Experimental design of fMRI studies

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SPM Course Lausanne
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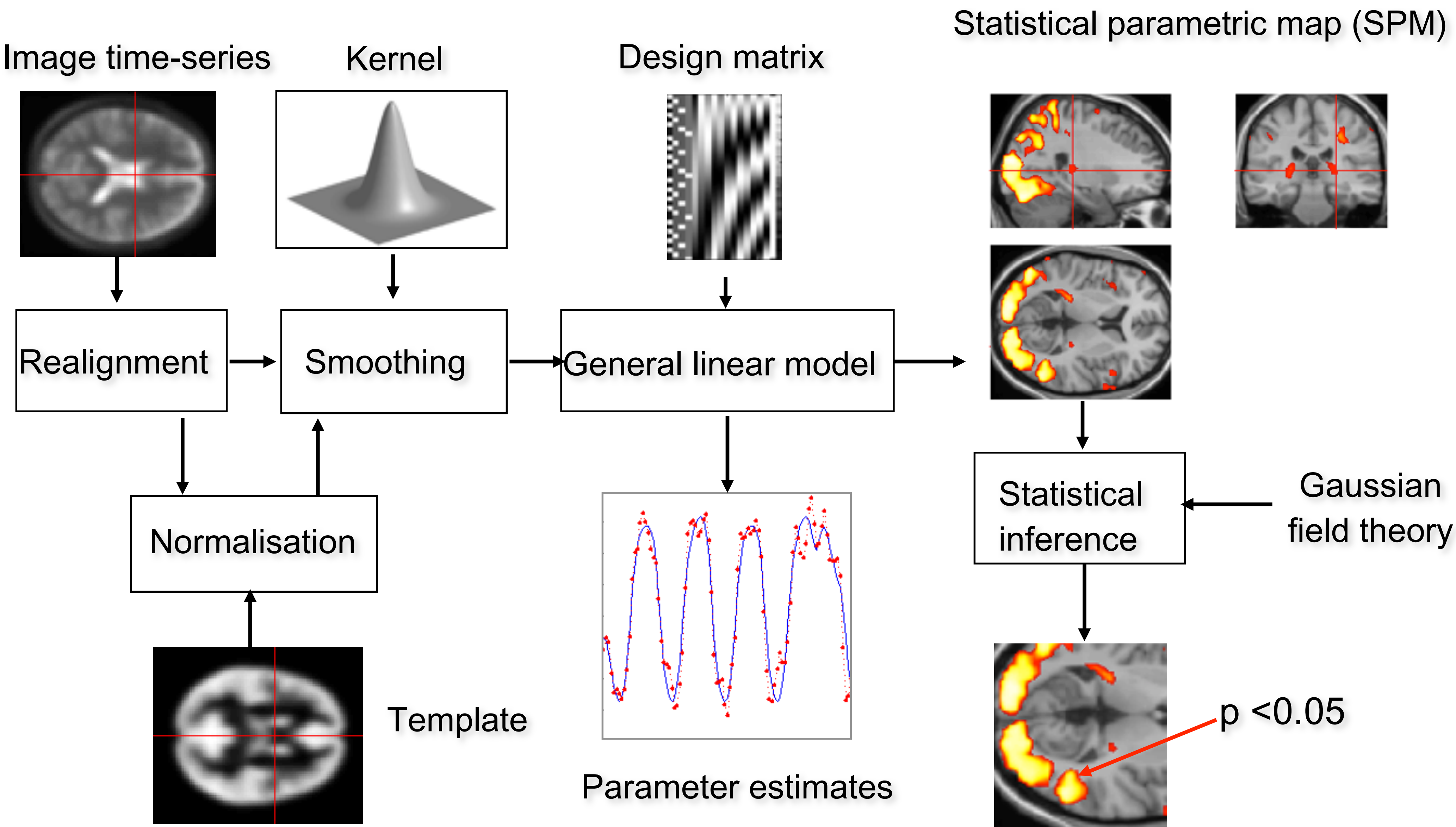
Essential reading

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

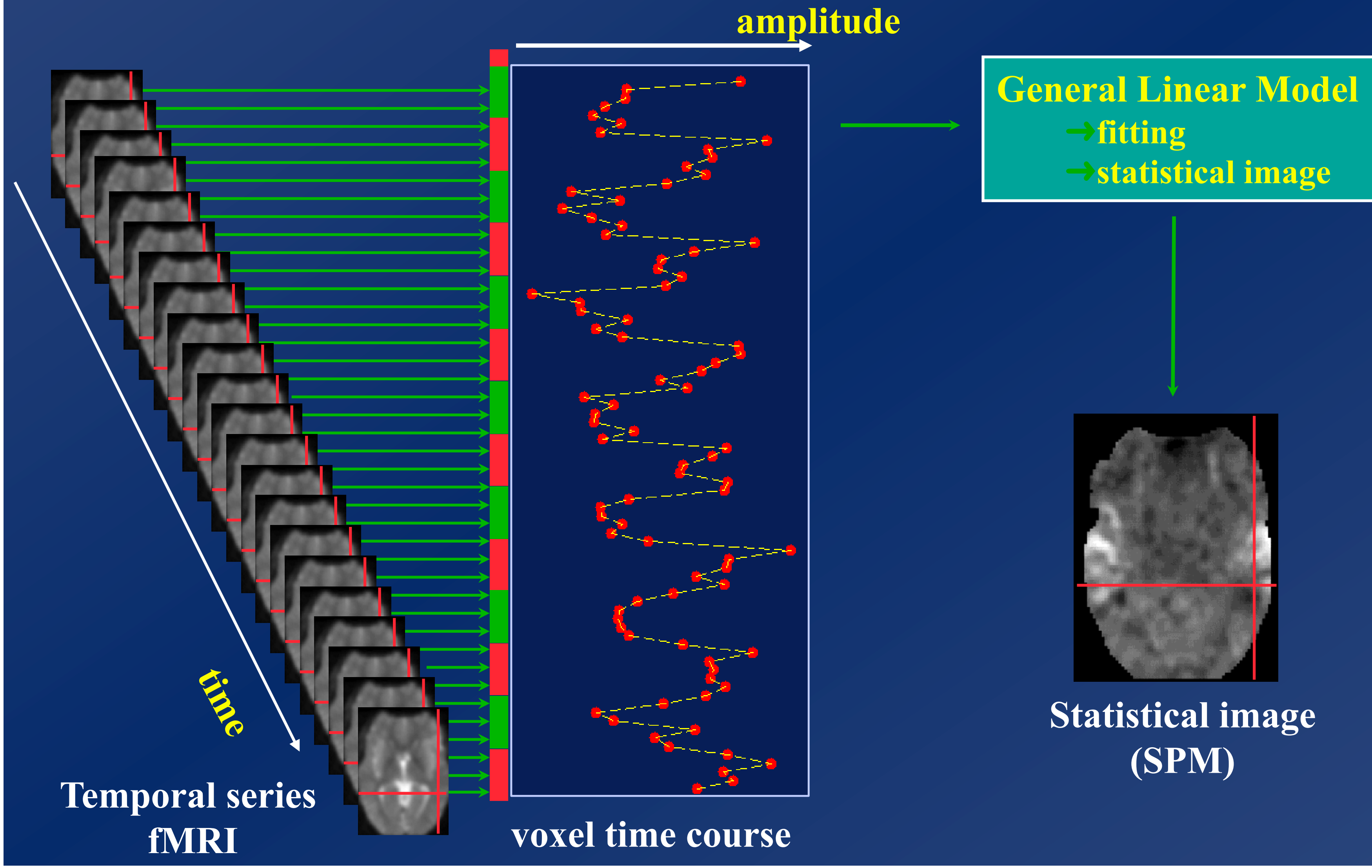
This book chapter covers the most common experimental designs along with how to efficiently design your experiments such that you maximize your chances of obtaining significant results.

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

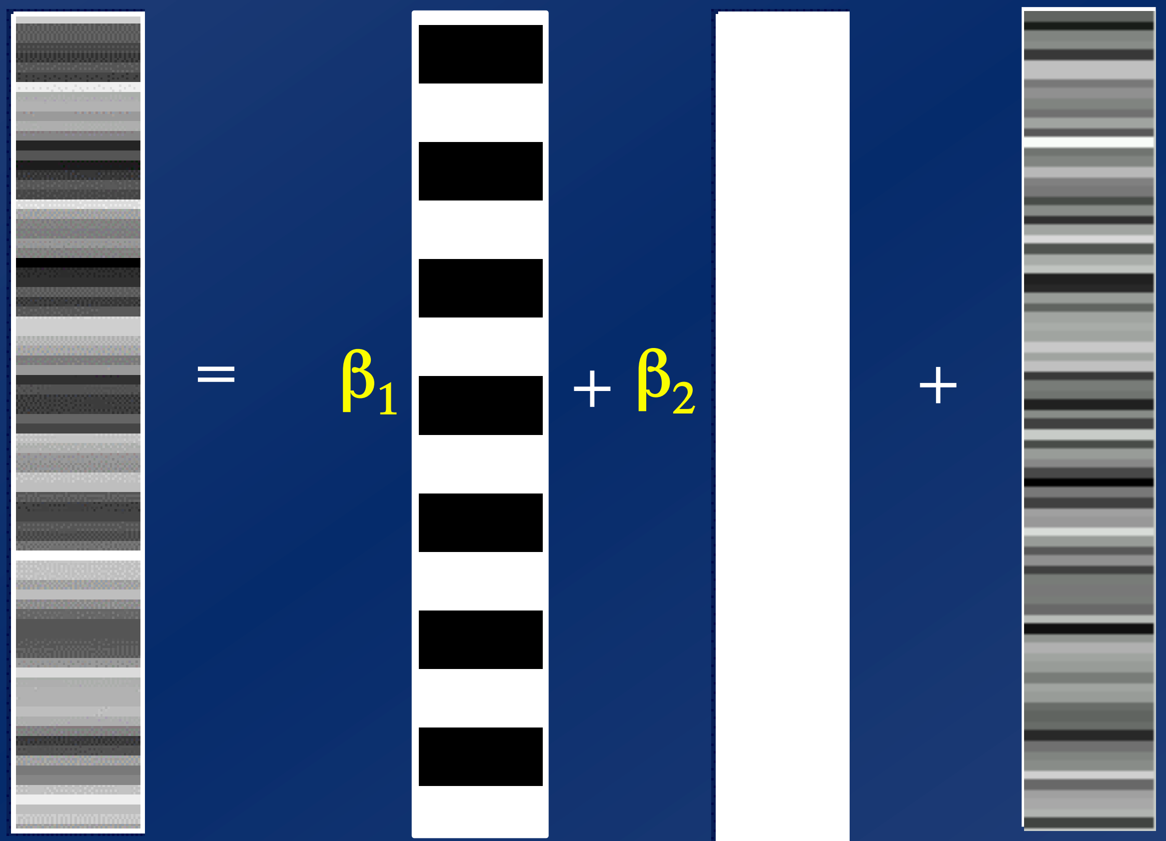
Overview of SPM



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

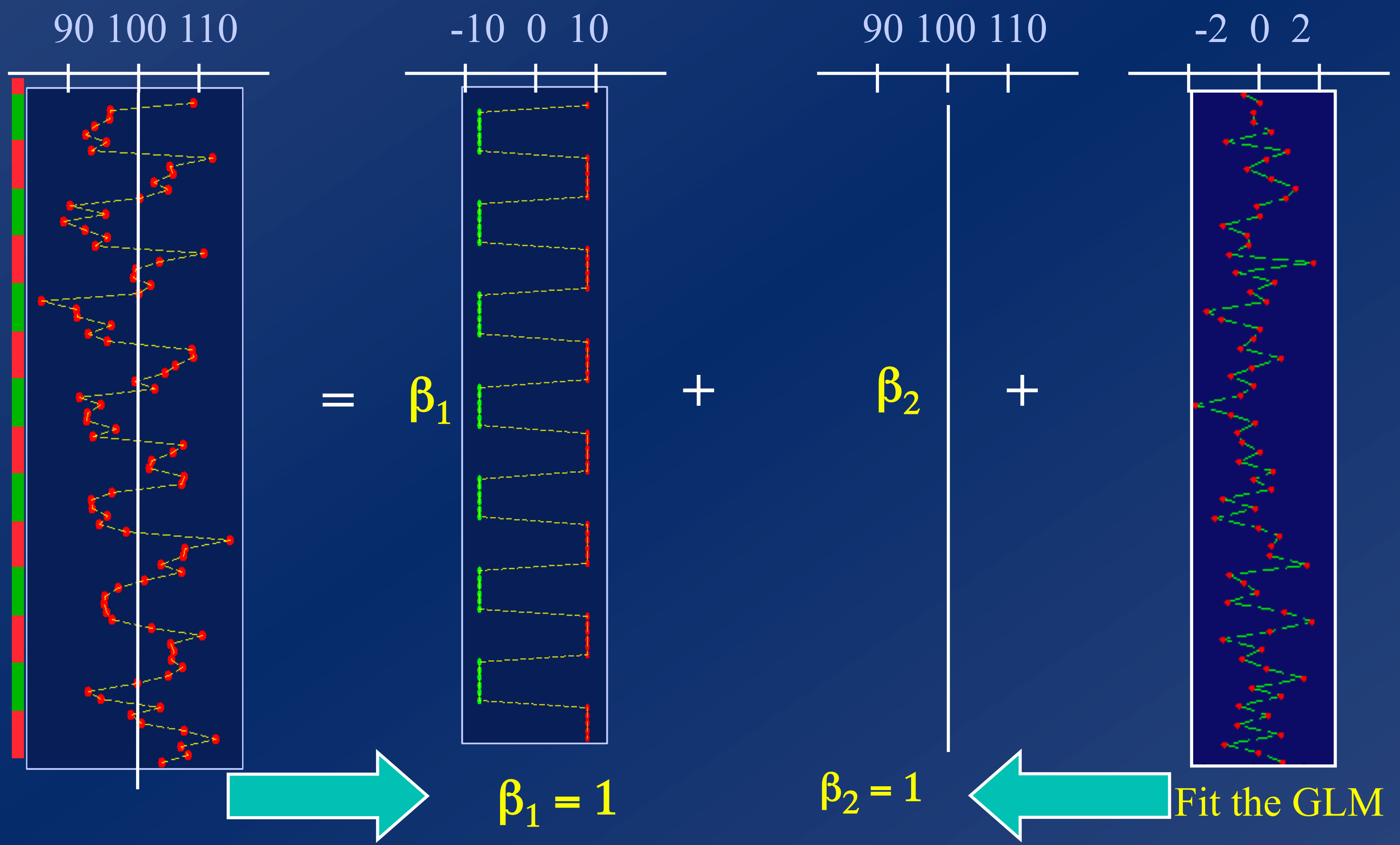


…revisited : matrix form



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

Regression example…



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

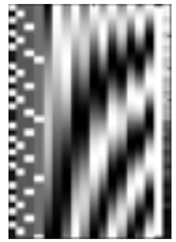
Overview of SPM

Research question:
Which neuronal structures support face recognition?

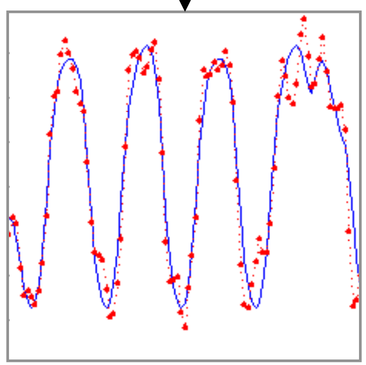
Hypothesis:
The fusiform gyrus is implicated in face recognition

Experimental design

Design matrix

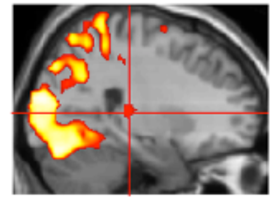


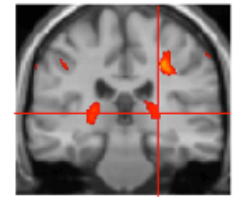
General linear model

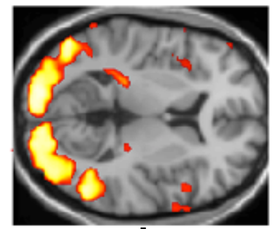


Parameter estimates

Statistical parametric map (SPM)

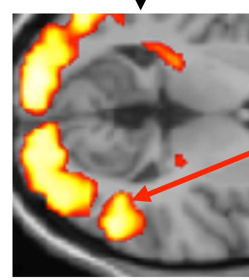






Statistical inference

Gaussian field theory



$p < 0.05$

Overview

- Categorical designs

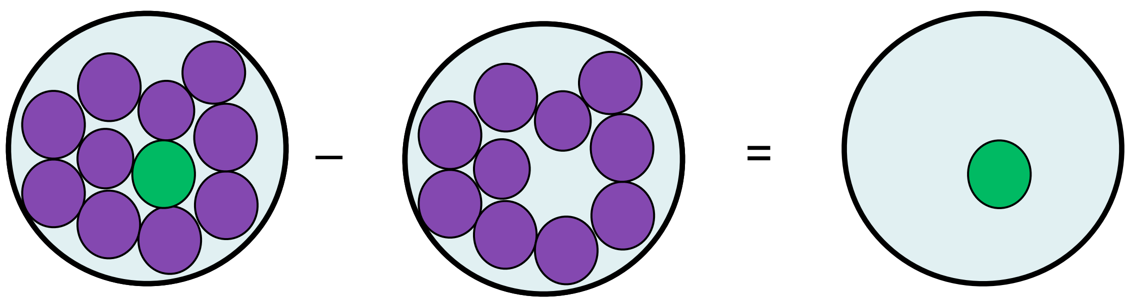
Subtraction	- Pure insertion, evoked / differential responses
Conjunction	- Testing multiple hypotheses

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



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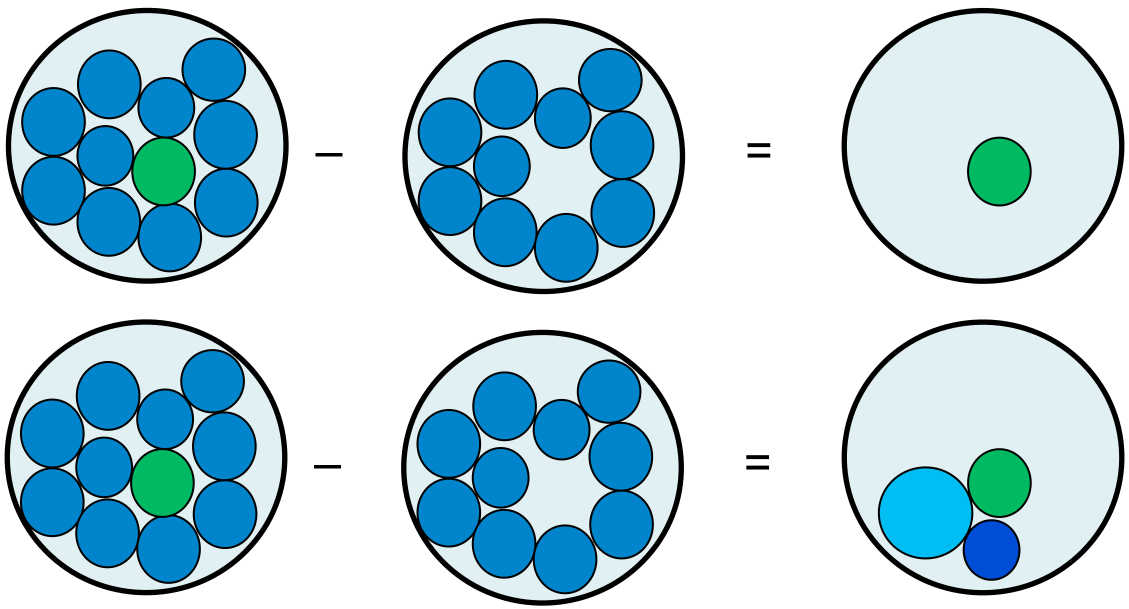
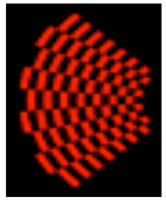


Cognitive subtraction: Baseline problems

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)?

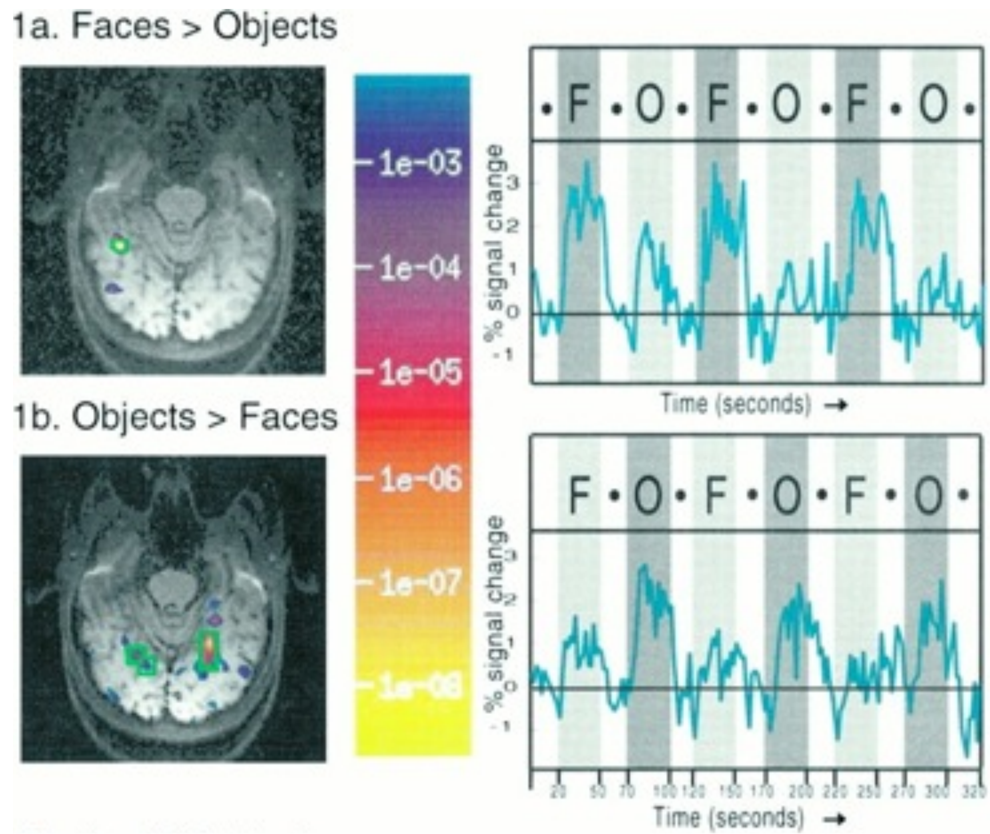
A categorical analysis

Experimental design

Face viewing F
Object viewing O

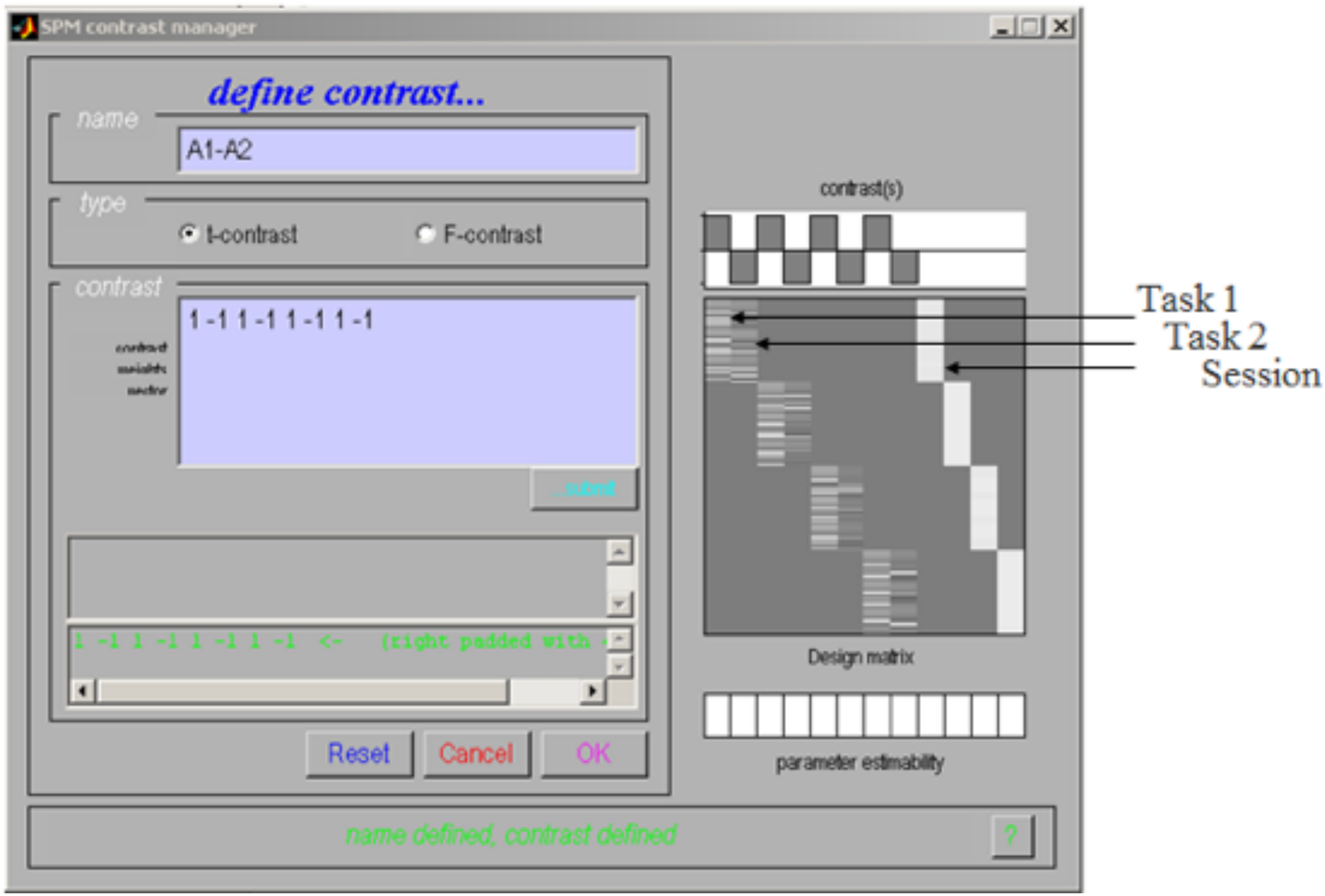
F - O = Face recognition
O - F = Object recognition

…under assumption of pure insertion



Kanwisher N et al. J. Neurosci. 1997;

Categorical design



Overview

- Categorical designs

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

- Parametric designs

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

- Factorial designs

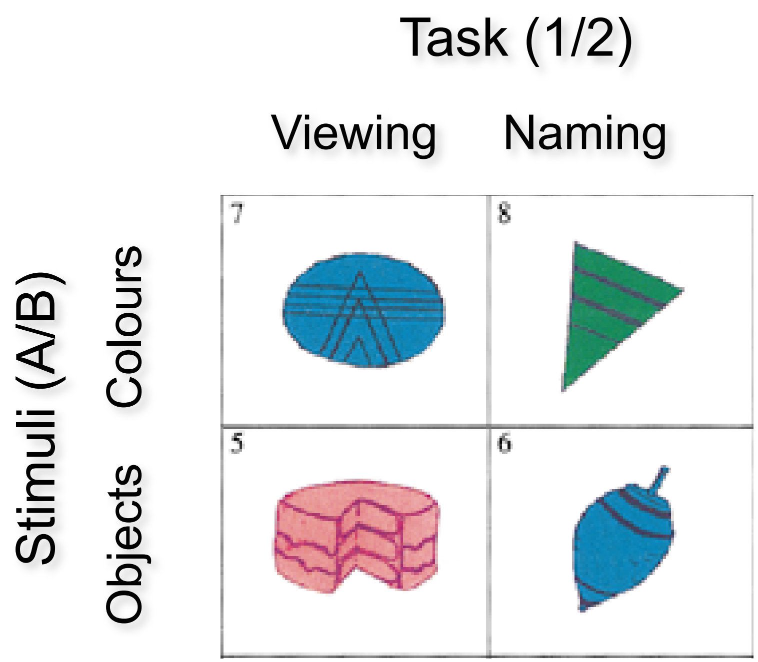
Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological Interactions

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)?



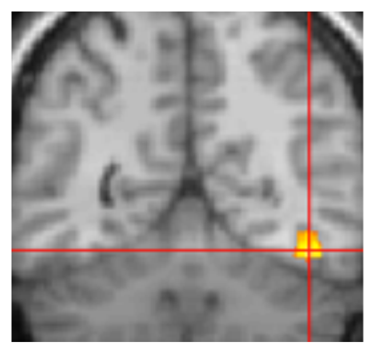
Stimuli (A/B)	Task (1/2)	Viewing	Naming
	Colours	A1 Visual Processing V	A2 Visual Processing V Phonological Retrieval P
	Objects	B1 Visual Processing V Object Recognition R	B2 Visual Processing V Phonological Retrieval P Object Recognition R

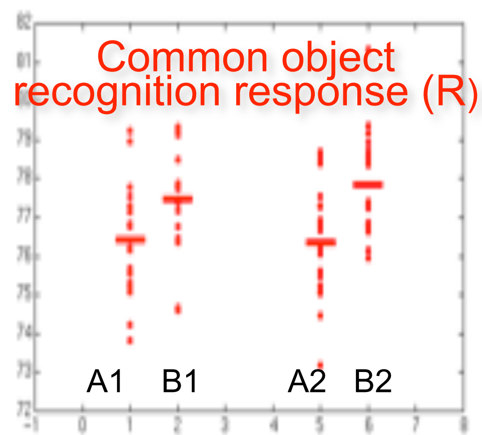
Which neural structures support object recognition?

(Object - Colour viewing) [B1 - A1]
&
(Object - Colour naming) [B2 – A2]

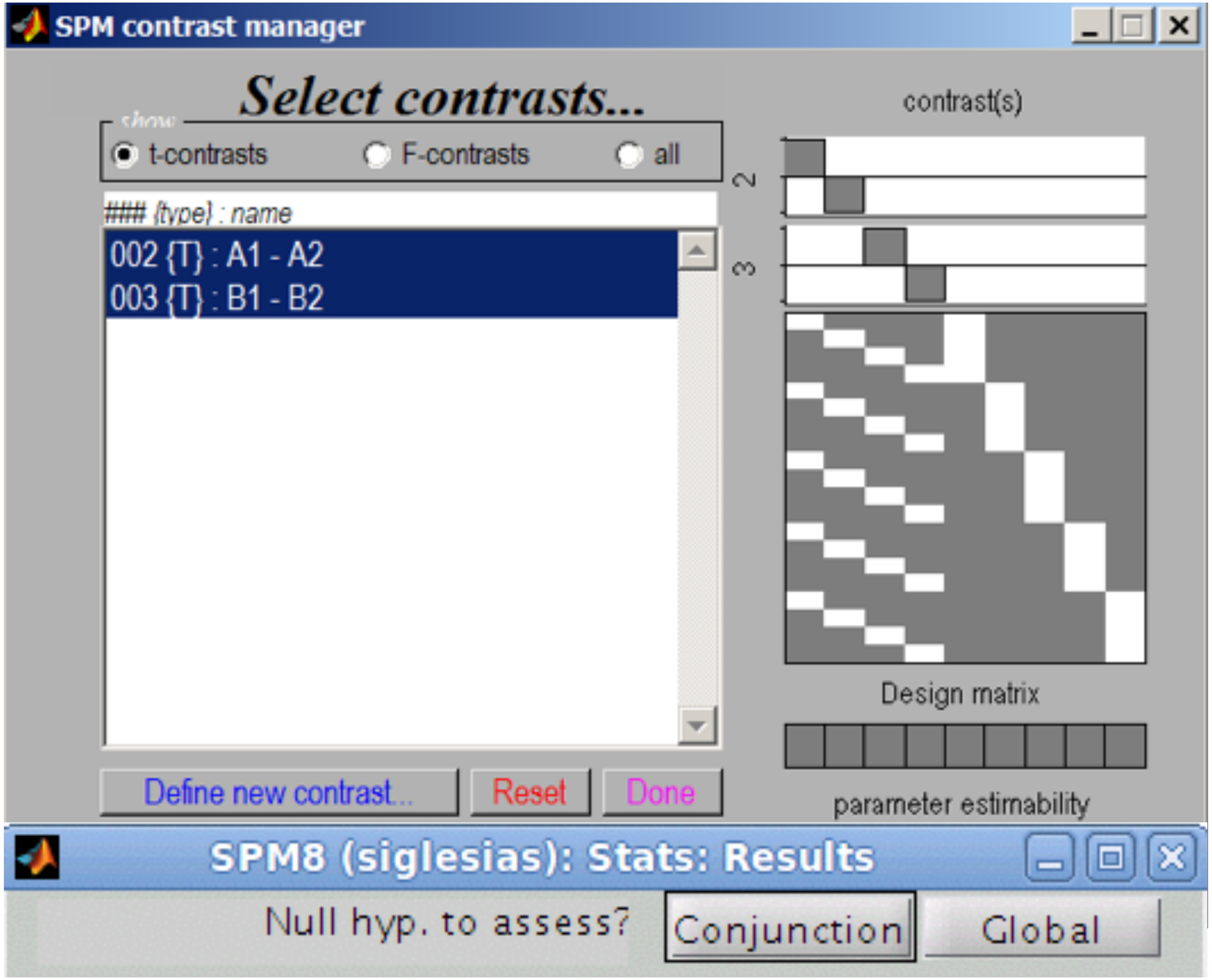
[V,R - V] & [P,V,R - P,V] = R & R = R

Price et al. 1997



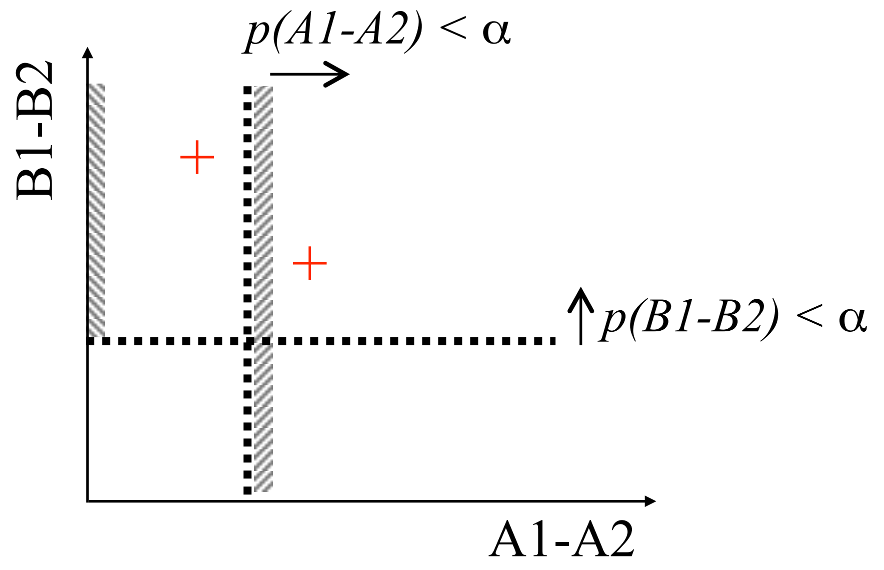


Conjunctions



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.

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- Factorial designs

Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
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Main effects and interactions

Stimuli (A/B)	Task (1/2)	Viewing	Naming
	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

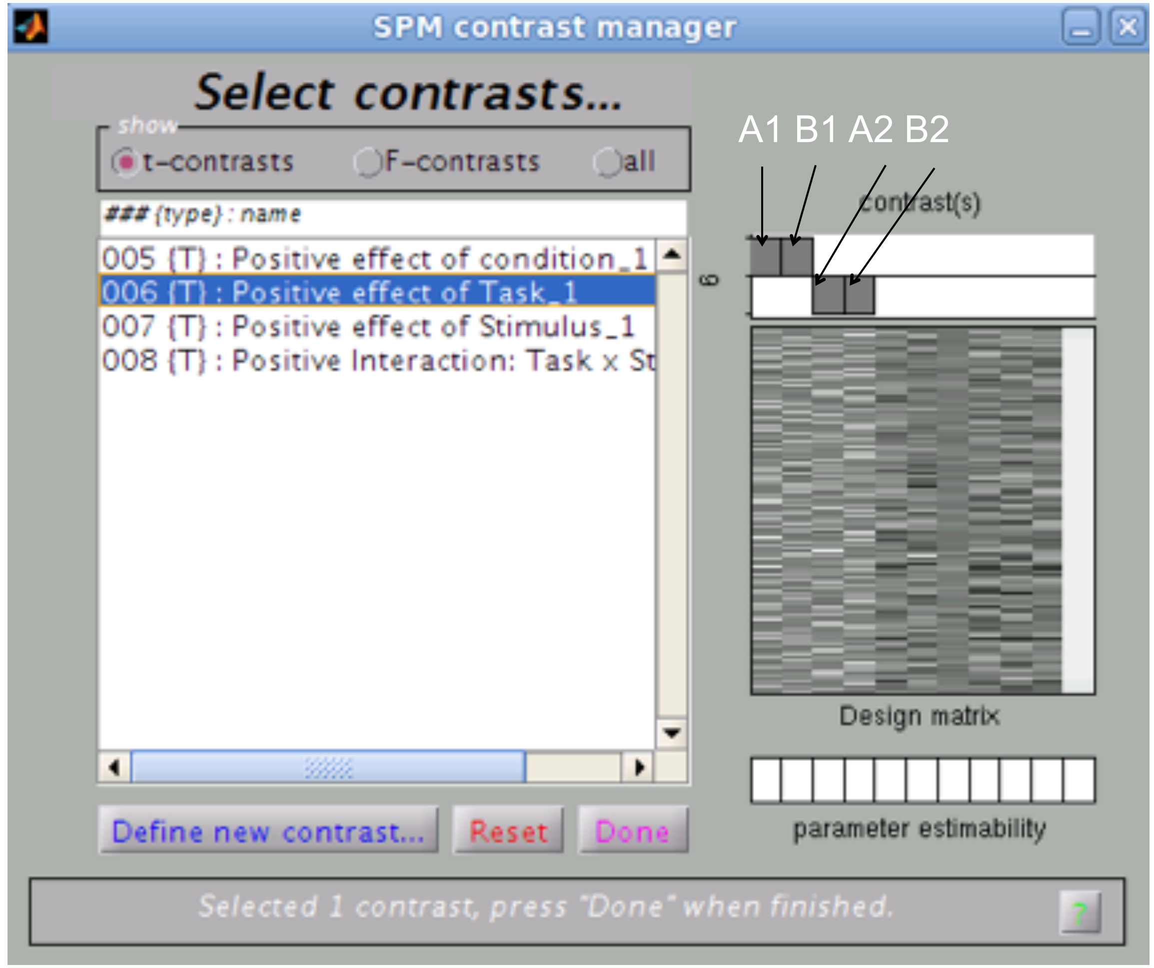
$$(A1 - B1) - (A2 - B2)$$

Factorial design

Task (1/2)

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

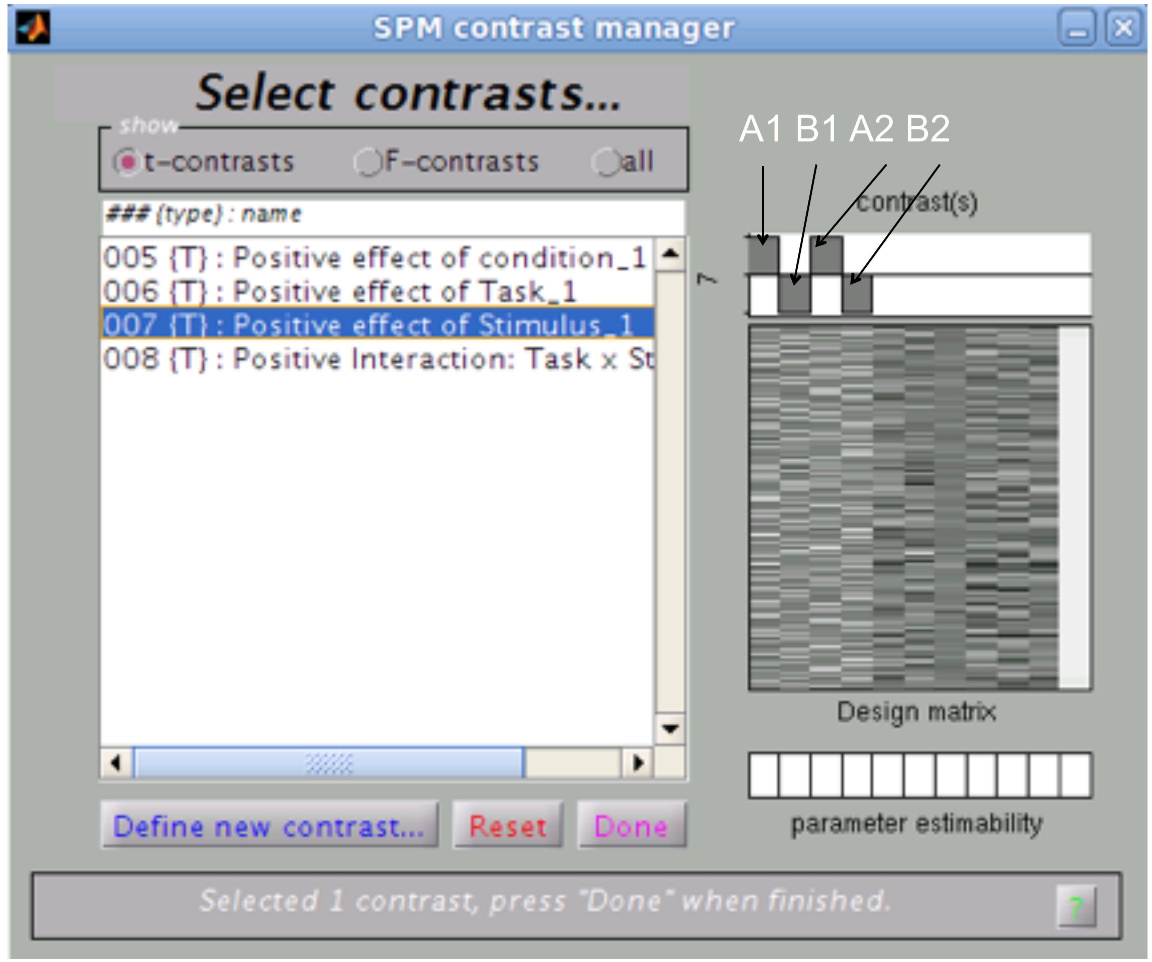
Main effect of task:
(A1 + B1) – (A2 + B2)



Factorial design

Task (1/2)

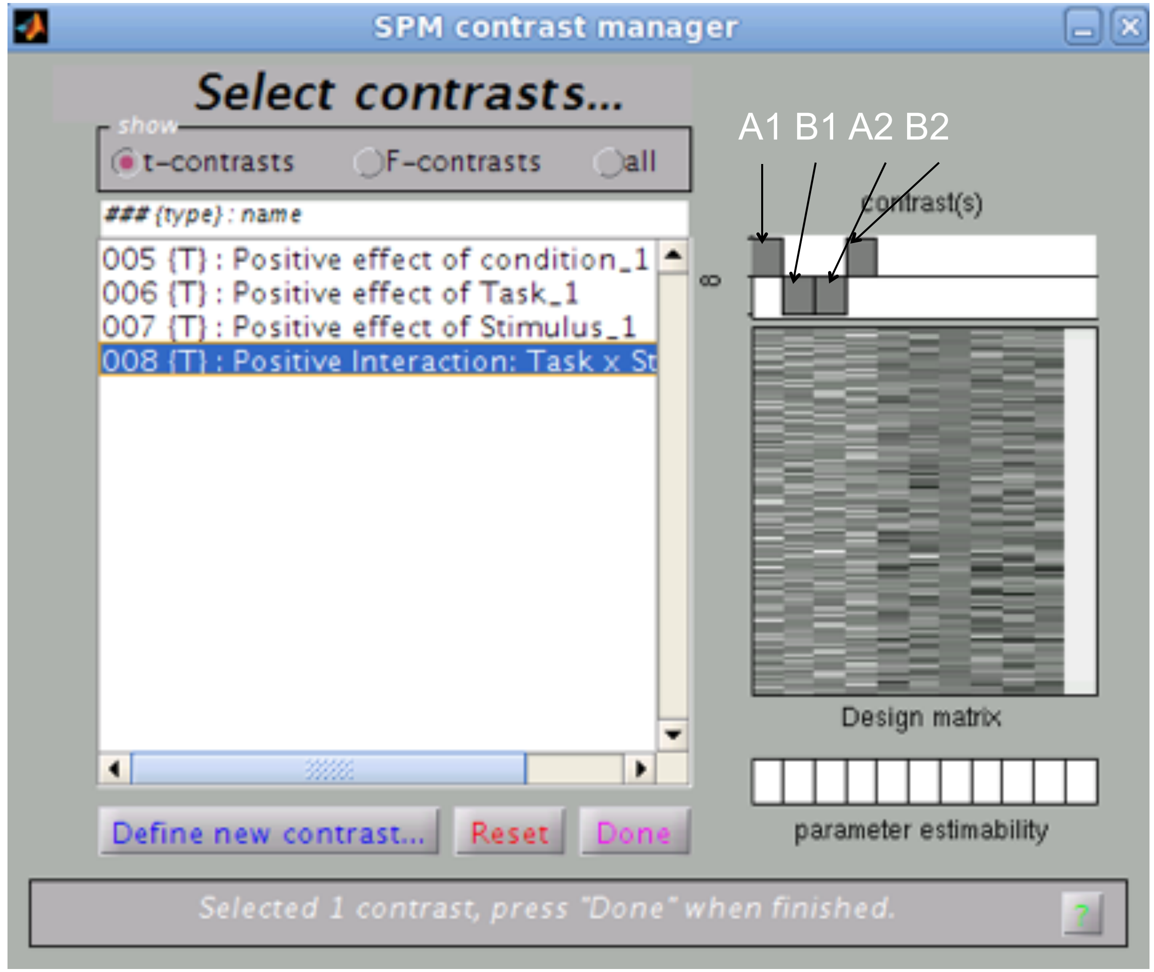
Stimuli (A/B)		Viewing	Naming
	Colours	A1	A2
	Objects	B1	B2



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

Factorial design

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



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

Main effects and interactions

Task (1/2)

Stimuli (A/B)	Viewing	Naming
Colours	A1	A2
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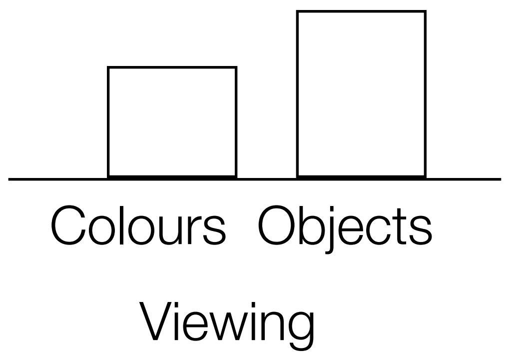
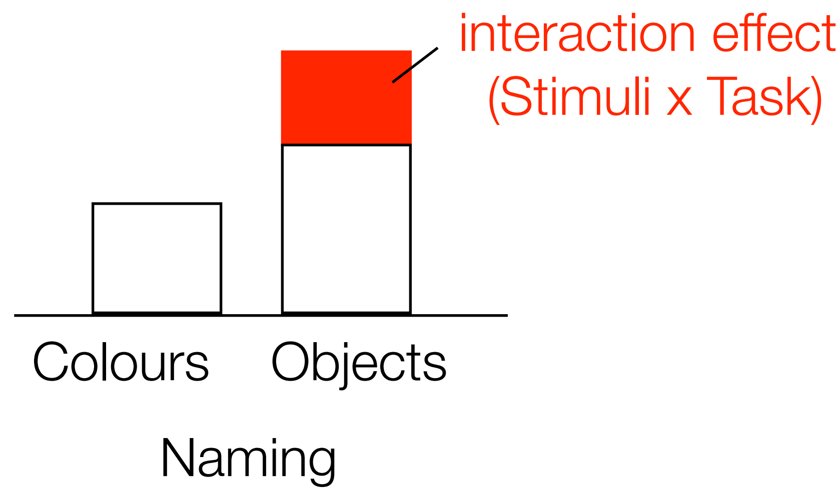
- Interaction of task and stimuli:
  Can show a failure of pure insertion

  (A1 – B1) – (A2 – B2)

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





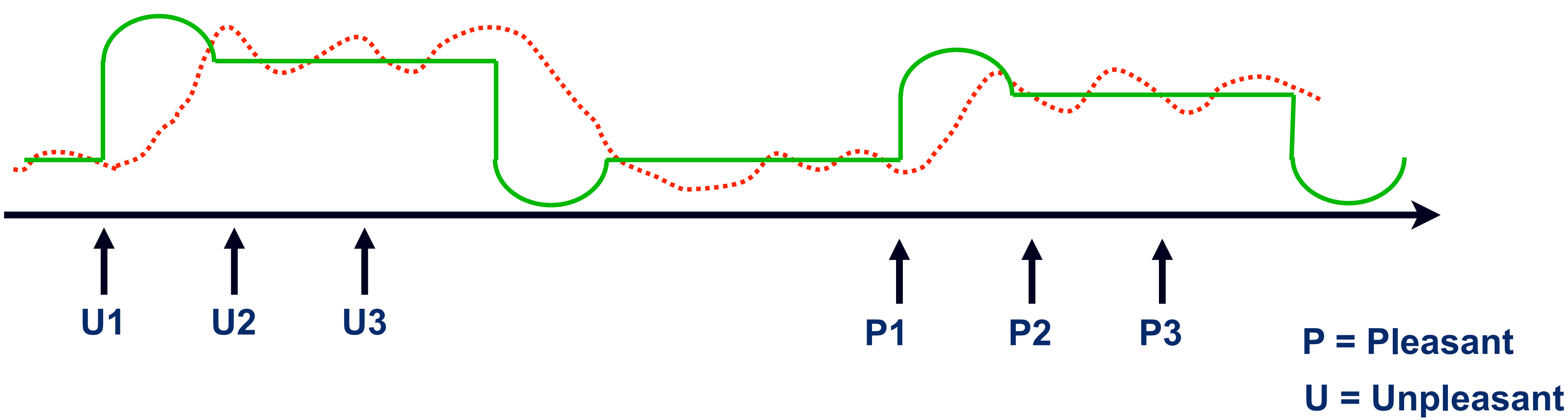
Event-related fMRI

Overview

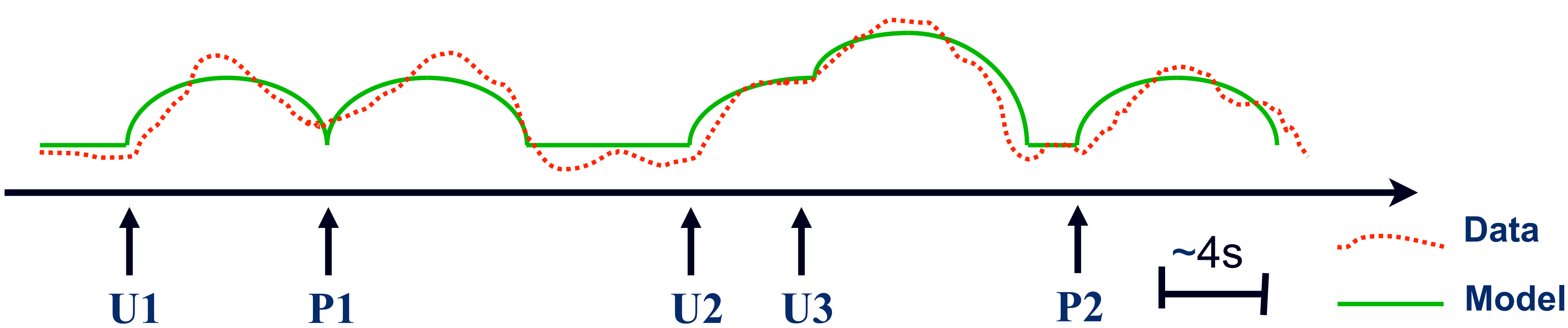
1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”

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

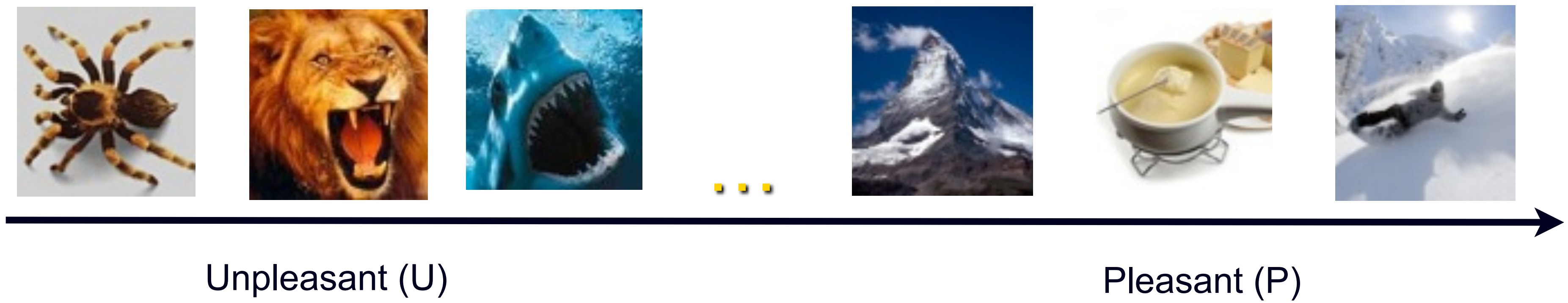


Advantages of event-related fMRI

1. Randomised trial order

efMRI: Randomised trial order

Blocked designs may trigger expectations and cognitive sets

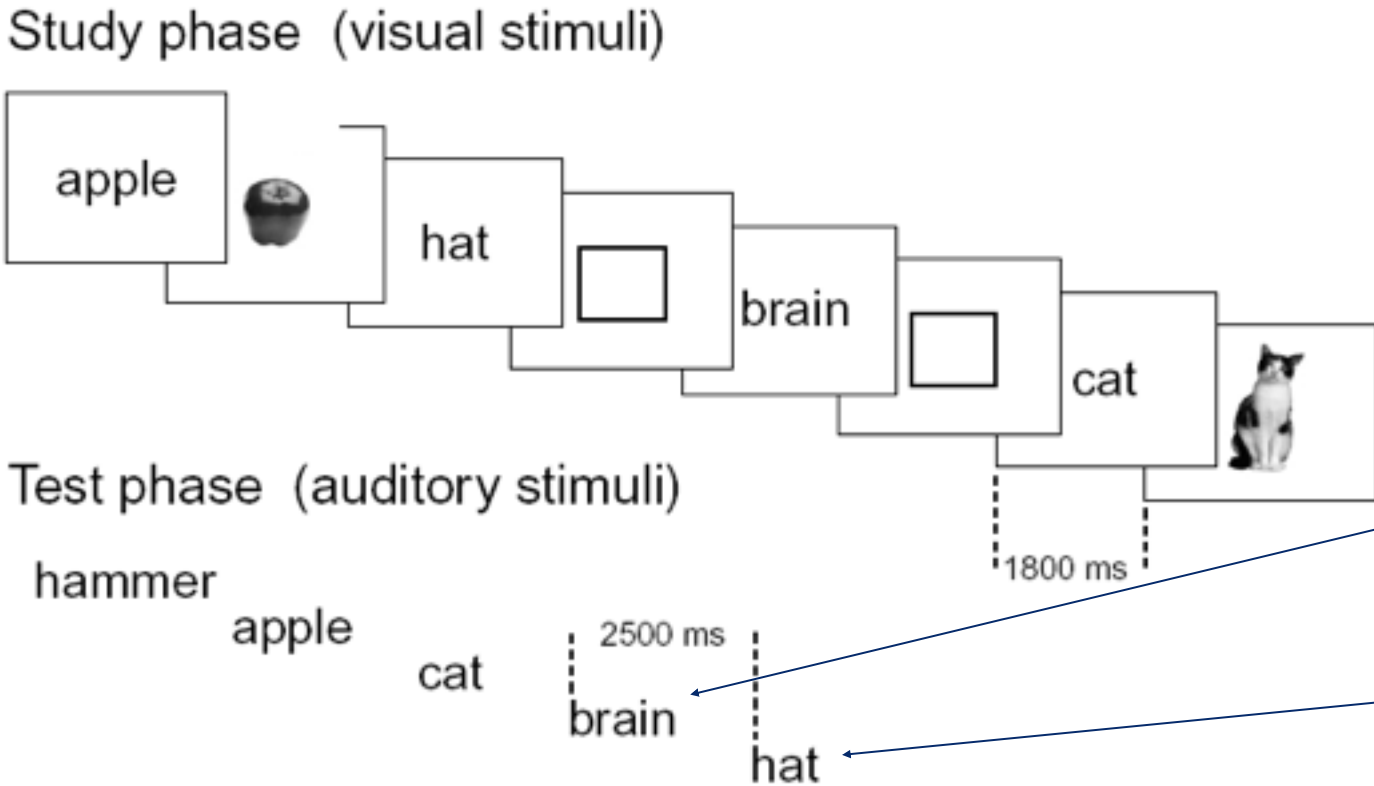


Intermixed designs can minimise this by stimulus randomisation

Advantages of event-related fMRI

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

efMRI: Post-hoc classification of trials



Participant response:

„was *not* shown as picture“

„was shown as picture“

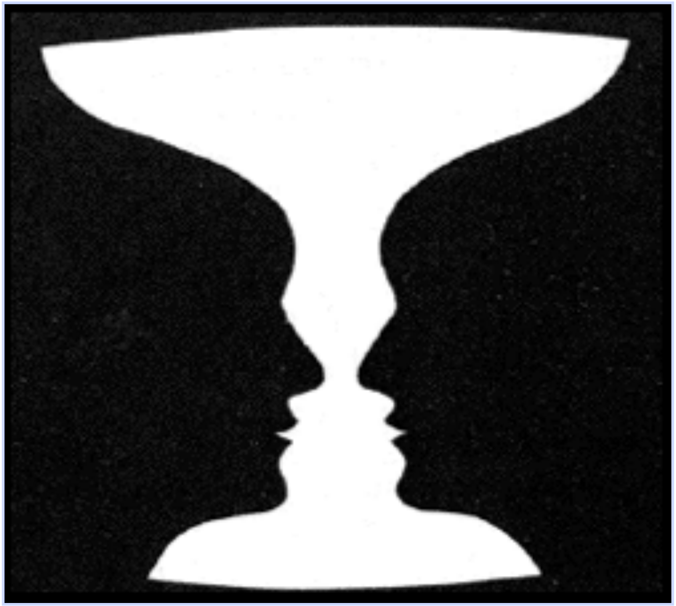
Items with wrong memory of picture („hat“) were associated with more occipital activity *at encoding* than items with correct rejection („brain“)

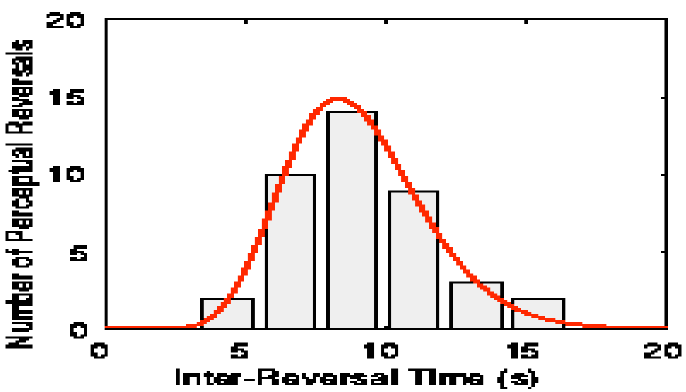
Gonsalves & Paller (2000) Nature Neuroscience

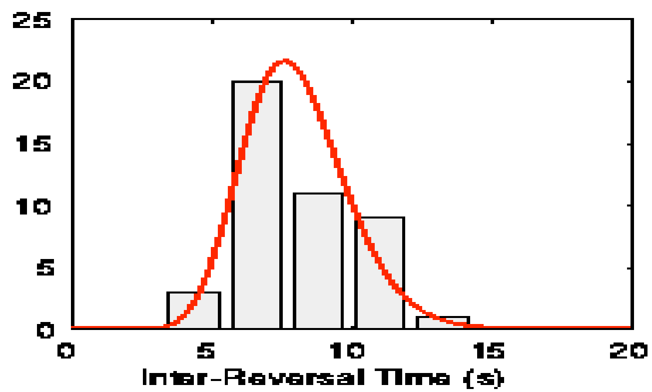
Advantages of event-related fMRI

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

efMRI: Online event definition



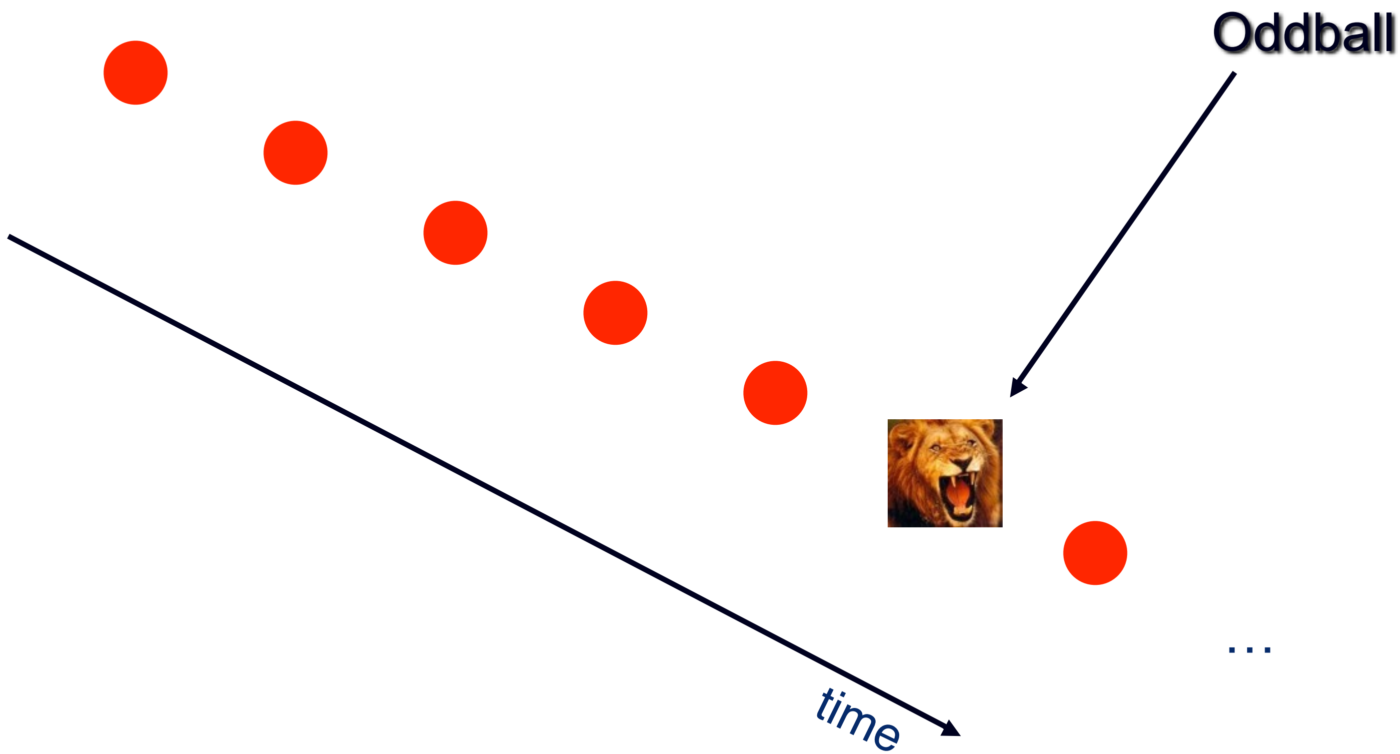




Advantages of event-related fMRI

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
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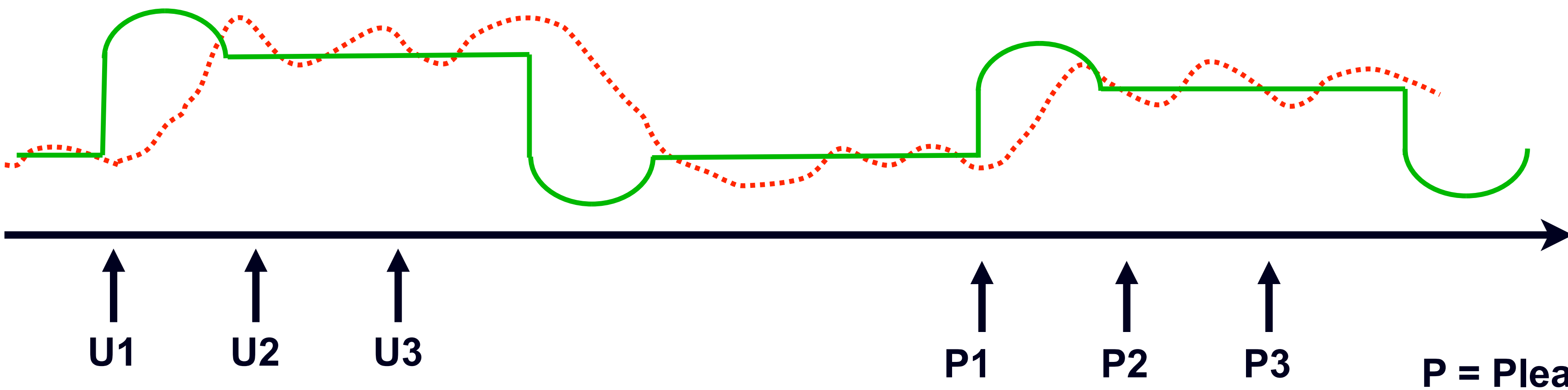
5. More accurate model even for epoch/block designs?

“Event” model of block design

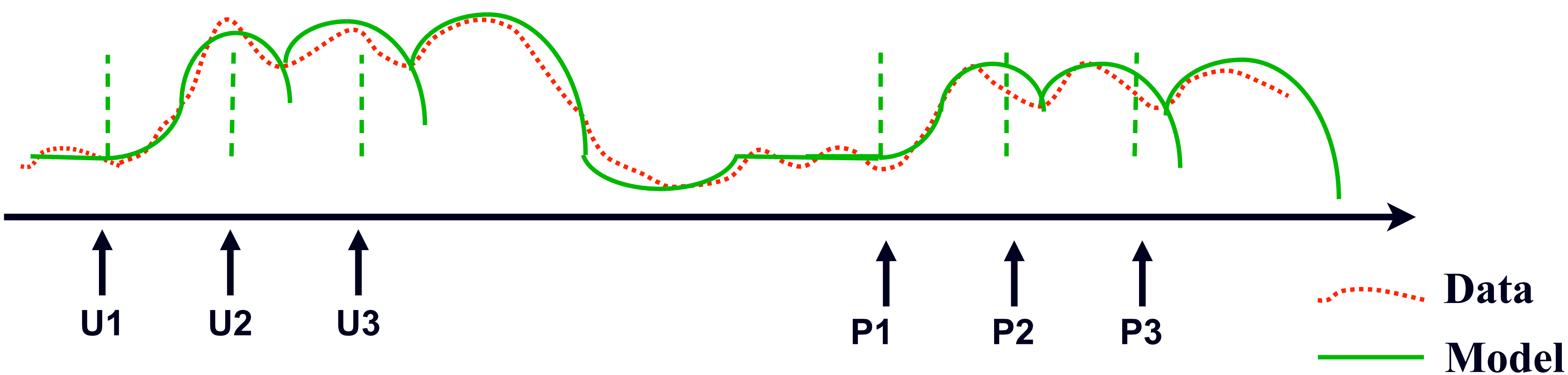
“Epoch” model assumes constant neural processes throughout block



P = Pleasant

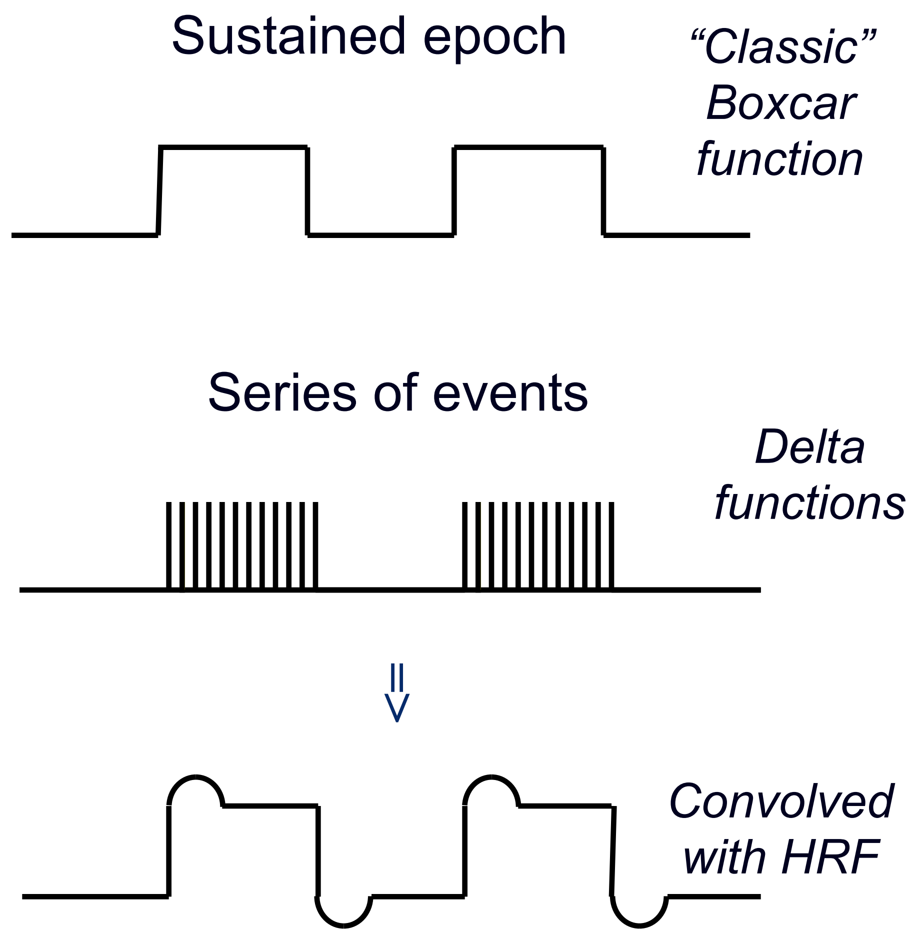
U = Unpleasant

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



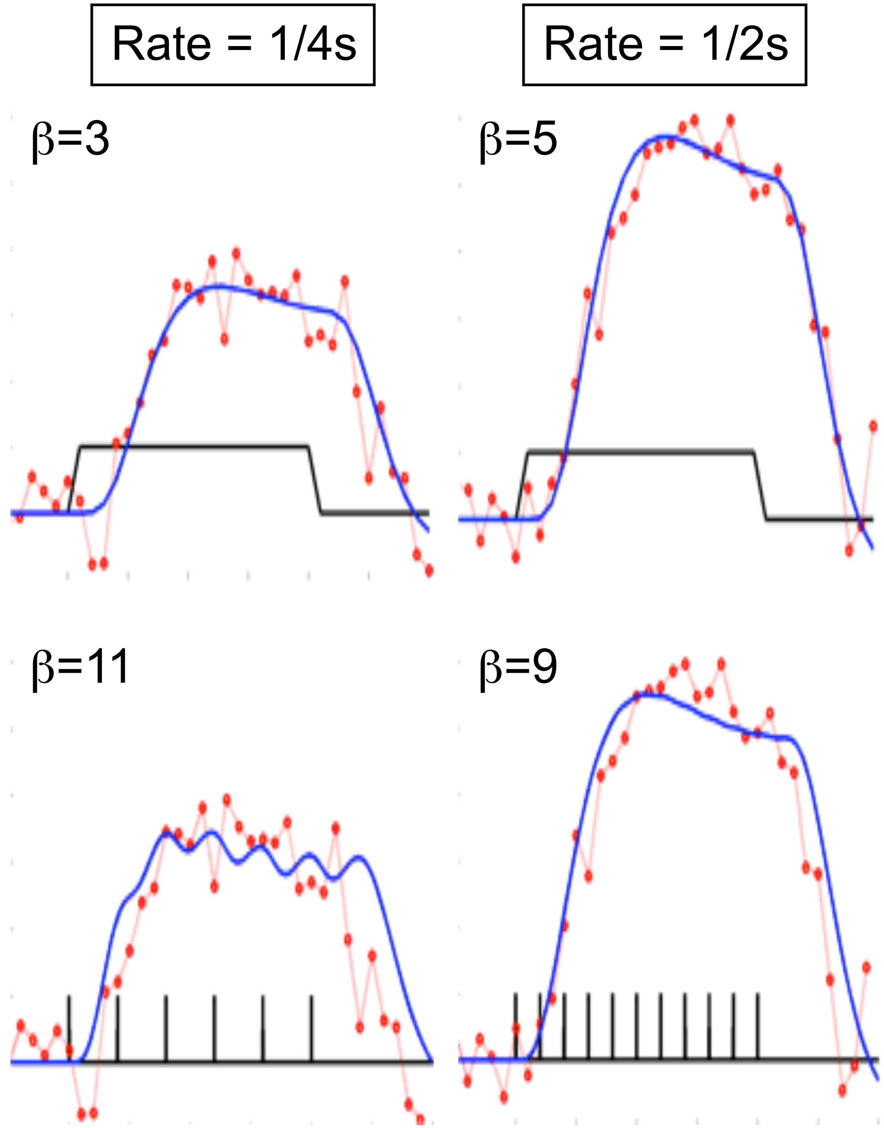
Modeling block designs: Epochs vs events

- 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<~3s)
- 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

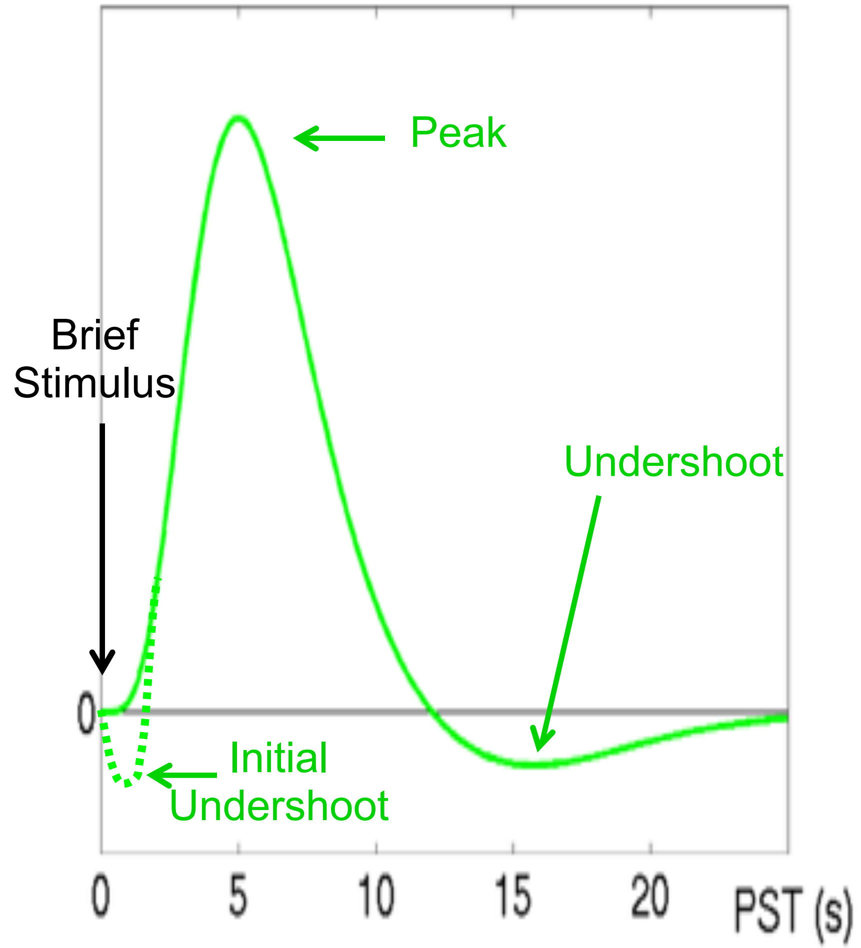
2. Some psychological processes have to/may be better blocked
   (e.g., if difficult to switch between states, or to reduce surprise effects)

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”

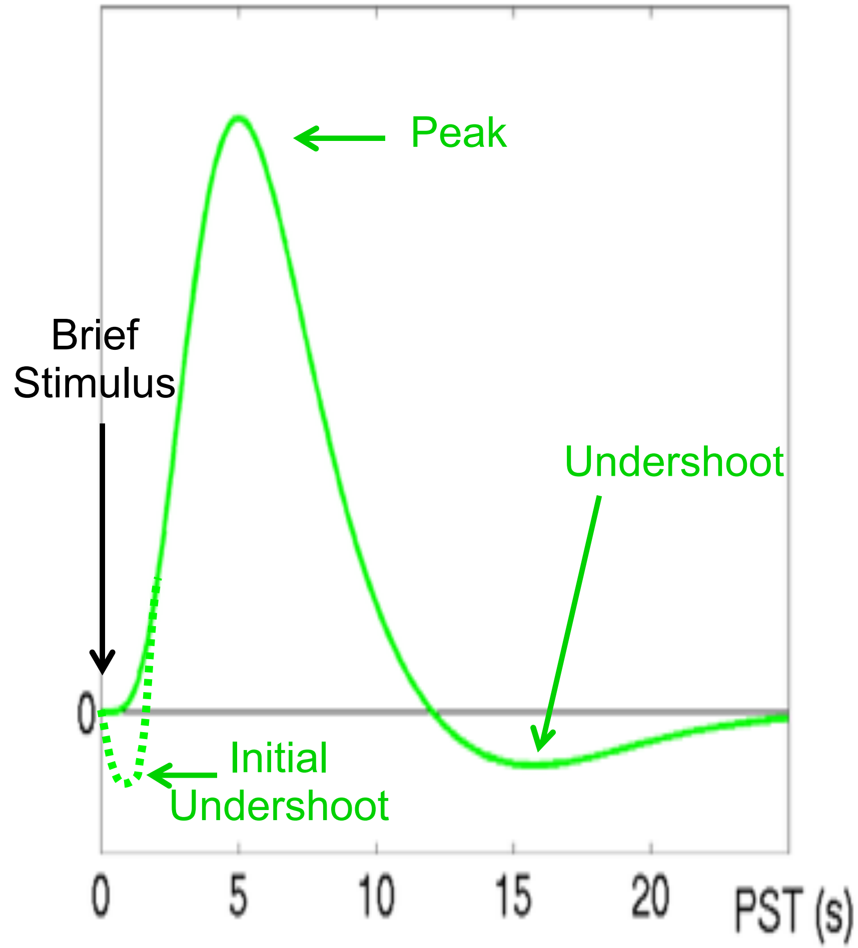
BOLD impulse response

- 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

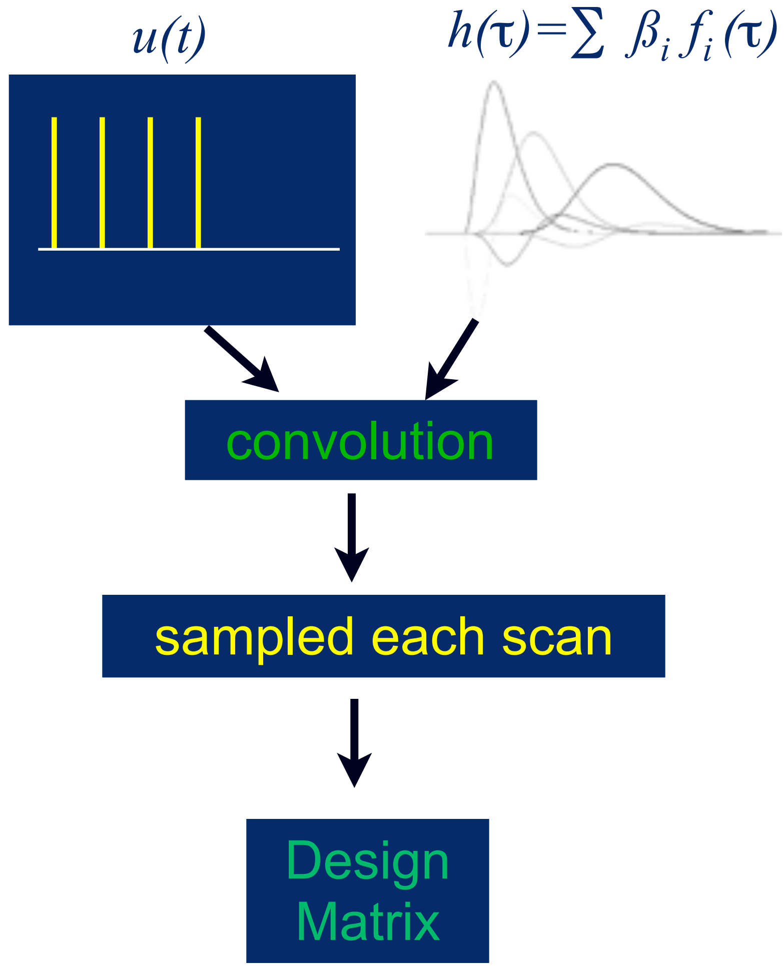


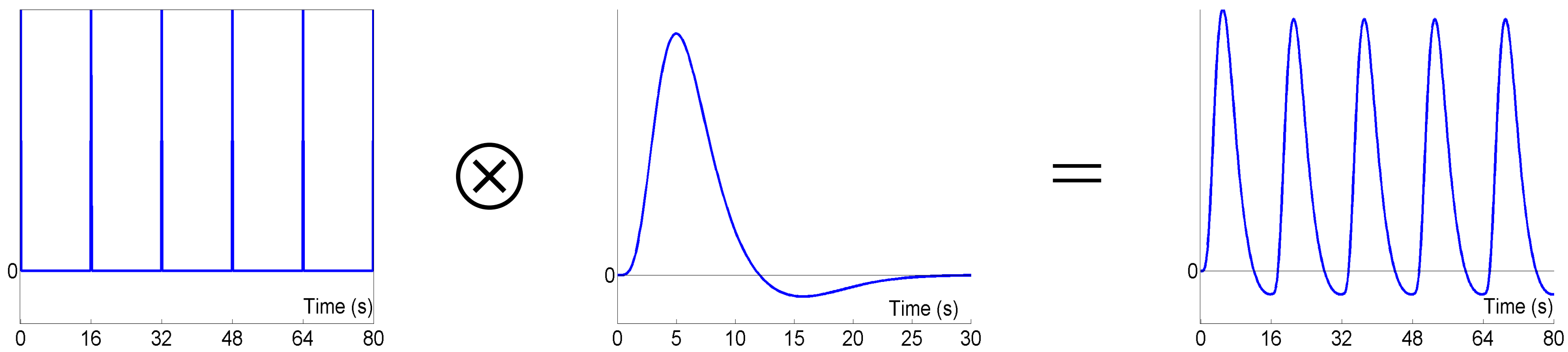
BOLD impulse response

- 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



General Linear (Convolution) Model





$$f \otimes g(t) = \int_0^t f(\tau)\, g(t-\tau)\, d\tau$$

expected BOLD response

= input function ⊗ impulse response function (HRF)

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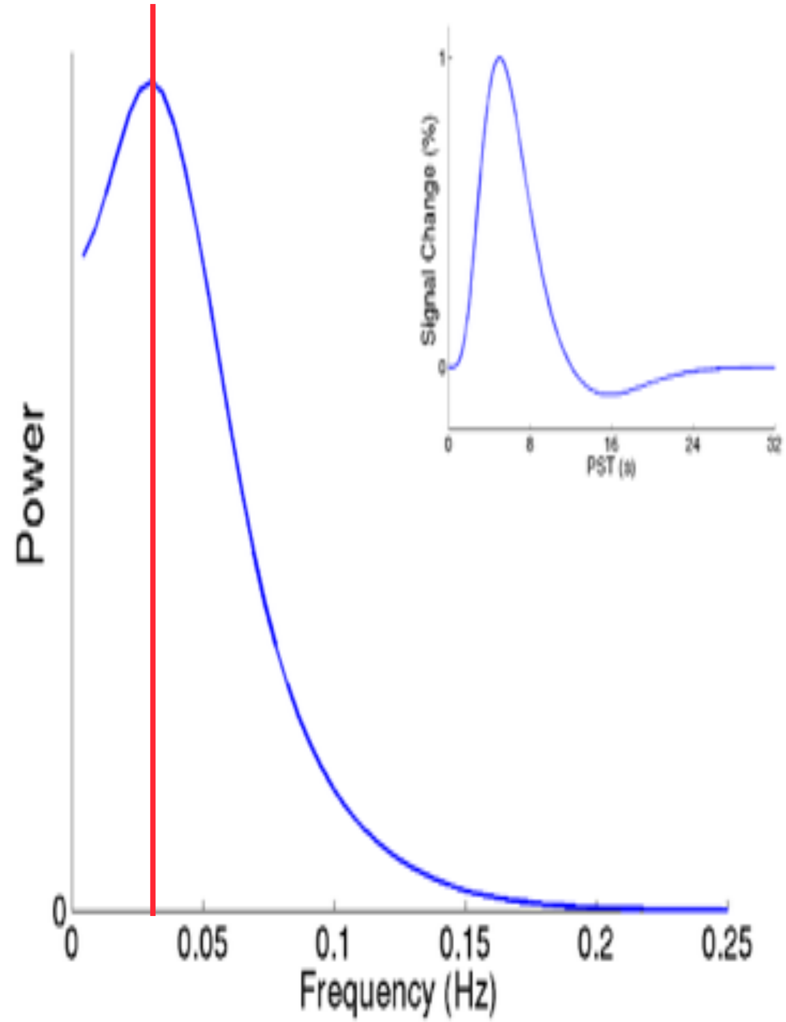
7. **Design Optimisation – "Efficiency"**

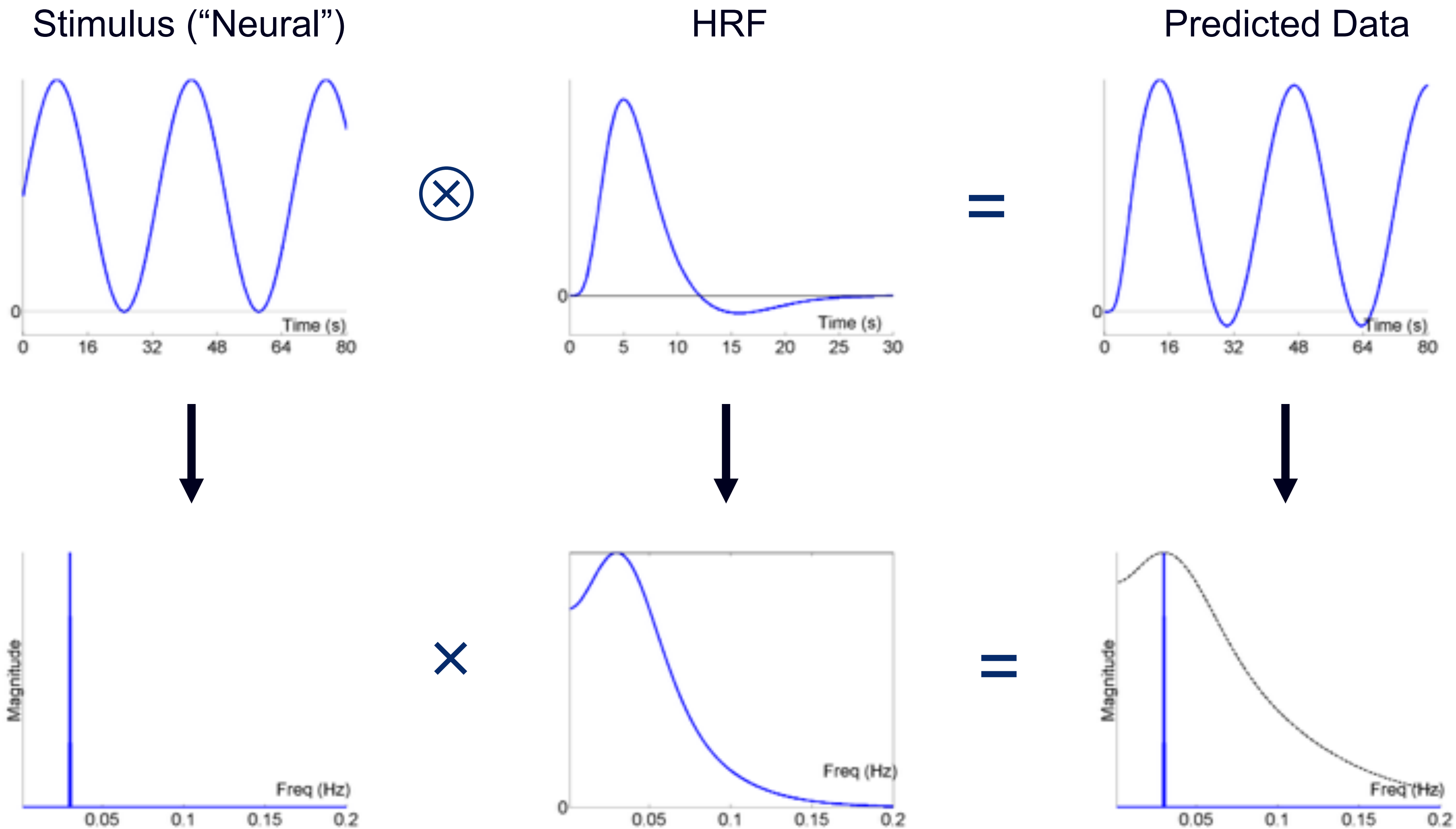
Design efficiency

- 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 ~0.04 Hz

➡ The most efficient design is a sinusoidal modulation of neural activity with period ~24s (e.g., boxcar with 12s on/ 12s off)

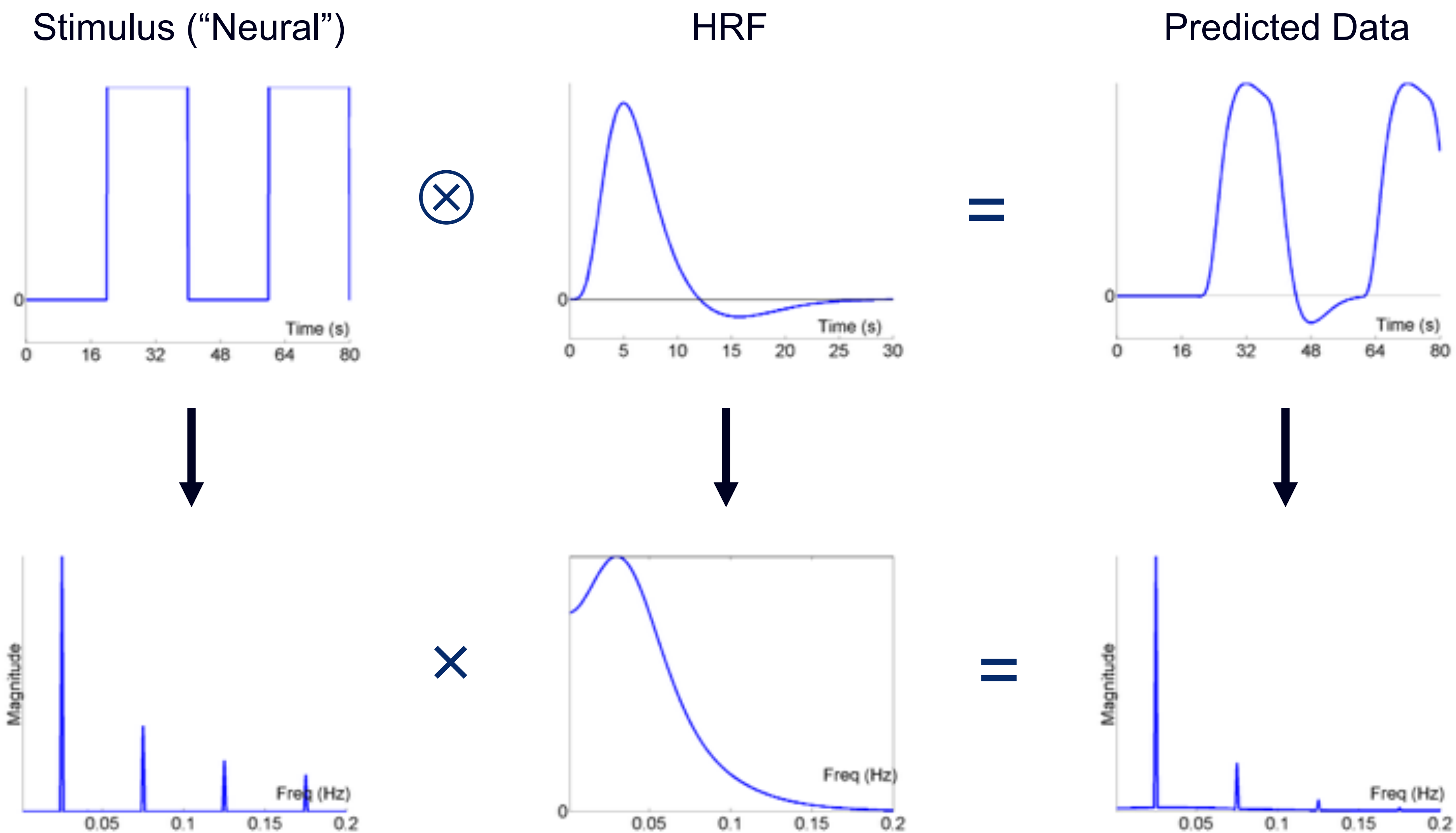


Sinusoidal modulation, f = 1/33



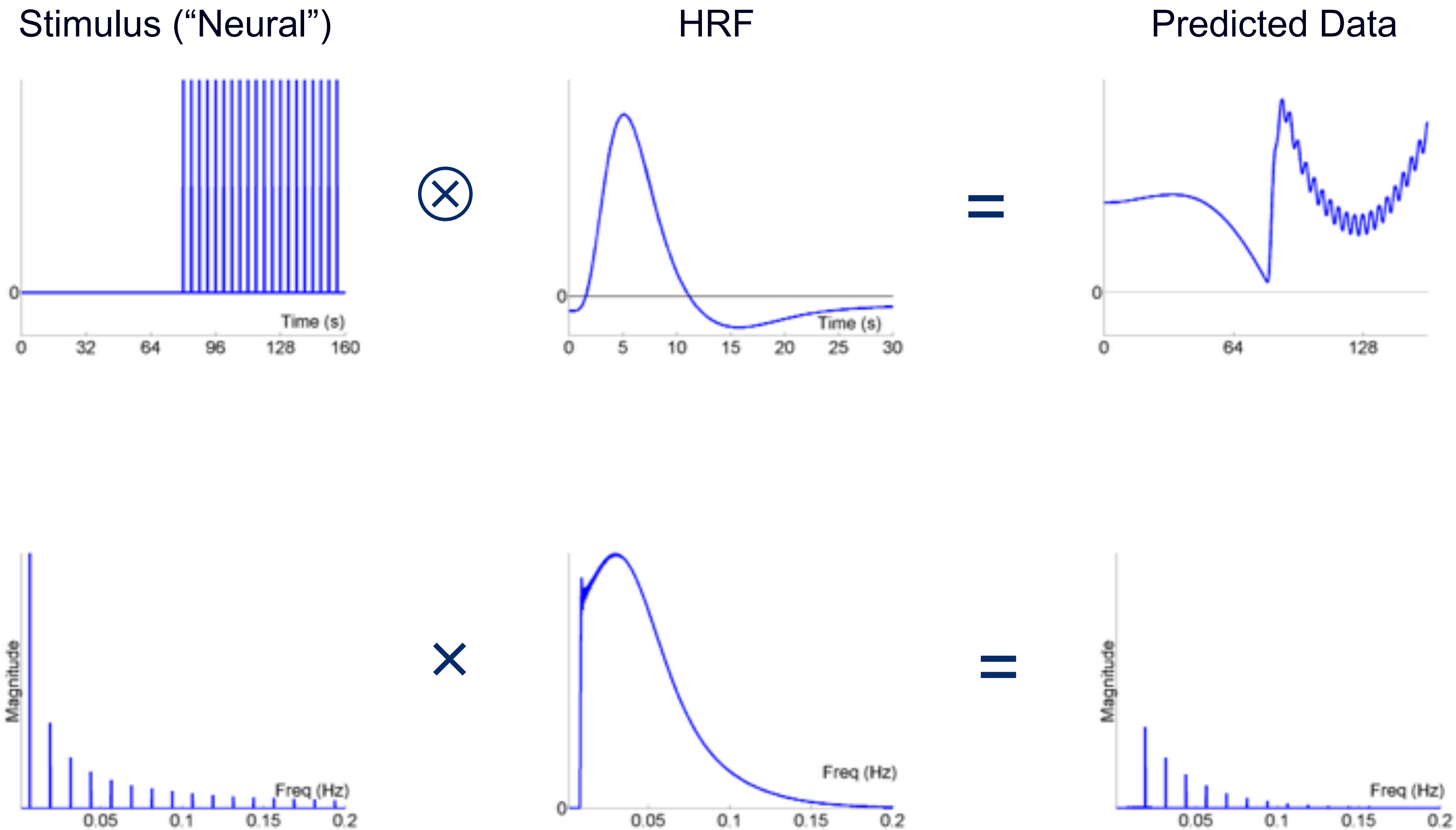
A very “efficient” design!

Blocked, epoch = 20 sec



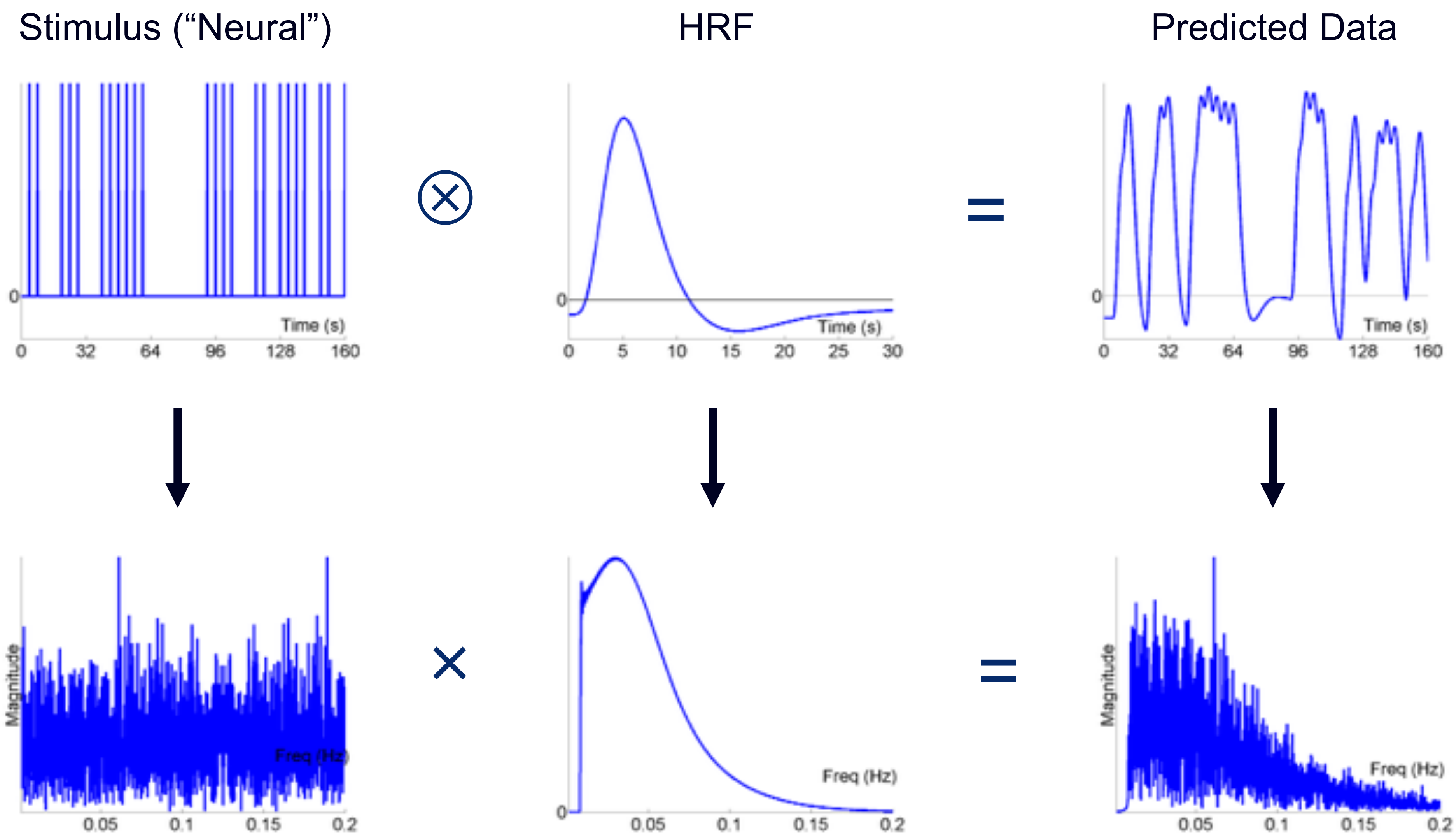
Blocked-epoch (with small SOA) quite “efficient”

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



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

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



Randomised design spreads power over frequencies

Design efficiency: Trial spacing

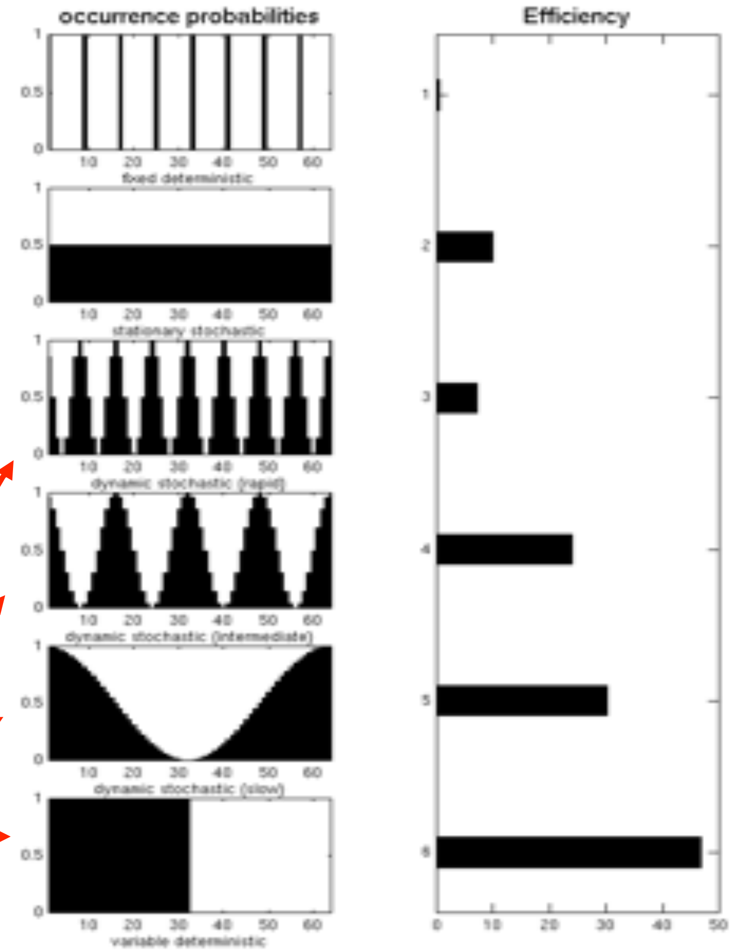
- Design parametrised by:

  - SOA_{min} Minimum SOA
  - $p(t)$ Probability of event at each SOA_{min}

- Deterministic
  p(t)=1 iff t=nSOAmin

- Stationary stochastic
  p(t)=constant

- Dynamic stochastic
  p(t) varies (e.g., blocked)

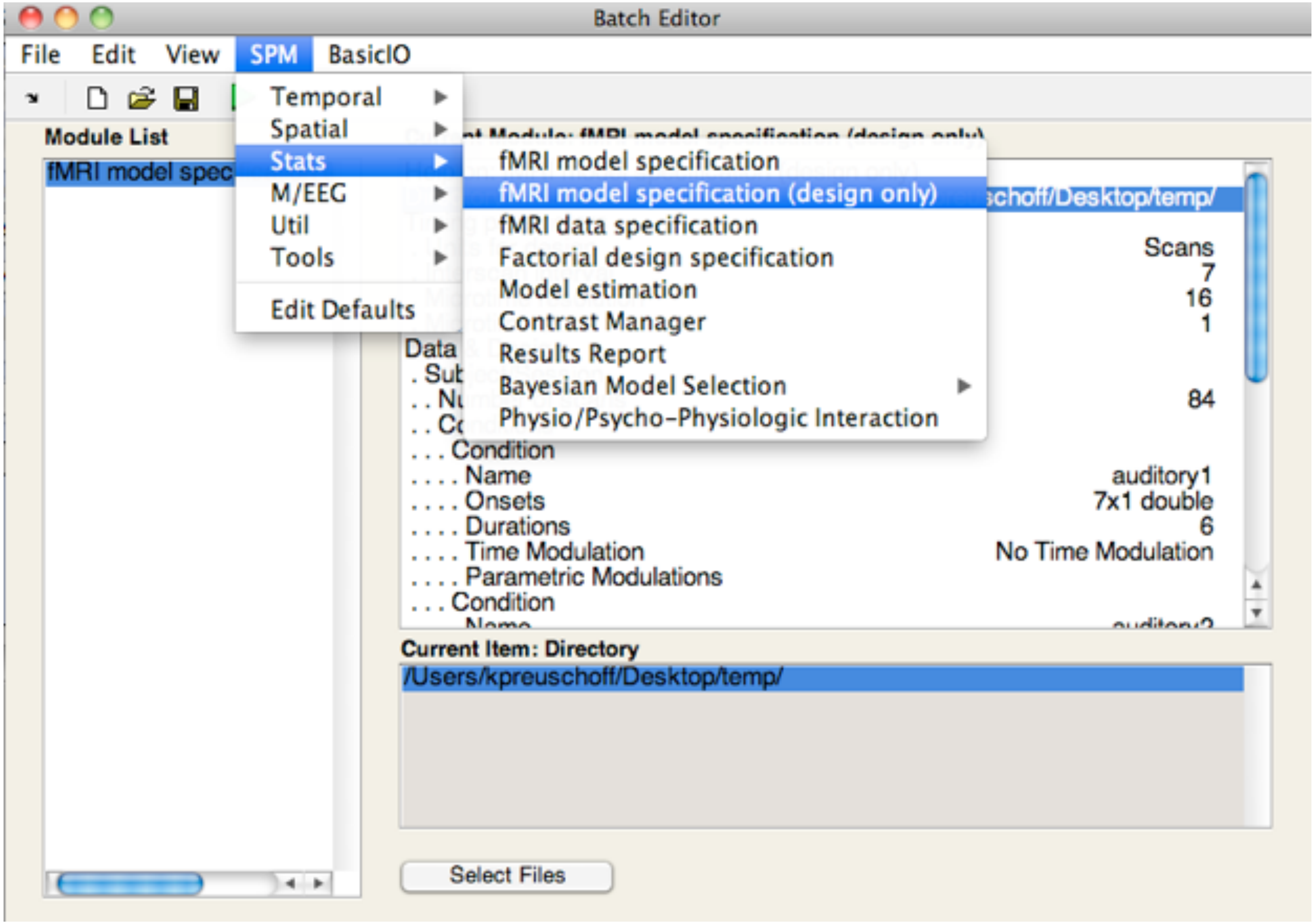


Blocked designs most efficient! (with small SOAmin)

Design efficiency: Conclusions

- Optimal design for one contrast may not be optimal for another
- Blocked designs generally most efficient (with short SOAs, given optimal block length is not exceeded)
- However, psychological efficiency often dictates intermixed designs, and often also sets limits on SOAs
- With randomised designs, optimal SOA for differential effect (A-B) is minimal SOA (>2 seconds, and assuming no saturation), whereas optimal SOA for main effect (A+B) is 16-20s
- Inclusion of null events improves efficiency for main effect at short SOAs (at cost of efficiency for differential effects)
- If order constrained, intermediate SOAs (5-20s) can be optimal
- If SOA constrained, pseudorandomised designs can be optimal (but may introduce context-sensitivity)

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

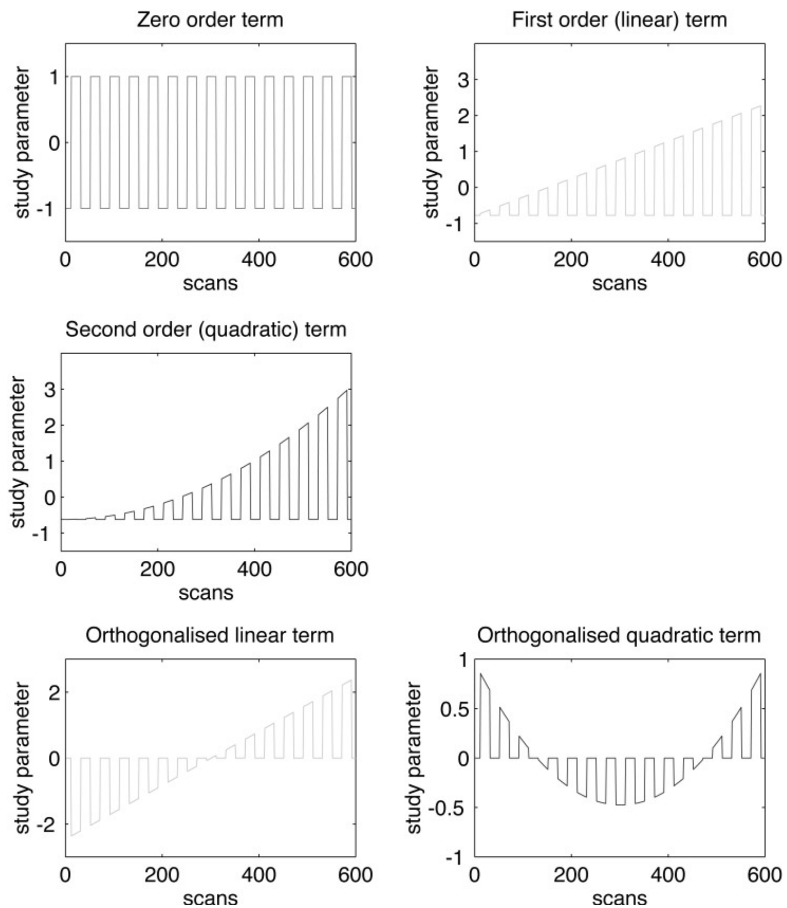
Categorical	- Interactions and pure insertion
Parametric	- Linear and nonlinear interactions
	- Psychophysiological Interactions

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

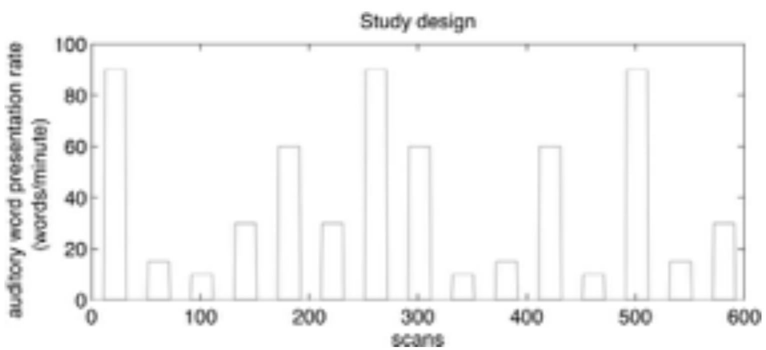
- Possible tests for such relations are manifold:
  - Linear
  - Nonlinear: Quadratic/cubic/etc. (polynomial expansion)
  - Model-based (e.g. predictions from learning models)

Parametric modulation of regressors by time

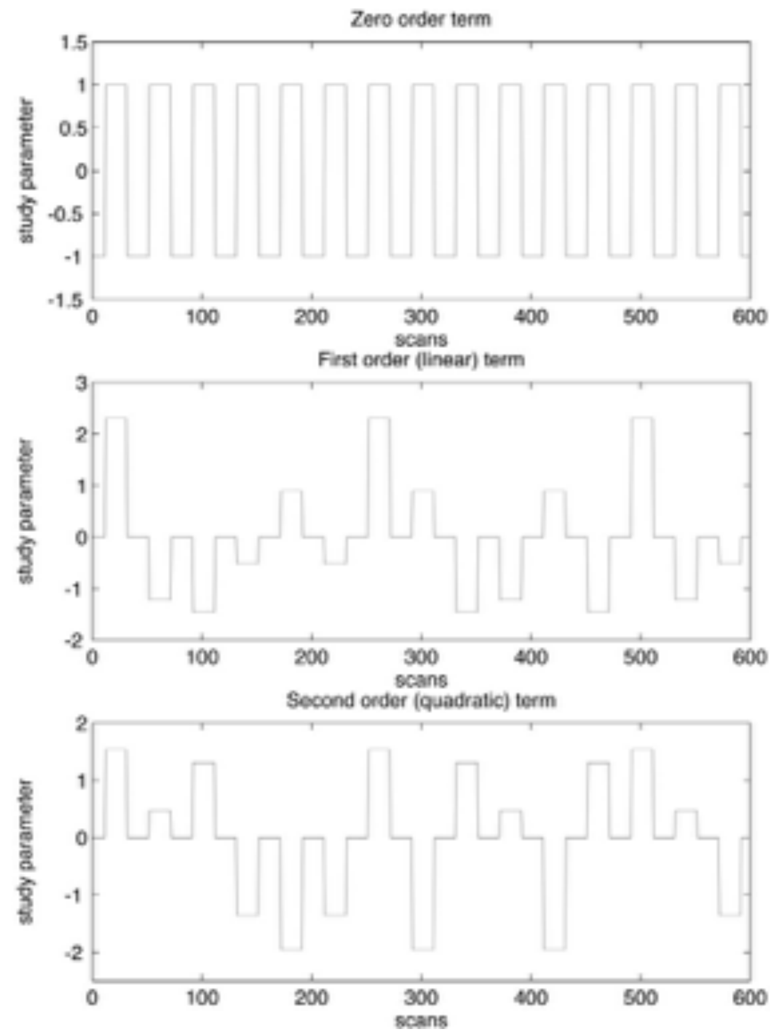


Büchel et al. 1998, *NeuroImage* 8:140-148

“User-specified” parametric modulation of regressors



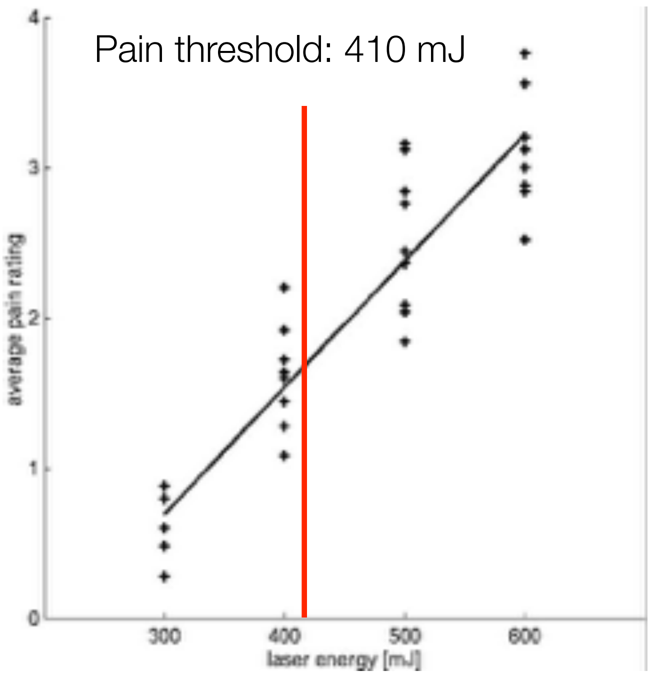
Polynomial expansion
&
orthogonalisation



Büchel et al. 1998, *NeuroImage* 8:140-148

Investigating neurometric functions

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

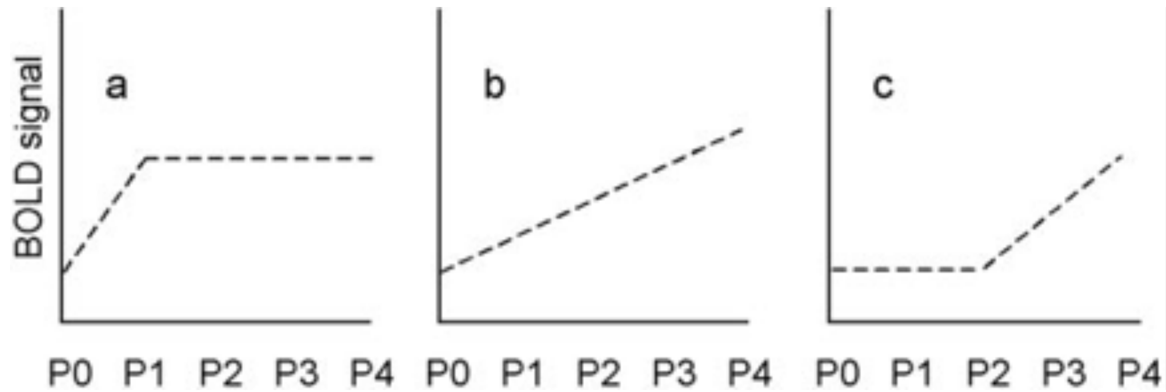


P0 P1 P2 P3 P4

Stimulus awareness

Stimulus intensity

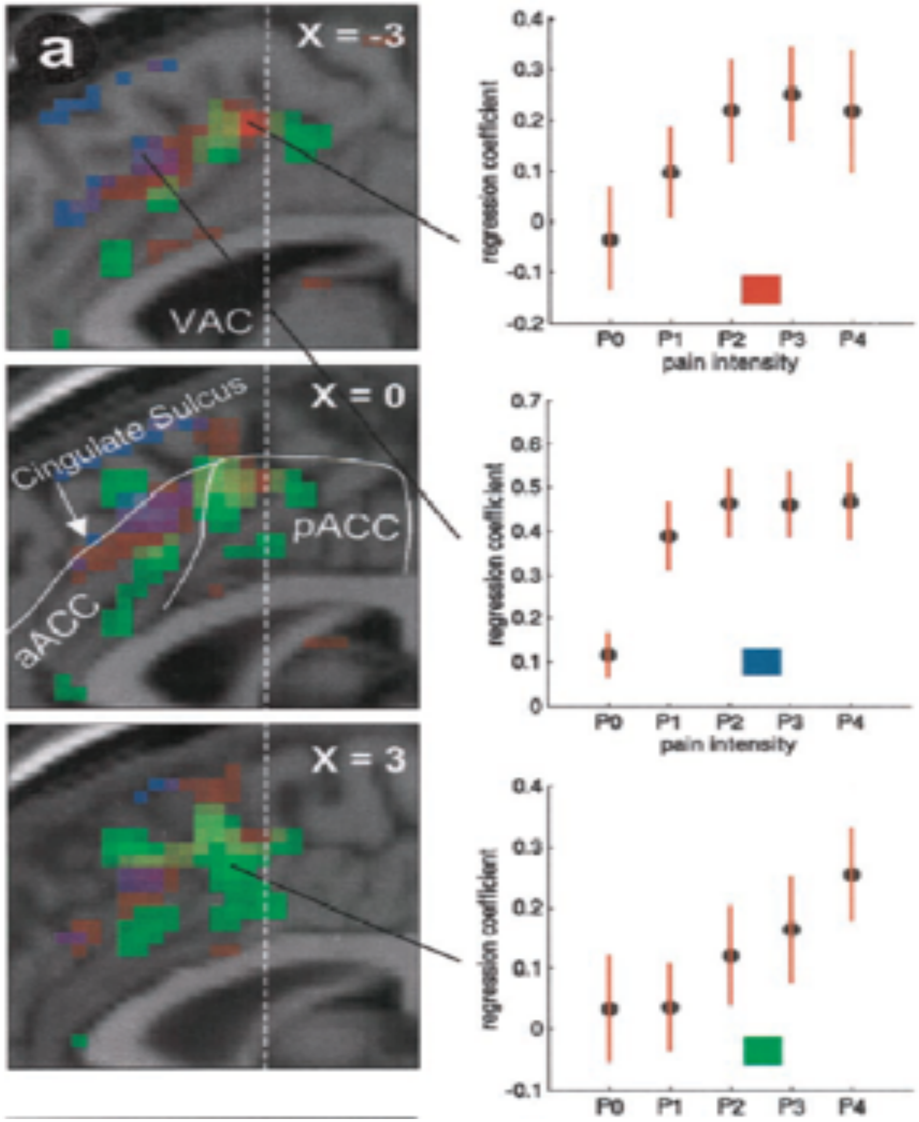
Pain intensity



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

Büchel et al. 2002, J. Neurosci. 22:970-976

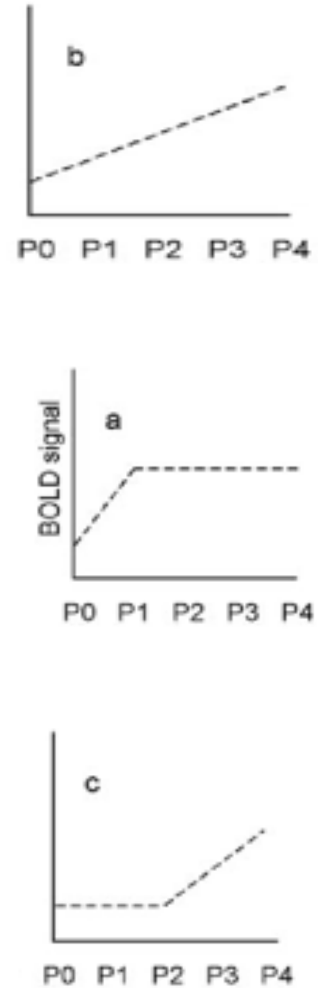
Neurometric functions



→ 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

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Thank you