Experimental design for fMRI

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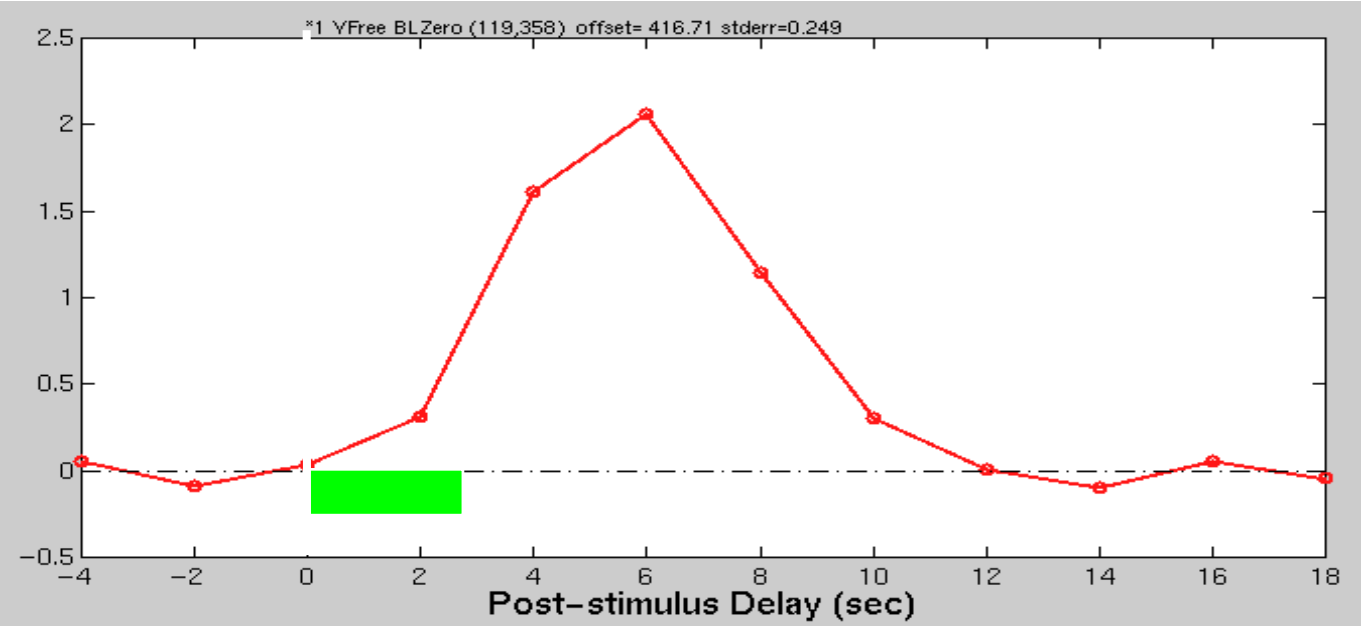
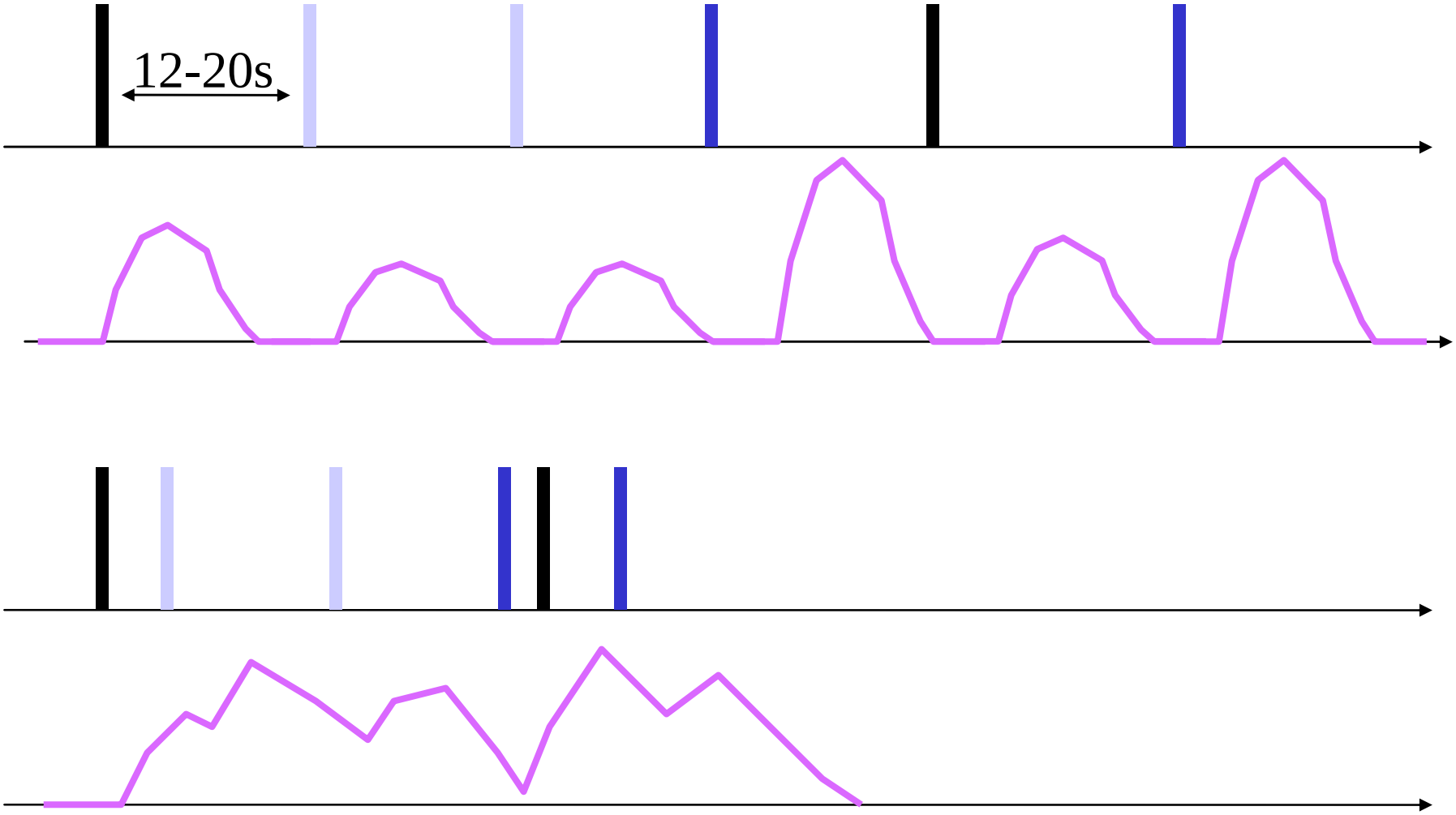
The problem with fMRI

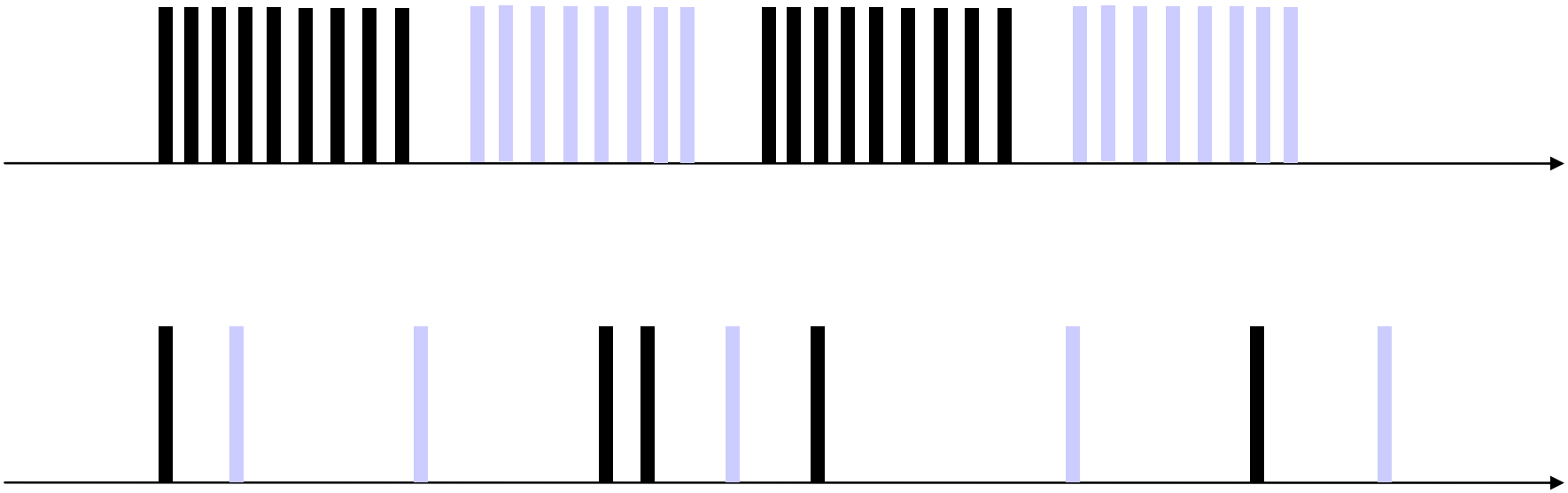


We are dealing with an indirect, temporally extended index of neural activity, which makes it difficult to estimate the neural response to any one event

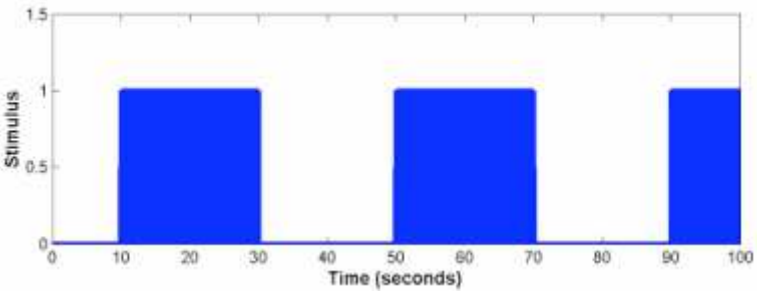
Overlap in BOLD responses

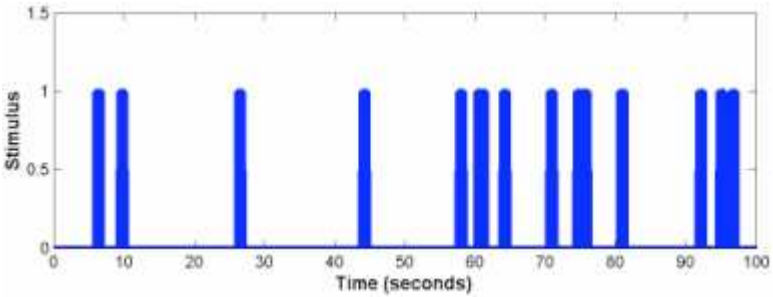


Blocked vs event-related designs



The advantages of being event-related





- Simple
- Very efficient
- Robust to uncertainty in BOLD response and timing
- Straightforward analysis

- Flexible
- Good estimation of time course of BOLD response
- Allows post-hoc sorting of events
- Can separate different task components

- Most tasks can’t be blocked
- Participants can anticipate upcoming stimuli
- No timing information

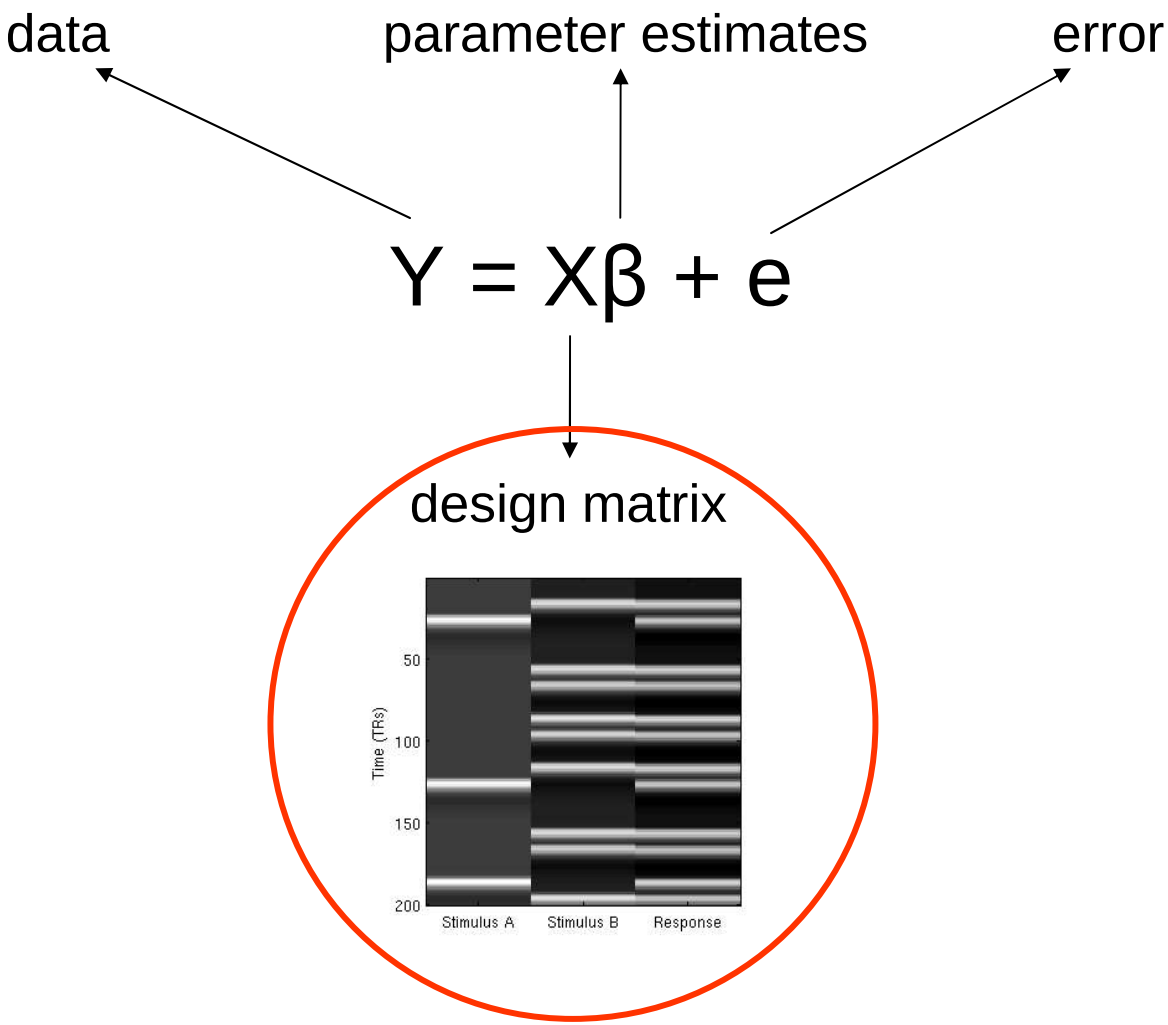
- More things can go wrong
- Reduced efficiency
- Requires longer experiments
- More dependent on accurate hrf modelling

Overview of the talk

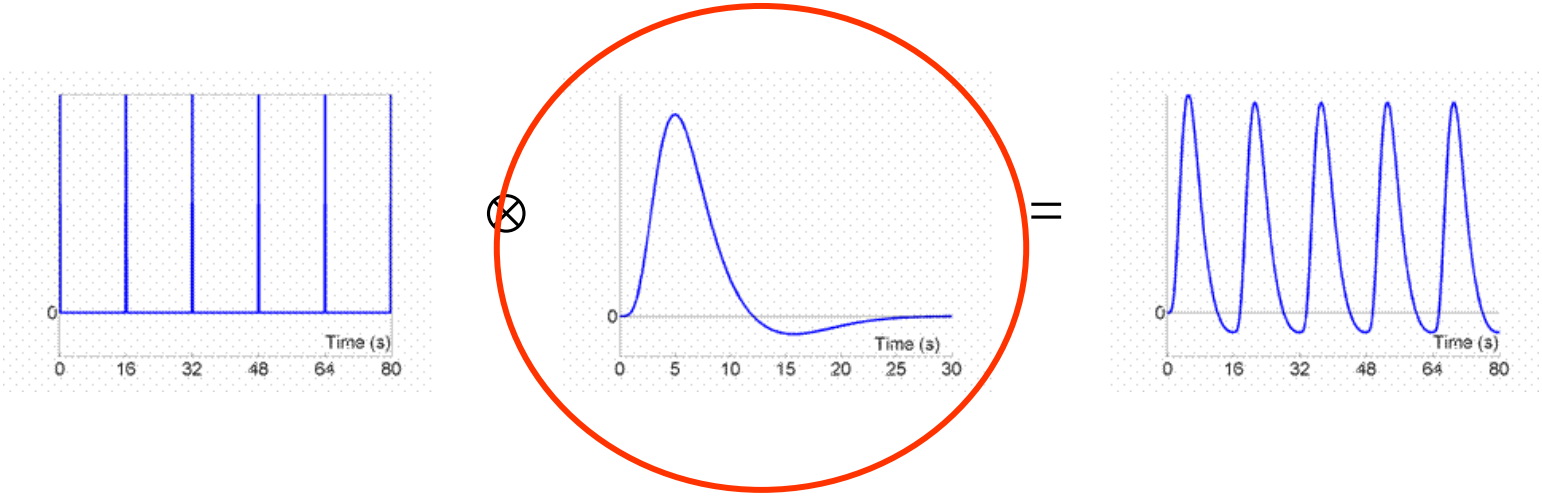
Goal of the talk is to find a way to build an event-related fMRI experiment, which will allow is to present stimuli in randomized order and at high rate, while still allowing us to reliably look at BOLD responses to different event types

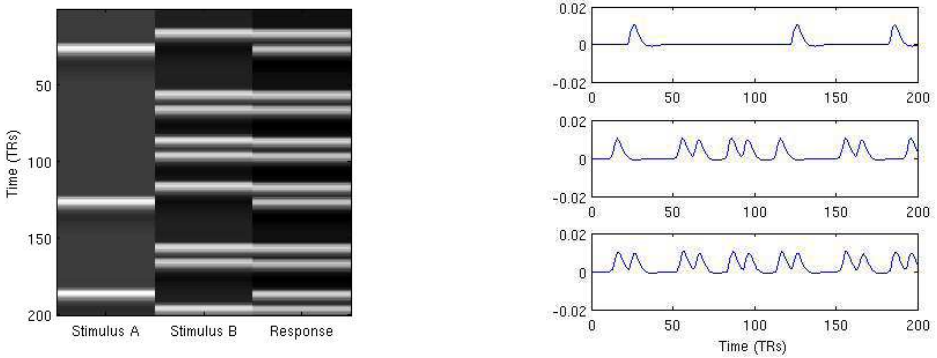
- What do we do in fMRI?
- What kind of responses are we dealing with?
- What constitutes a ‘good’ design?
- How can we evaluate the effectiveness of our design?
- Examples please!

What do we do in fMRI?



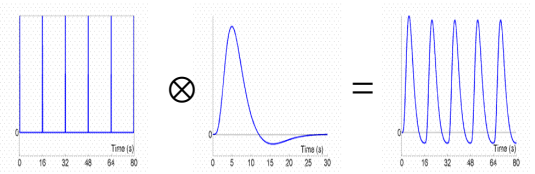
Design matrix





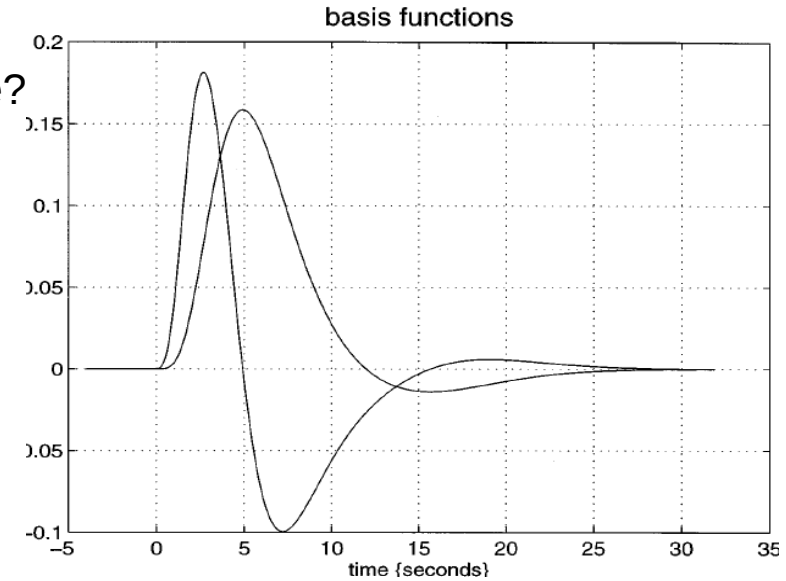
Modelling the BOLD response

We convolve the design matrix with a model of the hemodynamic response



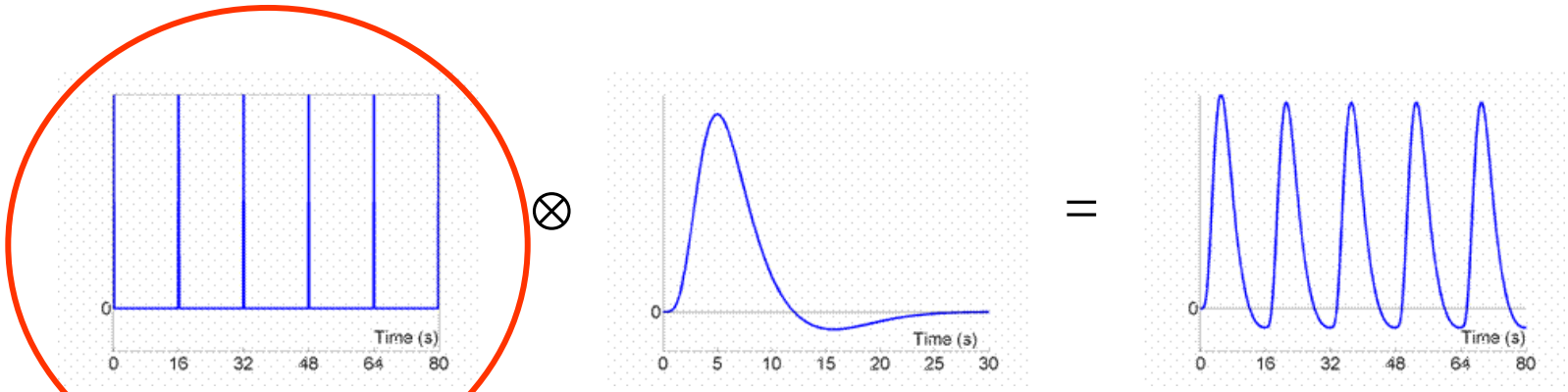
Question: how consistent is the BOLD response?

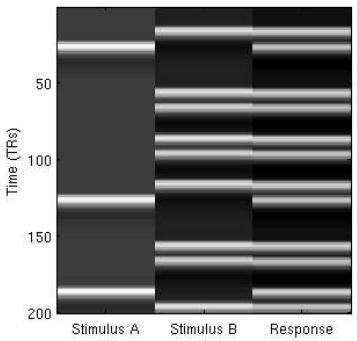
- variability in time
- variability in space
- variability across individuals (!)

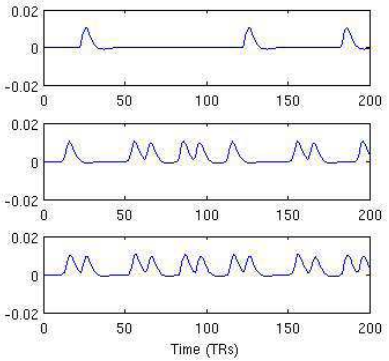


Josephs 1999; Friston 1998; Friston 1999

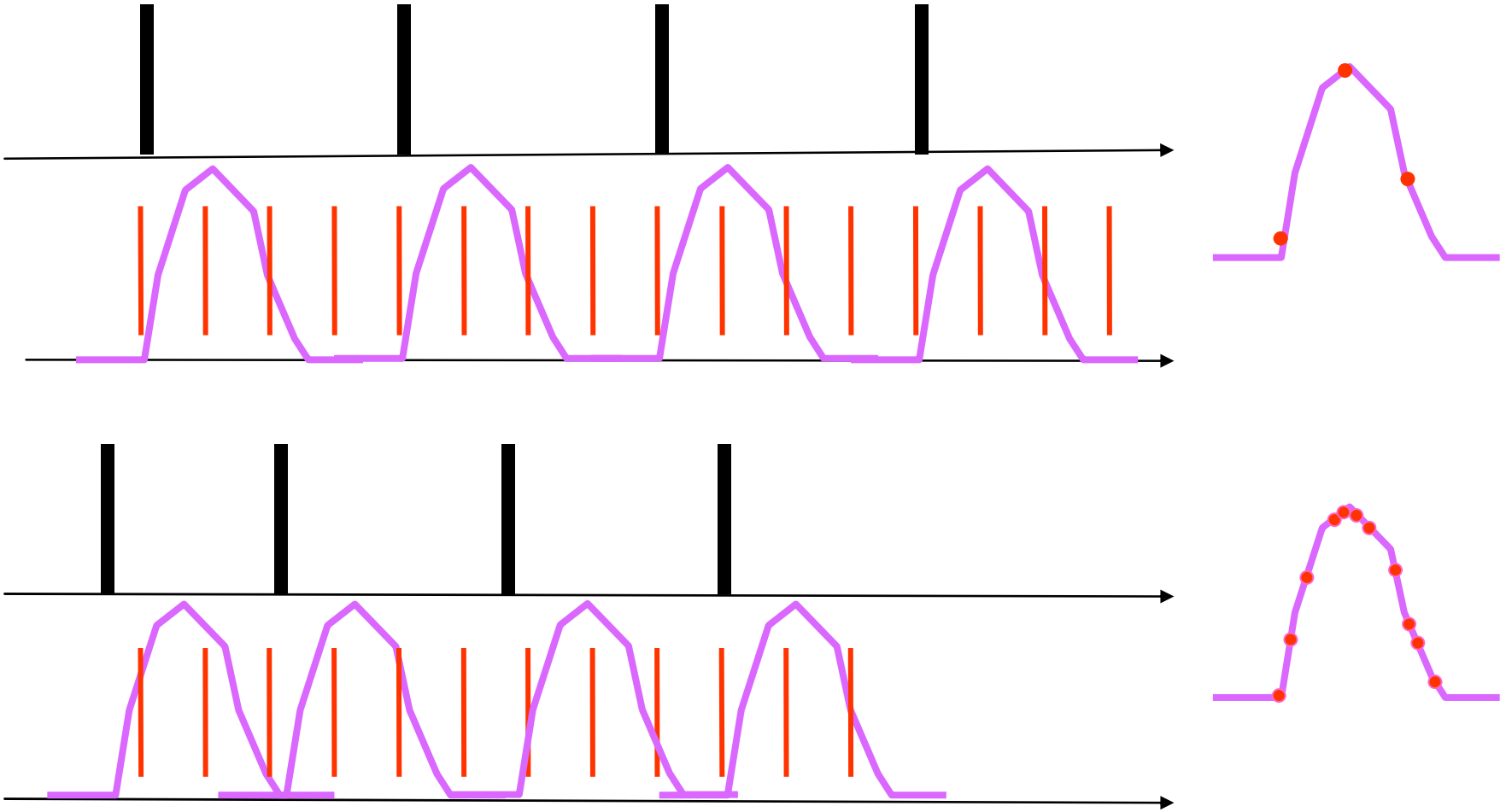
Design matrix





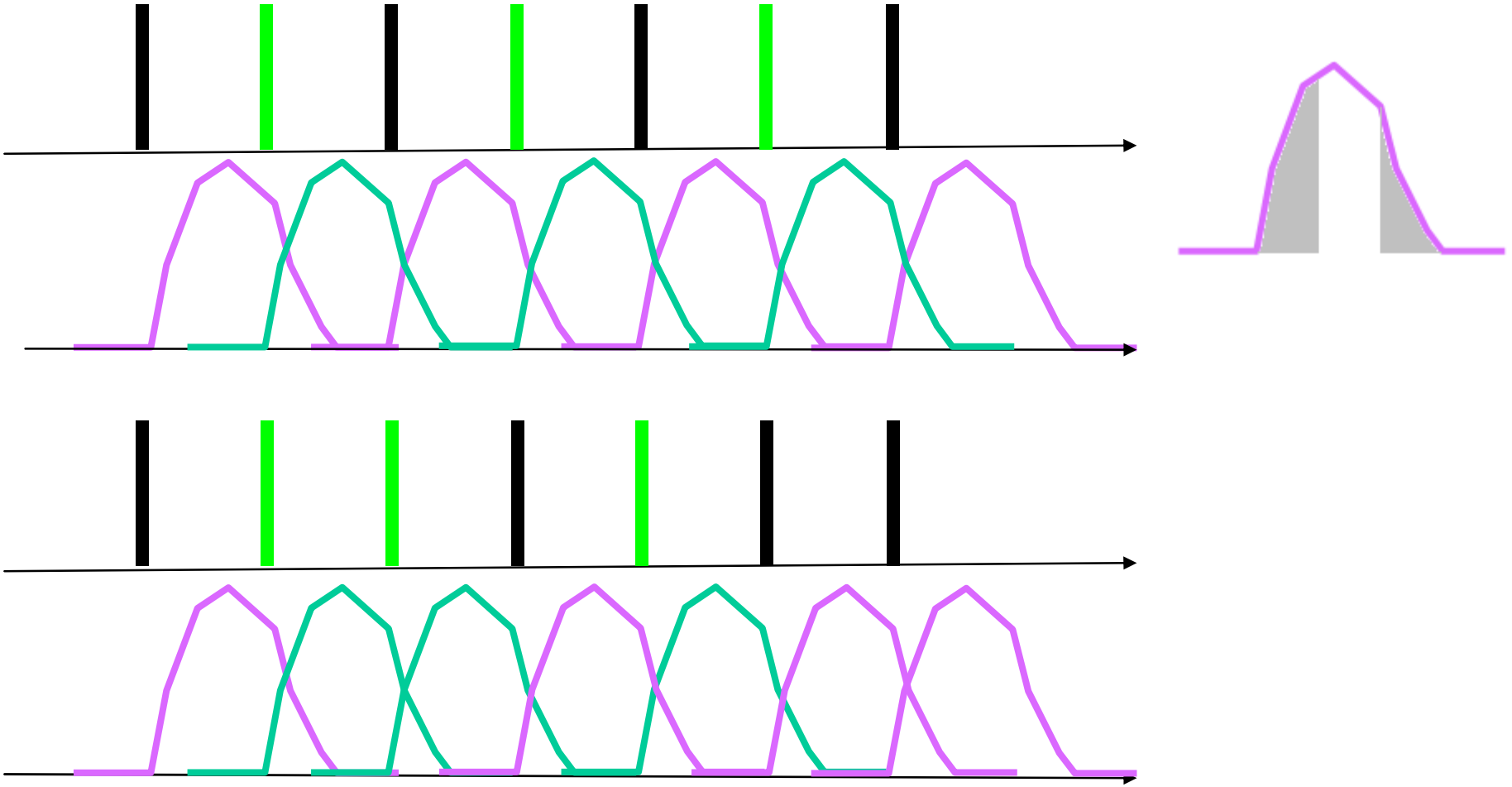


Intuitive approach



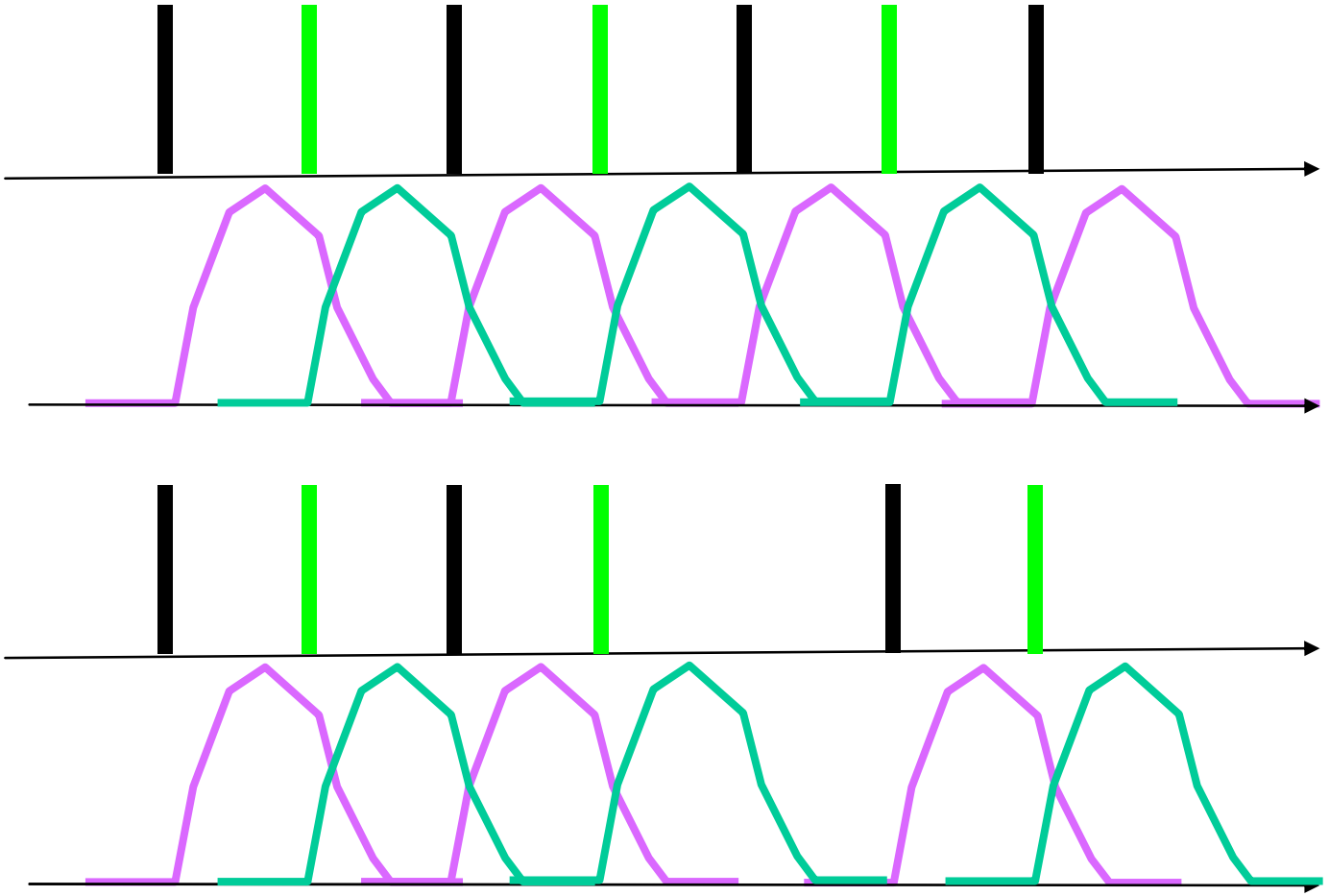
Jittering with respect to acquisition time allows better characterization of the BOLD response

Intuitive approach



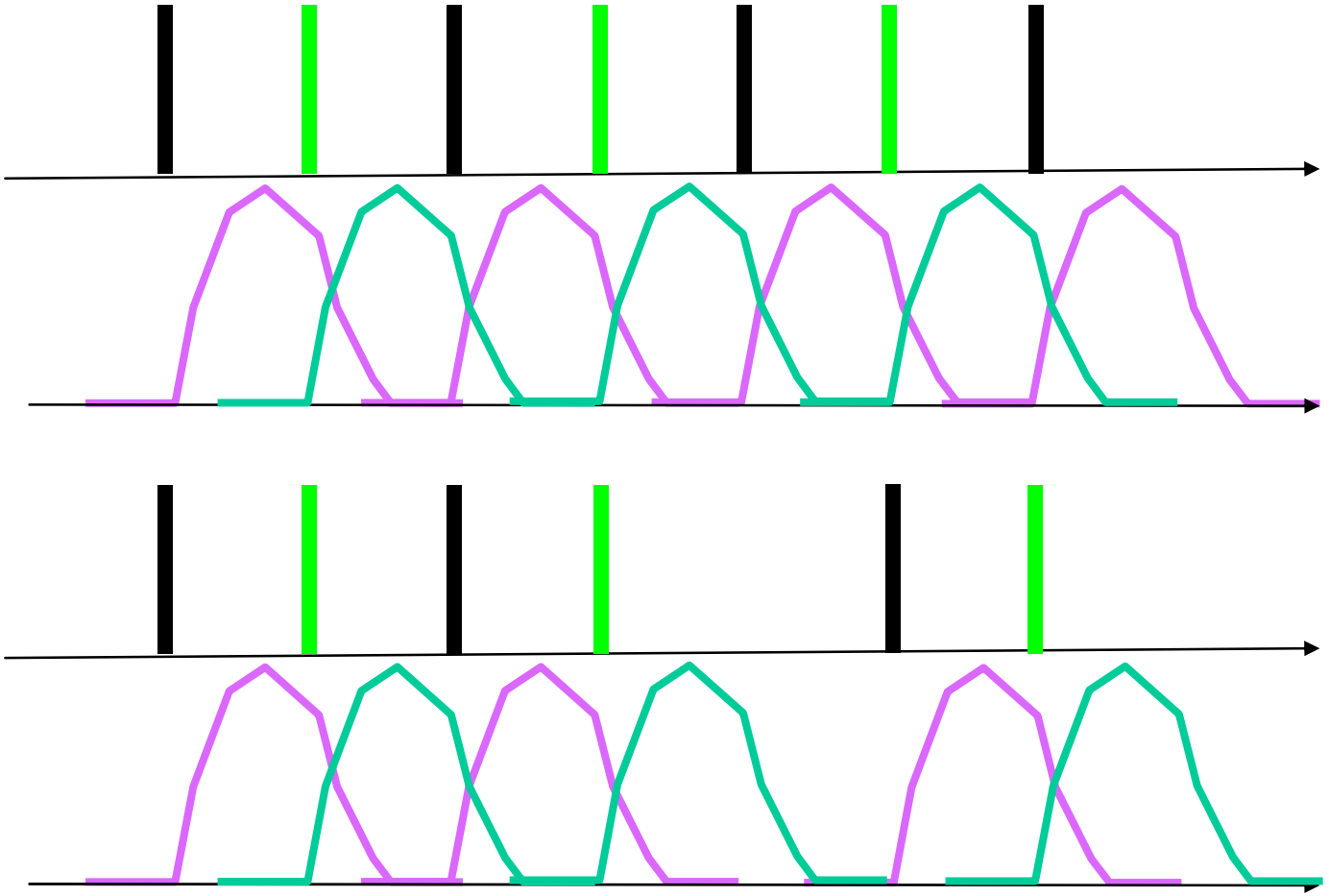
Changing the order of conditions allows us to deal with overlap in BOLD responses

'Null' events



Adding 'null' events creates a jitter and diminishes overlap between BOLD responses

Intuitive approach



Jittering and randomizing conditions is even better

Different types of event-related designs

So far, we looked at three possibilities to improve our quantification of the evoked hrf

- jittering with response to acquisition time
- randomizing conditions
- adding ‘null’ events, jittering time between different events

Of course, all these approaches can be combined!

....

What constitutes a ‘good’ design?

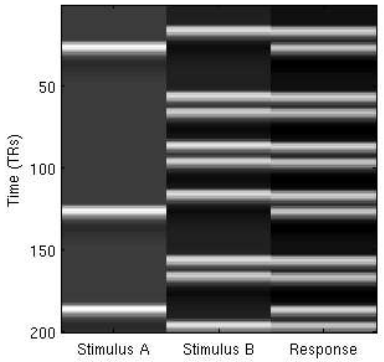
Now, we need to find some sort of formal definition of when our design is ‘good’

A number of authors have suggested measures of ‘estimability’ of contrasts, i.e., of a way to *quantify whether a particular response can be detected if it present in the data* (Dale, 1999; Liu et al., 2001; Smith et al., 2007)

Several software tools have been developed to help determine these various measure of estimability (Dale, 1999; Wager and Nichols, 2003; SPM hacks; Smith et al., 2007)

T contrast

$$Y = X\beta + e$$



c = [1 -1 0]

$$T = \frac{c' \times b}{\sqrt{\mathrm{var}(c' \times b)}}$$

Contrast estimability

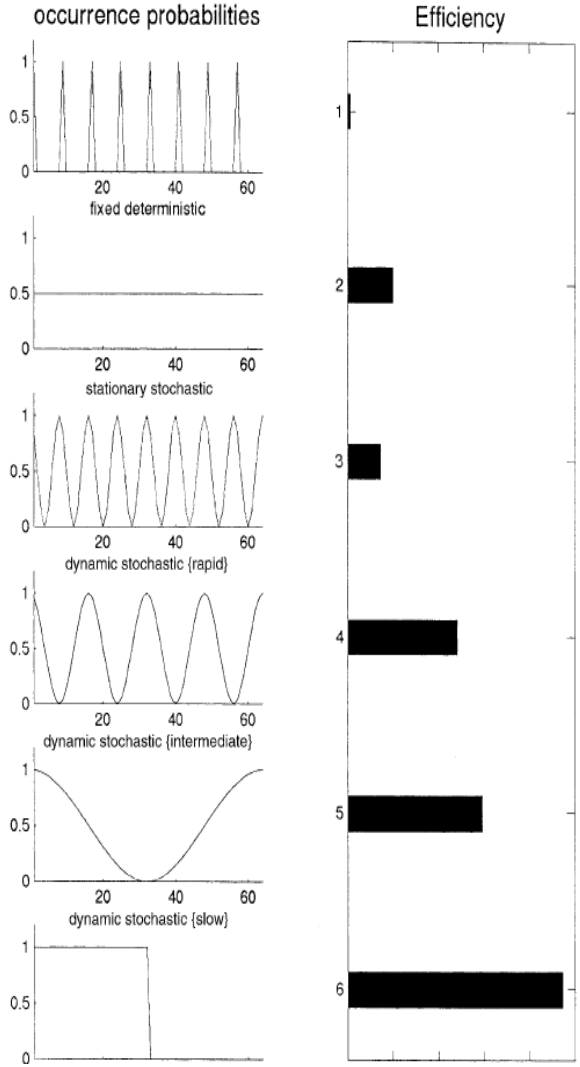
Some maths…

$$T = \frac{c' \times b}{\sqrt{\mathrm{var}(c' \times b)}}$$ } this we want to minimize

this we can play with

$$\mathrm{var}(c' \times b) = \sigma^2 c' (X' X)^{-1} c$$

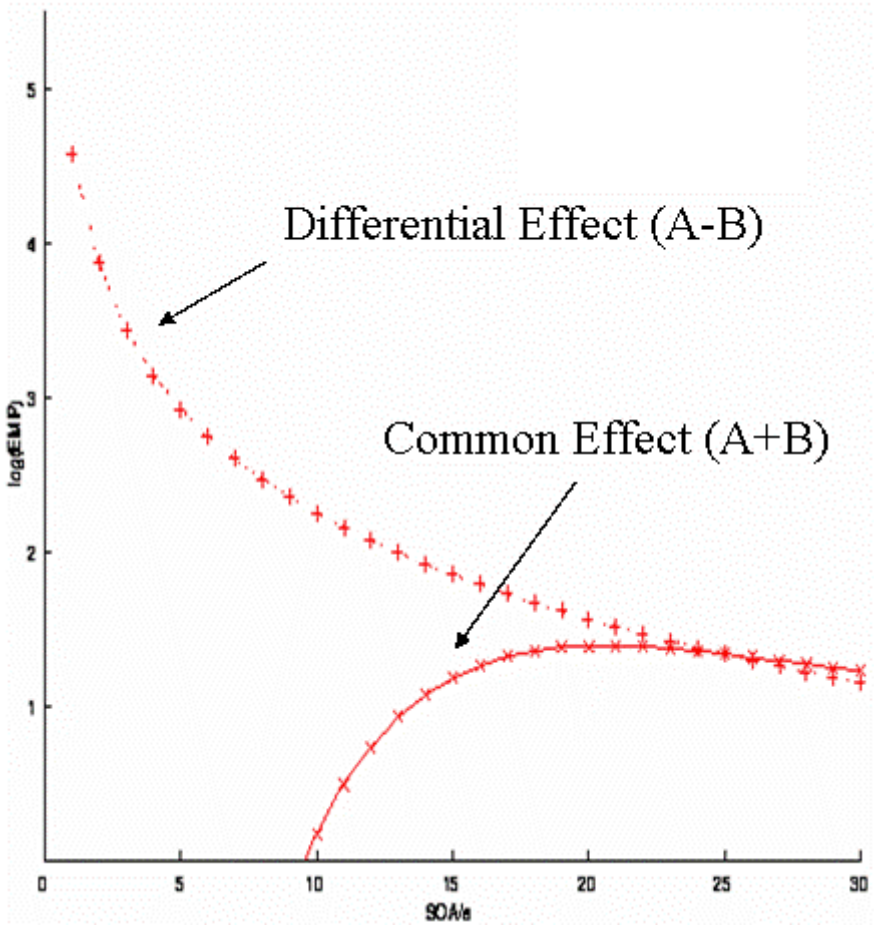
$$e(c, X) = trace(c' (X' X)^{-1} c)^{-1}$$



Friston 1999; Henson website

Not all contrasts have the same efficiency

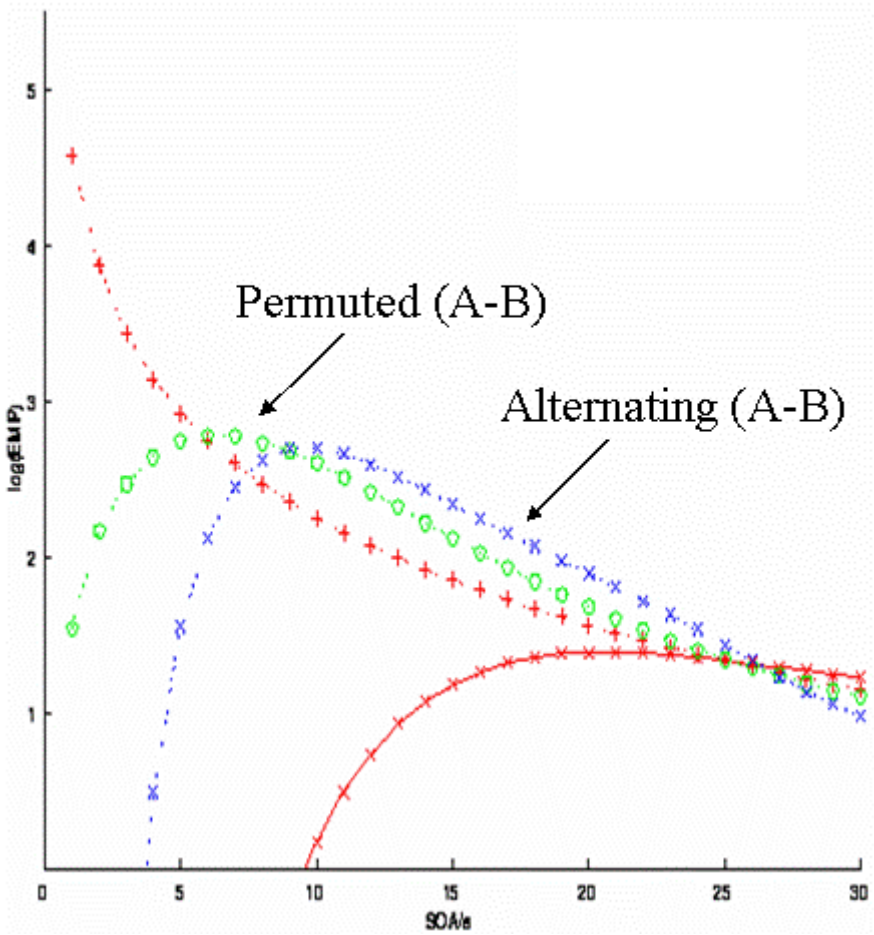
	A	B
A	0.5	0.5
B	0.5	0.5



Henson website

Not all contrasts have the same efficiency

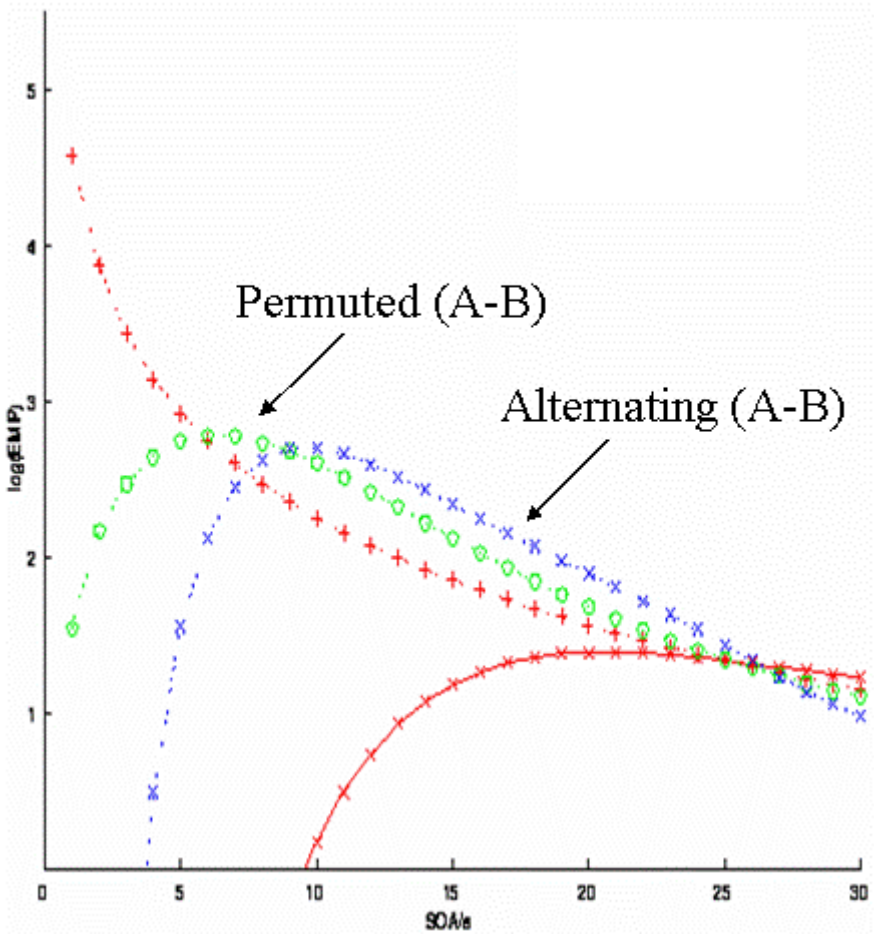
	A	B
A	0	1
B	1	0



Henson website

Not all contrasts have the same efficiency

	A	B
AA	0	1
AB	0.5	0.5
BA	0.5	0.5
BB	1	0

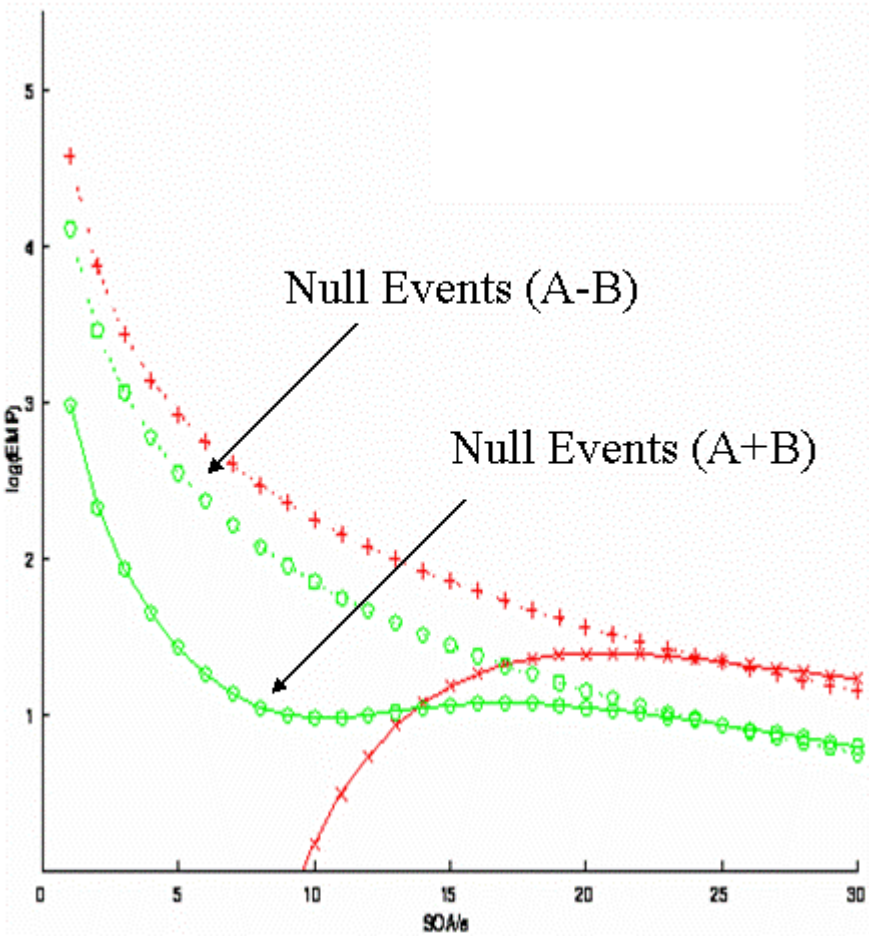


Henson website

Not all contrasts have the same efficiency

	A	B
A	0.5	0.5
B	0.5	0.5

	A	B
A	0.33	0.33
B	0.33	0.33

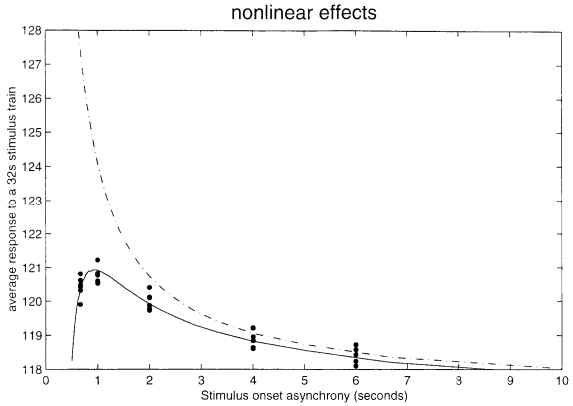


Henson website

Not all contrasts have the same efficiency

What if we overlay BOLD responses?

- Reasonable linearity may be expected for ITIs > 2 sec
- BOLD response saturates at high levels

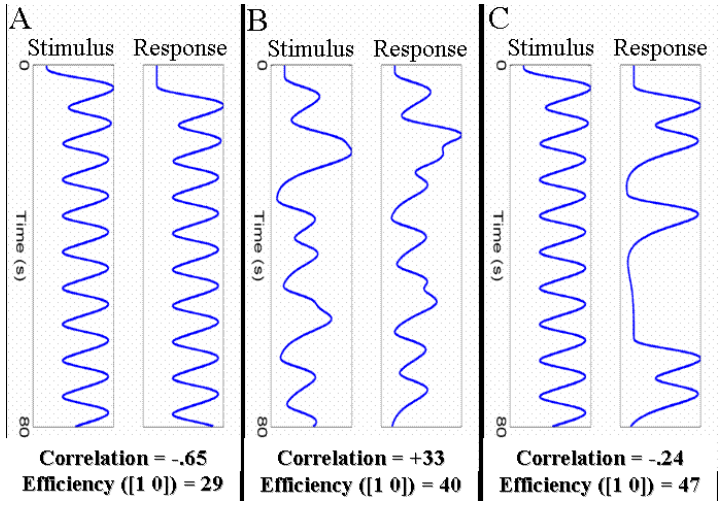


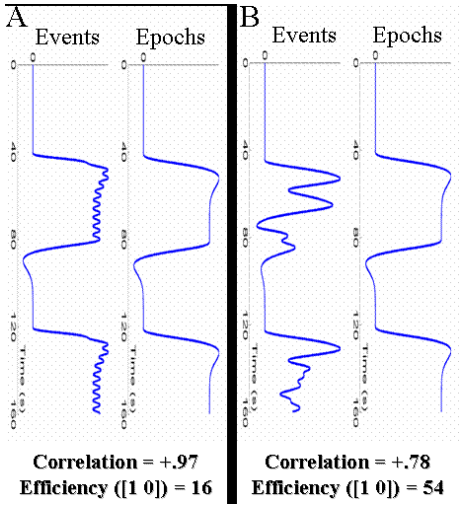
Henson website

Efficiency and correlation between regressors

$$e(c, X) = trace(c'(X'X)^{-1}c)^{-1}$$

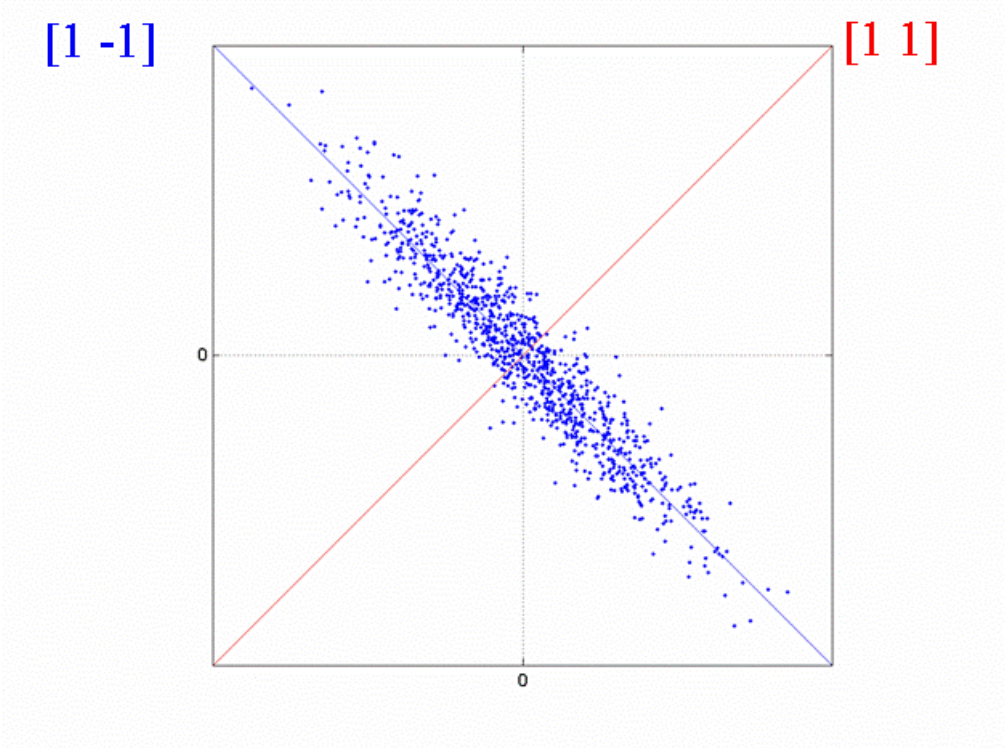
Correlation between regressors





Henson website

Not all contrasts have the same efficiency



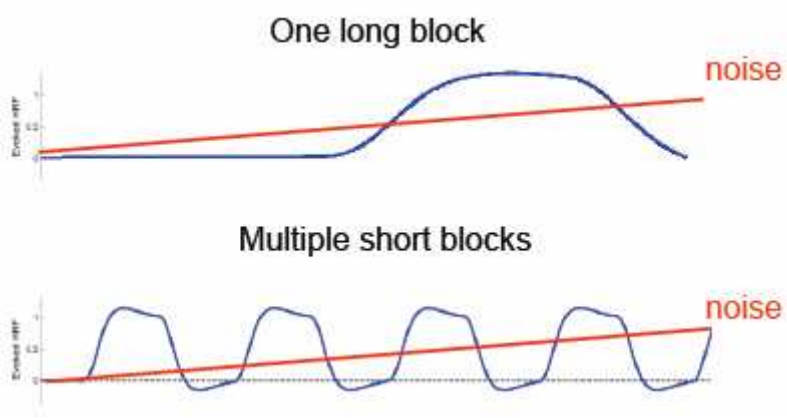
Different contrasts can have different efficiency even within the same design matrix

Henson website

Filtering

Before analyzing your fMRI data, you usually apply a highpass filter, to remove low frequency confounds, such as scanner drifts.

This creates some problems for designs in which trials that are place too far apart are contrasted



For the same reason, it is wise not to make the blocks of a blocked design experiment too long. Usually, blocks should be kept <30 seconds, with about 16 seconds considered optimal

Software tools

Optimal experimental design and toolboxes:

- SPM hack (allows you to evaluate designs in Matlab)
- Smith et al (2007) NeuroImage 34:127-136 (implemented in FSL)
- Optseq2 (http://surfer.nmr.mgh.harvard.edu/optseq/)
- Genetic algorithm (Wager, Nichols (2003) NeuroImage 19:293-309)
- M-sequences (Buracas, Boynton (2002) NeuroImage 16:801-813)

Summary of the first half

Optimal experimental design:

• Requires careful thinking about your experiment *before* you start scanning

• Needs to overcome a number of signal processing problems, mostly related to the nature of the BOLD response

• Maximizes the efficiency of the contrast of interest

• Is always a compromise

• Is fun!

Overview of second half of the talk

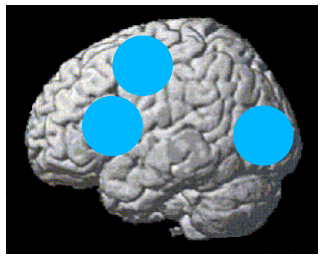
- Some general issues
- Different basic designs: subtraction, factorial, parametric
- Using model-based analyses
- Examples

The subtraction technique

In order to address the temporal insensitivity of the BOLD response, many authors have employed a subtraction technique to investigate the neural processes associated with certain cognitive aspects

Stimulus identification
Decision making
Button press

A+B



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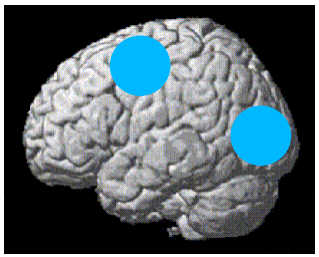
Stimulus identification

Button press

A



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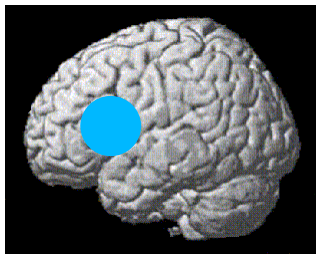
Decision making

B



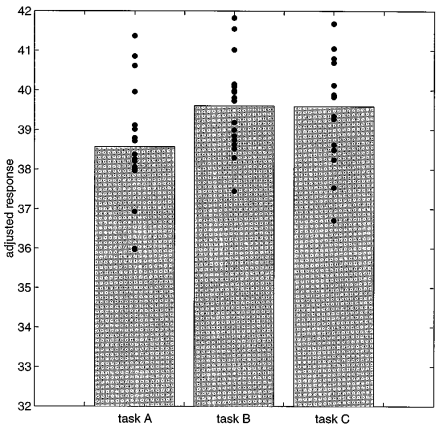
This approach assumes that a cognitive component of interest evokes an ‘additional’ neural activation

The trouble with cognitive subtraction

Is inferotemporal cortex involved in phonological retrieval during object naming?

- saying ‘yes’ when viewing colored shape (*visual, speech*)
- saying ‘yes’ when viewing colored object (*visual, speech, obj recognition*)
- naming viewed colored object (*visual, speech, obj recognition, phonological retrieval*)

Subtraction approach



Conclusion of the subtraction approach:

Inferotemporal cortex is not involved in phonological retrieval during object naming

But: this conclusion assumes that activity due to object naming is the same in both the presence and absence of phonological retrieval

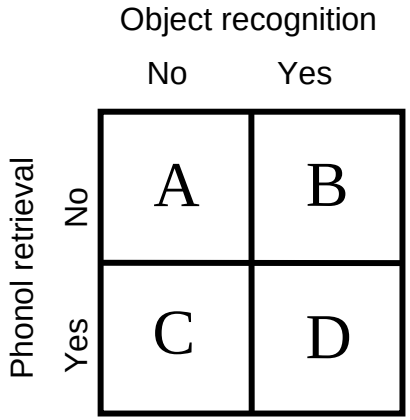
The subtraction technique relies on the assumption of *pure insertion*, i.e., the assumption that when a new cognitive component is added to the task, the implementation of previous remain unaffected

Friston 1996

Solution: Factorial design

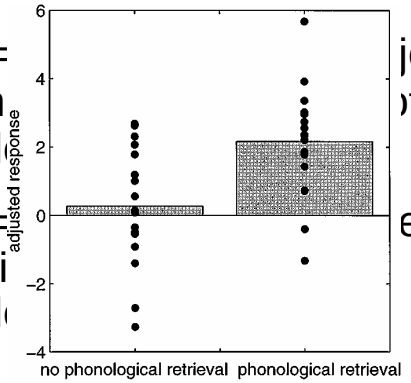
Is inferotemporal cortex involved in phonological retrieval during object naming?

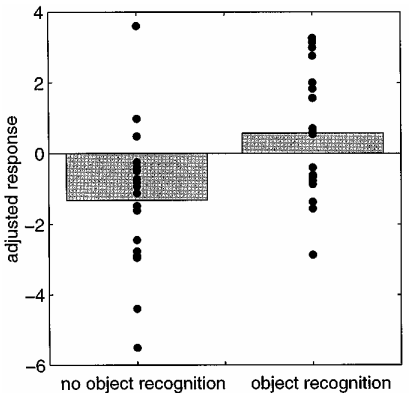
- saying ‘yes’ when viewing colored shape (*visual, speech*)
- saying ‘yes’ when viewing colored object (*visual, speech, obj recognition*)
- naming viewed colored object (*visual, speech, obj recognition, phonological retrieval*)
- naming color of presented shape (*visual, speech, phonological retrieval*)



B – A = ject recogn of phonol

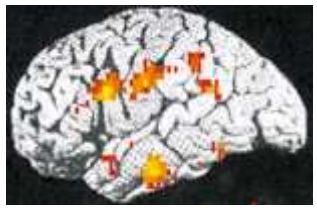
C – D = ent activati phonol





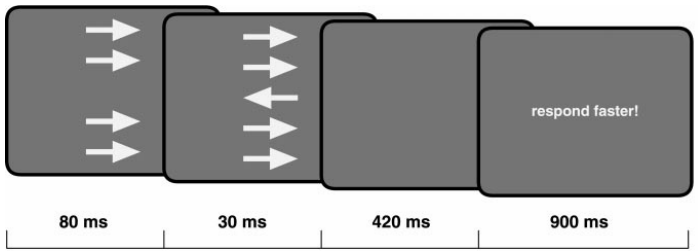
Main effect obj recogn

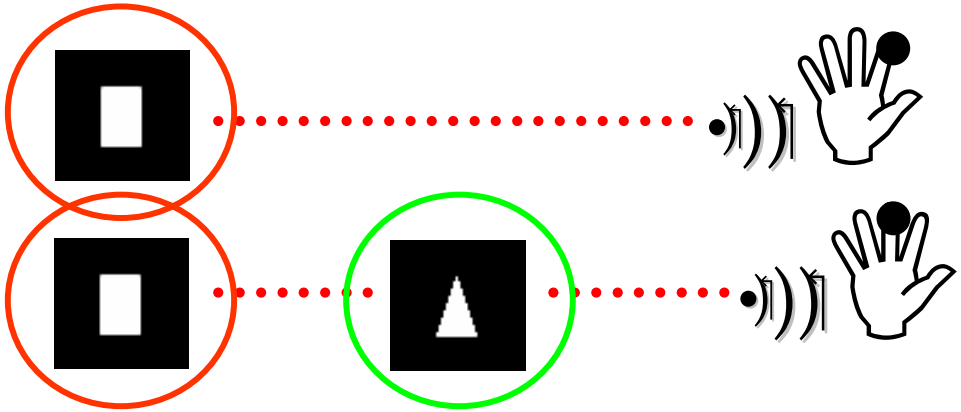
Main effect phon retriev

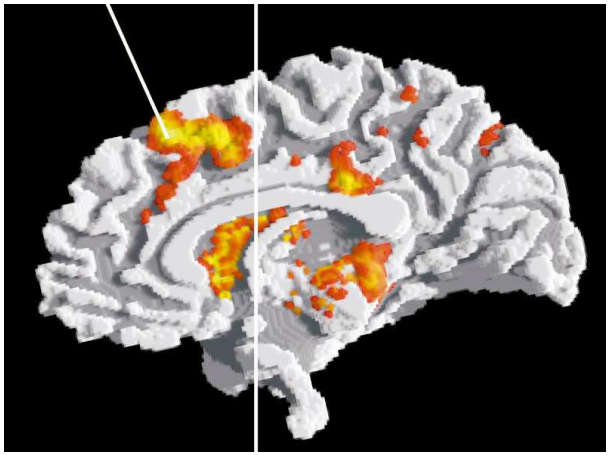


Interaction

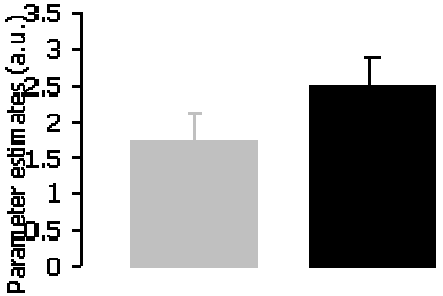
Solution: Separating events in time







Pre-SMA [0 8 52]

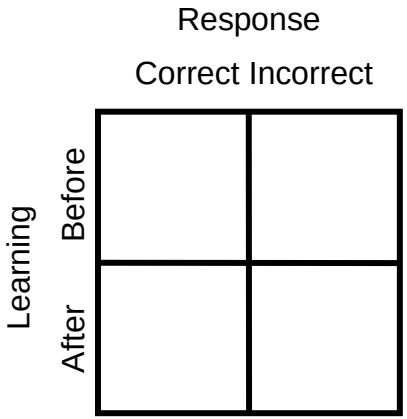


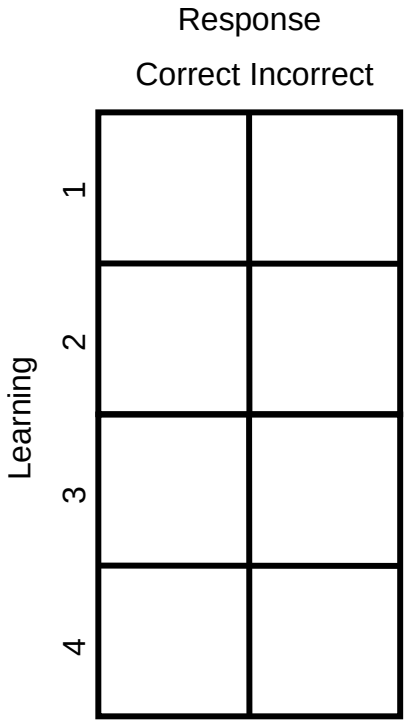
There is nothing wrong is *comparing* activity in one region between conditions, but there is a problem with using subtraction to *isolate* neural processes

Mars 2007

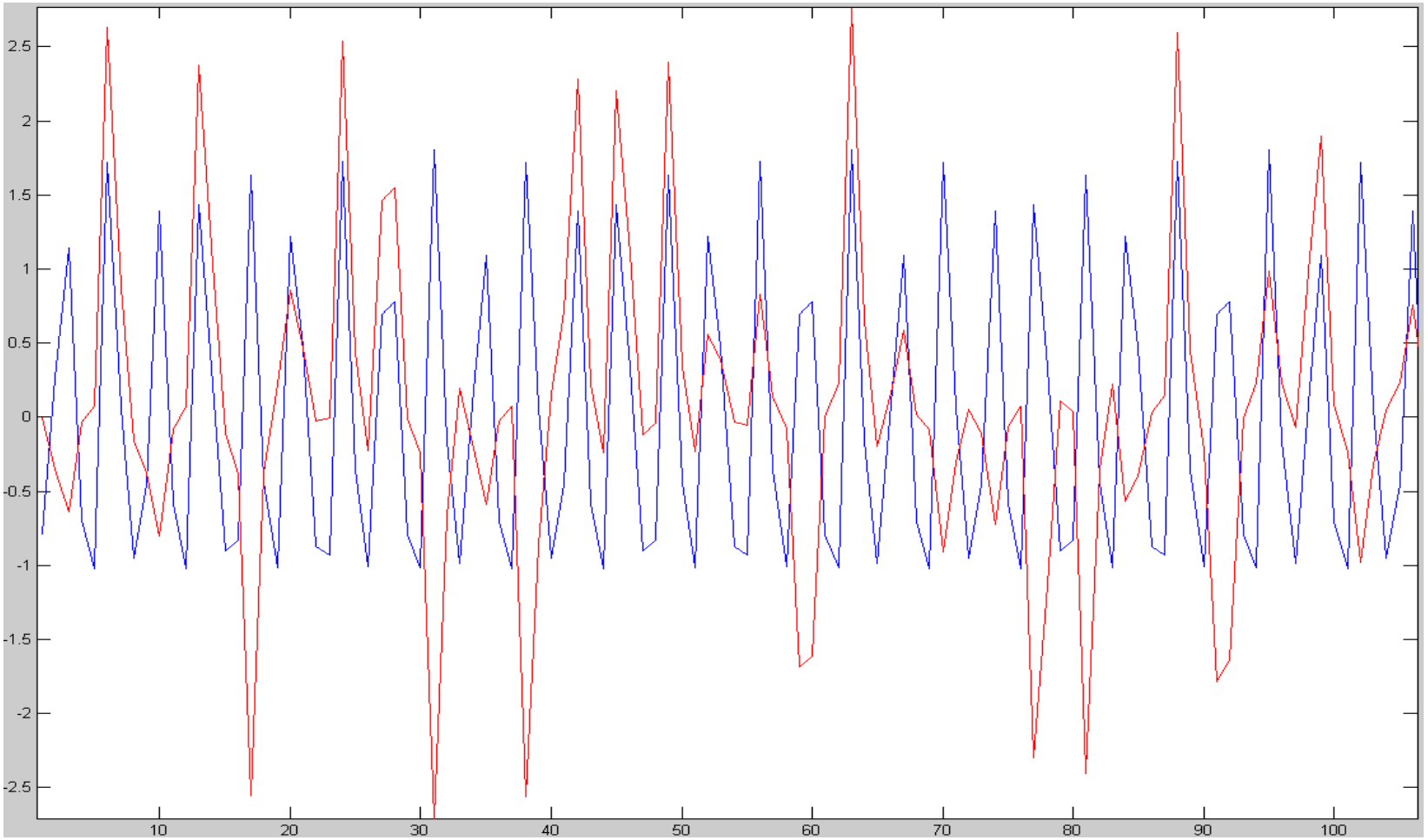
Parametric designs

Parametric designs treat cognitive components as dimensions rather than as categories



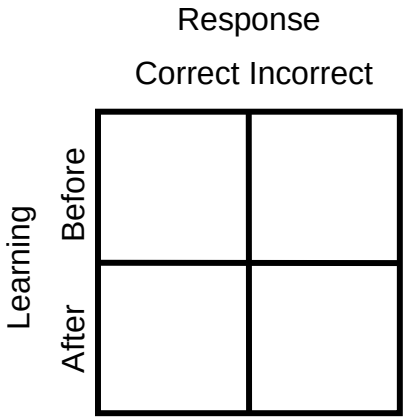


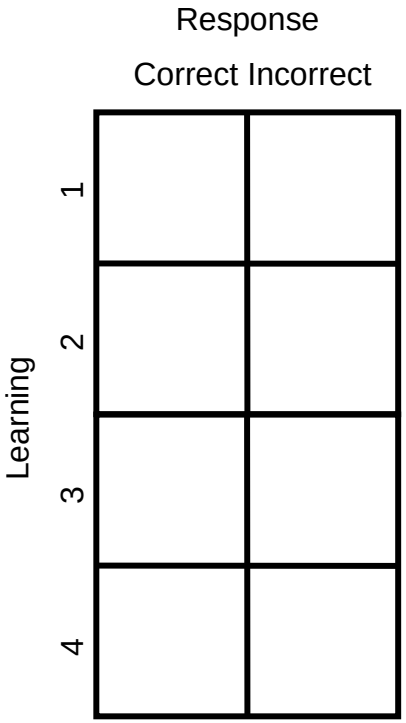
Parametric designs

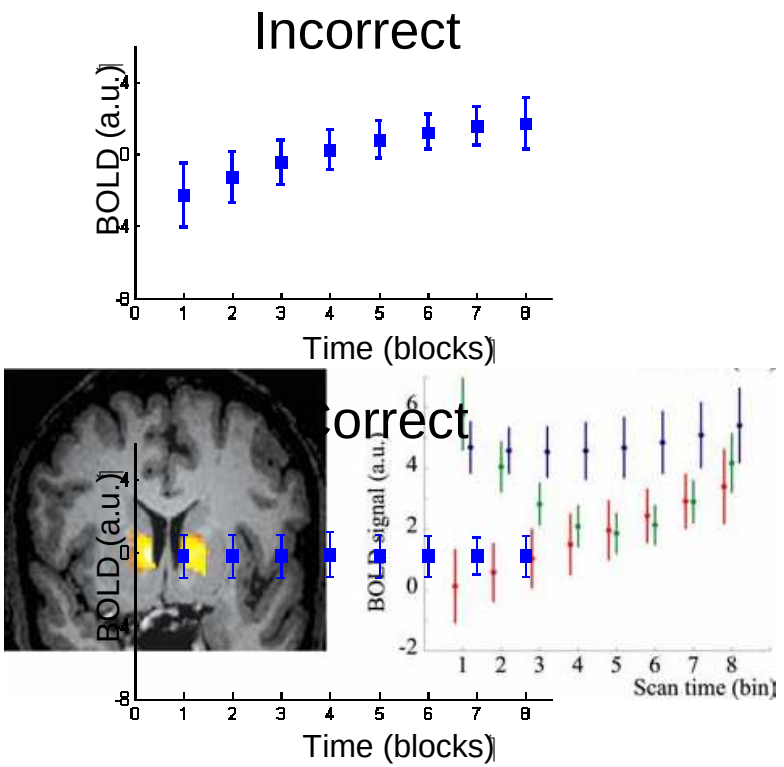


Parametric designs

Parametric designs treat cognitive components as dimensions rather than as categories



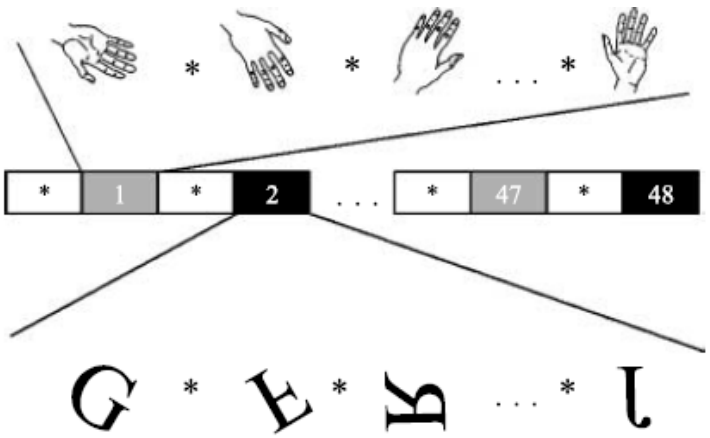


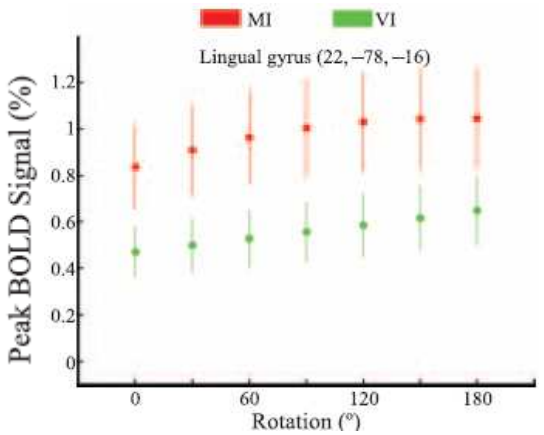


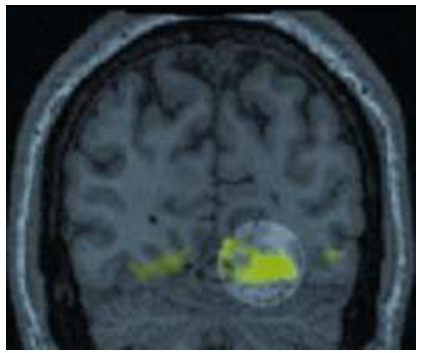
Mars 2005; Grol 2006

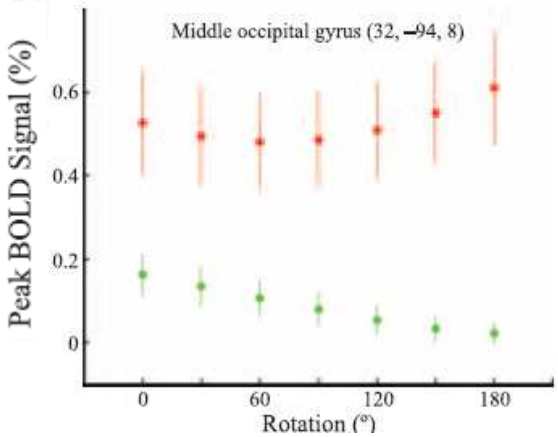
Example: De Lange 2005

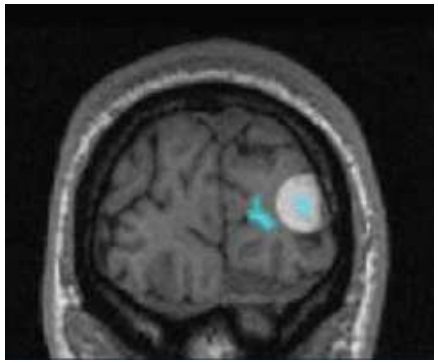
Which regions are implicated in movement representations and how are they implicated?







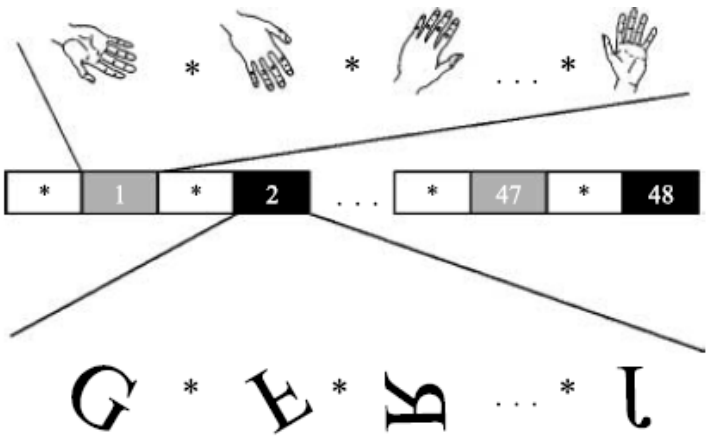


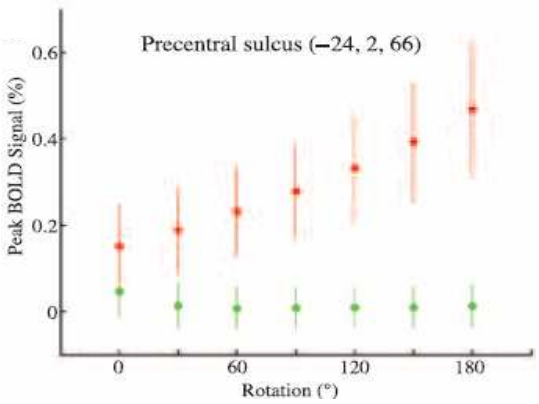


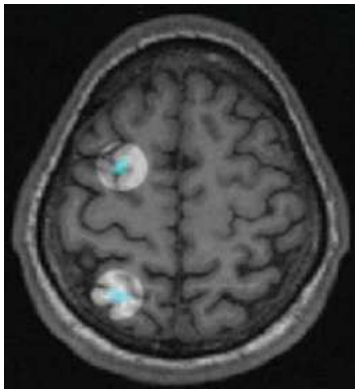
De Lange 2005

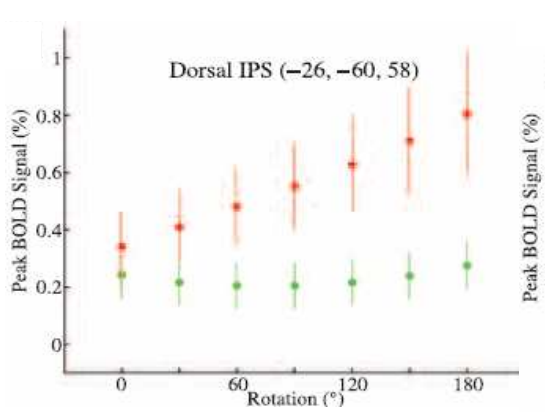
Example: De Lange 2005

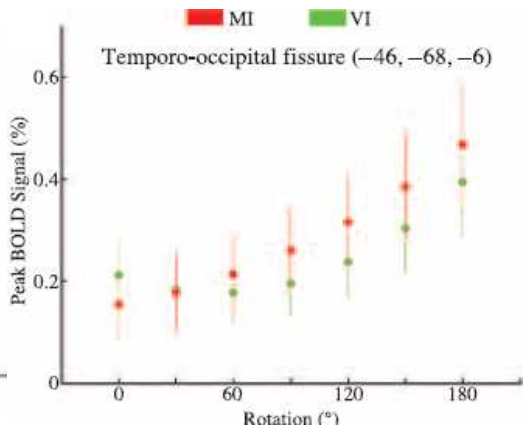
Which regions are implicated in movement representations and how are they implicated?







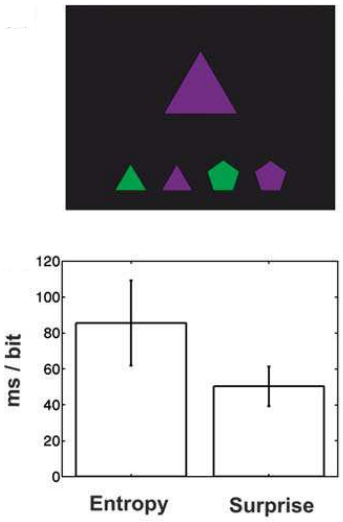


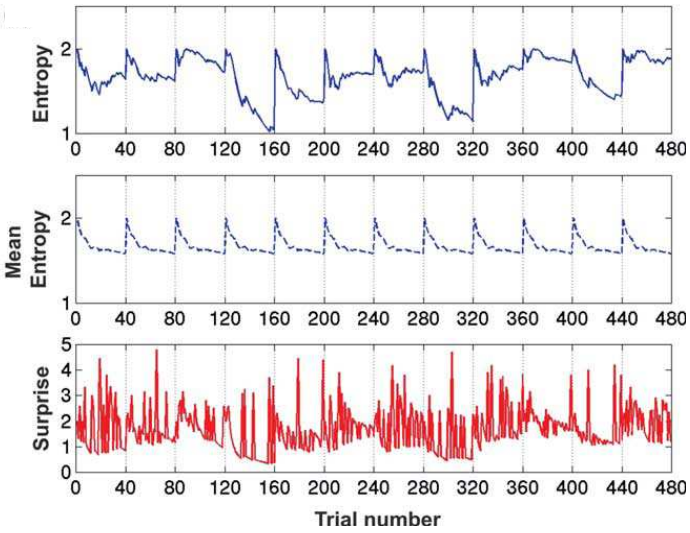


De Lange 2005

Parametric designs: Model-based analysis

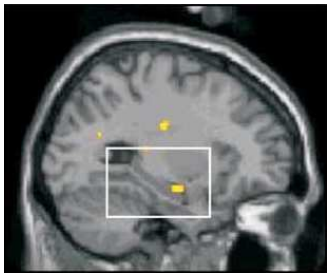
Rather than comparing activity in two or more conditions, regressors based on computational models allow for the detection of signals related to variables internal to the participant. Using computational models one can generate a predictor of the variance explained by such a process (cf. Corrado and Doya 2007)

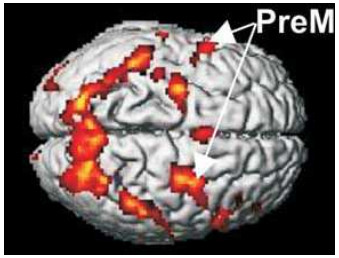




$$H(X) = \sum_{i=1}^{j} - p(x_i) \log p(x_i)$$

$$h(x_i) = -\log p(x_i)$$

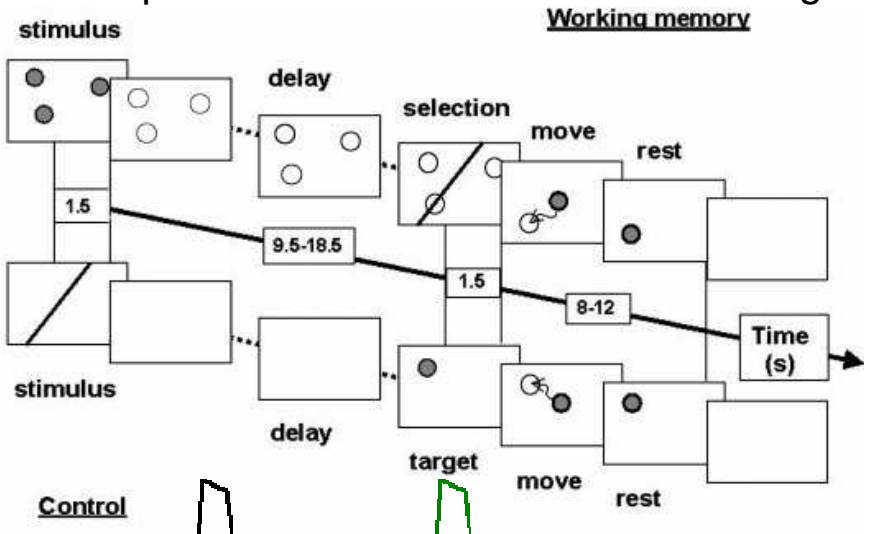




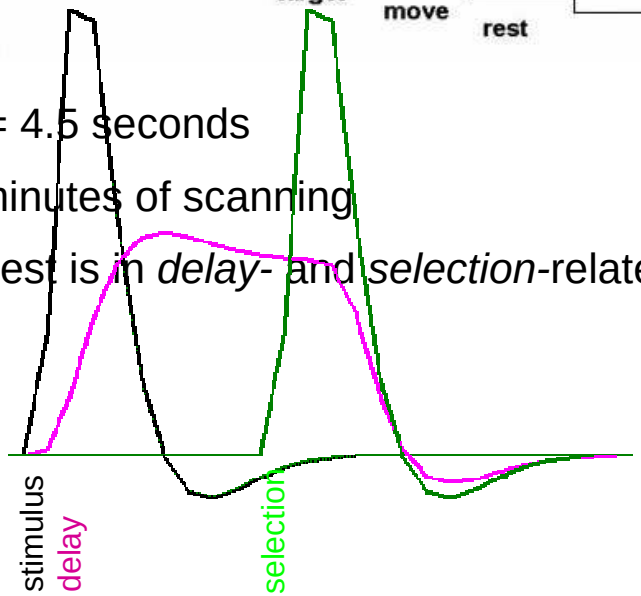
Strange 2005

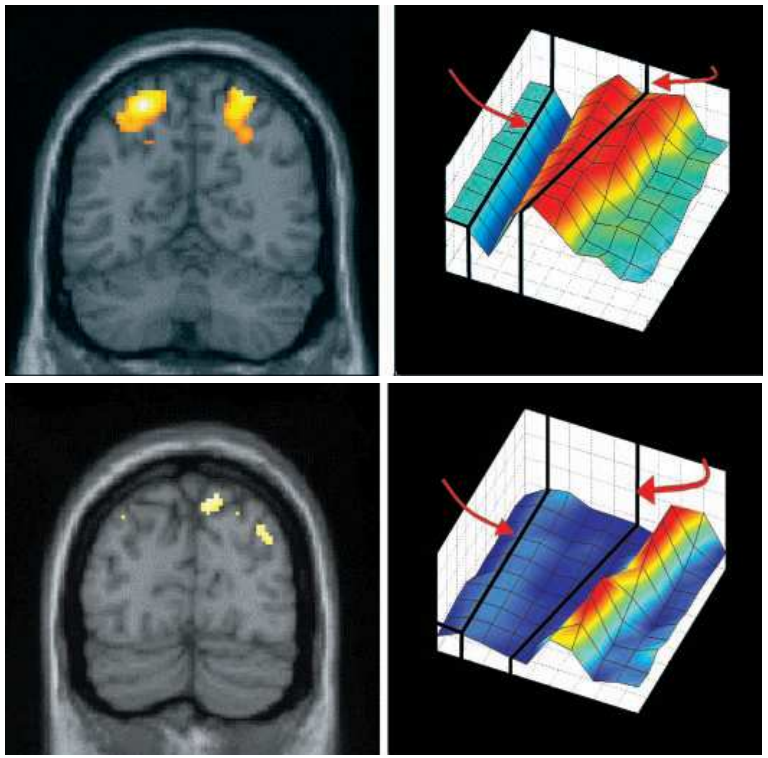
Example: Rowe et al (2000, Science)

Is the prefrontal cortex involved in working memory *maintenance* or *selection* from memory?



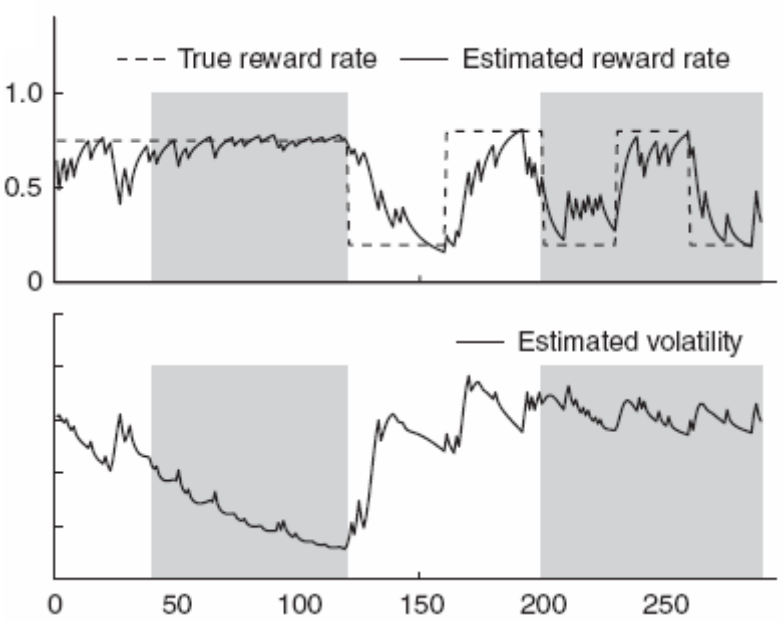
- TR = 4.5 seconds
- 40 minutes of scanning
- Interest is in *delay*- and *selection*-related activity

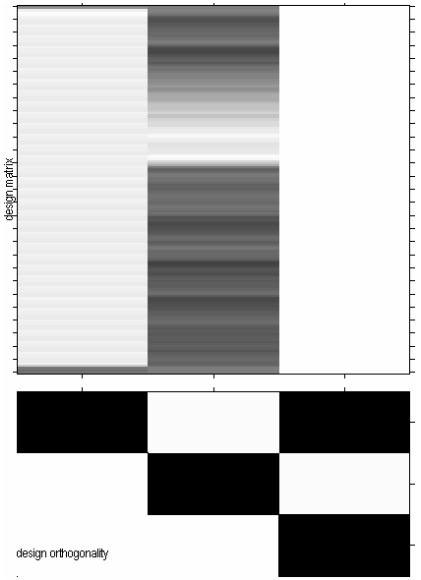


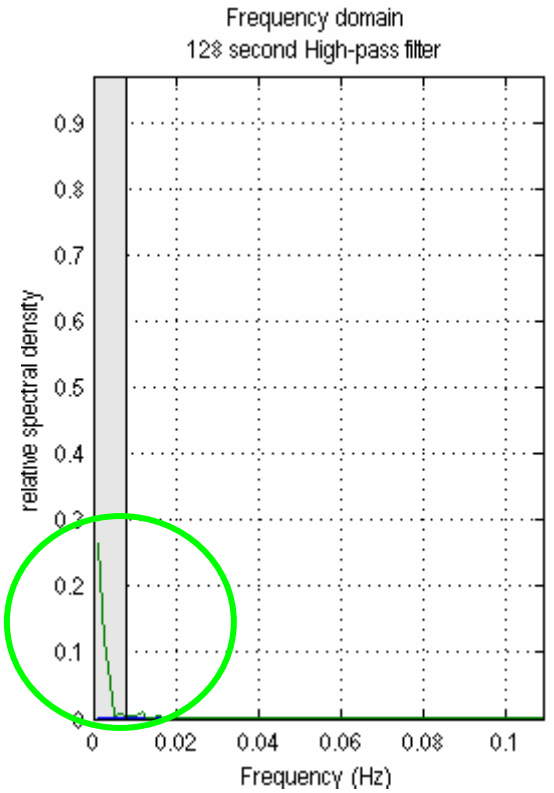


Rowe 2000

Example: Behrens et al (2007, Nat Neurosci)



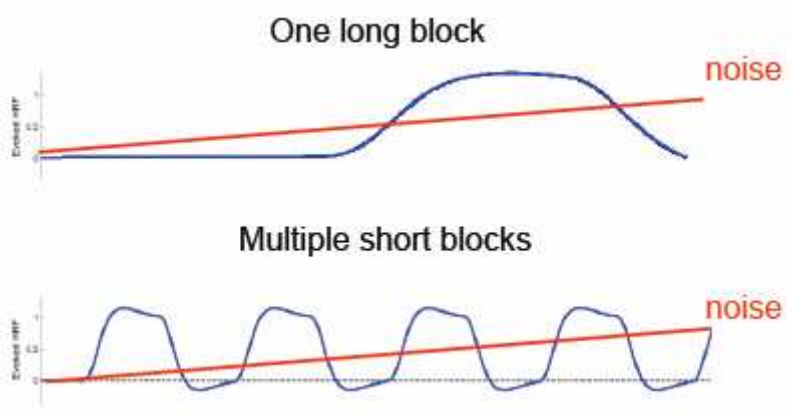




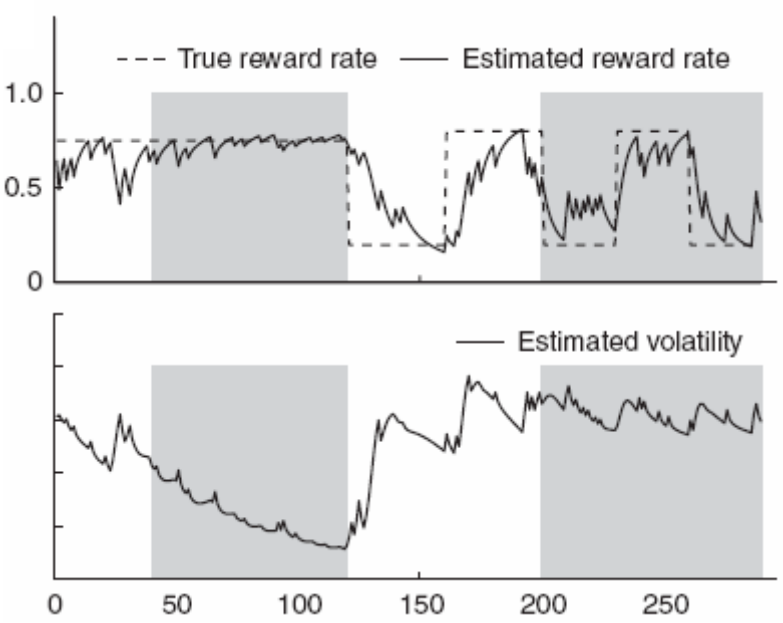
Regressor 1: stimulus

Regressor 2: parametric modulation volatility

Filtering



Example: Behrens et al (2007, Nat Neurosci)



Regressor 1: decide

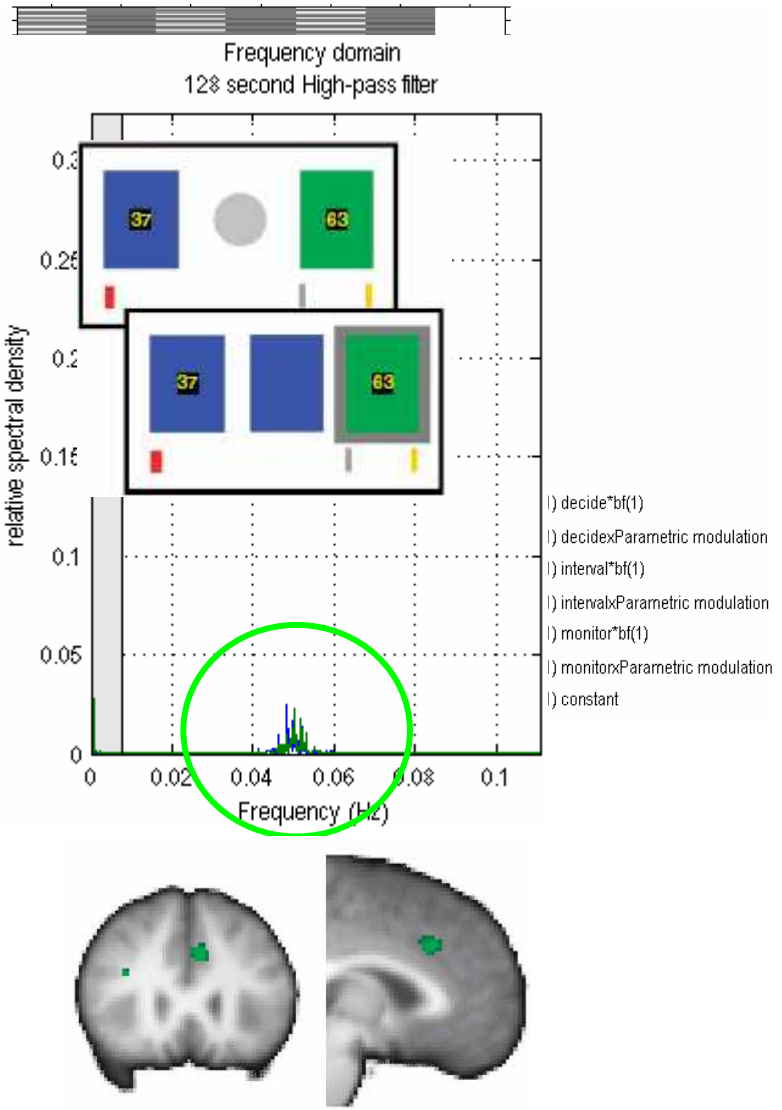
Regressor 2: decide×volatility

Regressor 3: interval

Regressor 4: interval×volatility

Regressor 5: monitor

Regressor 6: monitor×volatility



Papers mentioned in this talk

General papers on event-related fMRI:

- Josephs 1999 — Josephs, Henson (1999) Phil Trans R Soc B 354:1215-1228

Modelling the BOLD response:

- Friston 1998 — Friston et al. (1998) NeuroImage 7:30-40

Optimal experimental design:

- Henson homepage — http://imaging.mrc-cbu.cam.ac.uk/imaging/DesignEfficiency
- Friston 1999 — Friston et al (1999) NeuroImage 10:607-619
- Smith 2007 — Smith et al (2007) NeuroImage 34:127-136

Toolboxes:

- SPM hack/FSL
- Optseq2 — http://surfer.nmr.mgh.harvard.edu/optseq/
- Genetic algorithm — Wager, Nichols (2003) NeuroImage 19:293-309
- M-sequences — Buracas, Boynton (2002) NeuroImage 16:801-813

Design approaches:

- Friston 1996 — Friston et al (1996) NeuroImage 4:97-104

Papers mentioned in this talk

Examples:

• Behrens 2007	Behrens et al. (2007) Nat Neurosci 10:1214-1221
• Corrado 2007	Corrado, Doya (2007) J Neurosci 27:8178-8180
• De Lange 2005	De Lange et al (2005) J Cogn Neurosci 17:97-112
• Grol 2006	Grol et al. (2006) J Neurosci 26:117-125
• Mars 2005	Mars et al. (2005) NeuroImage 28:1007-1013
• Mars 2007	Mars et al. (2007) Cereb Cortex 17:2972-2979
• Rowe 2000	Rowe et al. (2000) Science 288:1656-1660
• Strange 2005	Strange et al. (2005) Neural Netw 18:225-230