Introduction à la statistique médicale

Statistical Parametric Mapping short course

Course 5:

Evoked response fMRI & Design efficiency

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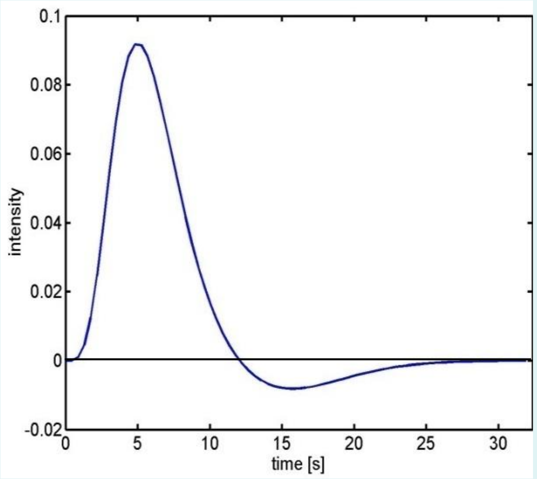
Content

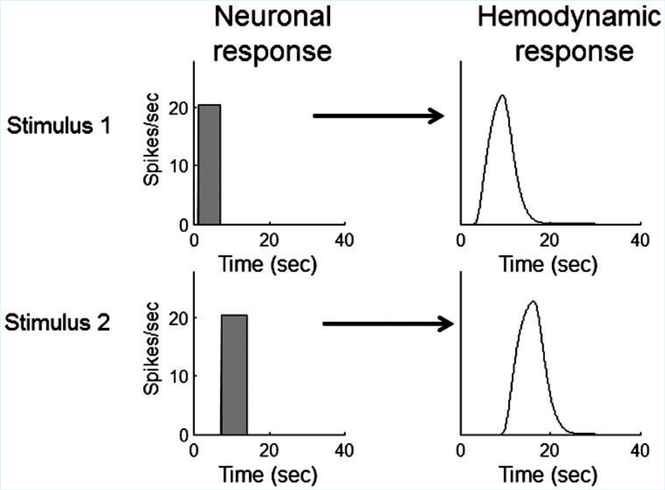
- **Evoked response models**
- Design efficiency

BOLD response

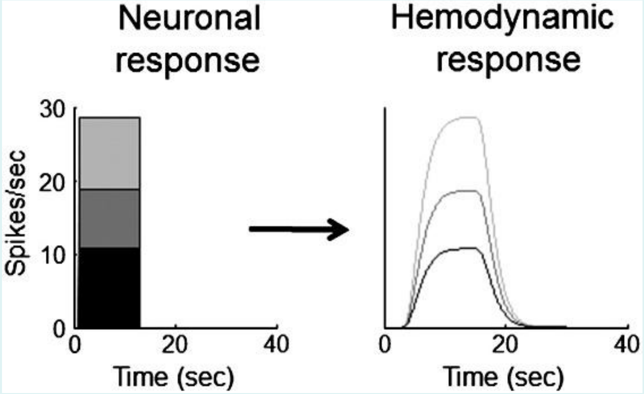
Hemodynamic response function (HRF):



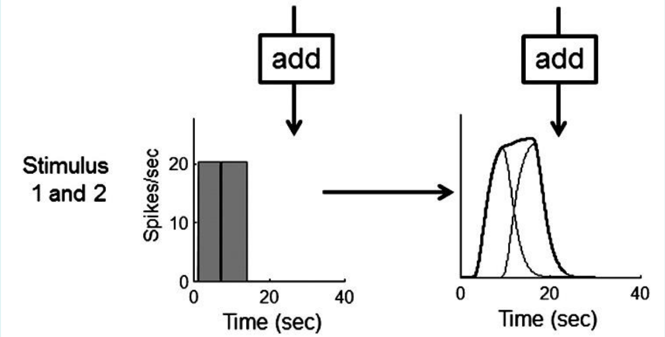
Shift invariance



Scaling



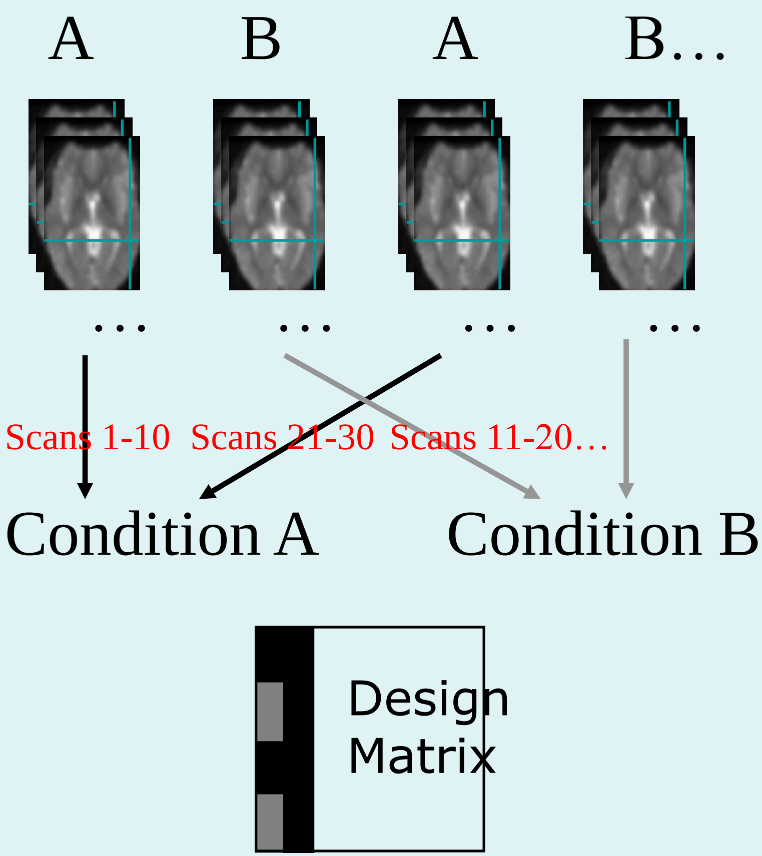
Additivity



Boynton et al, NeuroImage, 2012.

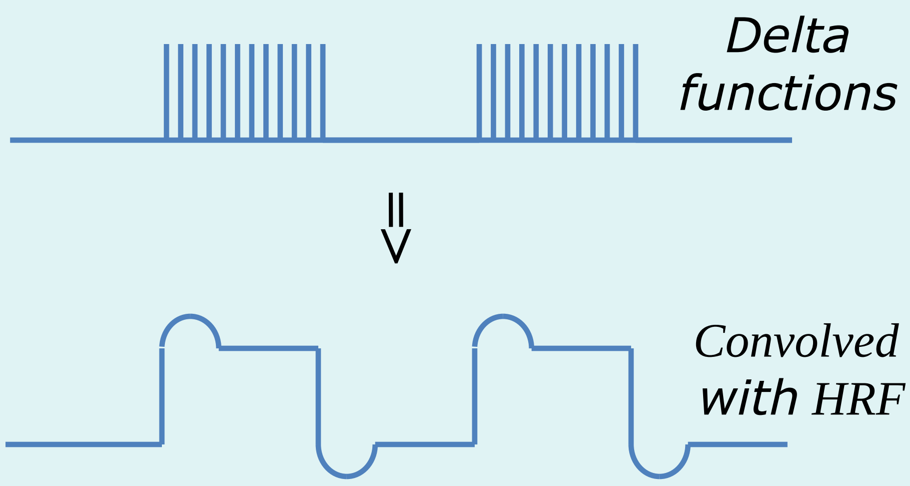
Epoch vs. event related design

"PET Blocked conception"
(scans assigned to conditions)



"fMRI Epoch conception"
(scans treated as timeseries)

"fMRI Event-related conception"



Advantages of Event-Related design

- Randomised trial order

  c.f. confounds of blocked designs

Blocked designs may trigger expectations and cognitive sets

Intermixed designs can minimise this by stimulus randomisation

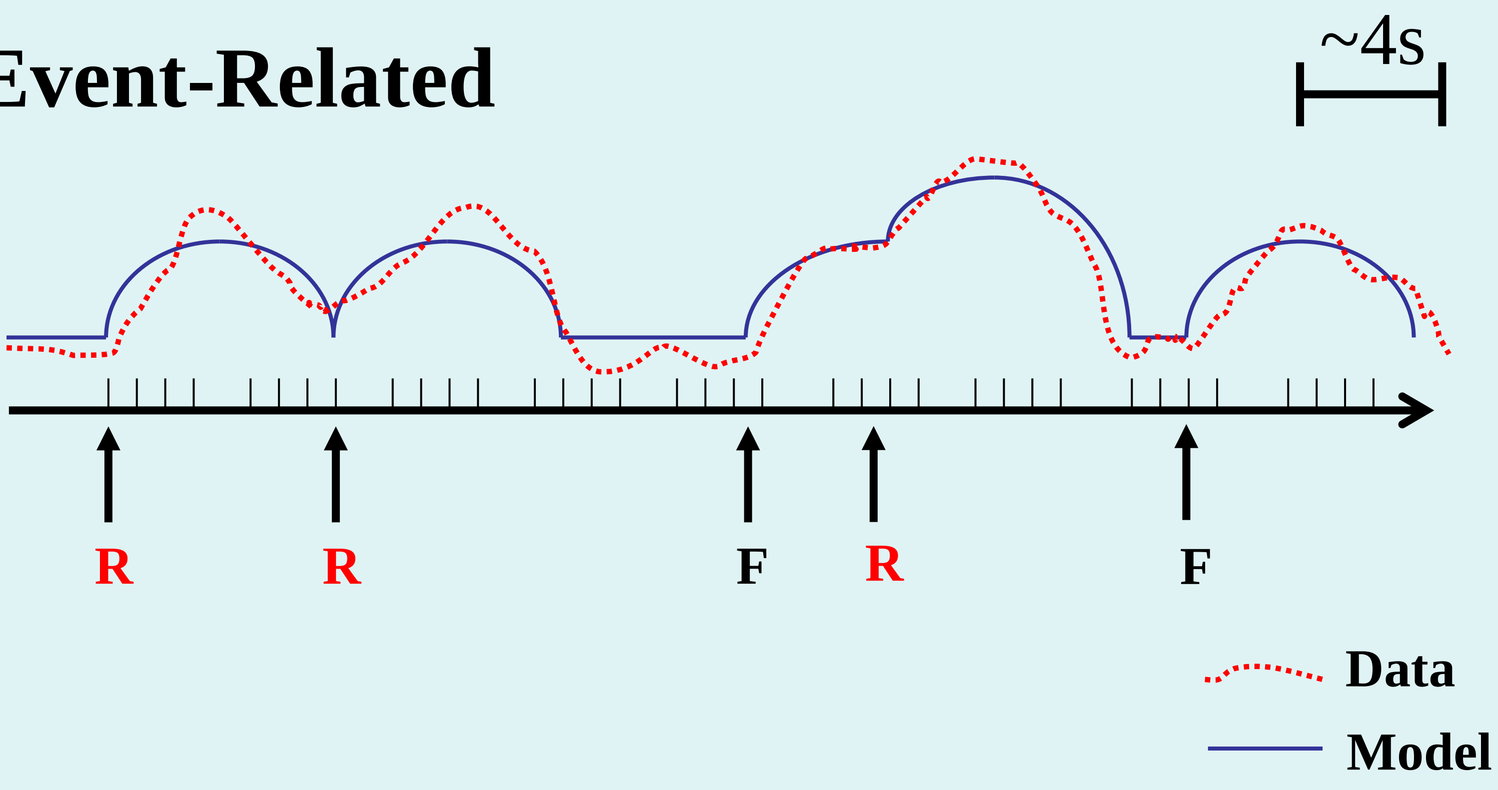
Advantages of Event-Related design

- Randomised trial order
  c.f. confounds of blocked designs
- Post hoc / subjective classification of trials
  e.g, according to subsequent memory

R = Words Later Remembered

F = Words Later Forgotten

Event-Related



Advantages of Event-Related design

- Randomised trial order
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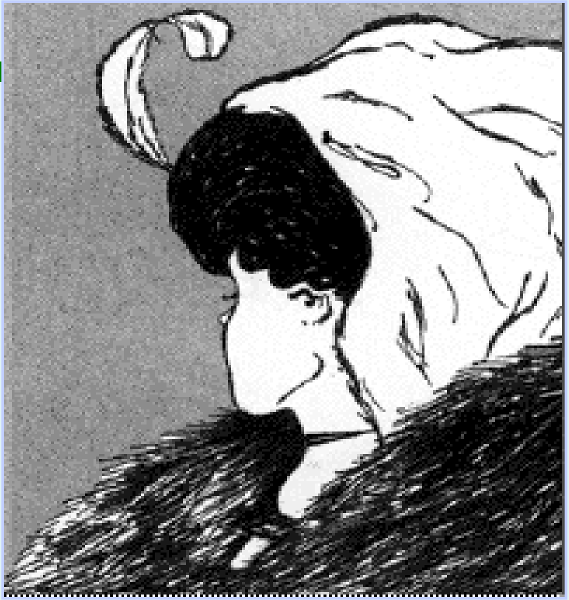
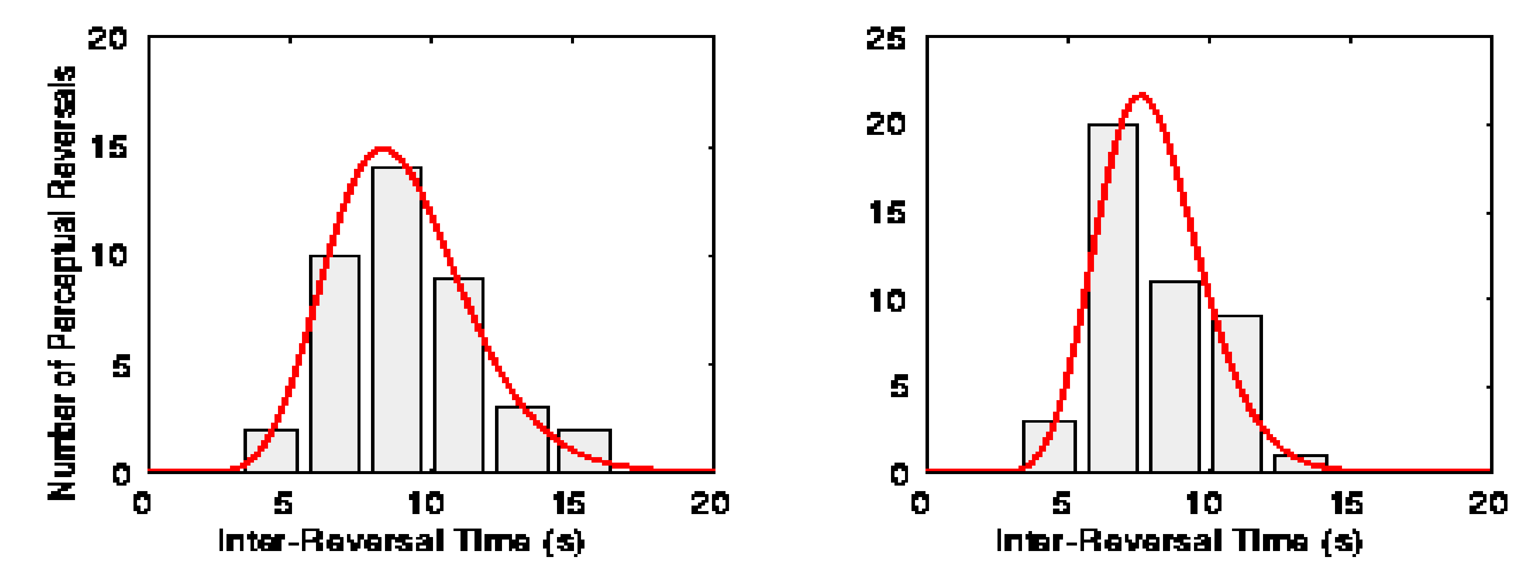
- Post hoc / subjective classification of trials
  e.g, according to subsequent memory
- Some events can only be indicated (in time)
  e.g, spontaneous perceptual changes

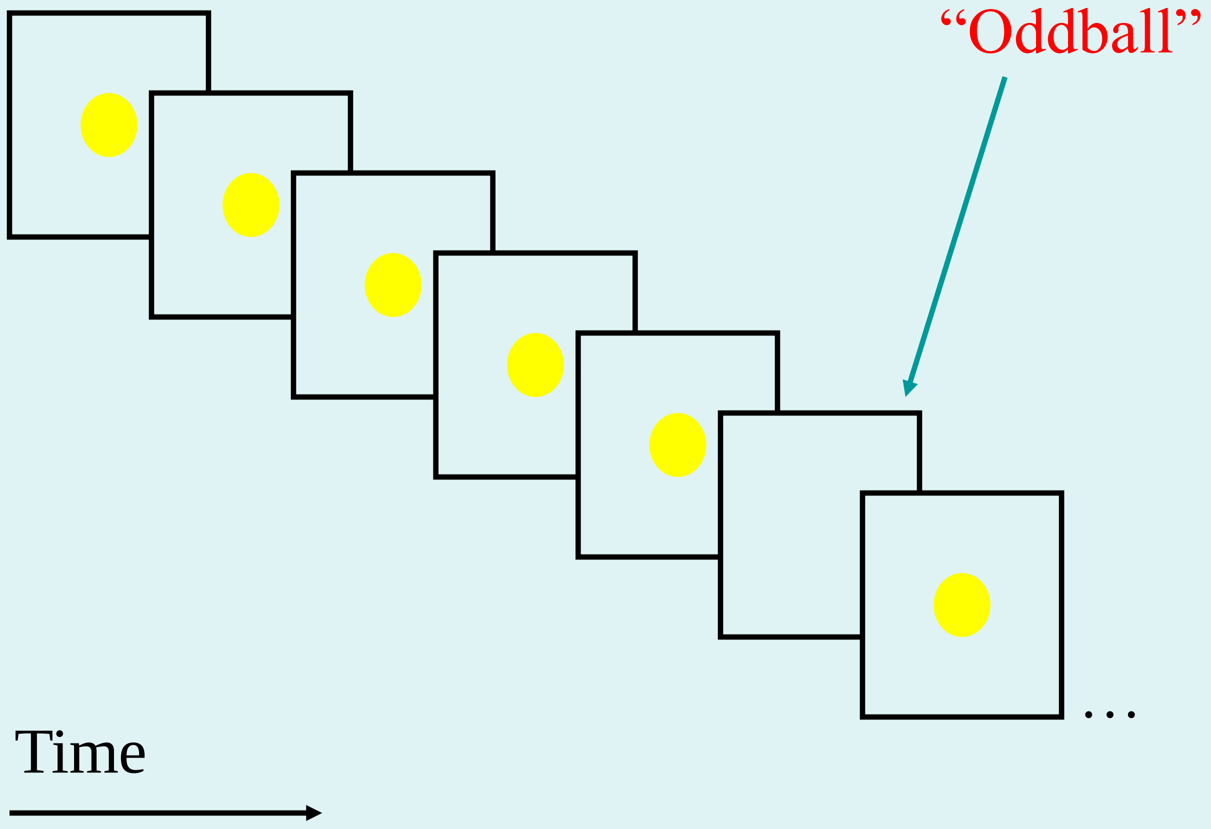




Number of Perceptual Reversals
Inter-Reversal Time (s)
Inter-Reversal Time (s)

Advantages of Event-Related design

- Randomised trial order
  c.f. confounds of blocked designs
- Post hoc / subjective classification of trials
  e.g, according to subsequent memory
- Some events can only be indicated (in time)
  e.g, spontaneous perceptual changes
- Some trials cannot be blocked
  e.g, "oddball" designs


"Oddball"
Time
. . .

Advantages of Event-Related design

- Randomised trial order
  c.f. confounds of blocked designs

- Post hoc / subjective classification of trials
  e.g, according to subsequent memory

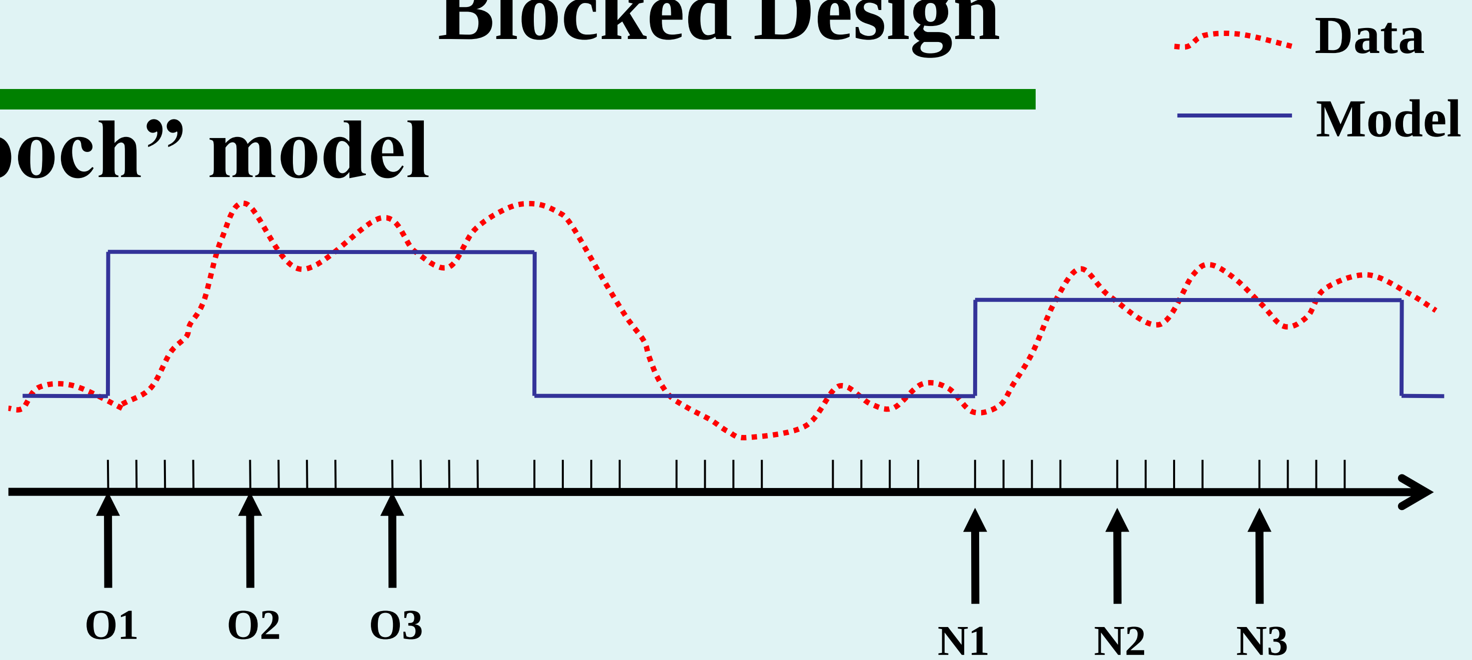
- Some events can only be indicated (in time)
  e.g, spontaneous perceptual changes

- Some trials cannot be blocked
  e.g, "oddball" designs

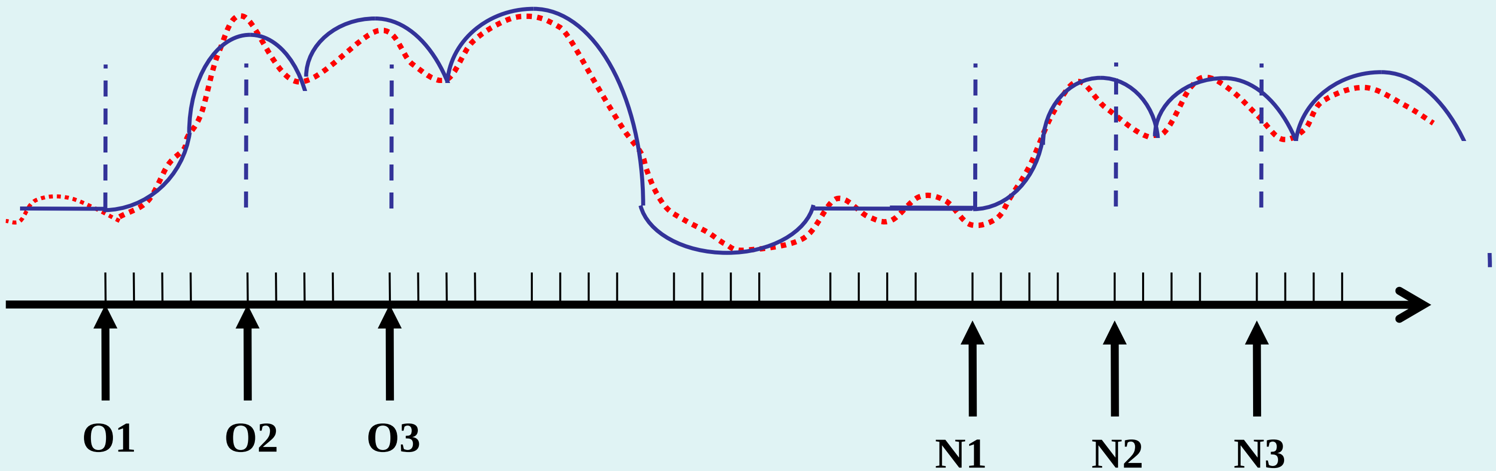
- More accurate models even for blocked designs?
  e.g, "state-item" interactions

Blocked Design

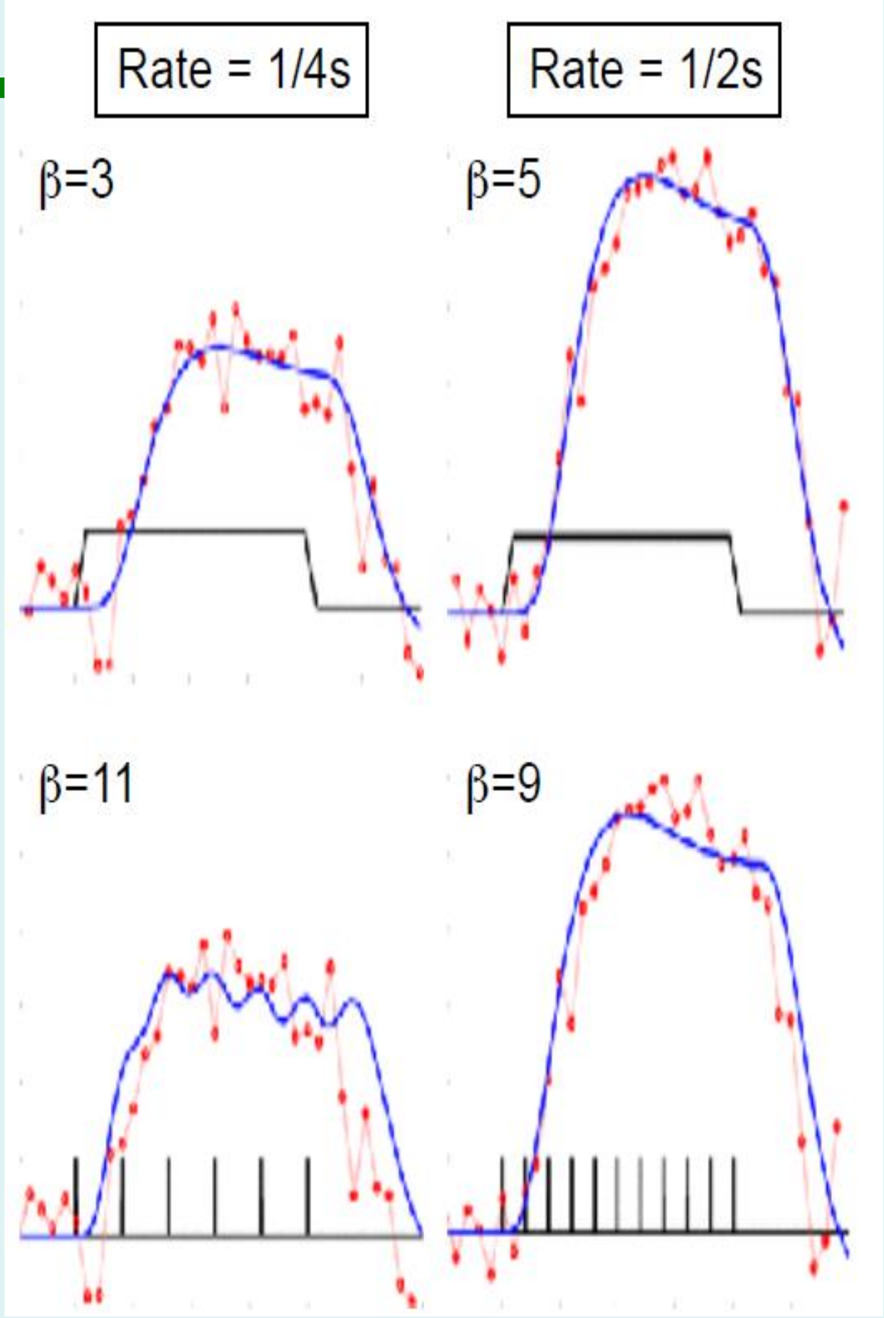
“Epoch” model



“Event” model



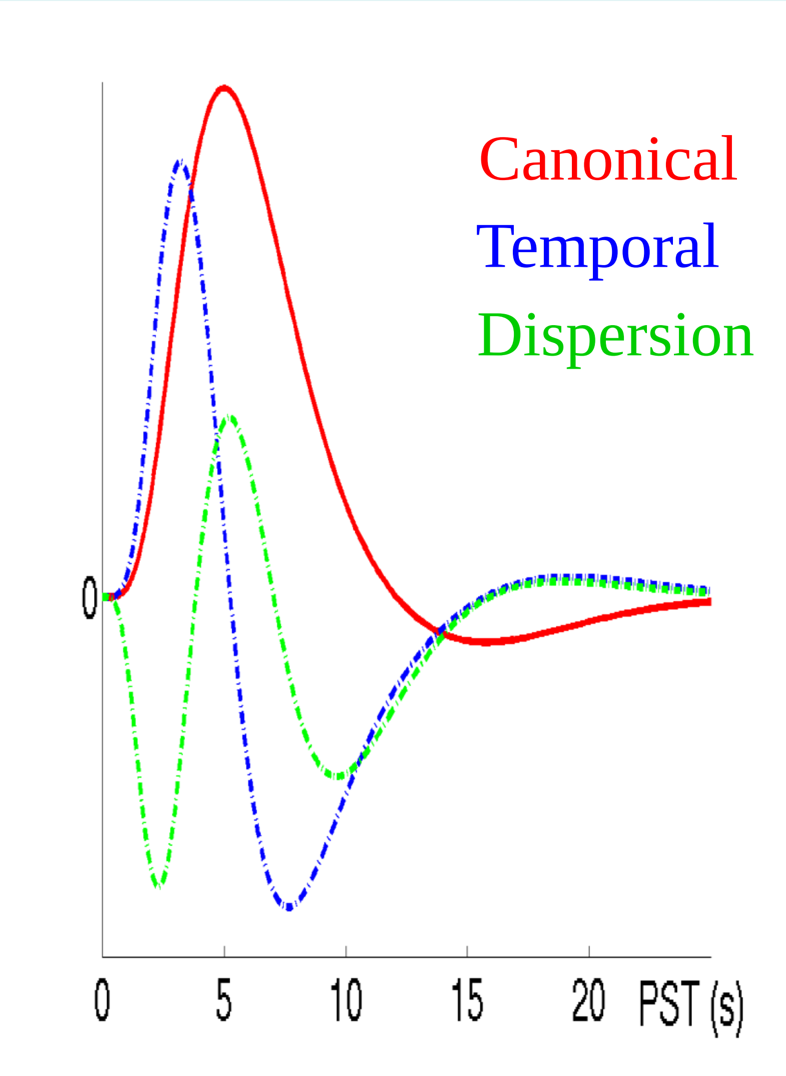
- Blocks of trials can be modeled as boxcars or runs of events
- BUT: interpretation of the parameter estimates may differ
- Consider an experiment presenting words at different rates in different blocks:
  - An “epoch” model will estimate parameter that increases with rate, because the parameter reflects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



Disadvantages of ER designs

- Less efficient for detecting effects than are blocked designs *(see later…)*
- Some psychological processes may be better blocked (e.g. task-switching, attentional instructions)

Temporal Basis Functions



- Informed Basis Set

  (Friston et al. 1998)
- Canonical HRF (2 gamma functions)

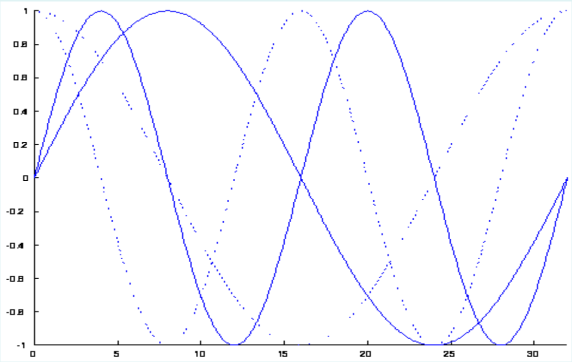
  plus Multivariate Taylor expansion in:

  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…)

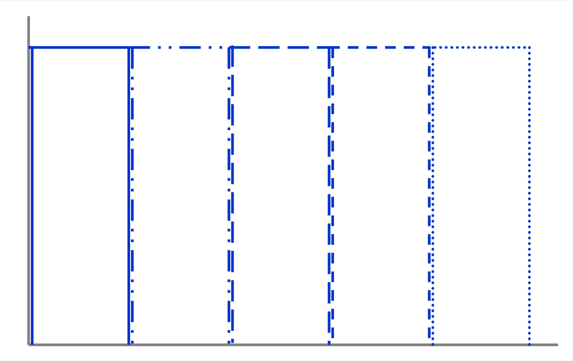
Temporal Basis Functions

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



Temporal Basis Functions

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



Temporal Basis Functions

- Fourier Set

  Windowed sines & cosines
  Any shape (up to frequency limit)
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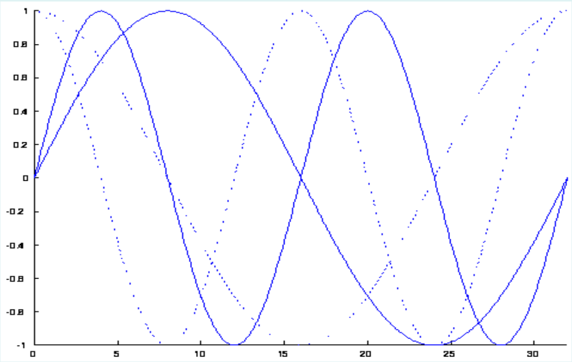
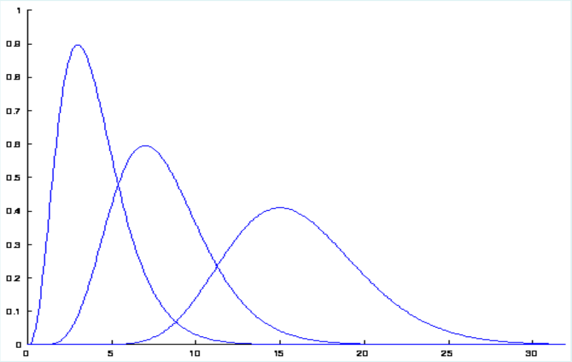


- Gamma Functions

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



Temporal Basis Functions

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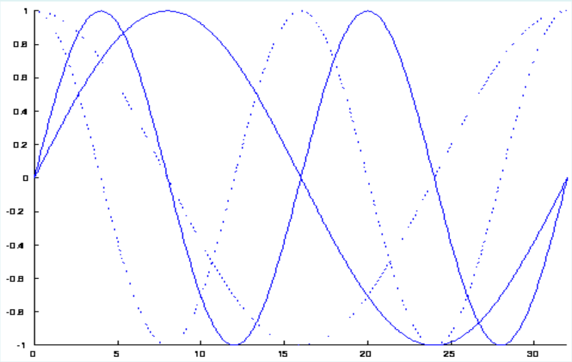

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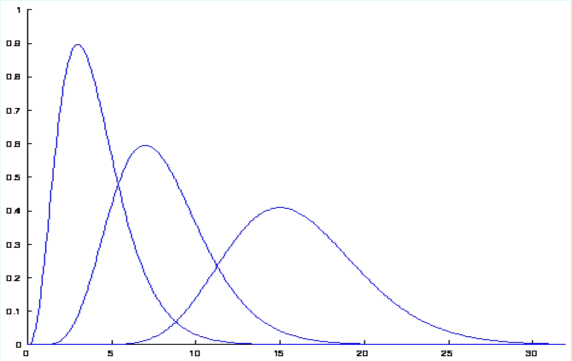
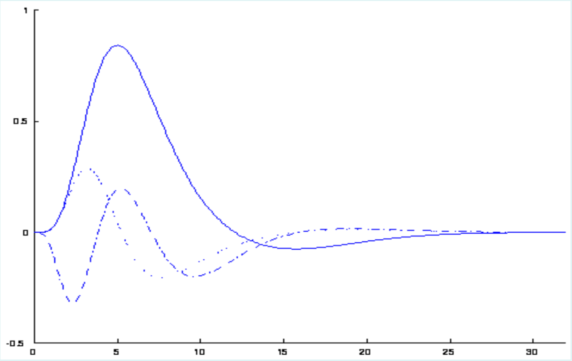
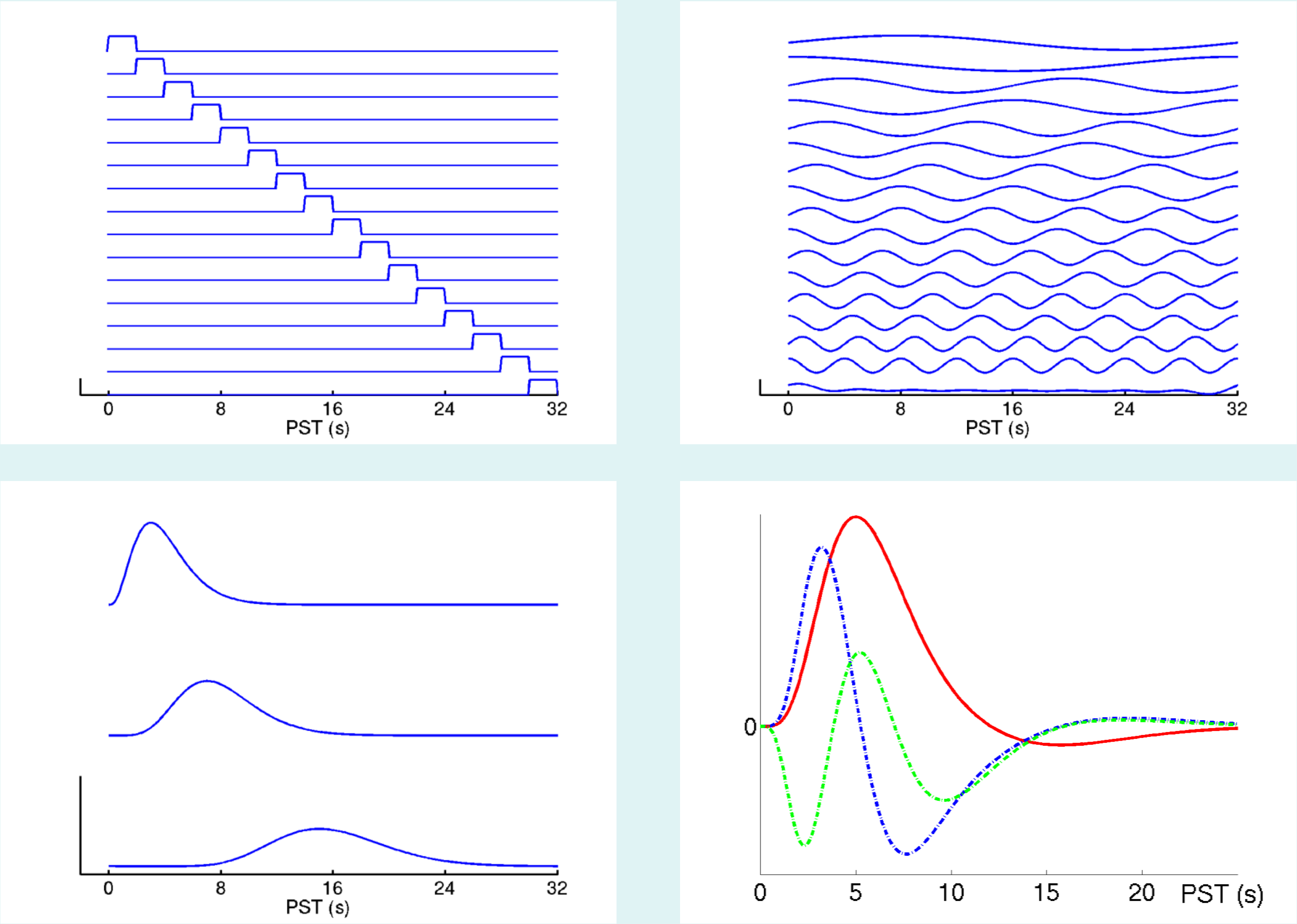


- Informed Basis Set

  Best guess of canonical BOLD response
  Variability captured by Taylor expansion
  "Magnitude" inferences via t-test…?

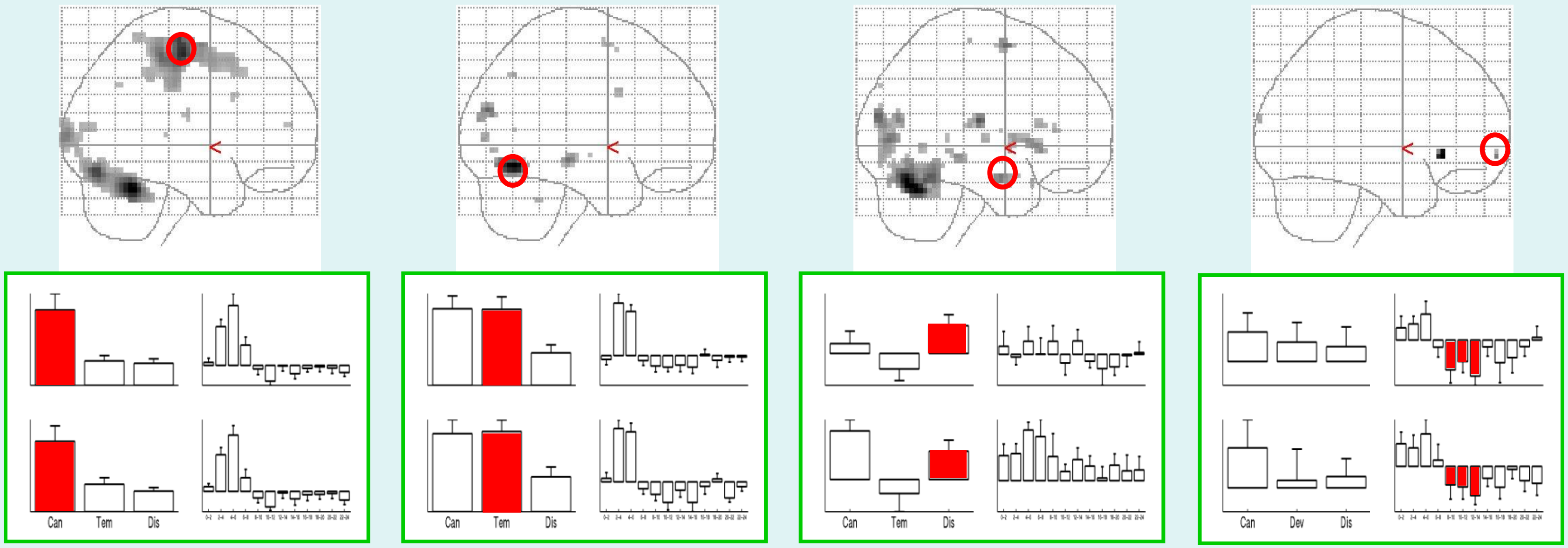


Temporal Basis Functions



Temporal Basis Functions, which one(s)?

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



Canonical + Temporal + Dispersion + FIR

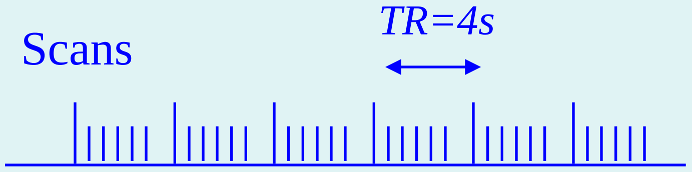
…canonical + temporal + dispersion derivatives appear sufficient

…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)

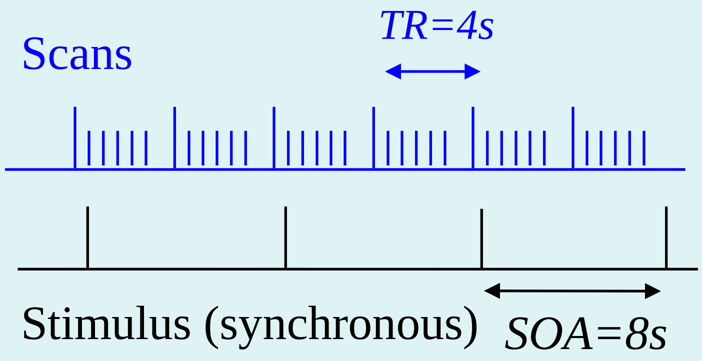
Timing Issues

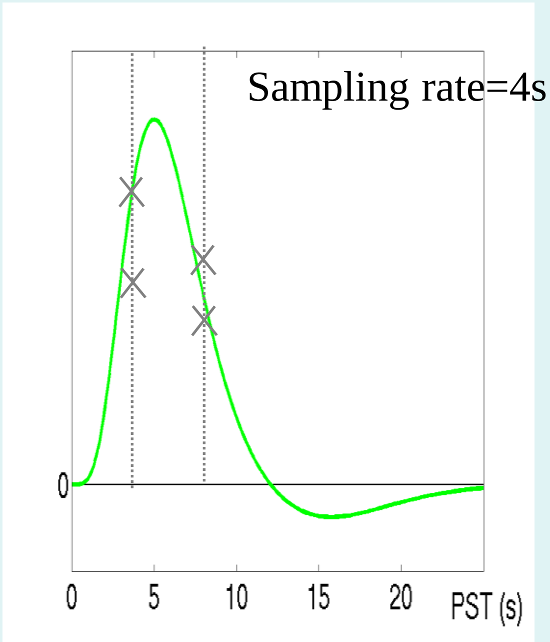
- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s



Timing Issues

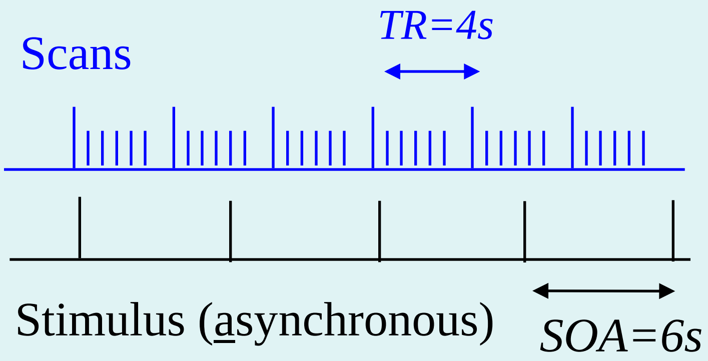
- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal

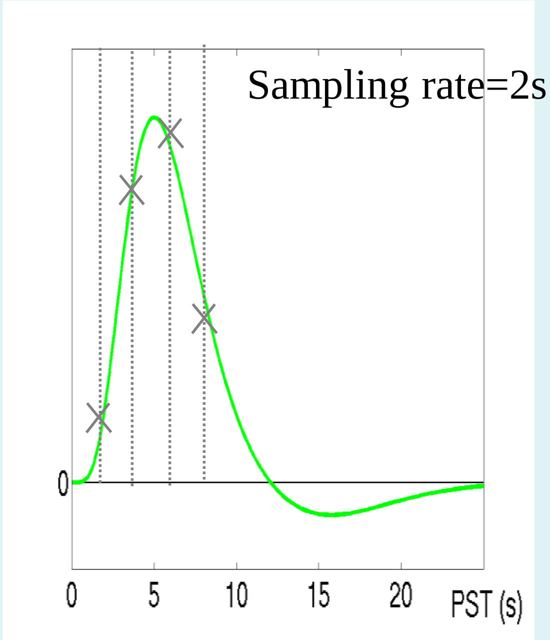




Timing Issues

- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal
- Higher effective sampling by:
  1. Asynchrony, *e.g. SOA=1.5TR*

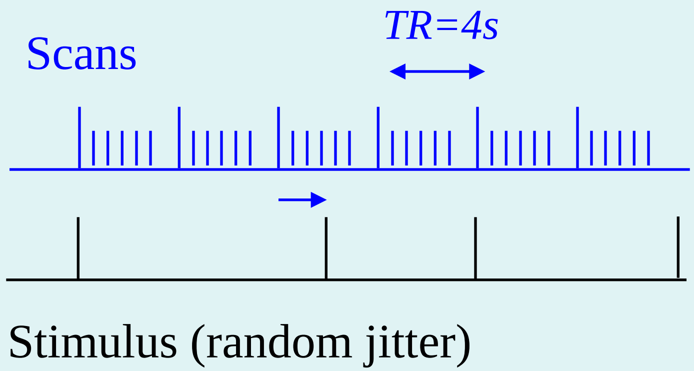


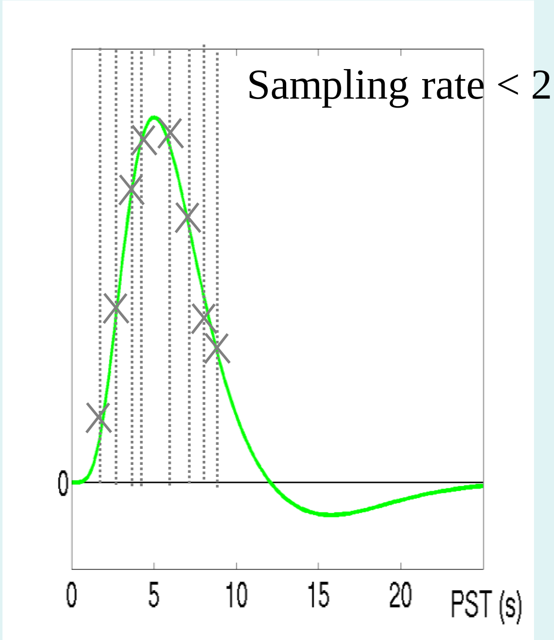


Timing Issues

- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal
- Higher effective sampling by:

  1. Asynchrony, *e.g. SOA=1.5TR*
  2. Random Jitter, e.g. *SOA=(2±0.5)TR*





BOLD Response Latency (Linear)

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

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

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

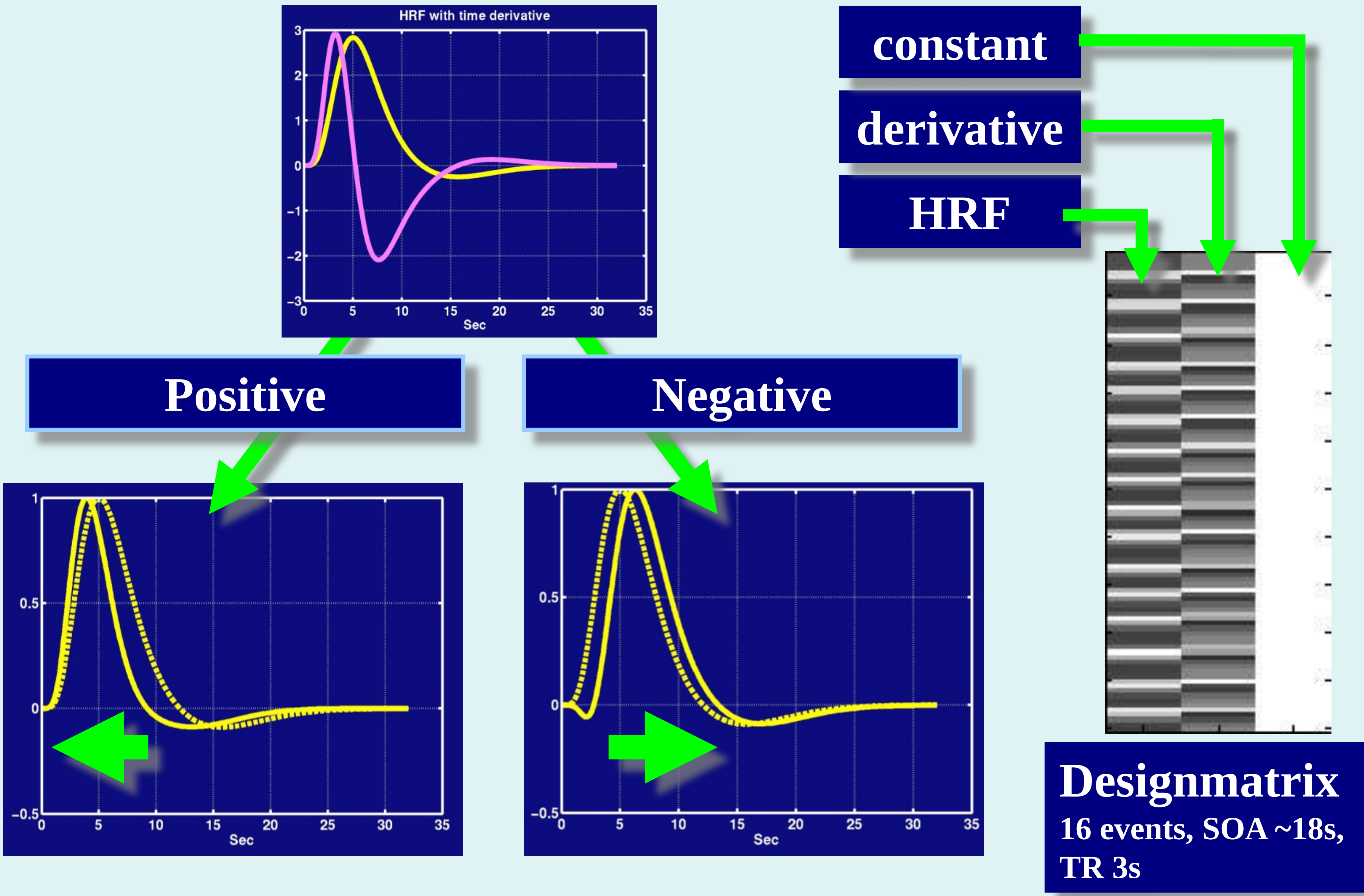
$$R(t) = ß_1 f(t) + ß_2 f'(t) \qquad \textit{GLM fit}$$

- Then canonical and derivative parameter estimates, $ß_1$ and $ß_2$, are such that:

$$\alpha = ß_1 , \quad dt = ß_2 / ß_1$$

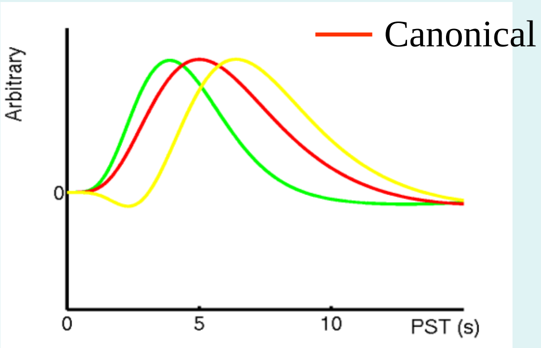
- *i.e. latency can be approximated by the ratio of derivative-to-canonical parameter estimates (within limits of first-order approximation, +/- 1s)*

BOLD Response Latency: example

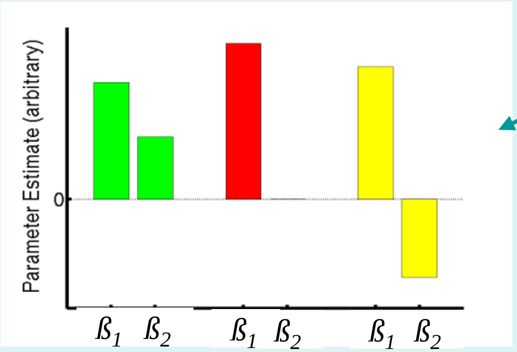


BOLD Response Latency (Linear)

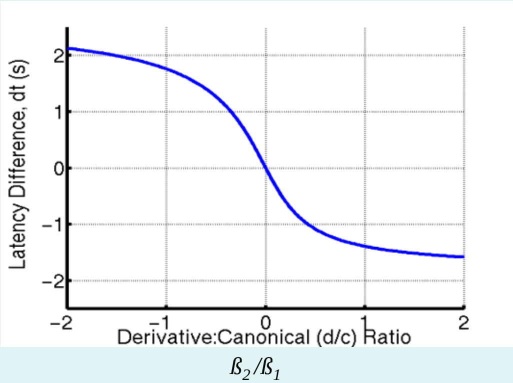
Delayed Responses (green/yellow)

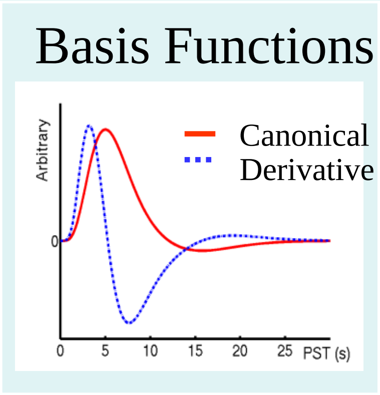


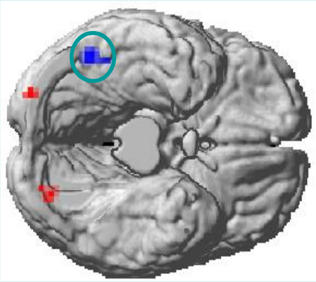
Parameter Estimates

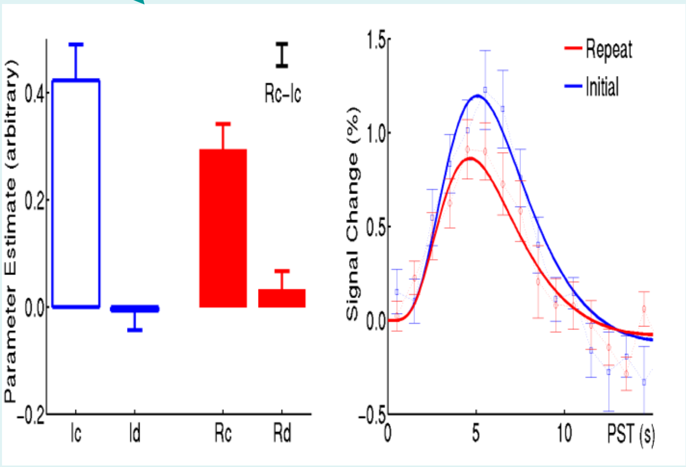


Actual latency, dt, vs. $ß_2 / ß_1$









Face repetition reduces latency as well as magnitude of fusiform response

Neural Response Latency

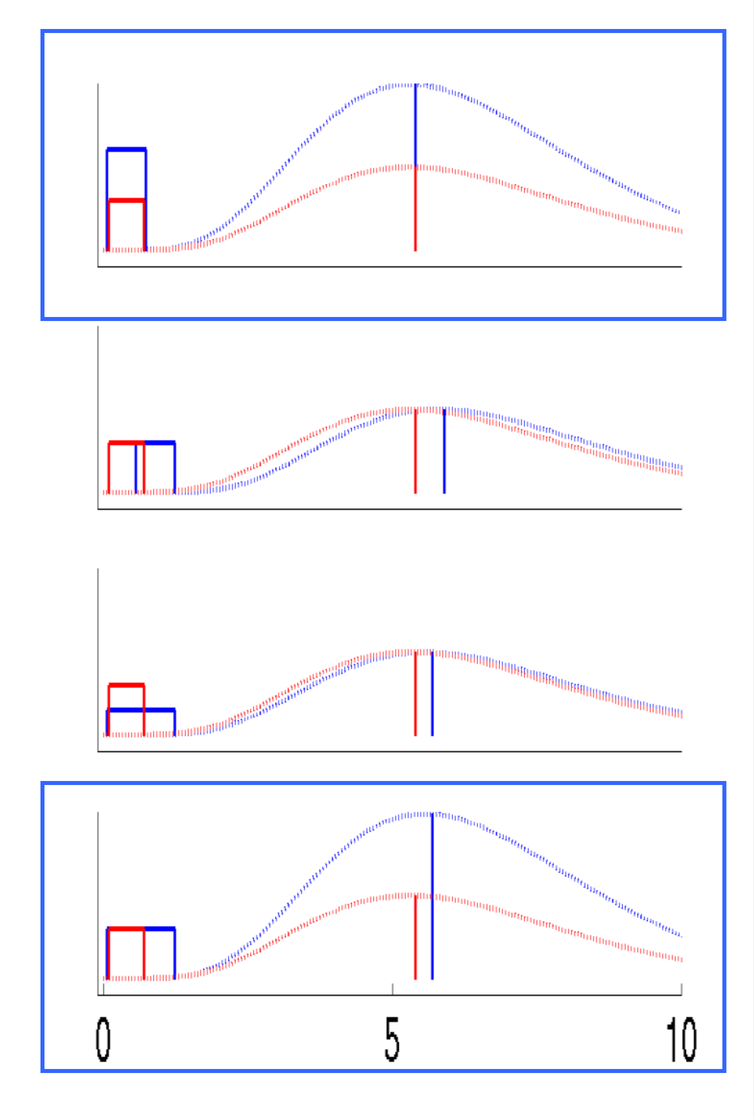
Neural

A. Decreased

B. Advanced

C. Shortened (same integrated)

D. Shortened (same maximum)



BOLD

A. Smaller Peak

B. Earlier Onset

C. Earlier Peak

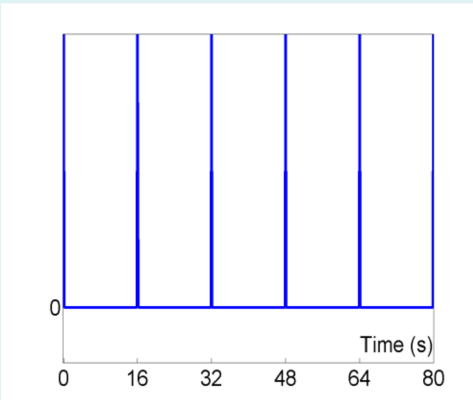
D. Smaller Peak *and earlier Peak*

Content

- Evoked response models
- **Design efficiency**

Fixed SOA = 16s

Stimulus (“Neural”)



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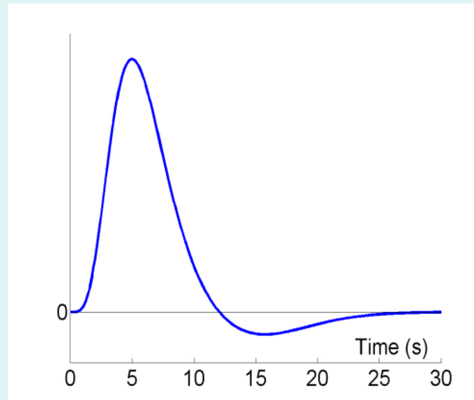
HRF



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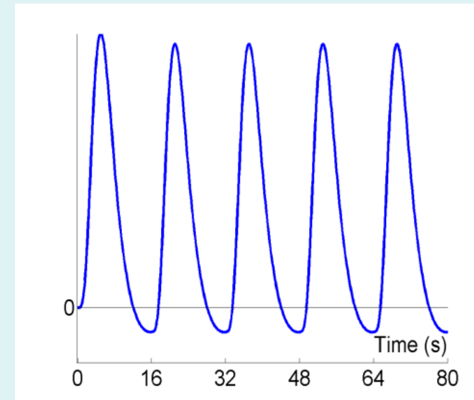
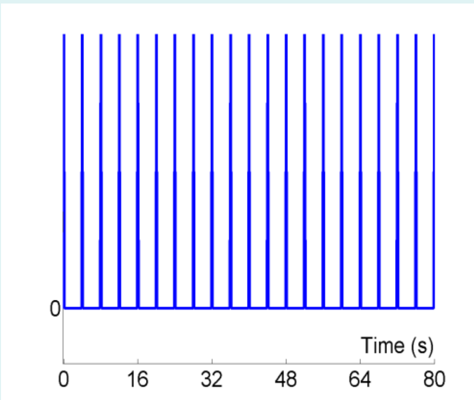
Predicted Data



Not particularly efficient…

Fixed SOA = 4s

Stimulus ("Neural")



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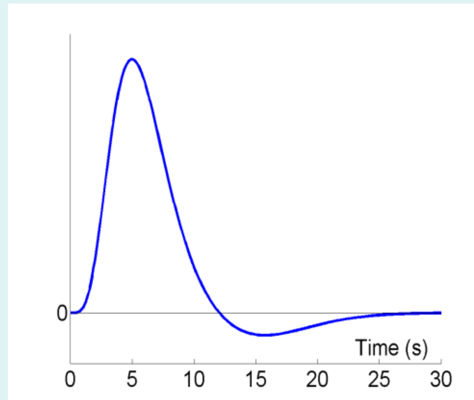
HRF



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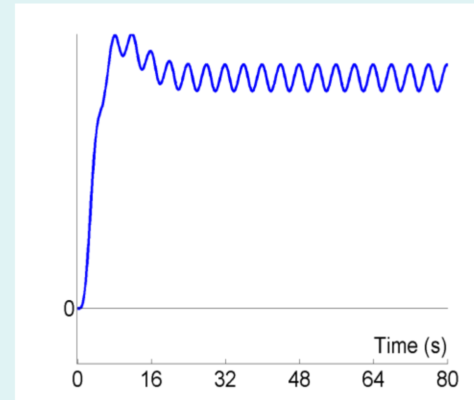
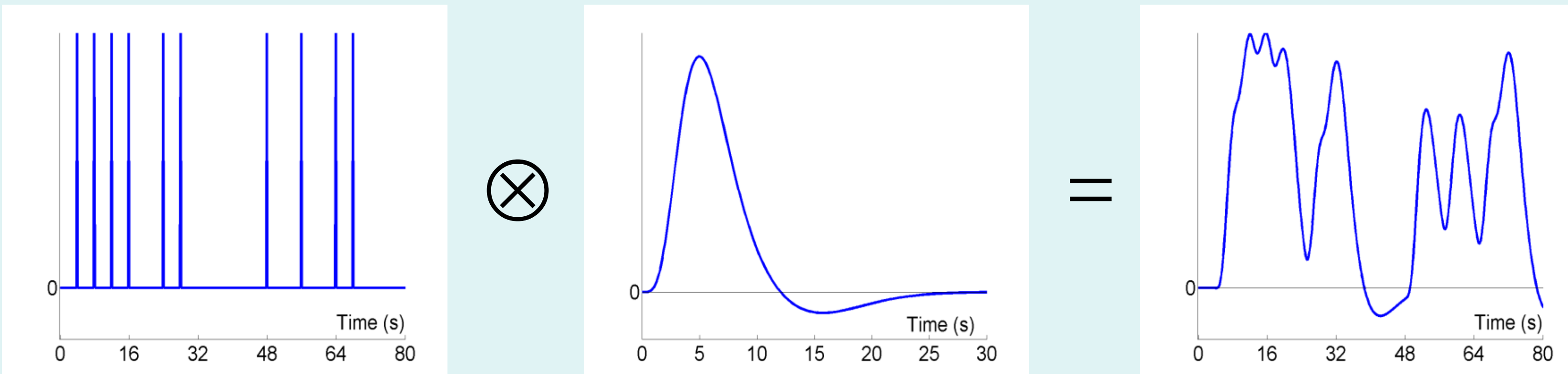
Predicted Data



Very Inefficient…

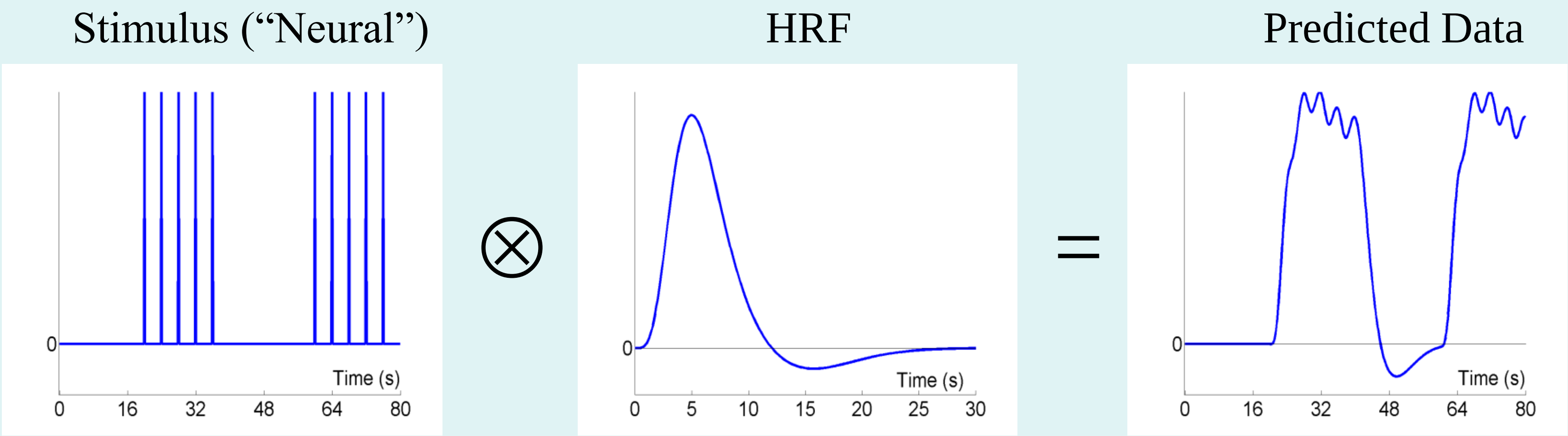
Randomised, SOA_{min} = 4s

Stimulus ("Neural") HRF Predicted Data



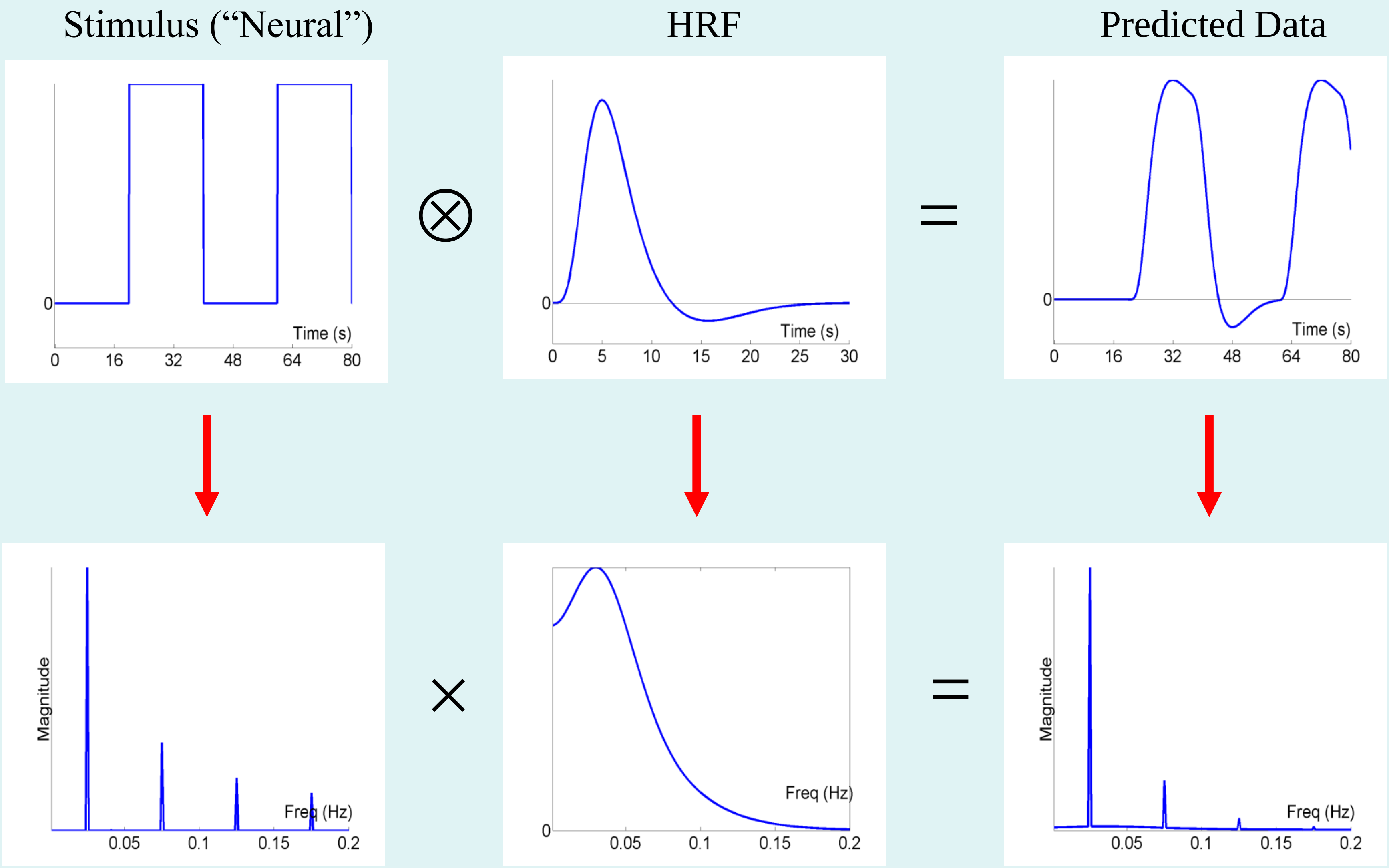
More Efficient…

Blocked, $SOA_{min} = 4s$



Even more Efficient…

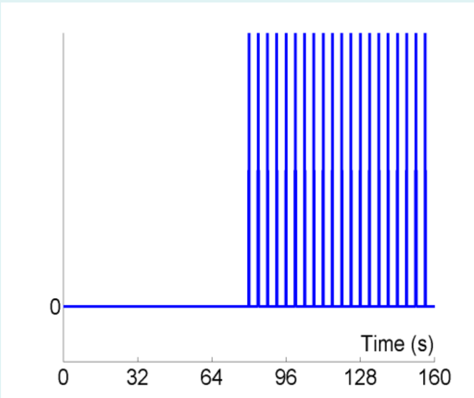
Blocked, epoch = 20s



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

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

Stimulus (“Neural”)



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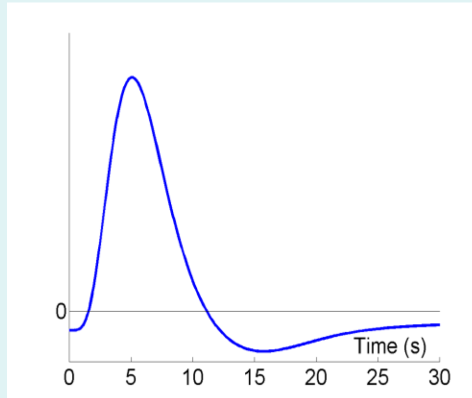
HRF



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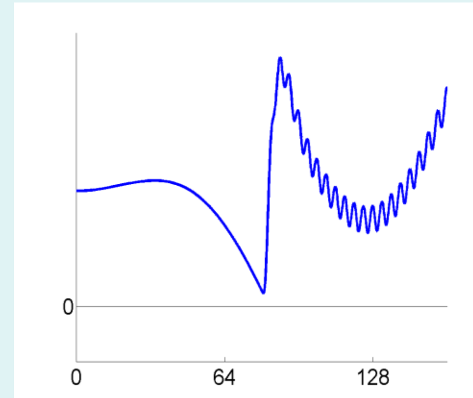
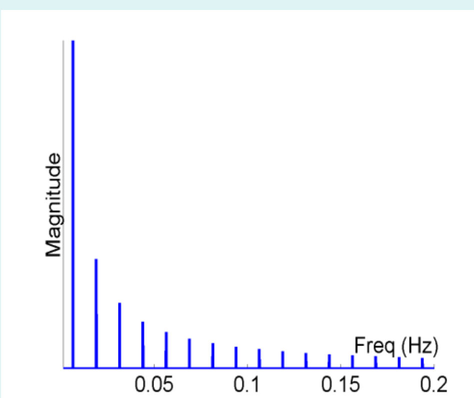


“Effective HRF” (after highpass filtering)
(Josephs & Henson, 1999)



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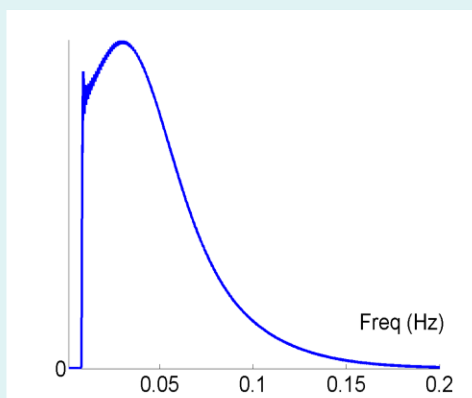

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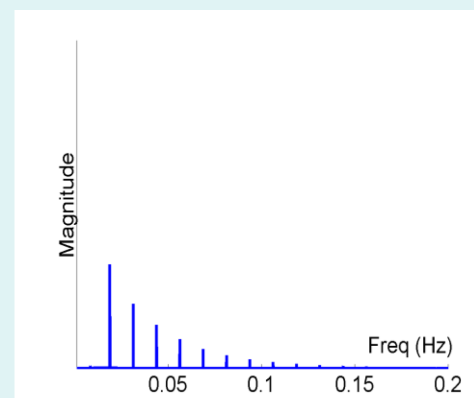
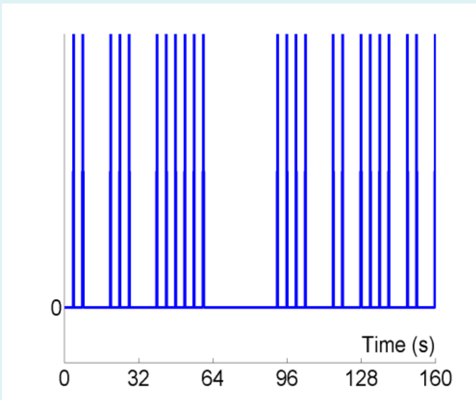


Don’t have long (>60s) blocks!

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

Stimulus (“Neural”)



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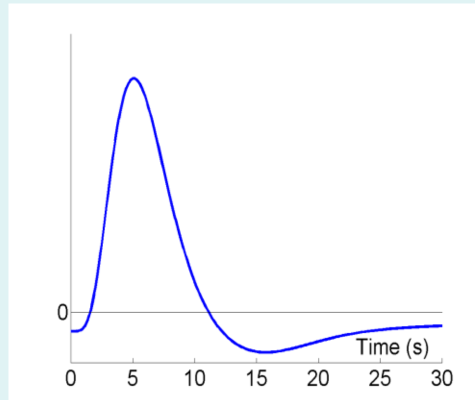
HRF



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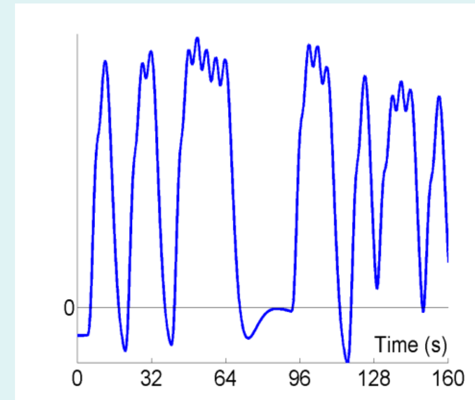
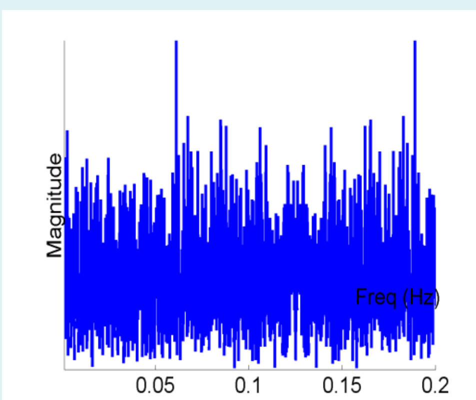
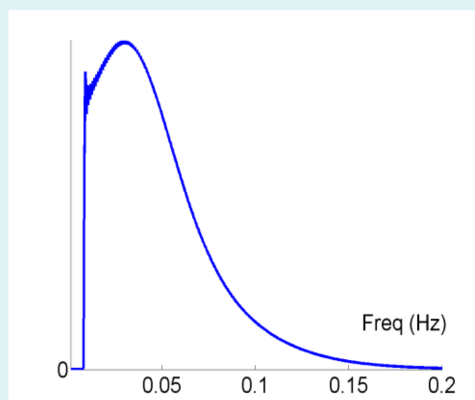
Predicted Data





$\times$



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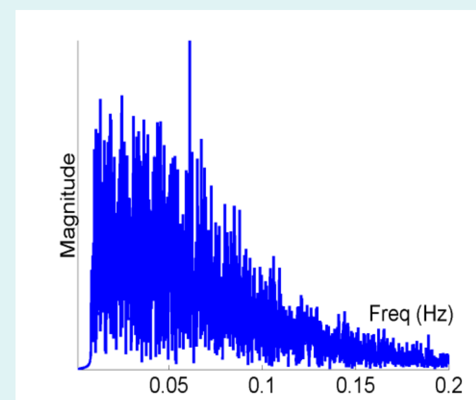

(Randomised design spreads power over frequencies)

Design Efficiency

Maximise efficiency by maximising t, by minimising the squared variance:

$$t = \frac{c^T \beta}{\sqrt{\mathrm{var}(c^T \beta)}}$$

X: design matrix
c: contrast vector
β: beta vector

Assuming that the error in our model is 'iid', each observation is drawn independently from a Gaussian distribution:

$$b \sim N(b, s^2 (X^T X)^{-1})$$

$$\mathrm{var}(c^T b) = s^2 c^T (X^T X)^{-1} c$$

Assuming σ is independent of our design, taking a fixed contrast we can only alter our design matrix to improve efficiency.

Formal definition of **design efficiency** minimises variance:

$$e \gg \frac{1}{\sqrt{c^T (X^T X)^{-1} c}}$$

Given the contrast of interest, **minimise covariance in the design matrix**

Efficiency can be estimated before using the design