Principles of fMRI

Part II

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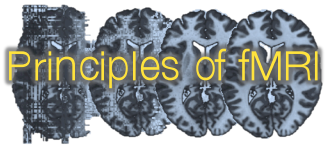
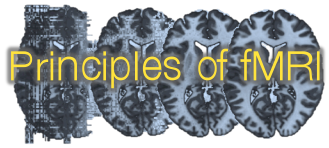
Bird's Eye View



- Goal
  - Induce human subject to do or experience the psychological states you're studying
  - Effectively detect brain signals related to those psychological states

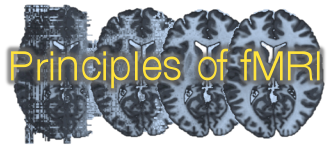
- Design method
  - You control what to present and when
  - Two kinds of considerations: Psychological and statistical

Eight Principles of fMRI Design



1) Sample size.
2) Scan time.
3) Number of conditions.
4) Grouping of events.
5) Temporal frequencies.
6) Randomization.
7) Nonlinearity.
8) Optimization.

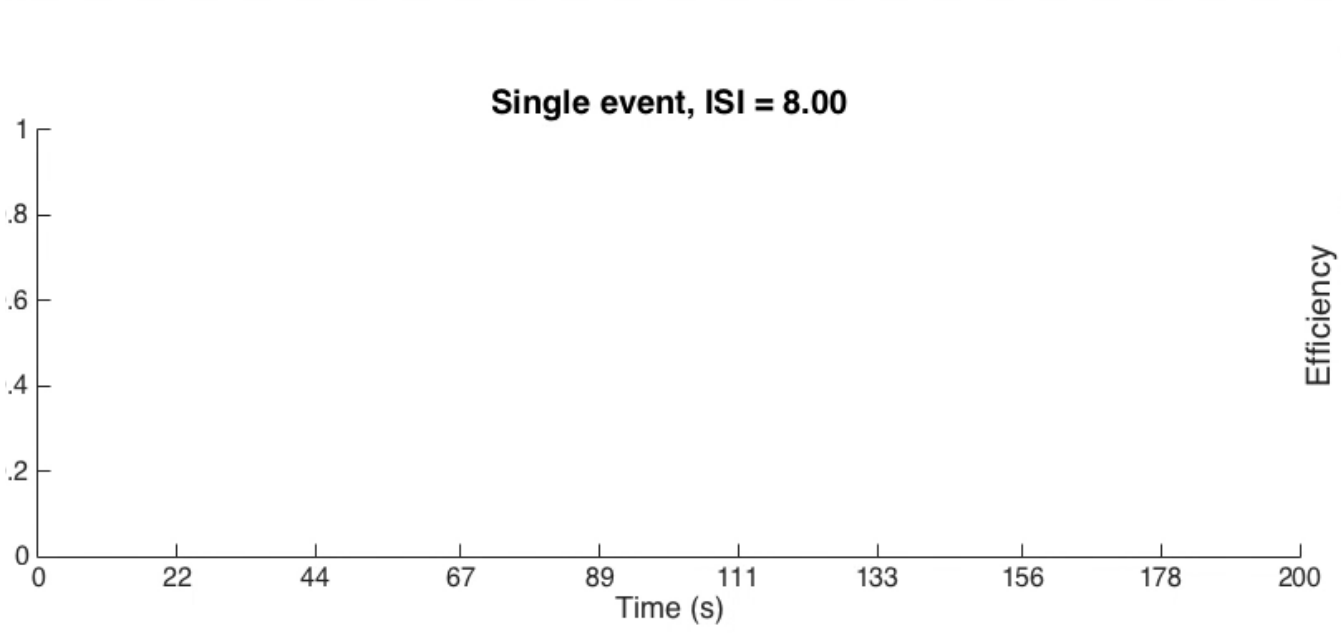
Eight Principles of fMRI Design

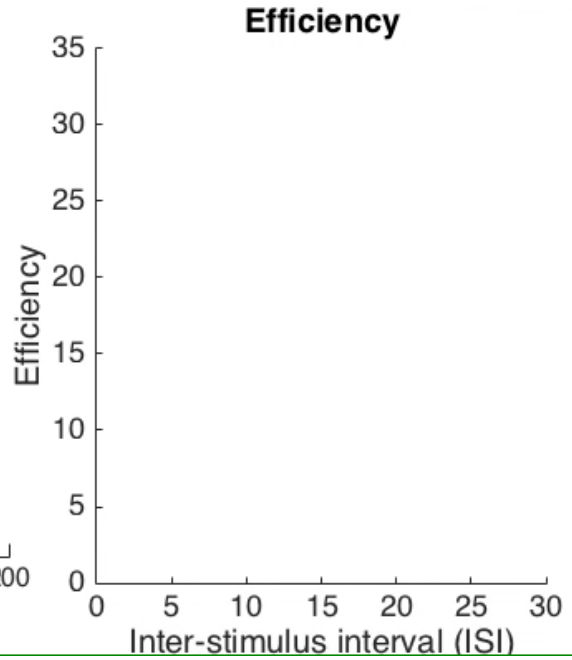


1) Sample size. Number of subjects is usually rate-limiting factor. Larger samples increase power dramatically.

2) Scan time. More time on task is helpful, but consider psychological effects (fatigue, habituation)

Within-person scan time: Maximize time on task





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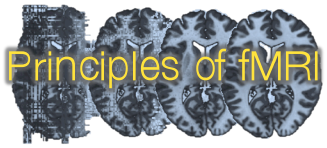

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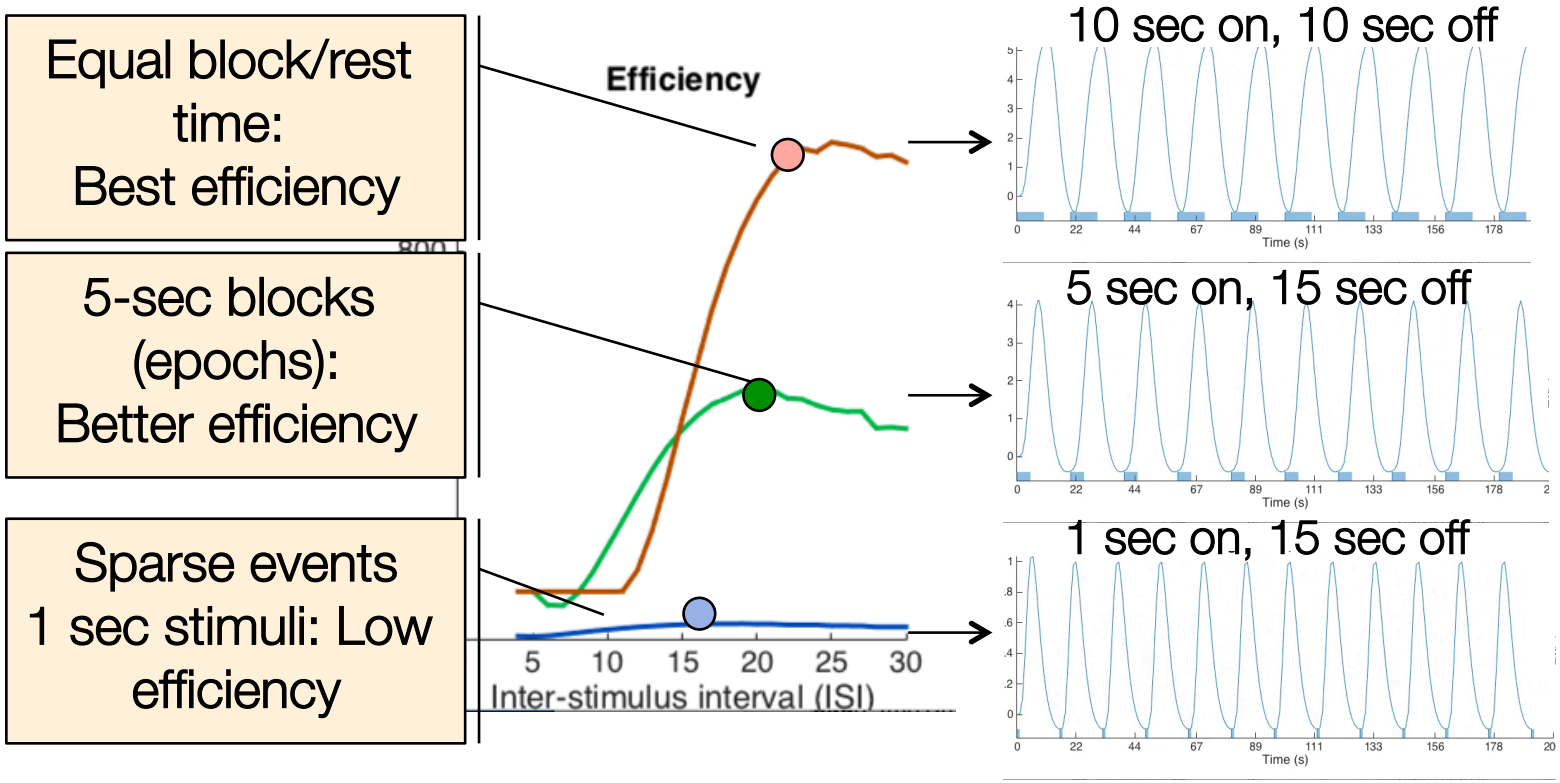
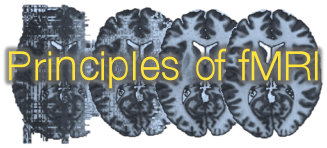


Efficiency in a Multi-level Setting



- In a group analysis, efficiency (and power) depend on within-person and between-person variance.

$$\hat{S}(c^T\beta) = \sqrt{\frac{\hat{\sigma}_w^2 c^T \left(X^T X\right)_{ii}^{-1} c + c^T \hat{\sigma}_B^2 c}{N}}$$

Sample size

Variance/ covariance of contrast values

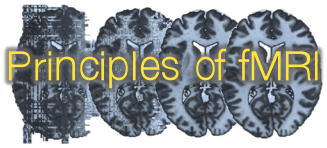
Within-person standard errors (1/efficiency)

Variance/covariance of individual differences between people

- Increasing within-person efficiency (e.g., by collecting more data) helps up to a point
- Increasing sample size always helps
- The greater the between-person variance, the more sample size is important.

e.g. Wager & Nichols, 2003

Sample Size and Scan Time



- Efficiency at the 1st level (single-subject) increases as the square root of the number of images

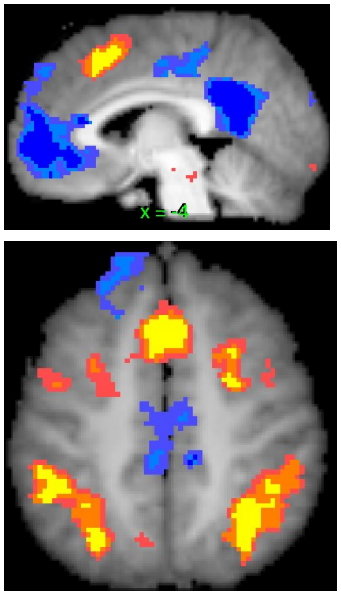
- However: Power in group analysis is limited by number of subjects collected, and this is often a bigger constraint on power

- Even if efficiency at 1st level is infinite, power and efficiency at group level limited by $\sqrt{\frac{\hat{s}_B^2}{N}}$

Balancing Scan Time and Participants

- Depends on the ratio of within-person to between-person variance in your task and brain regions of interest.
- Rule of thumb: 30-40 min functional time, scan as many participants as possible.
- Empirical example: N-back vs. Rest (data from van Ast et al. 2014)

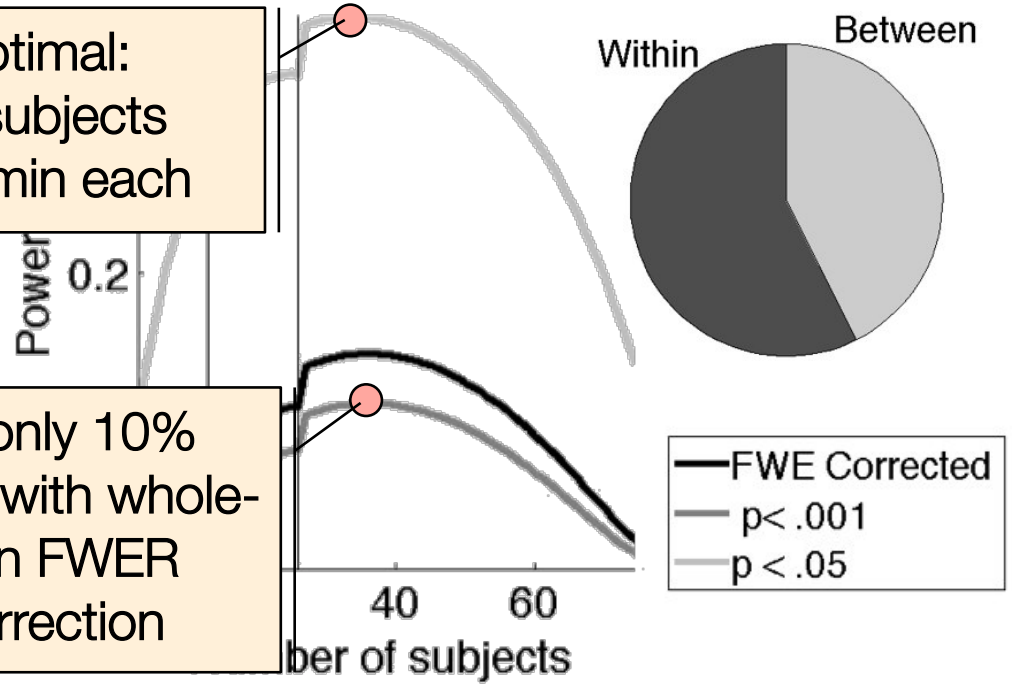
Power calculated in these voxels



Optimal allocation of 40 scan hours

Optimal:
40 subjects
~40 min each

Still only 10% power with whole-brain FWER correction



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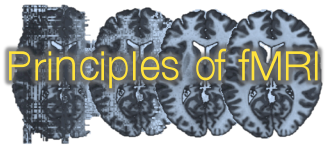
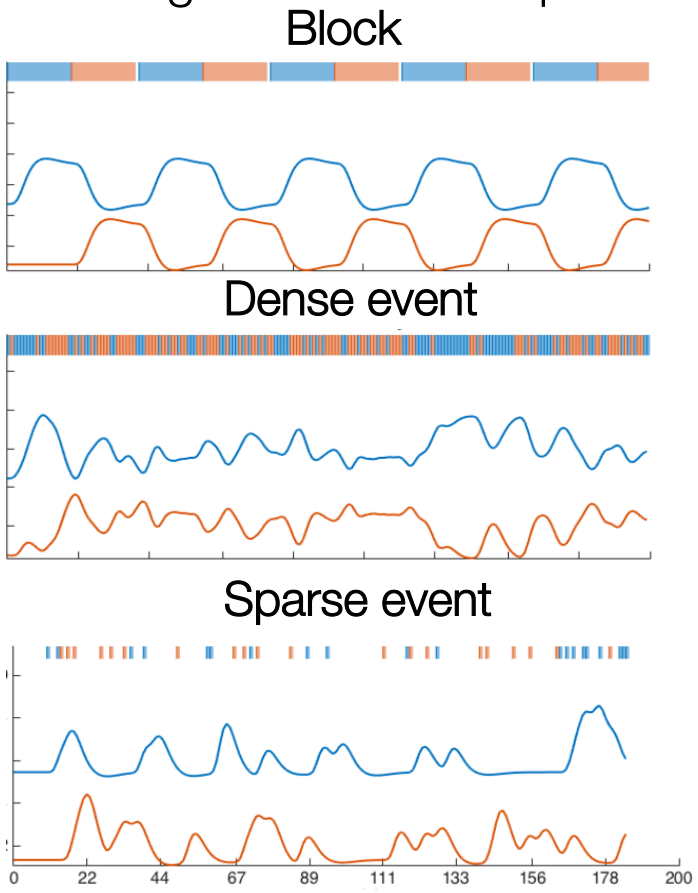
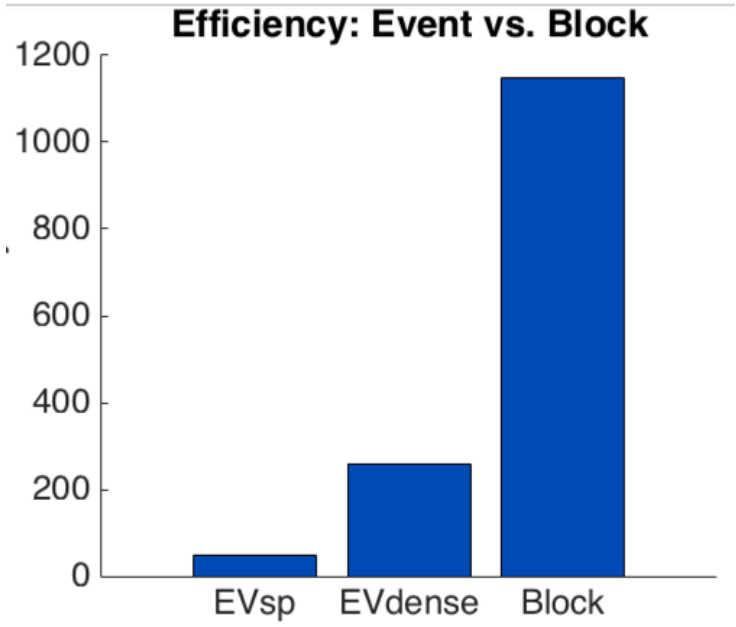


3) Number of conditions. For detection power, fewer conditions is better, and 2 (e.g., Task – Control) is optimal. For interpretability, more comparison conditions may be desirable.

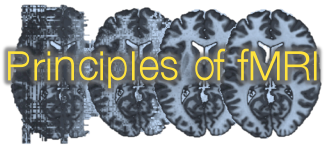
4) Grouping of conditions. For detection power and robustness, block designs. For more specific inferences, event-related designs.



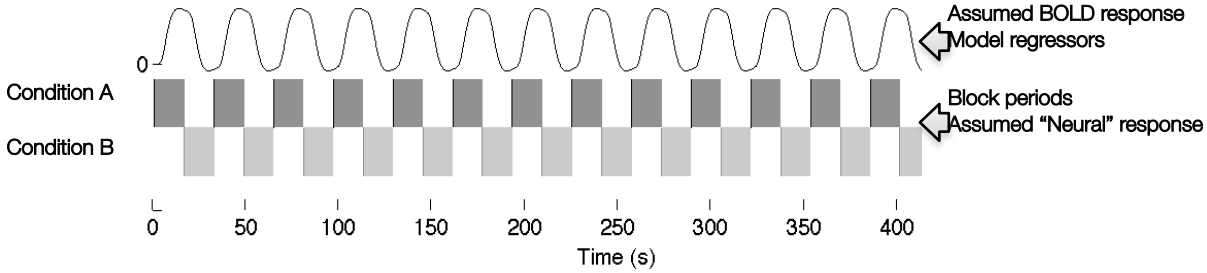


[1 -1 Contrast]

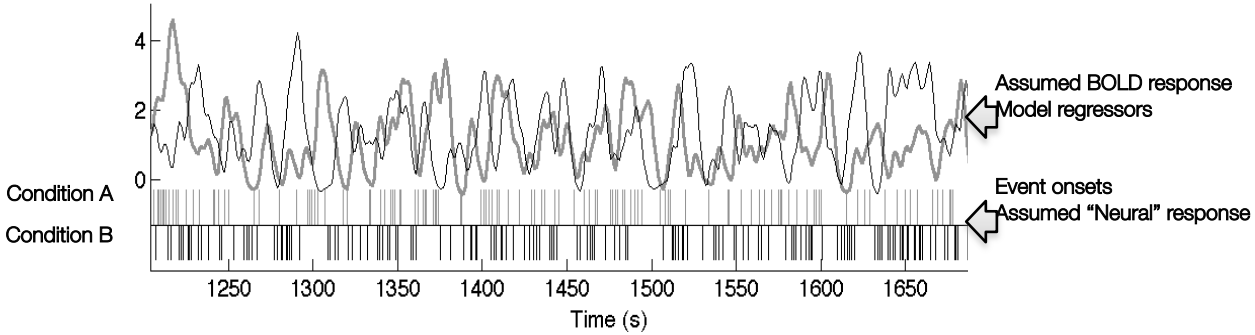
A fundamental tradeoff: contrast detection vs. HRF estimation



Blocks of the same trials: Greater power to detect differences among conditions



Unpredictable sequences of trials: Greater power to estimate the shape of the hemodynamic response



Josephs & Henson, 1999; Wager & Nichols, 2003; Liu, 2004; Smith et al., 2007; Buracas et al., 2004

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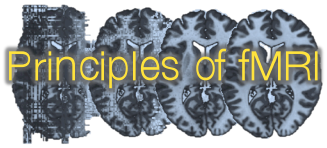

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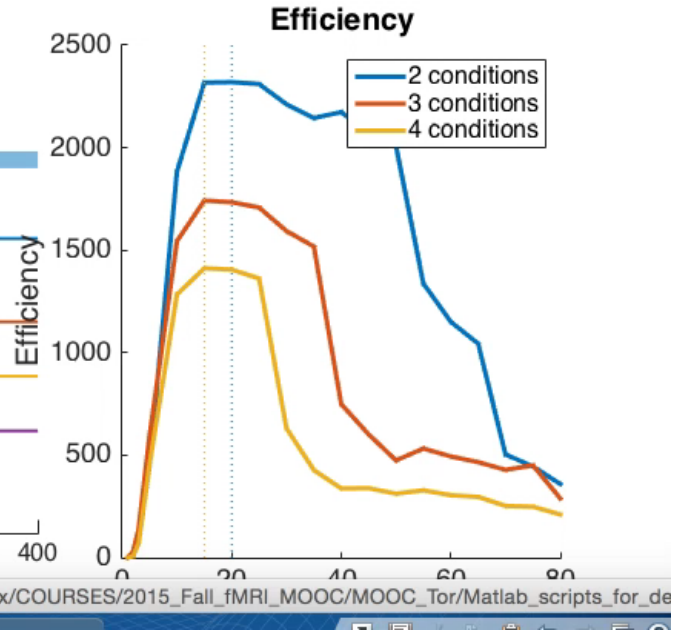
More blocks costs power



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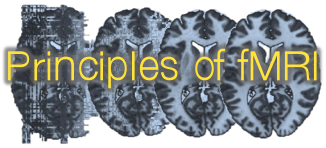
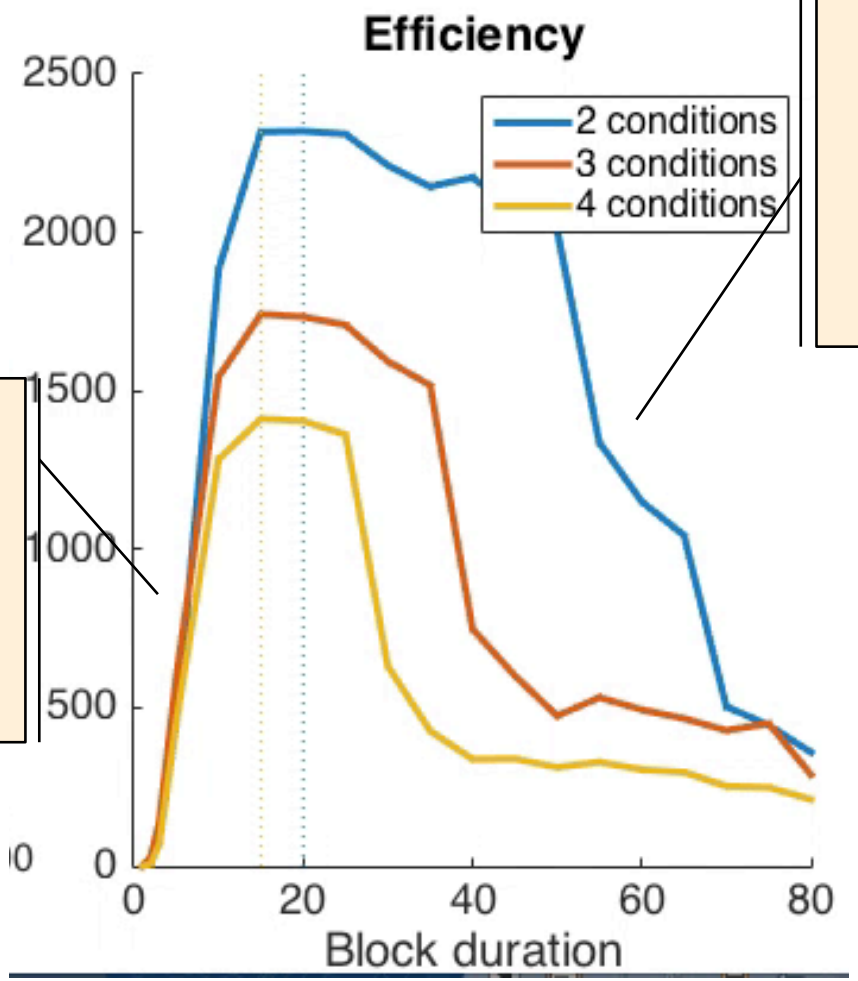


5) Temporal frequencies. Use short blocks (18-20 sec is optimal, > 40 sec is risky) or event-related designs without strong low-frequency components (stratified randomization).



Long blocks: High-pass filter removes design variance.

Short blocks: Low predictor variance. HRF is smoothing filter.

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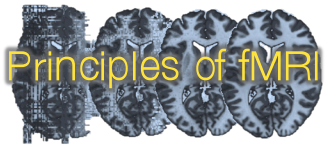


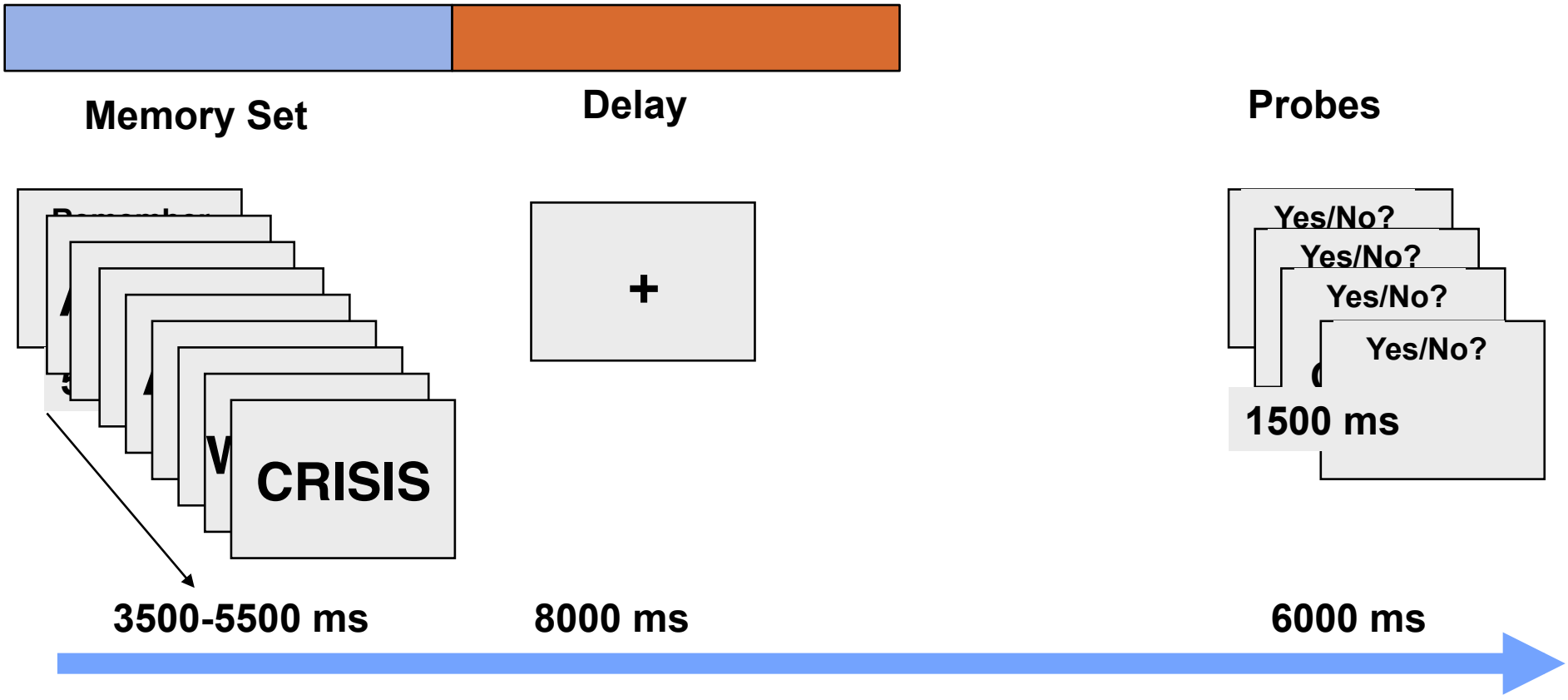
6) Randomization. Randomize event-related designs individually for each participant. Randomize (or pseudo-randomize) the ordering of and/or jitter between events that are close together in time, or use catch trials when you cannot.

- Causal inference that your experimental manipulations caused the brain response requires randomization to avoid confounds.

- For example: If Trial type A always precedes B, then the brain may show a spurious A > B difference even if the neural response to the two is identical, because of:
  - Neural habituation
  - Vascular inelasticity
  - Psychological changes caused by order

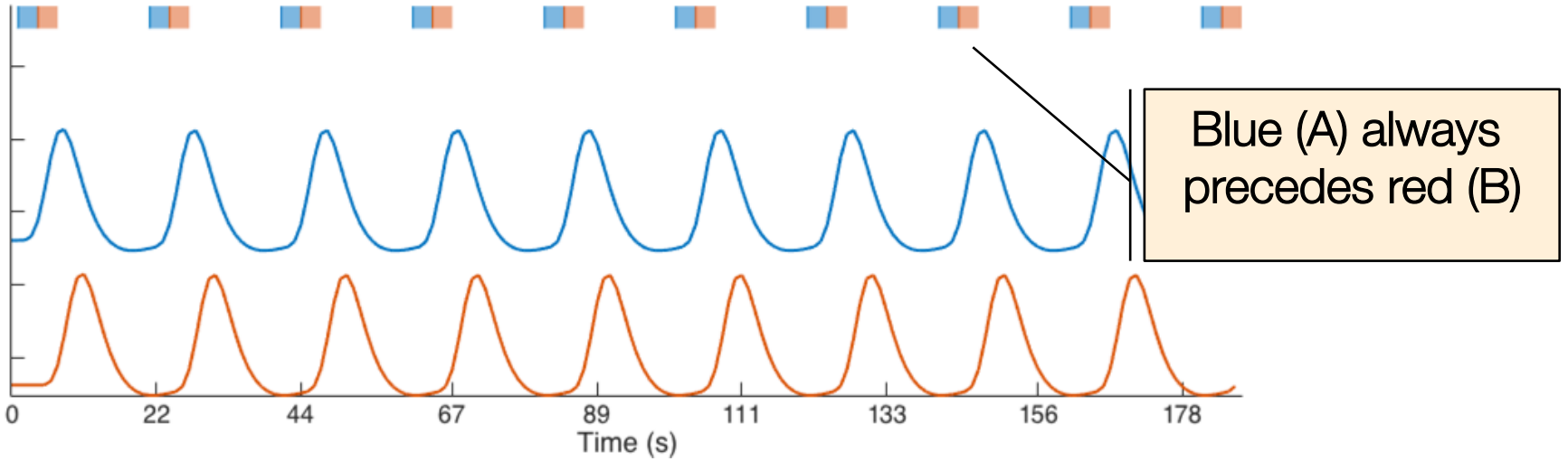
Temporally Dependent Events Example: Working memory

Memory encoding (A, blue) is always followed by maintenance during delay (B, red)



Example from Wager et al. 2014

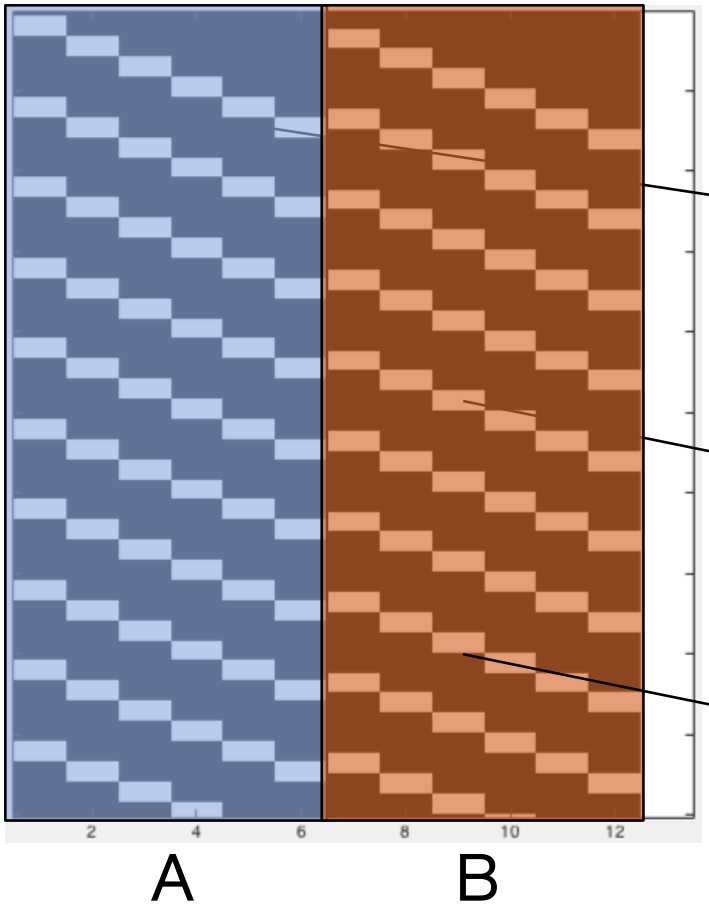
Dependent Event Fail



- Correlation between regressors is “only” r = 0.45 …
  But strong reliance that assumed HRF shape is correct!
- Identical HRF is not likely to be strictly true in practice
- If not, we will get a wrong answer (without knowing it’s wrong)

Dependent Event Fail

A more flexible model: FIR



Blue (A) always precedes red (B)

Fixed ISI (20 sec) fail:
A is correlated with itself shifted in time.

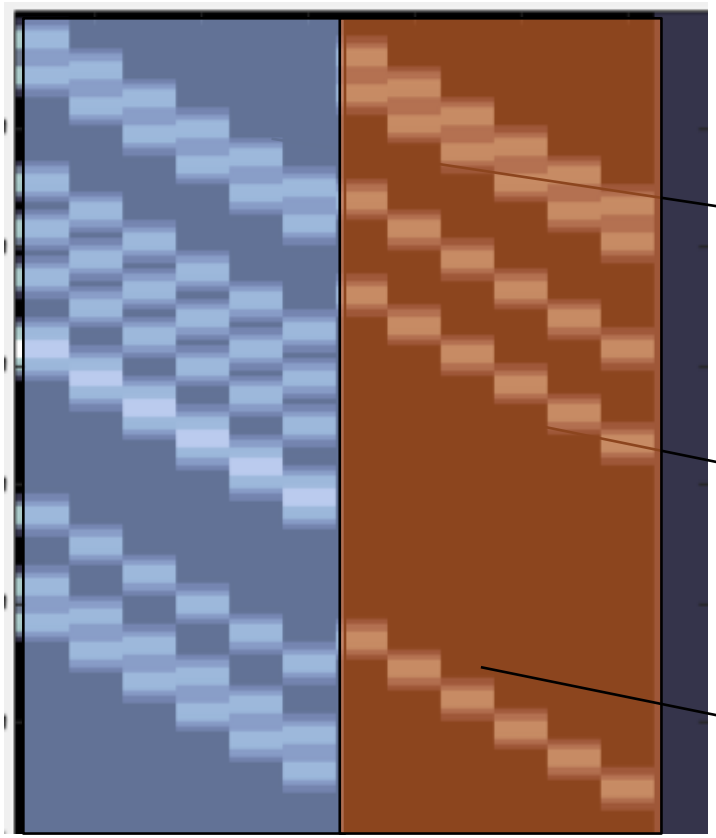
Later time points for A arecorrelated with earlier time points for B

Max correlation across regressors is r = 0.93!!

Catch Trials

Red (B) follows blue (A) on ½ the trials

A more flexible model: FIR



Jitter (variability in onsets) reduces correlations within trial type A

Catch trials (partial trials) reduce correlation between events dependent in time

Max correlation across regressors is r = 0.47. Better.

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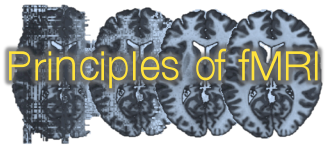
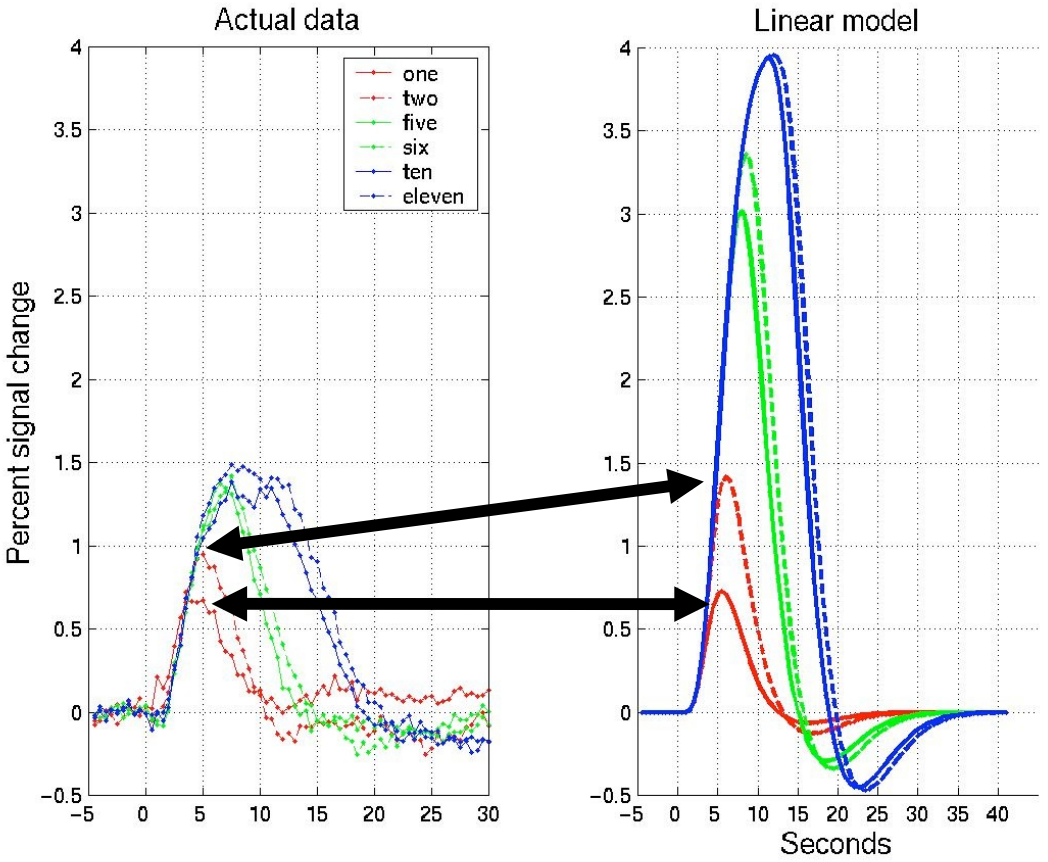


7) Nonlinearity. Avoid nonlinear interactions among events by spacing them by at least few seconds if possible, and avoid systematic differences in temporal grouping with stratified randomization.

BOLD Nonlinearity at Short ISIs

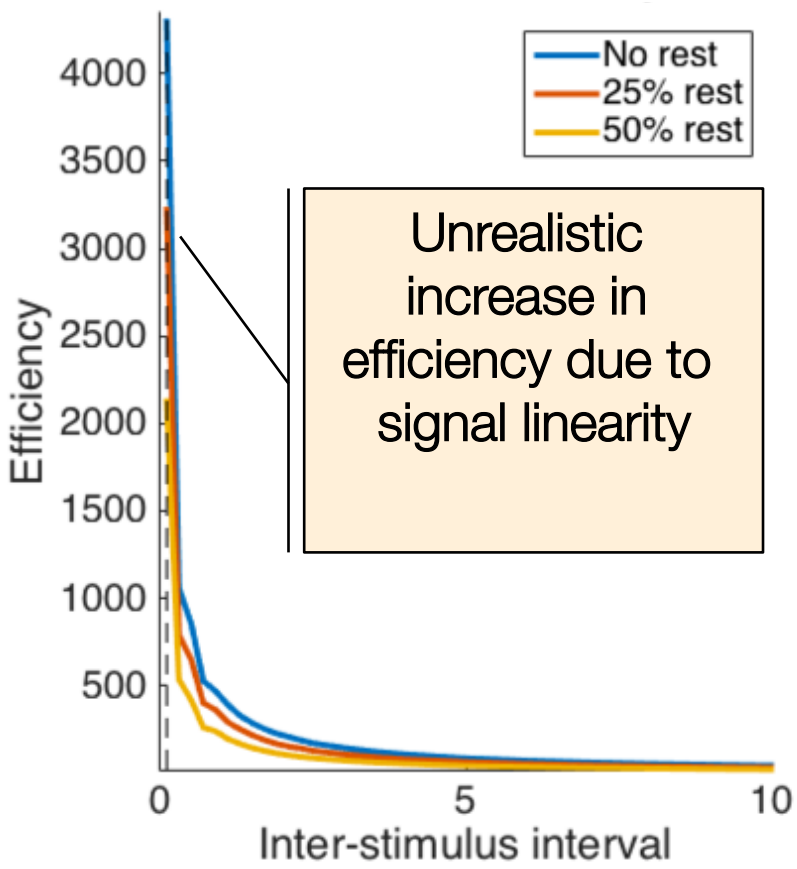
- Meizin et al. (2000): 10% nonlinear saturation at 5 s ISI
- Wager et al. 2005: Strong linearity at 1 sec ISI:

- Series of 1,2,5,6,10 or 11 events. Each event: 125 ms flashing checkerboard, 1s ISI. Series followed by 30s rest
- Note actual vs. predicted relative magnitude



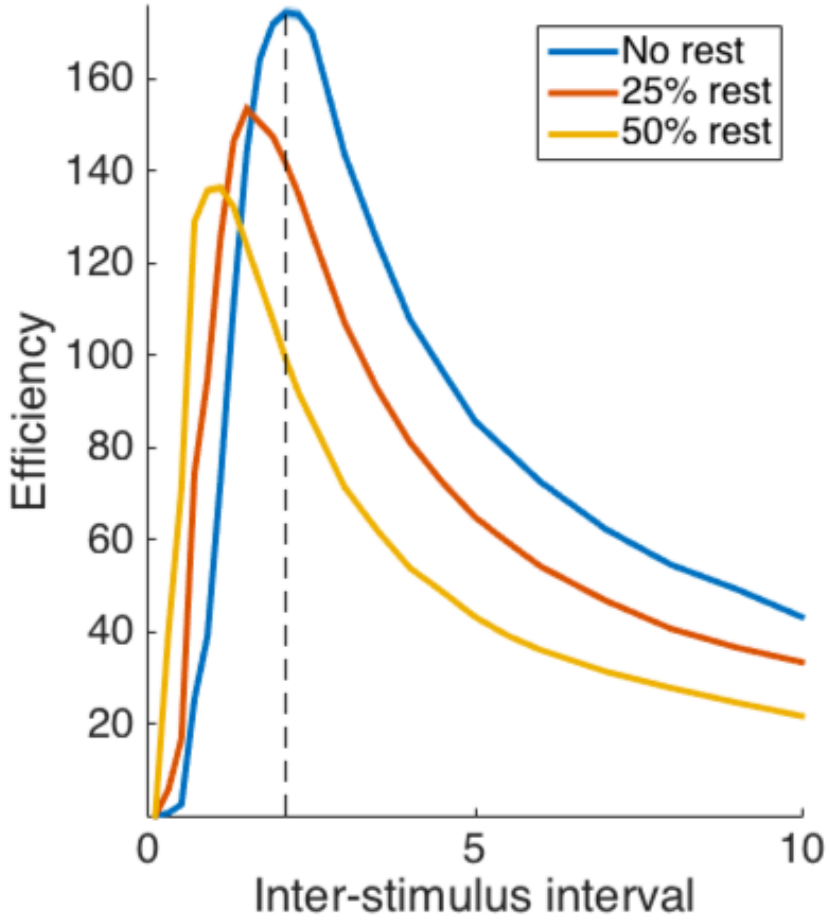
Efficiency of Randomized Designs

Contrast efficiency: LTI system



Contrast: [1 -1]
Best ISI = 0.10 (min in sim.)
Time between repetitions = 0.20 sec

A more realistic model



Contrast: [1 -1]
Best ISI = 2.10 sec
Time between repetitions = 4.19 sec

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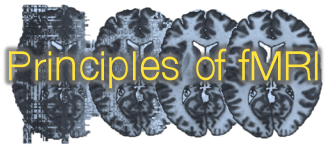
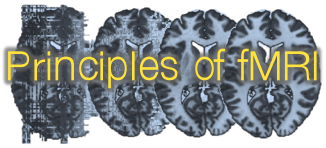


8) Optimization. Optimize your design choices with specific study goals and constraints (psychological, neural, and statistical) in mind

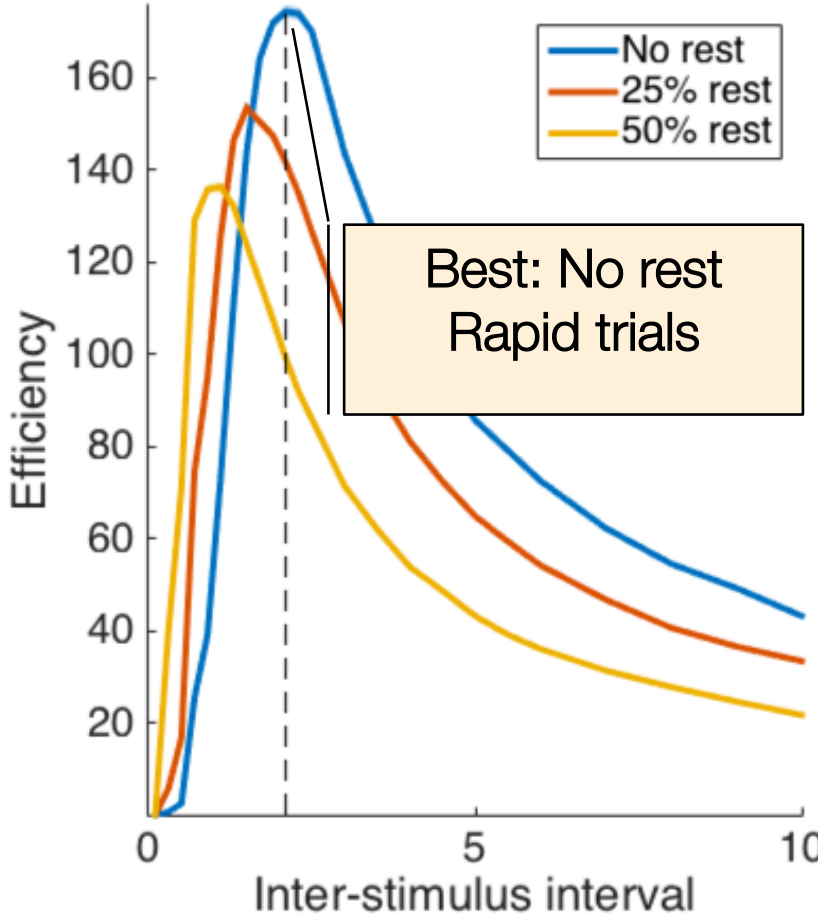
Specify:

- A set of contrasts that you care about
- Relative importance of contrasts
- Desired high-pass filtering cutoff
- Desired model (canonical HRF for detection, FIR for shape estimation, combination of both)

Efficiency of Randomized Designs

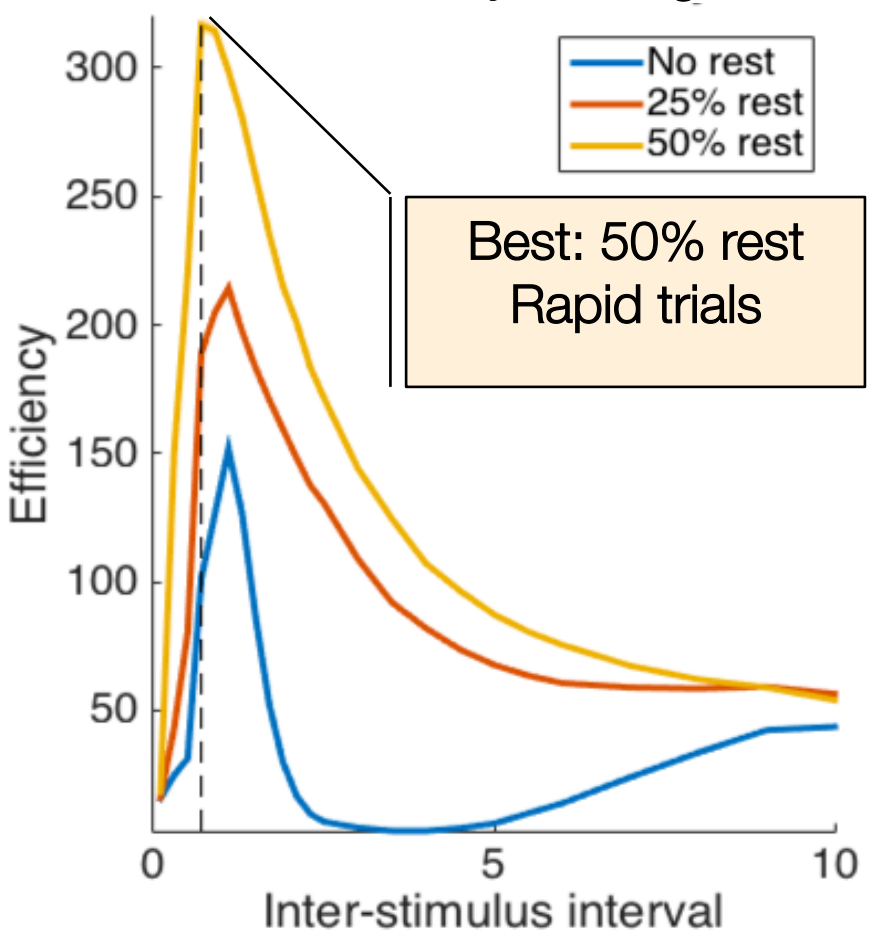


Contrast efficiency: Difference



Contrast: [1 -1]
Best ISI = 2.10 sec
Time between repetitions = 4.19 sec

Contrast efficiency: Average vs. rest



Contrast: [0.5 0.5]
Best ISI = 0.70 sec
Time between repetitions = 2.79 sec

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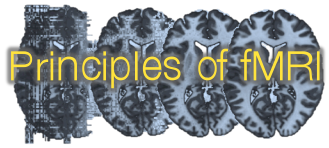

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End of this module.

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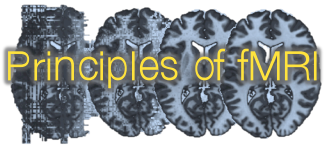
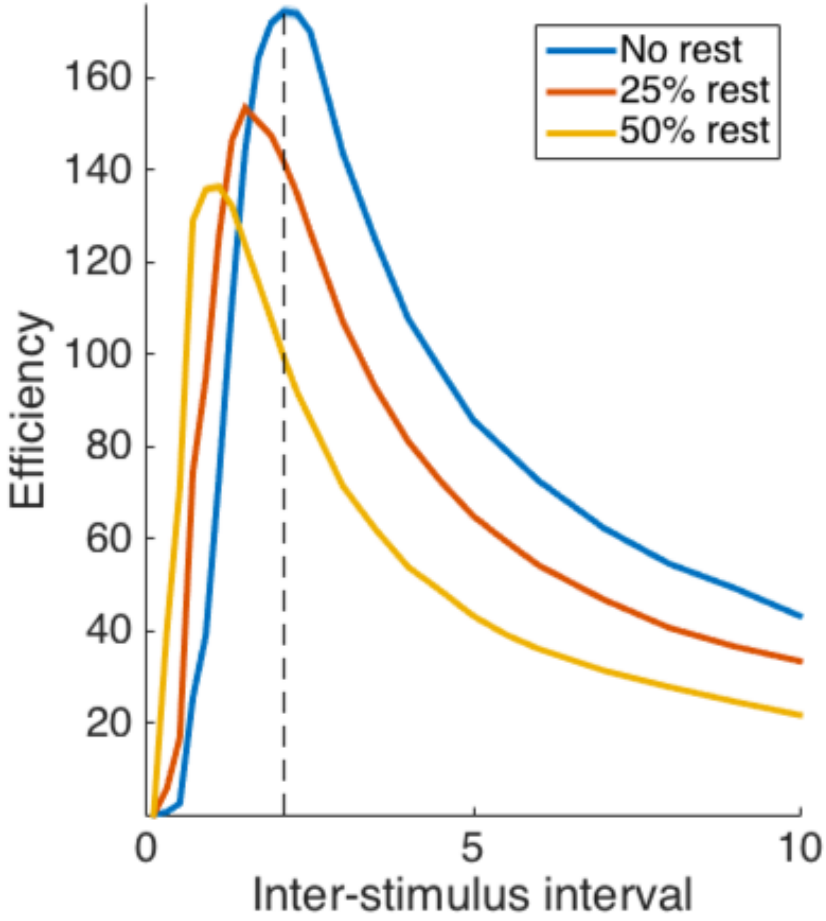
Efficiency of randomized designs

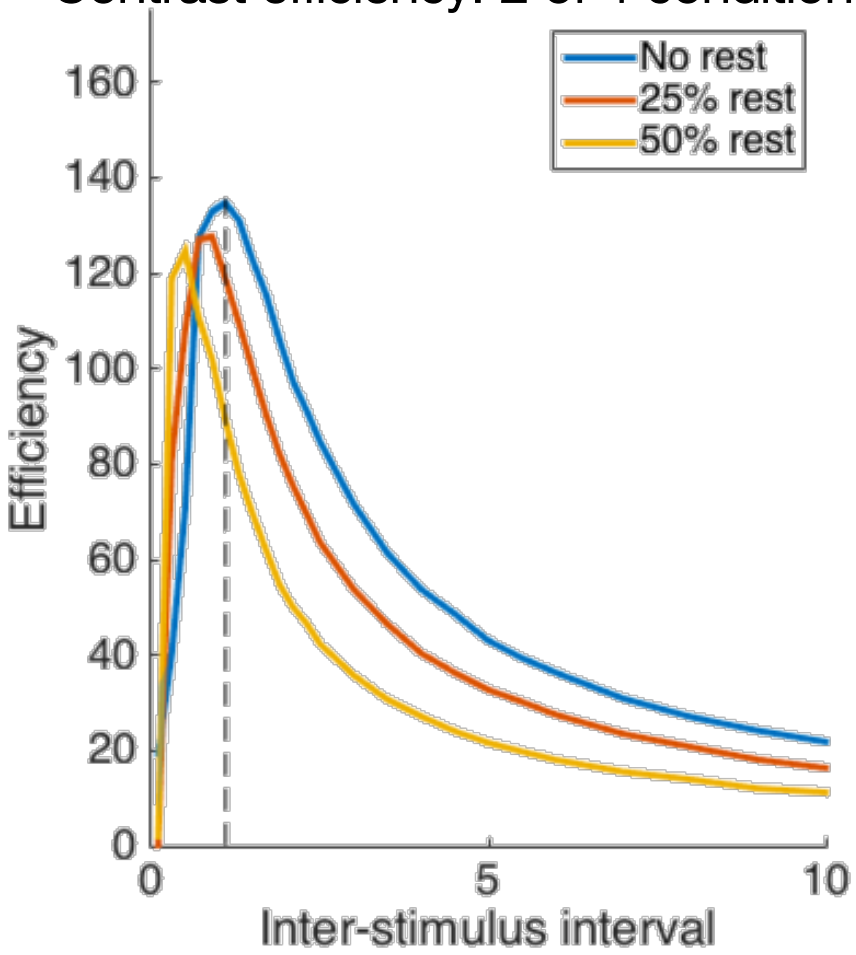


Contrast efficiency: Difference



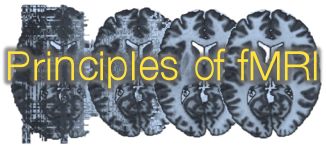
Contrast: [1 -1]
Best ISI = 2.10 sec
Time between repetitions = 4.19 sec

Contrast efficiency: 2 of 4 conditions

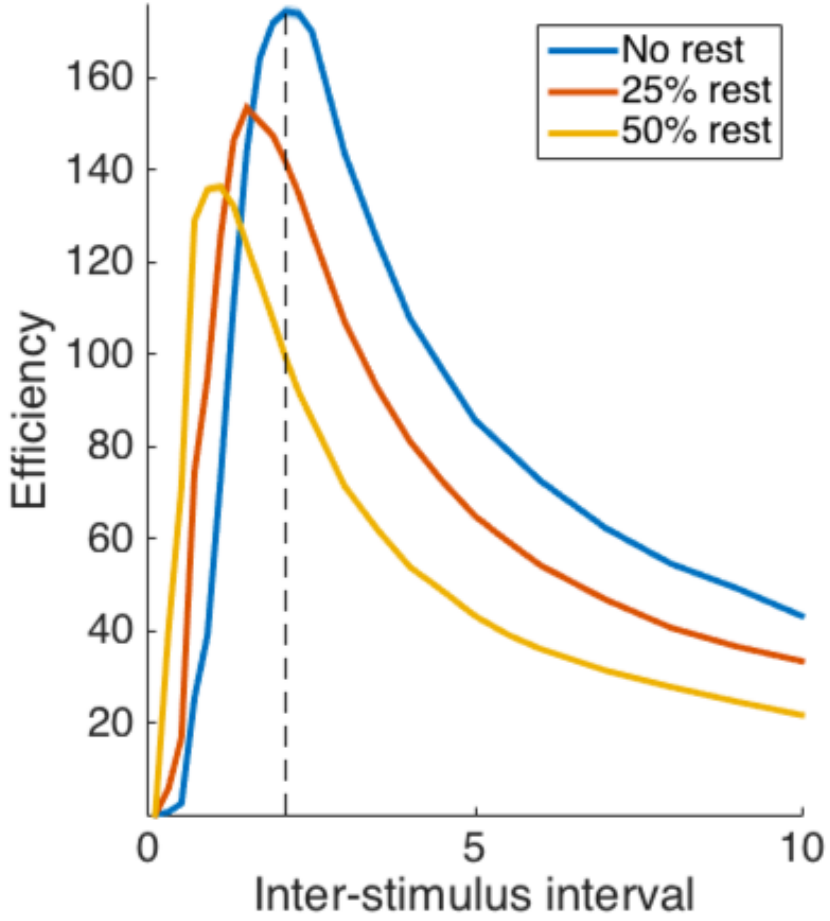


Contrast: [0.5 0.5]
Best ISI = 1.1 sec
Time between repetitions = 4.39 sec

Efficiency of randomized designs

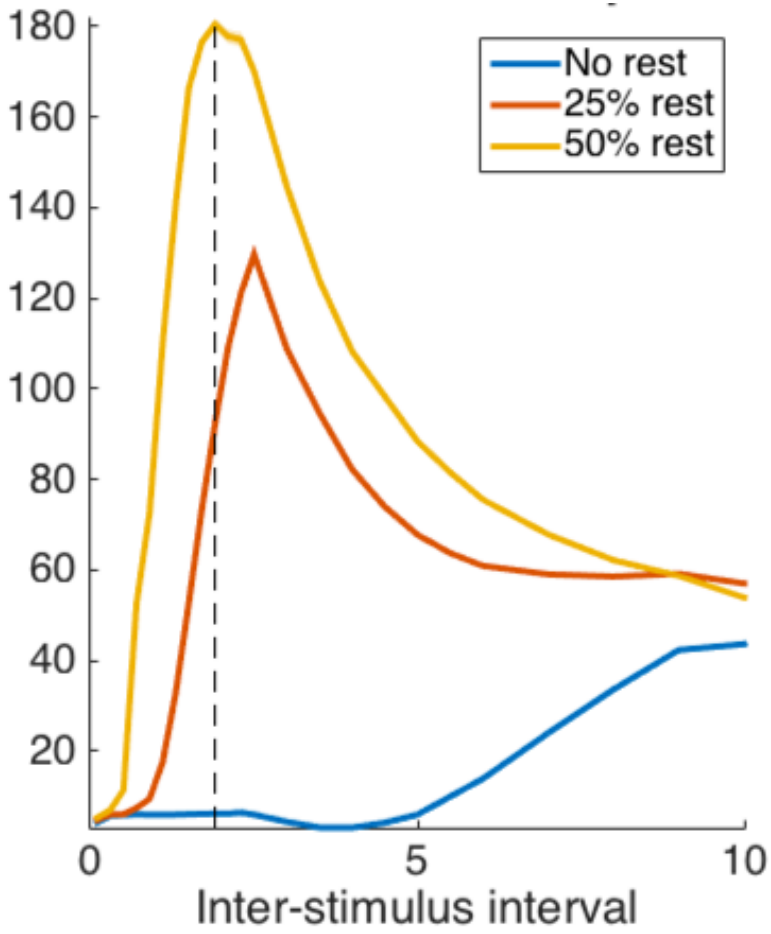


Contrast efficiency: Difference



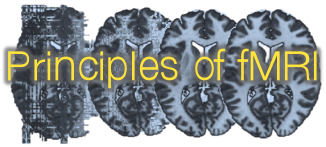
Contrast: [1 -1]
Best ISI = 2.10 sec
Time between repetitions = 4.19 sec

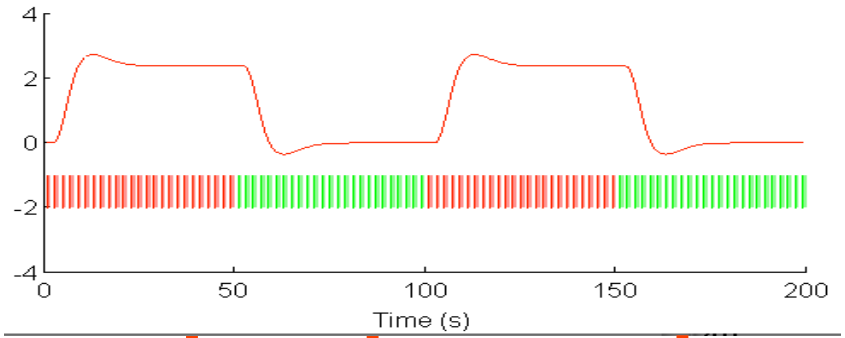
Contrast efficiency: Single-event



Contrast: [1]
Best ISI = 1.9 sec
Time between repetitions = 1.9 sec

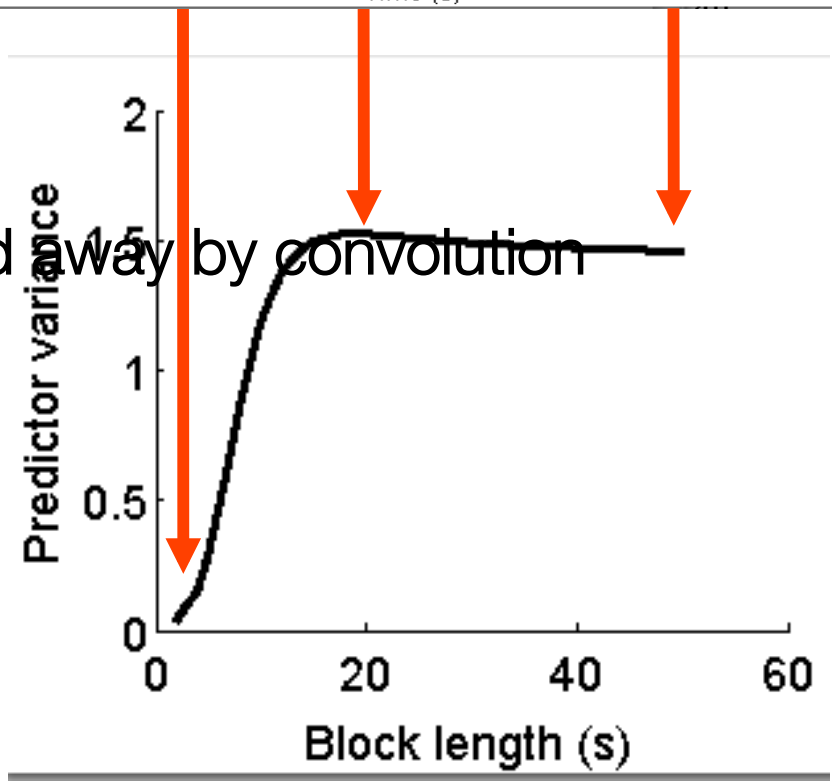
fMRI designs: Block length matters





Rise and fall:
High predictor variance

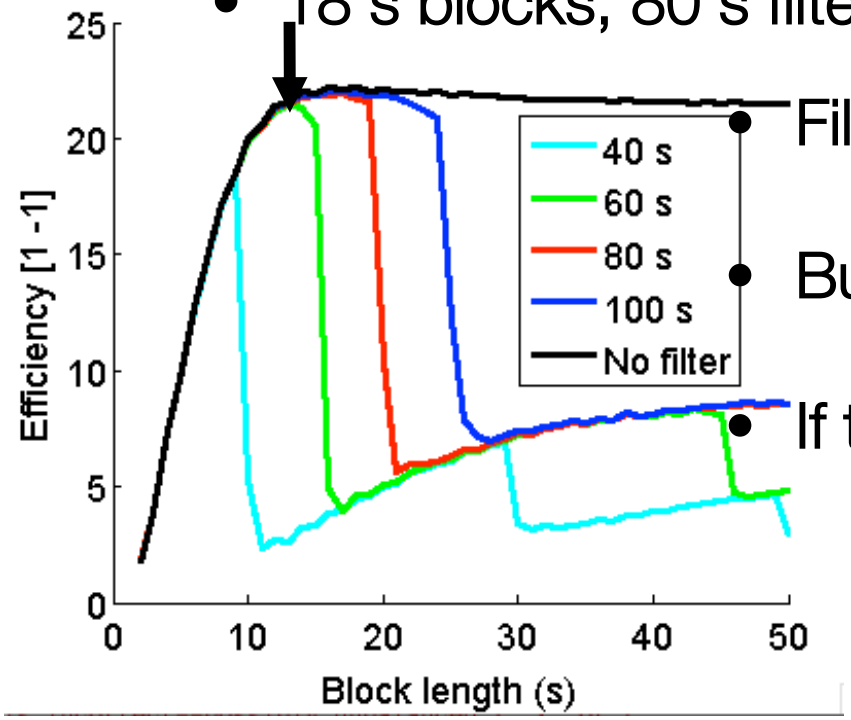
2 sec blocks:
Too fast!
Signal is blurred away by convolution



50 sec blocks:
About the same

Effects of filtering on efficiency

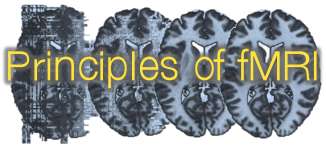
- 18 s blocks, 80 s filter



- Filtering reduces efficiency…
- But you're removing noise, too!
- If the noise reduction is great, it's

Considering nonlinearity

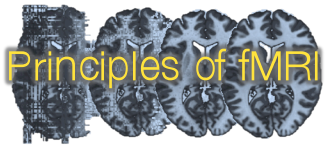
Optimizing trial order



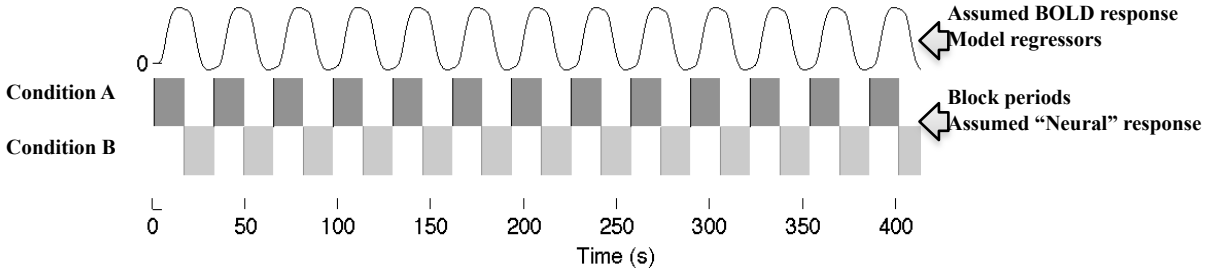
- Hemodynamic response blurs response to events close in time
- Other factors: Slow noise drift, filtering procedures, signal nonlinearity

- **Blocks of the same trials: Greater power to detect differences among conditions**
- **Unpredictable sequences of trials: Greater power to estimate the shape of the hemodynamic response**

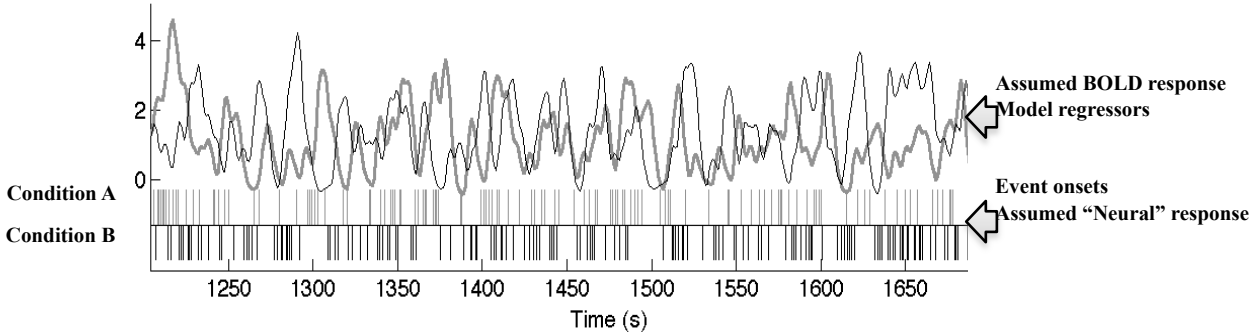
A fundamental tradeoff: contrast detection vs. HRF estimation



- **Blocks of the same trials: Greater power to detect differences among conditions**

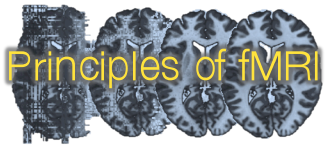


- **Unpredictable sequences of trials: Greater power to estimate the shape of the hemodynamic response**



Josephs & Henson, 1999; Wager & Nichols, 2003; Liu, 2004; Smith et al., 2007; Buracas et al., 2004

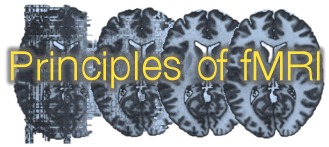
Design efficiency



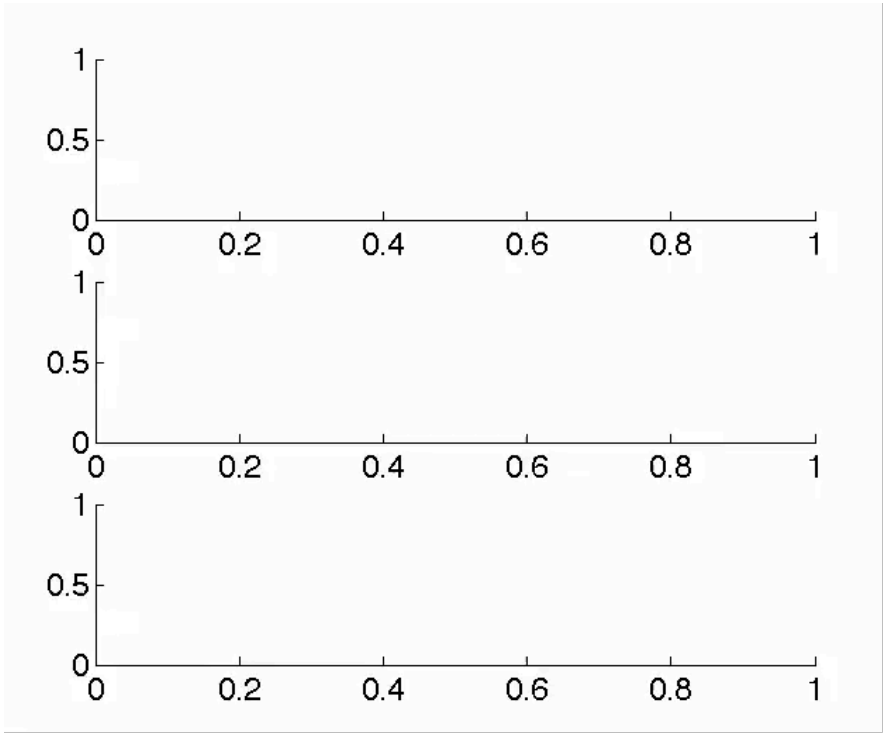
Computer-aided design
Genetic algorithm (Wager & Nichols; see website below)
OptSeq (Doug Greve)
M-sequence program (Buracas).

Genetic algorithm
Rapid convergence on optimal designs
Can optimize across multiple contrasts
User can specify the relative importance of each contrast
Account for high-pass filtering and autocorrelation
Account for nonlinearity (simple model)
Can optimize for combination of detection power, HRF estimation power, and counterbalancing

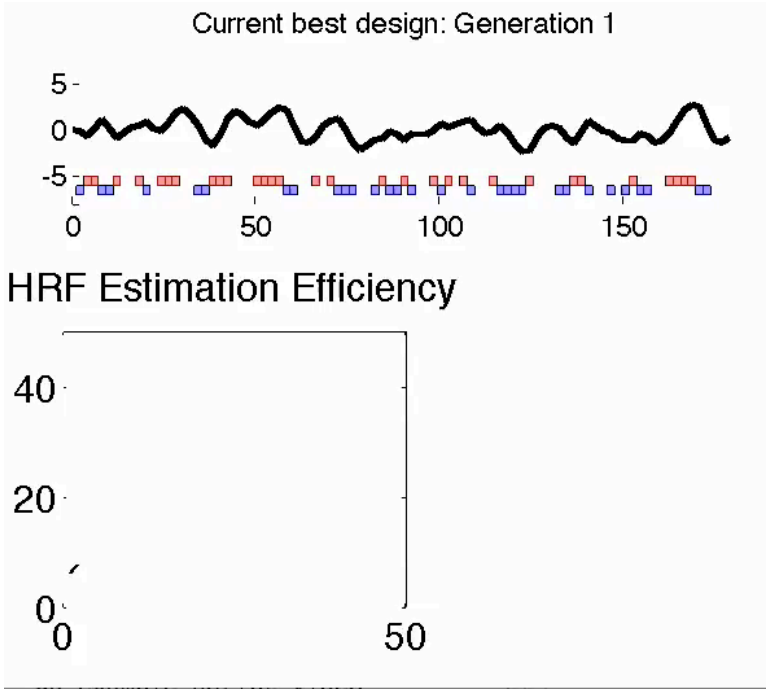
Optimizing with a genetic algorithm



[A - B] contrast power

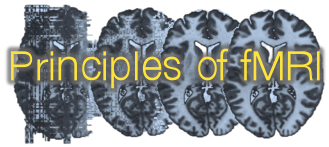


HRF estimation power



Wager & Nichols, 2003

Optimizing with a genetic algorithm



$$se(c^T\hat{\beta}) = \sqrt{\frac{\hat{\sigma}_\varepsilon^2 c^T (X^T X)^{-1} c + c^T \hat{\sigma}_\eta^2 c}{N}}$$

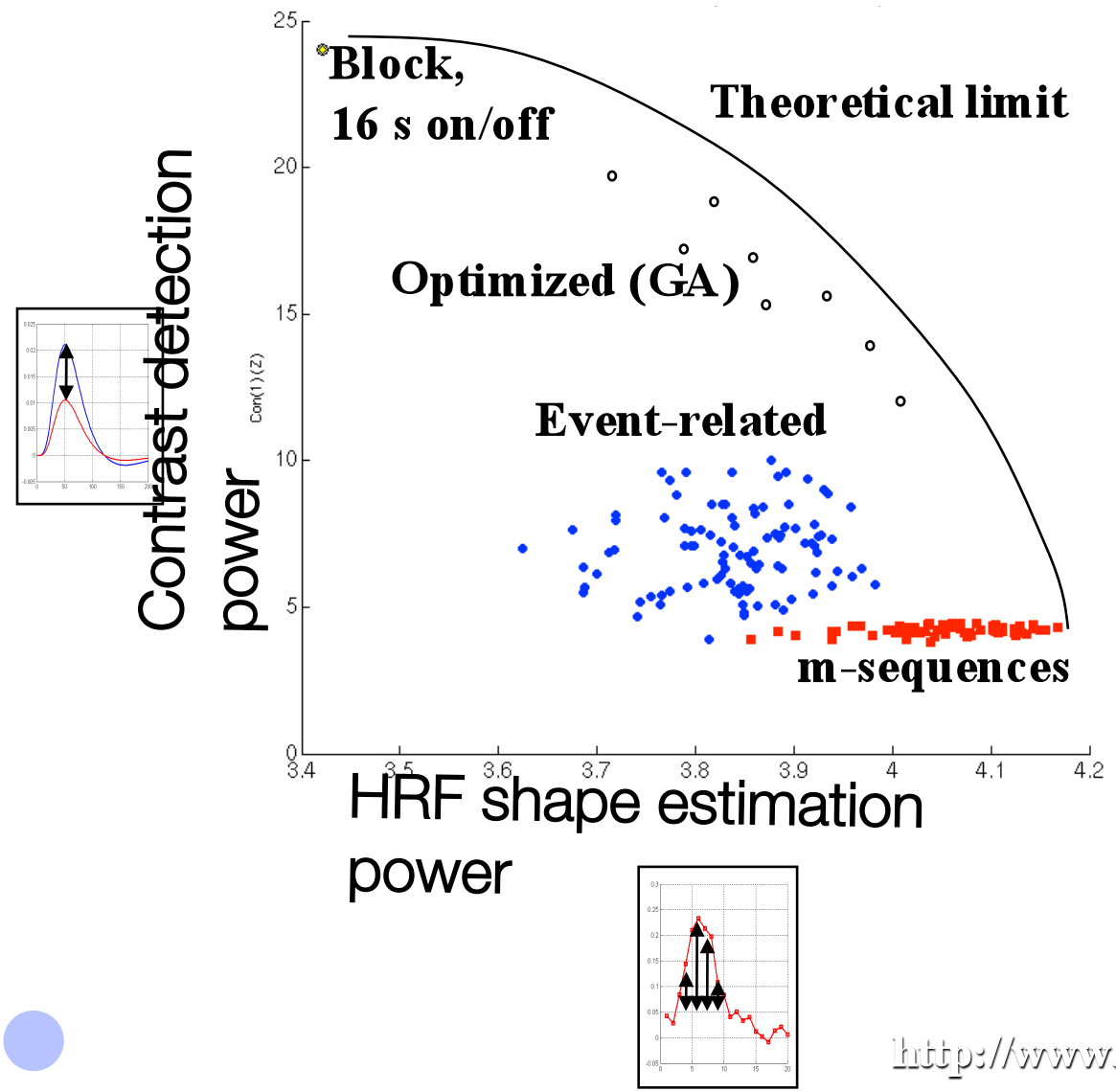
(1) Increase variation and balance in predictors
(2) Reduce correlation among predictors (colinearity)

How to handle the tradeoff between estimating contrasts and hemodynamic response shape?

c is either a set of contrasts of interest, an FIR design matrix that specifies hemodynamic response estimation, or a combination

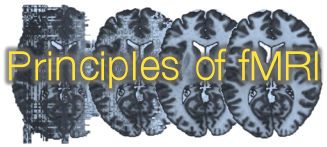
Wager & Nichols, 2003

Comparing efficiency for different design types



- Block best for detection
- M-sequence best for shape (Buracas et al.)
- Event-related designs so-so on both
- Optimized designs good tradeoff

A design scheme I like



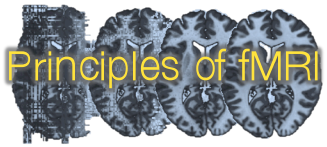
Event-related: for psychological specificity

Pseudorandomized trial types (using genetic algorithm)

Balance detection power for [A - B] contrast and HRF shape estimation

Minimum of 4 s between events to prevent nonlinear weirdness

Summary



Five psychological considerations

- **Stimulus predictability**
- **Time on task**
- **Participant strategy**
- **Temporal precision of psychological manipulations**
- **Unintended psychological activity**

Four analysis considerations

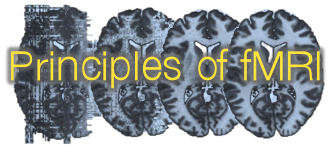
Statistical efficiency: Power to detect results

Effects of filtering, autocorrelation, and nonlinearity

Detection vs. response shape estimation

Computer-aided optimization

Extra stuff



Download the Genetic Algorithm toolbox at:
http://psych.colorado.edu/~tor/

Module Title Here

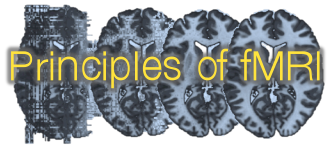
 @fMRIstats

A growing new field

Default text box

Default callout box

Neuroimaging



JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

University of Colorado Boulder

Goals of neuroimaging:

TOWARD MULTIDISCIPLINARY SCIENCE

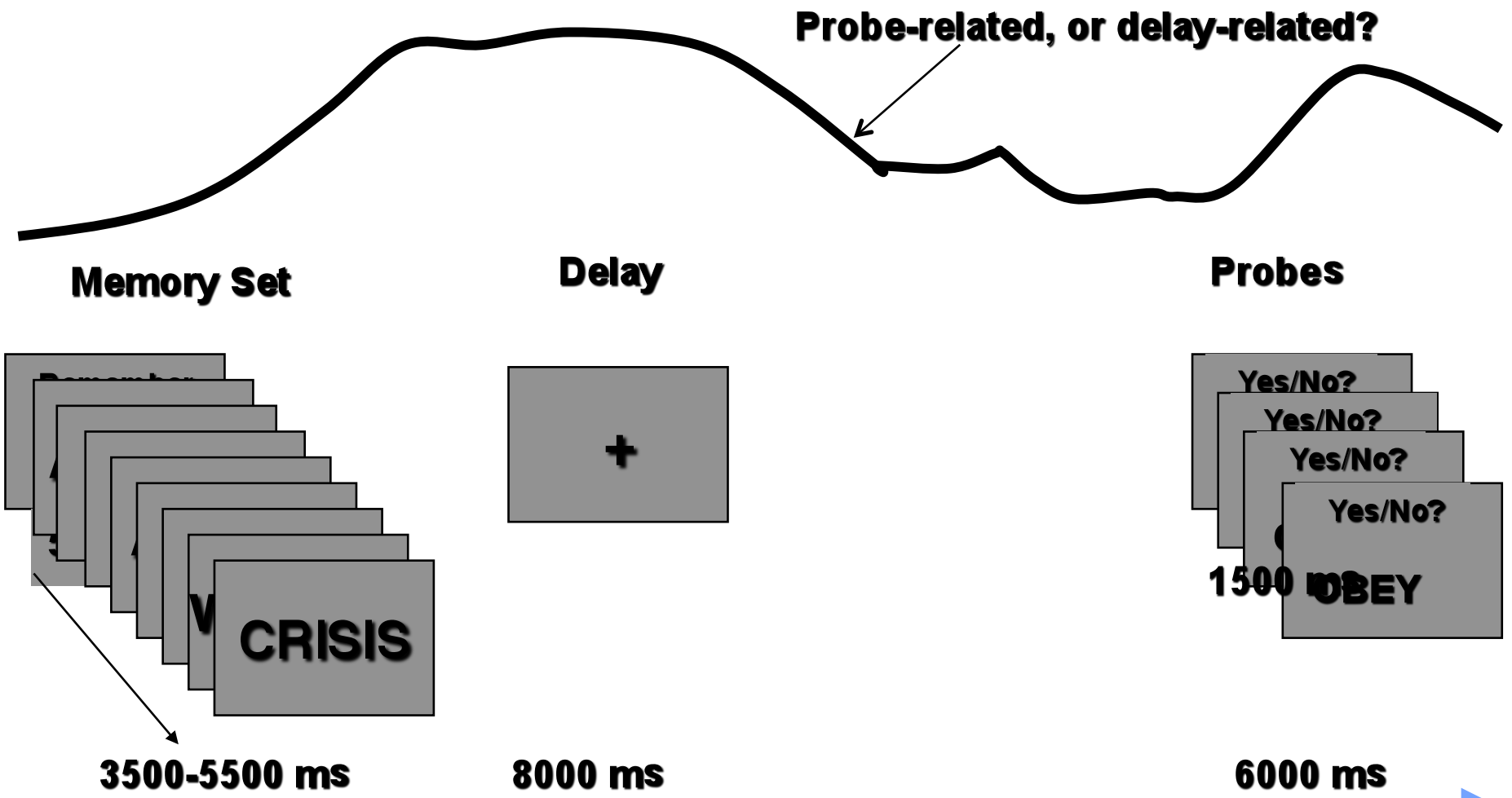
@fMRIstats

Lindquist & Wager

End of Module

@fMRIstats

Catch trials



Catch trials