Event-related fMRI

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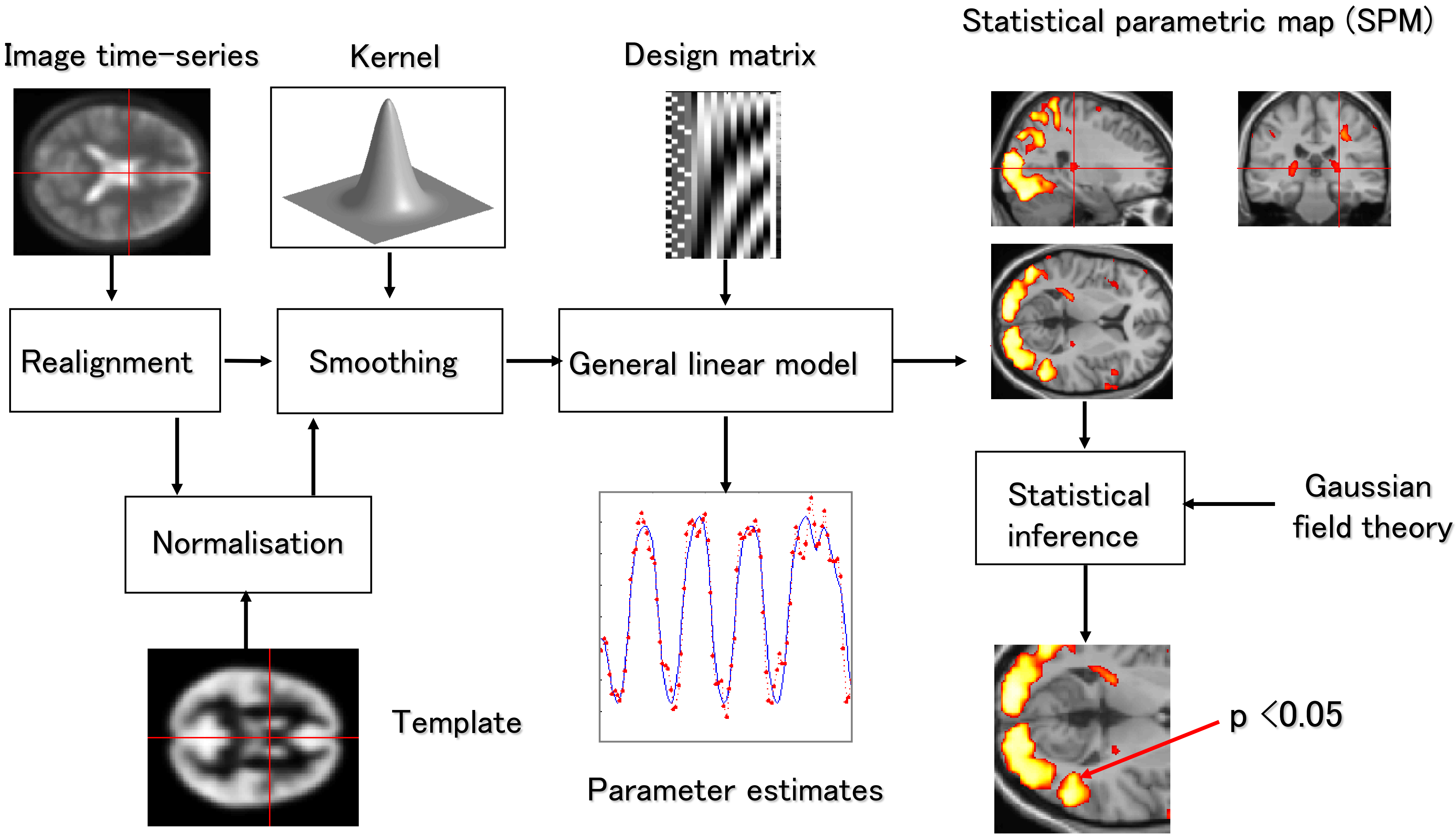
FIL Methods group, Klaas Enno Stephan, Rik Henson and Christian Ruff

Methods & models for fMRI data analysis
29 October 2019

Overview of SPM



Overview

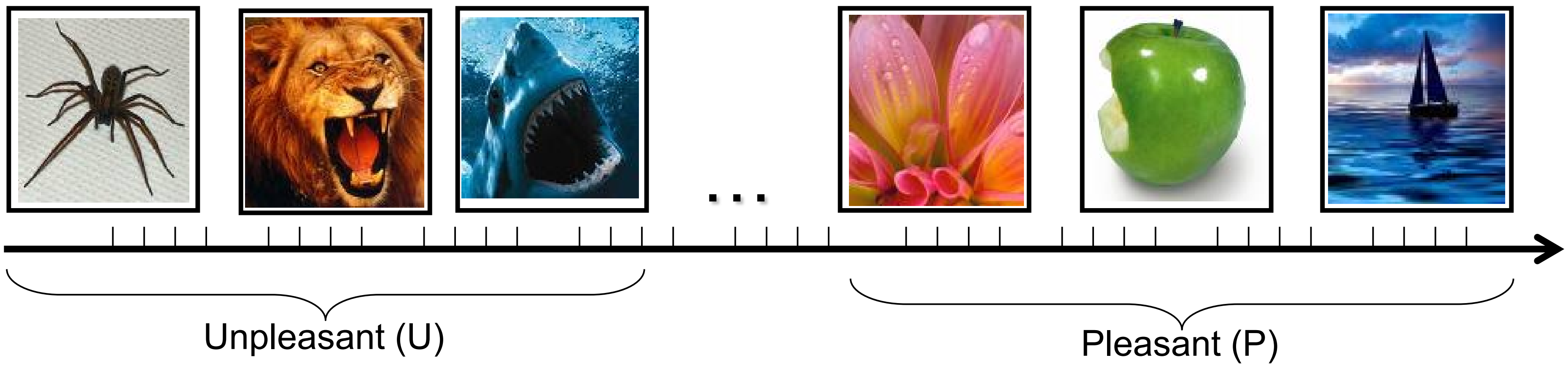
1. Advantages of er-fMRI
2. BOLD impulse response
3. General Linear Model
4. Temporal basis functions
5. Timing issues
6. Design optimisation

Advantages of er-fMRI

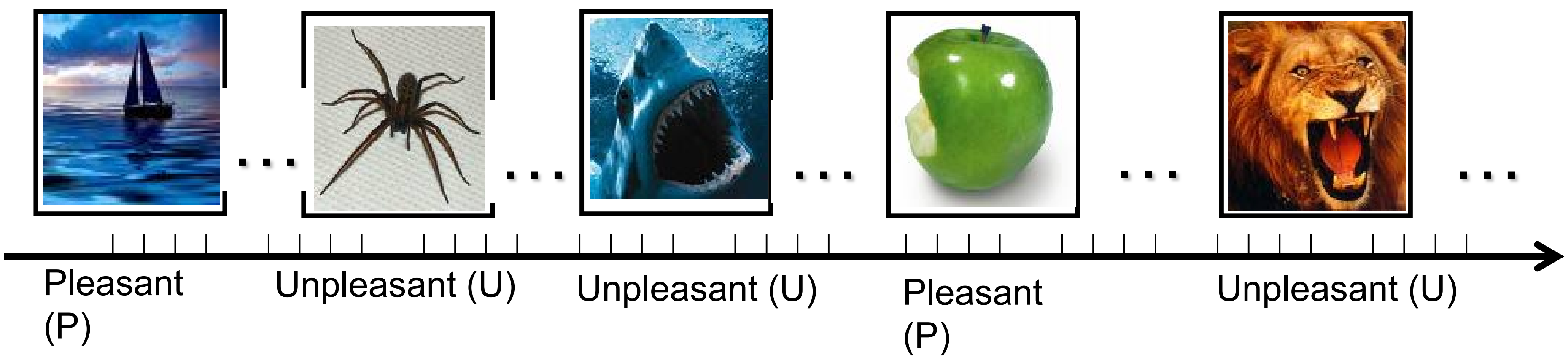
1. Randomised trial order
   cf. confounds of blocked designs

er-fMRI: Stimulus randomisation

Blocked designs may trigger expectations and cognitive sets



Intermixed designs can minimise this by stimulus randomisation

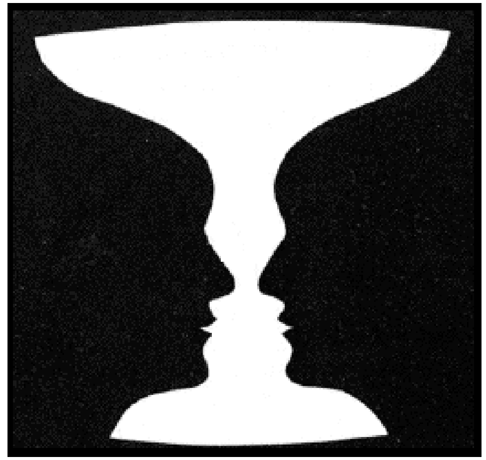


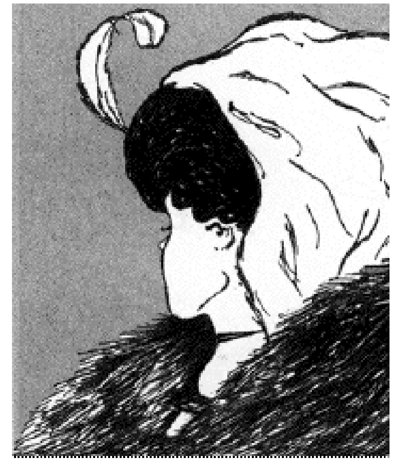
Advantages of er-fMRI

1. Randomised trial order
   cf. confounds of blocked designs
2. **Post hoc classification of trials:**
   according to performance, or because some events can only be indicated by the subject (e.g. spontaneous perceptual changes)

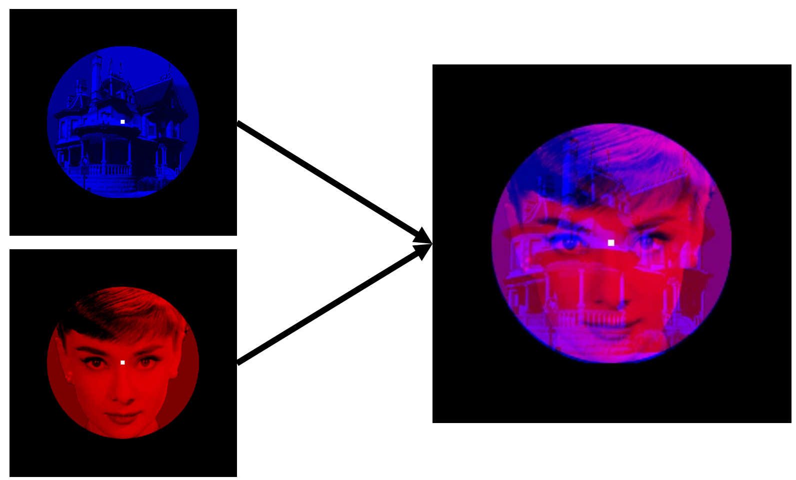
er-fMRI: "on-line" event-definition

Bistable percepts





Binocular rivalry



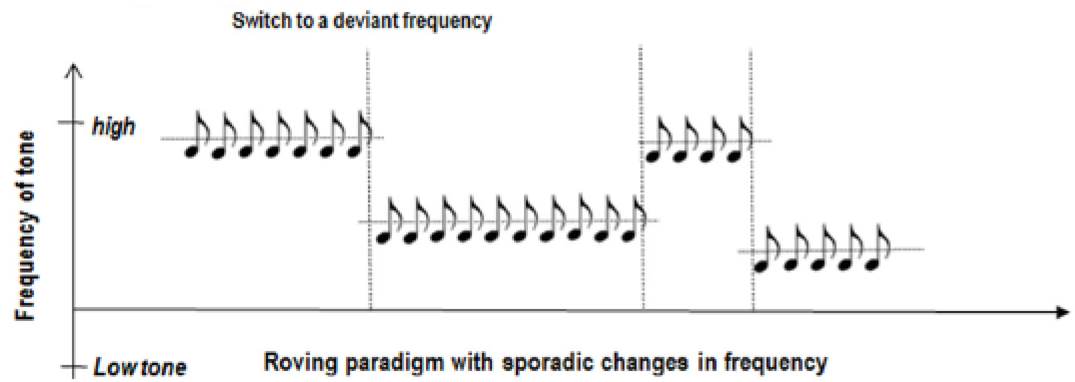
Advantages of er-fMRI

1. Randomised trial order
   cf. confounds of blocked designs

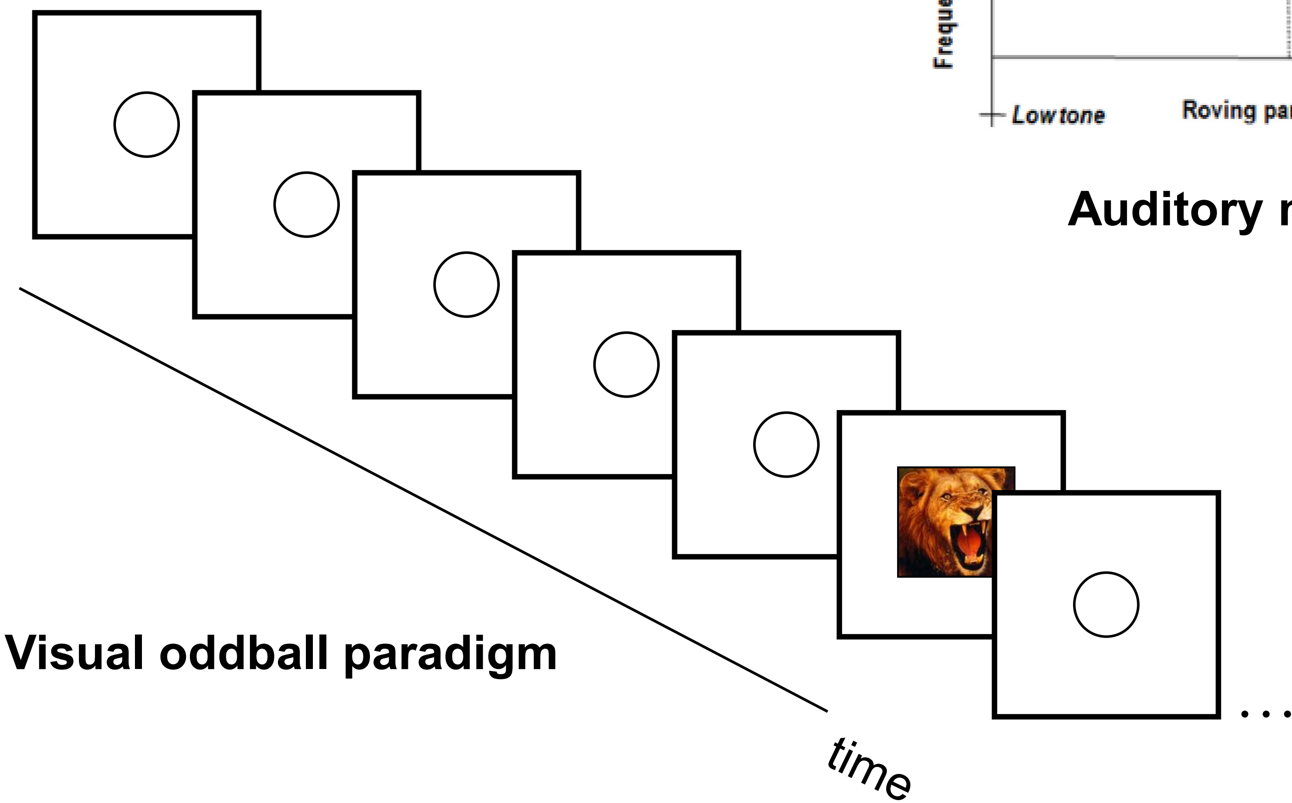
2. Post hoc classification of trials:
   according to performance, or because some events can only be indicated by the subject (e.g. spontaneous perceptual changes)

3. **Some trials cannot be blocked**
   e.g. “oddball” designs

er-fMRI: “oddball” designs



Auditory mismatch negativity (MMN)



Visual oddball paradigm

Advantages of er-fMRI

1. Randomised trial order
   cf. confounds of blocked designs

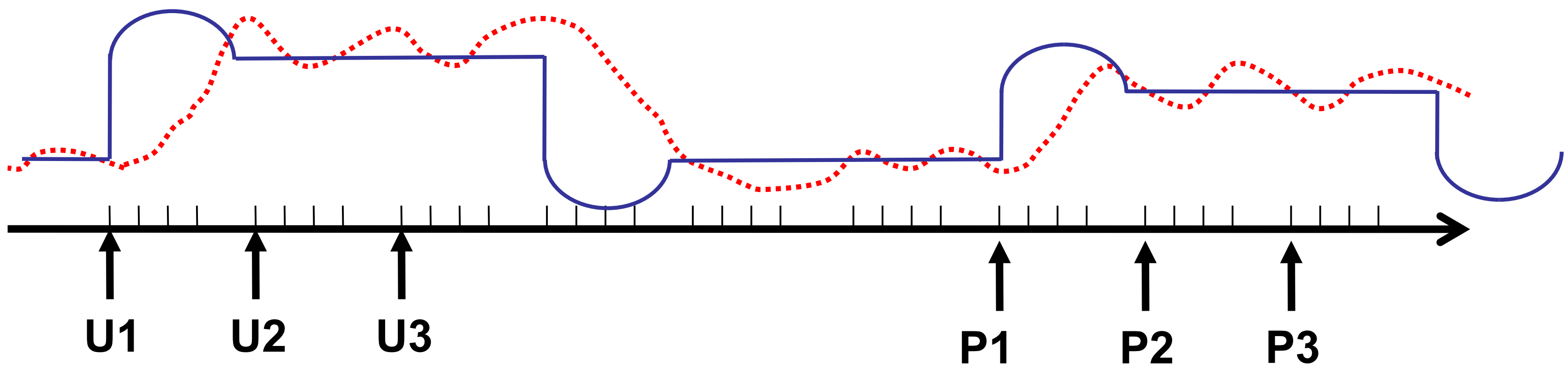
2. Post hoc classification of trials:
   according to performance, or because some events can only be indicated by the subject (e.g. spontaneous perceptual changes)

3. Some trials cannot be blocked
   e.g. “oddball” designs

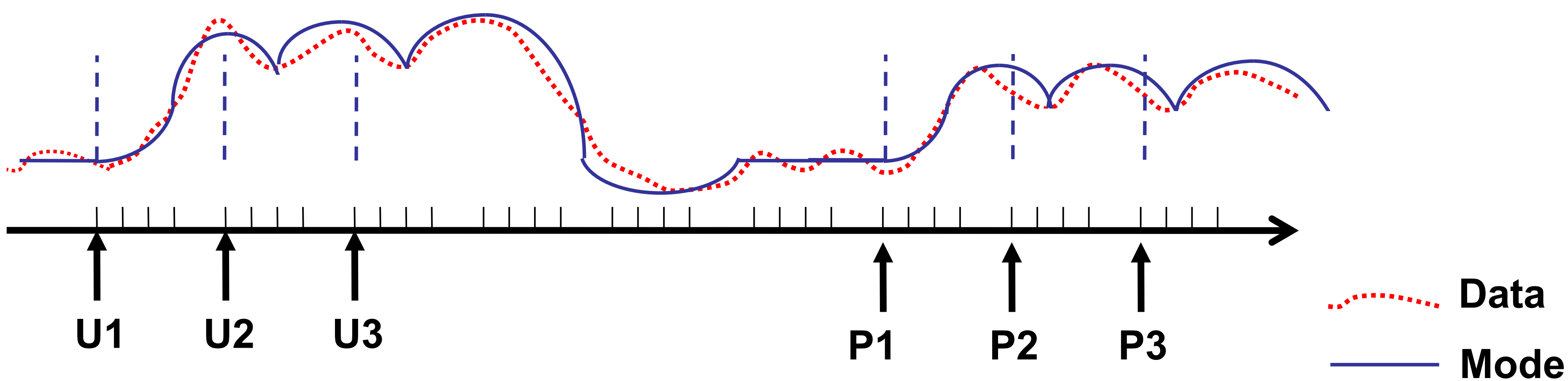
4. **More accurate models even for blocked designs?**

er–fMRI: "event-based" model of block-designs

"Epoch" model assumes constant neural processes throughout block

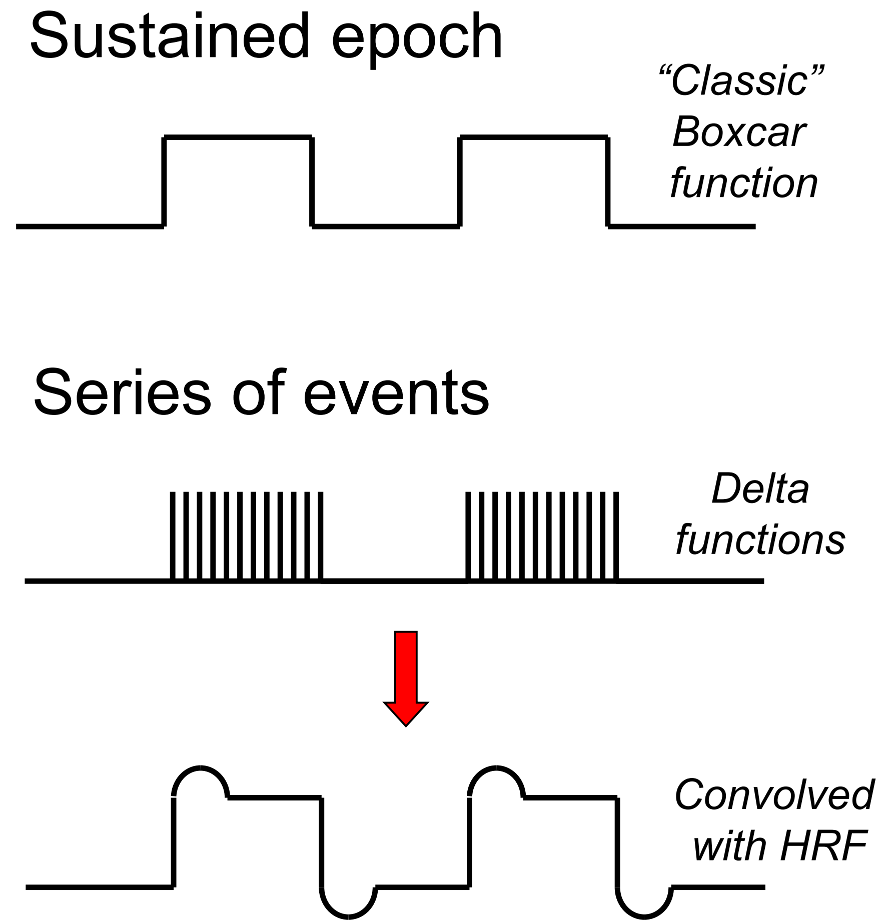


"Event" model may capture response better



Modeling block designs: epochs vs events

- *Models for ER designs are based on events* (delta functions)*...*
- ... but models for blocked designs can be epoch- or event-related
- Near-identical regressors can be created by 1) sustained epochs, 2) rapid series of events (SOAs<~3s)
- In SPM, all conditions are specified in terms of their 1) onsets and 2) durations
  - epochs: variable or constant duration, unit amplitude
  - events: zero duration, amplitude: 1/dt



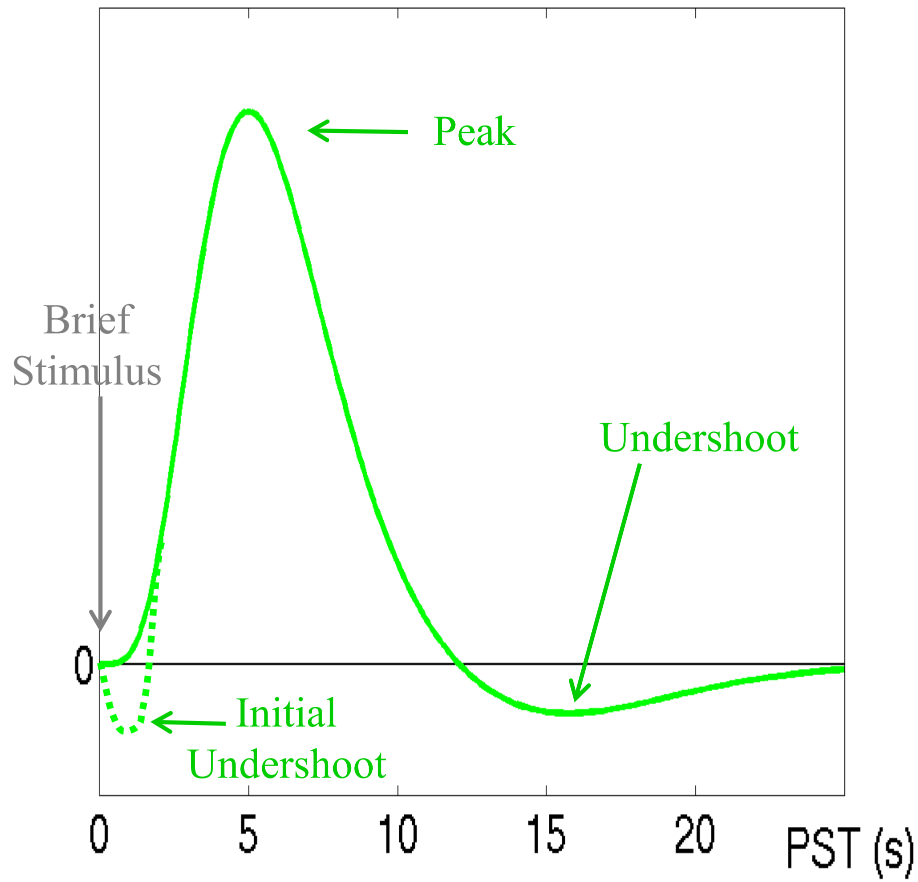
Disadvantages of er-fMRI

1. Less efficient for detecting effects than blocked designs (discussed in detail later).

2. Some psychological processes may be better blocked (e.g. task-switching, attentional instructions).

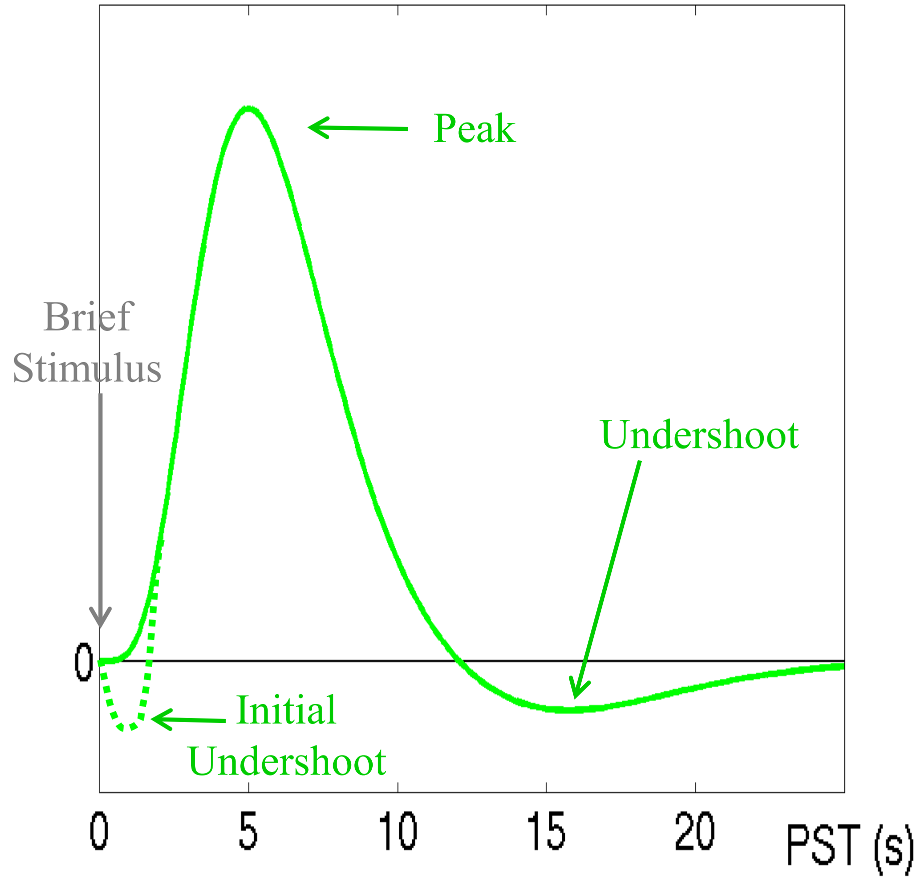
BOLD impulse response

- Function of blood volume and deoxyhemoglobin content (Buxton et al. 1998)
- Peak (max. oxygenation) 4-6s post-stimulus; return to baseline after 20-30s
- initial undershoot sometimes observed (Malonek & Grinvald, 1996)
- Similar across V1, A1, S1…
- … but differences across other regions (Schacter et al. 1997) and individuals (Aguirre et al. 1998)

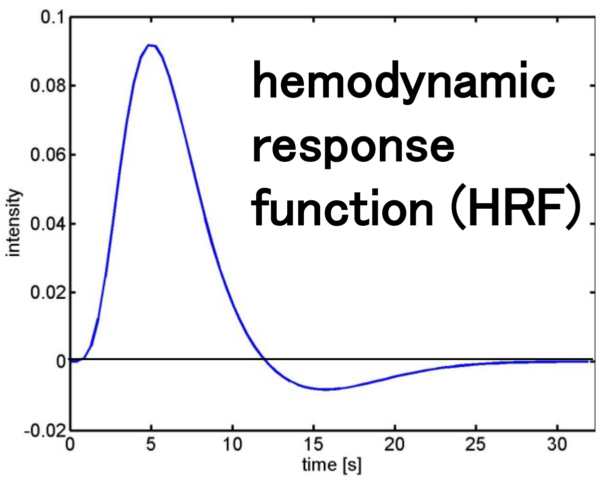


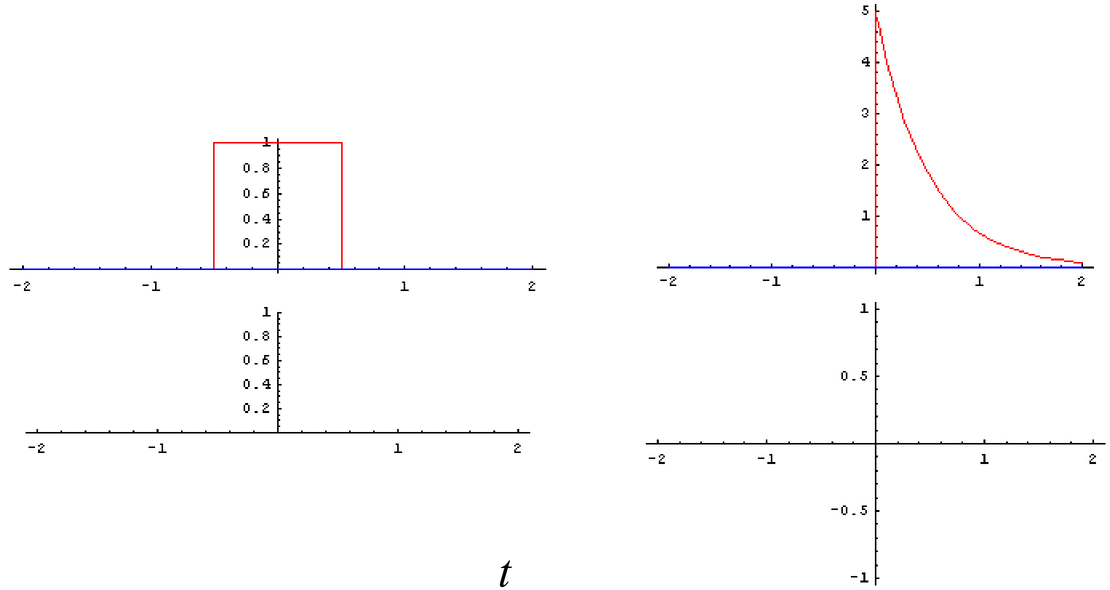
BOLD impulse response

- Early er-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 can give a more efficient design (see below).



Reminder: BOLD response as output from LTI





$$f \otimes g(t) = \int_0^t f(\tau) g(t-\tau) d\tau$$

The response of a linear time-invariant (LTI) system is the convolution of the input with the system's response to an impulse (delta function).

expected BOLD response

= input function ⊗ impulse response function (HRF)

General Linear (Convolution) Model

For block designs, the exact shape of the convolution kernel (i.e. HRF) does not matter much.

For event-related designs this becomes much more important.

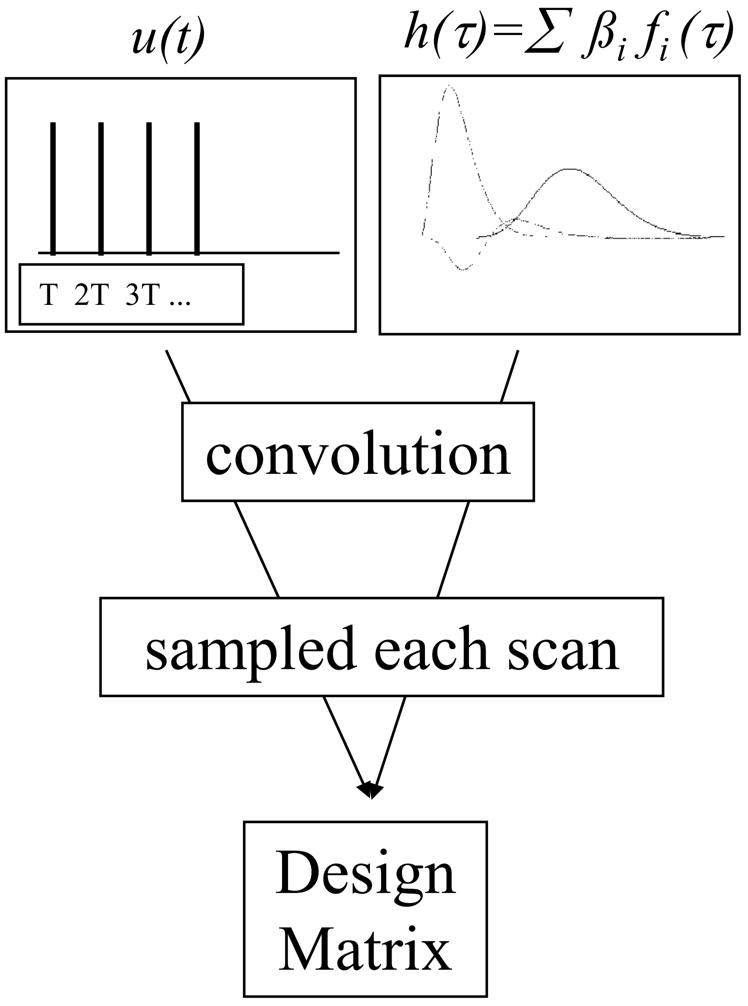
Usually, we use more than a single basis function to model the HRF.

GLM for a single voxel:

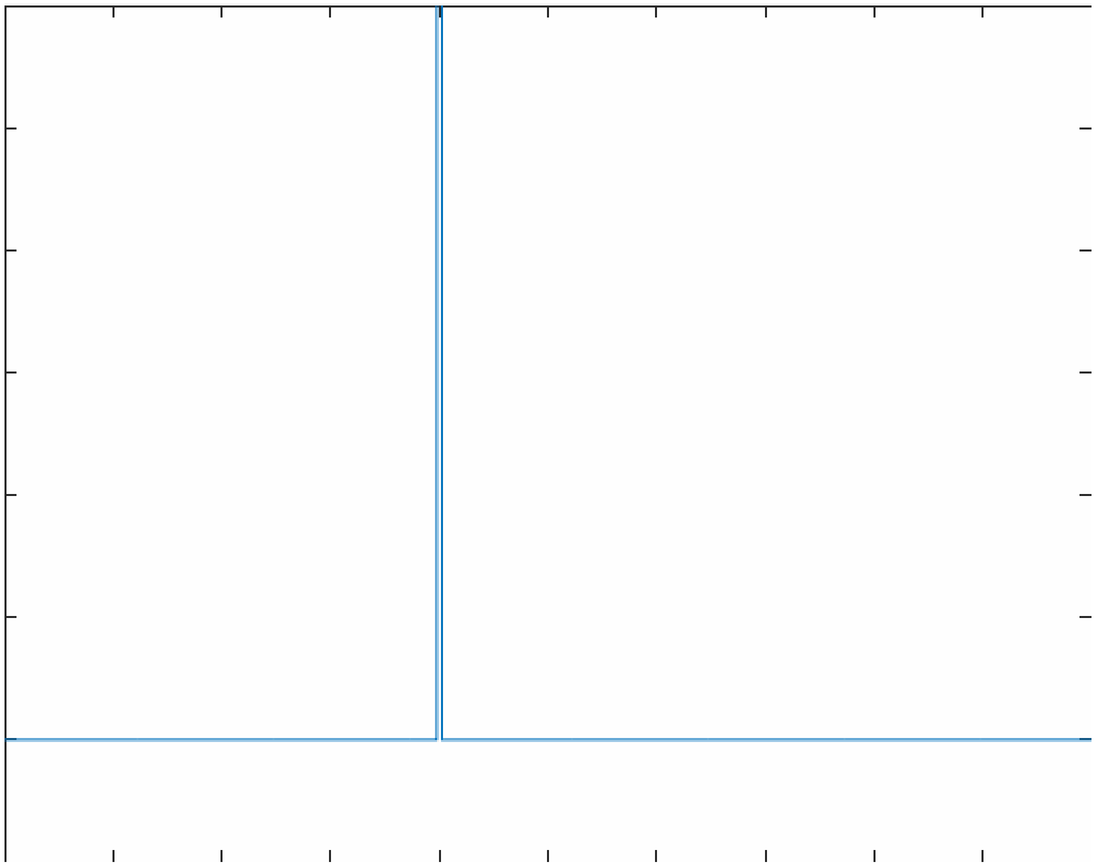
$$\mathbf{y(t)} = [\mathbf{u(t)} \otimes \mathbf{h(\tau)}]\boldsymbol{\beta} + \mathbf{e(t)}$$

Omitting time index:

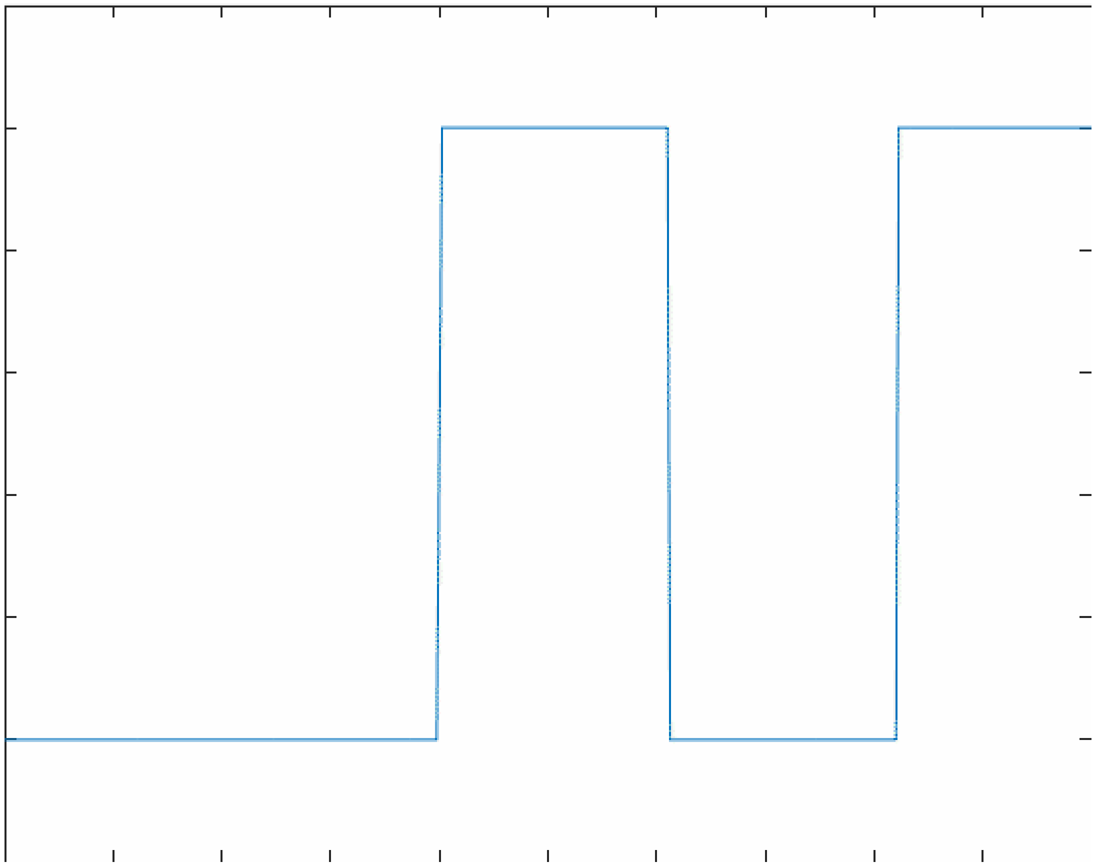
$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e}$$



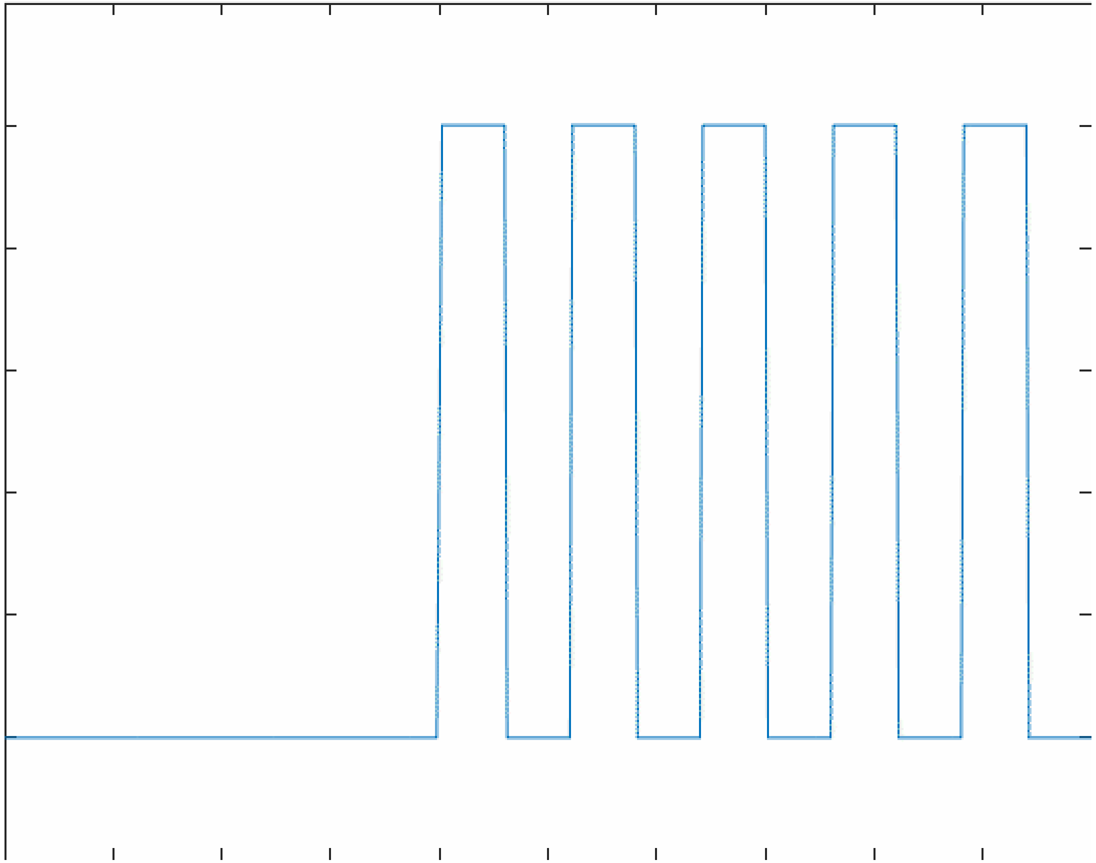
Convolution with BOLD 1



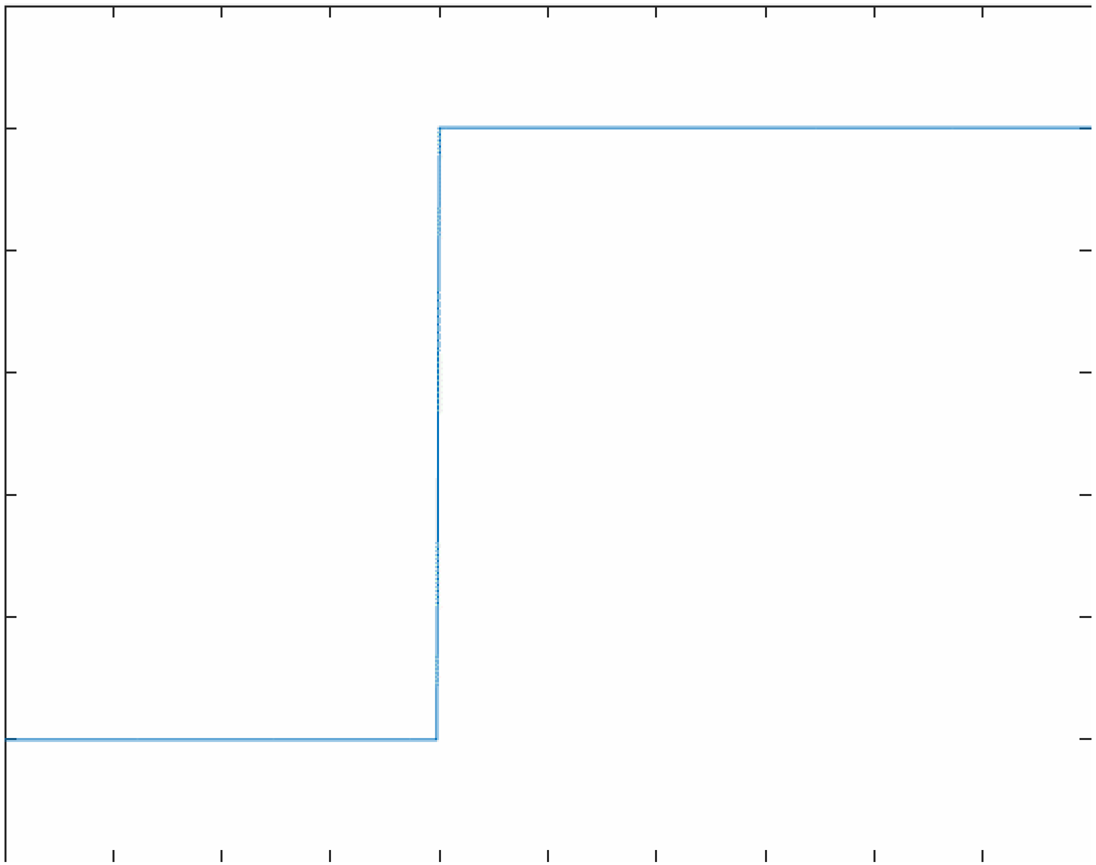
Convolution with BOLD 2



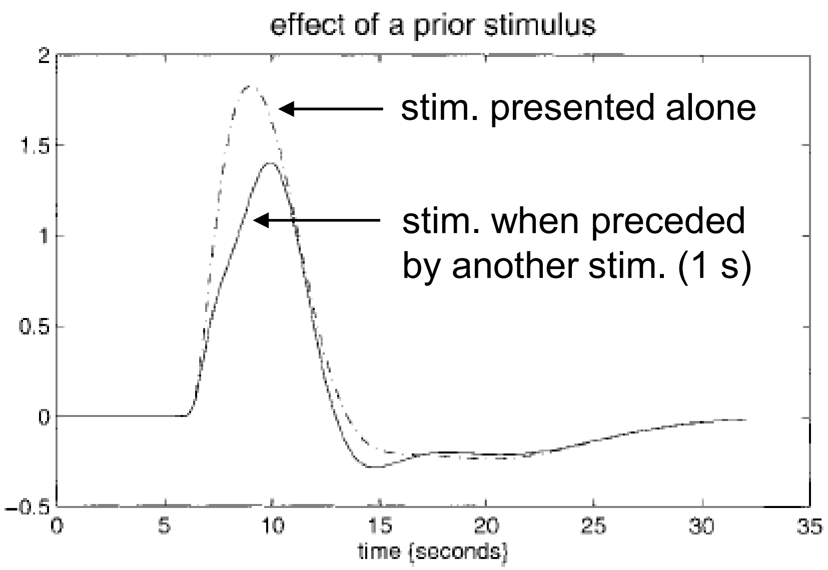
Convolution with BOLD 3

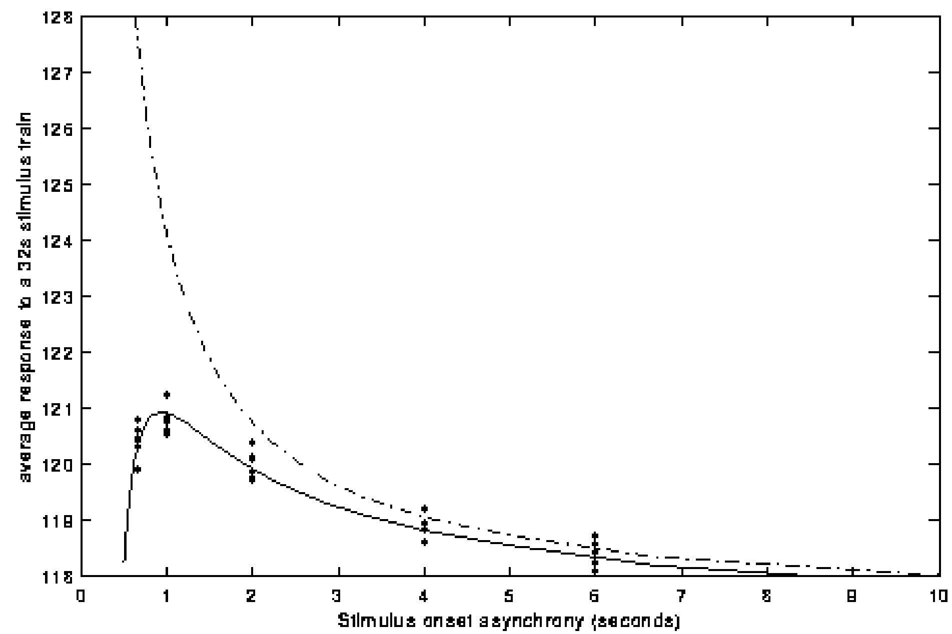


Convolution with BOLD 4



Nonlinearities at short SOAs



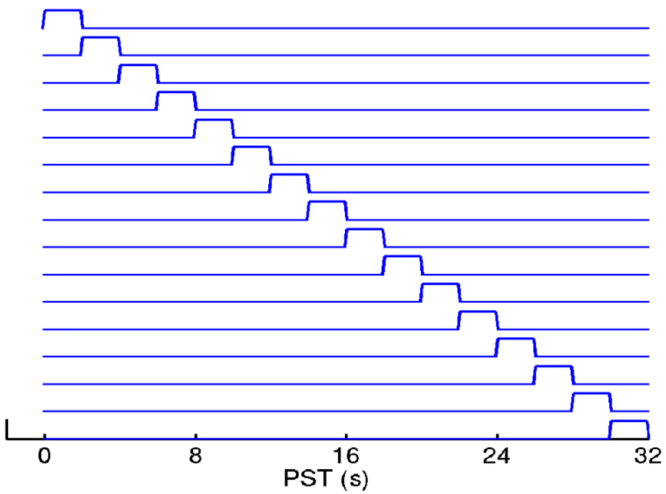


Friston et al. 2000, *NeuroImage*

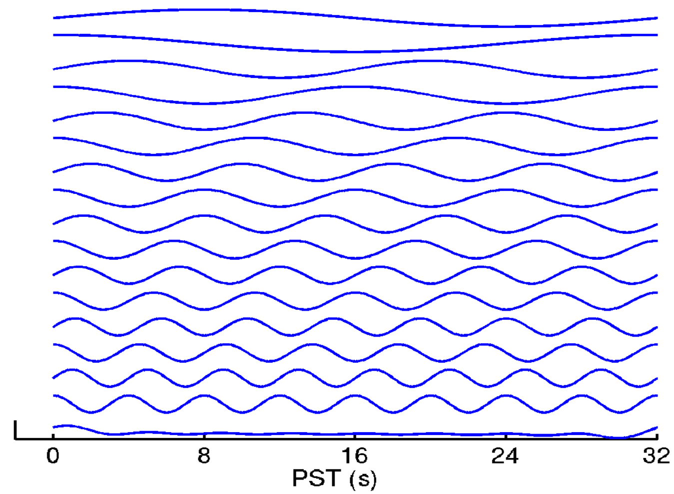
Friston et al. 1998, *Magn. Res. Med.*

Temporal basis functions

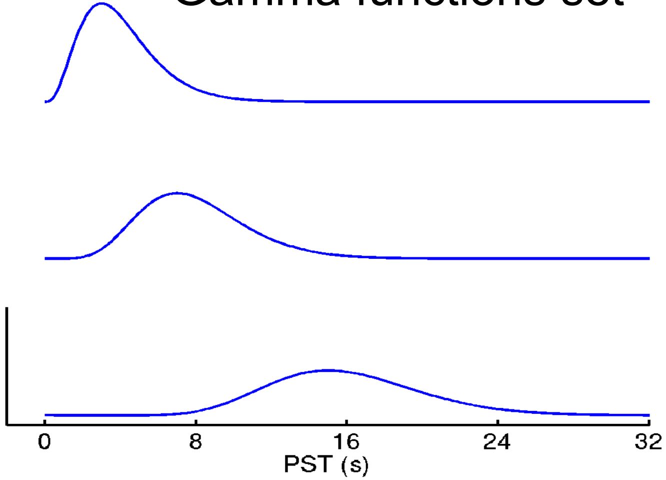
Finite Impulse Response (FIR) model



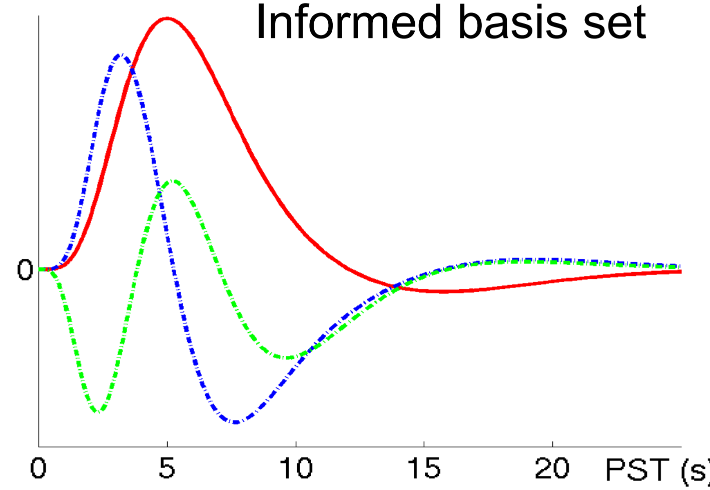
Fourier basis set



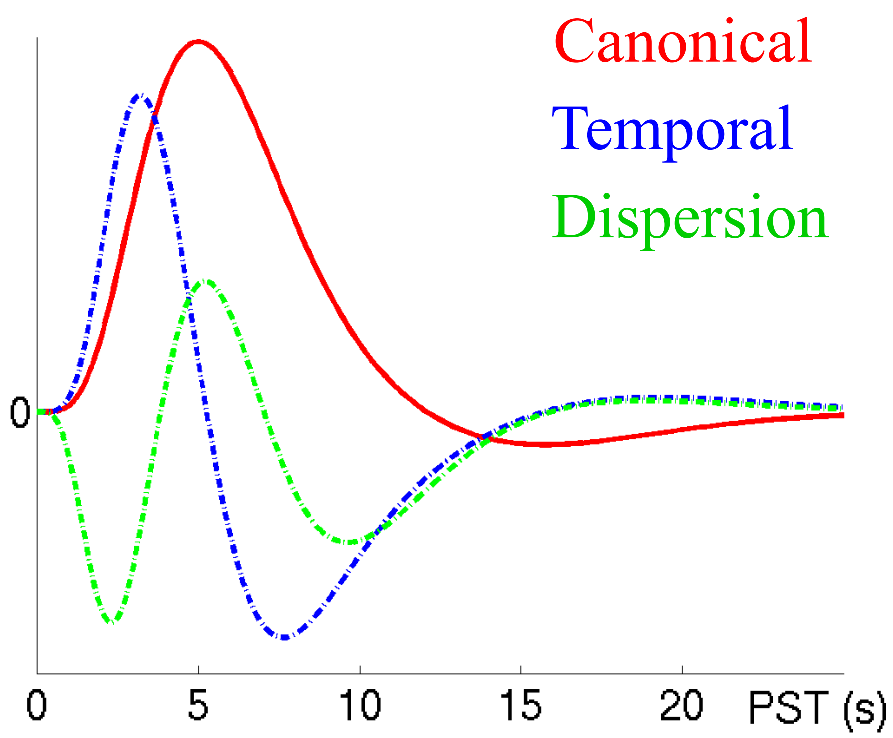
Gamma functions set



Informed basis set



Informed basis set



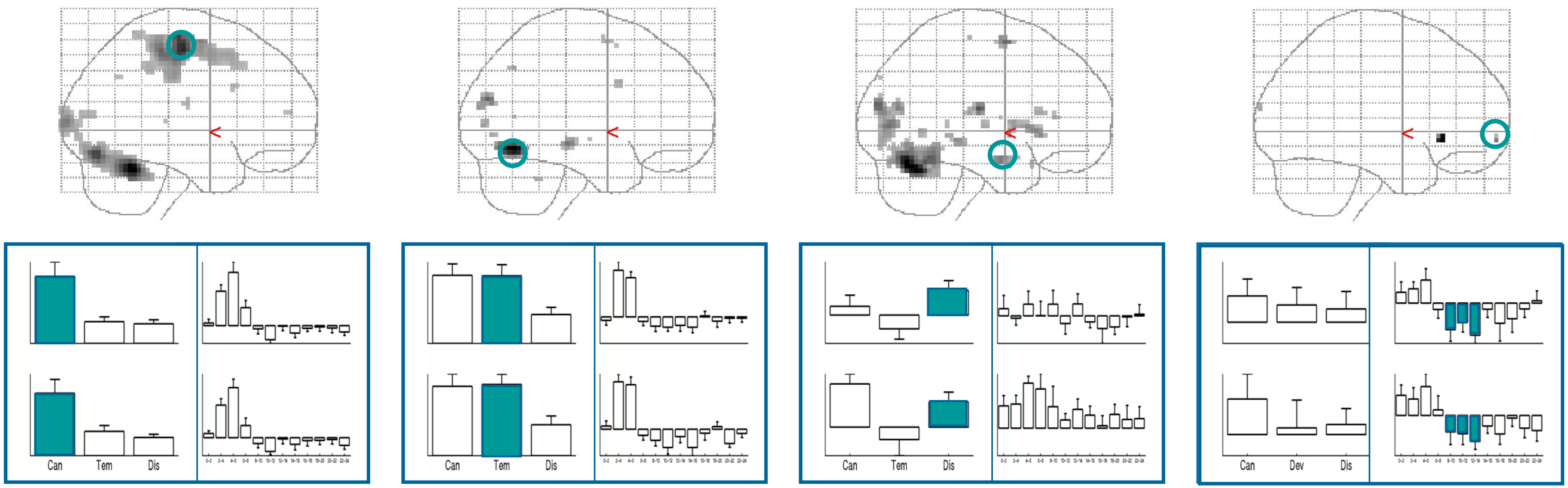
Friston et al. 1998, *NeuroImage*

- Canonical HRF:
  - linear combination of 2 gamma functions
  - 7 parameters, see spm_hrf
- *plus* multivariate Taylor expansion in:
  - time (*Temporal Derivative*)
  - width (*Dispersion Derivative;* partial derivative of canonical HRF wrt. parameter controlling the width)
- F-tests: testing for responses of any shape.
- T-tests on canonical HRF alone (at 1st level) can be improved by derivatives reducing residual error, and can be interpreted as “amplitude” differences, assuming canonical HRF is a reasonable fit.

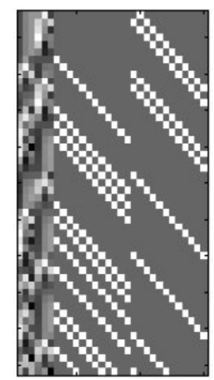
Matlab demo – time and dispersion derivatives

Temporal basis sets: Which one?

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



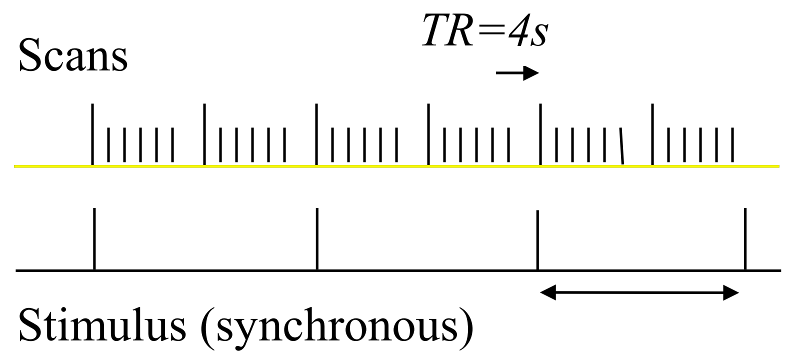
Canonical **+ Temporal** **+ Dispersion** **+ FIR**

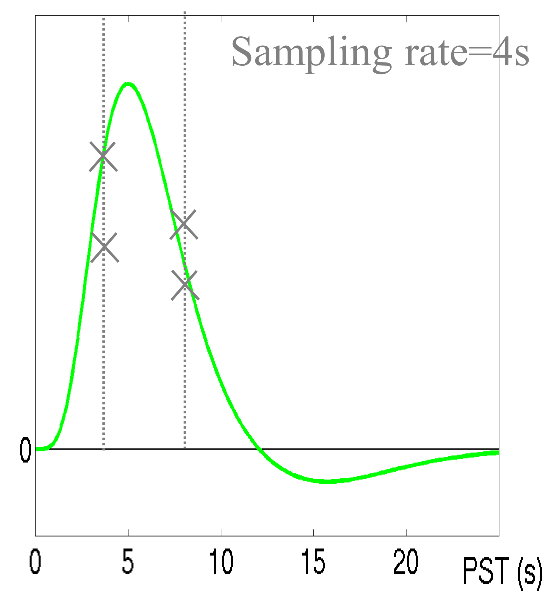


- canonical + temporal + dispersion derivatives appear sufficient
- may not be for more complex trials (e.g. stimulus-delay-response)
- but then such trials better modelled with separate neural components (i.e. activity no longer delta function) (Zarahn, 1999)

Timing Issues : Practical

- Assume TR is 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal





SOA = Stimulus onset asynchrony
(= time between onsets of two subsequent stimuli)

Timing Issues : Practical

- Assume TR is 4s
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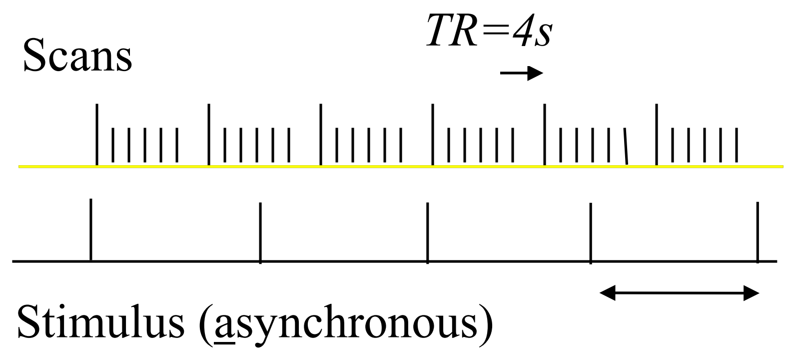
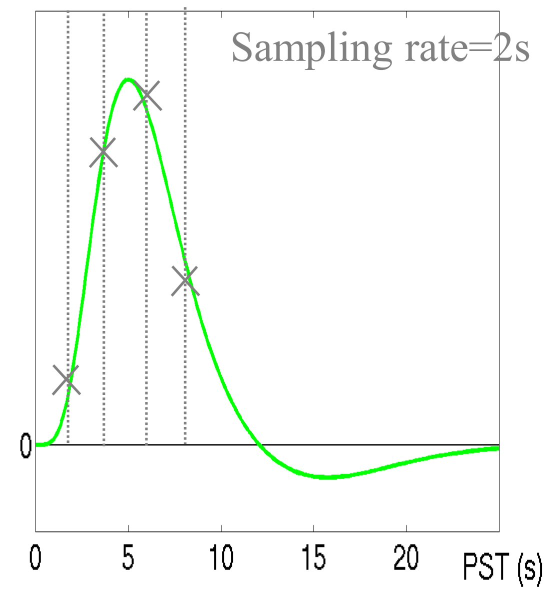
- Higher effective sampling by:
  - 1. Asynchrony, *e.g. SOA* = 1.5×TR





SOA = Stimulus onset asynchrony
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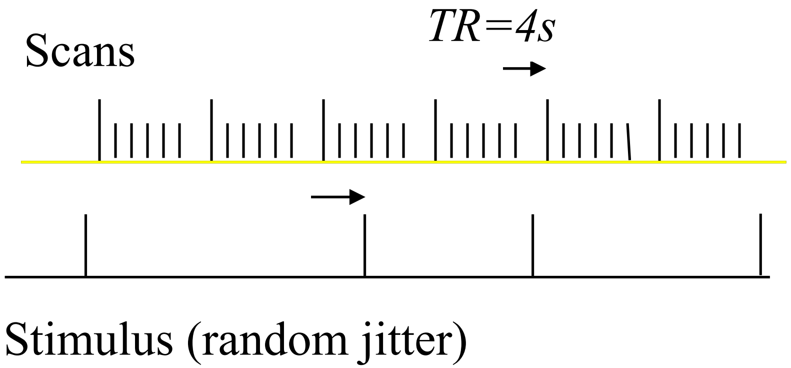
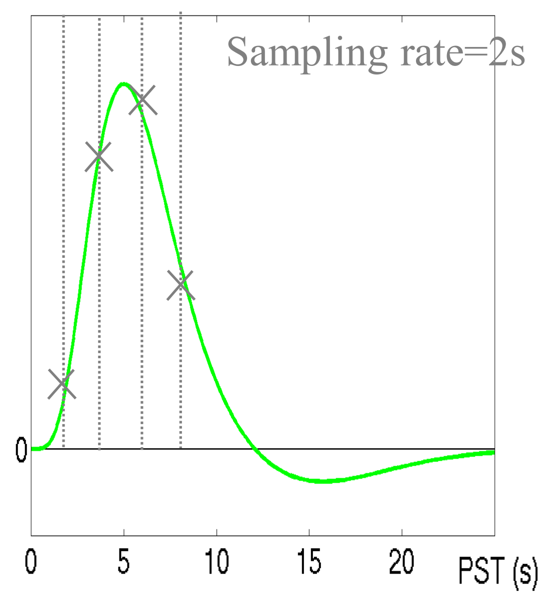
Timing Issues : Practical

- Assume TR is 4s
- Sampling at [0,4,8,12…] post- stimulus may miss peak signal
- Higher effective sampling by:
  - 1. Asynchrony, *e.g. SOA* = 1.5×TR
  - 2. Random jitter, e.g. SOA = (2 ± 0.5)×TR
- Better response characterisation (Miezin et al, 2000)





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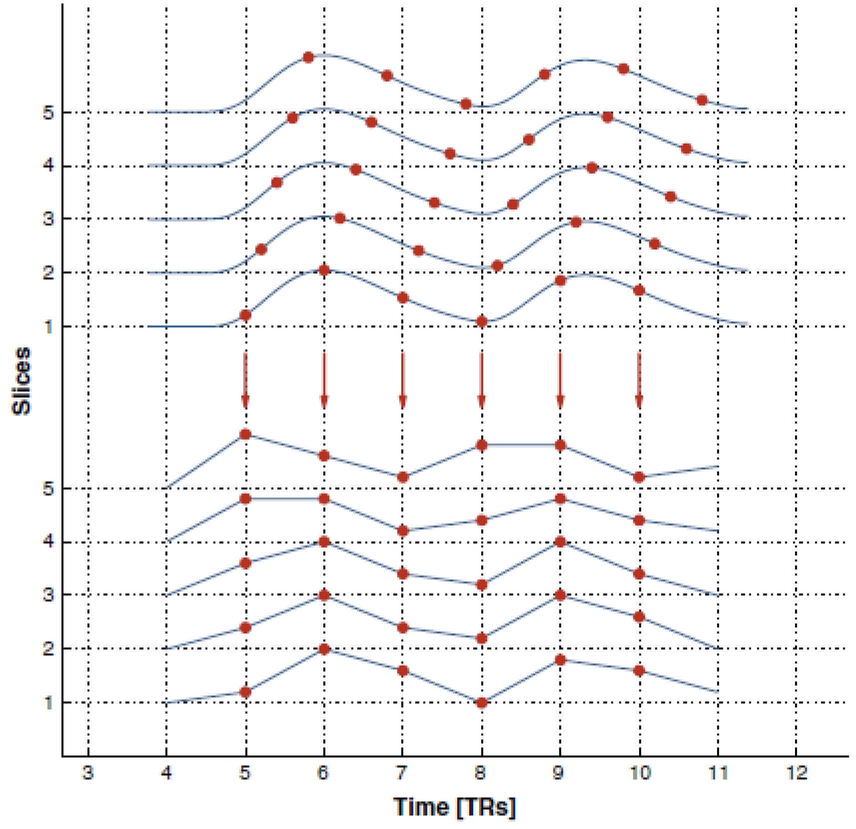
(= time between onsets of two subsequent stimuli)

Slice-timing



Sladky et al. 2011, NeuroImage

Slice-timing

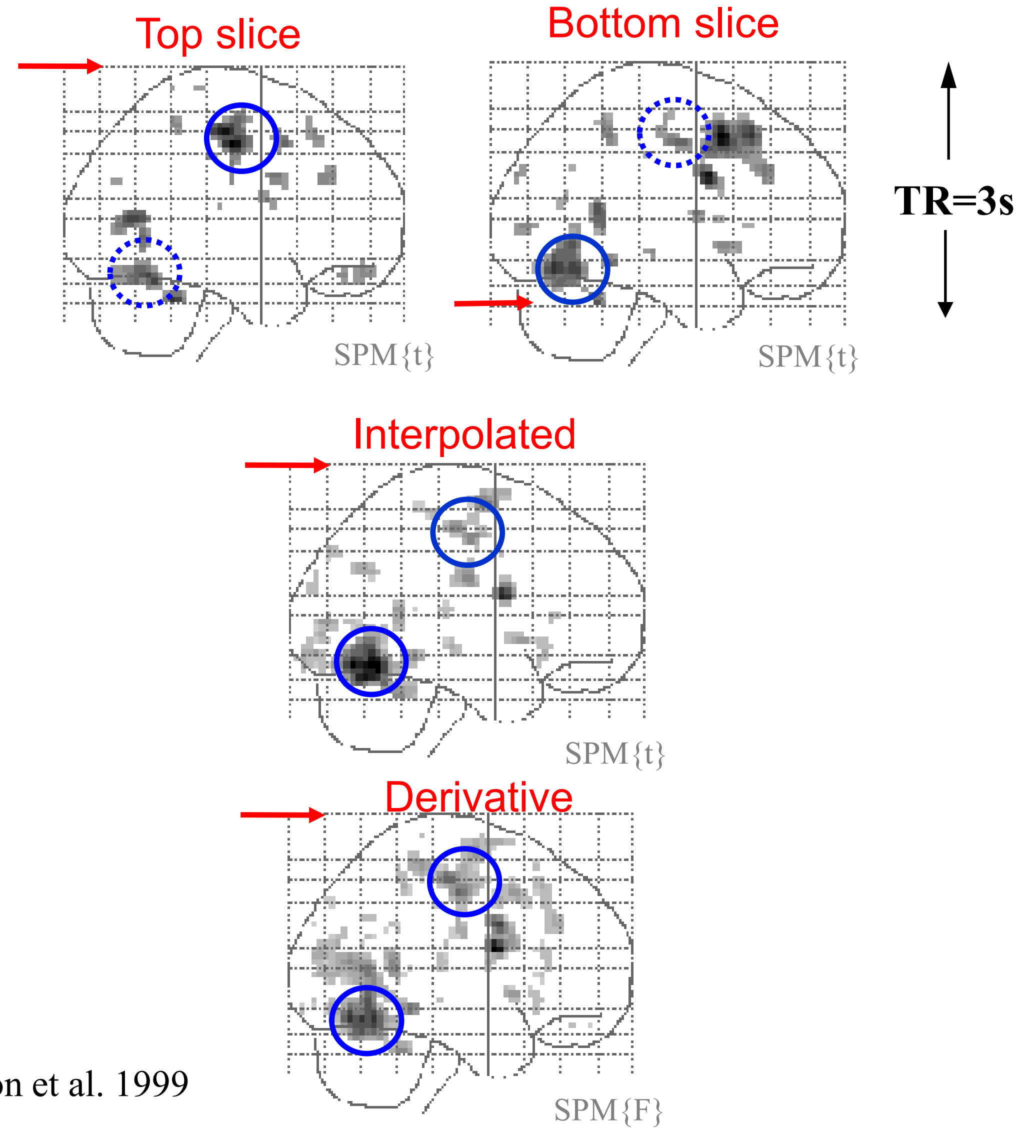
- Slices acquired at different times, yet model is the same for all slices

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

- Solutions:

1. Temporal interpolation of data
   … but may be problematic for longer TRs

2. More general basis set (e.g. with temporal derivatives)
   … but more complicated design matrix



Henson et al. 1999

Design efficiency

How can I make my experimental design as good (powerful) as possible?

Design efficiency

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

- The aim is to minimize the standard error of a *t*-contrast (i.e. the denominator of a t-statistic).

$$\mathrm{var}(c^T \hat{\beta}) = \hat{\sigma}^2 c^T (X^T X)^{-1} c$$

- This is equivalent to maximizing the efficiency *e*:

$$e(\hat{\sigma}^2, c, X) = (\underbrace{\hat{\sigma}^2}_{\text{Noise variance}} c^T \underbrace{(X^T X)}_{\text{Design variance}}{}^{-1} c)^{-1}$$

- If we assume that the noise variance is independent of the specific design:

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

- This is a relative measure: all we can really say is that one design is more efficient than another (for a given contrast).

Scaling issues – a x c

$$T = \frac{c^T \hat{\beta}}{\sqrt{\mathrm{var}(c^T \hat{\beta})}} = \frac{c^T \hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T \left(X^T X\right)^{-1} c}}$$

$$T_a = \frac{ac^T \hat{\beta}}{\sqrt{\mathrm{var}(ac^T \hat{\beta})}} = \frac{ac^T \hat{\beta}}{\sqrt{\hat{\sigma}^2 ac^T \left(X^T X\right)^{-1} ac}} = \frac{c^T \hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T \left(X^T X\right)^{-1} c}} = T$$

Multiplying the contrast with a scalar does not change the t-value?

Scaling issues – b x X

$$T_b = \frac{c^T \hat{\beta}_b}{\sqrt{\text{var}(c^T \hat{\beta}_b)}} = \frac{c^T \hat{\beta}_b}{\sqrt{\hat{\sigma}^2 c^T \left(bX^T bX\right)^{-1} c}}$$

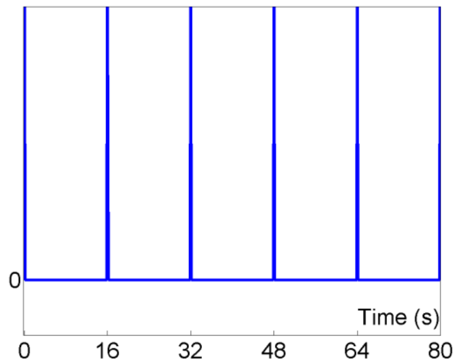
$$\widehat{\beta_b} = (bX^T bX)^{-1} bX^T y = \hat{\beta}/b$$

$$T_b = \frac{c^T \hat{\beta}/b}{b^{-1}\sqrt{\hat{\sigma}^2 c^T \left(X^T X\right)^{-1} c}} = T$$

Multiplying the design matrix with a scalar does not change the t-value?

Fixed SOA = 16s

Stimulus (“Neural”)



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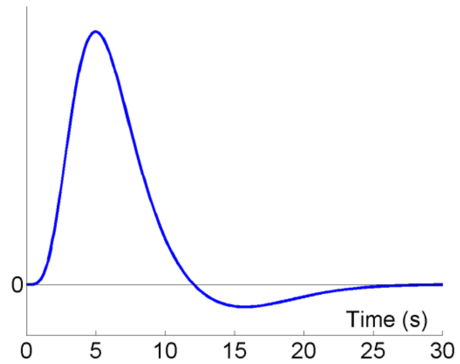
HRF



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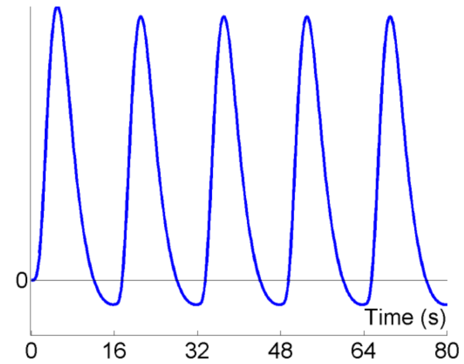
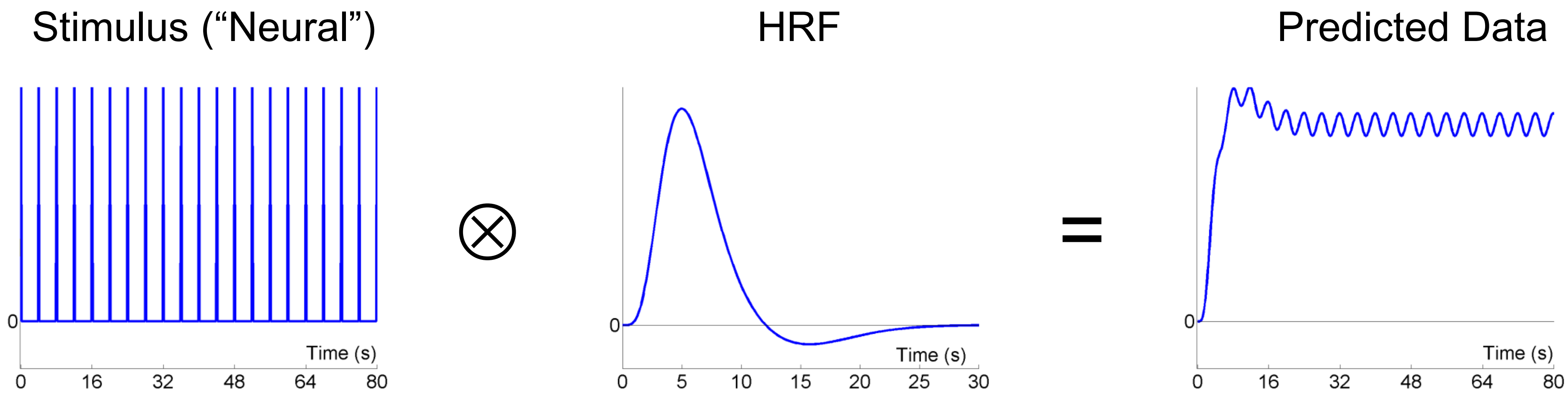
Predicted Data



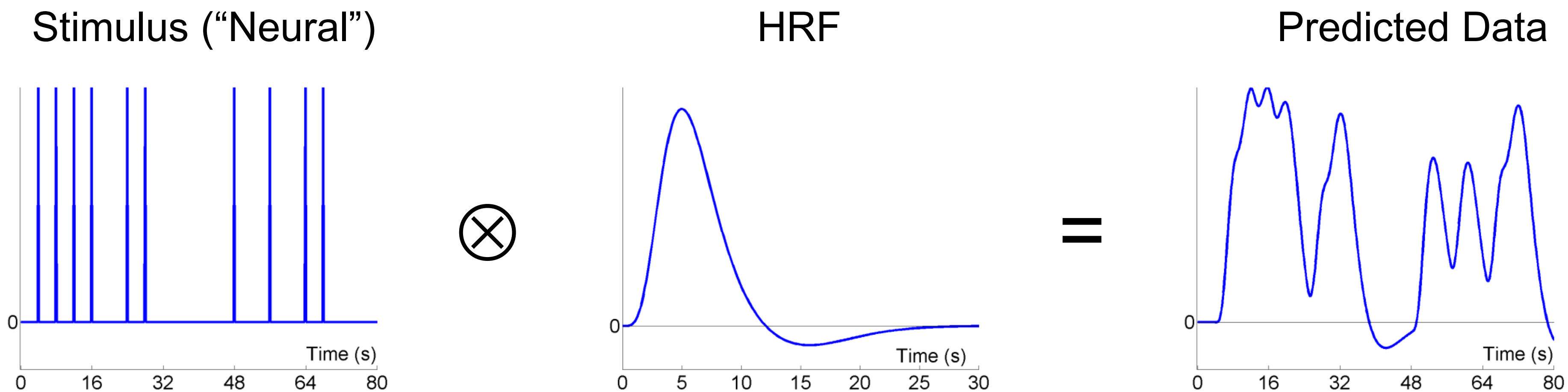
Not particularly efficient…

Fixed SOA = 4s



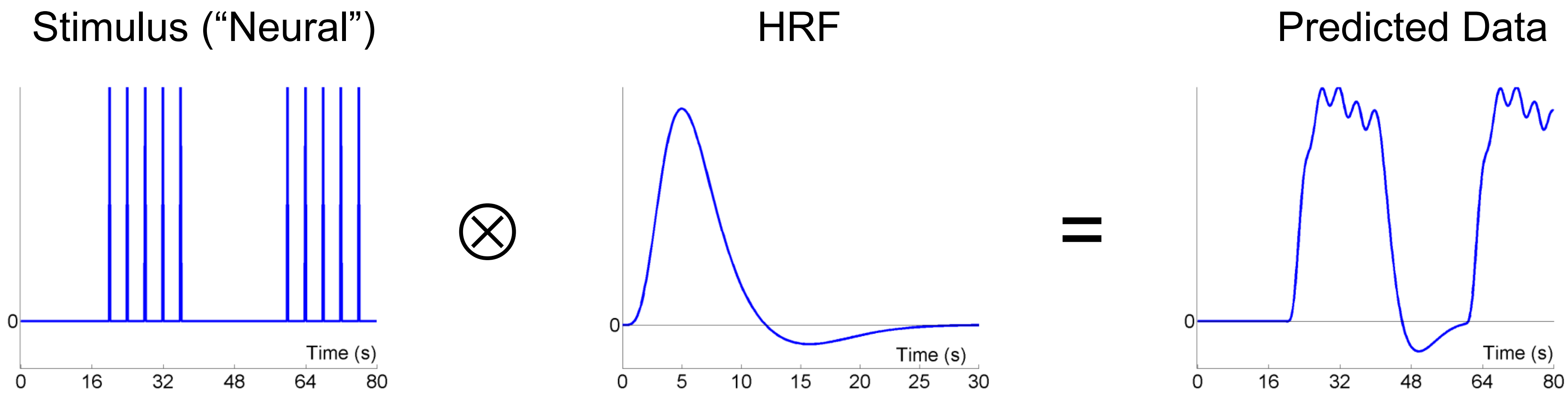
Very inefficient…

Randomised, SOA_{min}= 4s



More efficient …

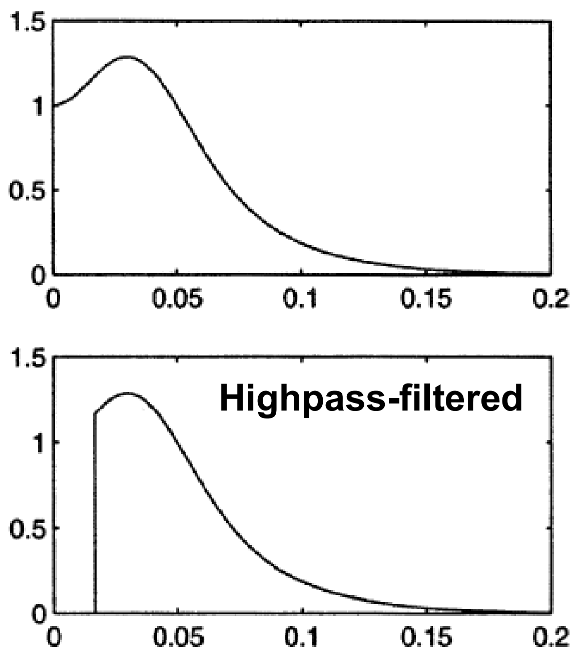
Blocked, SOA_{min}= 4s

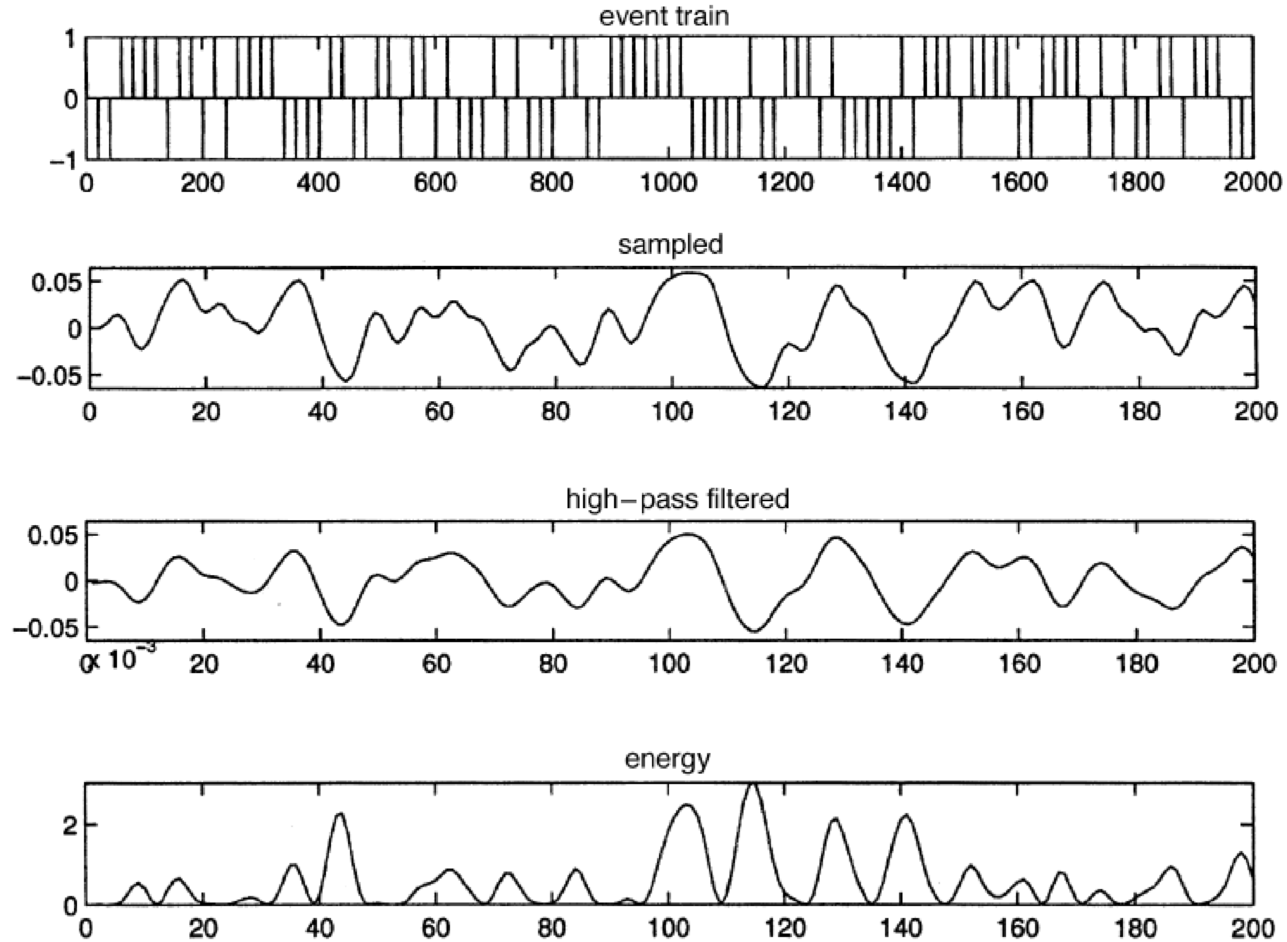


Even more efficient…

Another perspective on efficiency

Hemodynamic transfer function
(based on canonical HRF):
neural activity (Hz) → BOLD





efficiency = bandpassed signal energy

Josephs & Henson 1999, *Phil Trans B*

Fourier series

Sine wave

$$y(t) = A\sin(2\pi ft + \varphi) = A\sin(\omega t + \varphi)$$

where:

- A = the *amplitude*, the peak deviation of the function from zero.
- f = the *ordinary frequency*, the *number* of oscillations (cycles) that occur each second of time.
- $\omega = 2\pi f$, the *angular frequency*, the rate of change of the function argument in units of radians per second
- φ = the *phase*, specifies (in radians) where in its cycle the oscillation is at $t = 0$.

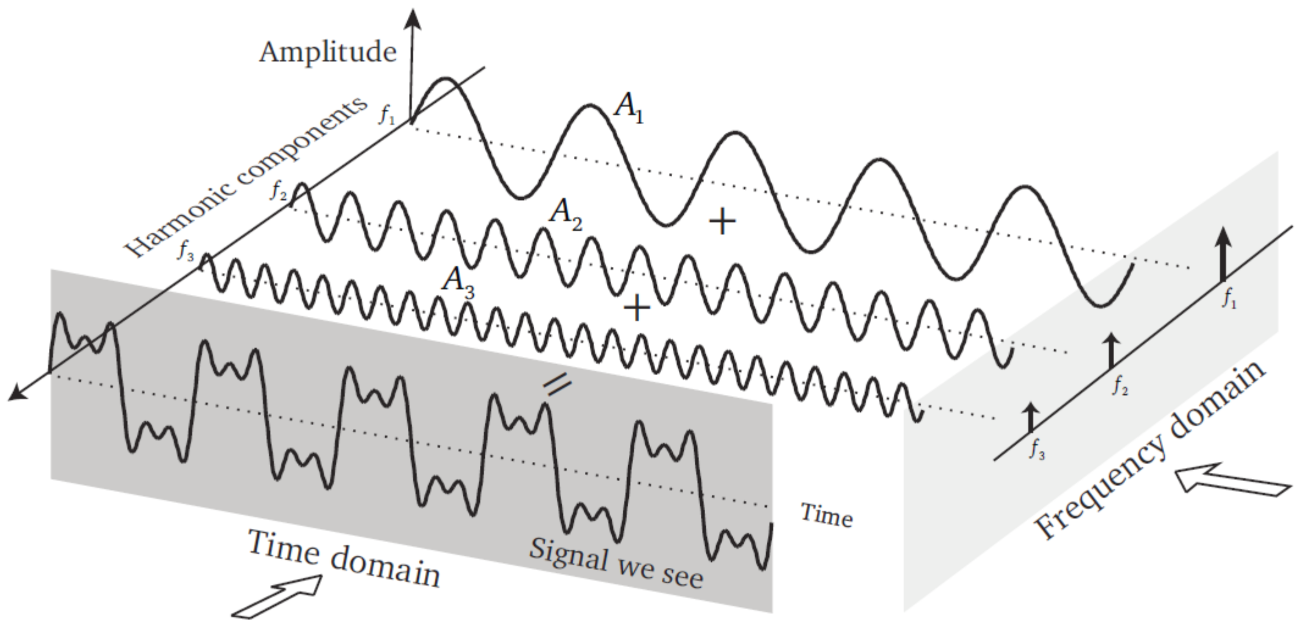
Power = squared amplitude (often represented in logs)

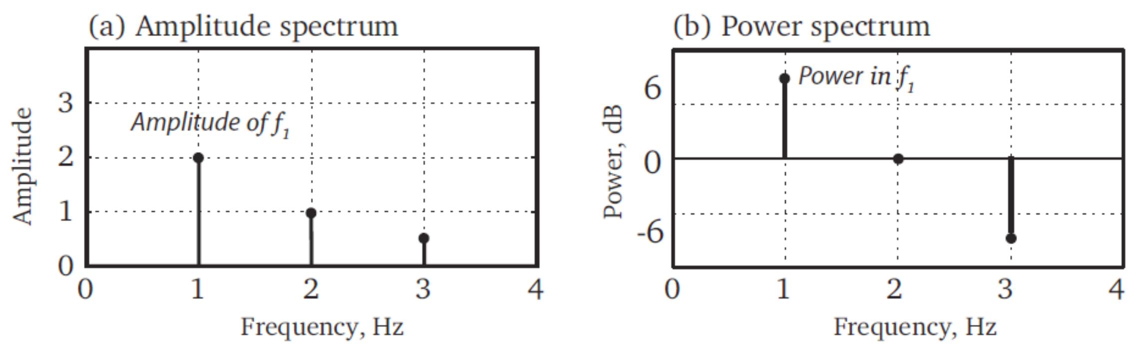
Signal energy = integral of power over time

Fourier series
= infinite sum of sines and cosines of different frequencies

$$\boxed{f(t) = a_0 + \sum_{k=1}^{\infty} a_k \cos(2\pi f_k t) + \sum_{k=1}^{\infty} b_k \sin(2\pi f_k t)}$$

Fourier series

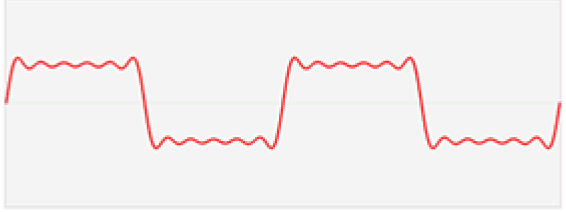




Langton & Levin (2016) Intuitive Guide to Fourier Analysis

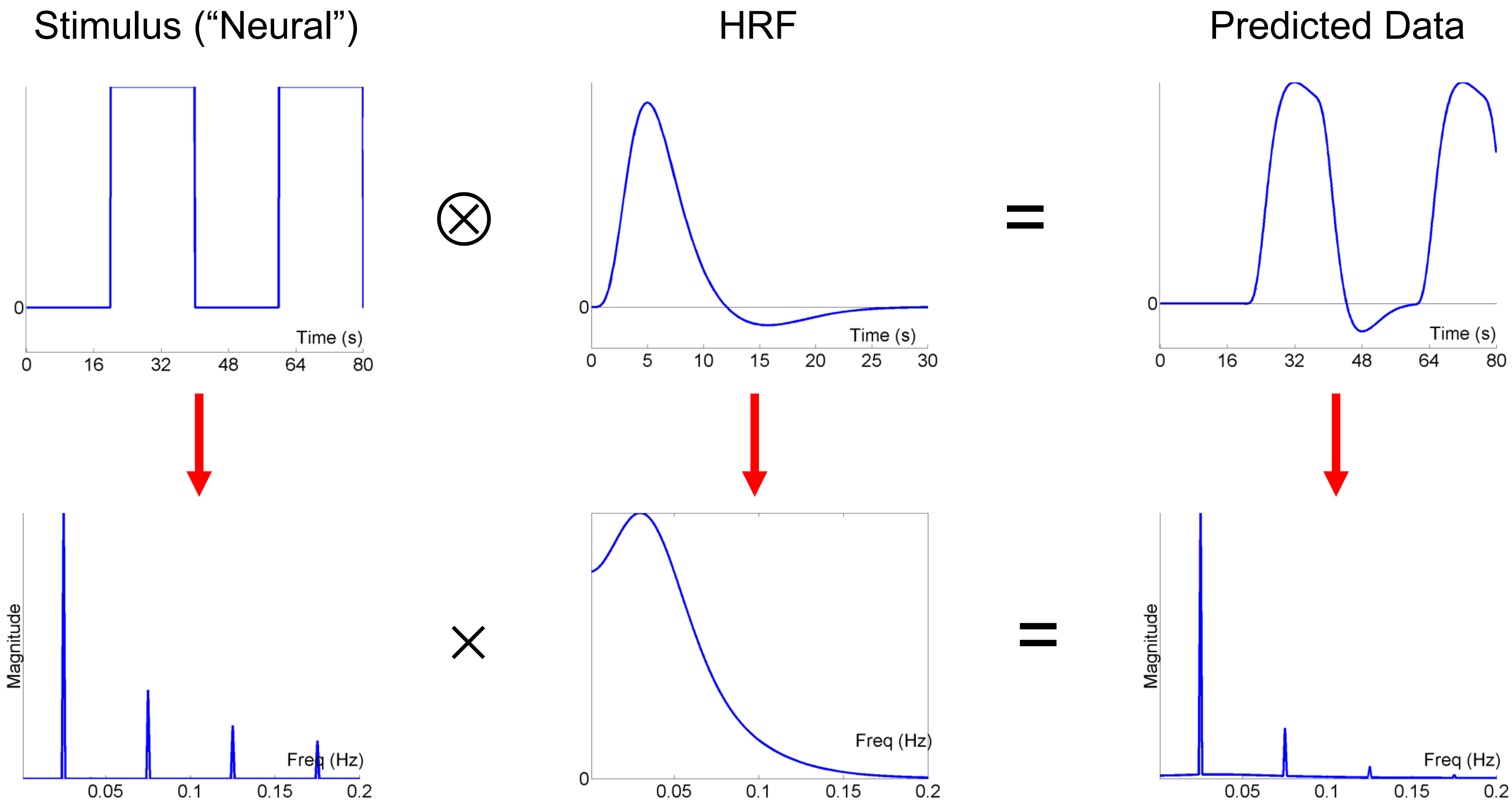
Fourier transform

- simply speaking, the Fourier transform F provides the Fourier series coefficients for a signal, i.e., it decomposes a function of time (a signal) into the frequencies it consists of
- linear operator
- convolution in time domain = multiplication in frequency domain: $F(f*g) = F(f)F(g)$



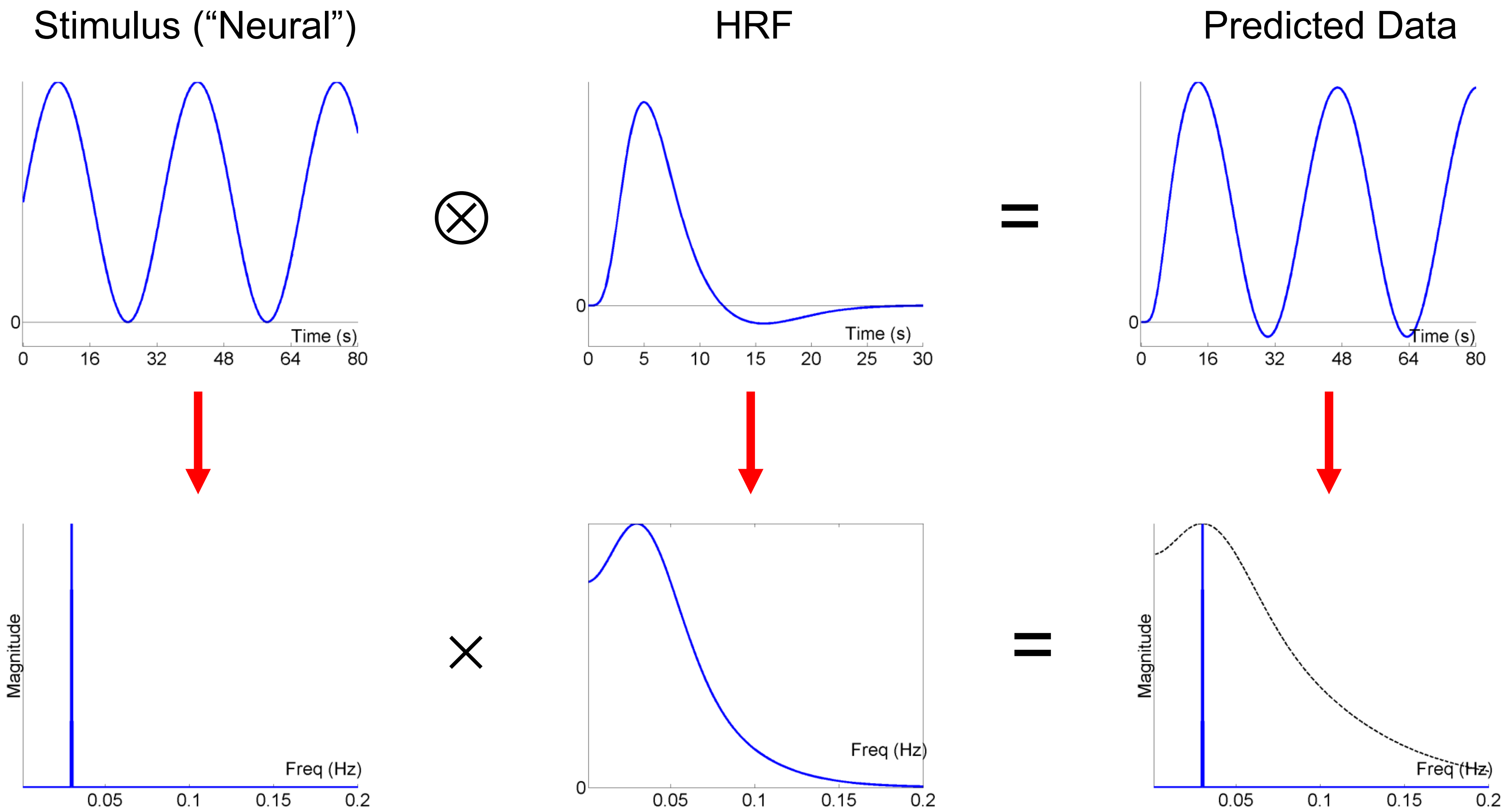
Animation: https://en.wikipedia.org/wiki/Fourier_transform

Blocked, epoch = 20s



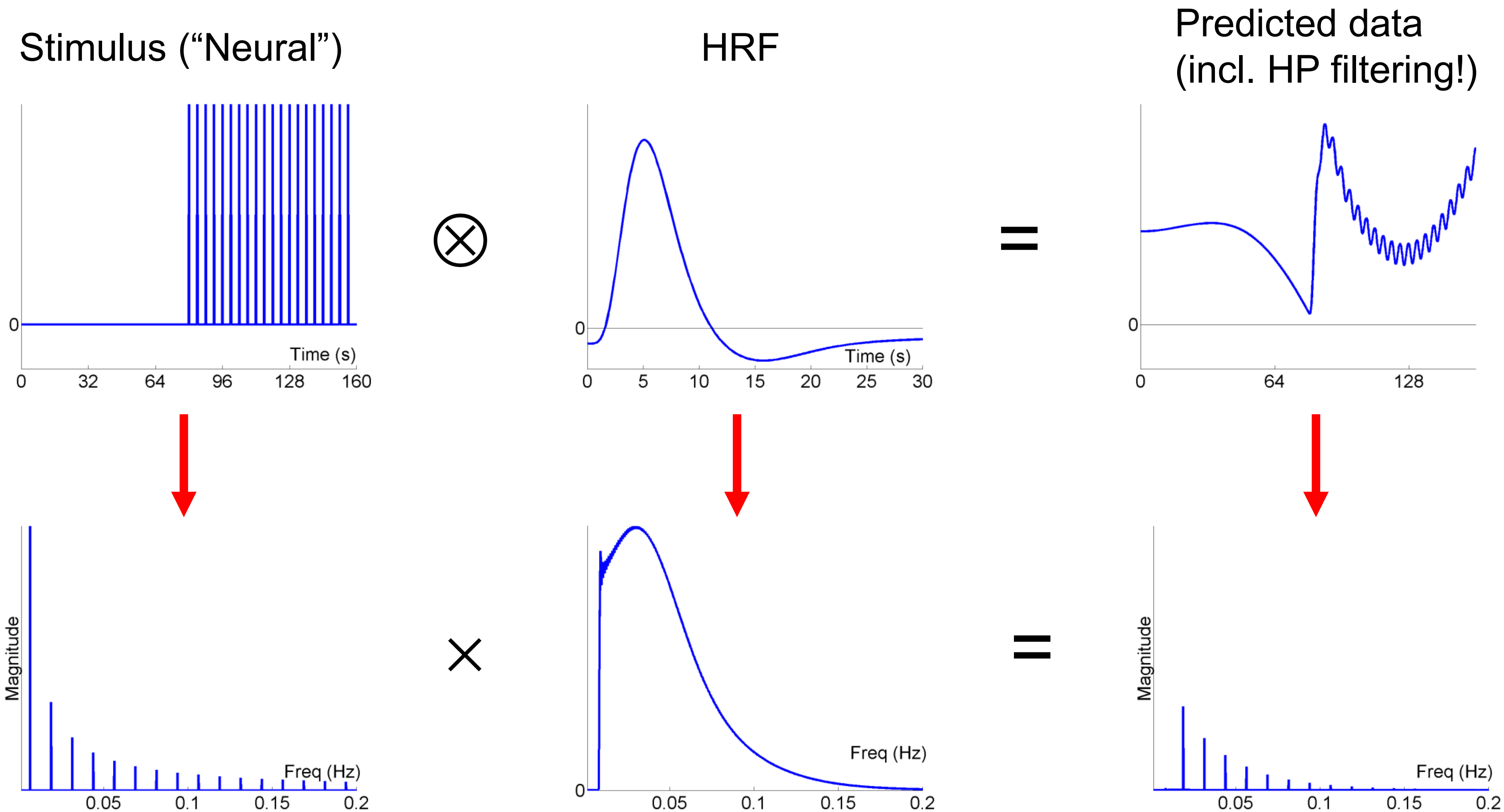
Blocked-epoch (with short SOA)

Sinusoidal modulation, f = 1/33s



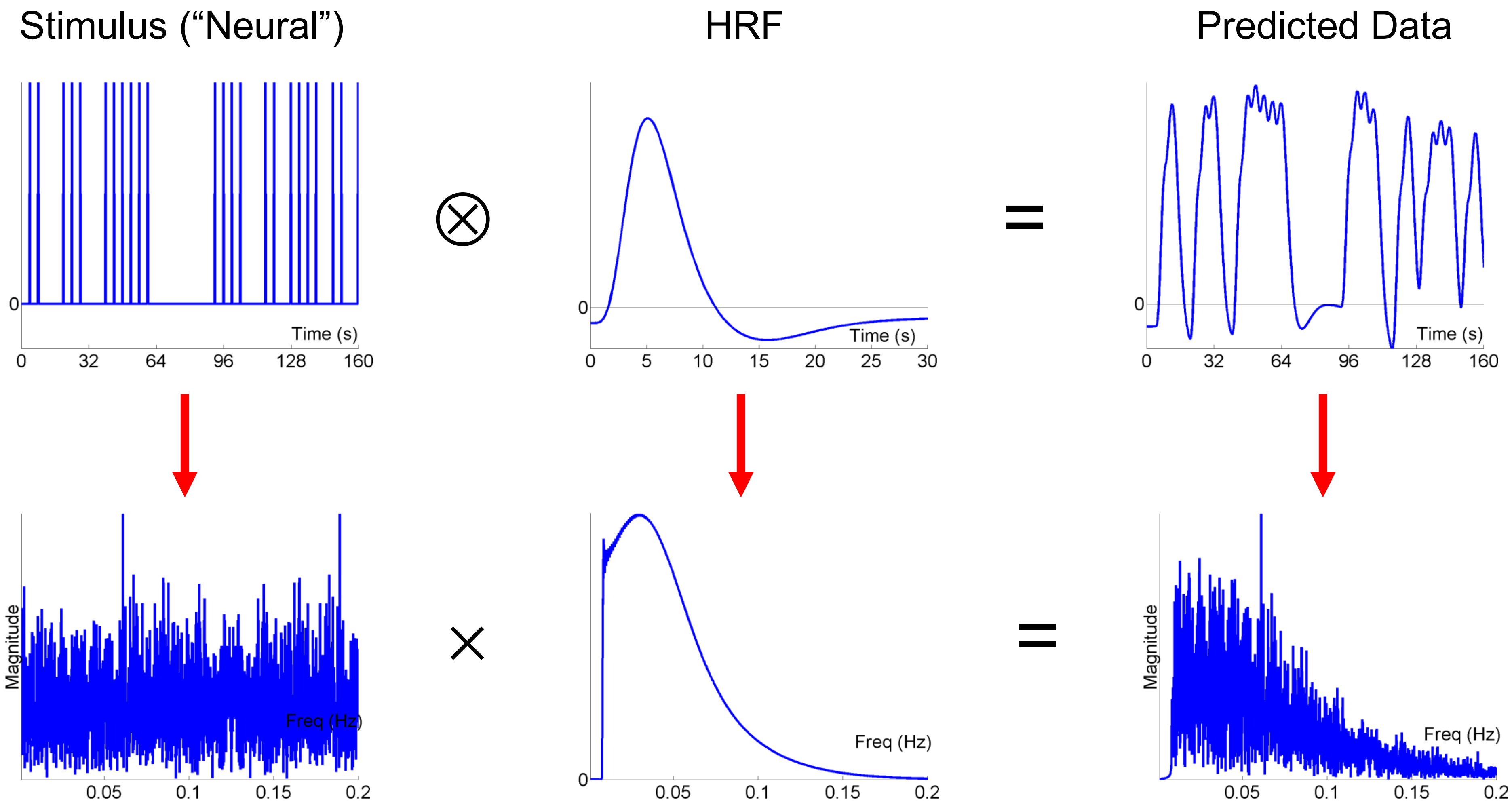
The most efficient design of all!

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



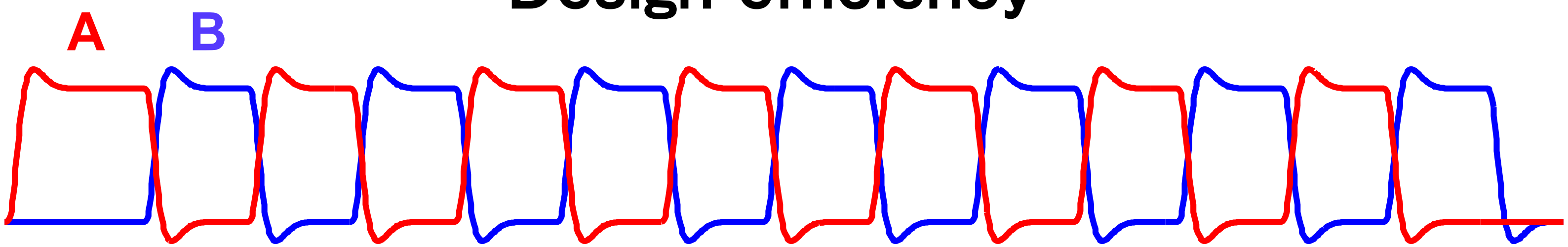
Don't use long (>60s) blocks!

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



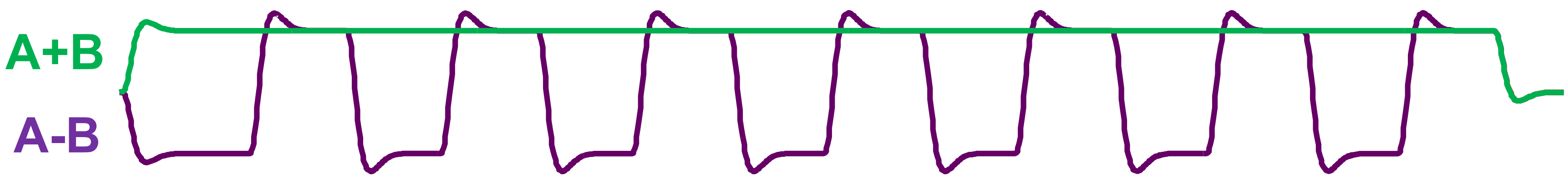
Randomised design spreads power over frequencies.

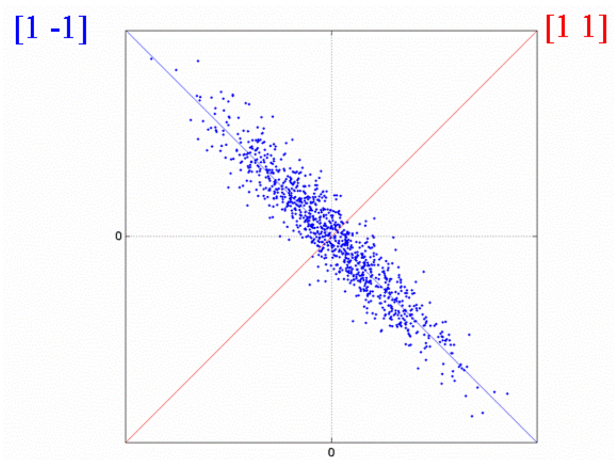
Design efficiency



$$X^T X = \begin{pmatrix} 1 & -0.9 \\ -0.9 & 1 \end{pmatrix}$$

$$c = [1\ 0]^T: \quad e(c, X) = 18.1$$
$$c = [0.5\ 0.5]^T: \quad e(c, X) = 19.0$$
$$c = [1\ -1]^T: \quad e(c, X) = 95.2$$





- ❑ **High correlation between regressors leads to low sensitivity to each regressor alone.**
- ❑ **We can still estimate efficiently the difference between them.**

Efficiency: Multiple event types

- Design parametrised by:

  SOA_{min} Minimum SOA

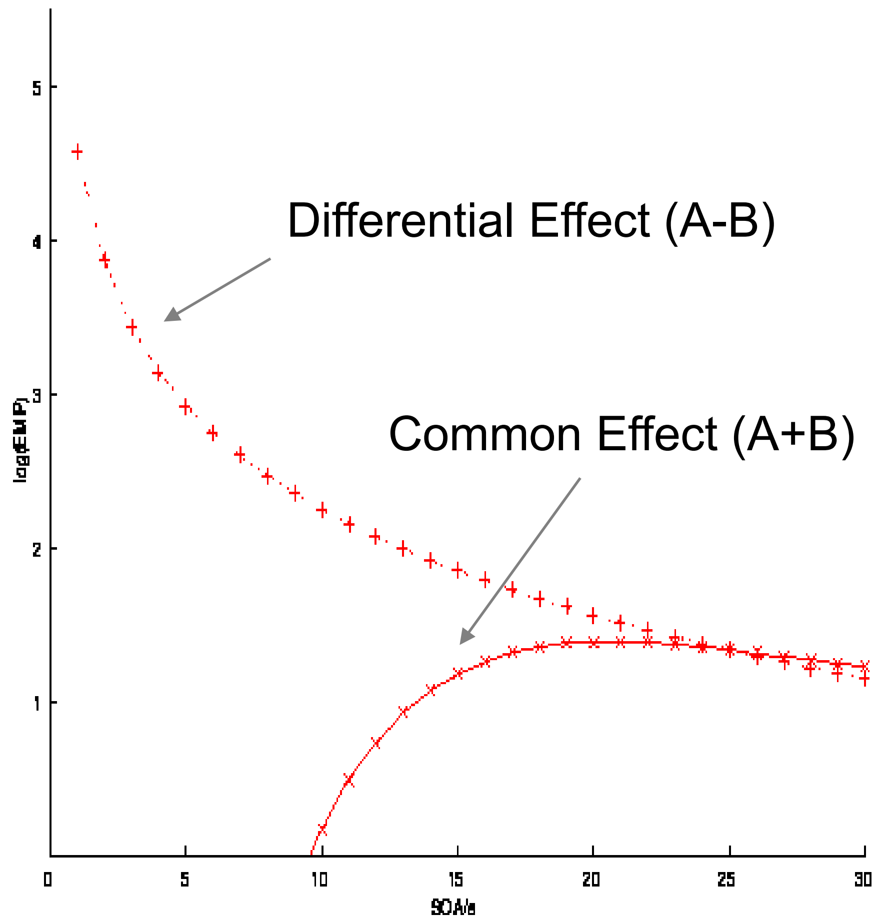
  $p_i(\boldsymbol{h})$ Probability of event-type i given history $\boldsymbol{h}$ of last m events

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

- Example: Randomised AB

	A	**B**
A	0.5	0.5
B	0.5	0.5

=> **ABBBABAABABAAA...**



4s smoothing; 1/60s highpass filtering

Efficiency: Multiple event types

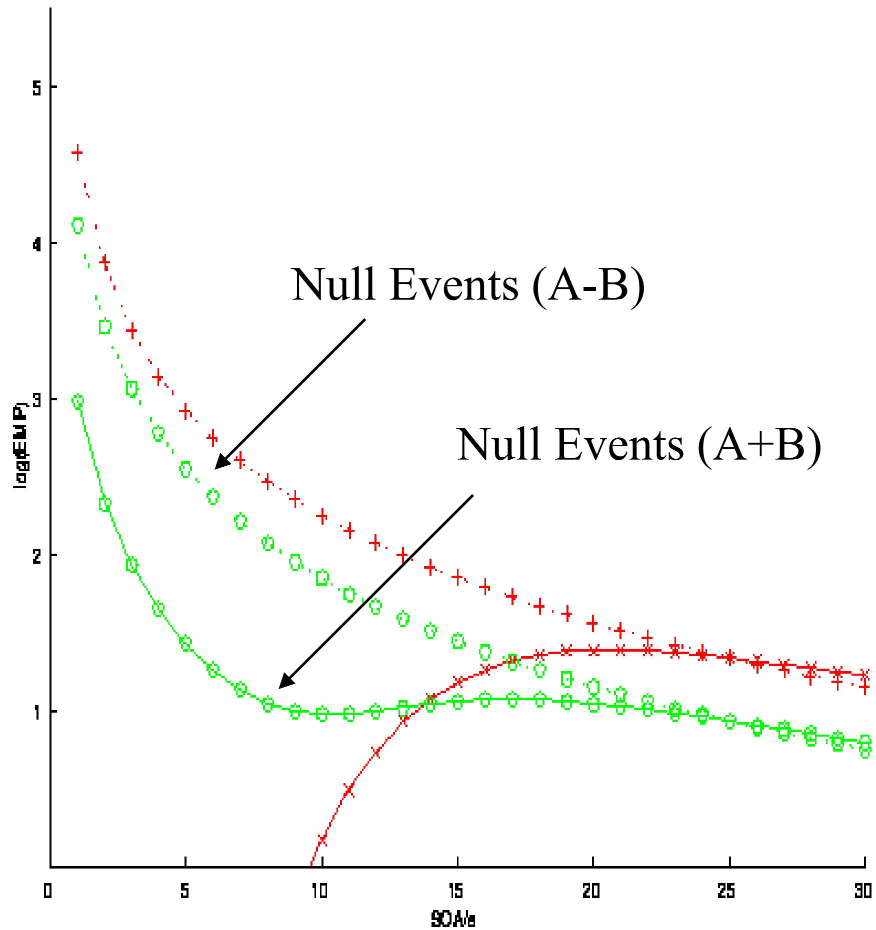
- Example: Null events

	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 corresponds to a third unmodelled event-type)



4s smoothing; 1/60s highpass filtering

Efficiency – main conclusions

- Optimal design for one contrast may not be optimal for another.

- Generally, blocked designs with short SOAs are the most efficient design.

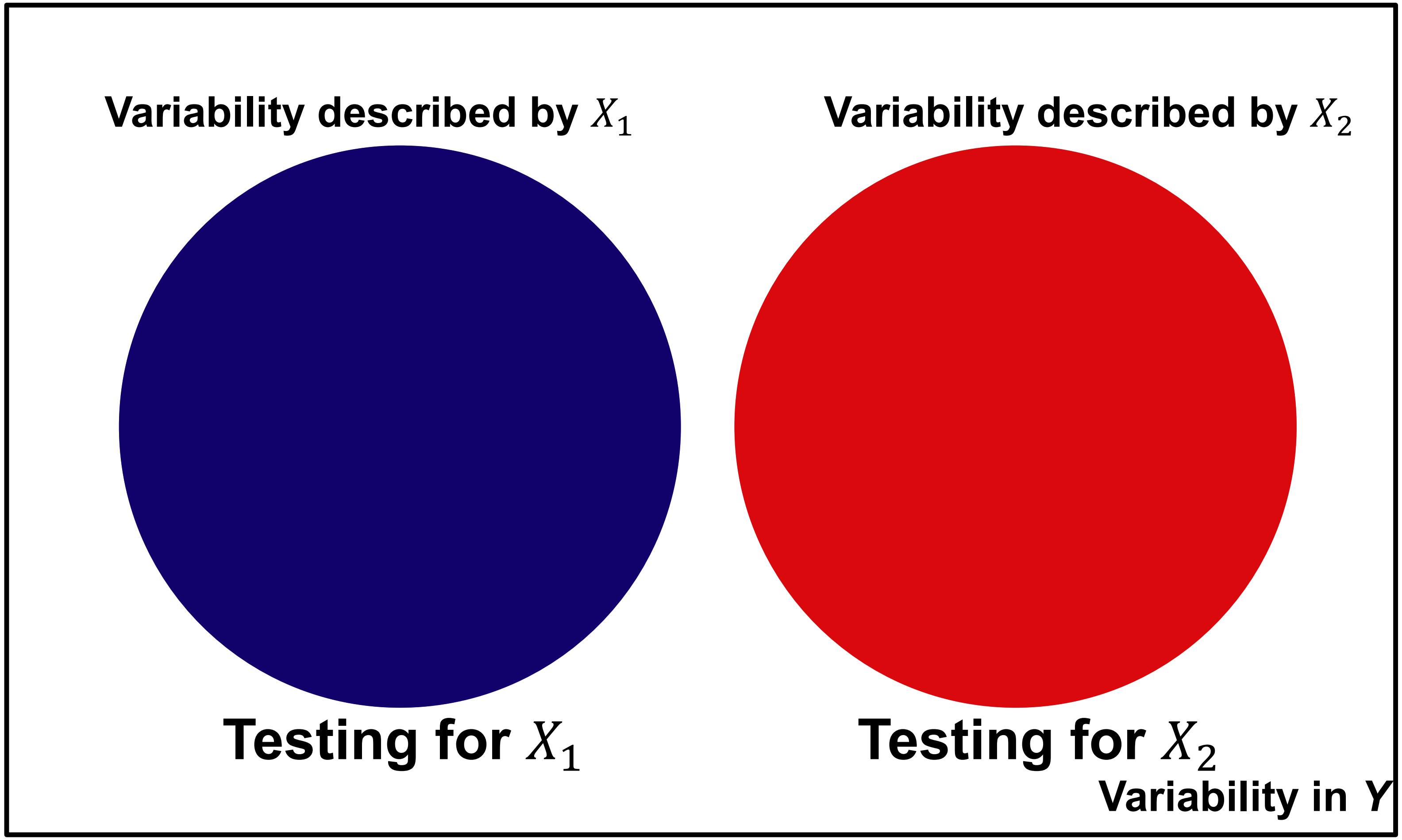
- With randomised designs, optimal SOA for differential effect (A-B) is minimal SOA (assuming no saturation), whereas optimal SOA for common effect (A+B) is 16-20s.

- Inclusion of null events gives good efficiency for both common and differential effects at short SOAs.

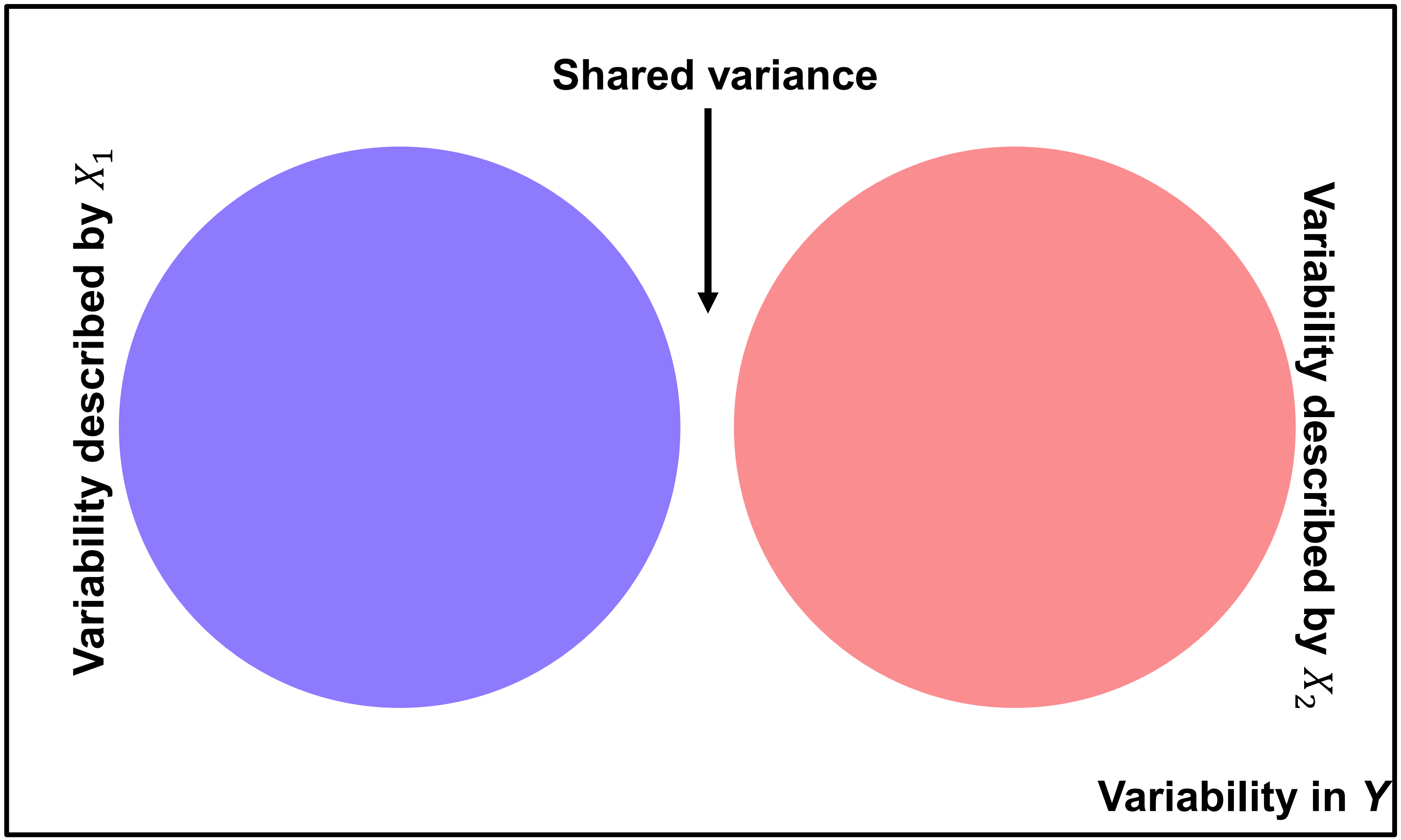
Appendix: Orthogonal regressors

What's (not) the problem if I use a design with correlated regressors?

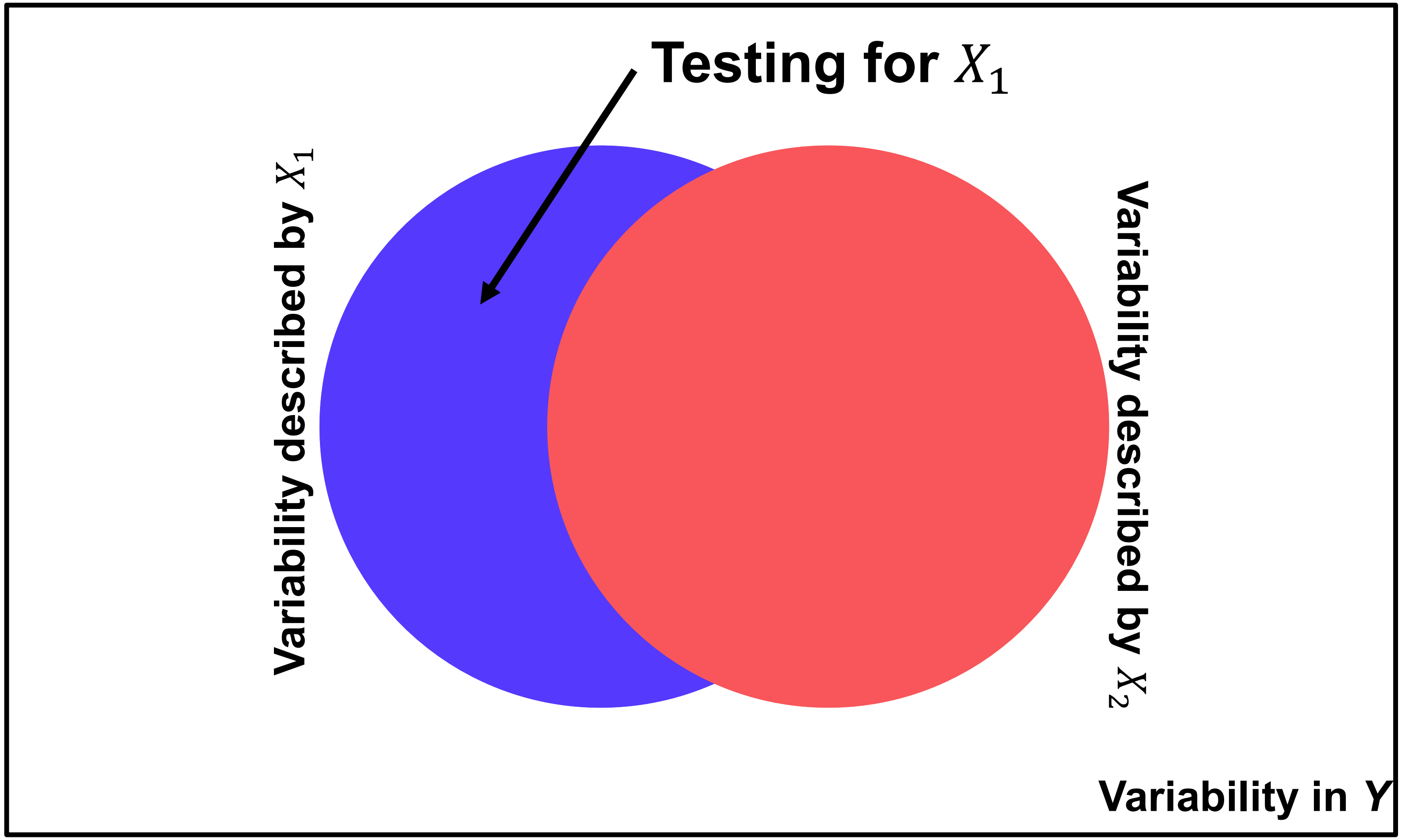
Orthogonal regressors



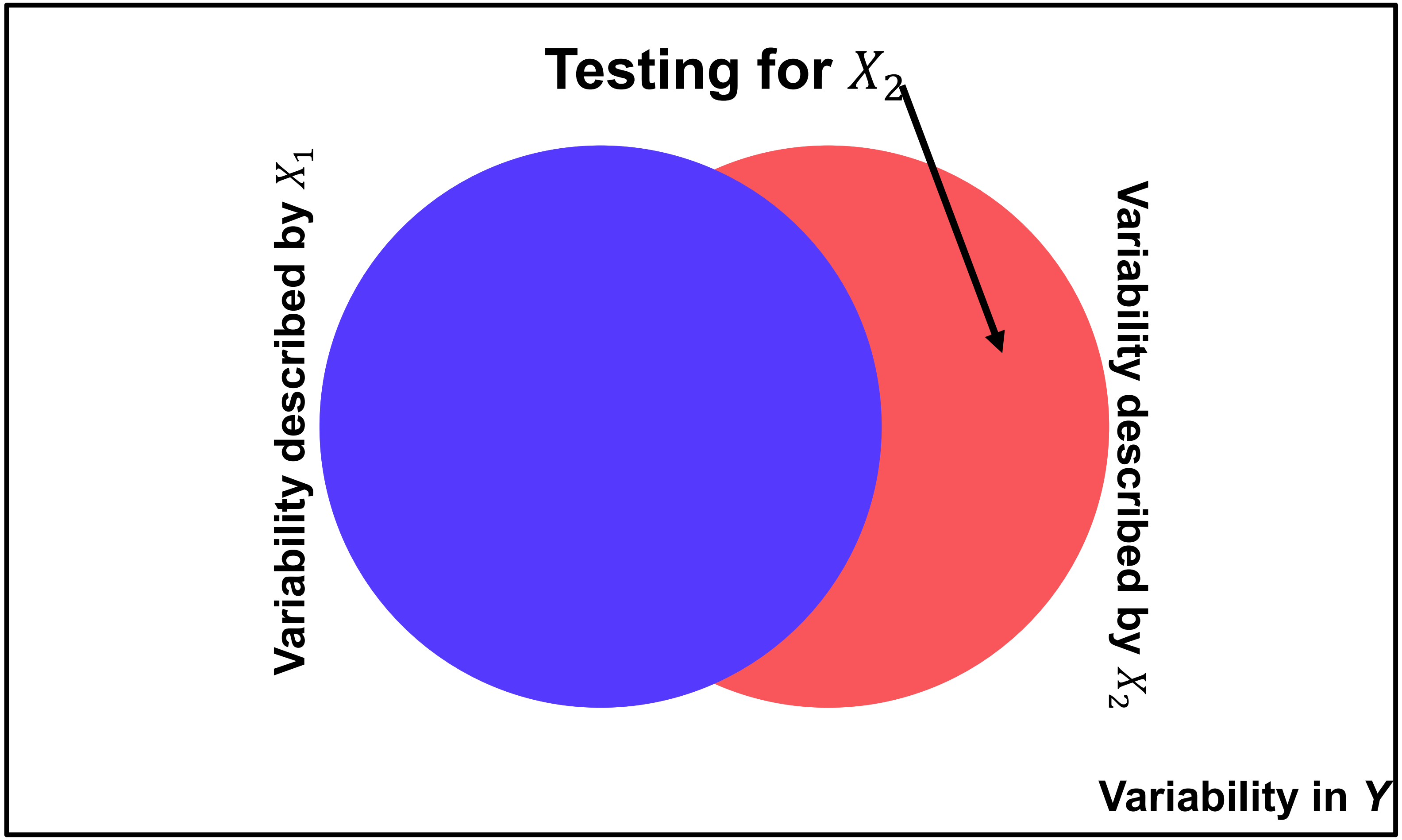
Correlated regressors



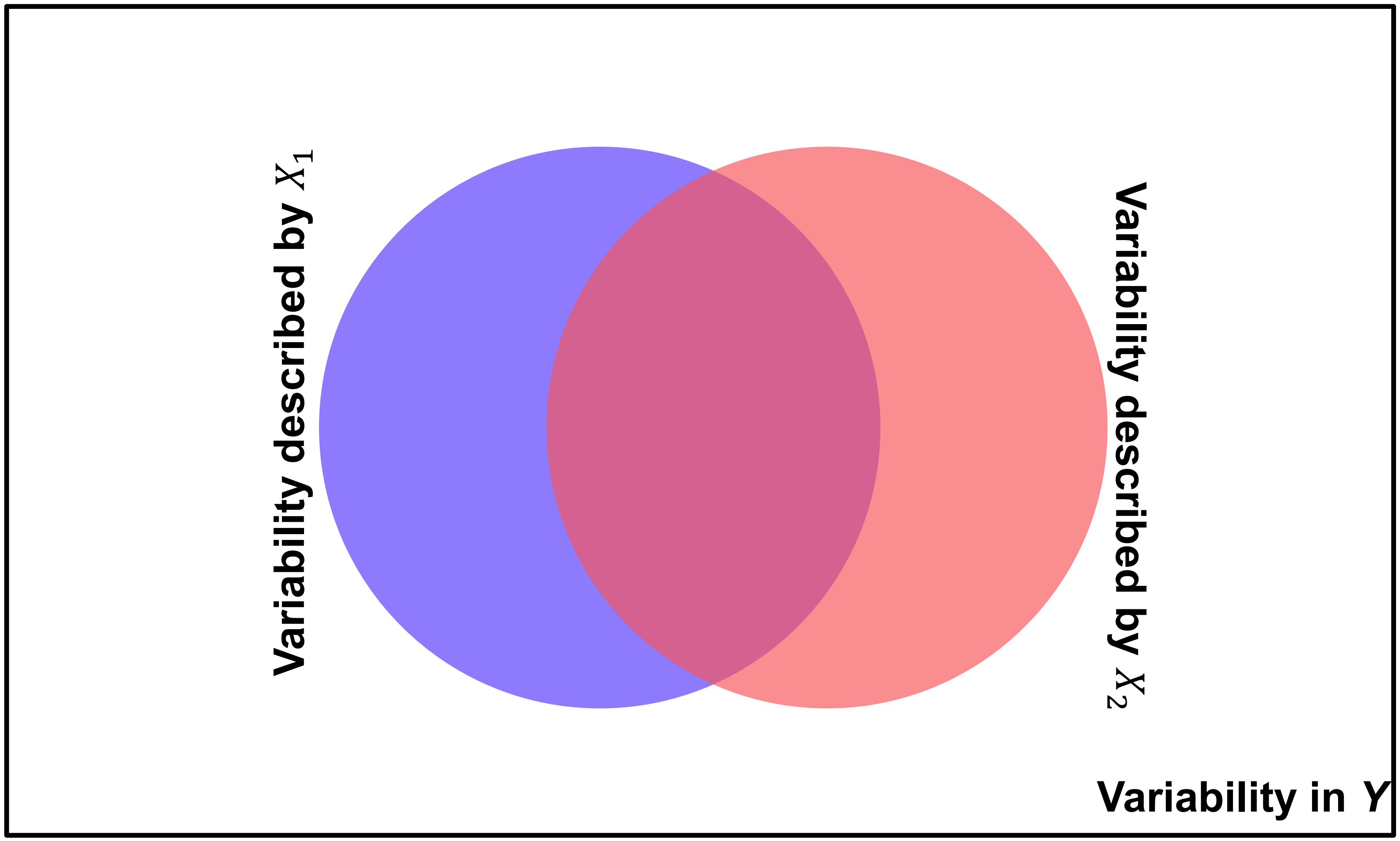
Correlated regressors



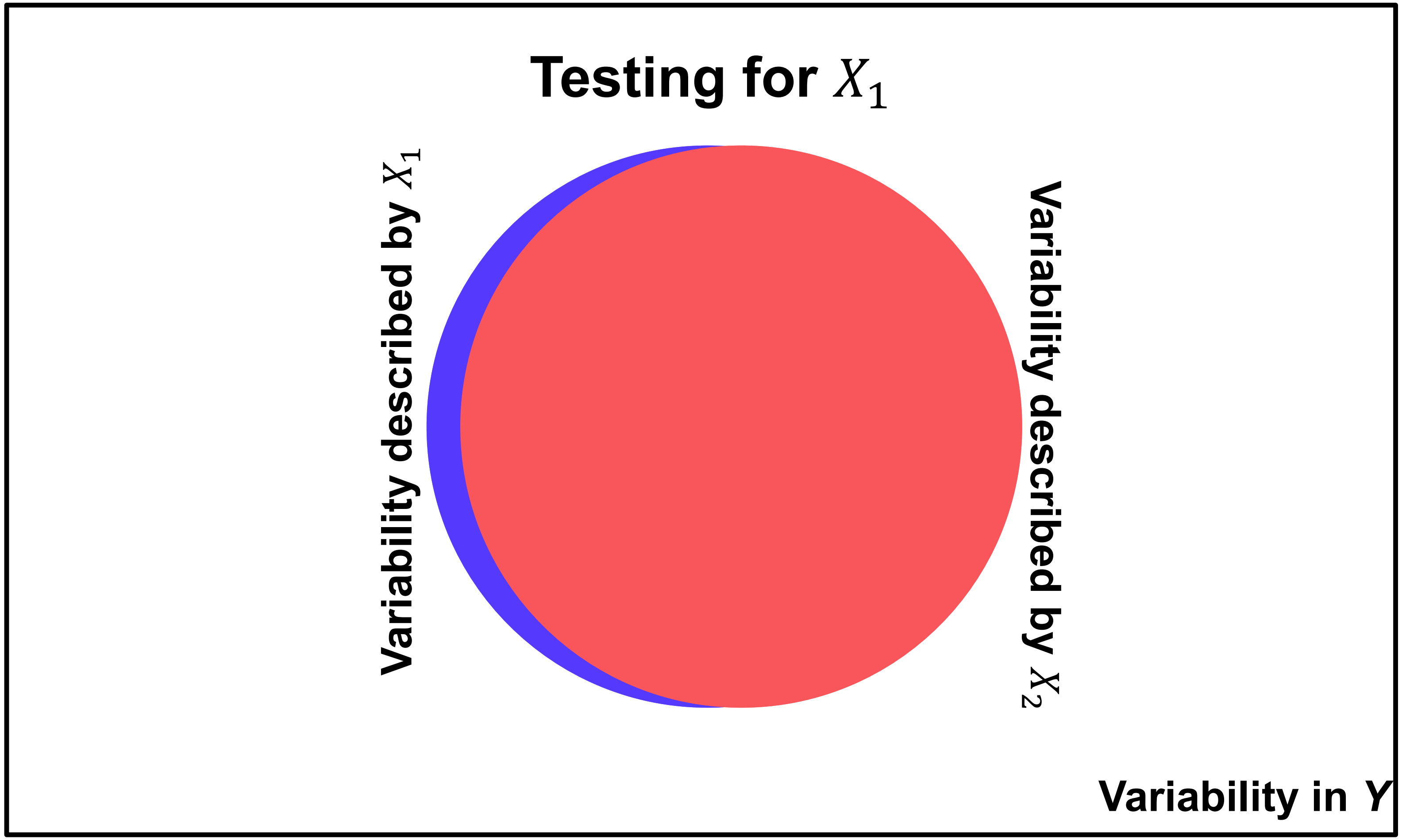
Correlated regressors



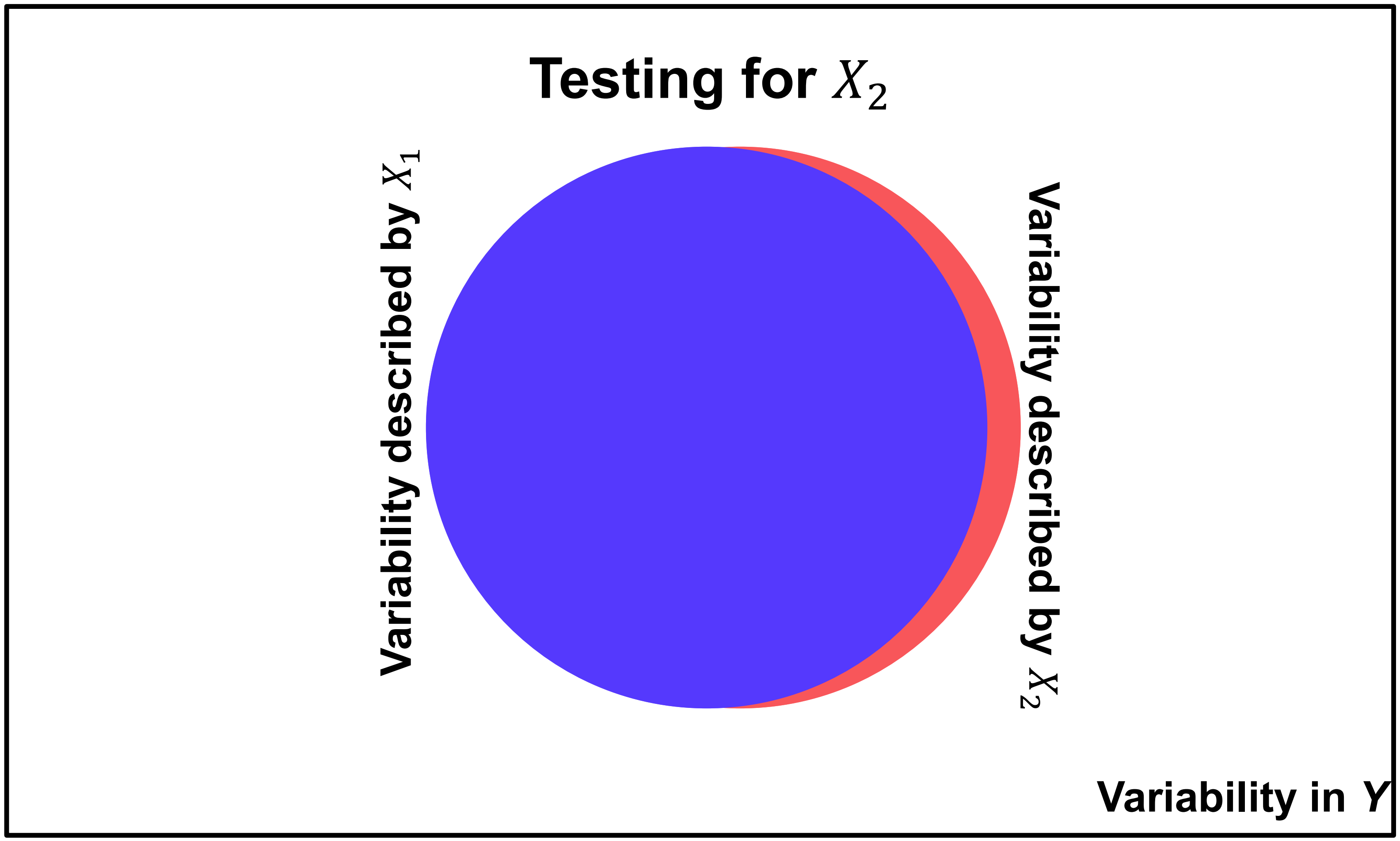
Correlated regressors



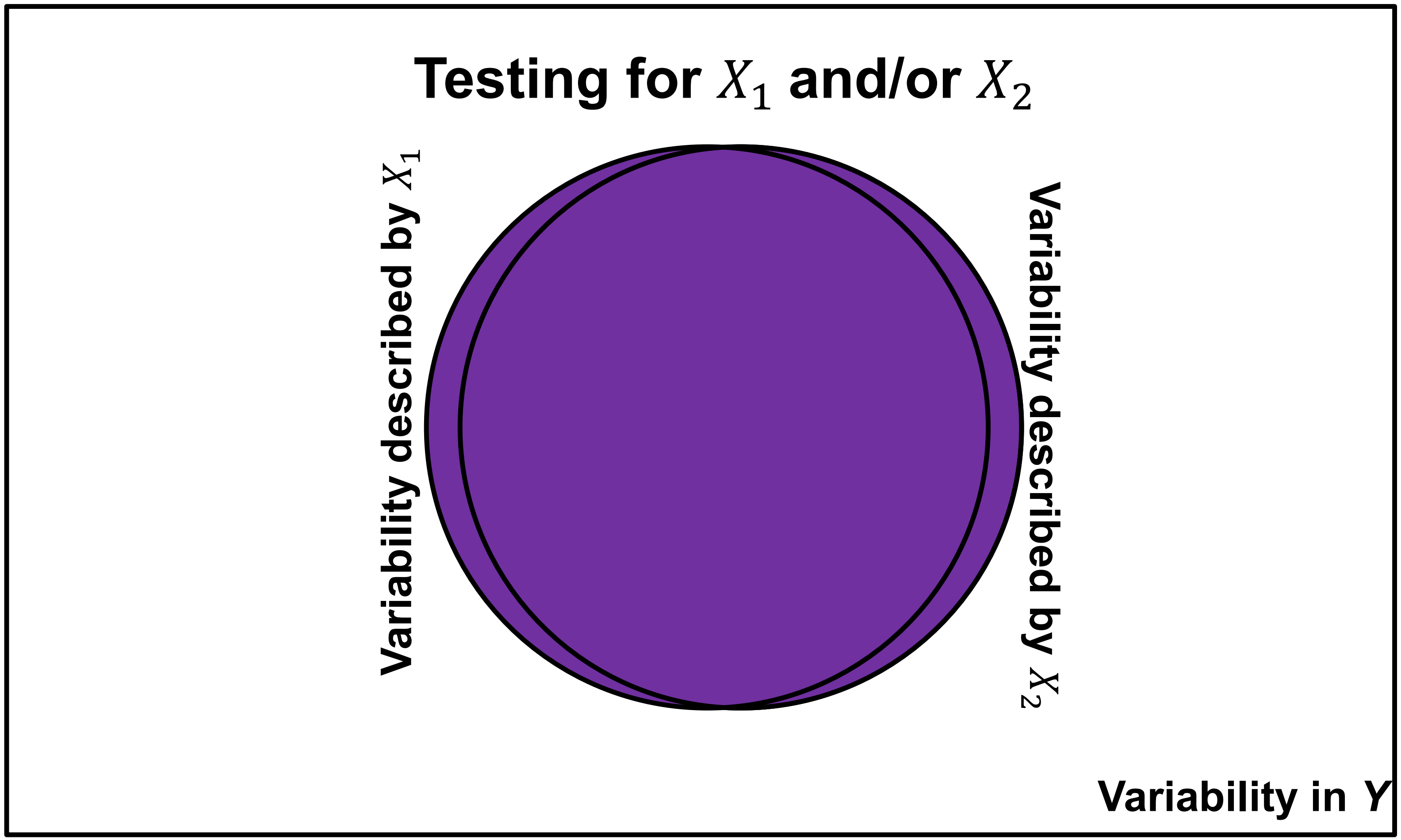
Correlated regressors



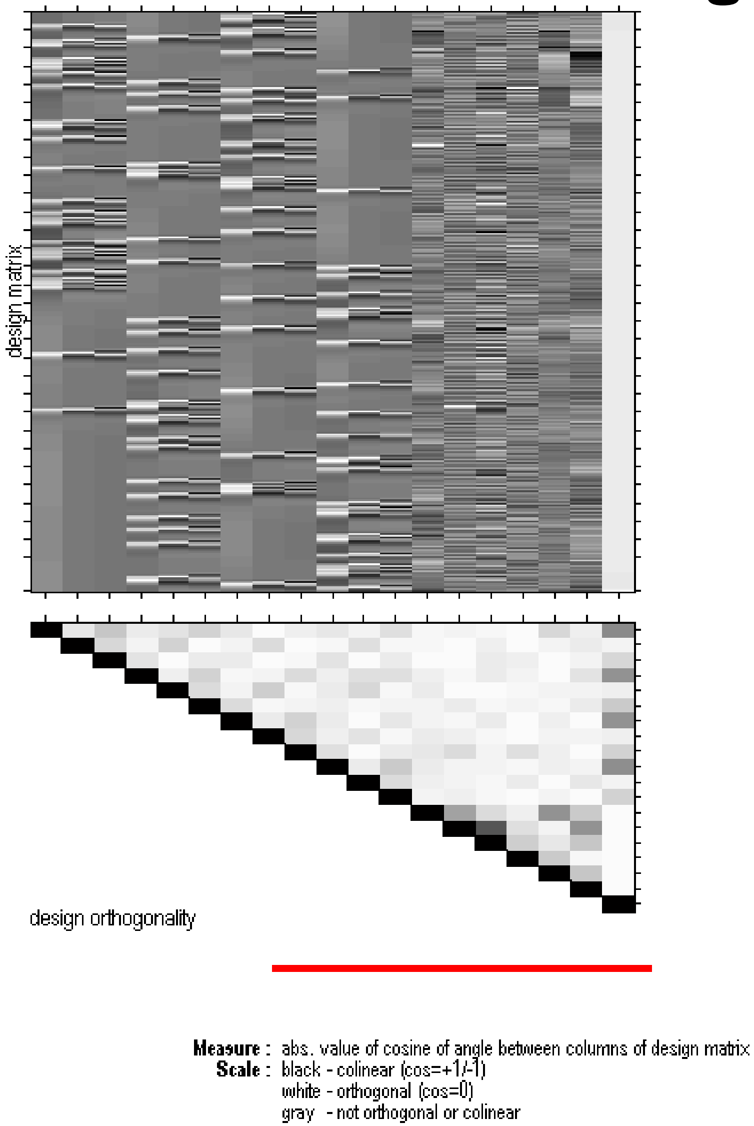
Correlated regressors



Correlated regressors



Design orthogonality

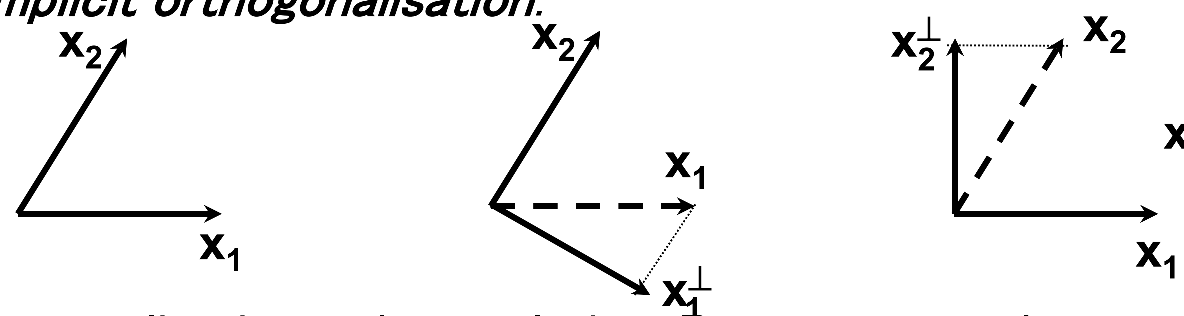


For each pair of columns of the design matrix, the orthogonality matrix depicts the magnitude of the **cosine of the angle** between them, with the range 0 to 1 mapped from white to black.

- **If both vectors have zero mean then the cosine of the angle between the vectors is the same as the correlation between the two variates.**

Correlated regressors: summary

- We implicitly test for an **additional** effect only. When testing for the first regressor, we are effectively removing the part of the signal that can be accounted for by the second regressor:
  ⇨ *implicit orthogonalisation.*



$$x_2^{\perp} = x_2 - x_1.x_2\ x_1$$

- Orthogonalisation = decorrelation. Parameters and test on the non modified regressor change.
  Rarely solves the problem as it requires assumptions about which regressor to uniquely attribute the common variance.
  ⇨ change regressors (i.e. design) instead, e.g. factorial designs.
  ⇨ use F-tests to assess overall significance.
- Original regressors may not matter: it's the contrast you are testing which should be as decorrelated as possible from the rest of the design matrix

Thank you