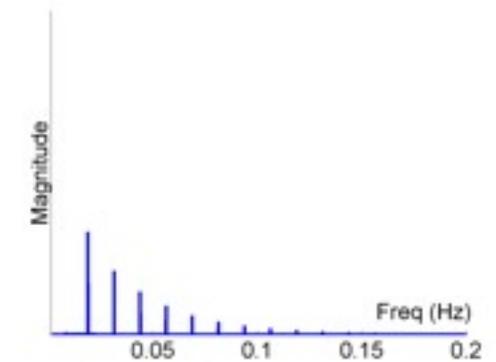
Predicted Data



×



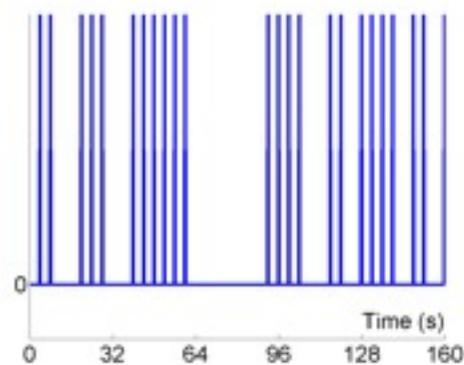
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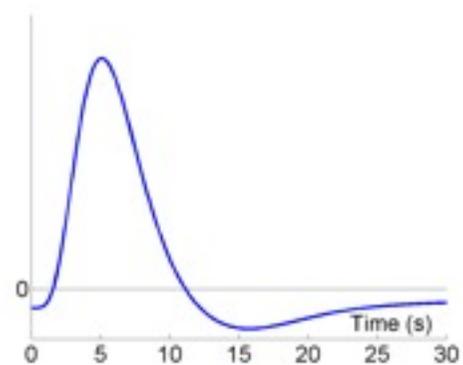
Very ineffective: Don't have long (>60s) blocks!

# Randomised, SOAmin=4s, highpass filter = 1/120s

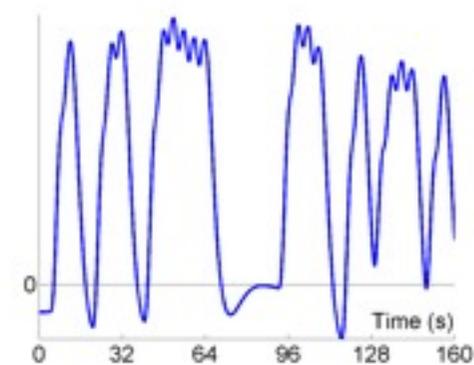
Stimulus ("Neural")



HRF

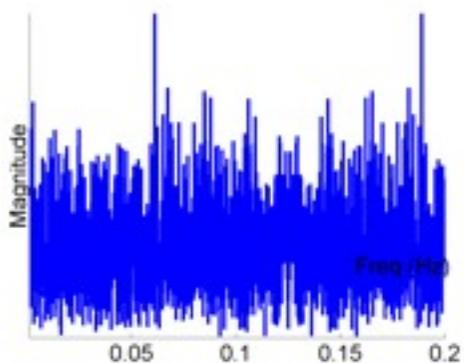


Predicted Data



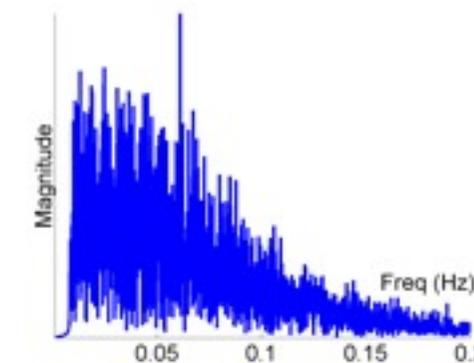
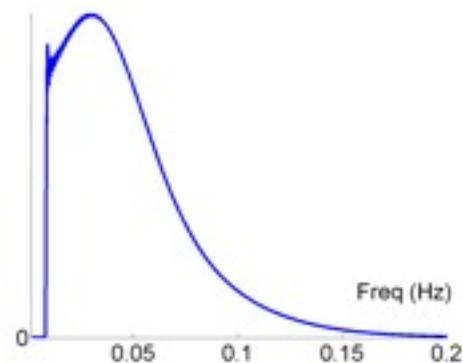
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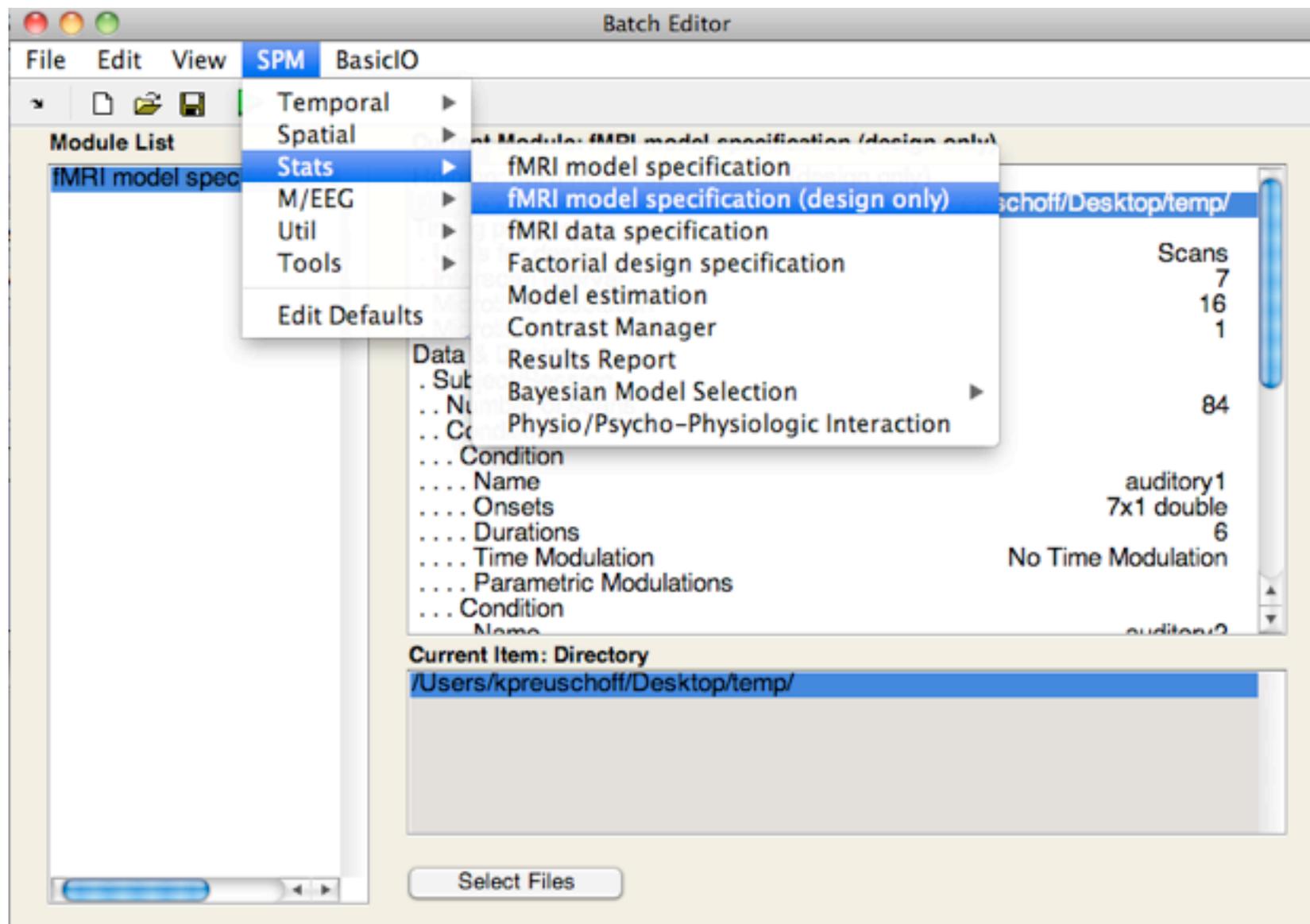
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Randomised design spreads power over frequencies

# Checking your design efficiency



# Overview

- 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

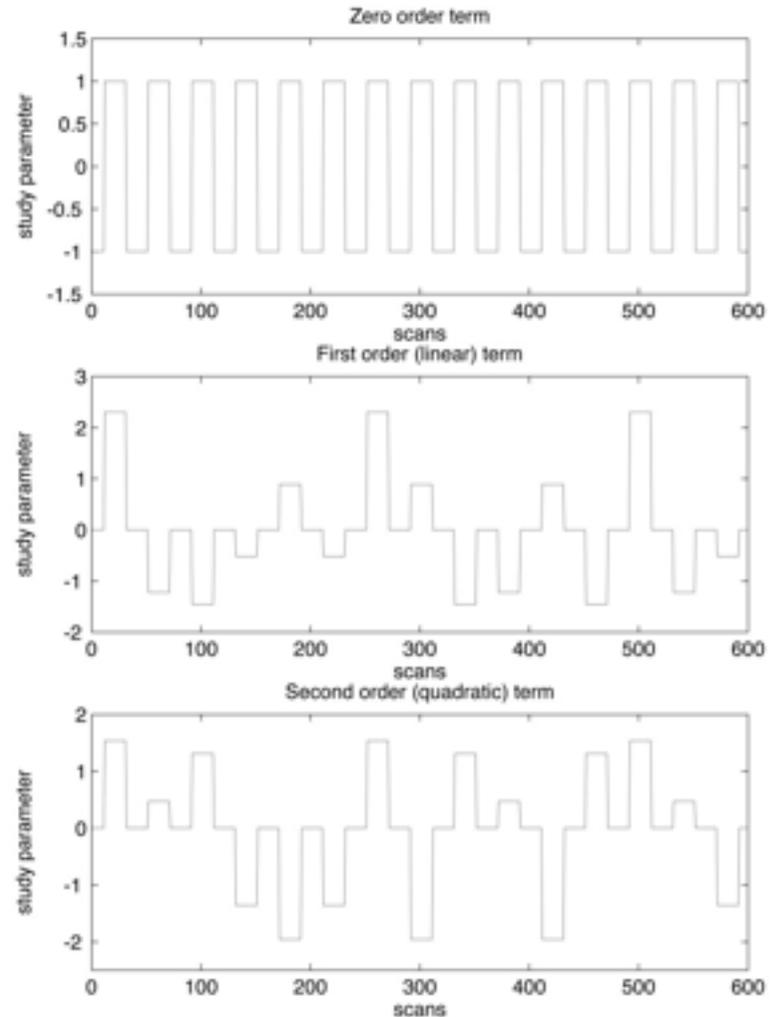
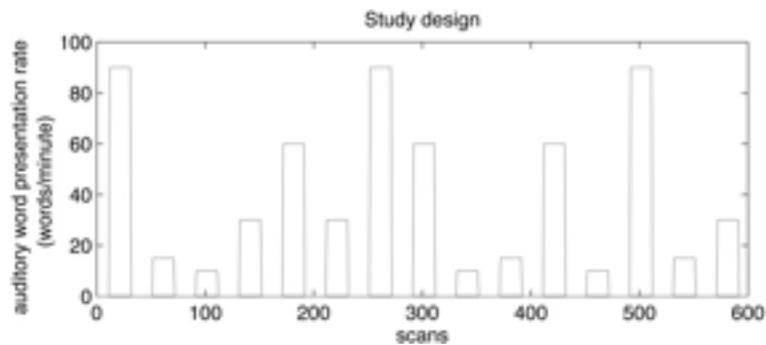
    - Psychophysiological Interactions

# 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)

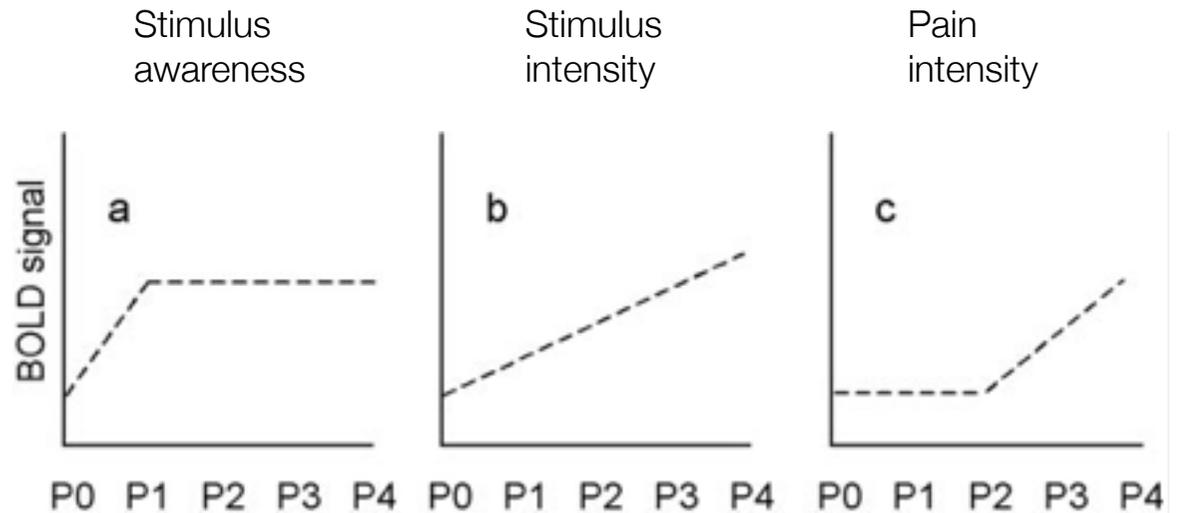
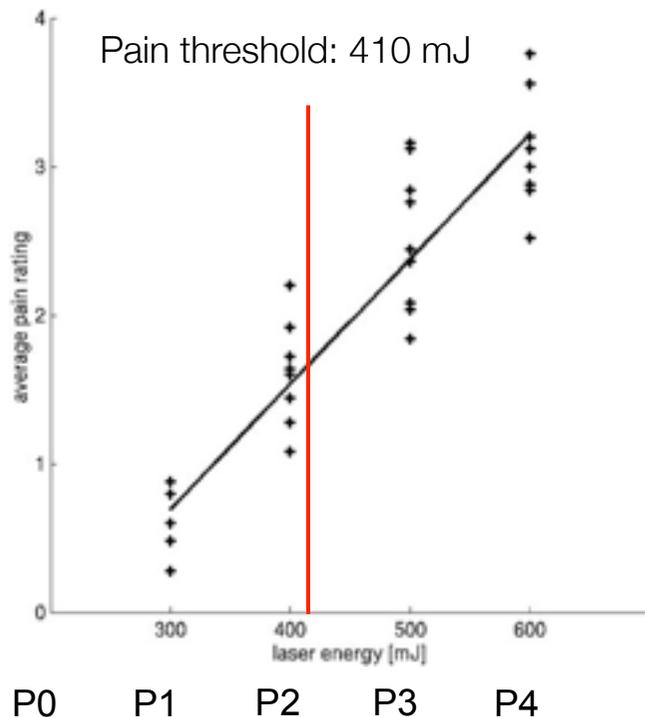
# “User-specified” parametric modulation of regressors

Polynomial expansion  
&  
orthogonalisation



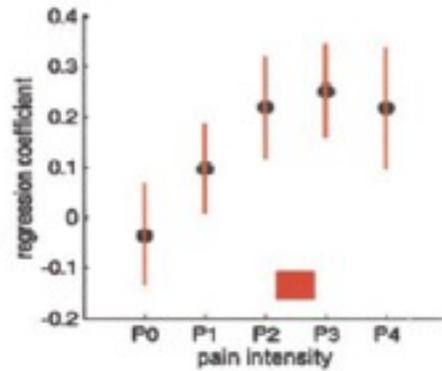
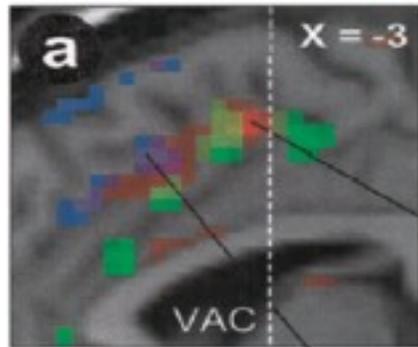
# Investigating neurometric functions

(= relation between a stimulus property and the neuronal response)

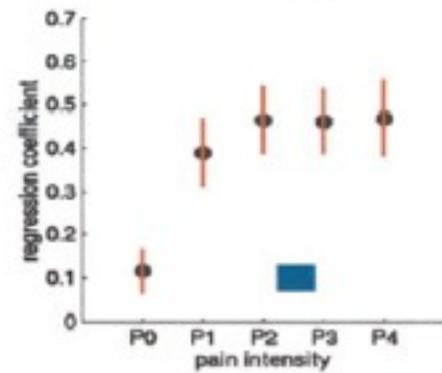
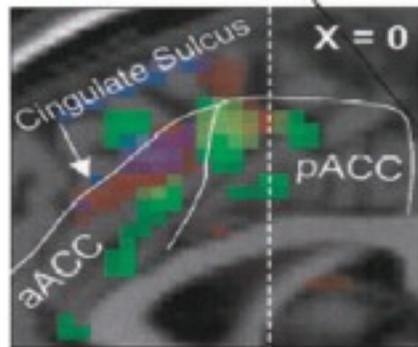
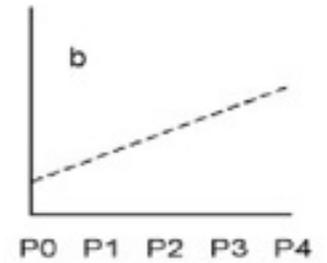


P0-P4: Variation of intensity of a laser stimulus applied to the right hand (0, 300, 400, 500, and 600 mJ)

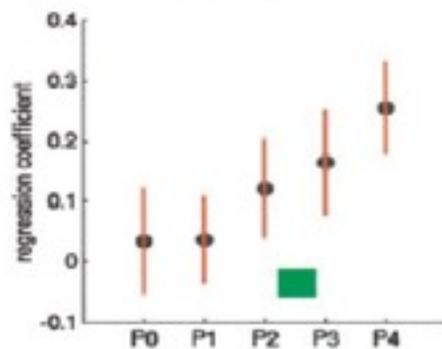
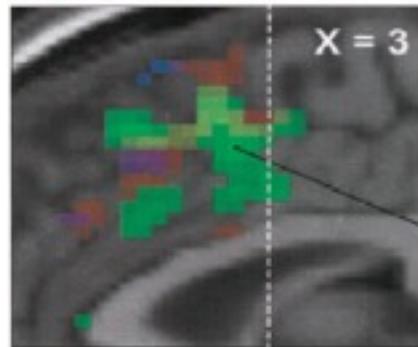
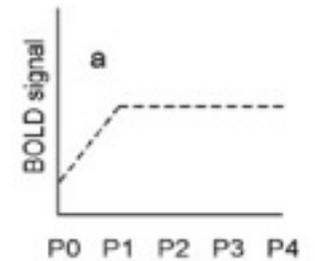
# Neurometric functions



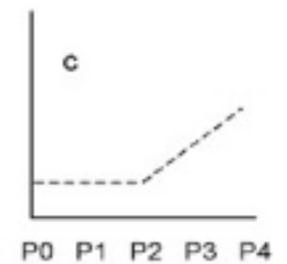
→ Stimulus intensity



→ Stimulus presence



→ Pain intensity



# Model-based regressors

- General idea:  
generate predictions from a computational model, e.g. of learning or decision-making
- Use these predictions to define regressors
- Include these regressors in a GLM and test for significant correlations with voxel-wise BOLD responses

# Summary I

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Thank you