

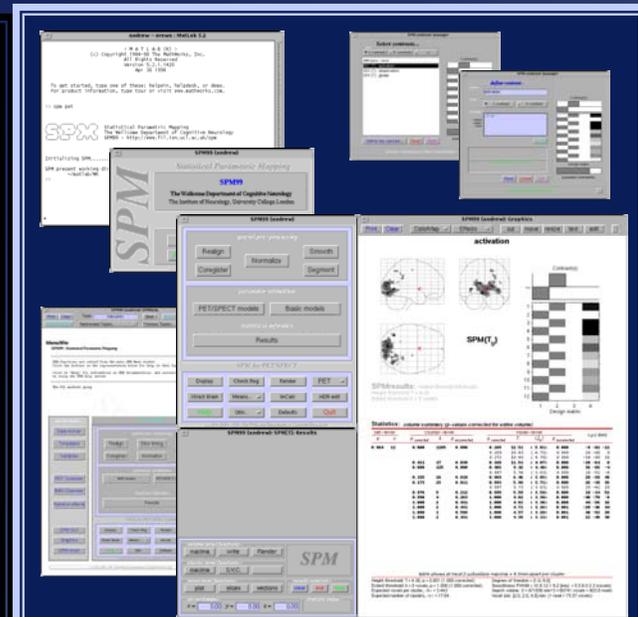
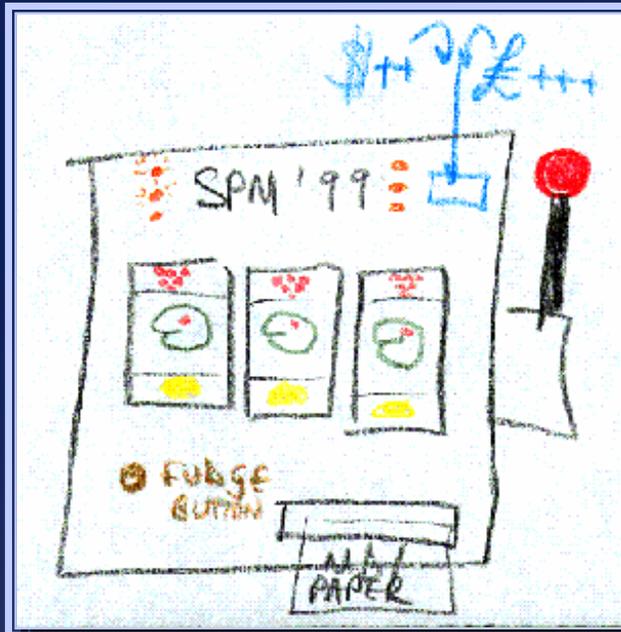
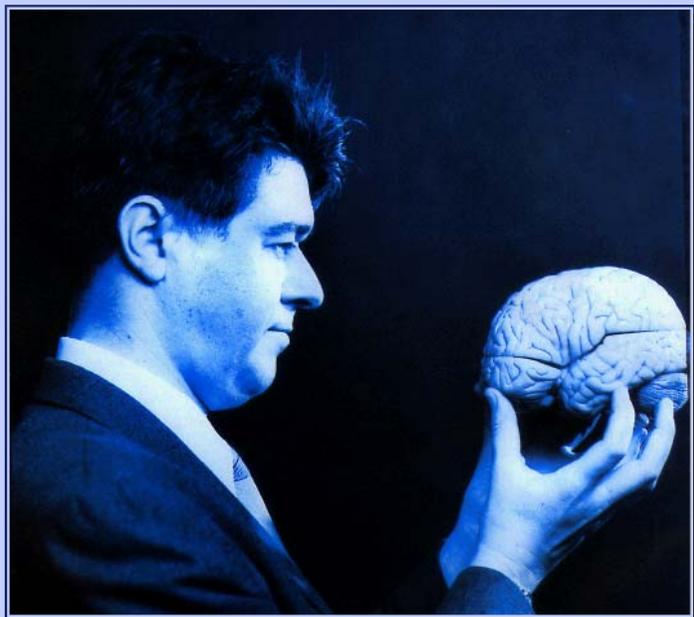


Experimental Design



Rik Henson

With thanks to:
Karl Friston, Andrew Holmes



Overview

1. A Taxonomy of Designs
2. Epoch vs Event-related
3. Mixed Epoch/Event Designs

A taxonomy of design

- Categorical designs

 - Subtraction

 - Additive factors and pure insertion

 - Conjunction

 - Testing multiple hypotheses

- Parametric designs

 - Linear

 - Cognitive components and dimensions

 - Nonlinear

 - Polynomial expansions

- Factorial designs

 - Categorical

 - Interactions and pure insertion

 - Adaptation, modulation and dual-task inference

 - Parametric

 - Linear and nonlinear interactions

 - Psychophysiological Interactions

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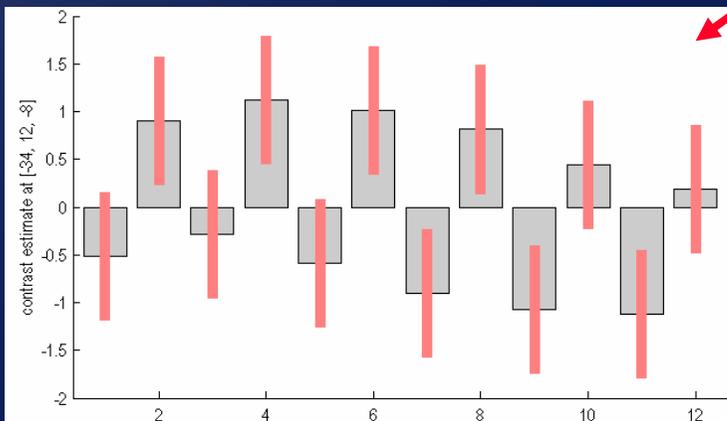
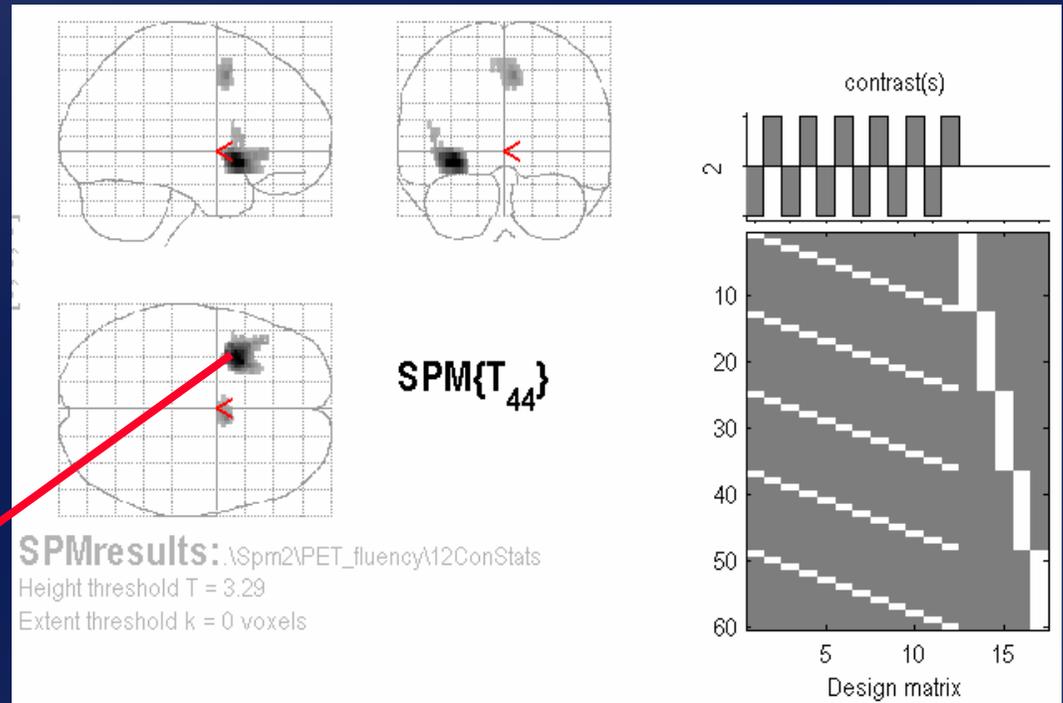
A categorical analysis

Experimental design

Word generation G

Word repetition R

R G R G R G R G R G



G - R = Intrinsic word generation

...under assumption of pure insertion,
ie, that G and R do not differ in other ways

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Cognitive Conjunctions

- One way to minimise problem of pure insertion is to isolate same process in several different ways (ie, multiple subtractions of different conditions)

Visual Processing	V
Object Recognition	R
Phonological Retrieval	P
Object viewing	R,V
Colour viewing	V
Object naming	P,R,V
Colour naming	P,V

$$\begin{aligned} &(\text{Object - Colour viewing}) \quad [1 \ -1 \ 0 \ 0] \\ &\quad \& \\ &(\text{Object - Colour naming}) \quad [0 \ 0 \ 1 \ -1] \end{aligned}$$

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

(assuming $R \times P = 0$; see later)

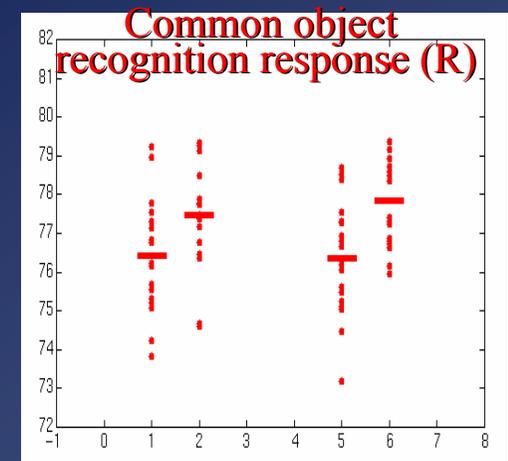
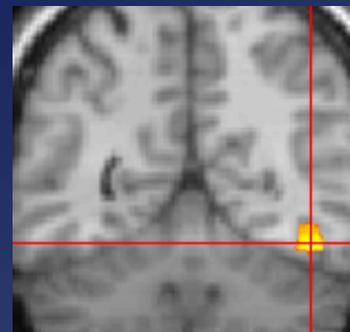
Task (1/2)

Viewing Naming

A1	A2
B1	B2

Stimuli (A/B)
Objects Colours

Price et al, 1997



Cognitive Conjunctions

SPM contrast manager

Select contrasts...

<how>

t-contrasts F-contrasts all

{type} : name

002 {T} : A1 - A2

003 {T} : B1 - B2

contrast(s)

Design matrix

parameter estimability

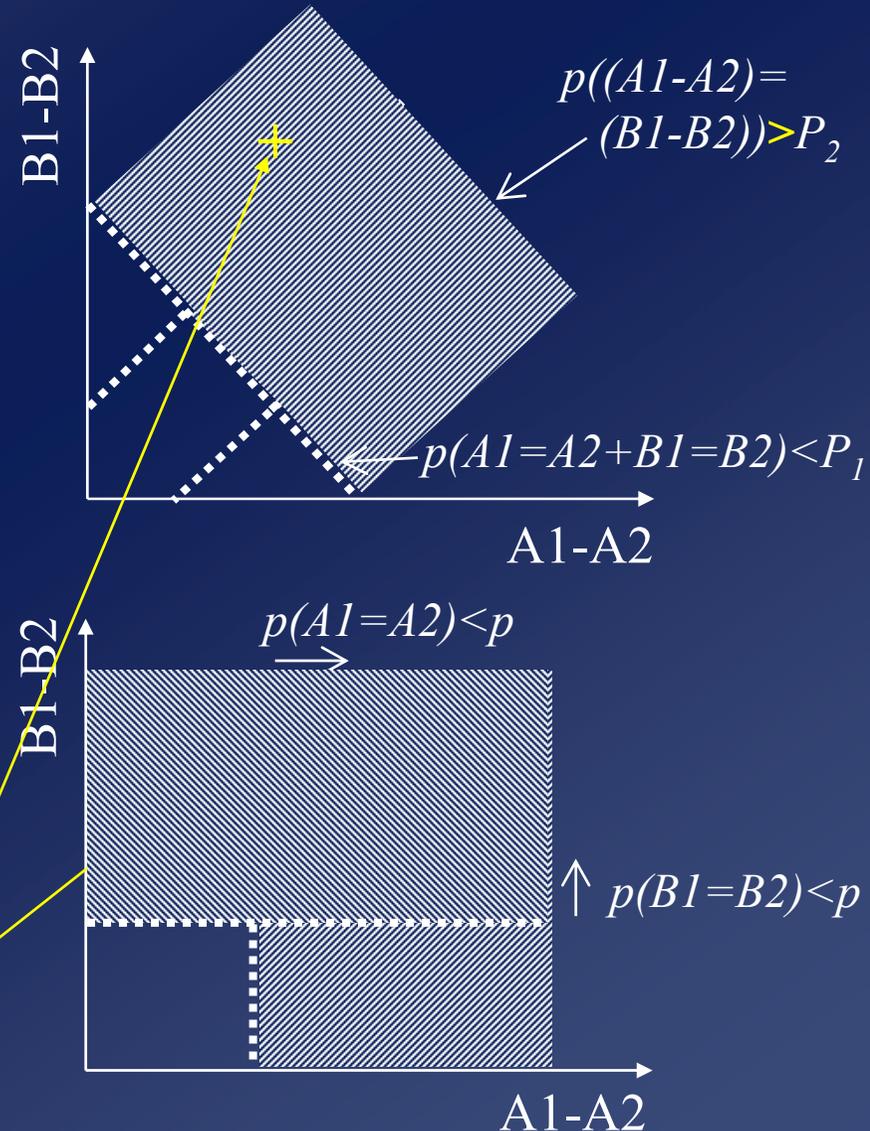
Define new contrast... Reset Done

Selected 2 contrasts for conjunction, press "Done" when finished. ?

Detailed description: The image shows a screenshot of the 'SPM contrast manager' software window. The window title is 'SPM contrast manager'. The main area is titled 'Select contrasts...'. At the top left, there are three radio buttons: 't-contrasts' (selected), 'F-contrasts', and 'all'. Below this is a list box containing two entries: '002 {T} : A1 - A2' and '003 {T} : B1 - B2'. To the right of the list box is a 'contrast(s)' section with a grid of gray and white squares representing the design matrix. Below the grid is a 'parameter estimability' section with a row of eight gray squares. At the bottom of the window, there are three buttons: 'Define new contrast...', 'Reset', and 'Done'. A status bar at the very bottom says 'Selected 2 contrasts for conjunction, press "Done" when finished.' followed by a question mark icon.

Cognitive Conjunctions

- Original (SPM97) definition of conjunctions entailed sum of two simple effects ($A1-A2 + B1-B2$) plus **exclusive** masking with interaction $(A1-A2) - (B1-B2)$
- Ie, “effects significant and of similar size”
- (Difference between conjunctions and masking is that conjunction p-values reflect the conjoint probabilities of the contrasts)
- SPM2 definition of conjunctions uses advances in Gaussian Field Theory (e.g, T^2 fields), allowing corrected p-values
- However, the logic has changed slightly, in that voxels can survive a conjunction even though they show an interaction



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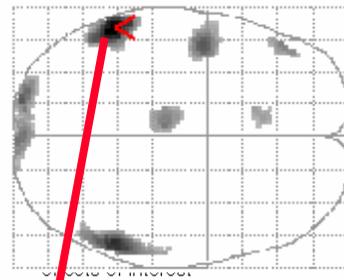
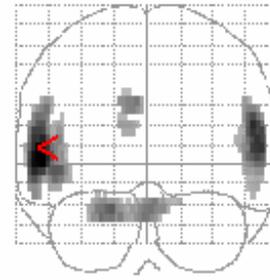
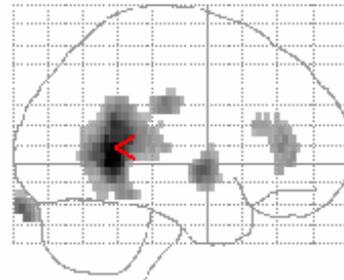
 - Parametric

 - Linear and nonlinear interactions

 - Psychophysiological Interactions

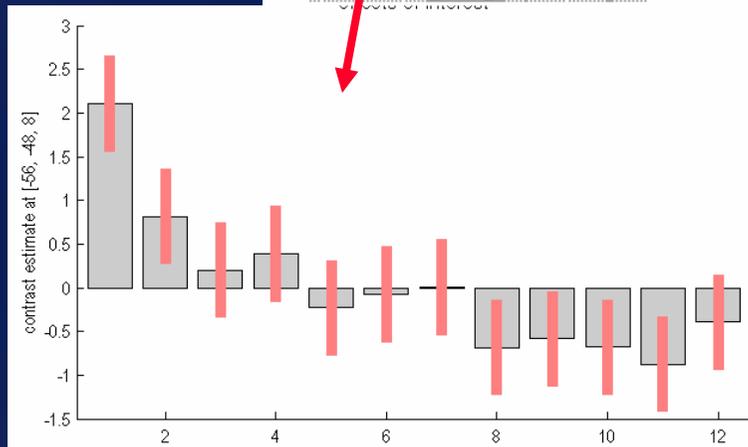
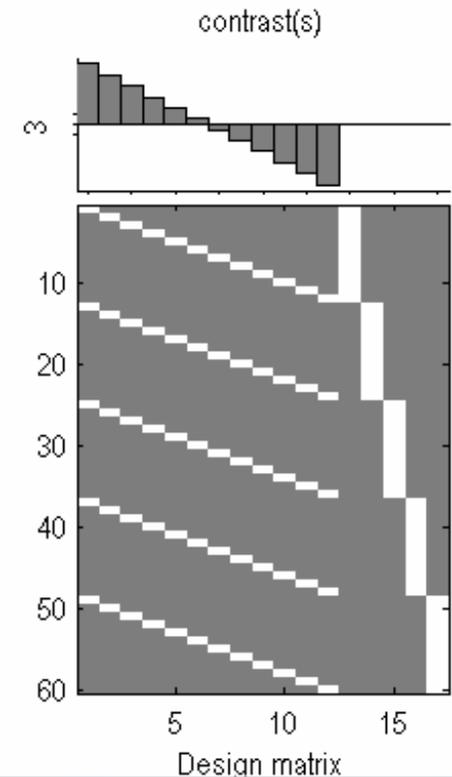
A (linear) parametric contrast

Linear effect
of time



SPM{T₄₄}

.12ConStats



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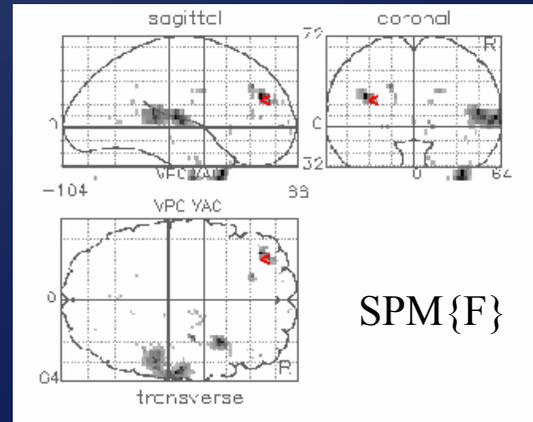
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Nonlinear parametric design matrix

E.g, F-contrast [0 1 0] on
Quadratic Parameter =>

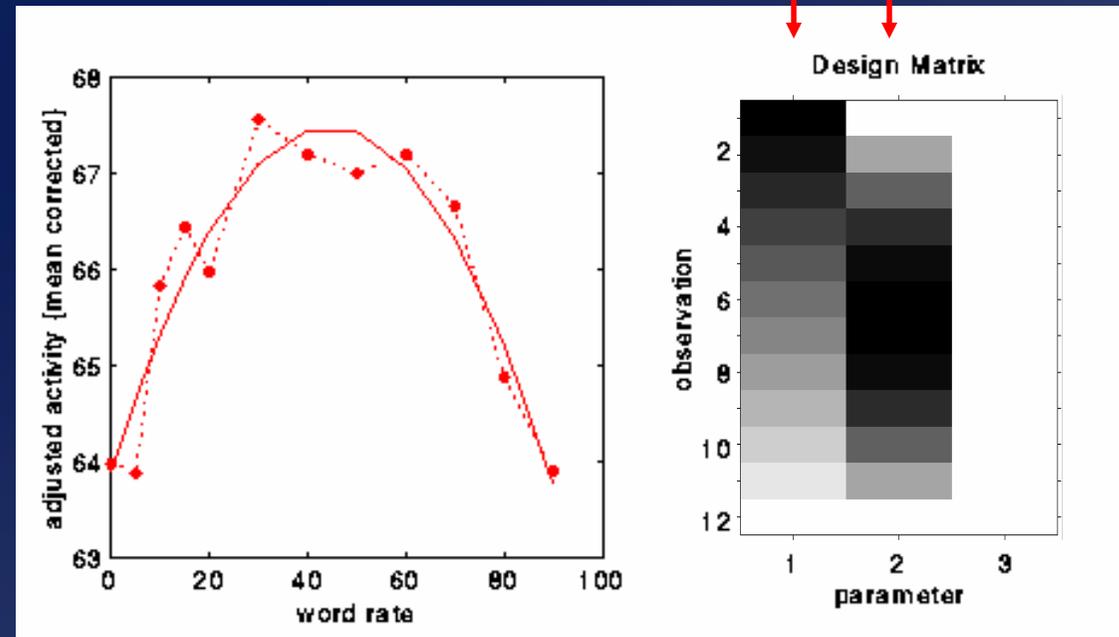
Inverted 'U' response to
increasing word presentation
rate in the DLPFC



Linear
Quadratic

Polynomial expansion:
 $f(x) \sim \beta_1 x + \beta_2 x^2 + \dots$

...(N-1)th order for N levels



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- **Interactions and pure insertion**

- Adaptation, modulation and dual-task inference

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Interactions and pure insertion

- Presence of an interaction can show a failure of pure insertion (using earlier example)...

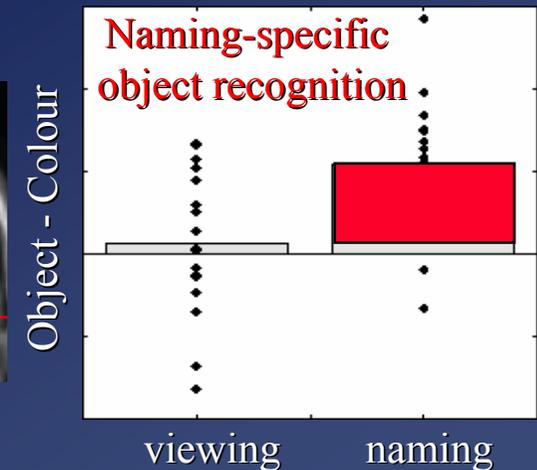
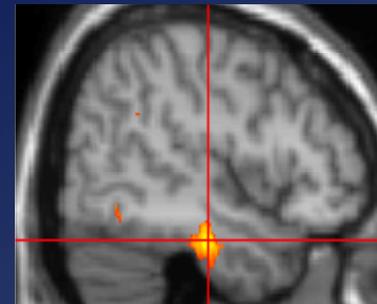
Visual Processing	V
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Phonological Retrieval	P
Object viewing	R, V
Colour viewing	V
Object naming	P, R, V, RxP
Colour naming	P, V

(Object – Colour) x (Viewing – Naming)

$$[1 \ -1 \ 0 \ 0] - [0 \ 0 \ 1 \ -1] = [1 \ -1] \otimes [1 \ -1] = [1 \ -1 \ -1 \ 1]$$

$$[R, V - V] - [P, R, V, RxP - P, V] = R - R, RxP = RxP$$

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



Interactions and pure insertion

SPM contrast manager

name **define contrast...**

name (A1 - A2) x (B1 - B2)

type t-contrast F-contrast

contrast

contrast
weights
vector

1 -1 -1 1

..submit

1 -1 -1 1 <- (right padded with 5

Reset Cancel OK

contrast(s)

Design matrix

parameter estimability

name defined, contrast defined ?

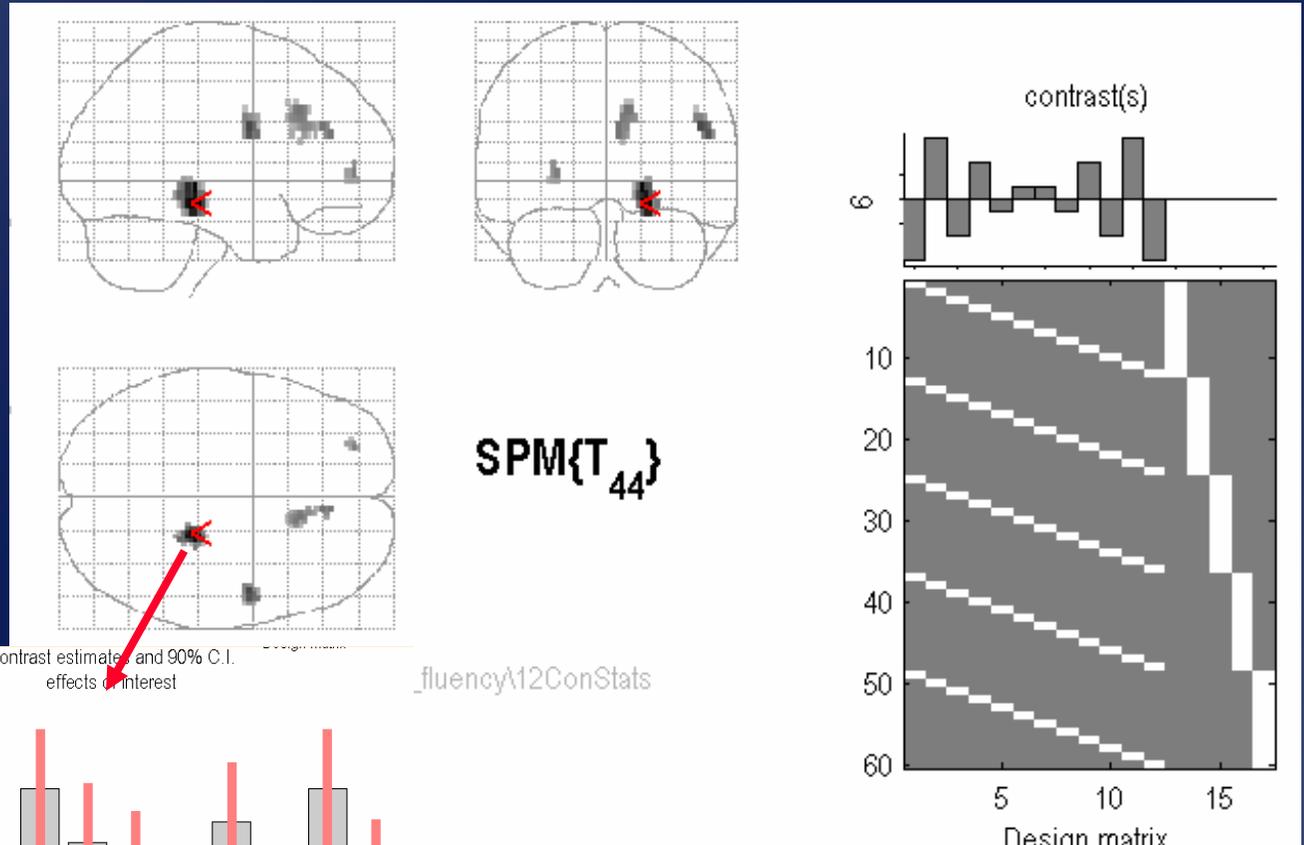
The dialog box is titled "SPM contrast manager" and contains several input fields and controls. The "name" field is labeled "define contrast..." and contains the text "(A1 - A2) x (B1 - B2)". The "type" section has two radio buttons: "t-contrast" (selected) and "F-contrast". The "contrast" section has a text area containing "1 -1 -1 1" and a ".submit" button. Below this is a scrollable list showing "1 -1 -1 1 <- (right padded with 5". At the bottom are "Reset", "Cancel", and "OK" buttons. On the right side, there is a visualization area labeled "contrast(s)" showing a grid of gray and white squares. Below that is a "Design matrix" visualization, also a grid of gray and white squares. At the bottom right of the visualization area is a "parameter estimability" bar consisting of ten gray squares. At the very bottom of the dialog, a status bar shows the text "name defined, contrast defined" in green, followed by a question mark icon in a box.

A taxonomy of design

- Categorical designs
 - Subtraction - Additive factors and pure insertion
 - Conjunction - Testing multiple hypotheses
- Parametric designs
 - Linear - Cognitive components and dimensions
 - Nonlinear - Polynomial expansions
- Factorial designs
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 - Adaptation, modulation and dual-task inference
 - Parametric
 - **Linear and nonlinear interactions**
 - Psychophysiological Interactions

(Linear) Parametric Interaction

A (Linear)
Time-by-Condition
Interaction
("Generation strategy"?)



Contrast: $[5 \ 3 \ 1 \ -1 \ -3 \ -5] \otimes [-1 \ 1]$

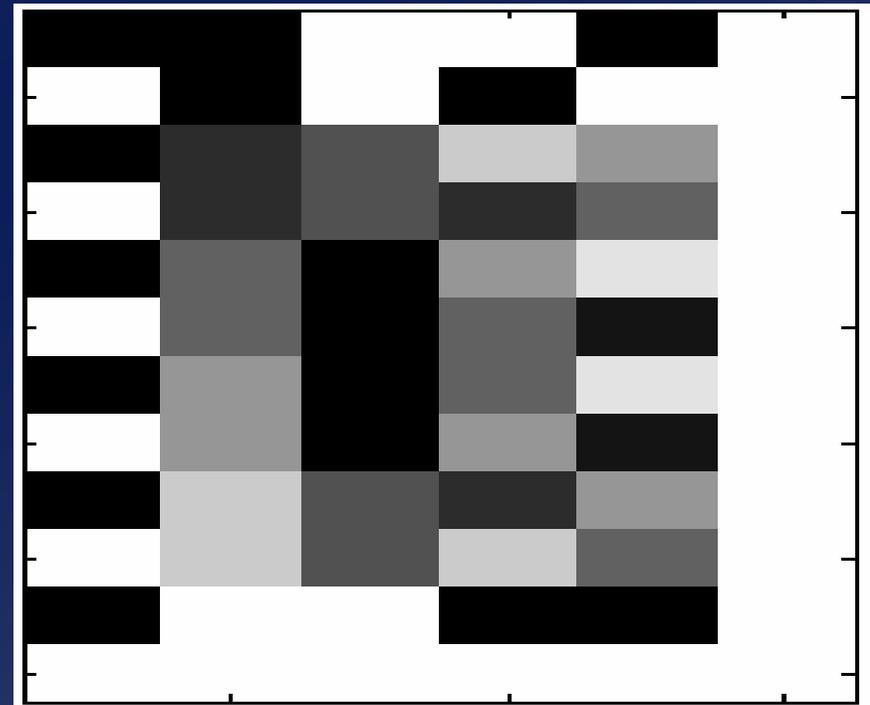
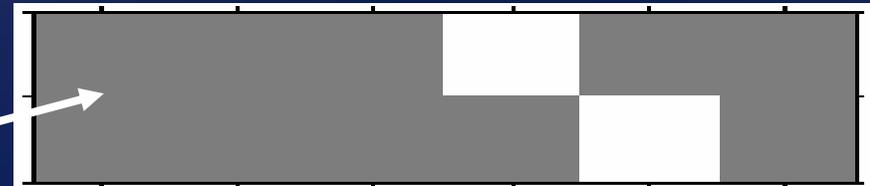
Nonlinear Parametric Interaction

F-contrast tests for nonlinear
Generation-by-Time interaction
(including both linear and
Quadratic components)

Factorial Design with 2 factors:

1. Gen/Rep (Categorical, 2 levels)
2. Time (Parametric, 6 levels)

Time effects modelled with both
linear and quadratic components...



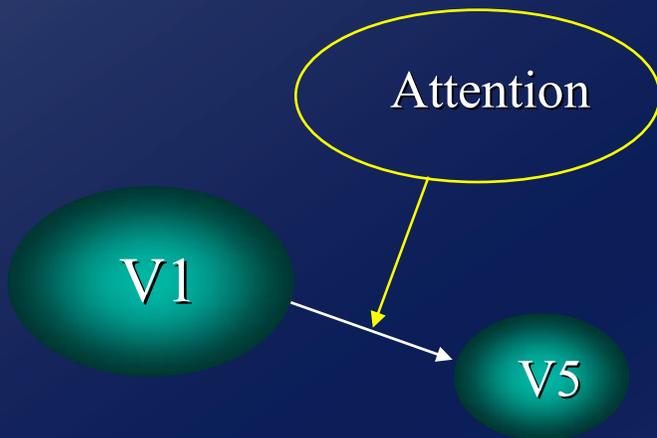
↑ ↑ ↑ ↑ ↑
G-R Time Time G x T G x T
 Lin Quad Lin Quad

A taxonomy of design

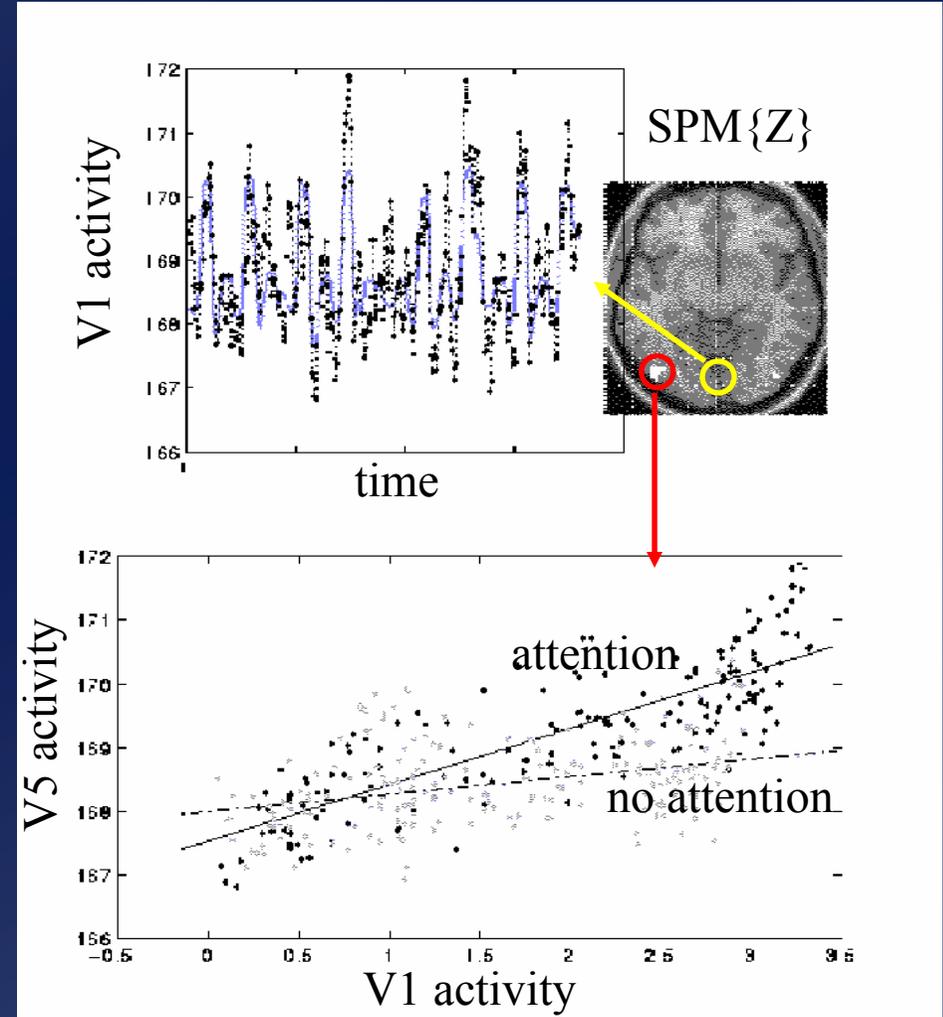
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Psycho-physiological Interaction (PPI)

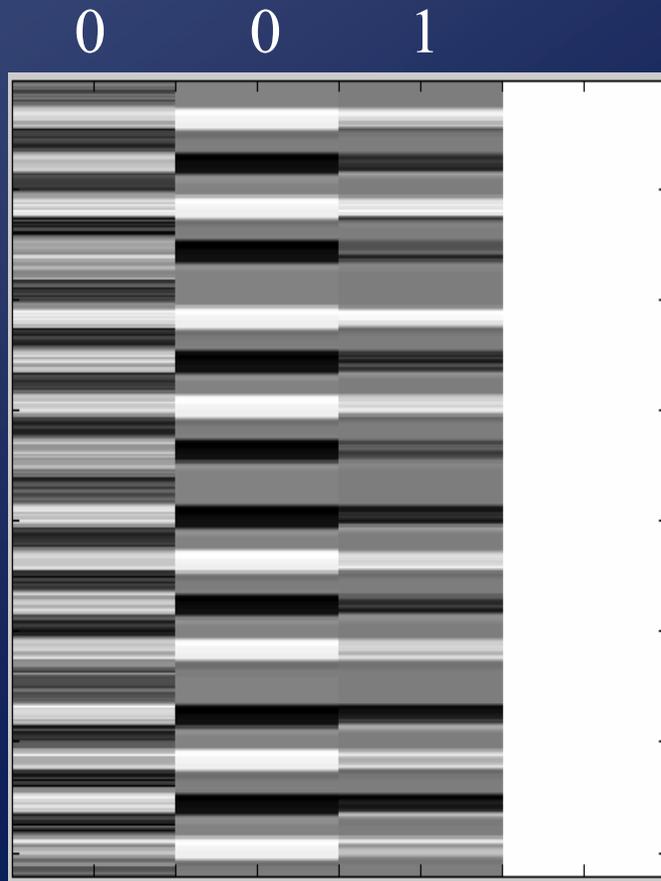
Parametric, factorial design, in which one factor is **psychological** (eg attention) ...and other is **physiological** (*viz. activity extracted from a brain region of interest*)



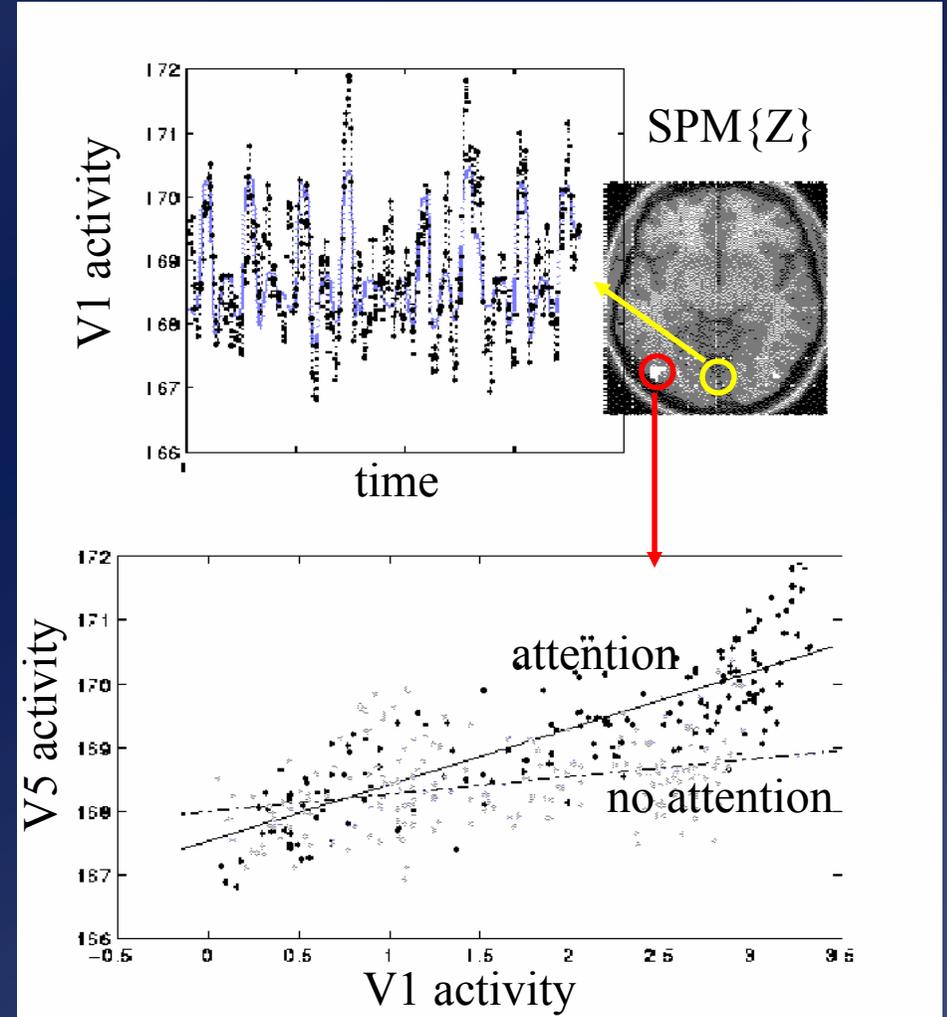
Attentional modulation of V1 - V5 contribution



Psycho-physiological Interaction (PPI)



↑ ↑ ↑
V1 Att Att V1 x Att



Psycho-physiological Interaction (PPI)

- PPIs tested by a GLM with form:

$$\mathbf{y} = (\mathbf{V1} \times \mathbf{A}) \cdot \beta_1 + \mathbf{V1} \cdot \beta_2 + \mathbf{A} \cdot \beta_3 + \varepsilon \quad \mathbf{c} = [1 \ 0 \ 0]$$

- However, the interaction term of interest, $\mathbf{V1} \times \mathbf{A}$, is the product of V1 activity and Attention block AFTER convolution with HRF
- We are really interested in interaction at neural level, but:

$$(\text{HRF} \otimes \text{V1}) \times (\text{HRF} \otimes \text{A}) \neq \text{HRF} \otimes (\text{V1} \times \text{A})$$

(unless A low frequency, eg, blocked; so problem for event-related PPIs)

- SPM2 can effect a **deconvolution** of physiological regressors (V1), before calculating interaction term and reconvolving with the HRF
- Deconvolution is ill-constrained, so regularised using smoothness priors (using ReML)

Overview

1. A Taxonomy of Designs

2. Epoch vs Event-related

3. Mixed Epoch/Event Designs

Epoch vs Events

- **Epochs** are periods of sustained stimulation (e.g, box-car functions)
- **Events** are impulses (delta-functions)
- In SPM99, epochs and events are distinct (eg, in choice of basis functions)
- In SPM2, all conditions are specified in terms of their 1) **onsets** and 2) **durations**...
... events simply have zero duration
- Near-identical regressors can be created by:
1) sustained epochs, 2) rapid series of events (SOAs < ~3s)
- i.e, *designs* can be **blocked** or **intermixed**
... *models* can be **epoch** or **event**-related

Sustained epoch



Blocks of events



Advantages of Event-related fMRI

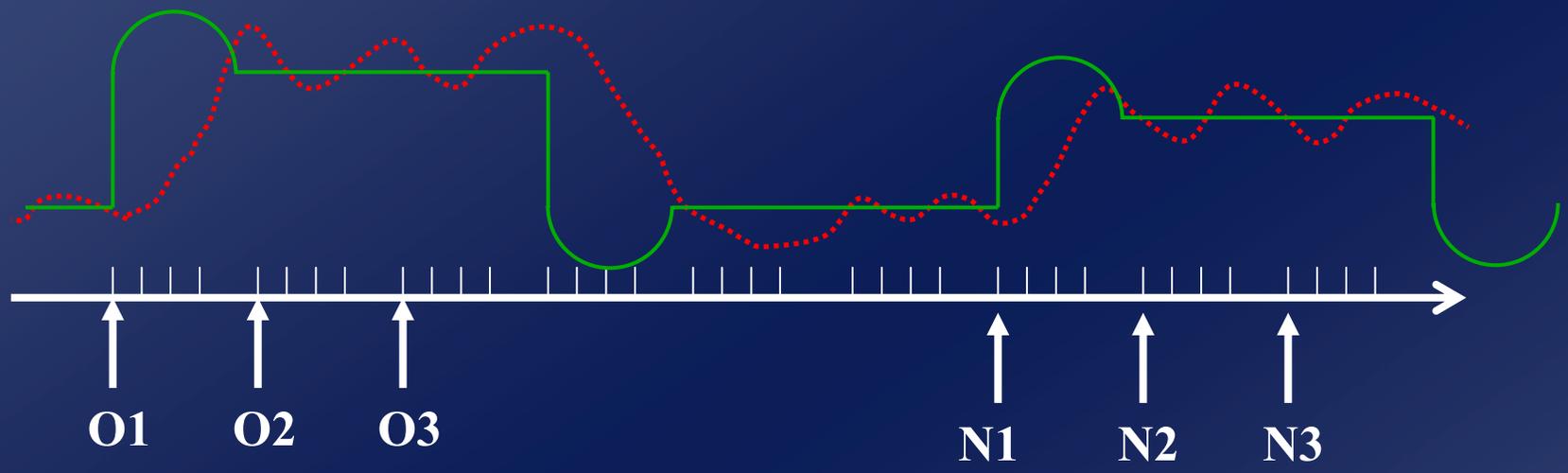
1. Randomised (intermixed) trial order

c.f. confounds of blocked designs (Johnson et al 1997)

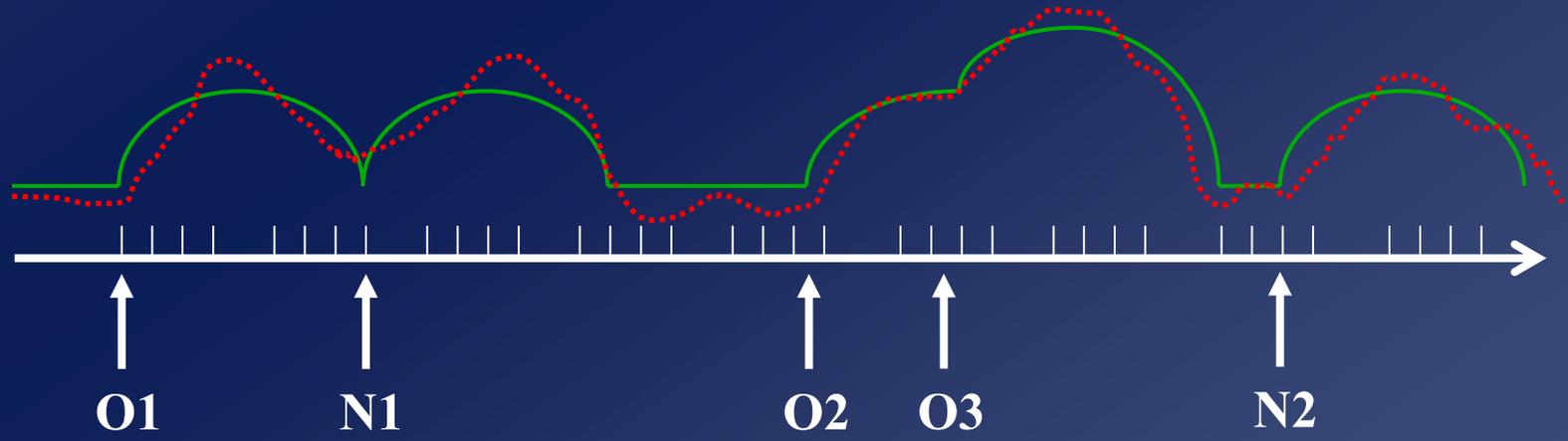
Blocked

..... Data
———— Model

O = Old Words
N = New Words



Randomised



Advantages of Event-related fMRI

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c.f. confounds of blocked designs (Johnson et al 1997)

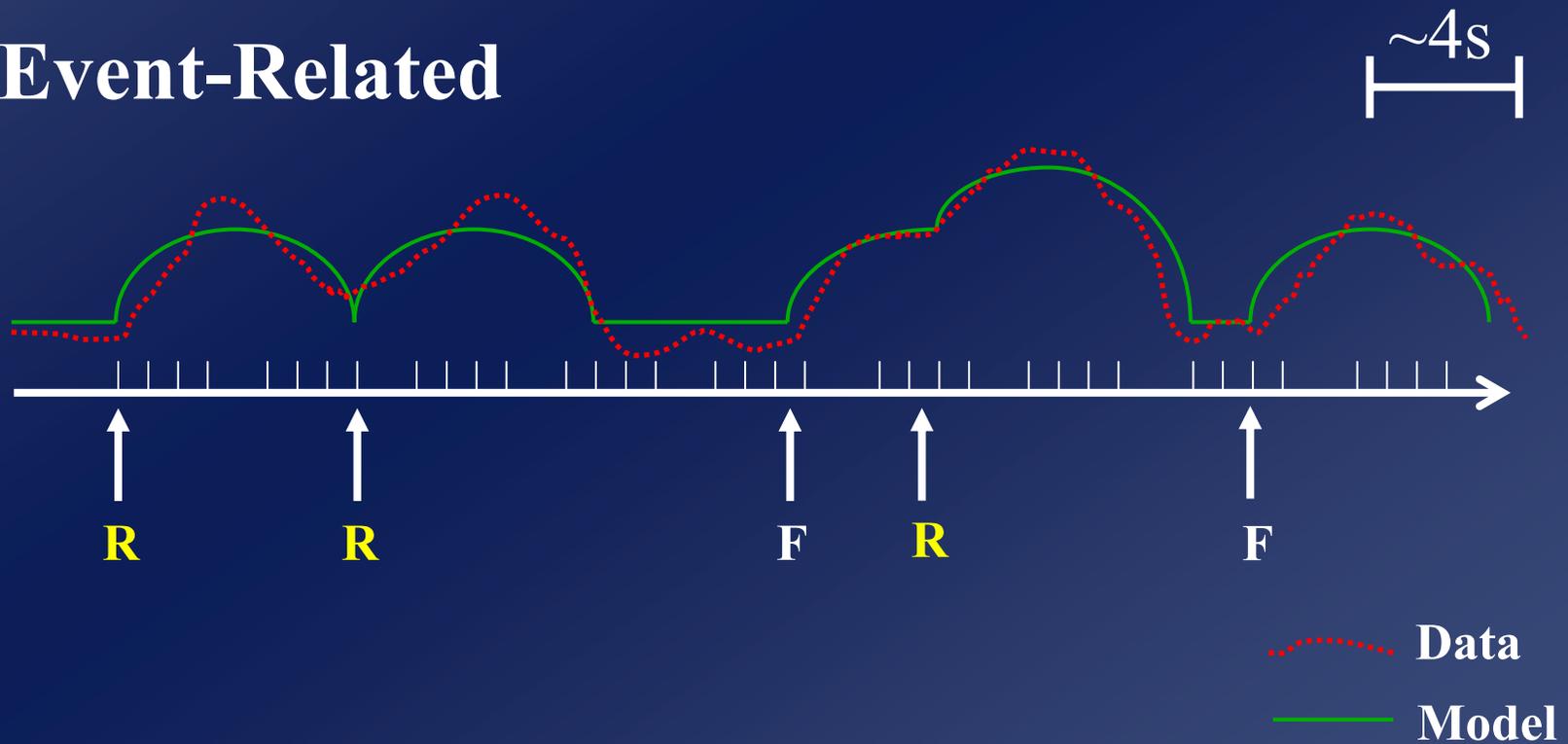
2. Post hoc / subjective classification of trials

e.g, according to subsequent memory (Wagner et al 1998)

R = Words Later Remembered

F = Words Later Forgotten

Event-Related



Advantages of Event-related fMRI

1. Randomised (intermixed) trial order

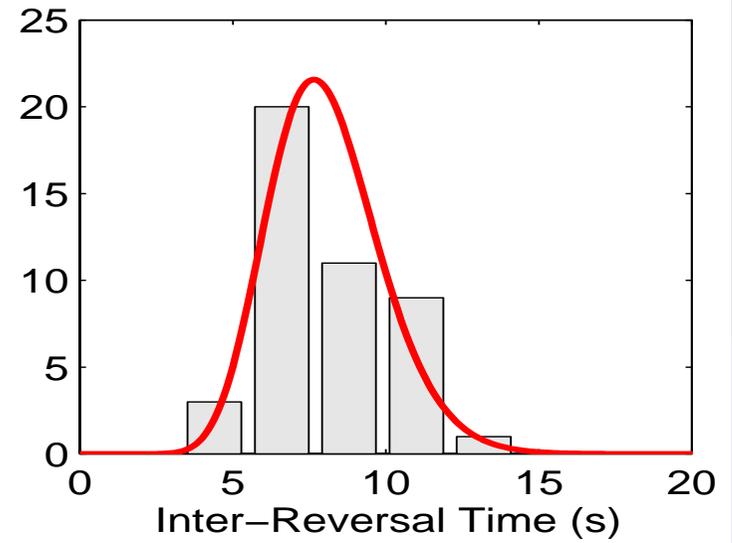
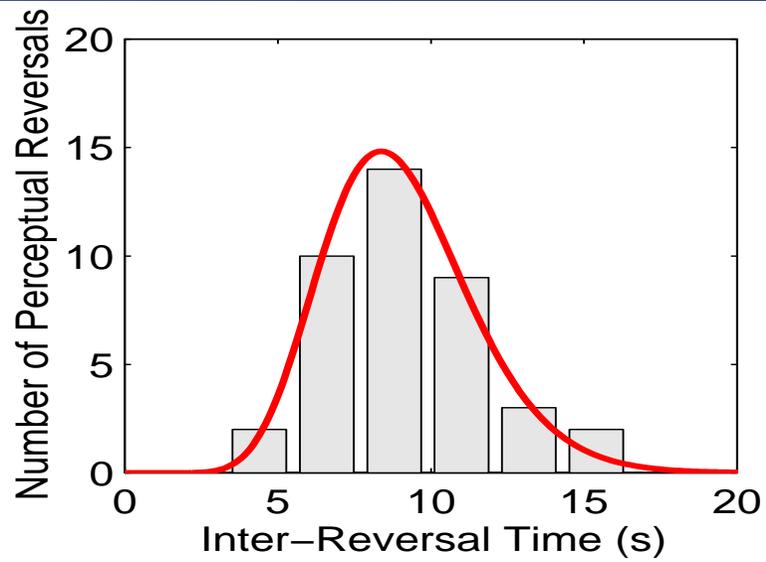
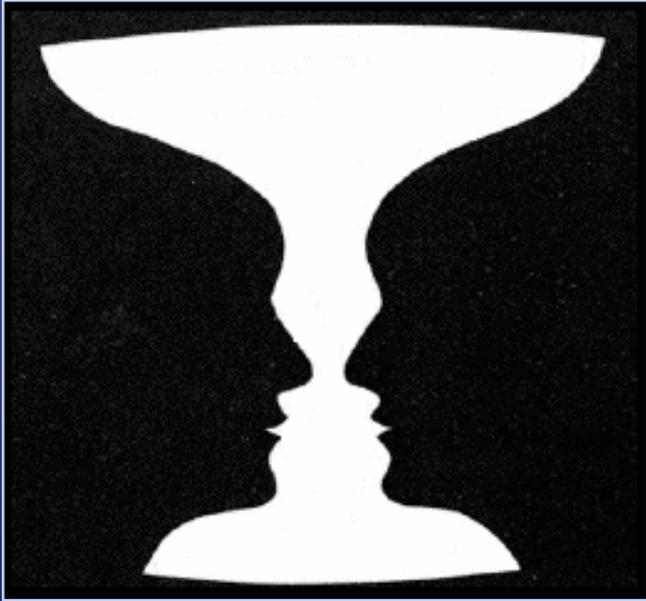
c.f. confounds of blocked designs (Johnson et al 1997)

2. Post hoc / subjective classification of trials

e.g, according to subsequent memory (Wagner et al 1998)

3. Some events can only be indicated by subject (in time)

e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)



Advantages of Event-related fMRI

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c.f. confounds of blocked designs (Johnson et al 1997)

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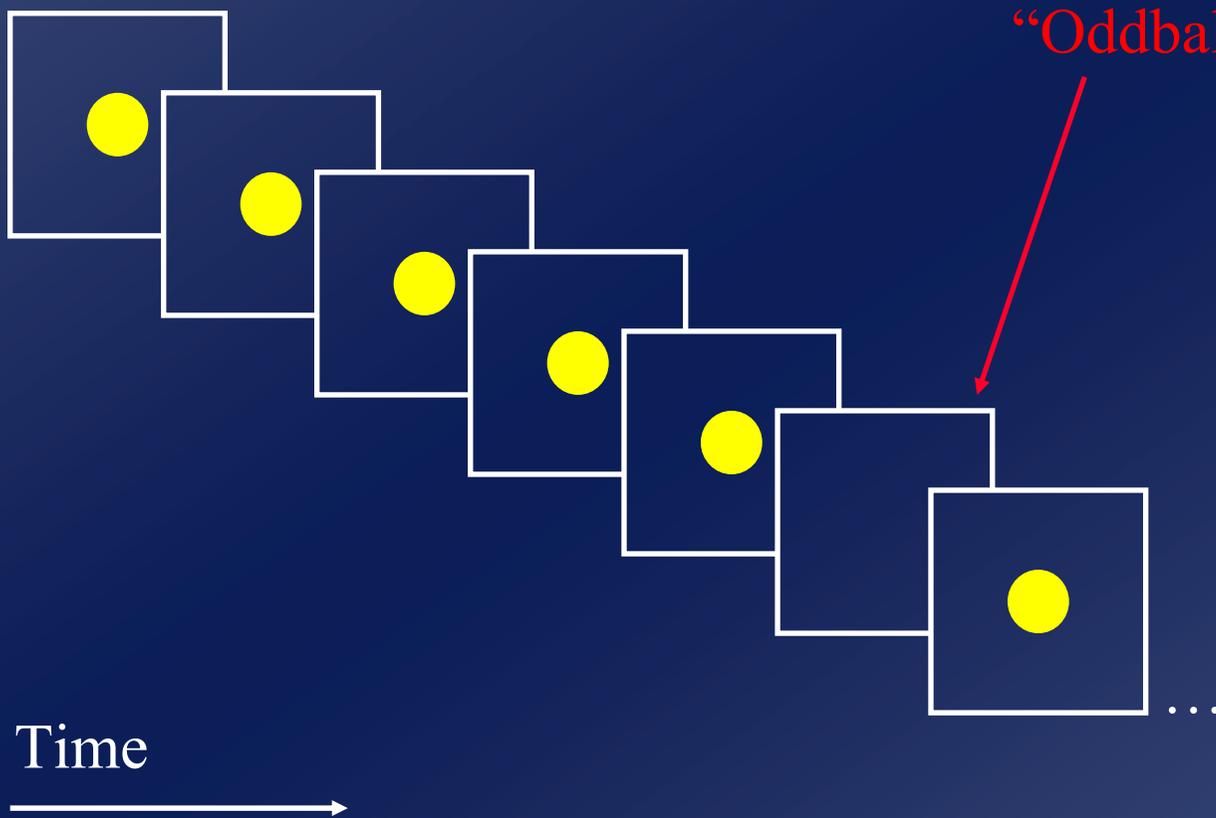
e.g, according to subsequent memory (Wagner et al 1998)

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e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)

4. Some trials cannot be blocked

e.g, “oddball” designs (Clark et al., 2000)



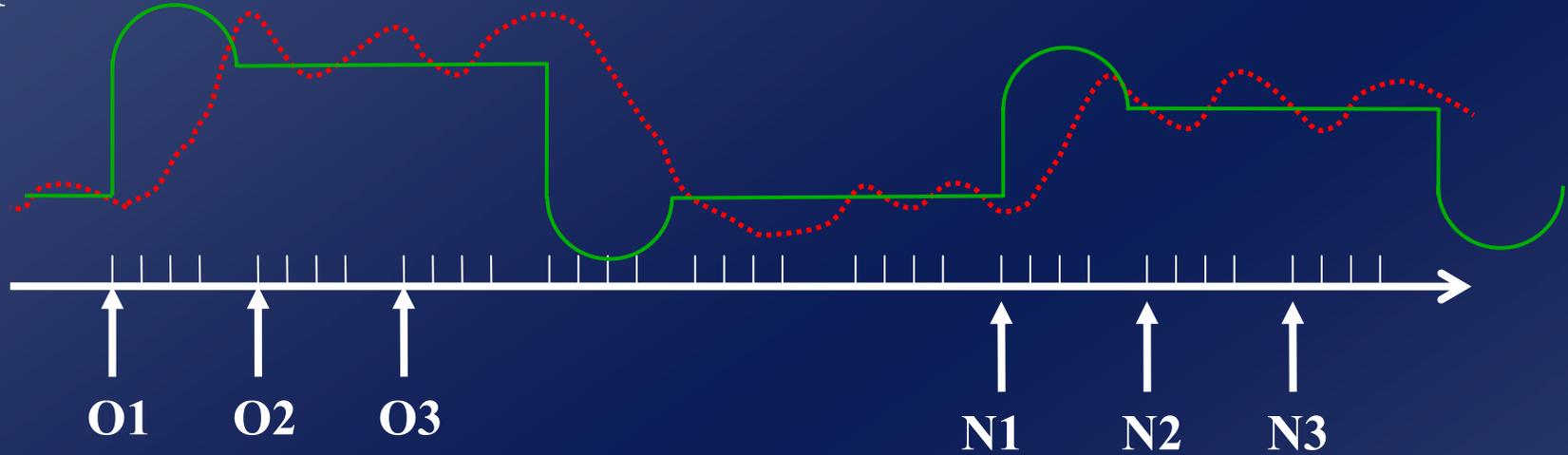
Advantages of Event-related fMRI

1. Randomised (intermixed) trial order
c.f. confounds of blocked designs (Johnson et al 1997)
2. Post hoc / subjective classification of trials
e.g, according to subsequent memory (Wagner et al 1998)
3. Some events can only be indicated by subject (in time)
e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)
4. Some trials cannot be blocked
e.g, “oddball” designs (Clark et al., 2000)
5. More accurate models even for blocked designs?
e.g, “state-item” interactions (Chawla et al, 1999)

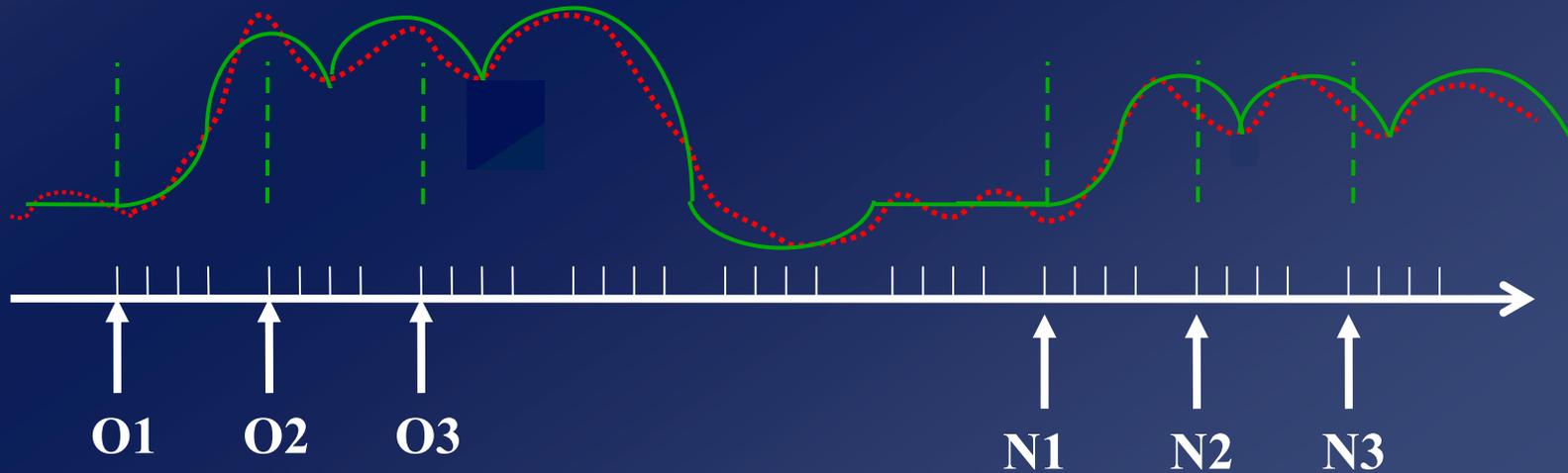
Blocked Design

..... Data
———— Model

“Epoch” model

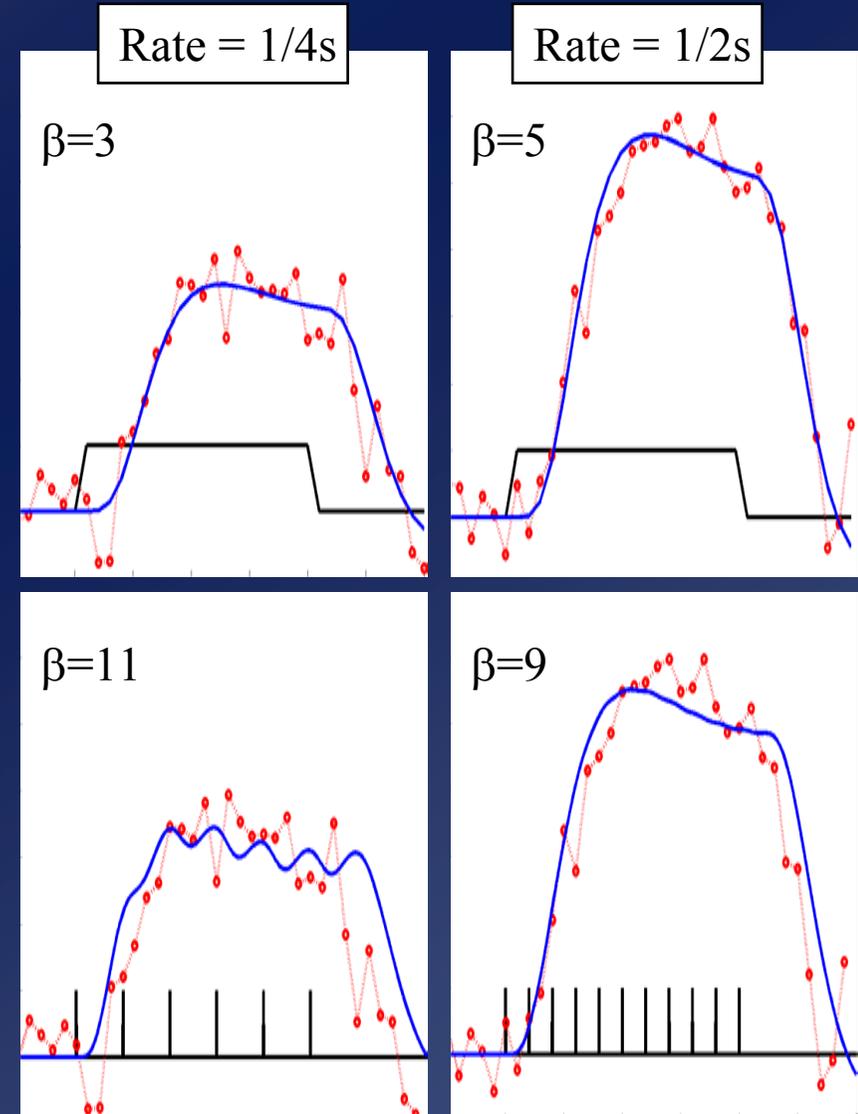


“Event” model



Epoch vs Events

- Though blocks of trials can be modelled as either epochs (boxcars) or runs of events...
... interpretation of parameters differs...
- 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 are blocked designs**
(see later...)
- 2. Some psychological processes may be better blocked**
(eg task-switching, attentional instructions)

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Mixed Designs

- **Recent interest in simultaneously measuring effects that are:**
 - **transient (“item- or event-related”)**
 - **sustained (“state- or epoch-related”)**
- **What is the best design to estimate both...?**

A bit more formally... “Efficiency”

- **Sensitivity, or “efficiency”, e (see later):**

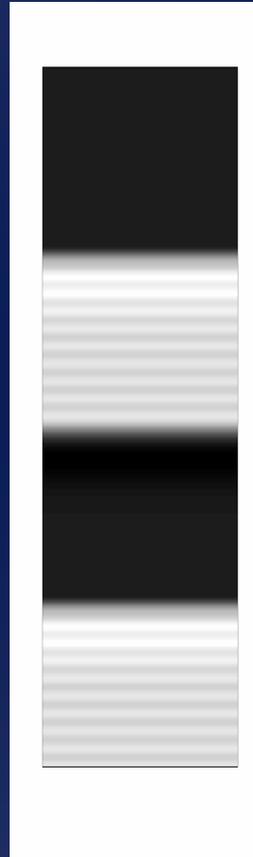
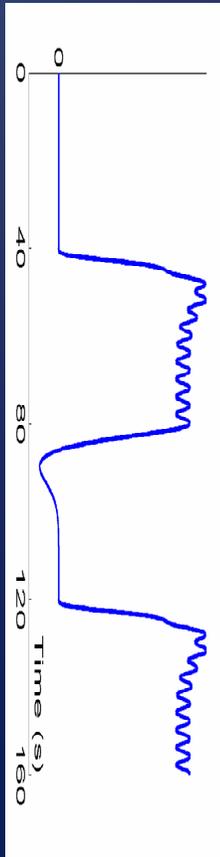
$$e(c, X) = \{ c^T (X^T X)^{-1} c \}^{-1}$$

- **$X^T X$ represents covariance of regressors in design matrix**
- **High covariance increases elements of $(X^T X)^{-1}$**

*=> So, when correlation between regressors is high,
sensitivity to each regressor alone is low*

Item effect only...

Blocks = 40s, Fixed SOA = 4s



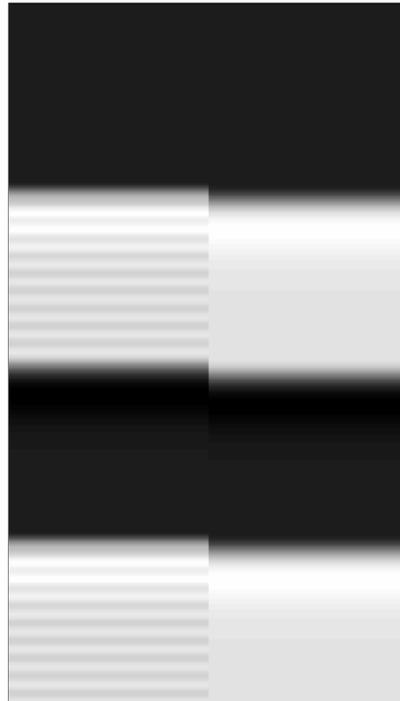
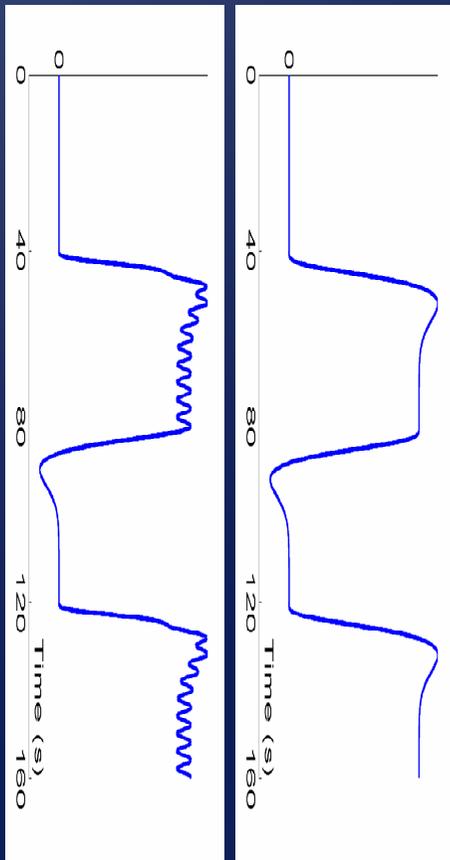
Efficiency = 565
(Item Effect)

Design Matrix (X)

OK...

Item and State effects

Blocks = 40s, Fixed SOA = 4s



Correlation = .97

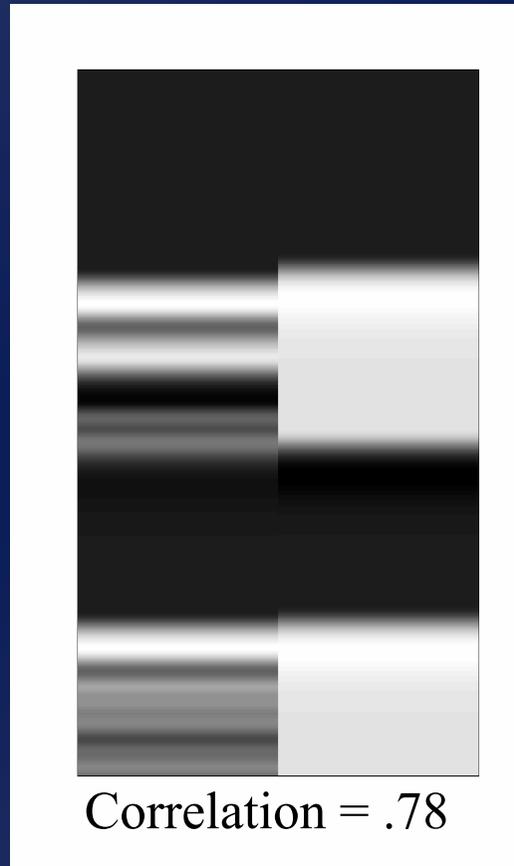
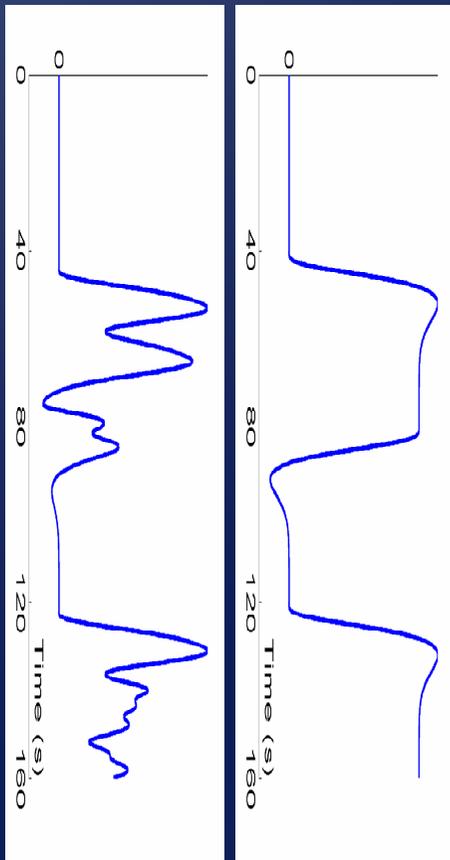
Design Matrix (X)

Efficiency = 16
(Item Effect)

Not good...

Item and State effects

Blocks = 40s, Randomised $SOA_{min} = 2s$



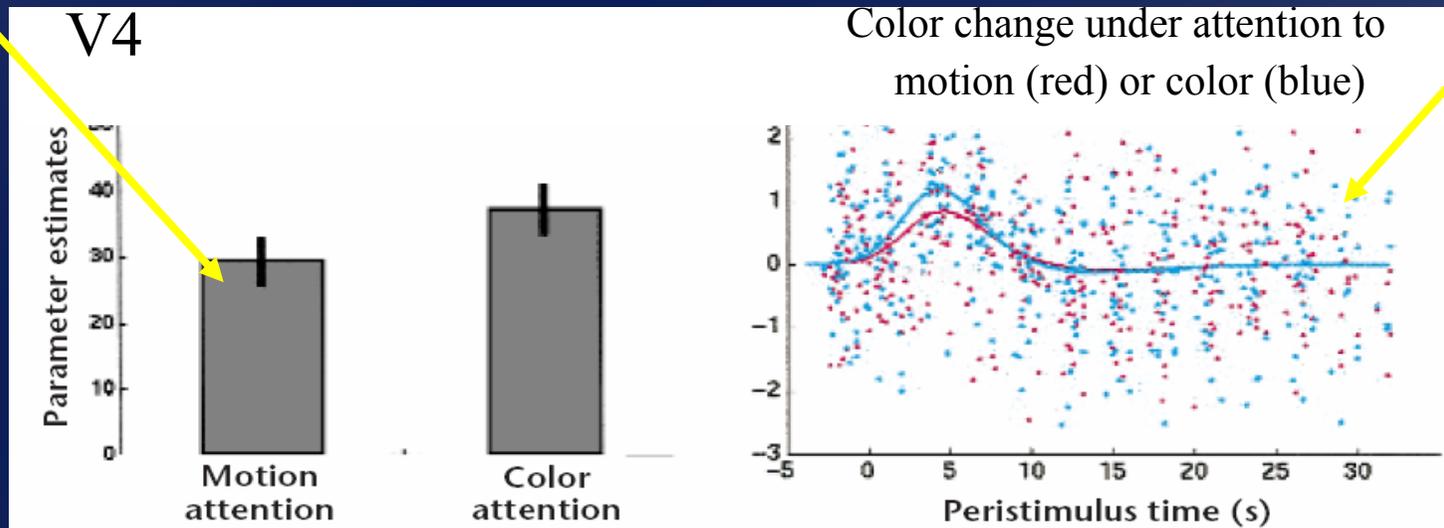
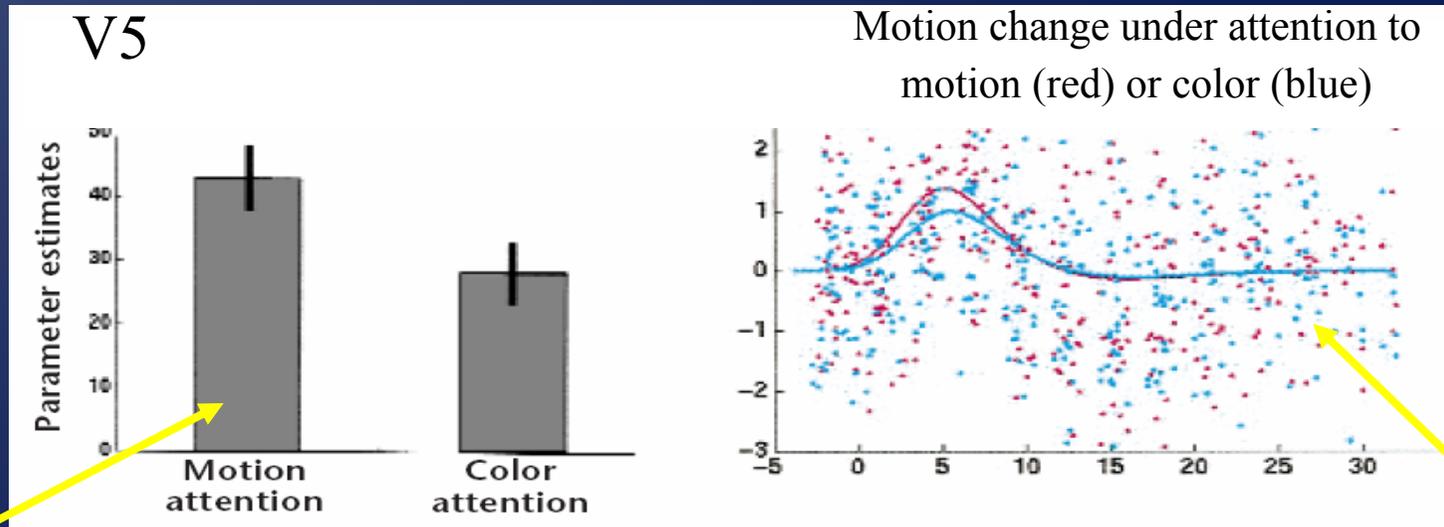
Efficiency = 54
(Item Effect)

Better!

Mixed Designs (Chawla et al 1999)

- Visual stimulus = dots periodically changing in colour or motion
- Epochs of attention to: 1) motion, or 2) colour
- Events are target stimuli differing in motion or colour
- **Randomised, long SOAs between events (targets) to decorrelate epoch and event-related covariates**
- Attention modulates BOTH:
 - 1) baseline activity (state-effect, additive)
 - 2) evoked response (item-effect, multiplicative)

Mixed Designs (Chawla et al 1999)



State Effect (Baseline)

Item Effect (Evoked)

