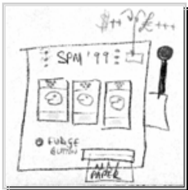
Event-related fMRI

Rik Henson

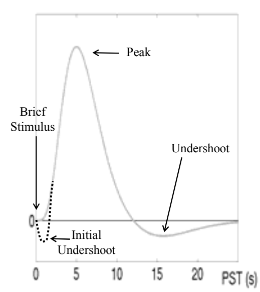
With thanks to:
Karl Friston, Oliver Josephs



Overview

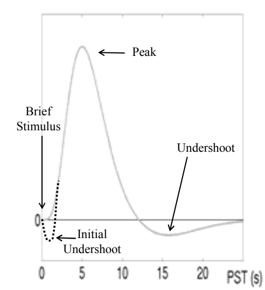
BOLD Impulse Response

- Function of blood oxygenation, flow, volume (Buxton et al, 1998)
- Peak (max. oxygenation) 4-6s poststimulus; baseline after 20-30s
- Initial undershoot can be observed (Malonek & Grinvald, 1996)
- Similar across V1, A1, S1…
- … but differences across:
  other regions (Schacter et al 1997)
  individuals (Aguirre et al, 1998)



BOLD Impulse Response

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



Overview

1. BOLD impulse response
2. General Linear Model
3. Temporal Basis Functions
4. Timing Issues
5. Design Optimisation
6. Nonlinear Models
7. Example Applications

General Linear (Convolution) Model

GLM for a single voxel:

$y(t) = u(t) \otimes h(\tau) + \varepsilon(t)$

$u(t)$ = neural causes (stimulus train)

$u(t) = \sum \delta(t - nT)$

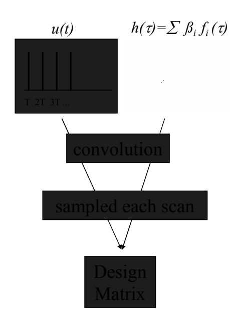
$h(\tau)$ = hemodynamic (BOLD) response

$h(\tau) = \sum \beta_i f_i(\tau)$

$f_i(\tau)$ = temporal basis functions

$y(t) = \sum\sum \beta_i f_i(t - nT) + \varepsilon(t)$

$\mathbf{y} = \mathbf{X\beta} + \boldsymbol{\varepsilon}$



General Linear Model (in SPM)

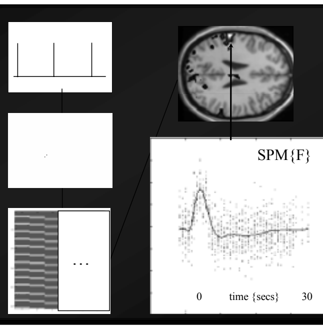
Auditory words every 20s

Gamma functions $f_i(\tau)$ of peristimulus time τ (Orthogonalised)

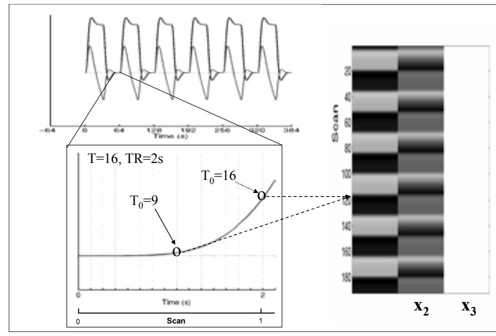
Sampled every TR = 1.7s

Design matrix, X

$[x(t)\otimes f_1(\tau) \mid x(t)\otimes f_2(\tau) \mid \ldots]$



A word about down-sampling



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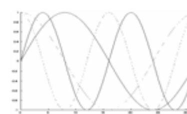
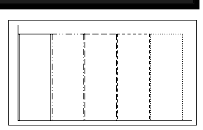
Temporal Basis Functions

- Fourier Set
  - Windowed sines & cosines
  - Any shape (up to frequency limit)
  - Inference via F-test



Temporal Basis Functions

- Finite Impulse Response
  - Mini "timebins" (selective averaging)
  - Any shape (up to bin-width)
  - Inference via F-test



Temporal Basis Functions

- Fourier Set
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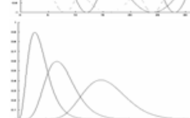
- Gamma Functions
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test



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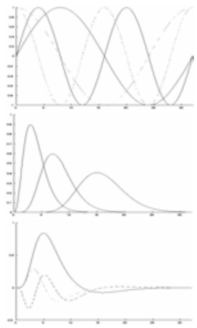
- Gamma Functions
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test
- "Informed" Basis Set
  - Best guess of canonical BOLD response
  - Variability captured by Taylor expansion
  - "Magnitude" inferences via t-test…?



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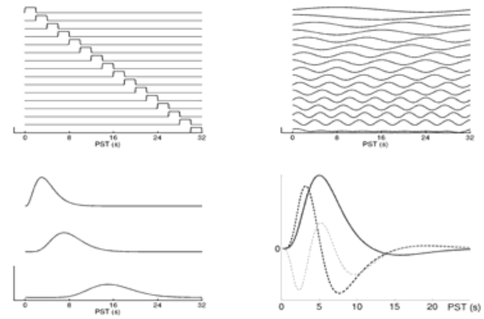
Temporal Basis Functions



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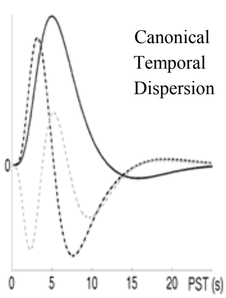
Temporal Basis Functions



"Informed" Basis Set (Friston et al. 1998)

- Canonical HRF (2 gamma functions)

  plus Multivariate Taylor expansion in:

  time (*Temporal Derivative*)

  width (*Dispersion Derivative*)

- "Magnitude" inferences via t-test on canonical parameters (providing canonical is a good fit…more later)
- "Latency" inferences via tests on *ratio* of derivative : canonical parameters (more later…)

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(Other Approaches)

- **Long Stimulus Onset Asychrony (SOA)**
  - Can ignore overlap between responses (Cohen et al 1997)
  - *... but long SOAs are less sensitive*
- **Fully counterbalanced designs**
  - Assume response overlap cancels (Saykin et al 1999)
  - Include fixation trials to "selectively average" response even at short SOA (Dale & Buckner, 1997)
  - *... but unbalanced when events defined by subject*
- **Define HRF from pilot scan on each subject**
  - May capture intersubject variability (Zarahn et al, 1997)
  - *... but not interregional variability*
- **Numerical fitting of highly parametrised response functions**
  - Separate estimate of magnitude, latency, duration (Kruggel et al 1999)
  - *... but computationally expensive for every voxel*

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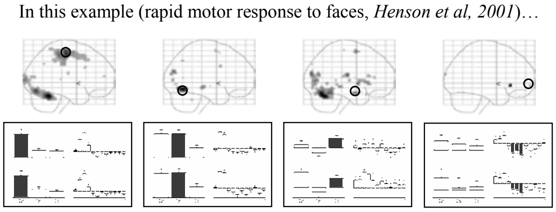
Temporal Basis Sets: Which One?

In this example (rapid motor response to faces, *Henson et al, 2001*)…



Canonical | + Temporal | + Dispersion | + FIR

…canonical + temporal + dispersion derivatives appear sufficient

…may not be for more complex trials (eg stimulus-delay-response)

…but then such trials better modelled with separate neural components (ie activity no longer delta function) + constrained HRF (Zarahn, 1999)

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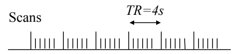
Timing Issues : Practical

- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s



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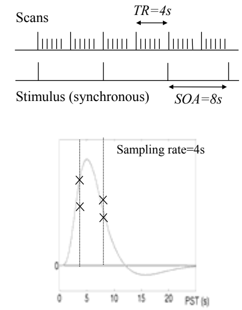

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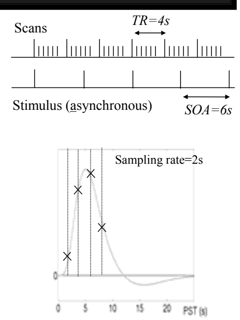
- Higher effective sampling by:
  1. Asynchrony
     eg SOA=1.5TR



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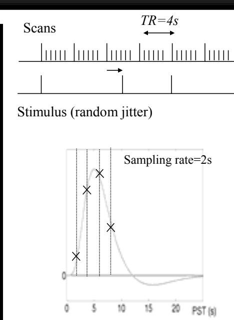
  2. Random Jitter
     eg SOA=(2±0.5)TR



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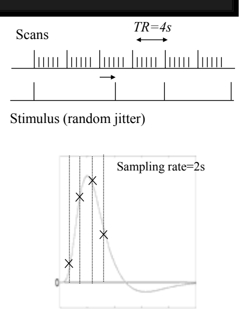
- Higher effective sampling by:
  1. Asynchrony
     eg SOA=1.5TR
  2. Random Jitter
     eg SOA=(2±0.5)TR
- Better response characterisation (Miezin et al, 2000)



Timing Issues : Practical

- …but "Slice-timing Problem"
  (Henson et al, 1999)

Slices acquired at different times, yet model is the same for all slices

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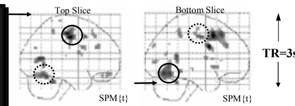
=> different results (using canonical HRF) for different reference slices



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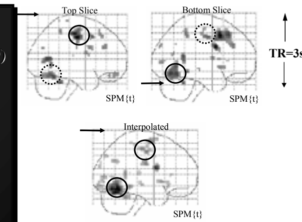
- Solutions:

1. Temporal interpolation of data
   … but less good for longer TRs



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Timing Issues : Practical

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(Henson et al, 1999)

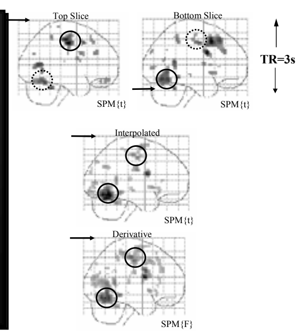
Slices acquired at different times, yet model is the same for all slices

=> different results (using canonical HRF) for different reference slices

- Solutions:

1. Temporal interpolation of data
   … but less good for longer TRs

2. More general basis set (e.g., with temporal derivatives)
   … but inferences via F-test



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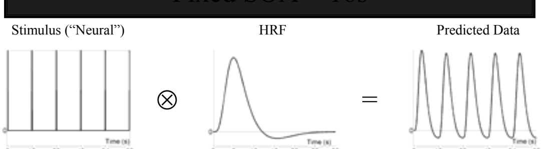
Fixed SOA = 16s



Not particularly efficient…

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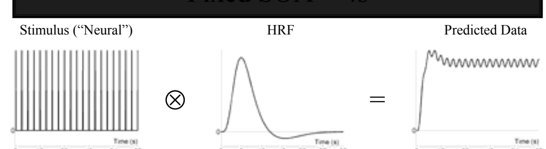
Fixed SOA = 4s



Very Inefficient…

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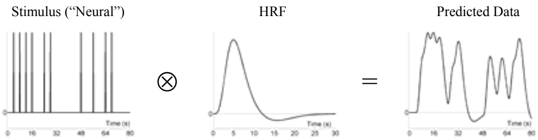
Randomised, SOA_{min} = 4s



More Efficient…

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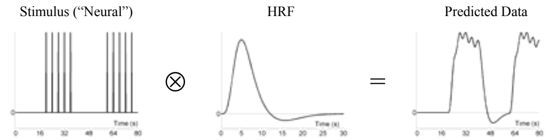
Blocked, SOA_{min} = 4s



Even more Efficient…

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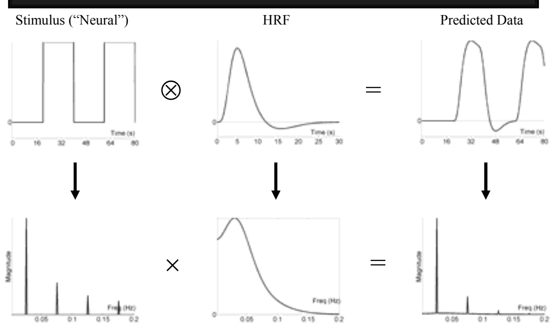
Blocked, epoch = 20s



Blocked-epoch (with small SOA) and Time-Freq equivalences

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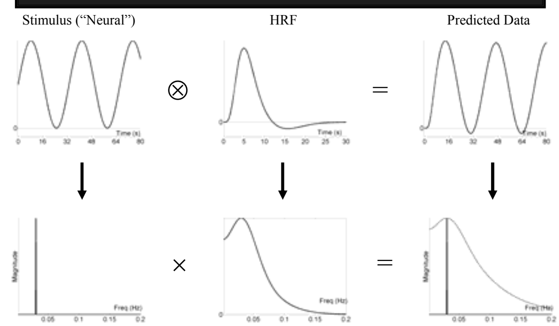
Sinusoidal modulation, f = 1/33s



The most efficient design of all!

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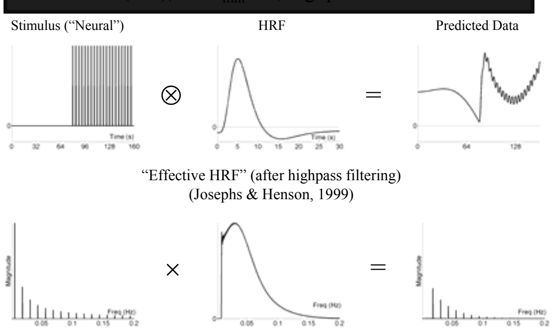
Blocked (80s), SOA_{min}=4s, highpass filter = 1/120s



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

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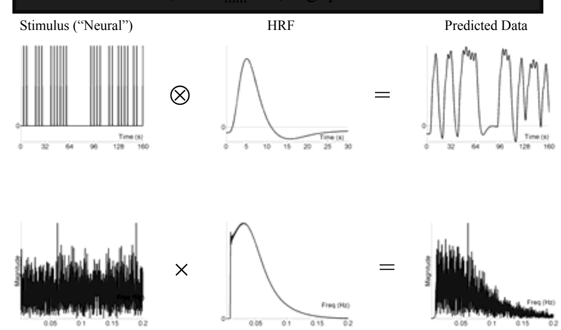
Randomised, SOA_{min}=4s, highpass filter = 1/120s



(Randomised design spreads power over frequencies)

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Design Efficiency

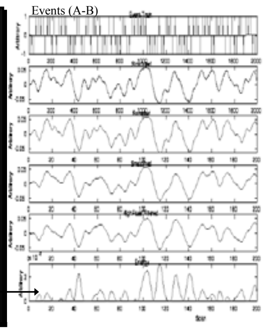
$T = c^T\beta / \text{var}(c^T\beta)$

$\text{Var}(c^T\beta) = \text{sqrt}(\sigma^2 c^T (X^T X)^{-1} c)$ (i.i.d)

- For max. T, want min. contrast variability (Friston et al, 1999)
- If assume that noise variance (σ^2) is unaffected by changes in X…
- …then want maximal efficiency, e:

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

- = maximal bandpassed signal energy (Josephs & Henson, 1999)



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Efficiency - Single Event-type

- Design parametrised by:

SOA_{min} Minimum SOA

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

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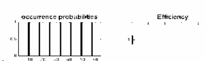
SOA_{min} Minimum SOA
$p(t)$ Probability of event at each SOA_{min}

- Deterministic
  $p(t)=1$ iff $t=nT$



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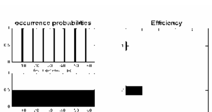
Efficiency - Single Event-type

- Design parametrised by:

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

- Deterministic
  $p(t)=1$ iff $t=nSOA_{min}$
- Stationary stochastic
  $p(t)=constant<1$



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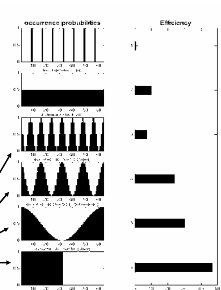
Efficiency - Single Event-type

- Design parametrised by:

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

- Deterministic
  $p(t)=1$ iff $t=nT$
- Stationary stochastic
  $p(t)=constant$
- Dynamic stochastic
  $p(t)$ varies (eg blocked)



Blocked designs most efficient! (with small SOAmin)

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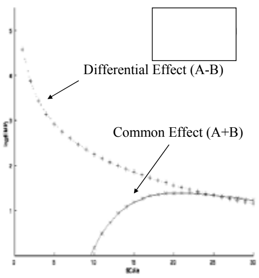
Efficiency - Multiple Event-types

- Design parametrised by:
  SOA_{min} Minimum SOA
  $p_i(h)$ Probability of event-type i given history h of last m events
- With n event-types $p_i(h)$ is a $n^m \times n$ *Transition Matrix*
- Example: Randomised AB

	A	B
A	0.5	0.5
B	0.5	0.5

=> ABBBABAABABAAA...



4s smoothing; 1/60s highpass filtering

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Efficiency - Multiple Event-types

- Example: Alternating AB

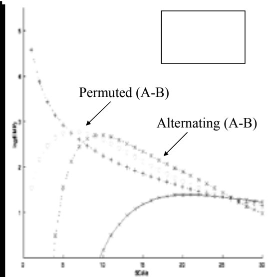
	A	B
A	0	1
B	1	0

=> ABABABABABAB...

- Example: Permuted AB

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

=> ABBAABABABBA...



4s smoothing; 1/60s highpass filtering

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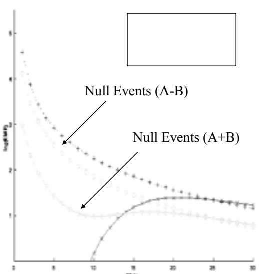
Efficiency - Multiple Event-types

- Example: Null events

	A	B
A	0.33	0.33
B	0.33	0.33

=> AB-BAA--B---ABB...

- Efficient for differential *and* main effects at short SOA
- Equivalent to stochastic SOA (Null Event like third unmodelled event-type)
- Selective averaging of data (Dale & Buckner 1997)



4s smoothing; 1/60s highpass filtering

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Efficiency - Conclusions

- Optimal design for one contrast may not be optimal for another
- Blocked designs generally most efficient with short SOAs (but earlier restrictions and problems of interpretation…)
- With randomised designs, optimal SOA for differential effect (A-B) is minimal SOA (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)

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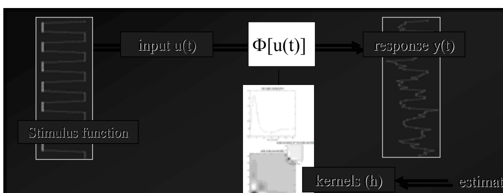
Nonlinear Model



Volterra series - a general nonlinear input-output model

$$y(t) = \Phi_1[u(t)] + \Phi_2[u(t)] + \ldots + \Phi_n[u(t)] + \ldots$$

$$\Phi_n[u(t)] = \sum \ldots \sum h_n(t_1, \ldots, t_n)u(t - t_1) \ldots u(t - t_n)dt_1 \ldots dt_n$$

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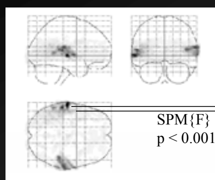
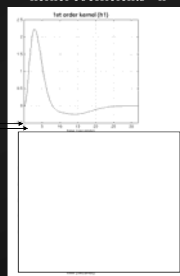
Nonlinear Model

Friston et al (1997)



kernel coefficients - h



SPM{F} testing H_0: kernel coefficients, h = 0

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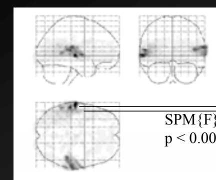
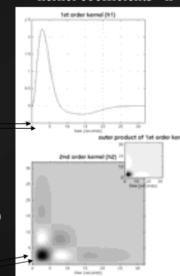
Nonlinear Model

Friston et al (1997)



kernel coefficients - h



SPM{F} testing H_0: kernel coefficients, h = 0

Significant nonlinearities at SOAs 0-10s:
(e.g., underadditivity from 0-5s)

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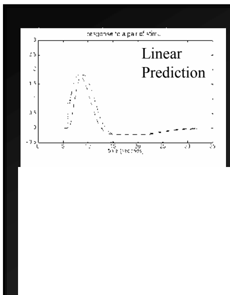
Nonlinear Effects



Underadditivity at short SOAs

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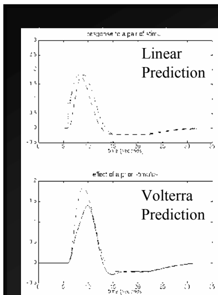
Nonlinear Effects



Underadditivity at short SOAs

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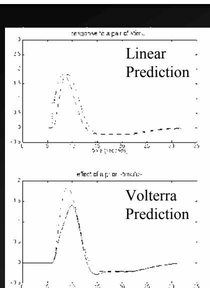
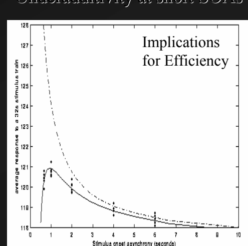
Nonlinear Effects



Underadditivity at short SOAs



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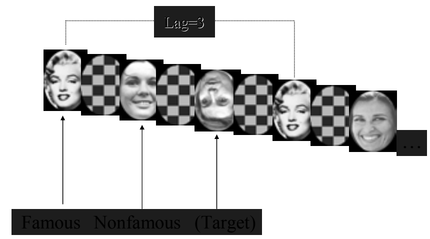
Overview

1. BOLD impulse response
2. General Linear Model
3. Temporal Basis Functions
4. Timing Issues
5. Design Optimisation
6. Nonlinear Models
7. Example Applications

Example 1: Intermixed Trials (Henson et al 2000)

- Short SOA, fully randomised, with 1/3 null events
- Faces presented for 0.5s against chequerboard baseline, SOA=(2 ± 0.5)s, TR=1.4s
- Factorial event-types:
  1. Famous/Nonfamous (F/N)
  2. 1st/2nd Presentation (1/2)



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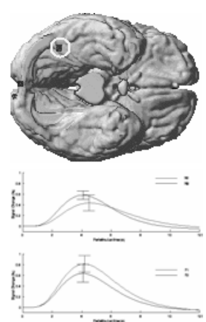
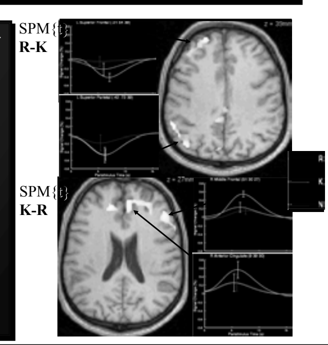
- Faces presented for 0.5s against chequerboard baseline, SOA=(2 ± 0.5)s, TR=1.4s
- Factorial event-types:
  1. Famous/Nonfamous (F/N)
  2. 1st/2nd Presentation (1/2)
- Interaction (F1-F2)-(N1-N2) masked by main effect (F+N)
- Right fusiform interaction of repetition priming and familiarity



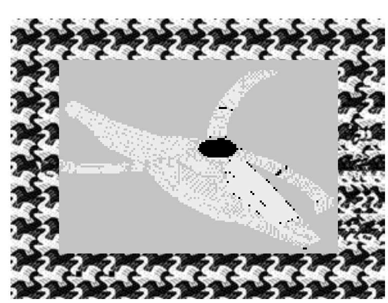
Example 2: Post hoc classification (Henson et al 1999)

- Subjects indicate whether studied (Old) words:
  i) evoke recollection of prior occurrence (R)
  ii) feeling of familiarity without recollection (K)
  iii) no memory (N)
- Random Effects analysis on canonical parameter estimate for event-types
- Fixed SOA of 8s => sensitive to differential but not main effect (de/activations arbitrary)



Example 3: Subject-defined events (Portas et al 1999)

- Subjects respond when “pop-out” of 3D percept from 2D stereogram



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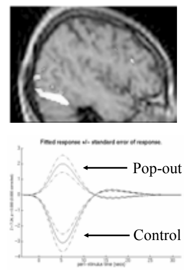
Example 3: Subject-defined events (Portas et al 1999)

- Subjects respond when "pop-out" of 3D percept from 2D stereogram
- Popout response also produces tone
- Control event is response to tone during 3D percept

Temporo-occipital differential activation



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Example 4: Oddball Paradigm (Strange et al, 2000)

- 16 same-category words every 3 secs, plus …
- … 1 perceptual, 1 semantic, and 1 emotional oddball

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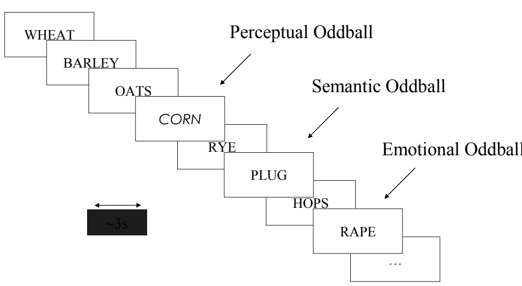

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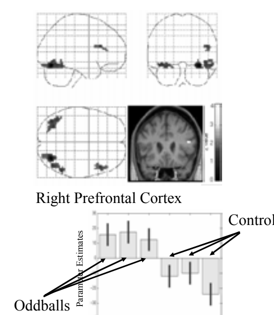
Example 4: Oddball Paradigm (Strange et al, 2000)

- 16 same-category words every 3 secs, plus …
- … 1 perceptual, 1 semantic, and 1 emotional oddball
- 3 nonoddballs randomly matched as controls
- Conjunction of oddball vs. control contrast images: generic deviance detector



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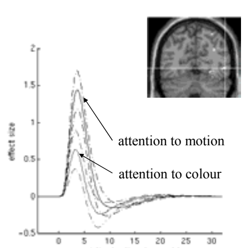
Example 5: Epoch/Event Interactions (Chawla et al 1999)

- Epochs of attention to: 1) motion, or 2) colour
- Events are target stimuli differing in motion or colour
- Randomised, long SOAs to decorrelate epoch and event-related covariates
- Interaction between epoch (attention) and event (stimulus) in V4 and V5

Interaction between attention and stimulus motion change in V5



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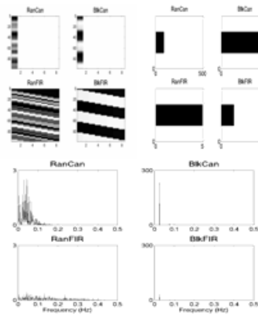
Efficiency – Detection vs Estimation

- "Detection power" vs "Estimation efficiency" (Liu et al, 2001)
- Detect response, or characterise shape of response?
- Maximal detection power in blocked designs;
  Maximal estimation efficiency in randomised designs

=> simply corresponds to choice of basis functions:

detection = canonical HRF
estimation = FIR



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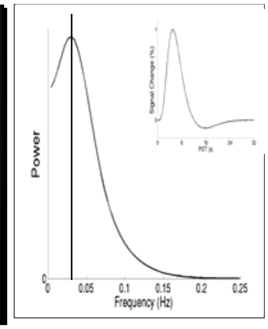
Design Efficiency

- HRF can be viewed as a filter (Josephs & Henson, 1999)
- Want to maximise the signal passed by this filter
- Dominant frequency of canonical HRF is ~0.04 Hz
- So most efficient design is a sinusoidal modulation of neural activity with period ~24s
- (eg, boxcar with 12s on/ 12s off)



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Timing Issues : Latency

- Assume the real response, $r(t)$, is a scaled (by α) version of the canonical, $f(t)$, but delayed by a small amount dt:

$$r(t) = \alpha f(t+dt) \sim \alpha f(t) + \alpha f'(t)\, dt \qquad \text{1st-order Taylor}$$

- If the fitted response, $R(t)$, is modelled by the canonical + temporal derivative:

$$R(t) = \beta_1 f(t) + \beta_2 f'(t) \qquad \text{GLM fit}$$

- Then canonical and derivative parameter estimates, β_1 and β_2, are such that :

$$\Rightarrow \qquad \alpha = \beta_1 \qquad dt = \beta_2 / \beta_1$$

(Henson et al, 2002)
(Liao et al, 2002)

ie, Latency can be approximated by the ratio of derivative-to-canonical parameter estimates (within limits of first-order approximation, +/-1s)

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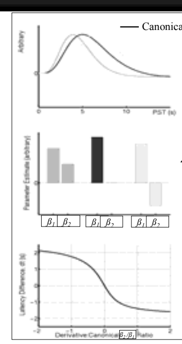
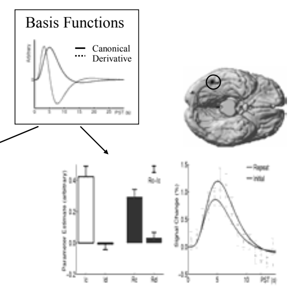
Timing Issues : Latency

Delayed Responses (green/ yellow)

Parameter Estimates

Actual latency, dt, vs. β_2 / β_1





Face repetition reduces latency as well as magnitude of fusiform response

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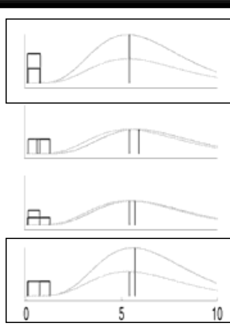
Timing Issues : Latency

Neural		*BOLD*
A. Decreased		A. Smaller Peak
B. Advanced		B. Earlier Onset
C. Shortened (same integrated)		C. Earlier Peak
D. Shortened (same maximum)		D. Smaller Peak *and earlier Peak*



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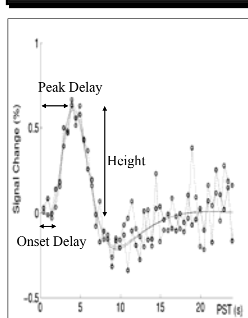
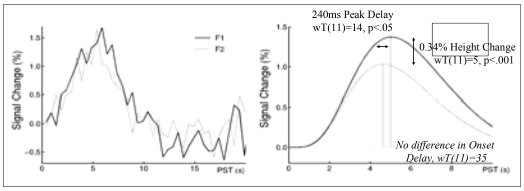
BOLD Response Latency (Iterative)



- Numerical fitting of explicitly parameterised canonical HRF *(Henson et al, 2001)*
- Distinguishes between *Onset* and *Peak* latency…
  …unlike temporal derivative…
  …and which may be important for interpreting neural changes (see previous slide)
- Distribution of parameters tested nonparametrically (Wilcoxon's T over subjects)

BOLD Response Latency (Iterative)



Neural

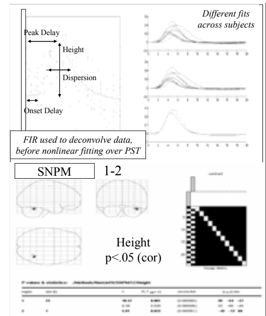
D. Shortened (same maximum)

BOLD

D. Smaller Peak *and earlier Peak*

Most parsimonious account is that repetition reduces ***duration*** *of neural activity…*

BOLD Response Latency (Iterative)



- Four-parameter HRF, nonparametric Random Effects (SNPM99)
- Advantages of iterative vs linear:
  1. Height "independent" of shape
     Canonical "height" confounded by latency (e.g, different shapes across subjects); no slice-timing error
  2. Distinction of onset/peak latency
     Allowing better neural inferences?
- Disadvantages of iterative:
  1. Unreasonable fits (onset/peak tension)
     Priors on parameter distributions? (Bayesian estimation)
  2. Local minima, failure of convergence?
  3. CPU time (~3 days for above)

Temporal Basis Sets: Inferences

- How can inferences be made in hierarchical models (eg, "Random Effects" analyses over, for example, subjects)?

1. Univariate T-tests on canonical parameter alone?
may miss significant experimental variability
canonical parameter estimate not appropriate index of "magnitude" if real responses are non-canonical (see later)

2. Univariate F-tests on parameters from multiple basis functions?
need appropriate corrections for nonsphericity (Glaser et al, 2001)

3. Multivariate tests (eg Wilks Lambda, Henson et al, 2000)
not powerful unless ~10 times as many subjects as parameters