# Event-related fMRI: Modelling of hemodynamic timeseries

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With thanks to the FIL methods group and Rik Henson

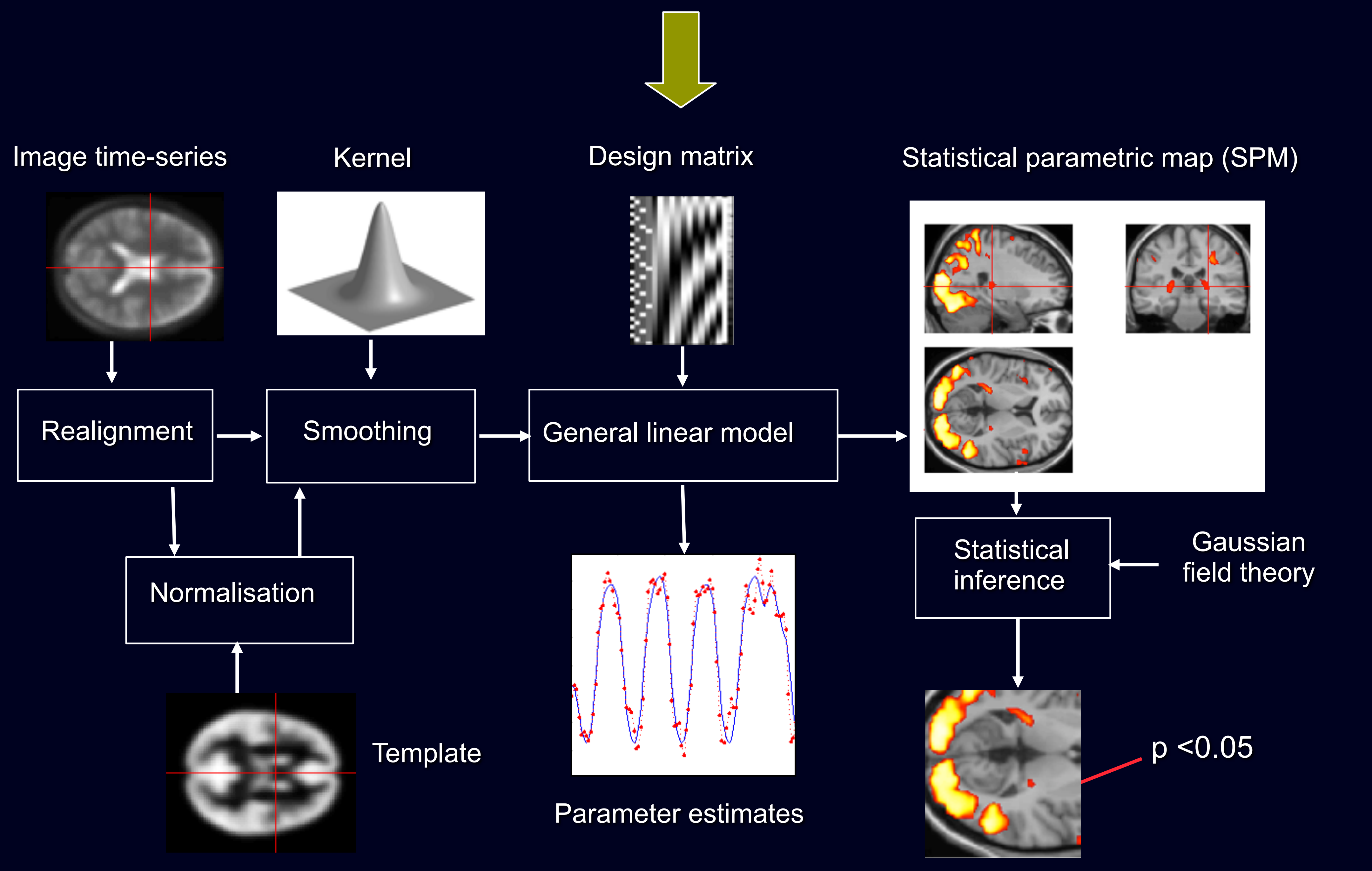


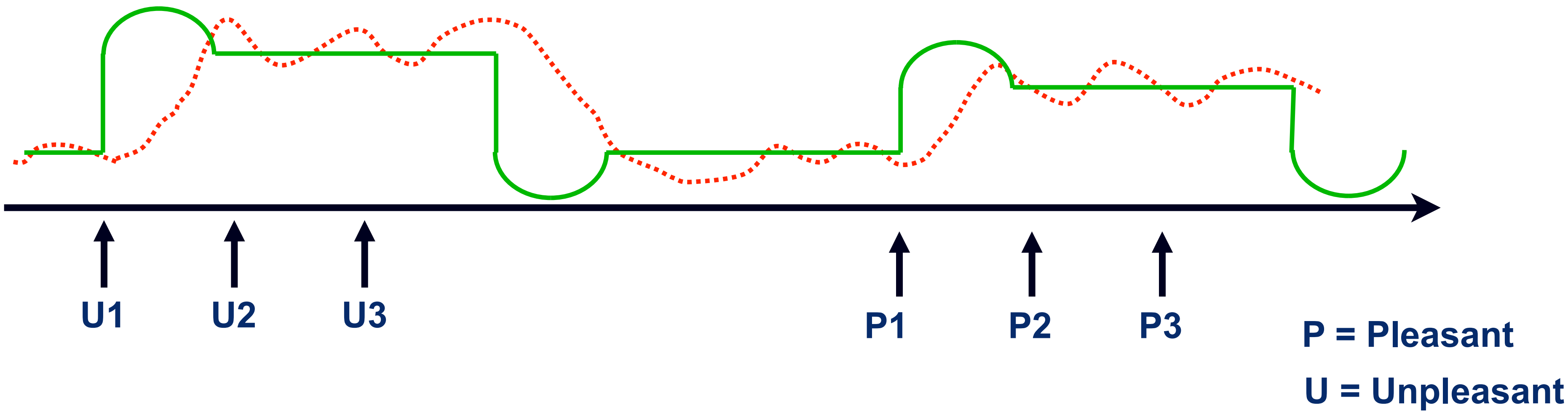
Image time-series
Kernel
Design matrix
Statistical parametric map (SPM)
Realignment
Smoothing
General linear model
Normalisation
Template
Parameter estimates
Statistical inference
Gaussian field theory
p <0.05

# Overview

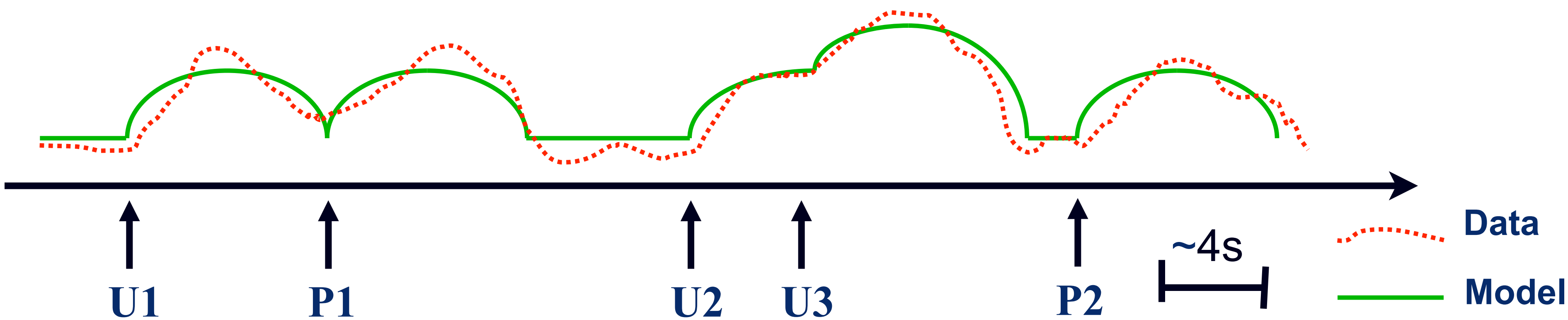
1. Block/epoch vs. event-related fMRI
2. (Dis)Advantages of efMRI
3. GLM: Convolution
4. BOLD impulse response
5. Temporal Basis Functions
6. Timing Issues
7. Design Optimisation – “Efficiency”

# Block/epoch designs vs event-related designs

**Block/epoch designs examine responses to series of similar stimuli**




**Event-related designs account for response to each single stimulus**

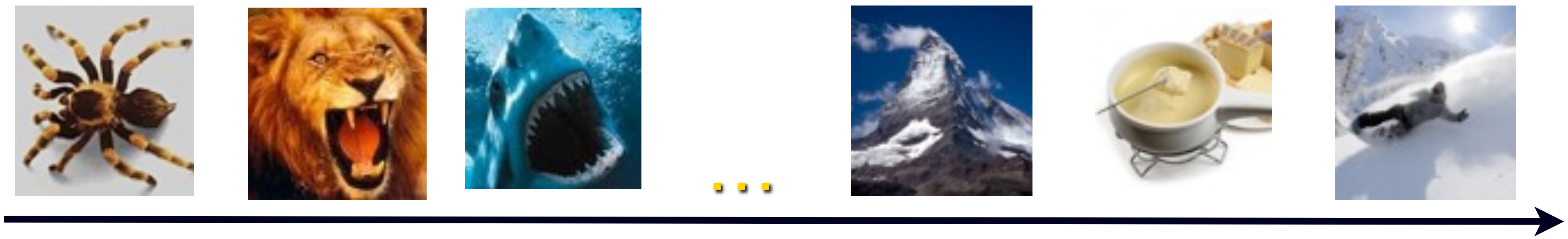


# Advantages of event-related fMRI

1. Randomised trial order

# efMRI: Randomised trial order

Blocked designs may trigger expectations and cognitive sets



Unpleasant (U) Pleasant (P)

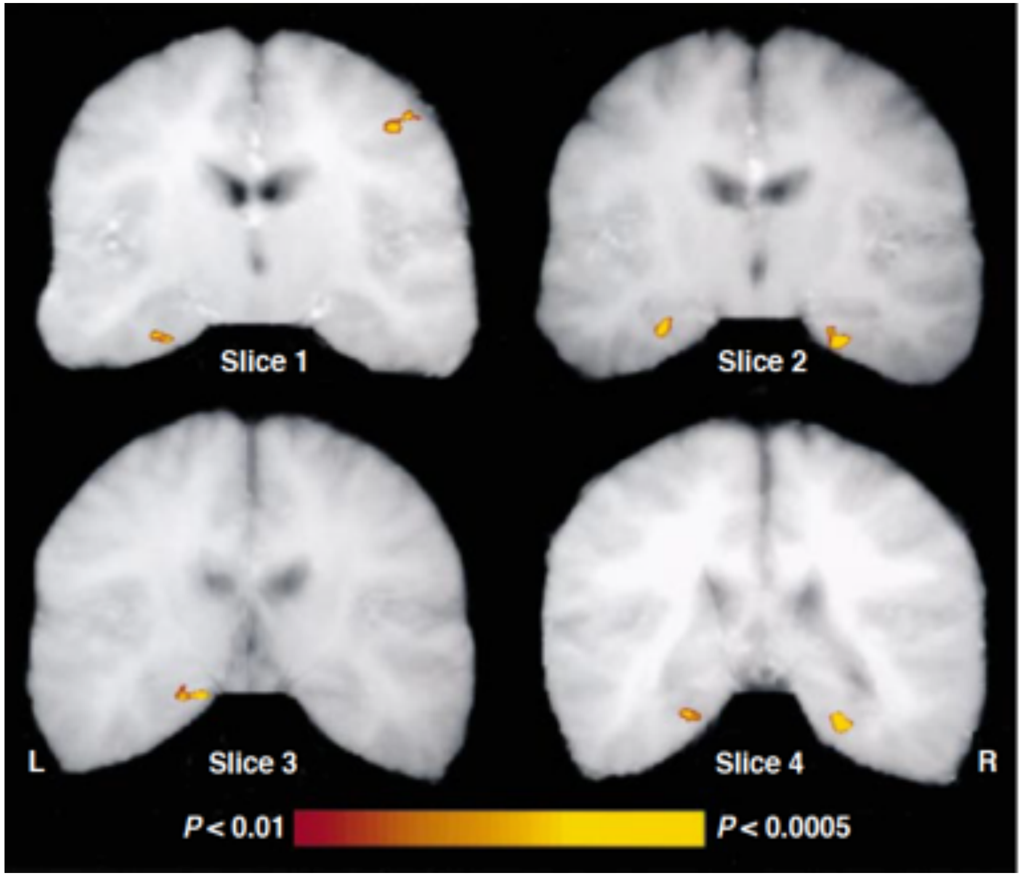
Intermixed designs can minimise this by stimulus randomisation

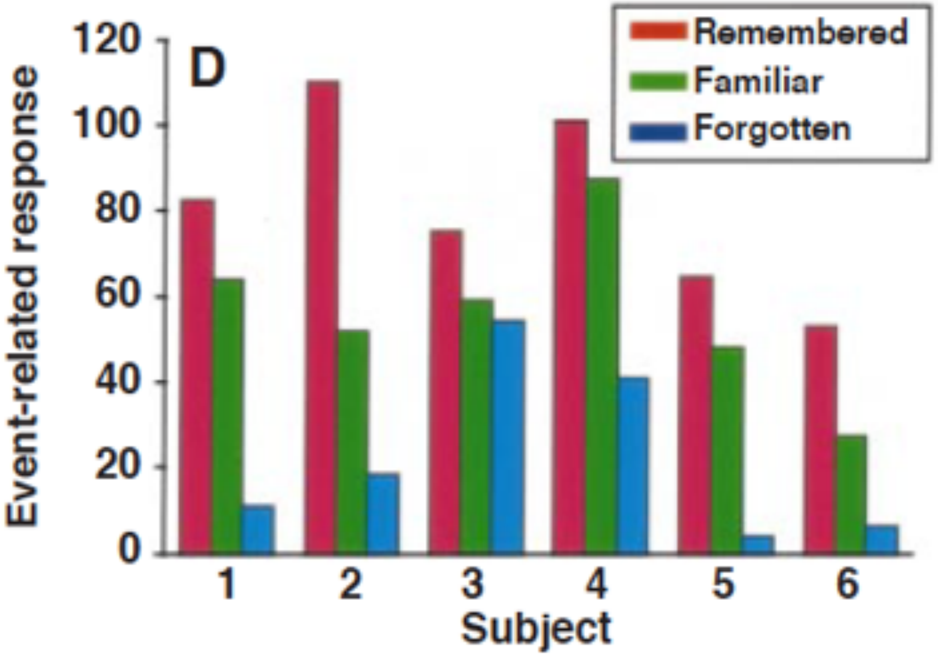
Pleasant (P) Unpleasant (U) Unpleasant (U) Pleasant (P) Unpleasant (U)

# Advantages of event-related fMRI

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

# efMRI: Post-hoc classification of trials



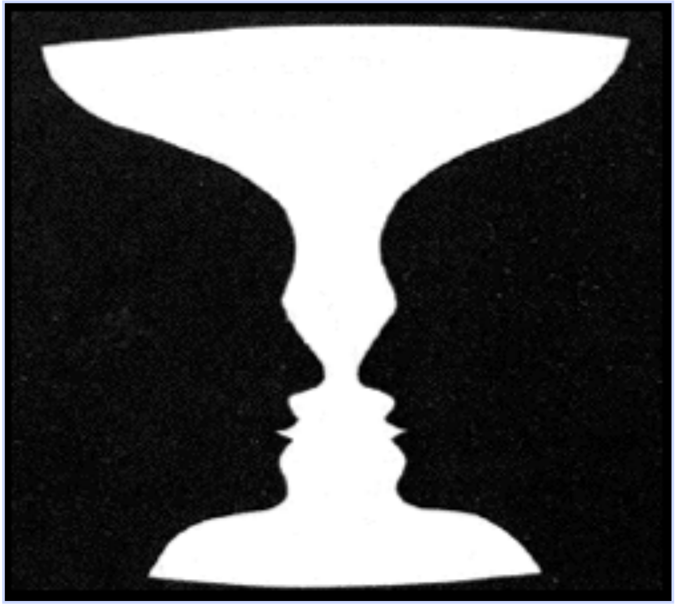



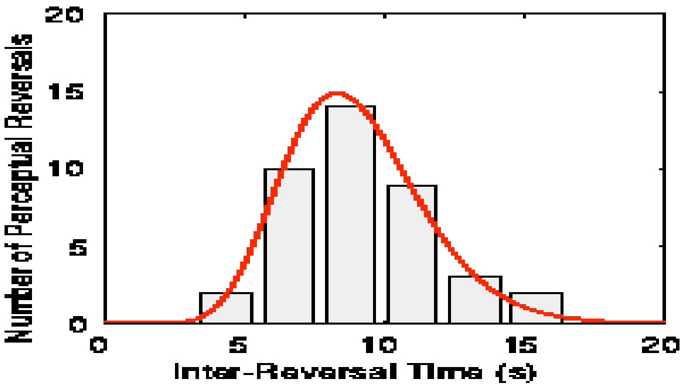

*Brewer et al (1999) Science*

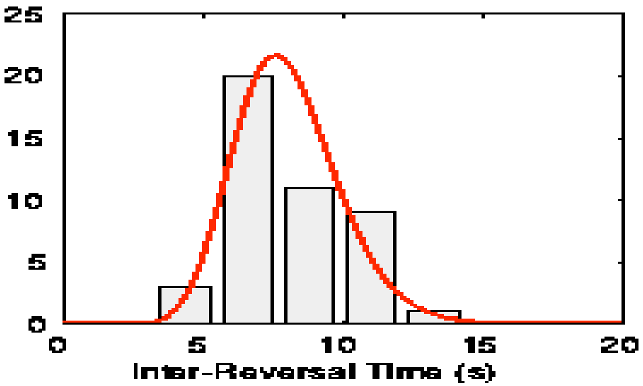
# Advantages of event-related fMRI

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

# efMRI: Online event definition



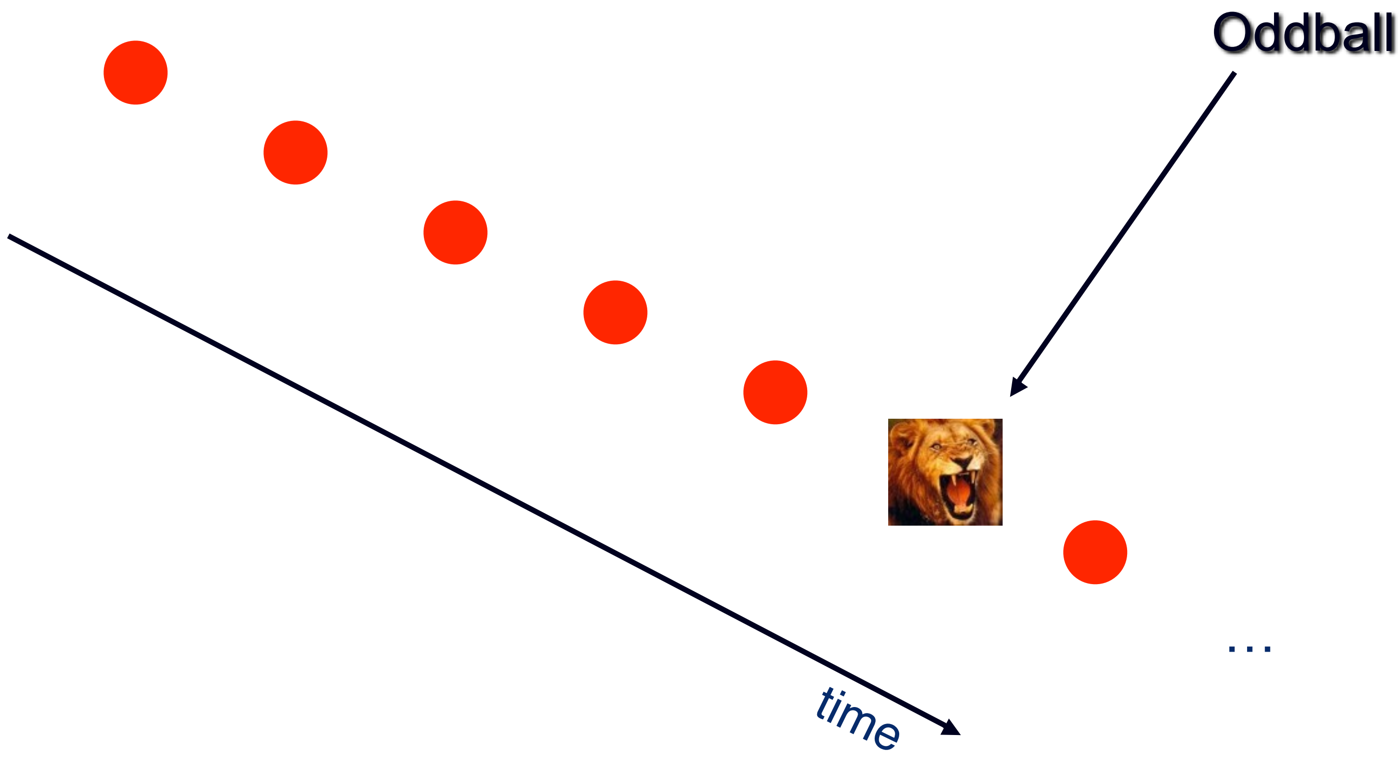


# Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context

# efMRI: Stimulus context

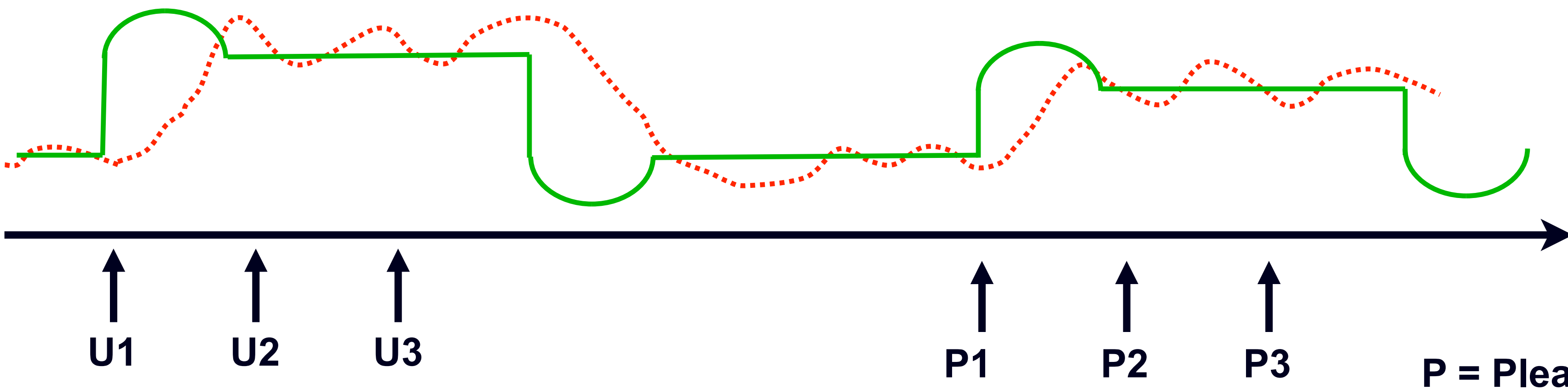


# Advantages of event-related fMRI

1. Randomised trials order
2. Post-hoc subjective classification of trials
3. Some events can only be indicated by participant
4. Some events cannot be blocked due to stimulus context
5. More accurate model even for epoch/block designs?

# “Event” model of block design

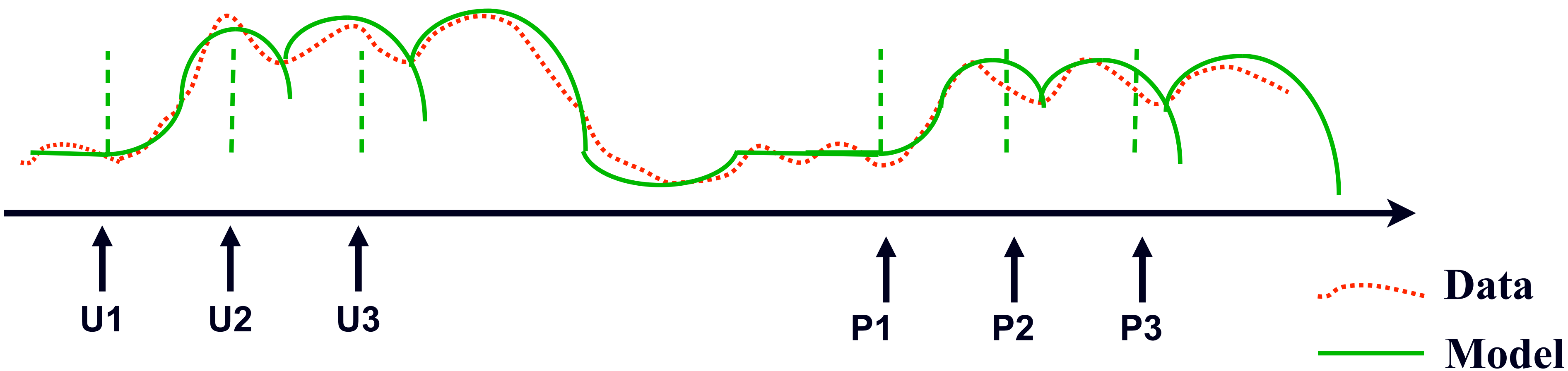
“Epoch” model assumes constant neural processes throughout block




P = Pleasant

U = Unpleasant

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



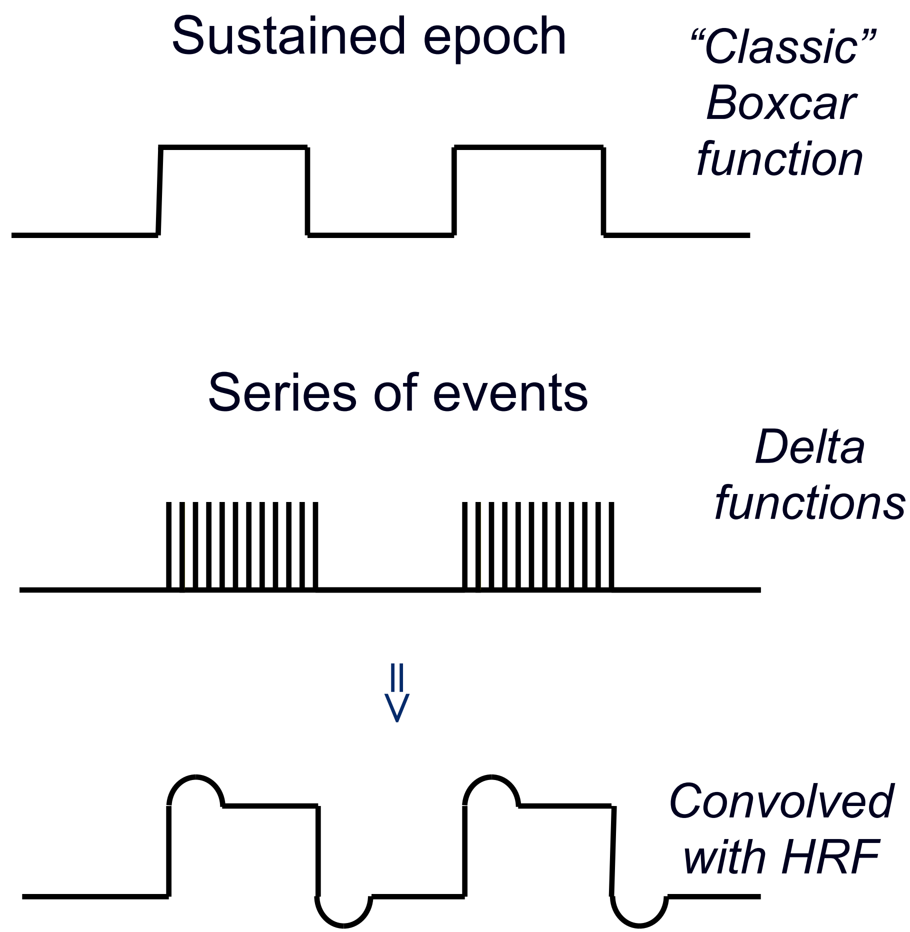
# Modeling block designs: Epochs vs events

Designs can be blocked or intermixed, BUT models for blocked designs can be epoch- or event-related

Epochs are periods of sustained stimulation (e.g, box-car functions)
Events are impulses (delta-functions)

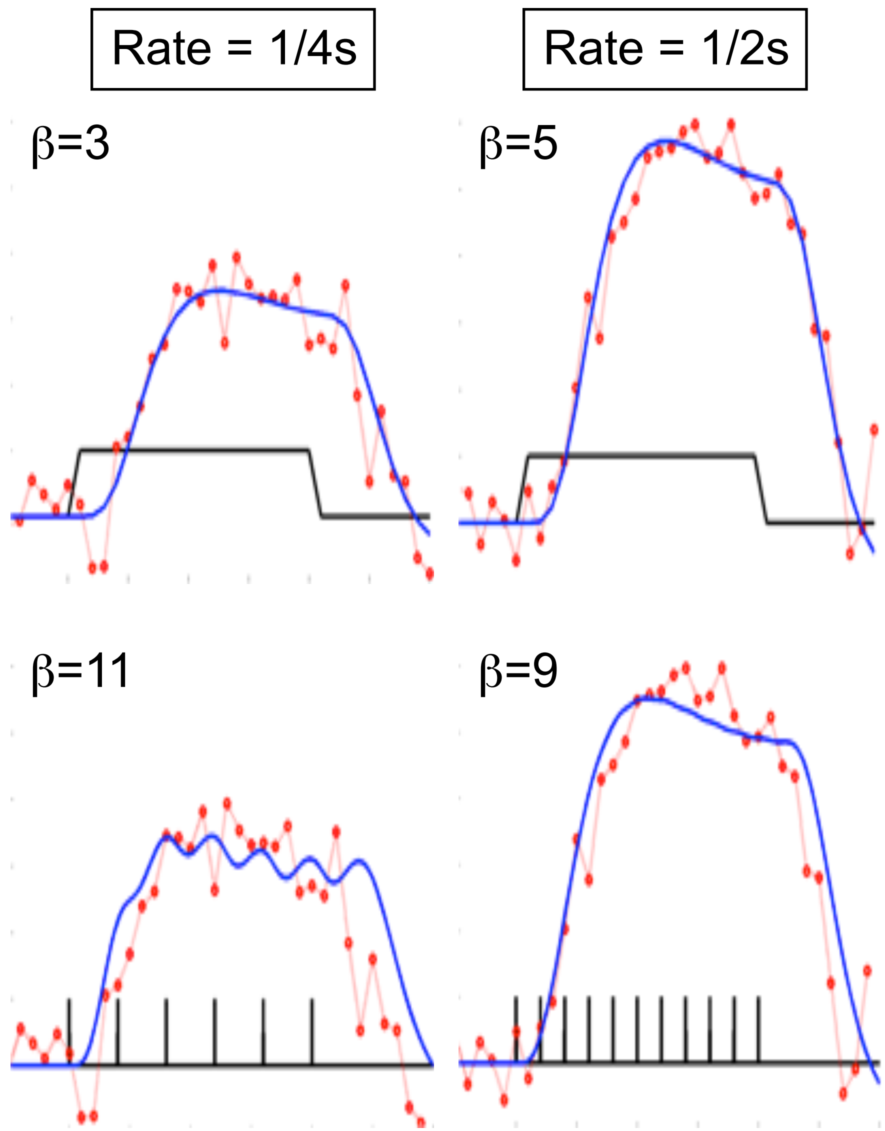
Near-identical regressors can be created by 1) sustained epochs, 2) rapid series of events (SOAs<~3s)

In SPM12, all conditions are specified in terms of their 1) onsets and 2) durations
… epochs: variable or constant duration
… events:  zero duration



# Modeling block designs: Epochs vs events

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



# Disadvatages of intermixed designs

1. Less efficient for detecting effects than blocked designs
   (see later…)

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

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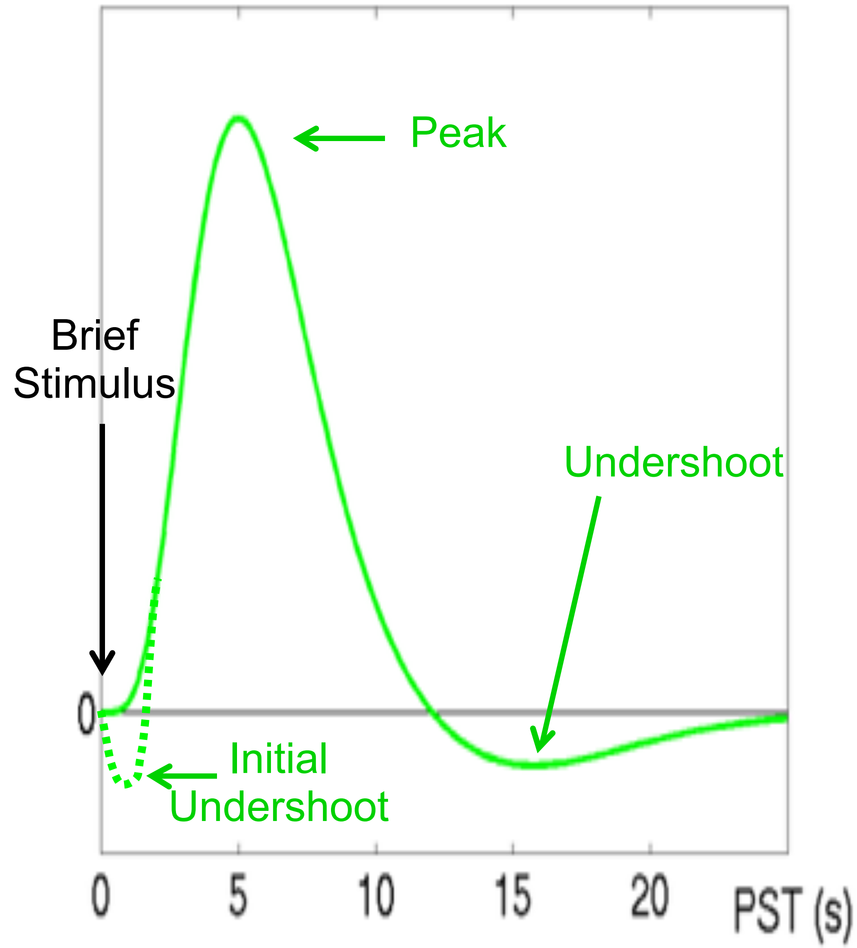
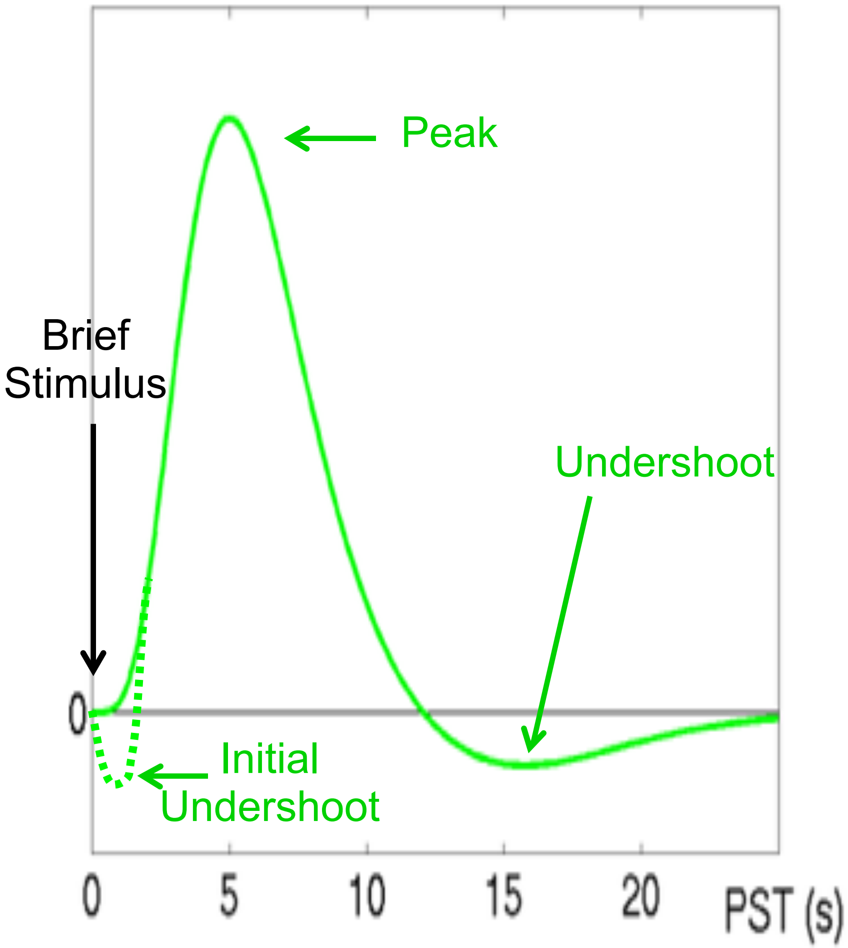
# BOLD impulse response

- Function of blood oxygenation, flow, volume
- Peak (max. oxygenation) 4-6s poststimulus; baseline after 20-30s
- Initial undershoot can be observed
- Similar across V1, A1, S1…
- … but possible differences across:
  - other regions
  - individuals



# BOLD impulse response

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



# General Linear (Convolution) Model

GLM for a single voxel:

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

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

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

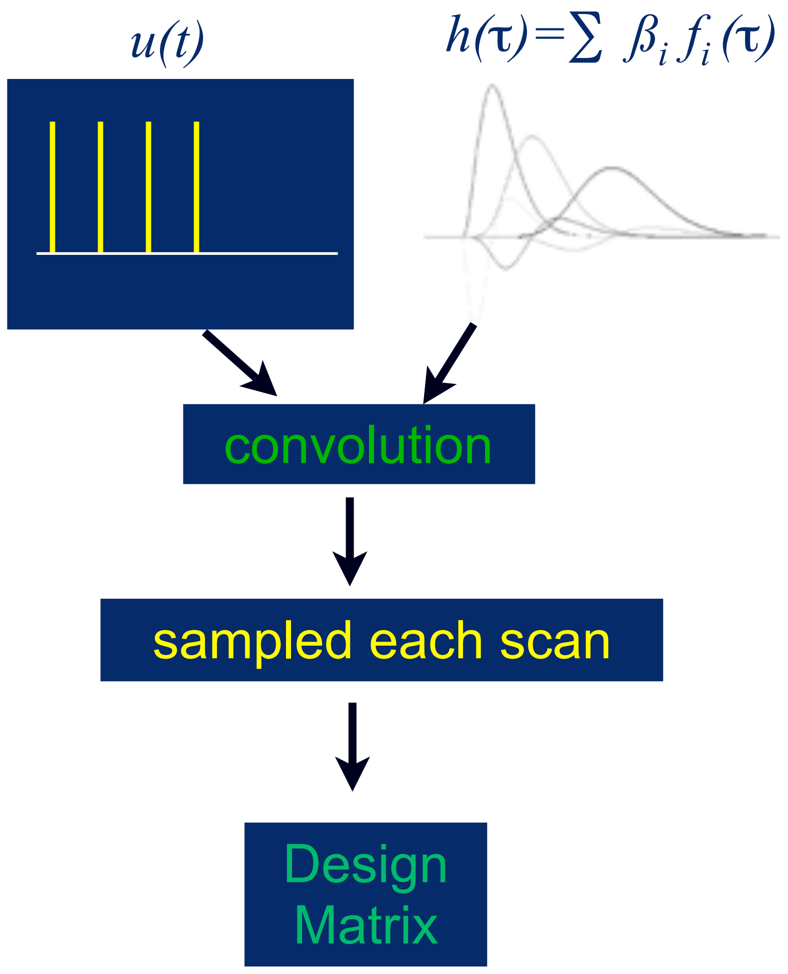
$h(\tau)$ = hemodynamic (BOLD) response

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

$f_i(\tau)$ = temporal basis functions

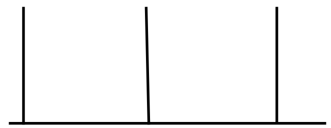
$$y(t) = \sum \sum \beta_i f_i(t - nT) + \varepsilon(t)$$

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

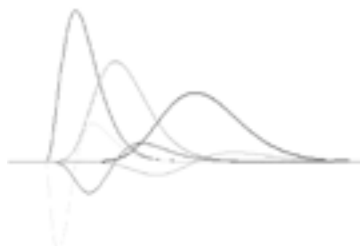


# General Linear Model in SPM

Stimulus every 20s



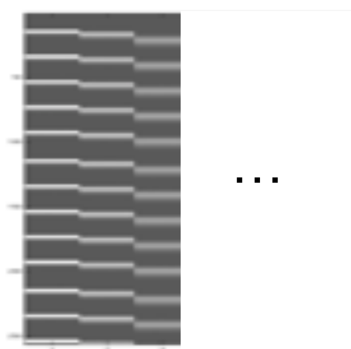
Gamma functions $f_i(\tau)$ of peristimulus time $\tau$ (Orthogonalised)



Sampled every TR = 1.7s

Design matrix, $\mathbf{X}$

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



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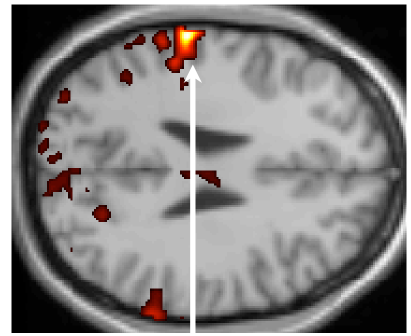

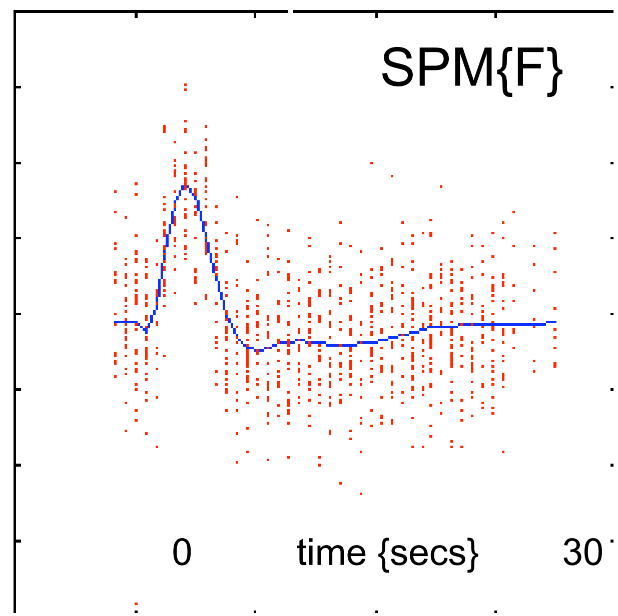

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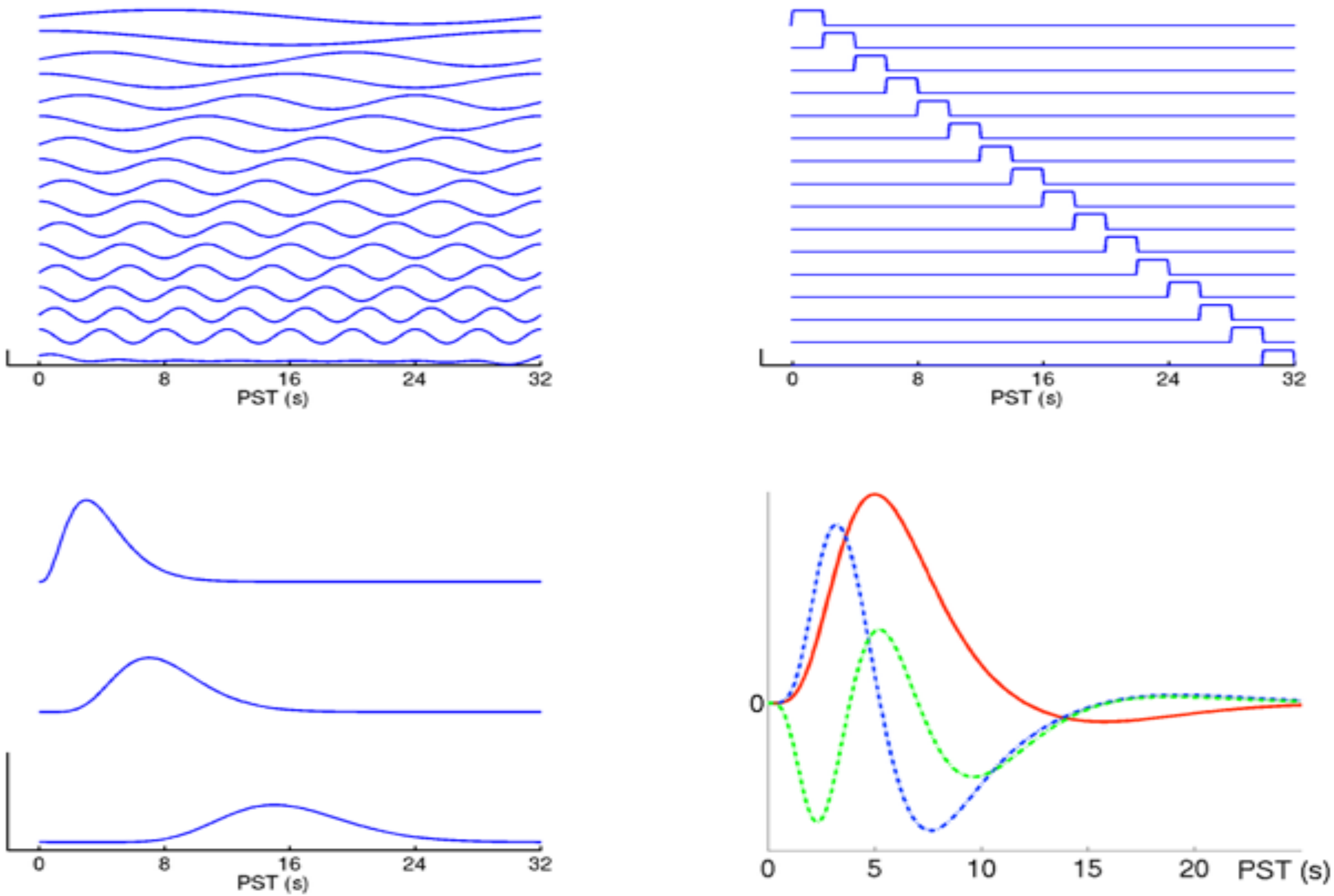
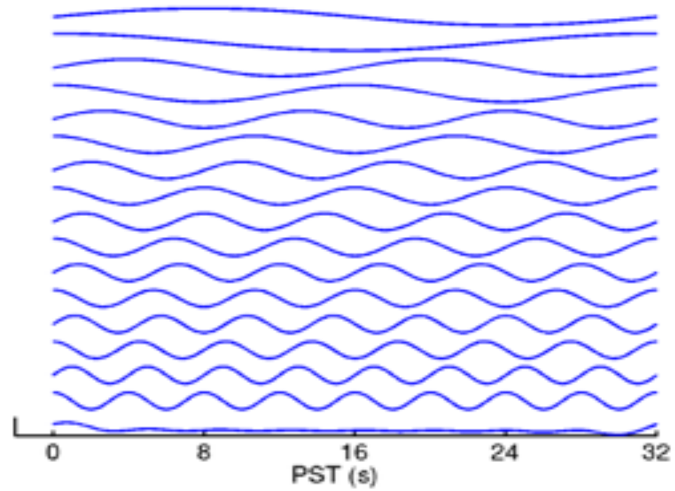
# Temporal basis functions

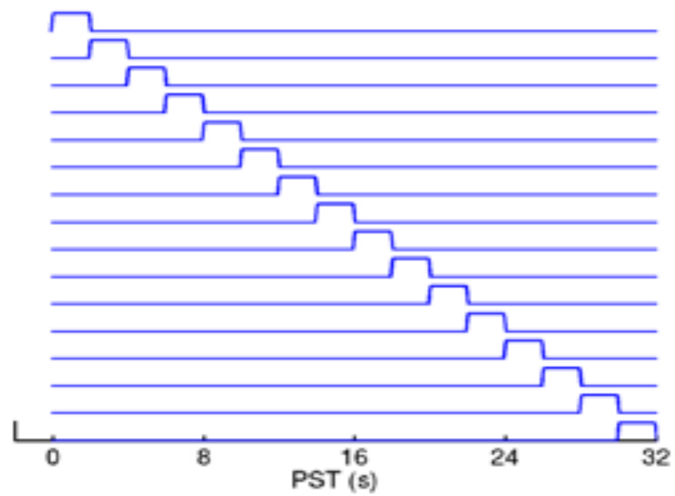


# Temporal basis functions

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

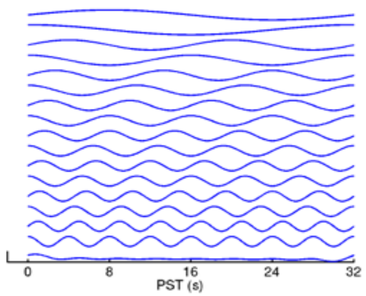


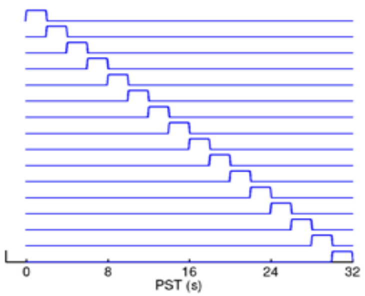

- **Finite Impulse Response**
  - Mini “timebins” (selective averaging)
  - Any shape (up to bin-width)
  - Inference via F-test



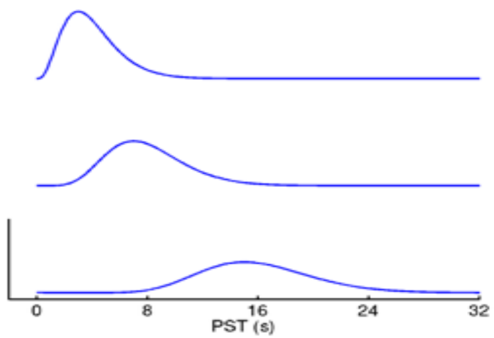
# Temporal basis functions

- **Fourier Set / FIR**
  - Any shape (up to frequency limit / bin width)
  - Inference via F-test

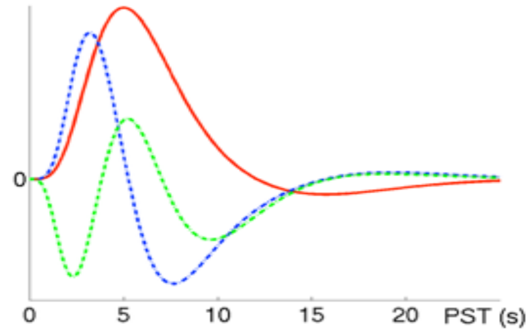


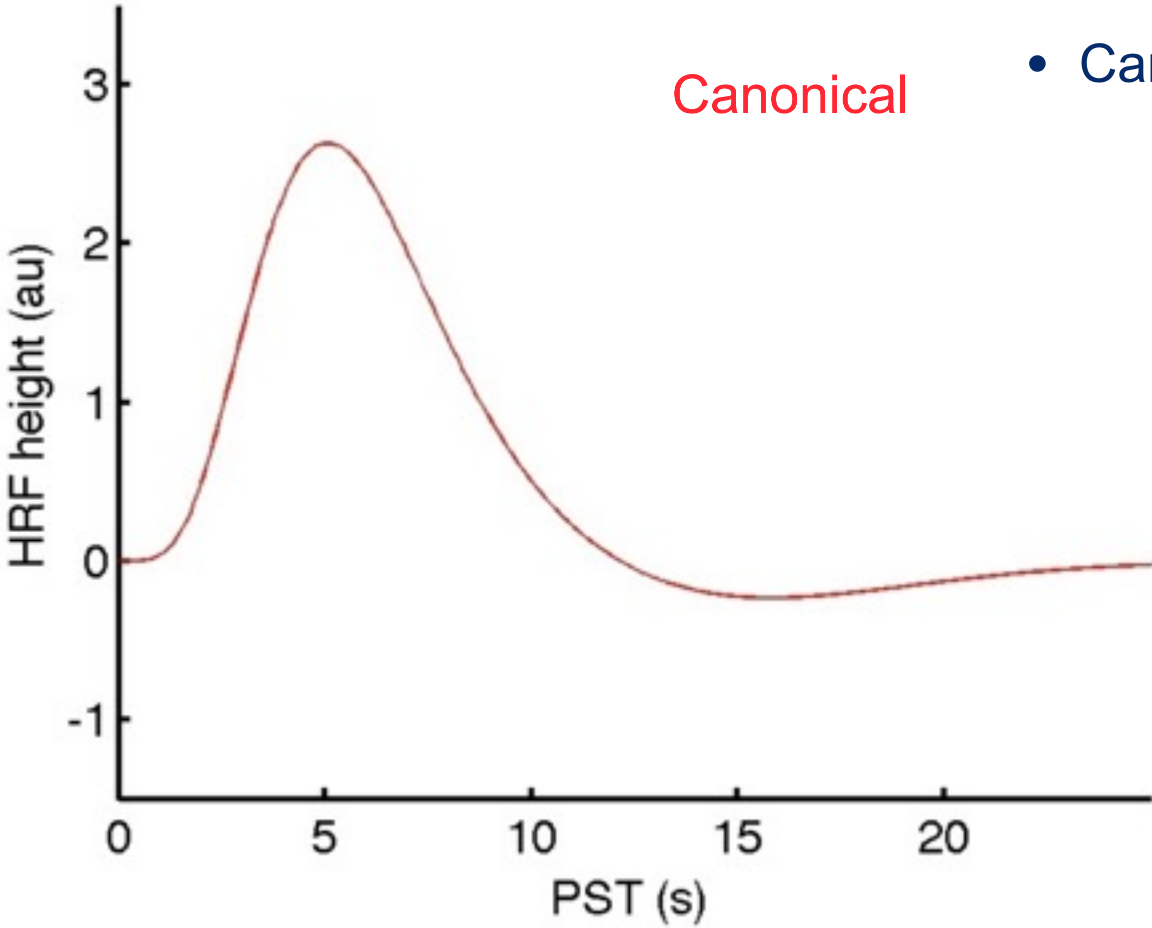

- **Gamma Functions**
  - Bounded, asymmetrical (like BOLD)
  - Set of different lags
  - Inference via F-test




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

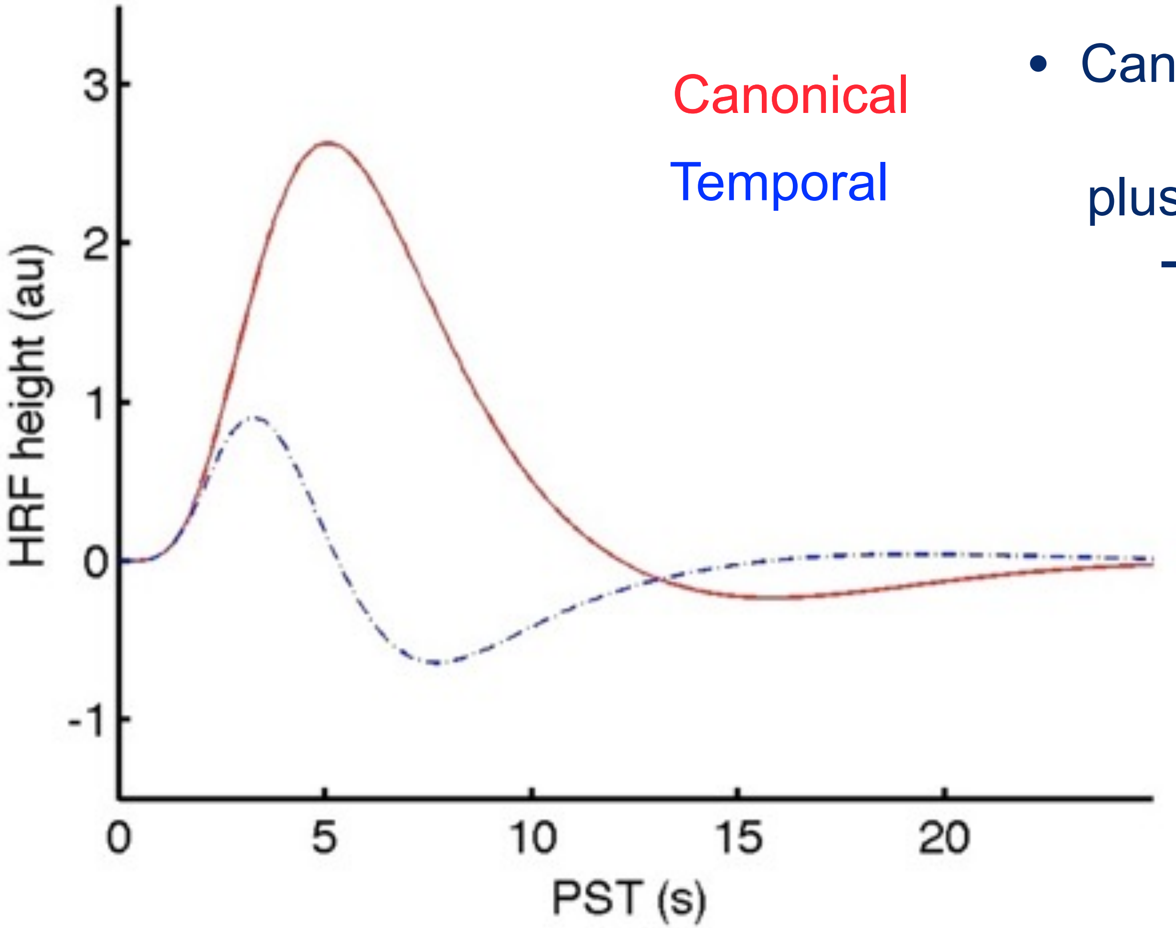


# Informed basis set




- Canonical HRF (2 gamma functions)

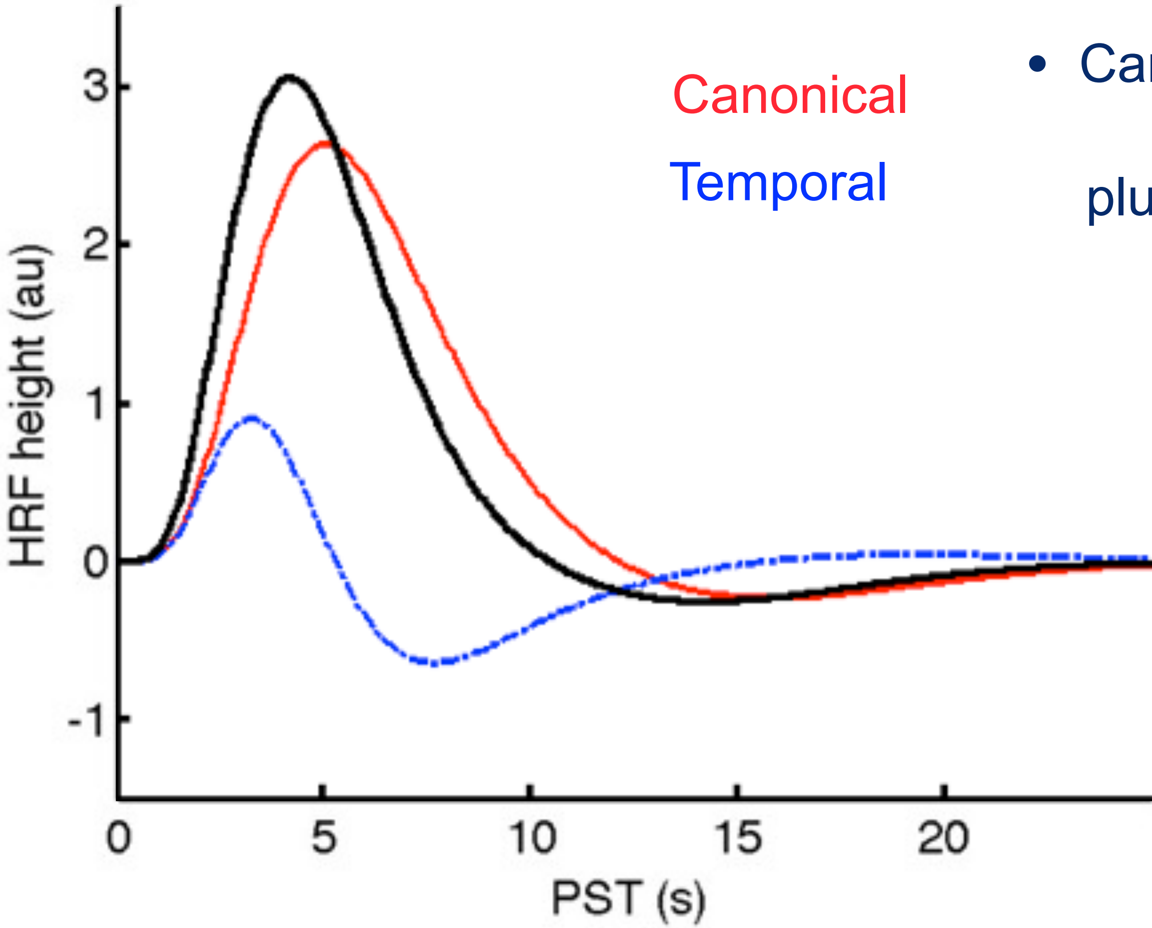
# Informed basis set




- Canonical HRF (2 gamma functions)

  plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)

# Informed basis set




- Canonical HRF (2 gamma functions)

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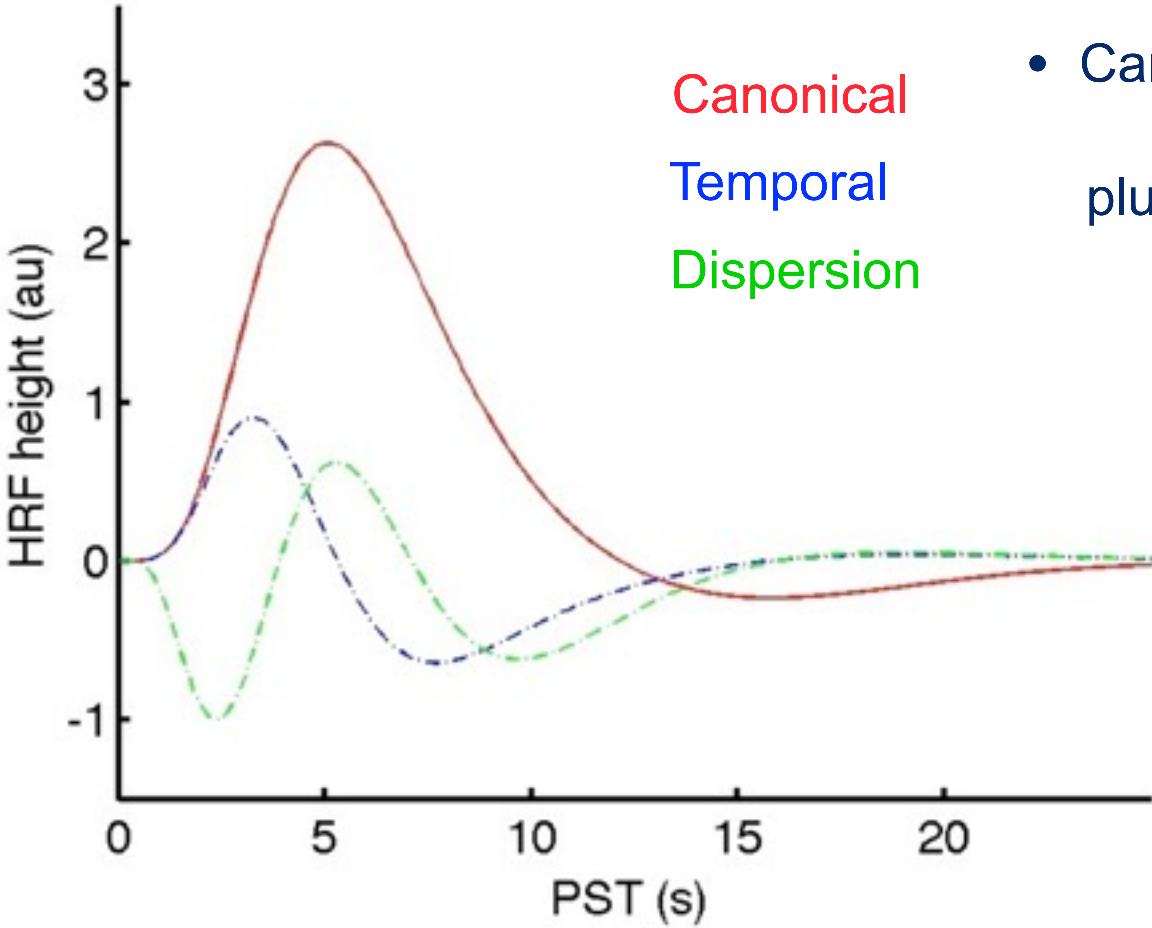
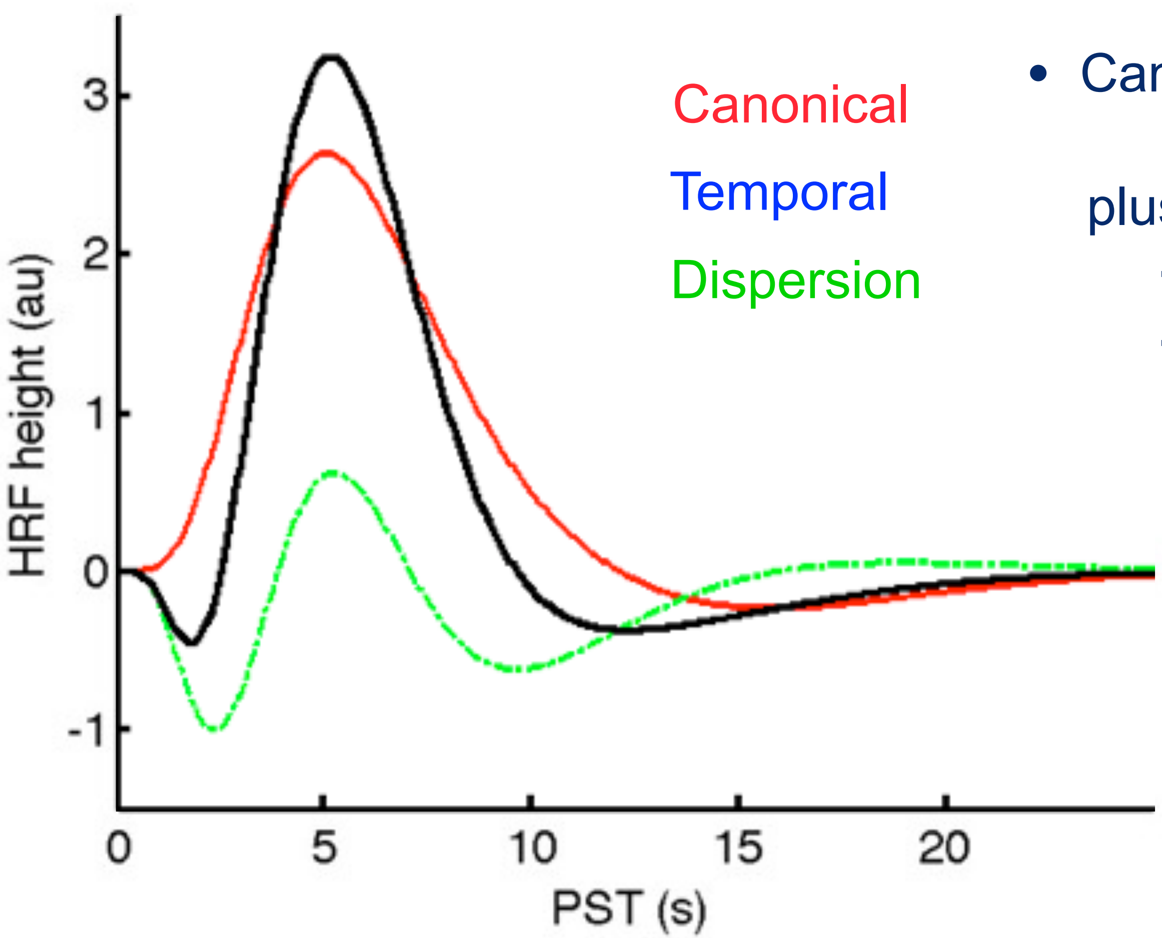
# Informed basis set




- Canonical HRF (2 gamma functions)

  plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)
  - width (Dispersion Derivative)

# Informed basis set

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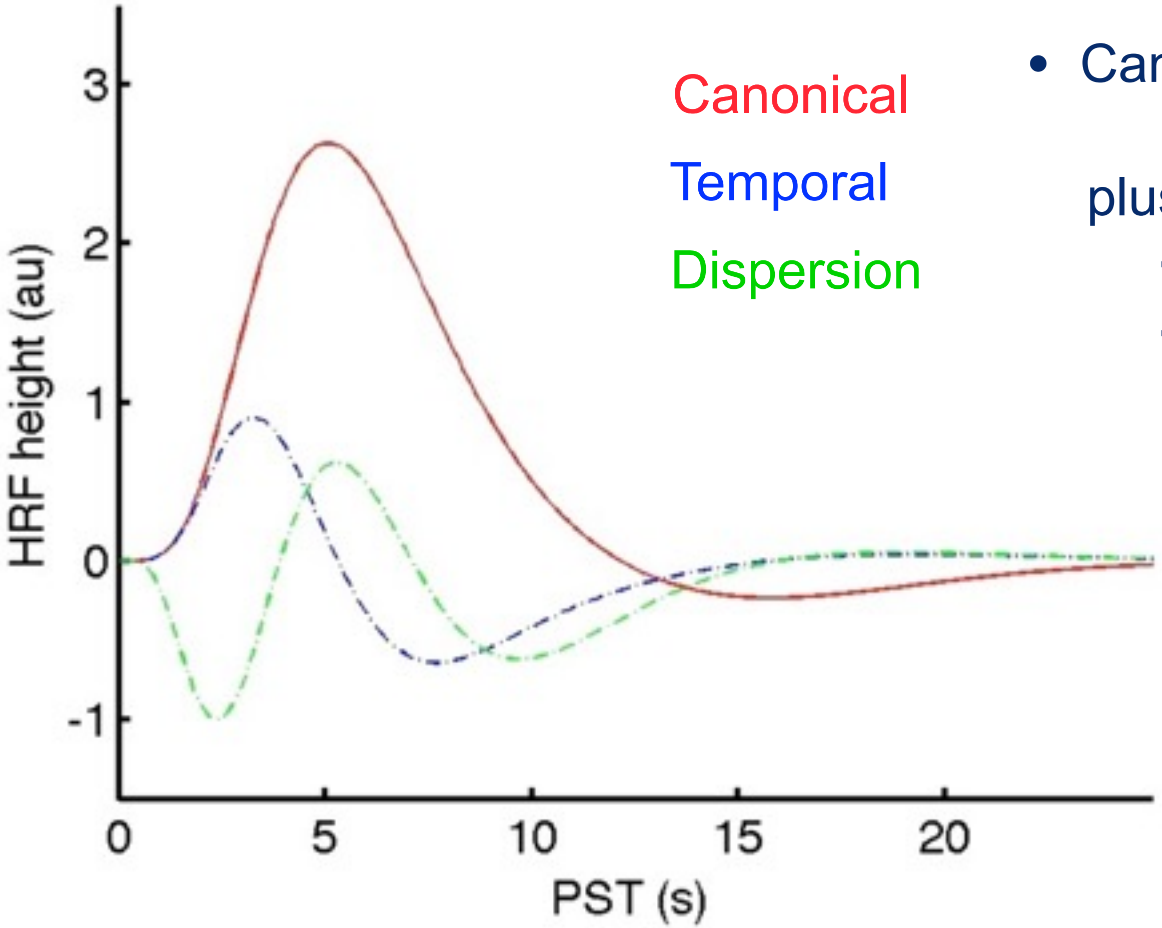



- Canonical HRF (2 gamma functions)

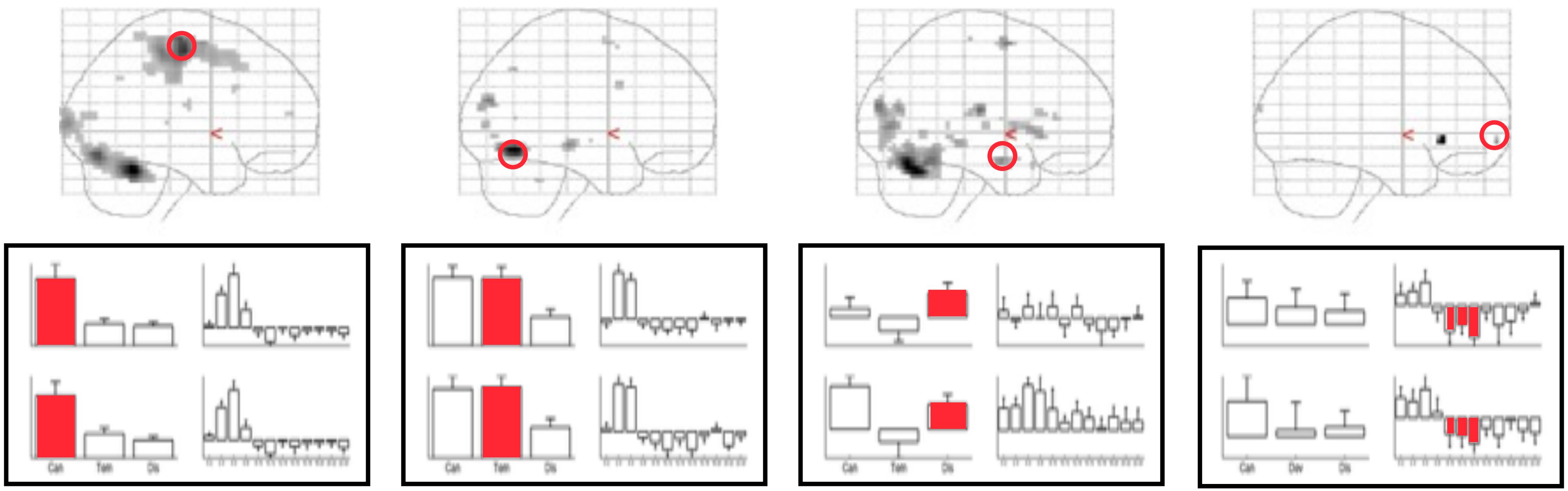
  plus Multivariate Taylor expansion in:
  - time (Temporal Derivative)
  - width (Dispersion Derivative)

- "Magnitude" inferences via t-test on canonical parameters (providing canonical is a reasonable fit)

- "Latency" inferences via tests on ratio of derivative : canonical parameters

# Which temporal basis set?

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



Canonical + Temporal + Dispersion + FIR

… canonical + temporal + dispersion derivatives appear sufficient to capture most activity

… may not be true for more complex trials (e.g. stimulus-prolonged delay (>~2 s)-response)

… but then such trials better modelled with separate neural components (i.e., activity no longer delta function) + constrained HRF

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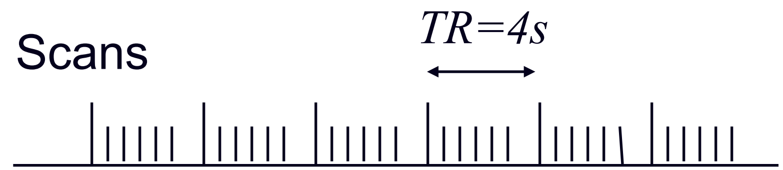
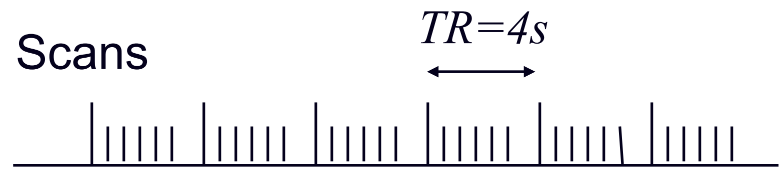
# Timing issues: Sampling

- TR for 80 slice EPI at 2 mm spacing is ~ 4s

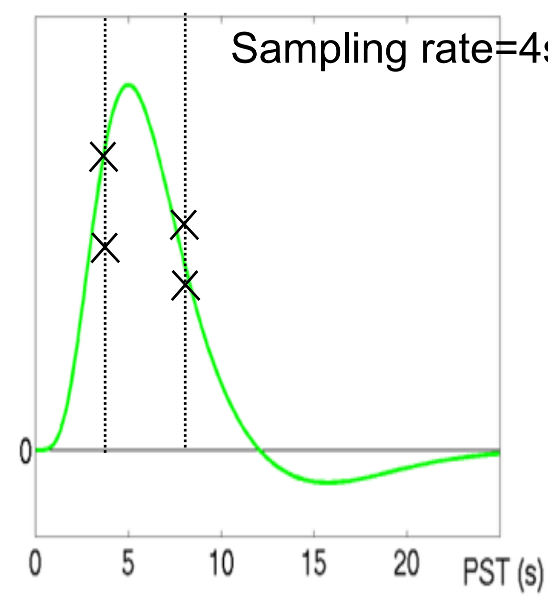


# Timing issues: Sampling

- TR for 80 slice EPI at 2 mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal




Stimulus (synchronous)



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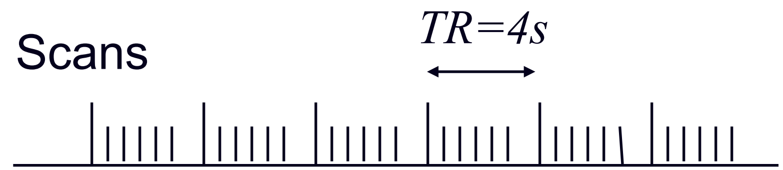
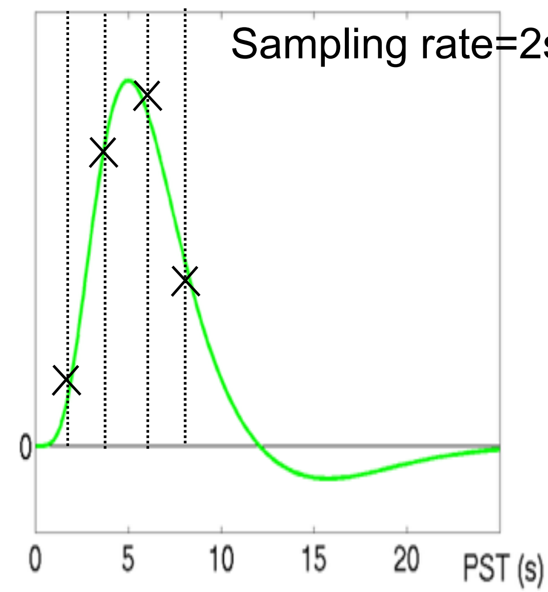
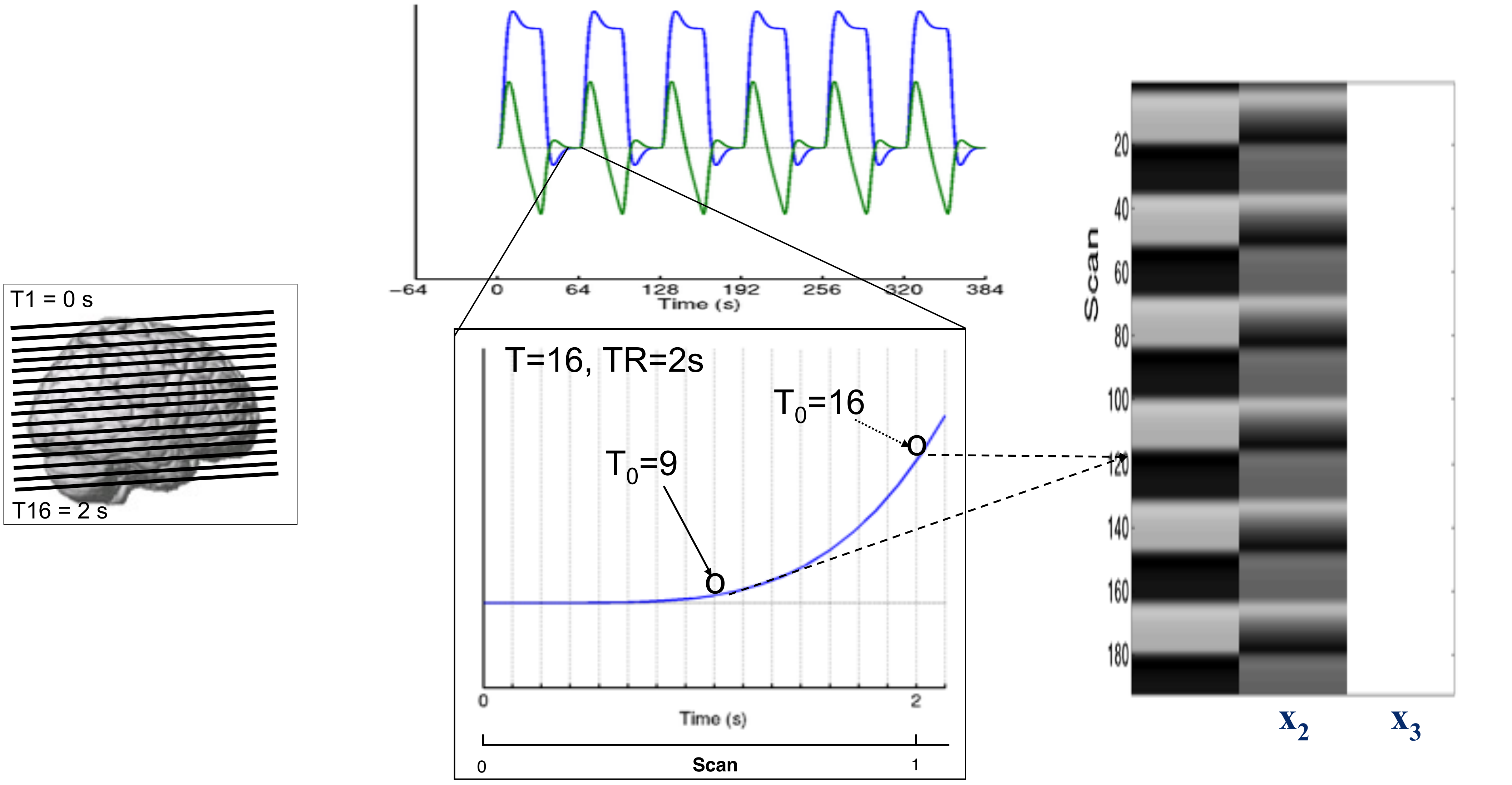



Stimulus (random jitter)

- Higher effective sampling by:
  1. Asynchrony; e.g., SOA=1.5TR
  2. Random Jitter; e.g., SOA=(2±0.5)TR
- Better response characterisation



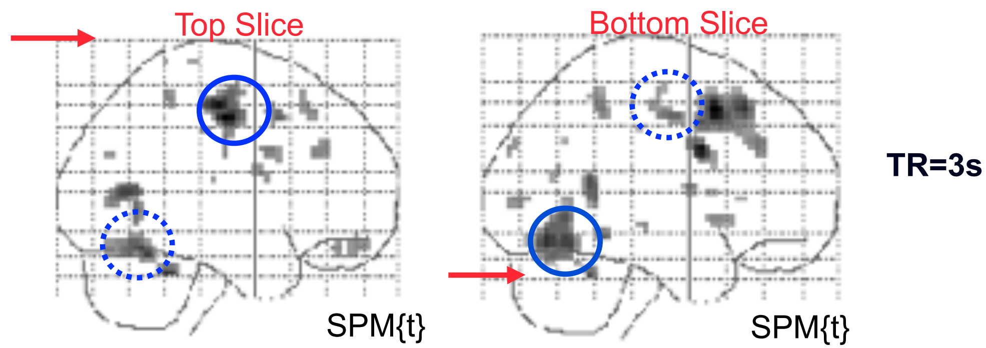
# Timing issues: Slice Timing



# Timing issues: Slice Timing

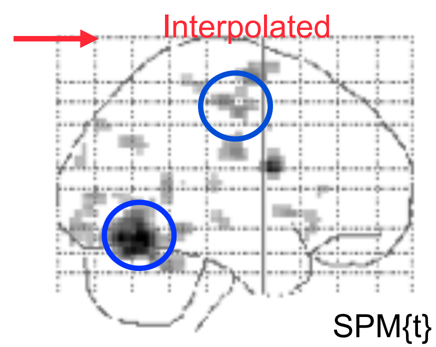
**"Slice-timing Problem":**

- Slices acquired at different times, yet model is the same for all slices
- different results (using canonical HRF) for different reference slices
- (slightly less problematic if middle slice is selected as reference, and with short TRs)

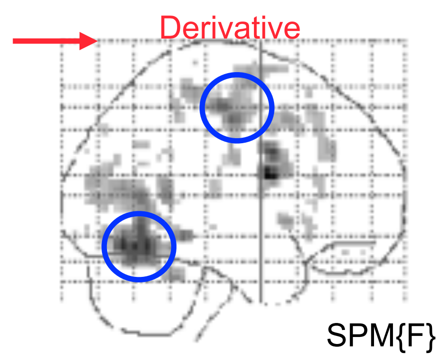



**Solutions:**

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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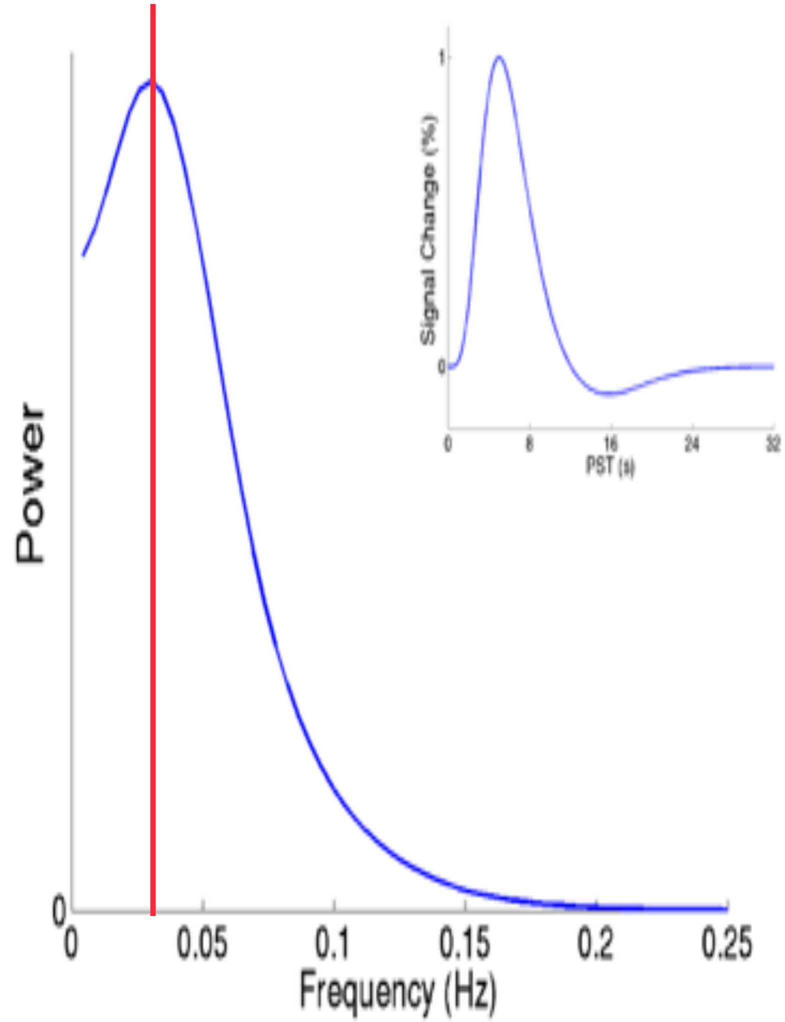
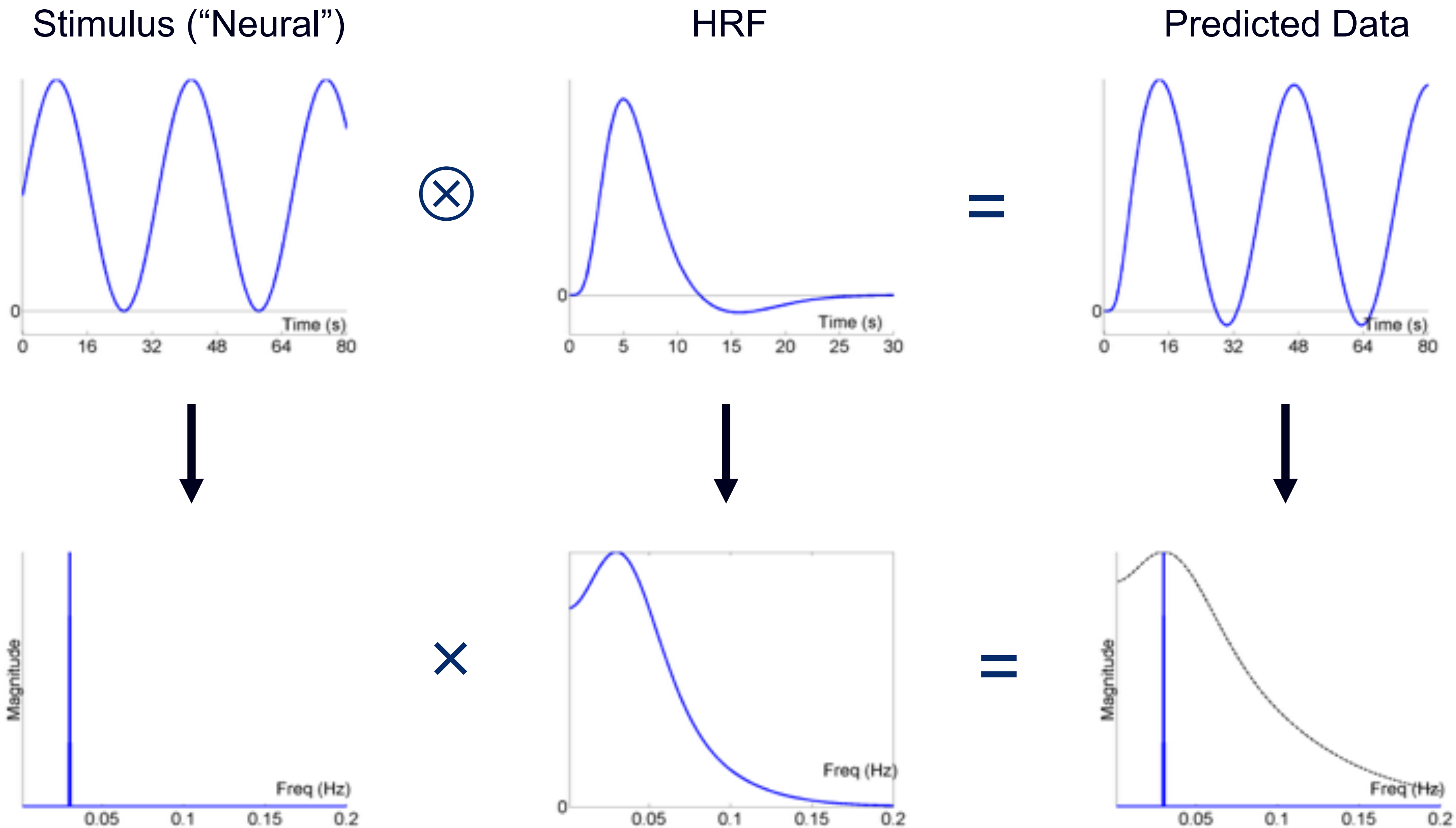
# Design efficiency

- HRF can be viewed as a filter (Josephs & Henson, 1999)
- We want to maximise the signal passed by this filter
- Dominant frequency of canonical HRF is ~0.04 Hz

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

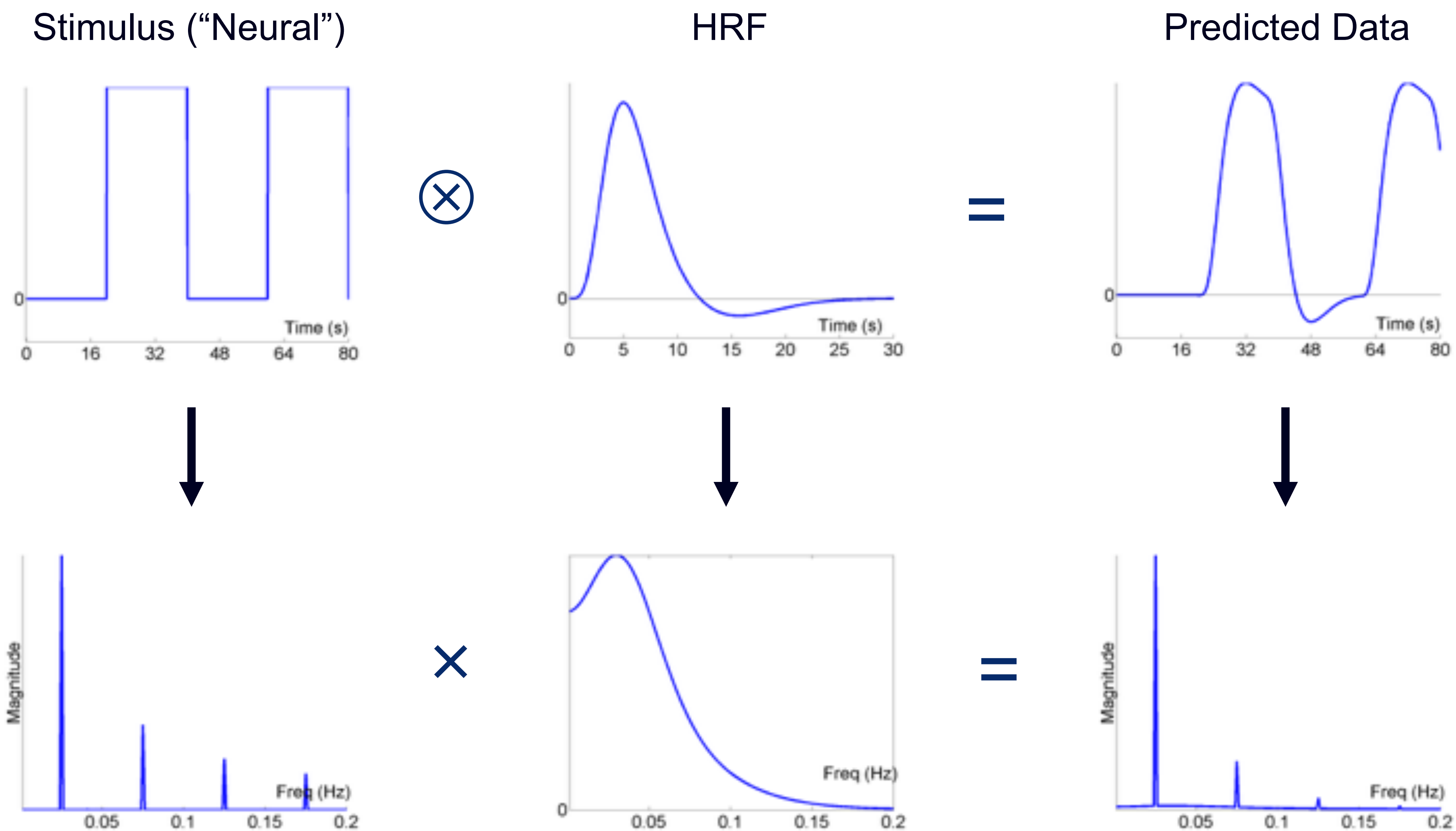


# Sinusoidal modulation, f = 1/33




A very “efficient” design!

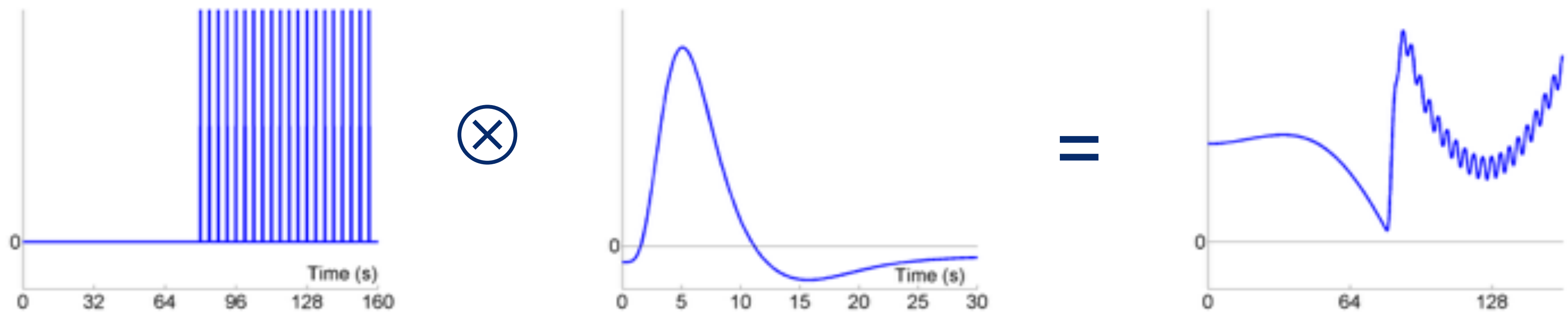
# Blocked, epoch = 20 sec



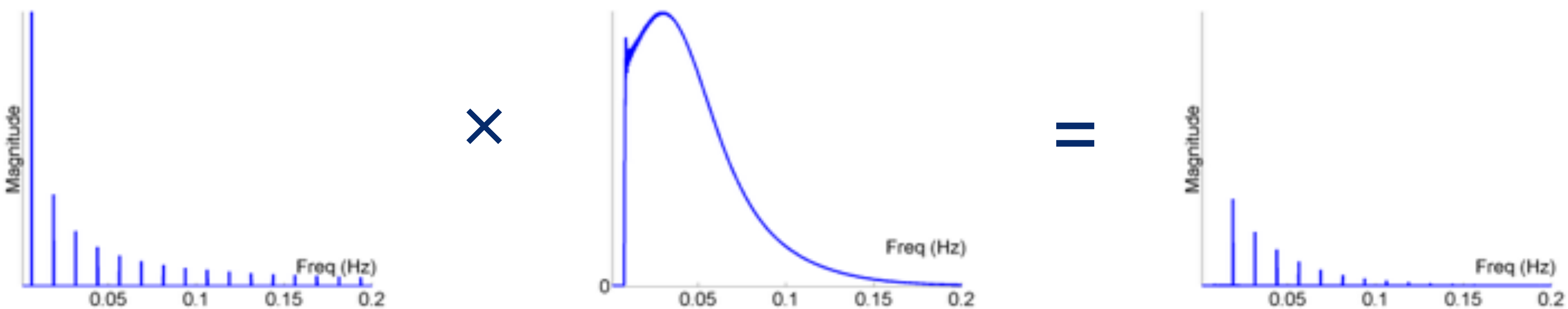

Blocked-epoch (with small SOA) quite “efficient”

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

Stimulus ("Neural") HRF Predicted Data

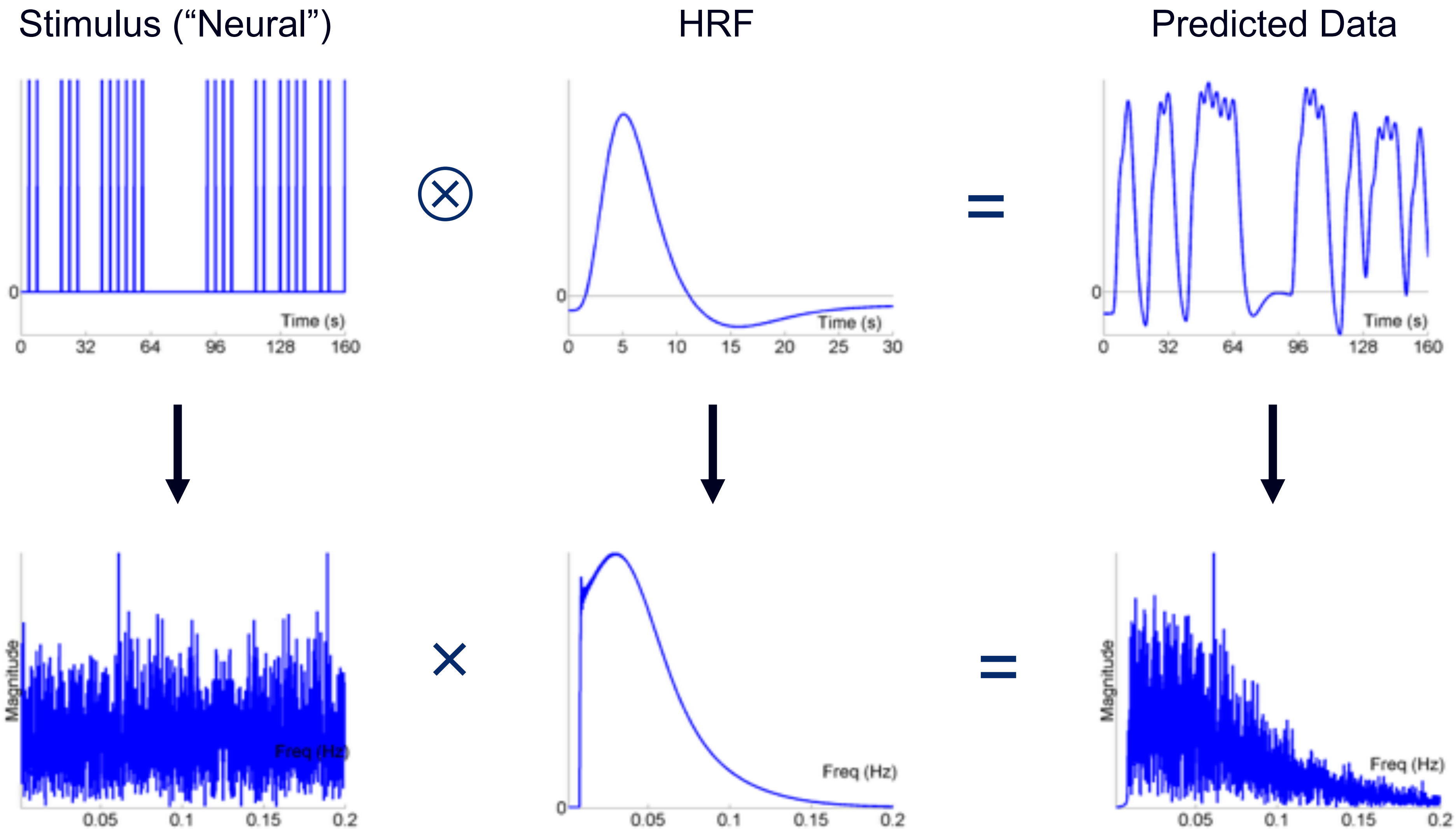



"Effective HRF" (after highpass filtering)
(Josephs & Henson, 1999)




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

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




Randomised design spreads power over frequencies

# Design efficiency

- T-statistic for a given contrast: $T = c^T b / var(c^T b)$

- For maximum T, we want maximum precision and hence minimum standard error of contrast estimates ($var(c^T b)$)

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

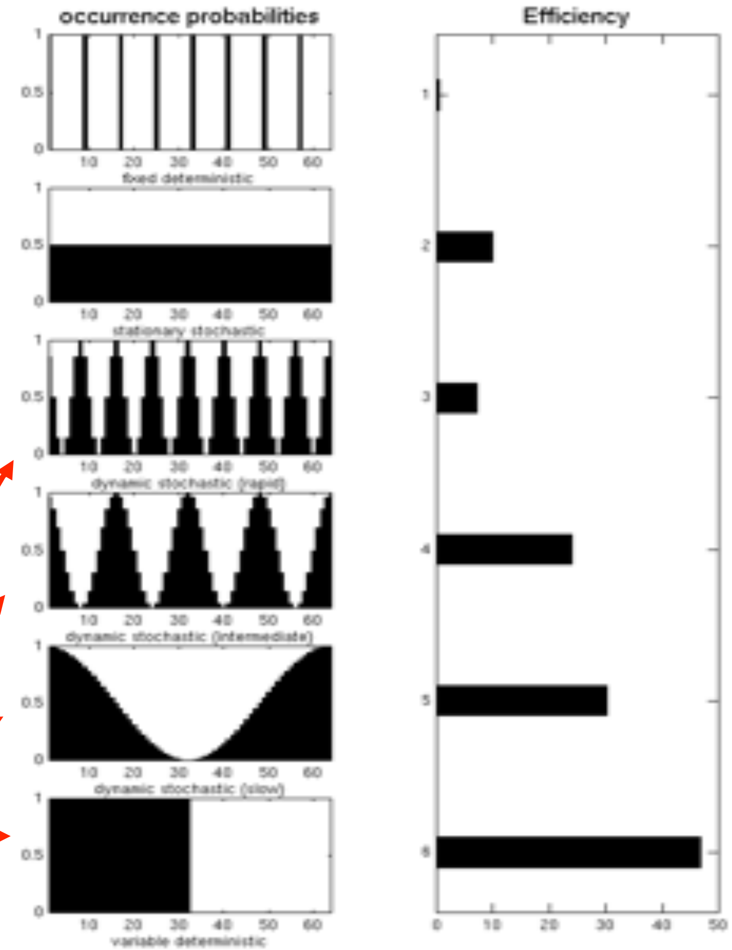
- If we assume that noise variance ($\sigma^2$) is unaffected by changes in X, then our precision for given parameters is proportional to the *design efficiency:* $e(c,X) = \{ \mathbf{c}^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{c} \}^{-1}$

➡ We can influence *e* (a priori) by the spacing and sequencing of epochs/events in our design matrix

➡ *e* is specific for a given contrast!

# Design efficiency: Trial spacing

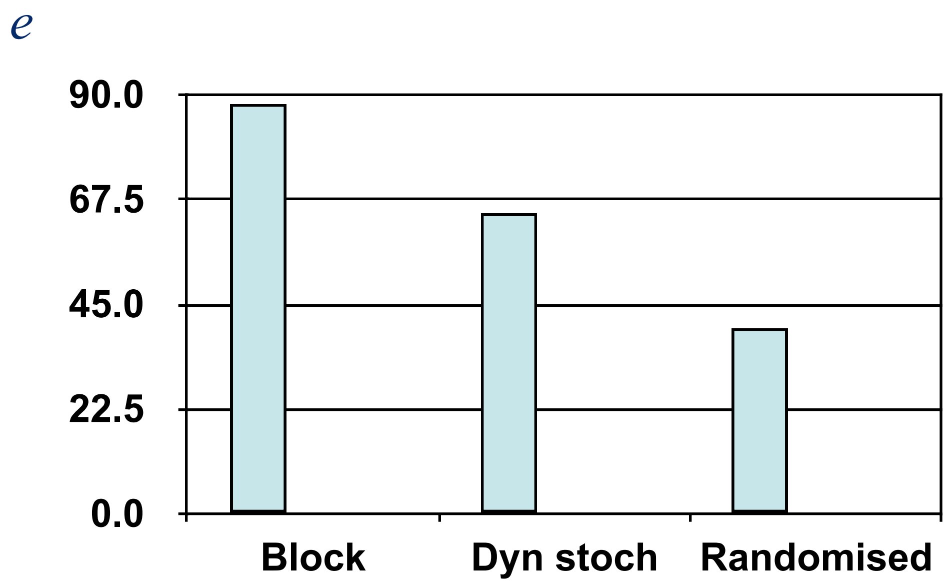
- Design parametrised by:
  - $SOA_{min}$ Minimum SOA
  - $p(t)$ Probability of event at each $SOA_{min}$
- Deterministic
  *p(t)=1 iff t=nSOAmin*
- Stationary stochastic
  *p(t)=constant*
- Dynamic stochastic
  *p(t) varies (e.g., blocked)*

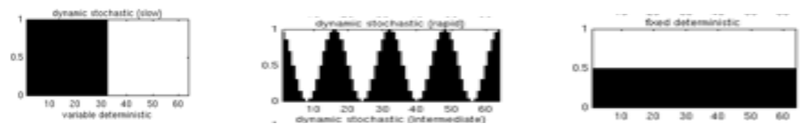



*Blocked designs most efficient!* (with small SOAmin)

# Design efficiency: Trial spacing

- However, block designs are often not advisable due to interpretative difficulties (see before)
- Event trains may then be constructed by modulating the event probabilities in a dynamic stochastic fashion
- This can result in intermediate levels of efficiency




3 sessions with 128 scans
Faces, scrambled faces
SOA always 2.97 s
Cycle length 24 s

# Design efficiency: Trial sequencing

- Design parametrised by:

  $SOA_{min}$ Minimum SOA

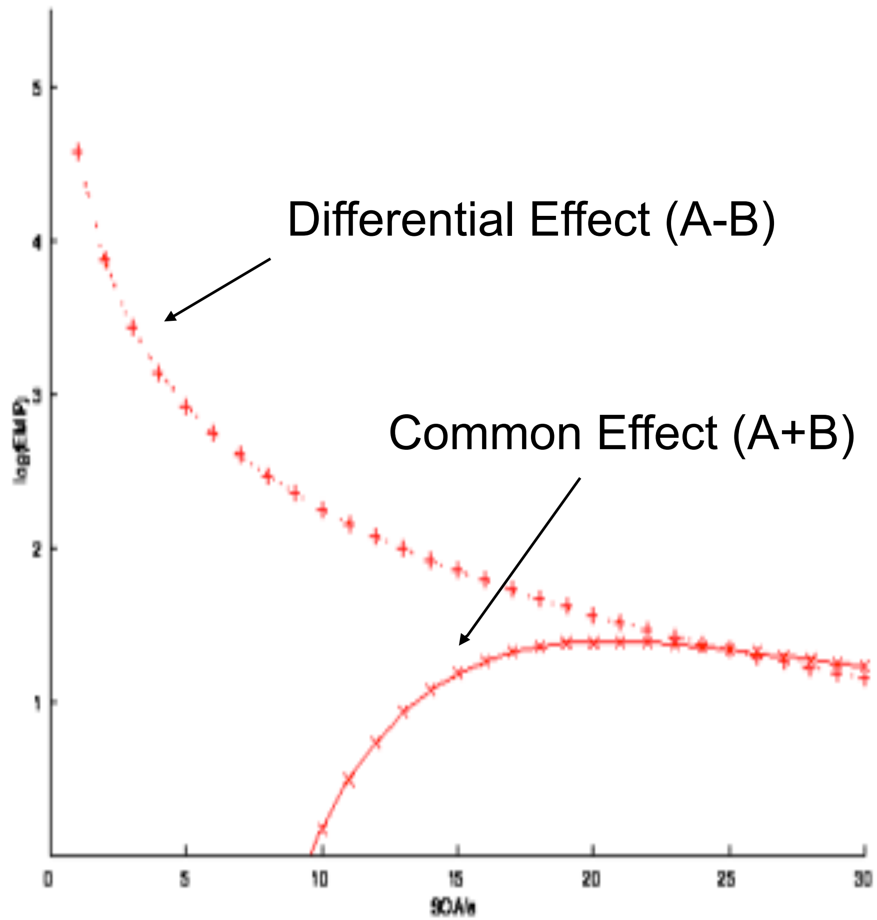
  $p_i(\boldsymbol{h})$ Probability of event-type $i$ given history $\boldsymbol{h}$ of last $m$ events

- With $n$ event-types $p_i(\boldsymbol{h})$ is a *n x n Transition Matrix*

- Example: Randomised AB

| | **A** | **B** |
|---|---|---|
| **A** | 0.5 | 0.5 |
| **B** | 0.5 | 0.5 |

=> **ABBBABAABABAAA...**



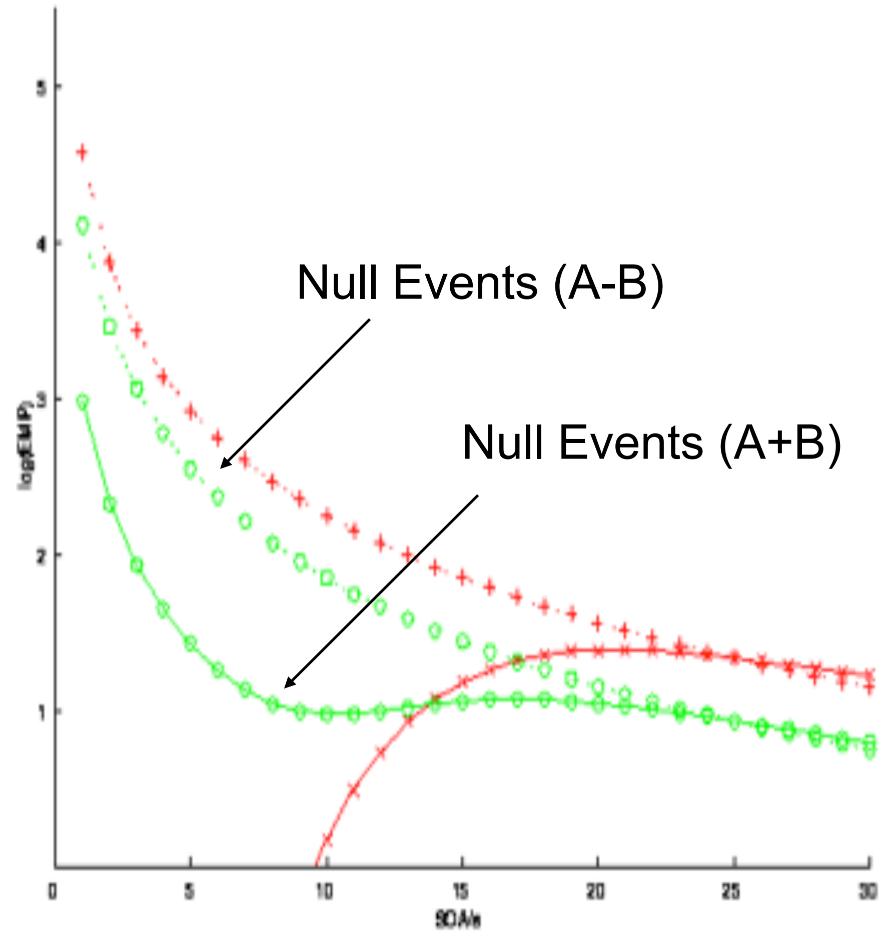
# Design efficiency: Trial sequencing

- 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)



# Design efficiency: Trial sequencing

- Example: Alternating AB

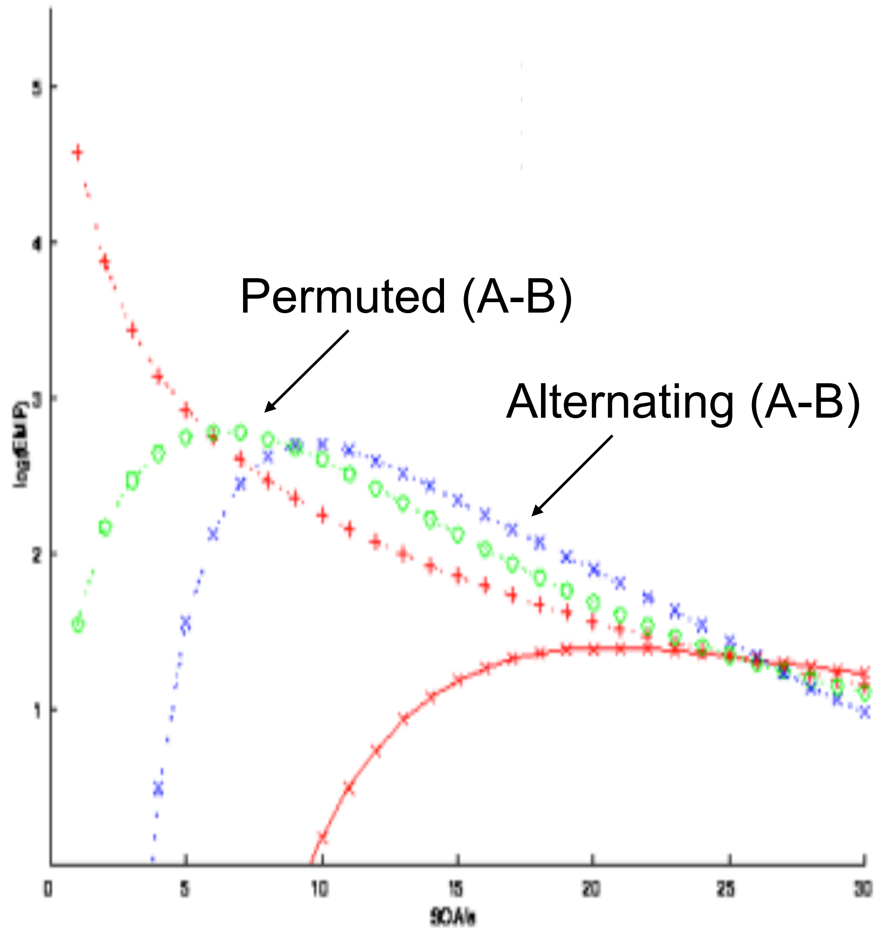
| | A | B |
|---|---|---|
| **A** | 0 | 1 |
| **B** | 1 | 0 |

=> **ABABABABABAB...**

- Example: Permuted AB

| | A | B |
|---|---|---|
| **AA** | 0 | 1 |
| **AB** | 0.5 | 0.5 |
| **BA** | 0.5 | 0.5 |
| **BB** | 1 | 0 |

=> **ABBAABABABBA...**



# Design efficiency: Conclusions

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