Event-Related fMRI Experimental Design

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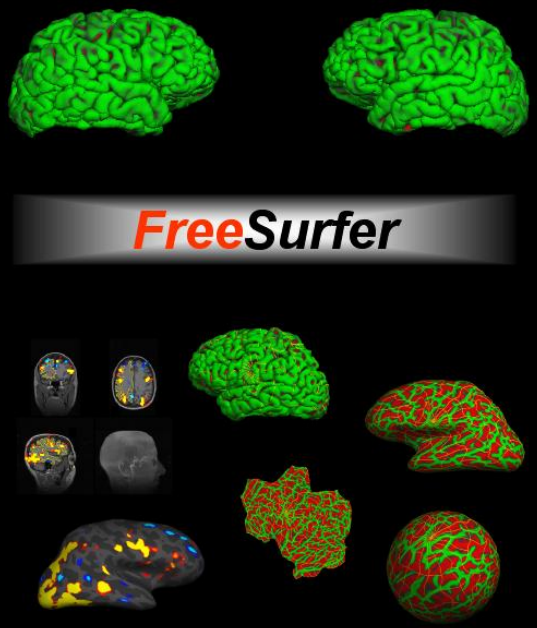
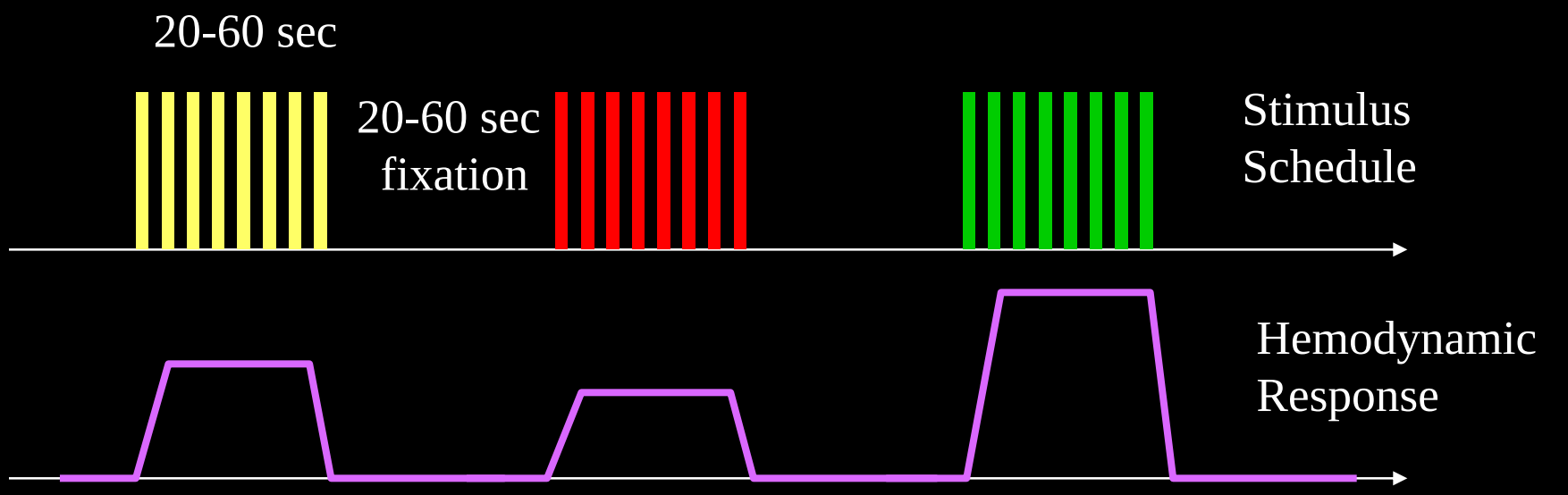


Overview

- Stimulus schedule
  - which stimulus is presented when and for how long
- Blocked design
- Event-related designs
  - Motivation
  - Types
  - Analysis
  - Efficiency
- Optseq

http://surfer.nmr.mgh.harvard.edu/optseq/

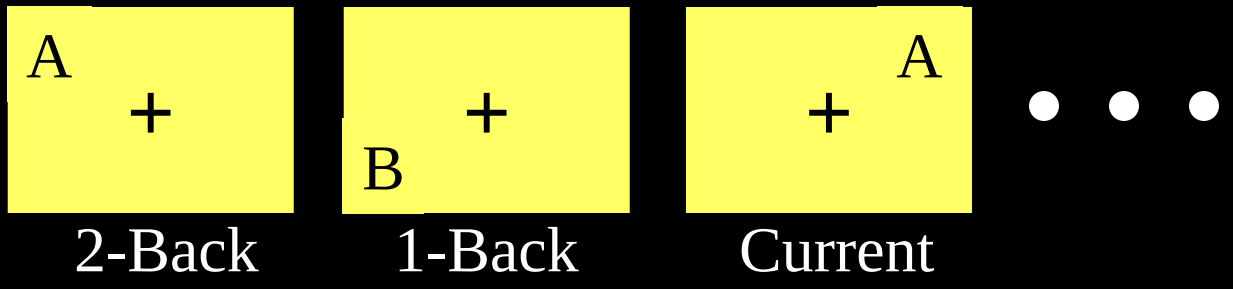
Blocked Design



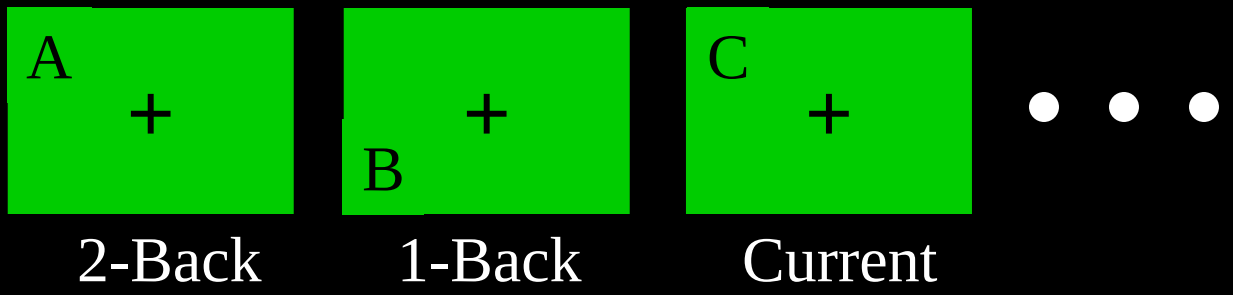
- Sequence of the same event type
- Usually presented periodically
- Measure Set, Strategy, State or as a Localizer
- Individual stimulus not important

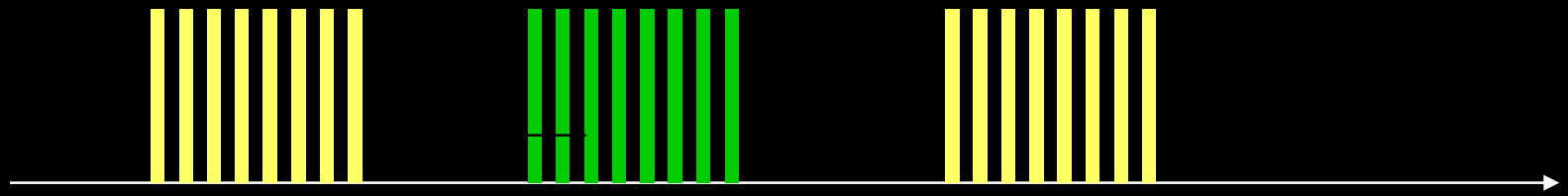
Blocked Design – Attention Task

Match-to-Letter
2-Back



Match-to-Position
2-Back

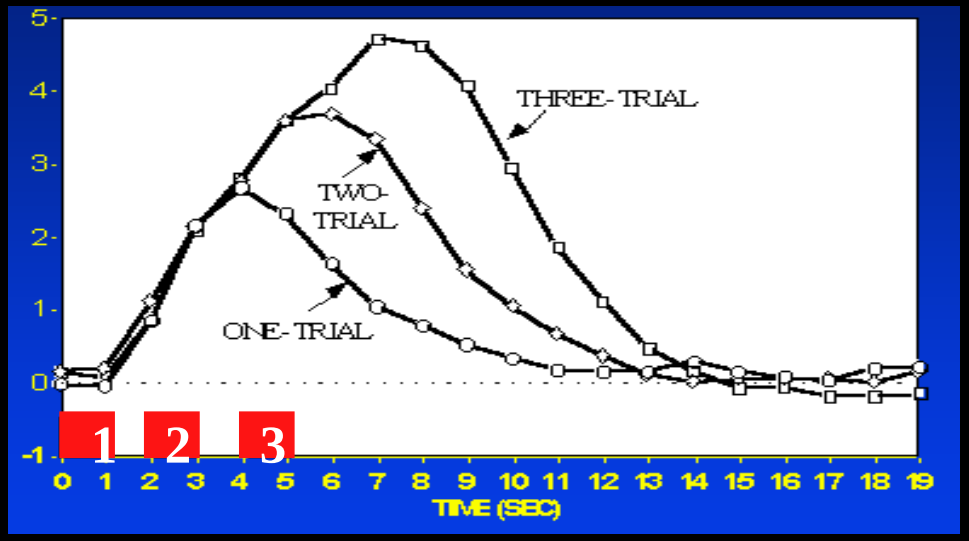




- Probe Attention to Letter vs Spatial Position
- Don’t really care about individual stimuli

Blocked Design – Localizer

- Find areas in the brain that respond to Faces vs Buildings
- Use as ROI for some other analyses
- Efficiency (no adaptation)
- Use overlap to build a larger signal (better SNR)



Event-related Design

- Care about response to individual event type
- Random order of events
- Often random timing of events

Motivation

- Avoid Set, Strategy, State, Adaptation
- More natural than blocked
- Want information about the shape (dynamics)

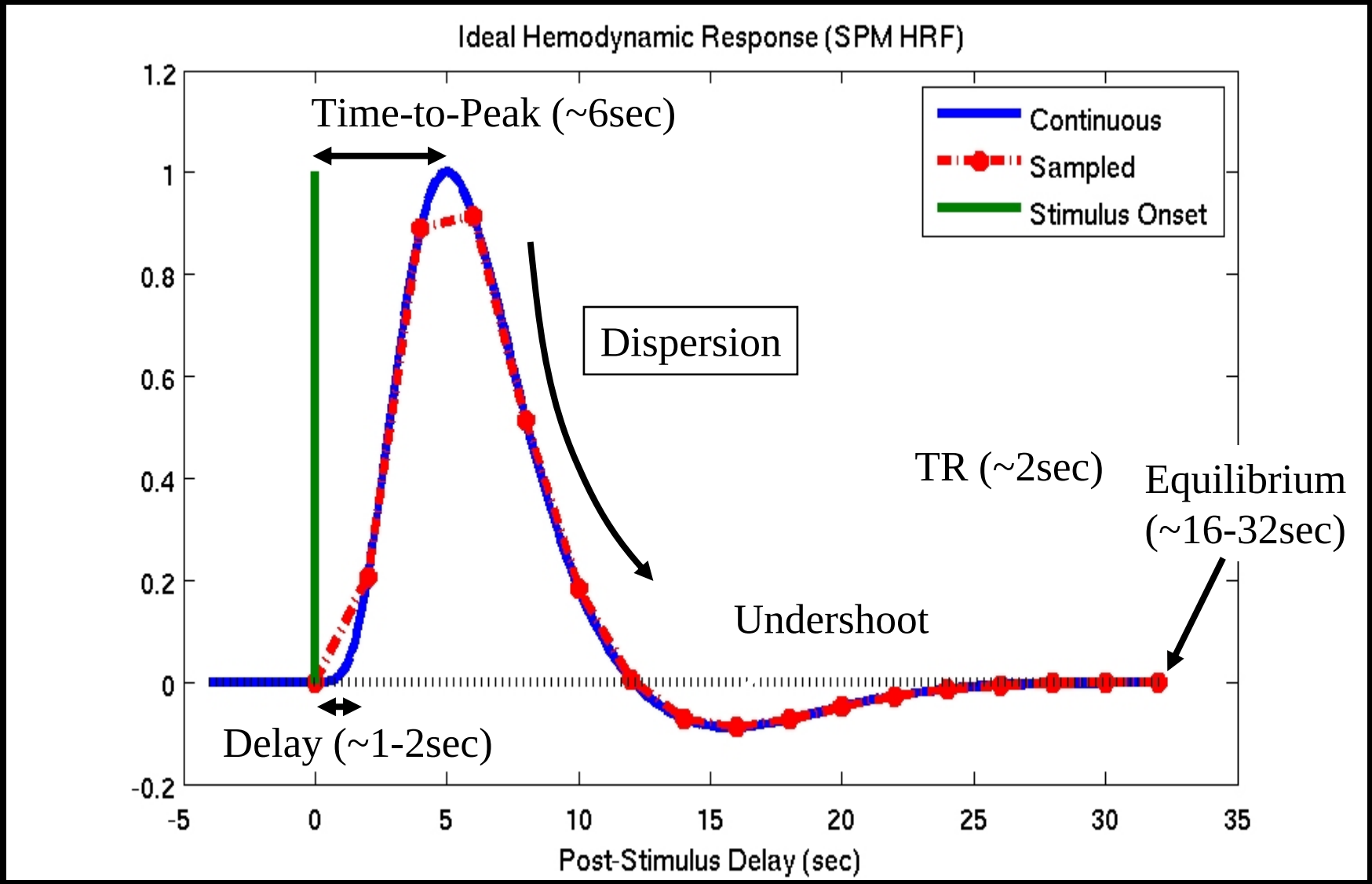
Dealing with overlap in responses

- Fixed Interval (no overlap)
- Randomized (overlap)
- Efficiency

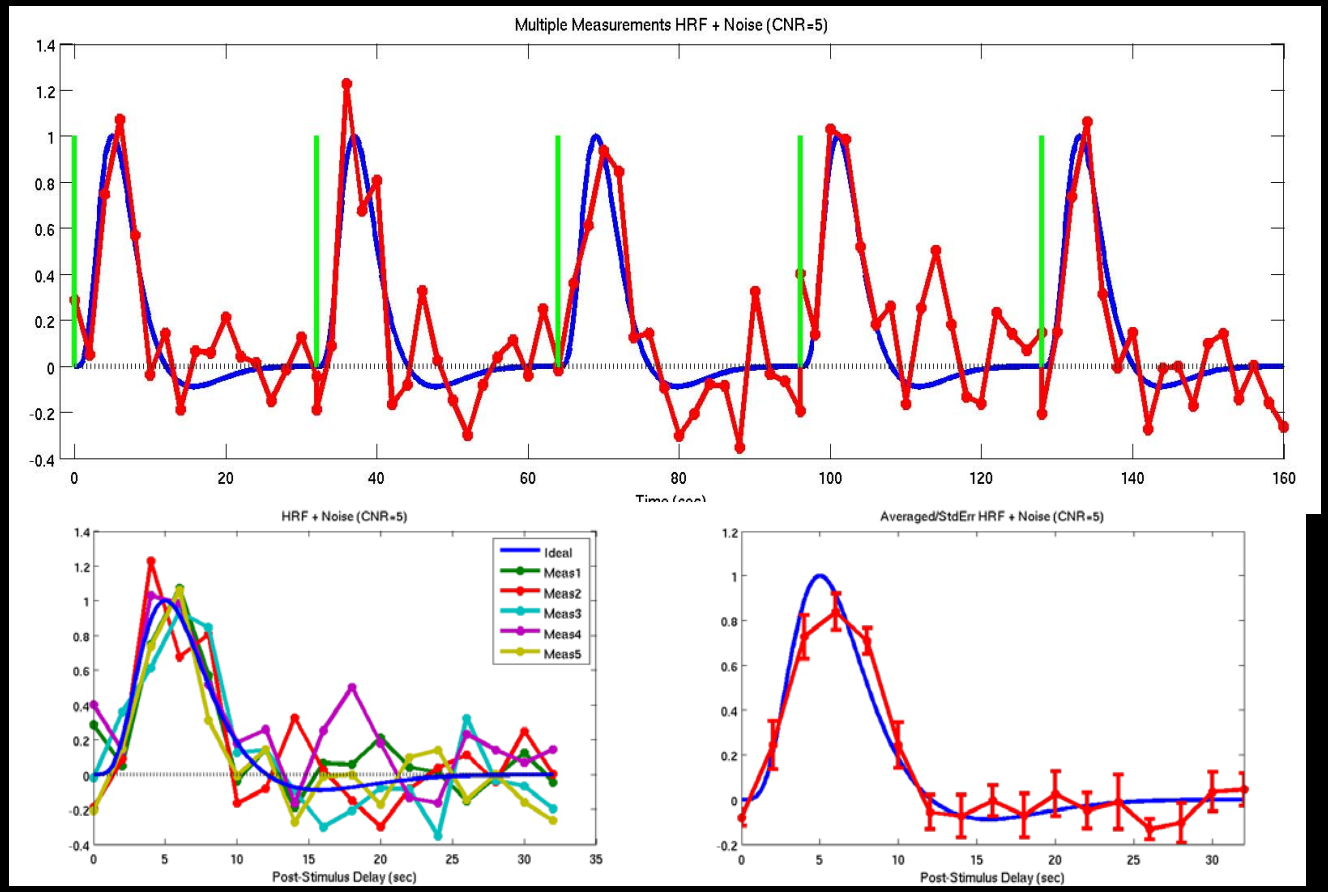
Motivation: Psychology

- Words vs Non-words
- Press key 1 for words
- Press key 2 for non-words
- cannot have a block of words, then a block of non-words

Motivation: Shape Estimation

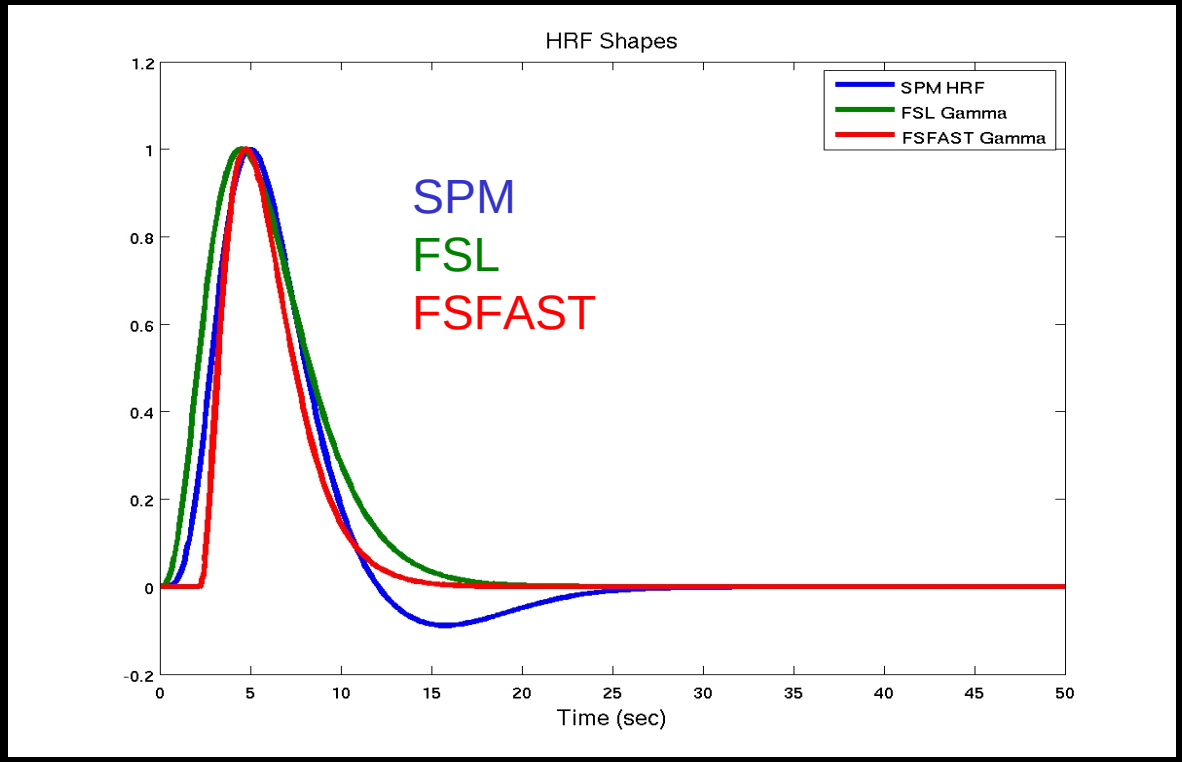


Estimating Shape (FIR)



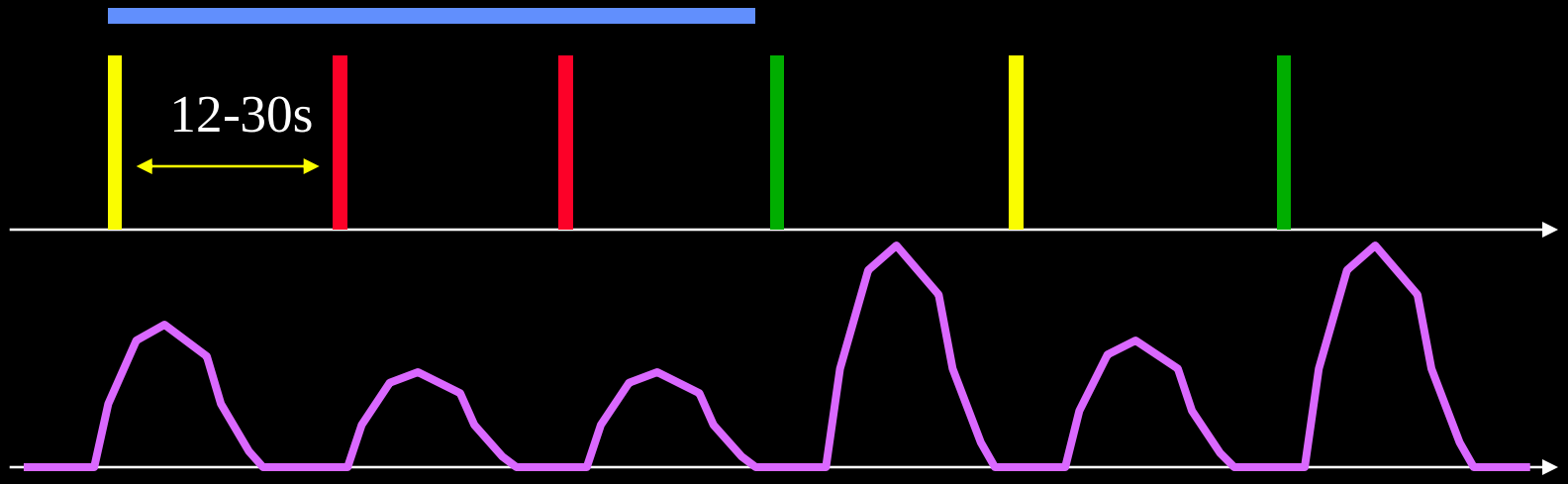
- FIR = Finite [Time] Impulse Response
- Within General Linear Model (GLM)
- Less efficient than blocked (usually)
- Non-linear (estimate delay and dispersion)
- Schedule is extremely important

Alternative: Assume an HRF Shape



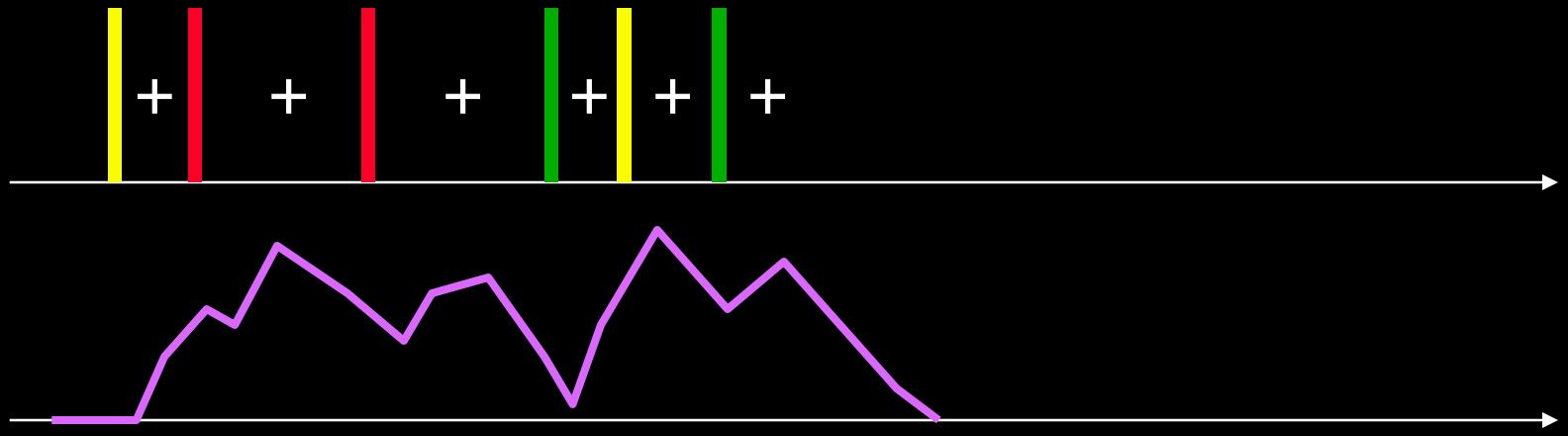
- Assume a shape in analysis (most common)
- Fit amplitude
- Usually more powerful than not assuming a shape
- Used in most analyses of blocked design

Fixed-Interval Event-Related



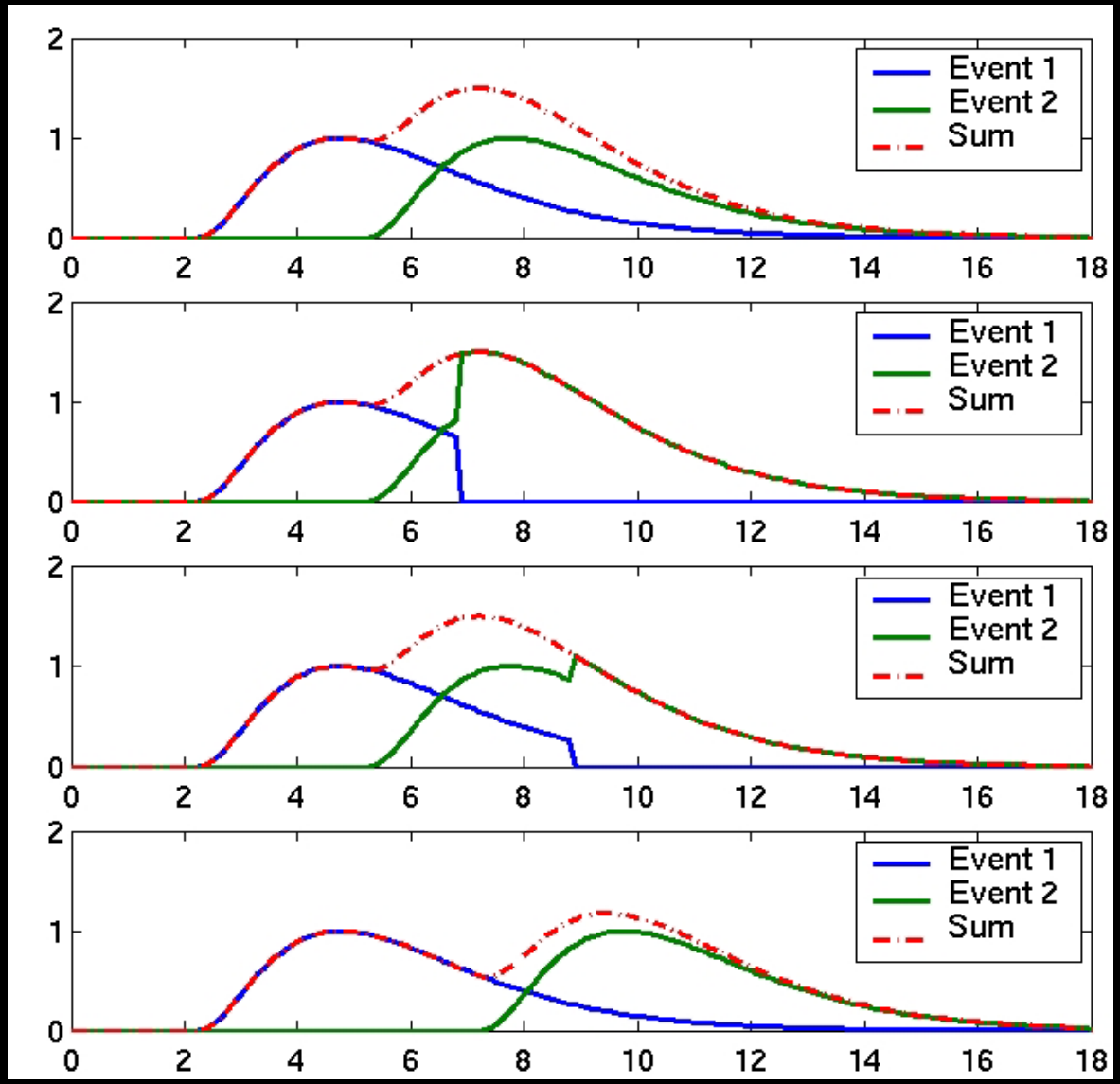
- Push trials apart enough to prevent overlap.
- Interval fixed at minimum is most efficient.
- Random Sequence (Counter-balanced)
- Expectation?
- Inflexible/Inefficient/Boring
- Can shorten interval if assuming an HRF

Rapid-Presentation Event-Related

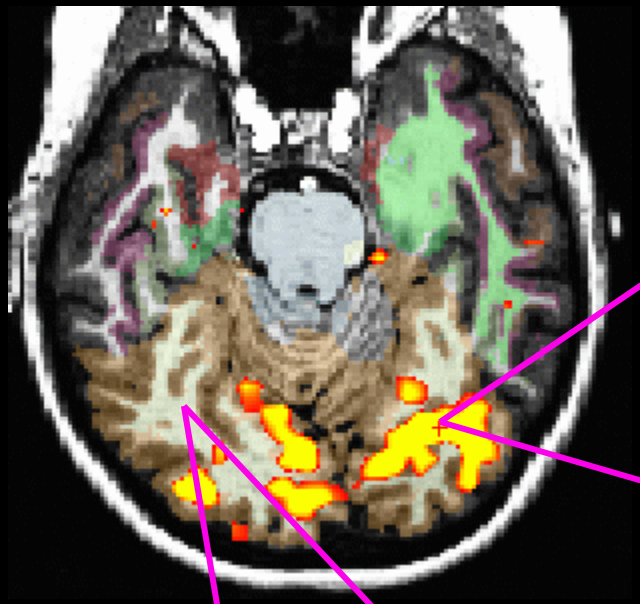


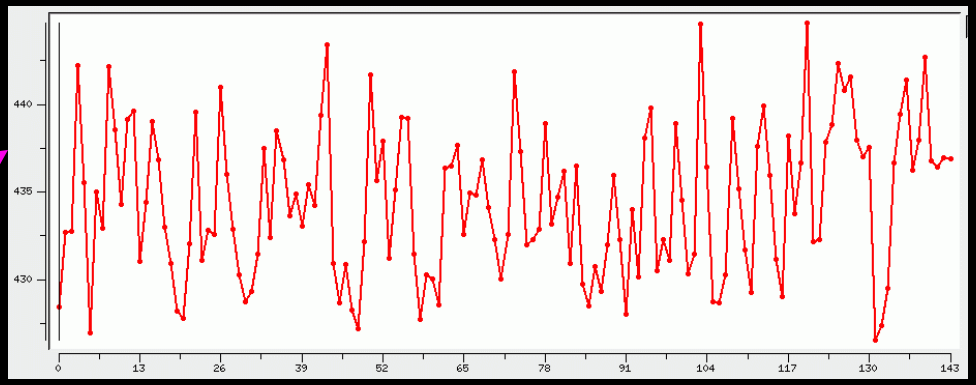
- Closely Spaced Task Trials (Overlap!)
- Raw signal uninterpretable
- More Stimulus Presentations for given scanning interval
- Random Sequence
- Jitter = “Random” Inter-Stimulus Interval (ISI/SOA)
- Linearity Assumption
- Do not need to assume a shape (but can)

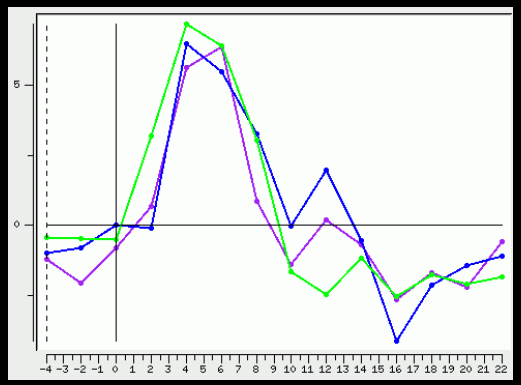
Deconvolving with Jitter



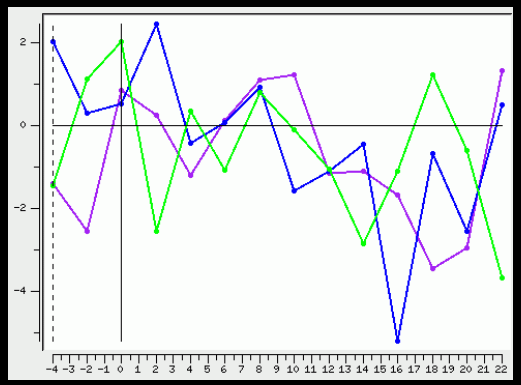
Example hemodynamic response

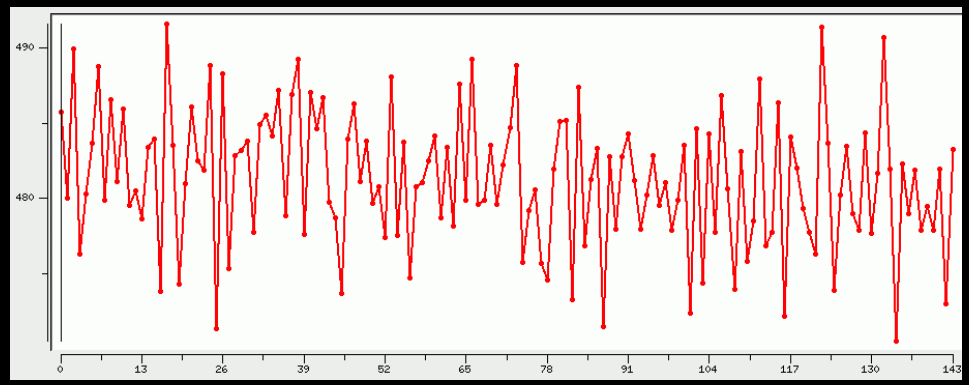






They don’t all look this good!

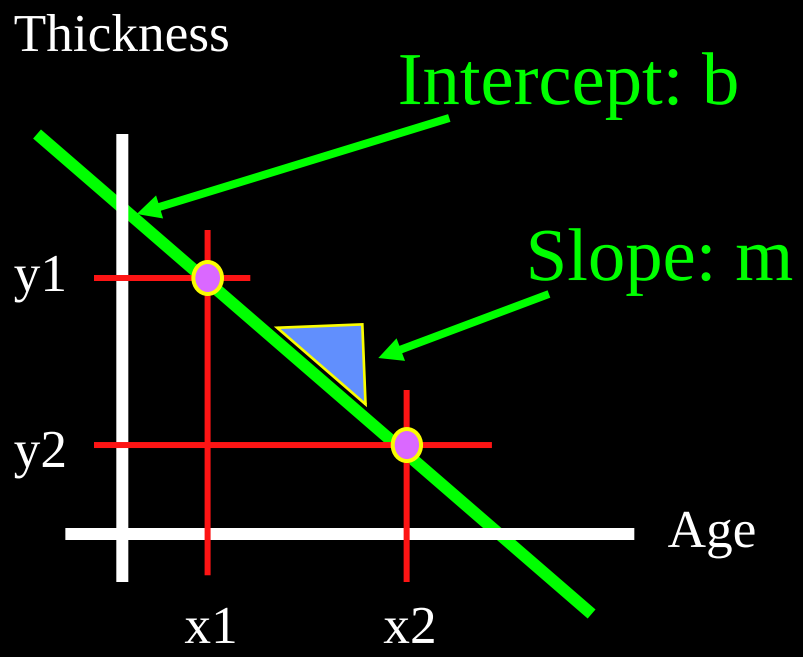




Scheduling Random Designs

- Choose:
  - Stimulus order
  - Stimulus onset time
- Enormous flexibility
- How to choose?
- Efficiency
  - Linear model
  - Minimize parameter variance

Linear Model



System of Linear Equations

$y1 = b + x1*m$

$y2 = b + x2*m$

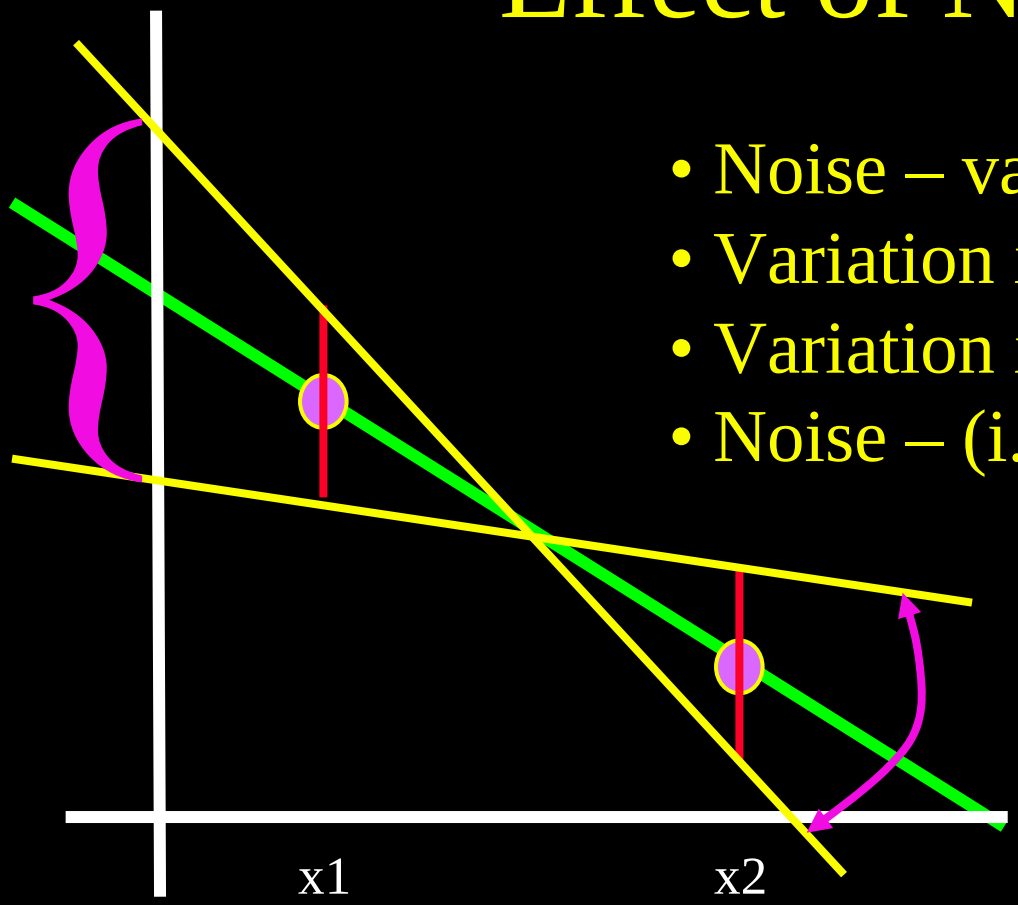
Independent Variable (x)

-- you get to choose

-- how?

Intercept = Offset

Effect of Noise

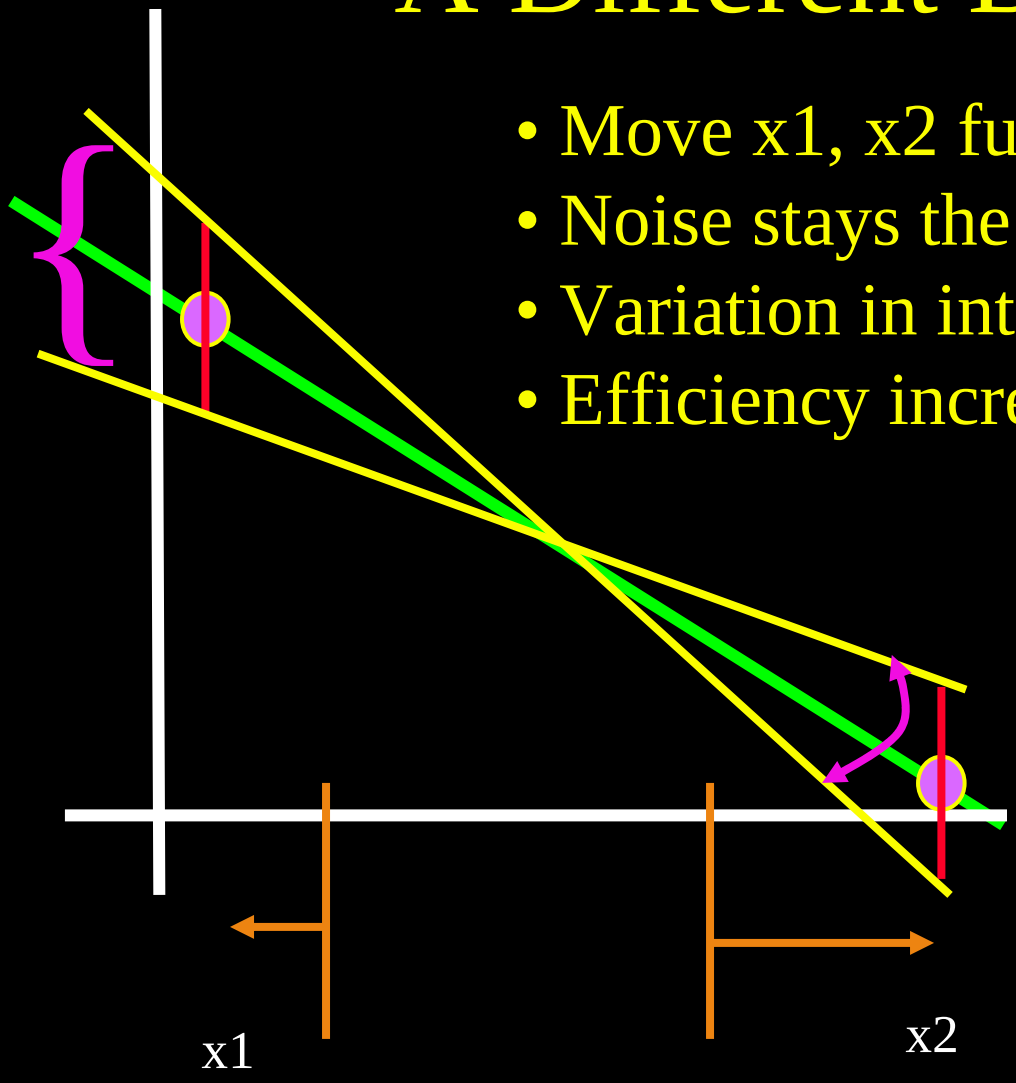


- Noise – variance (σ_n)
- Variation in intercept (σ_b)
- Variation in slope (σ_m)
- Noise – (i.i.d) same for all X

$$\sigma_b^2 = \sigma_n^2 / \xi_b$$

ξ_b is efficiency for b

A Different Design



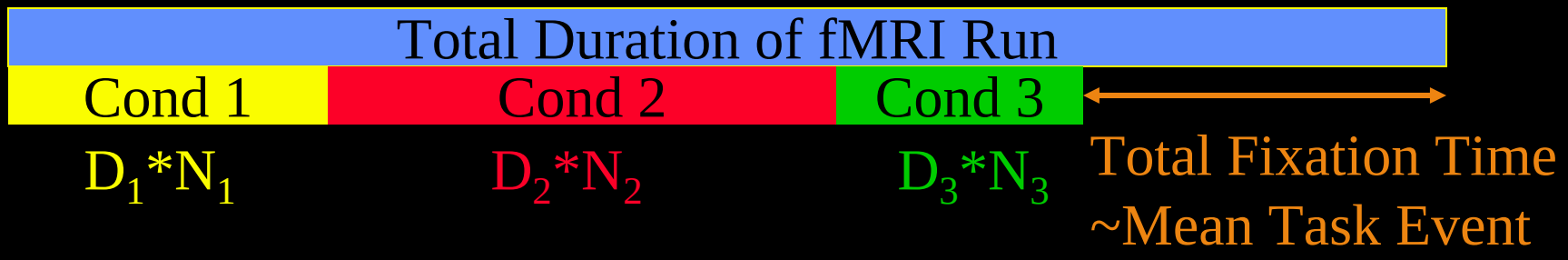
- Move x1, x2 further apart
- Noise stays the same (i.i.d)
- Variation in intercept and slope drops.
- Efficiency increases

Can compute efficiency from x before doing experiment. Choose x to maximize efficiency.

For an event-related design, x = stimulus onset times (design matrix X)

Optseq (optseq2)

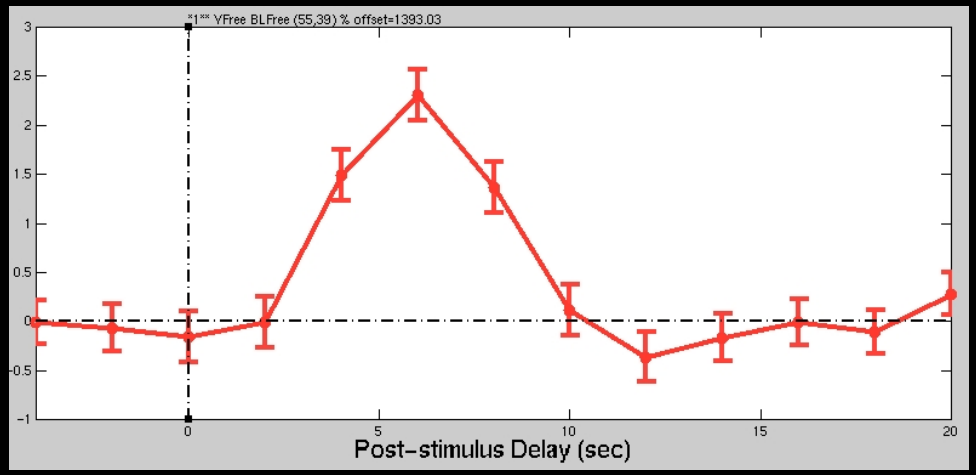
- Software to aid in the design of event-related experiments
- Chooses stimulus onset times given:
  - TR, Ntp
  - Duration and # of Repetitions of each Event Type



1. Randomly orders events
2. Chops fixation time into random bits
3. Inserts fixation between events (may be 0)
4. Builds FIR design matrix (X)
5. Computes efficiency, compares to max, keeps if greater
6. Return to step 1, repeat Nsearch times

Sample optseq2 command

```
optseq2
  --ntp 60
  --tr 2
  --psdwin -4 20
  --ev EnglishWord    2 12
  --ev EnglishNonWord 2 12
  --ev SpanishWord    2 12
  --ev SpanishNonWord 2 12
  --nsearch 10000
  --o bilingual
```



- 60 time points, TR=2, run time = 60*2=120 sec
- FIR Post-stimulus Delay Window (psdwin) -4 to +20 sec
- 4 event types, each 2 sec long, each presented 12 times (24 sec)
- 4*2*12 = 96 sec of Task; 120-96= 24 sec Fixation
- Search over 10000 iterations
- Save output in a file called “bilingual”

optseq2 output

Onset Time	Code	Duration	Weight	Name
0.0000	3	2.000	1.0000	SpanishWord
2.0000	0	2.000	1.0000	NULL
4.0000	2	2.000	1.0000	EnglishNonWord
6.0000	0	2.000	1.0000	NULL
8.0000	1	2.000	1.0000	EnglishWord
10.0000	0	2.000	1.0000	NULL
12.0000	4	2.000	1.0000	SpanishNonWord
14.0000	0	4.000	1.0000	NULL
18.0000	2	2.000	1.0000	EnglishNonWord
20.0000	0	2.000	1.0000	NULL
…				

Code: depends on order in the command line

Weight: usually 1.0.

Summary

- Random sequence of events
- Often random timing of events
- Psychology – avoid set, adaptation
- Measure shape of HRF
- Fixed interval (no overlap)
- Jittered (overlap), linearity, deconvolve
- Choose schedule based on efficiency
- optseq
  - Part of FreeSurfer
  - Docs and tutorial at

    http://surfer.nmr.mgh.harvard.edu/optseq

Mathematical Concepts

$$y = X\beta + n$$

Forward Model
(X = design matrix)

$$\hat{\beta} = (X^T X)^{-1} X y$$

Inverse Model

$$e = y - \hat{y} = y - X\hat{\beta}$$

Residual Error

$$\gamma = C\hat{\beta}$$

Contrast, Contrast Vector (or Matrix), Contrast Effect Size, COPE (FSL)

$$t_{DOF} = \frac{\gamma}{\sqrt{\sigma_e^2 (C(X^T X)^{-1} C^T)}}$$

t-Ratio

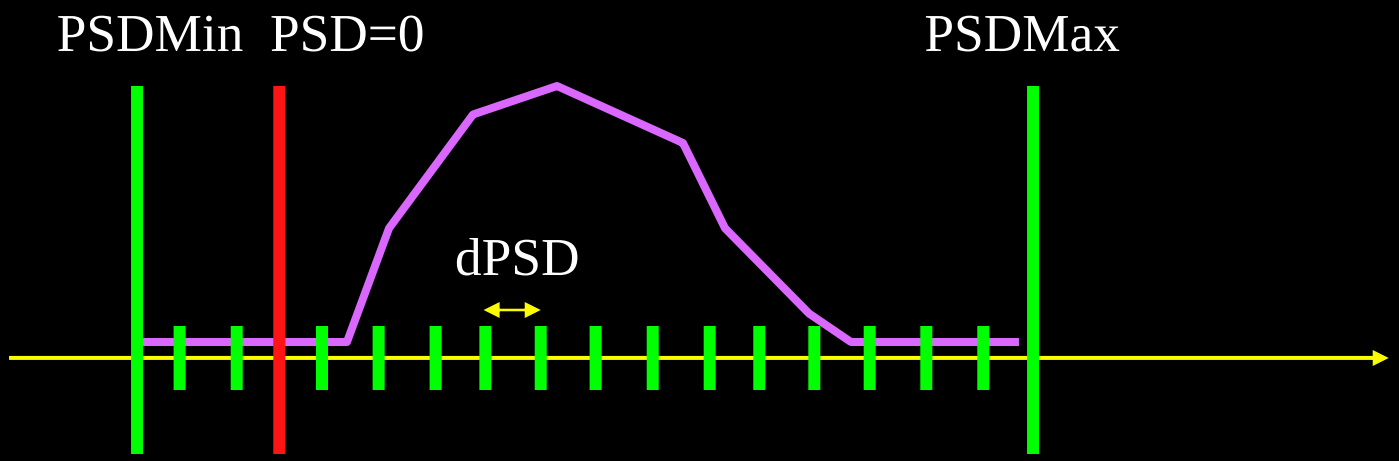
$$eff = \frac{1}{trace(C(X^T X)^{-1} C^T)}$$

Efficiency

$$VRF_i = \frac{1}{d_i}, d = diag(C(X^T X)^{-1} C^T)$$

Variance Reduction Factor

Event Response Model (FIR)



- PSD: Post-Stimulus Delay (PSD = 0 = Stimulus Onset)
- PSDMin: Response is zero for PSD < PSDMin
- PSDMax: Response is zero for PSD > PSDMax
- PSD Window should be long enough to capture response
- Response can be anything in between (FIR model)
- dPSD: sets basic temporal resolution for schedule
- DOF Constraint: Nbeta = nPSD*Nc < Ntp