EXPERIMENTAL DESIGN IN FMRI

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EXPERIMENTAL DESIGN IN FMRI

1- Categorical Designs (Subtraction Based)

2- Factorial Designs

3- Parametric Designe

1- Subtraction Method

Interested in process P?

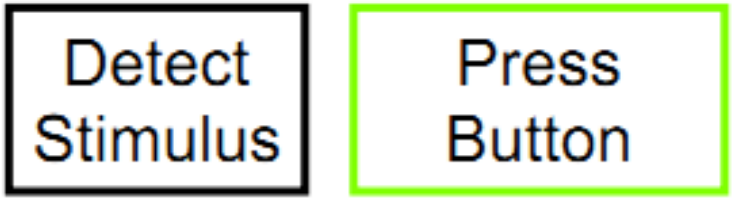
Task A contains P; Task B is similar to task A without P.

Subtraction: A – B = P

Simple Subtraction Method

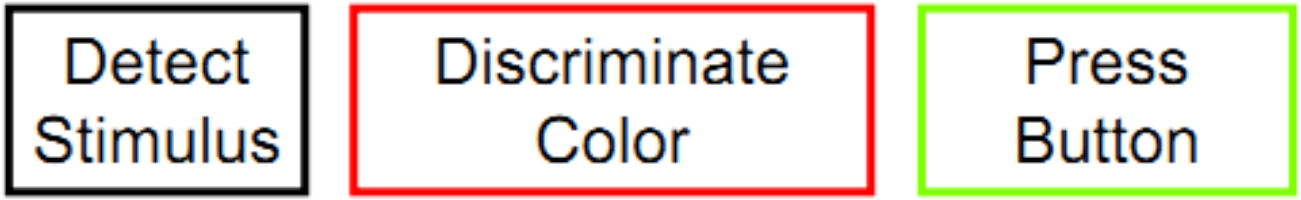
T1: Simple Reaction Time

- Hit button when you see a light



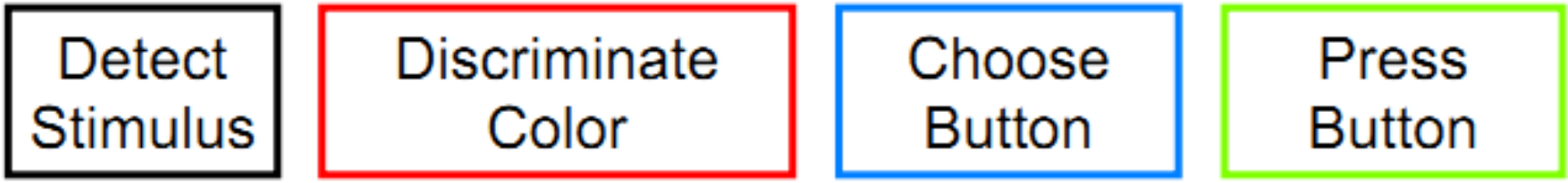
T2: Discrimination Reaction Time

- Hit button when light is green but not red

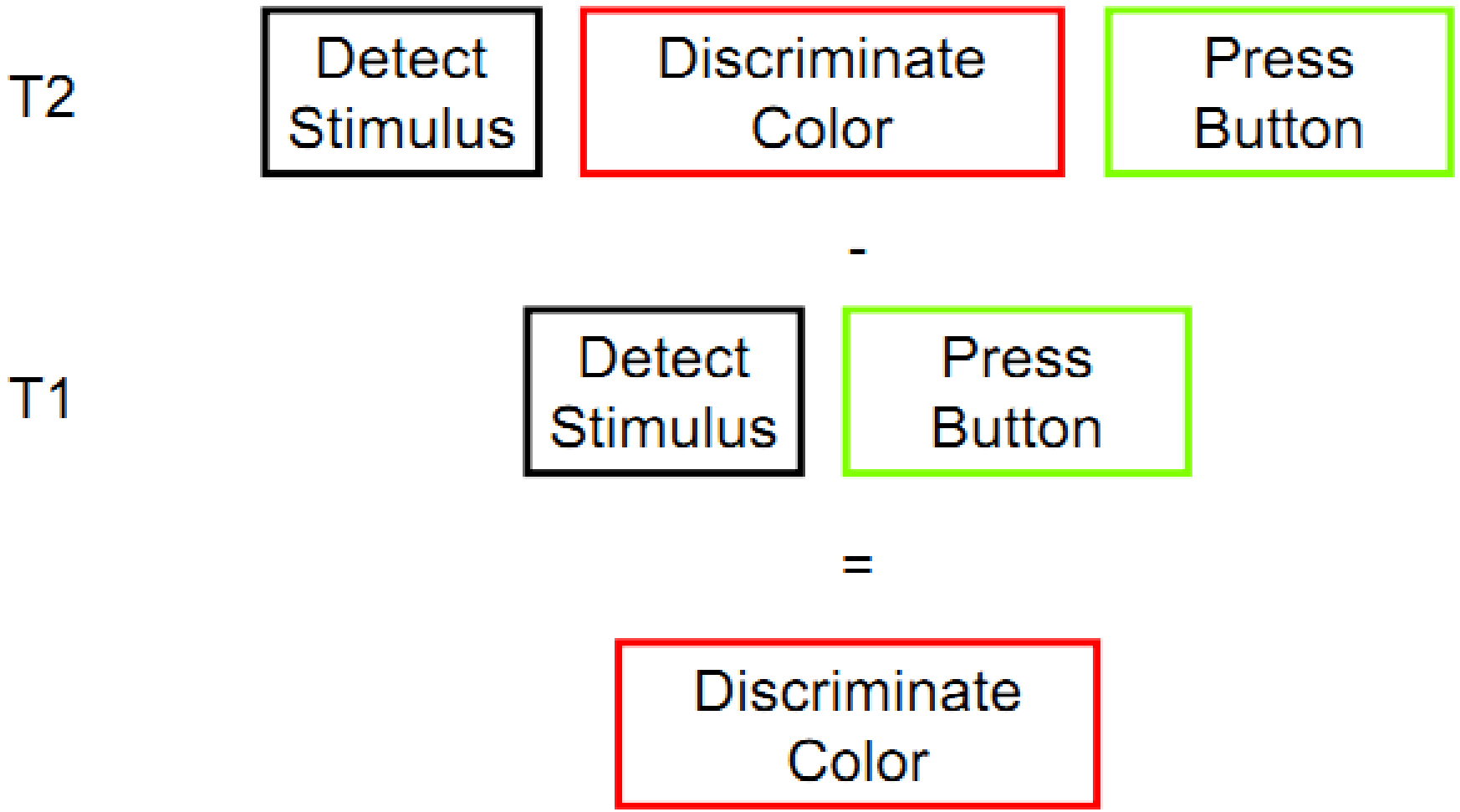


T3: Choice Reaction Time

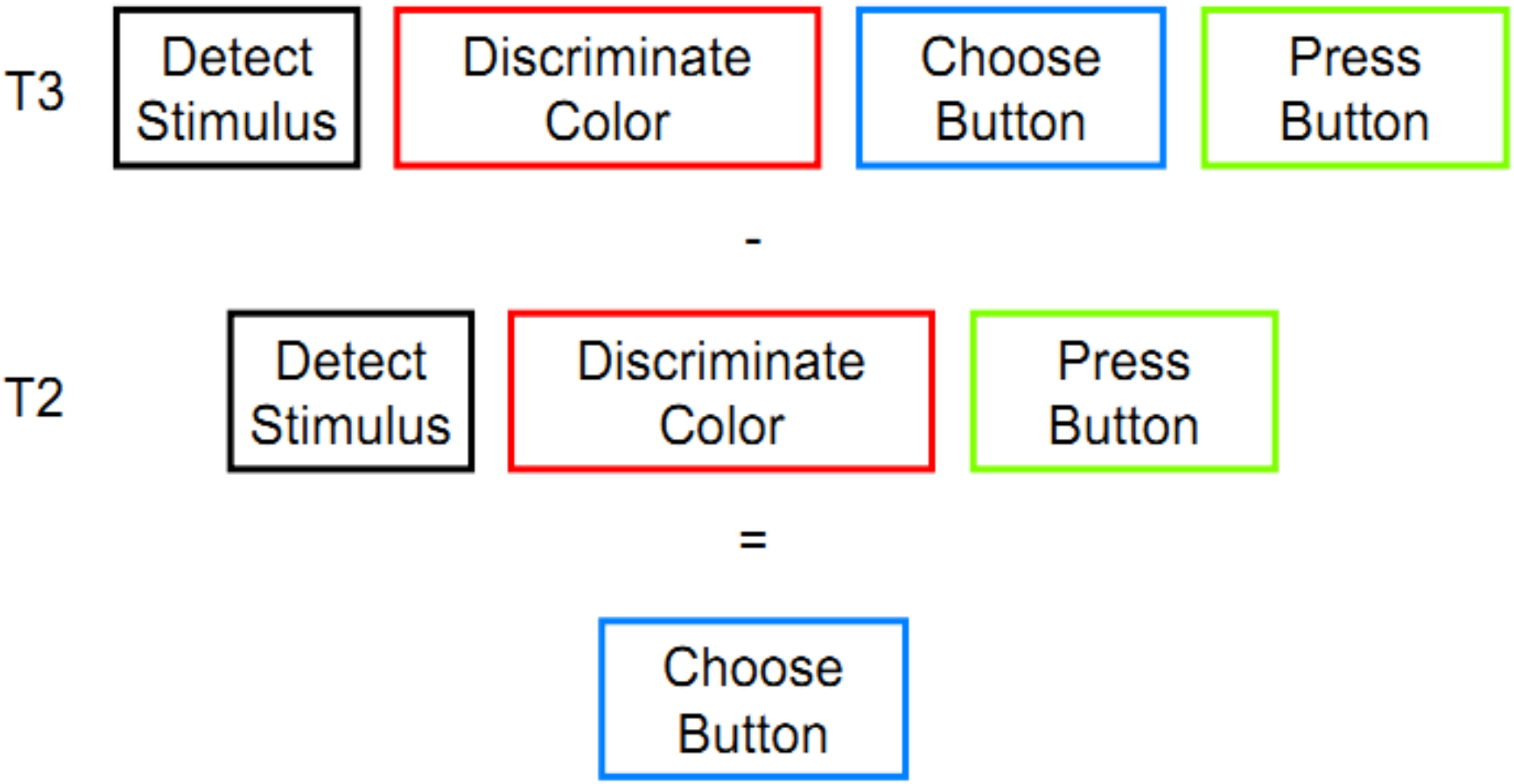
- Hit left button when light is green and right button when light is red



Simple Subtraction Method

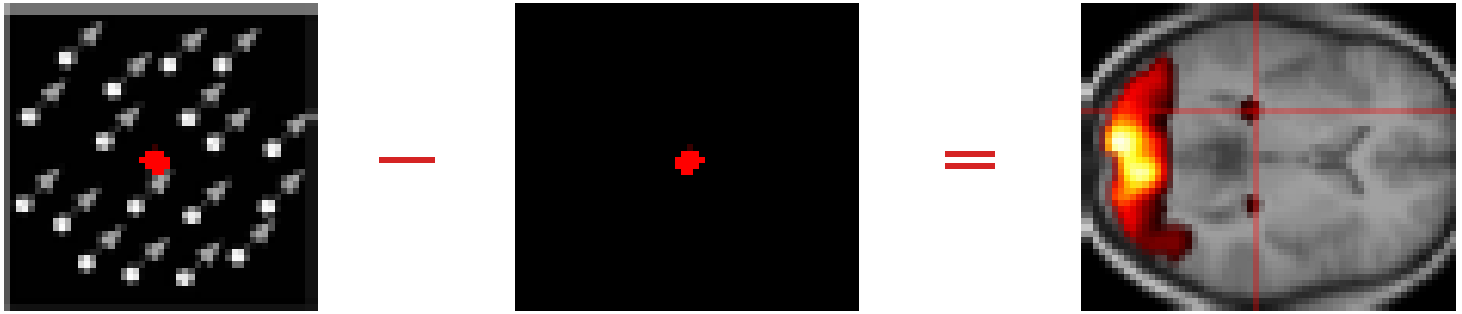


Simple Subtraction Method



Simple subtraction

- you can identify functionally specialised regions with regionally specific activation differences



moving dots — fixation =

Serial Subtraction Method

Serial subtraction

Question: Is inferior temporal cortex (IT) involved in phonological retrieval during object recognition?

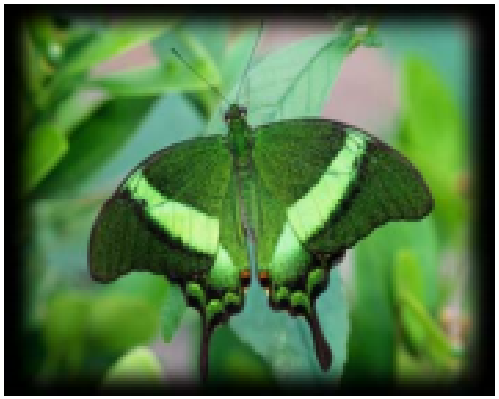
Cognitive processes

⇒ visual analysis: occipital cortex

⇒ object recognition: ???

⇒ phonological retrieval: ???

⇒ verbal output: Broca's area

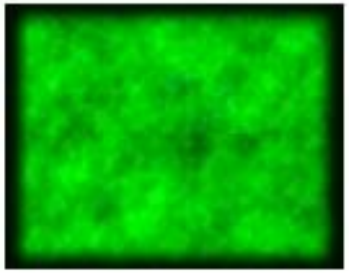


Subtraction Method

Experimental design

A say „yes“ when you see an abstract image

(*vis. analysis, verbal output*)



⇒ yes

B say „yes“ when you see a concrete object

(*vis. analysis, object recognition, verbal output*)

⇒ yes

C name concrete object

(*vis. analysis, object recognition, phonological retrieval, verbal output*)

⇒ butterfly

Subtraction Method

A visual analysis verbal output	----------
B visual analysis object recognition verbal output	C visual analysis object recognition phonological retrieval verbal output

B - A ⇒ significant IT activation ⇒ object recognition!

C - B ⇒ no significant IT activation ⇒ no evidence for IT involvement in phonological retrieval!

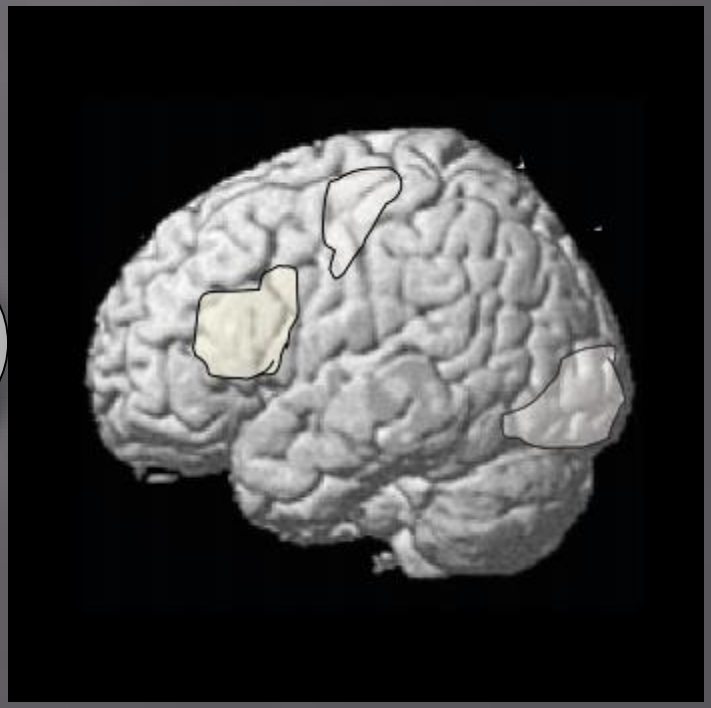
Conjunction Method

Find the Commonalities

Conjunction Method

Find the Commonalities

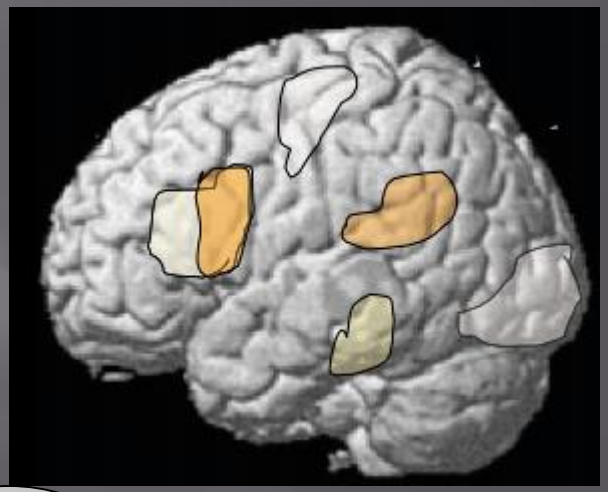
Task **A**



Conjunction Method

Find the Commonalities

Task **A**

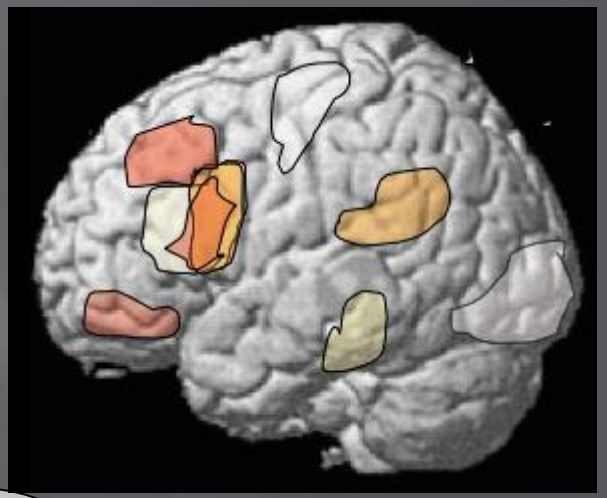


Task **B**

Conjunction Method

Find the Commonalities

Task **A**



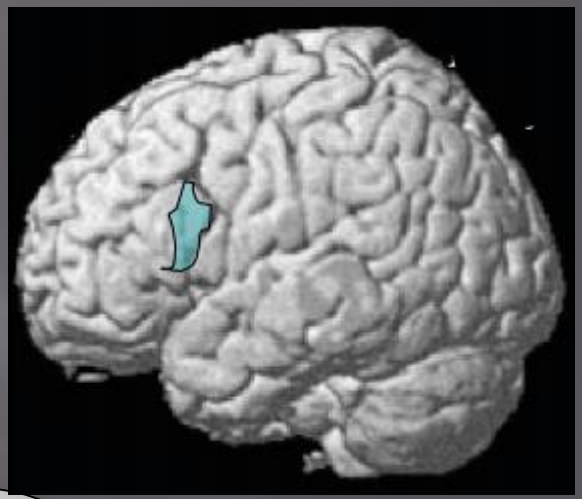
Task **B**

Task **C**

Conjunction Method

Find the Commonalities

Task **A**



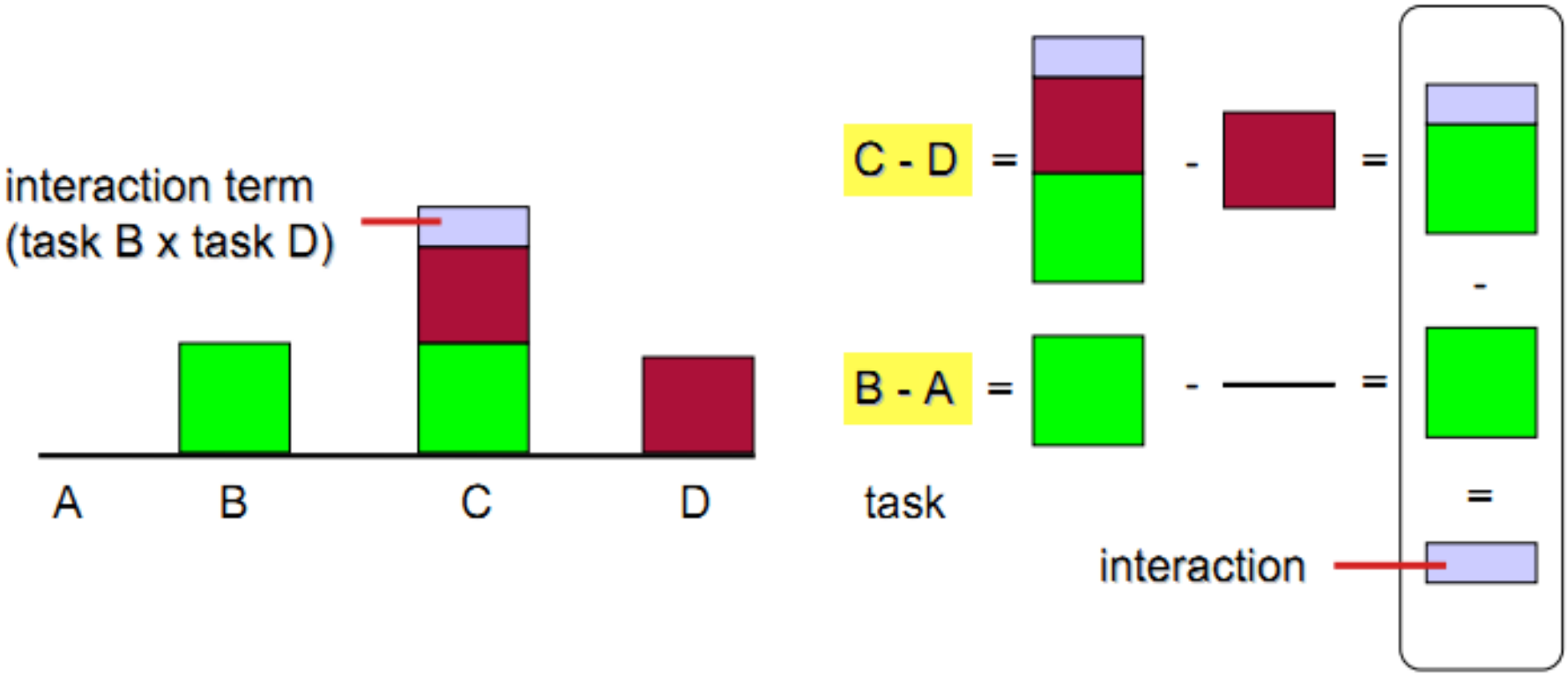
Task **B**

Task **C**

2- Factorial Design

Background

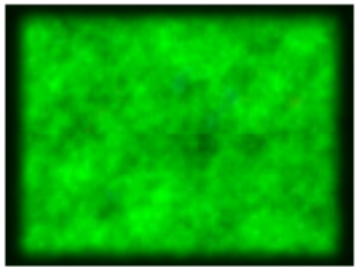
- "the whole is more than just the sum of its parts"
- cognitive processes are interdependent ⇒ task A interacts with task B, A modulates sensitivity to B ...



Factorial Design

D Name colour of abstract image

(*vis. analysis, phonological retrieval, verbal output*)



⇒ green

	no phonolog. retrieval	phonolog. retrieval
no object recogn.	**A** visual analysis verbal output	**D** visual analysis phonological retrieval verbal output
object recognit.	**B** visual analysis object recognition verbal output	**C** visual analysis object recognition phonological retrieval verbal output

Interaction: (C - D) – (B - A) ⇒ significant IT activation

- phonological retrieval modulates IT response to object recognition
  ⇒ IT also involved in phonological retrieval!

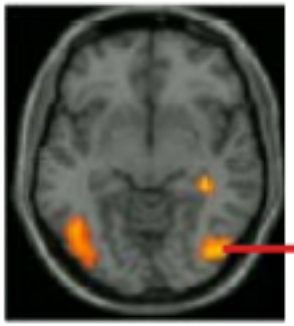
Parametric Design

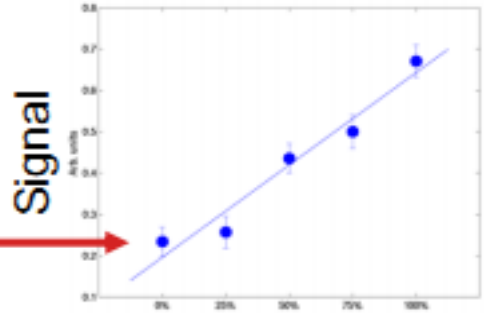
	cognitive processes
categorical/factorial designs	binary
parametric designs	continuous

Systematic variation of regional activation with endo-/exogenous parameters

⇒ task stays the same while the amount of processing varies; thus, changes to the nature of the task are less of a problem

⇒ you can test for both linear (i.e.level of sensorimotor/cognitive processing) and non-linear effects (i.e. time effects)





Rose et al. (2005). *Cerebral Cortex*.

Example 1: linear activation increase in LOC with increasing object visibility!

Parametric Design

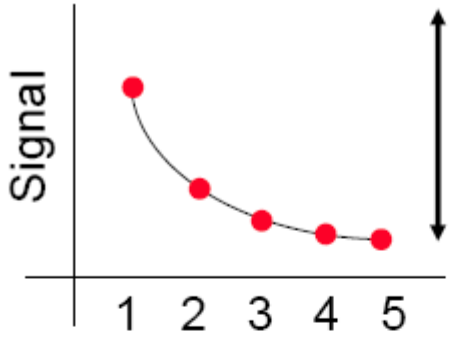
Variables Studied:

Sensory: Flicker Frequency, Speech Presentation Rate, Stimulus intensity and pain

Motor: Tapping Rate

Cognitive : Attention Load, Working Memory Load

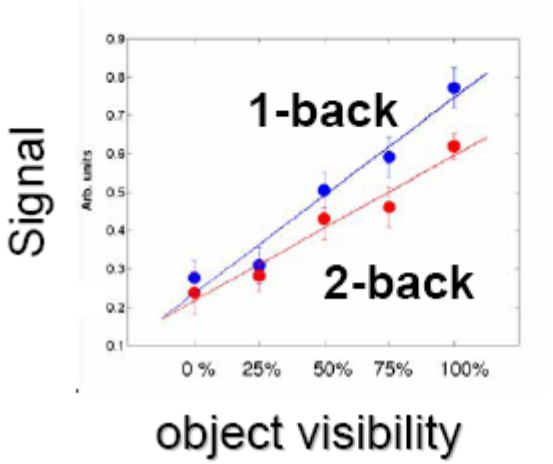
Parametric Design



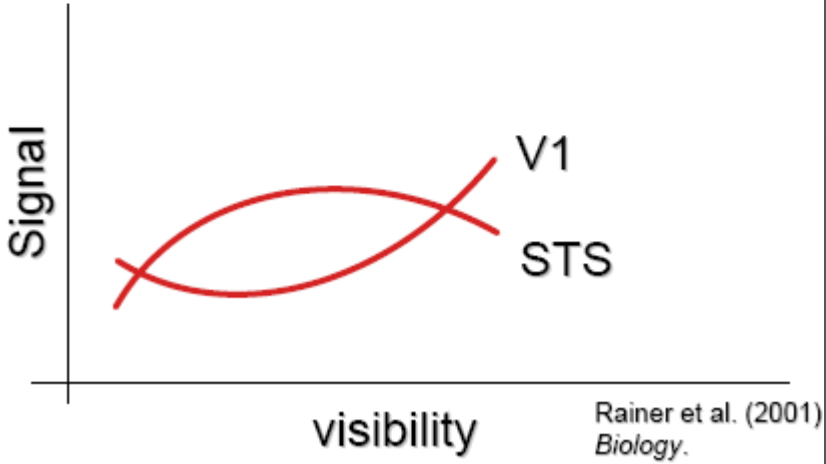
Example 2: Non-linear decrease of prefrontal activation over time during procedural learning!

Combining parametric and factorial designs

linear interaction



non-linear interaction



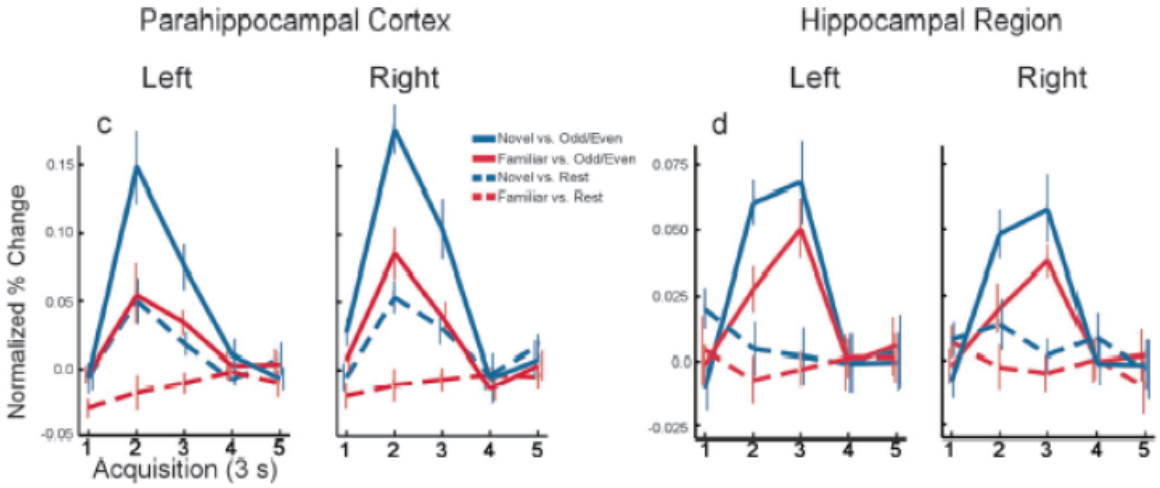
Rainer et al. (2001) *Biology*.

Control Condition

Problem

- fMRI = contrastive method

  ⇒ for many designs, you need to include adequate control conditions



Stark & Squire (2001) – When zero is not zero... *PNAS*, 98(22), 12760-12766.

„Rest“ = often substantial activation in many areas!

⇒ reason: mental imagery / rehearsal / eye movements…

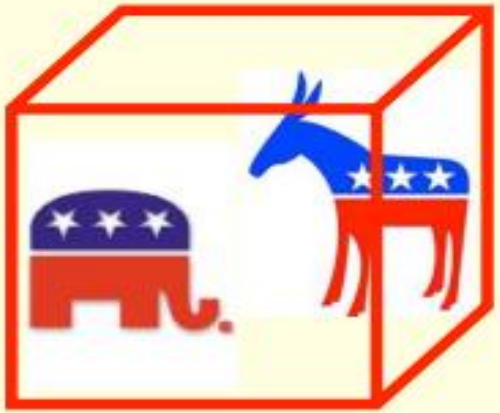
⇒ loss of sensitivity!

Adaptation in fMRI

Two stimuli: can neurons tell the difference?

- A voxel containing neurons that respond to all politicians, irrespective of party

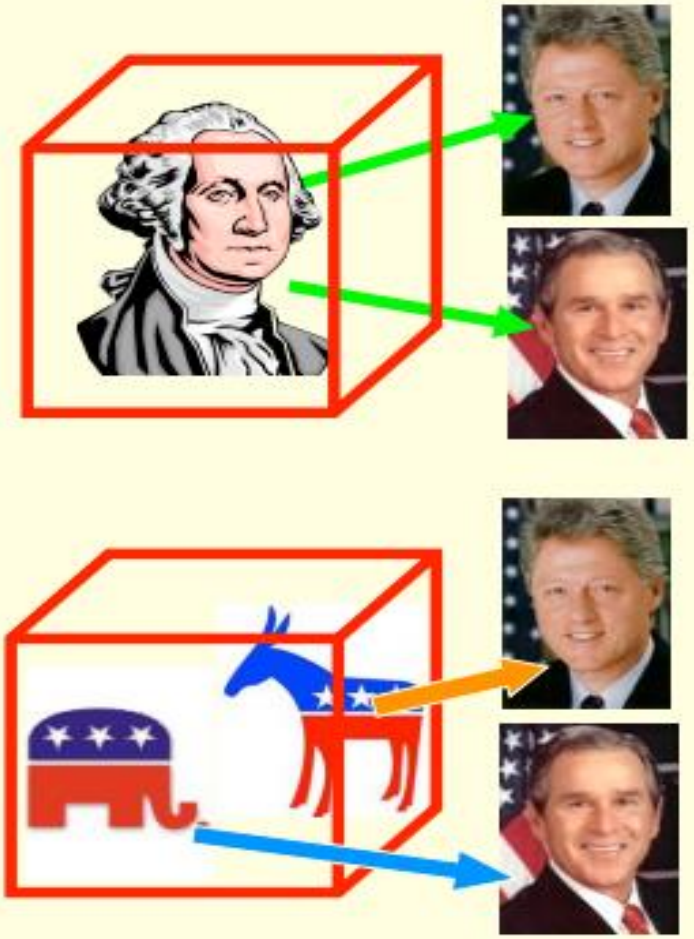
- A voxel containing some specifically Democratic neurons, and other specifically Republican neurons.



From R. Raizada

Adaptation in fMRI

Responses to individual stimuli do not show whether neurons can tell the



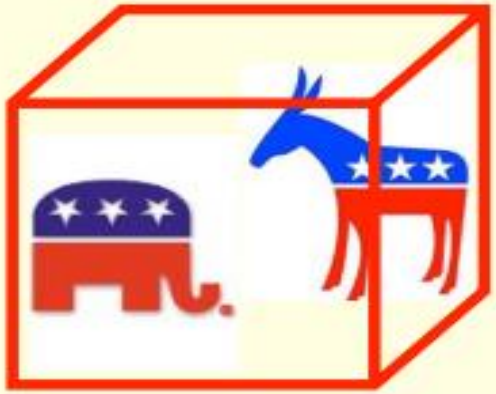
- Different sets of neurons are active within the voxel, but overall fMRI responses are indistinguishable

From R. Raizada

Adaptation in fMRI

Neural adaptation to repeated stimuli does show the difference:
What counts as repetition for neurons in a voxel?

Same neurons, adapting:
It's a politician again



Different, fresh neurons:
It's a Democrat

From R. Raizada

2- Trail Timing (Design types)

Blocked Designs

Event-Related Designs

Intermixed Designs

Goal of Design

- Goal of the design: optimization (efficiency)

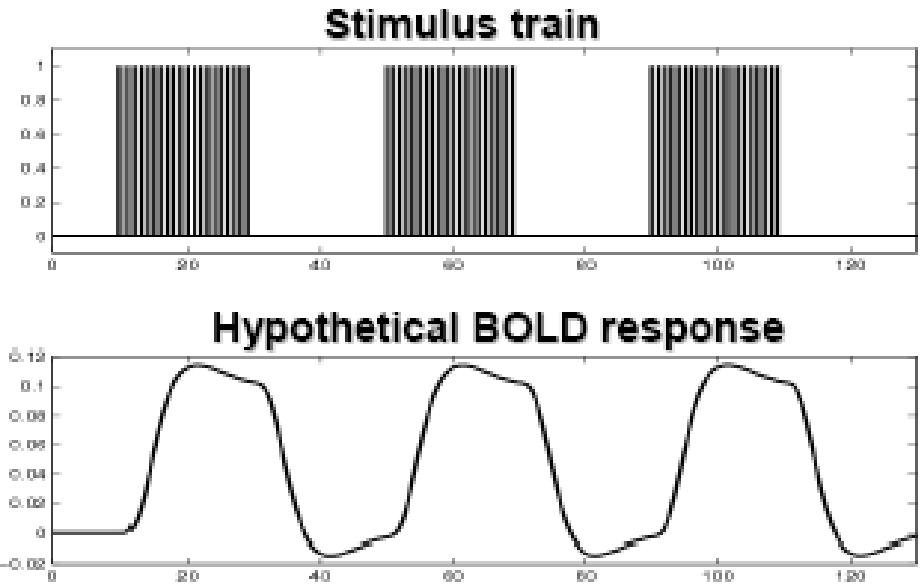
⇒ Have a sufficiently high frequency (avoid noise)

⇒ Increase the number of observations (statistical design)

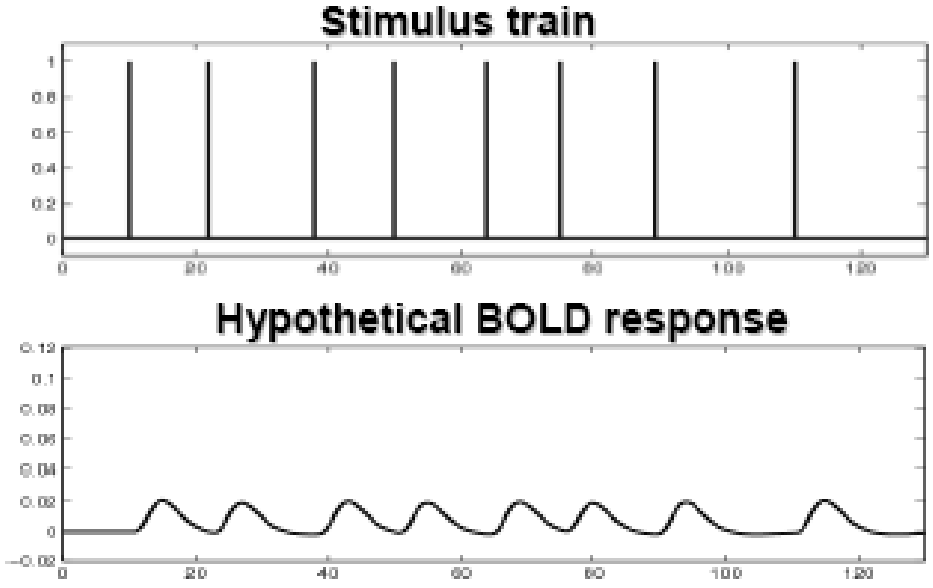
⇒ Increase the variability (NRJ = Σ signal^2 = f(var)), i.e. decrease the overlap between same BOLD responses & increase the differential overlap (event-related design)

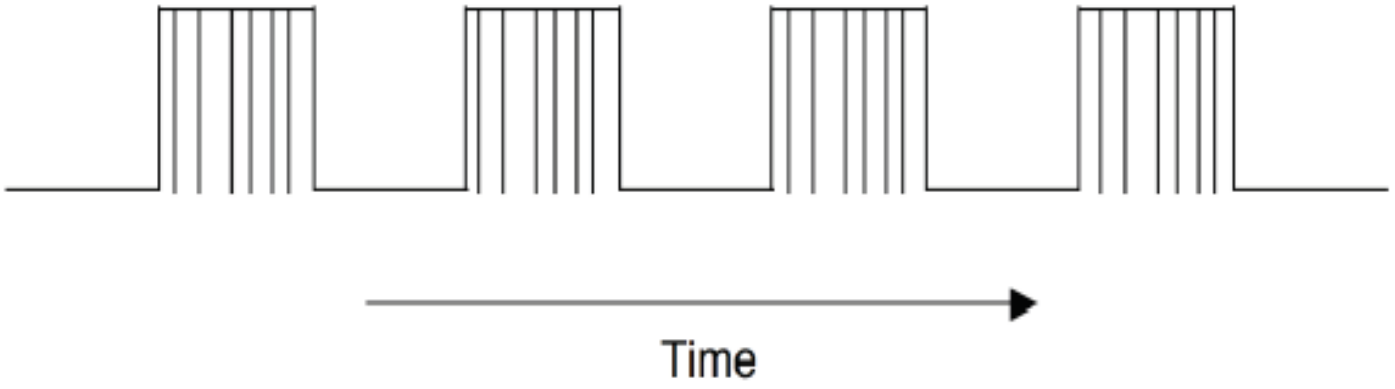
Trail Timing (Design types)

Block Design



Event-Related Design

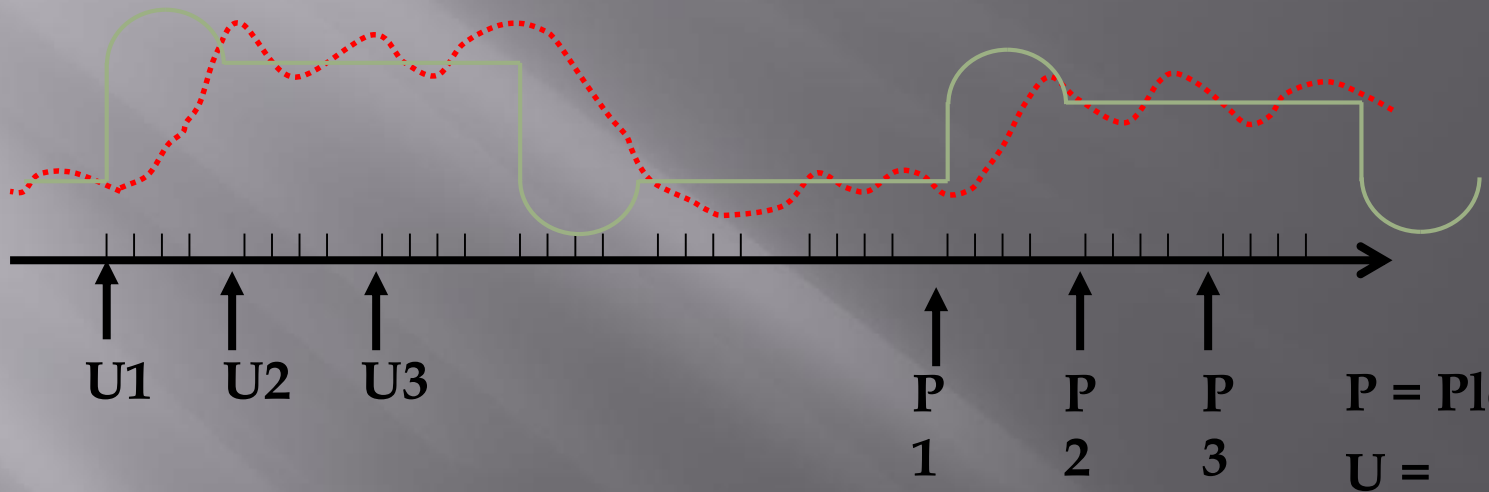




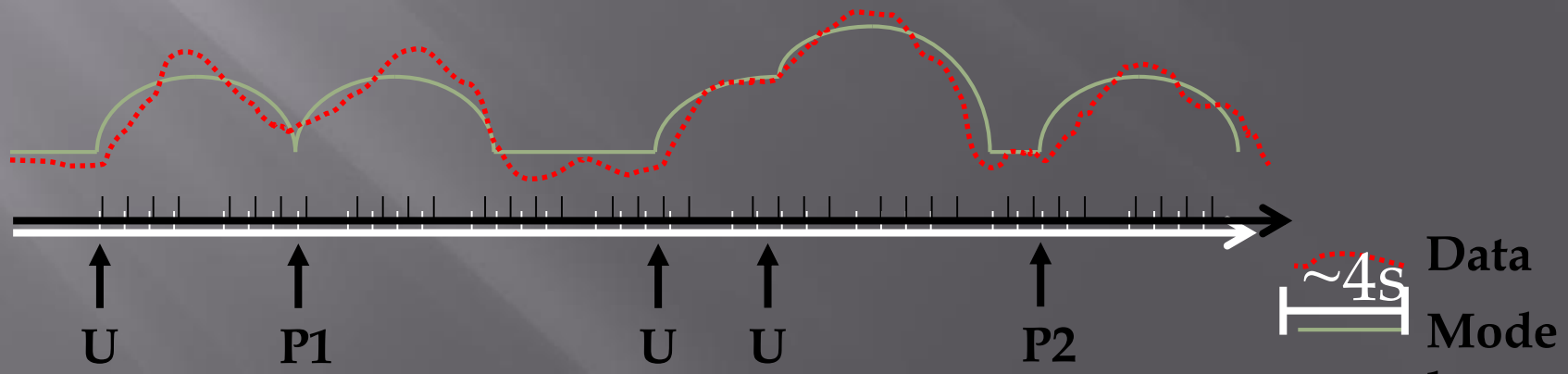
mixed

Designs: Block/epoch- vs event-related

Block/epoch designs examine responses to series of similar stimuli

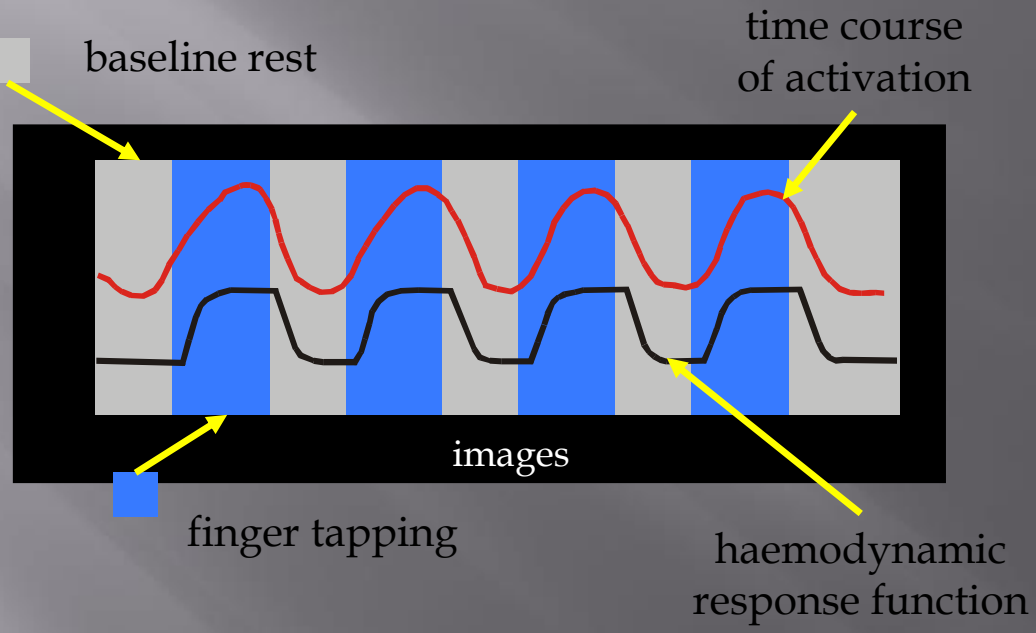


Event-related designs account for response to each single stimulus



Block Design

Consider the simplest case, a block design with two conditions
e.g. **alternate tapping of two fingers vs. rest**
let's assume 2 sec/volume



How long should a run be?

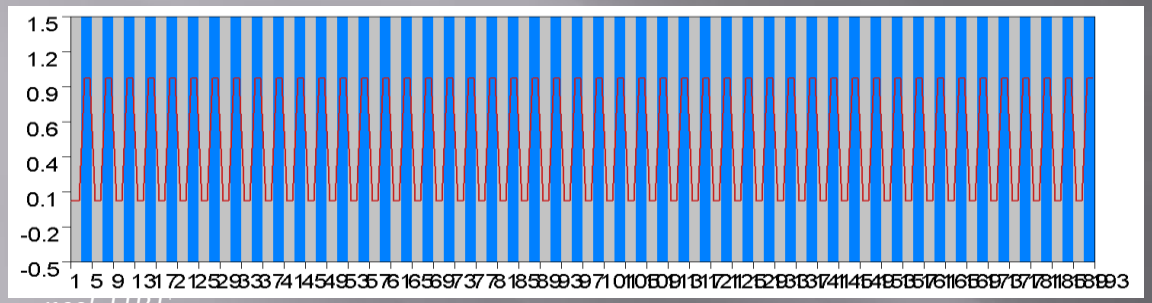
- Short enough that the subject can remain **comfortable** without moving or swallowing.
- Long enough that you're not wasting a lot of time restarting the scanner.
- Ideal is ~5 ± 2 minutes

Source: Jody Culham's web slides

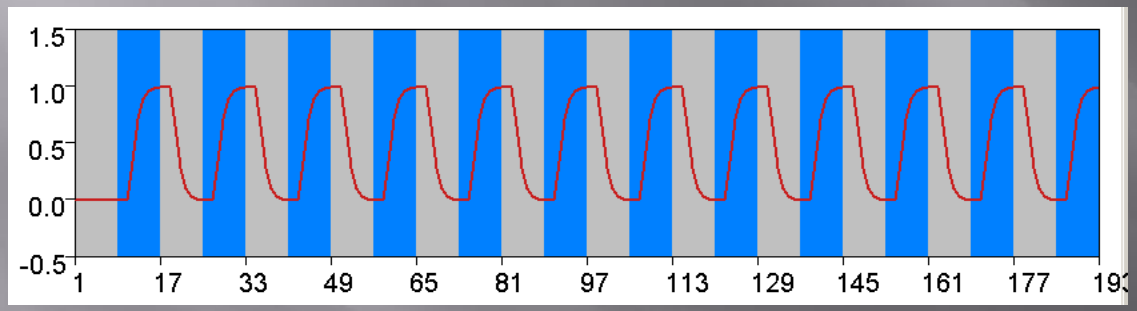
Block Design

How fast should the conditions cycle?

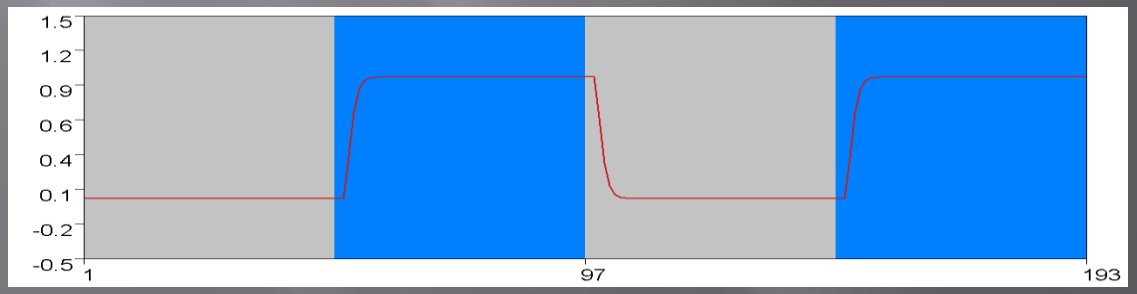
pre-HRF



post-HRF



post-HRF



Every 4 sec (2 images)

- signal amplitude is weakened by HRF
- not too far from range of breathing frequency (every 4-10 sec) → could lead to respiratory artifacts

Every 16 sec (8 images)

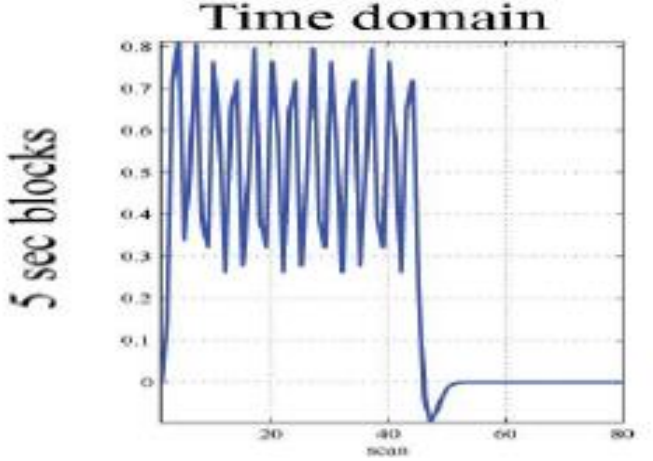
- allows enough time for signal to oscillate fully
- not near artifact frequencies
- a reasonable time for subjects to keep doing the same thing

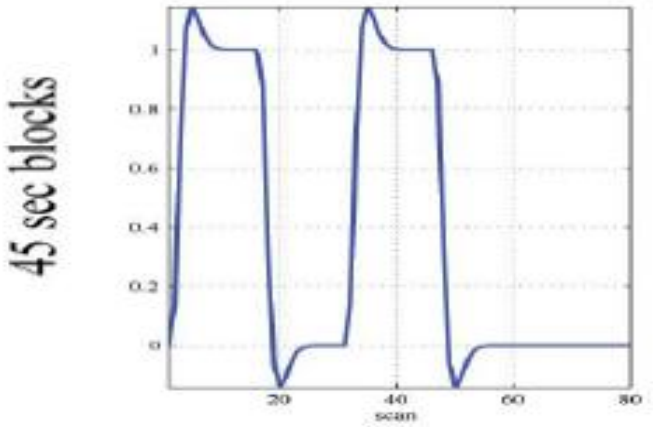
Every 96 sec (48 images)

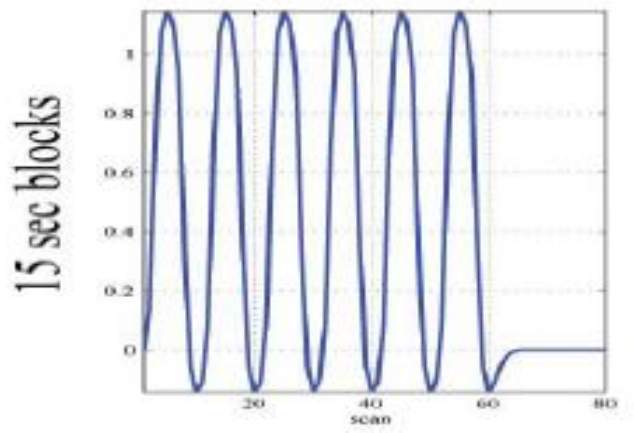
- more noise at low frequencies
- linear trend confound
- subject will get bored
- very few repetitions – hard to do eyeball test of significance

Block Design Optimization

we want short ISI and Long Blocks







Advantages of event-related fMRI

confounds of blocked designs

(Johnson et al 1997)

Advantages of event-related fMRI

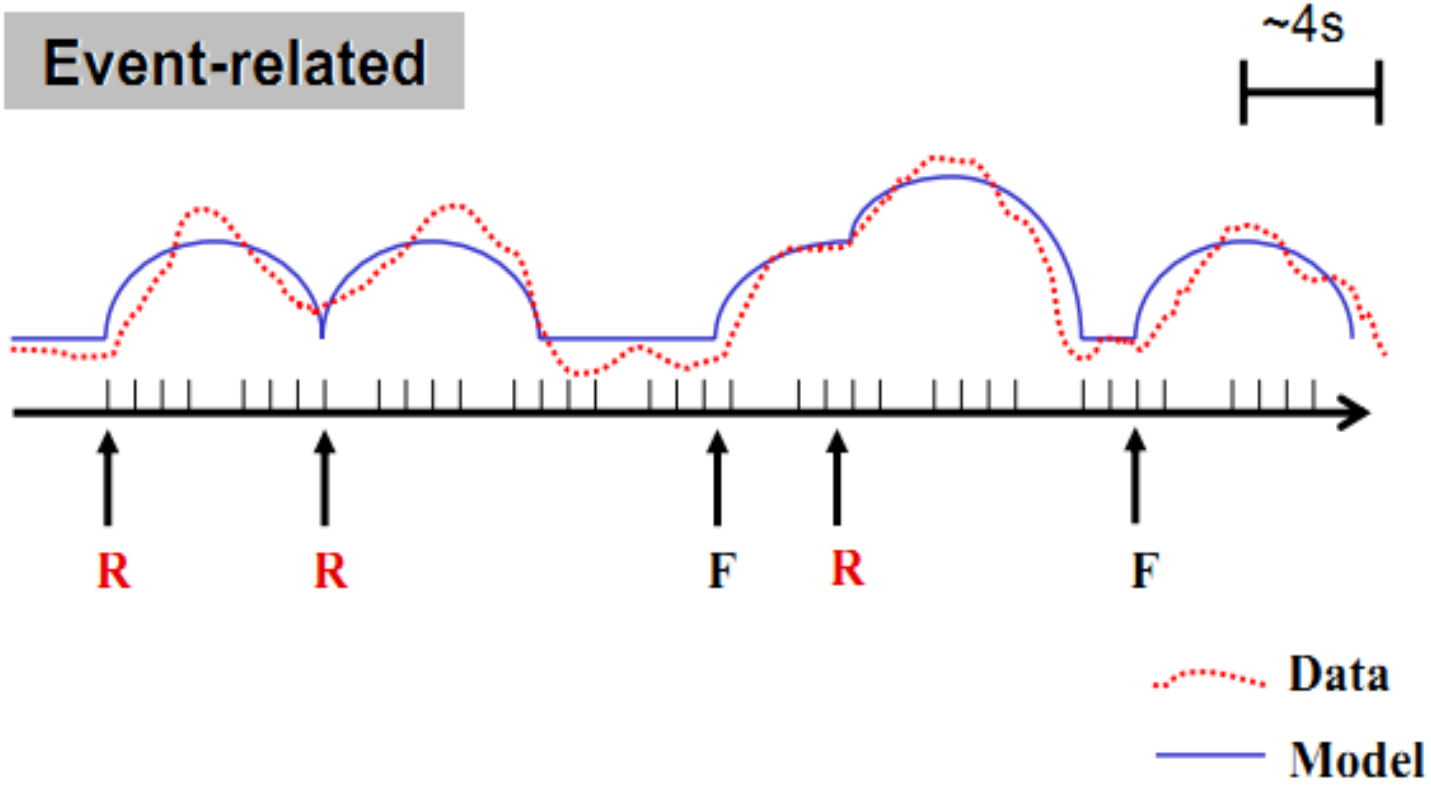
1. **Randomized trial order:** *confounds of blocked designs (Johnson et al 1997)*

2. **Post hoc / subjective classification of trials** *e.g, according to subsequent memory (Gonsalves & Paller 2000)*

Advantages of event-related fMRI

R = Words Later Remembered

F = Words Later Forgotten



Slide from Rick Henson

Advantages of event-related fMRI

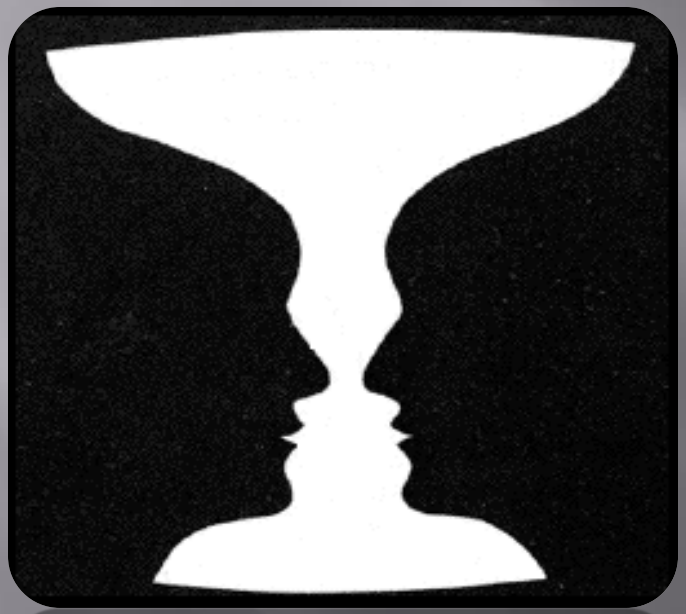
1. **Randomized trial order:** *confounds of blocked designs (Johnson et al 1997)*

2. **Post hoc / subjective classification of trials** *e.g, according to subsequent memory (Gonsalves & Paller 2000)*

3. **Some events can only be indicated by subject (in time)**

e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)

Advantages of event-related fMRI



Bistable Perception

Advantages of event-related fMRI

1. **Randomized trial order:** *confounds of blocked designs (Johnson et al 1997)*

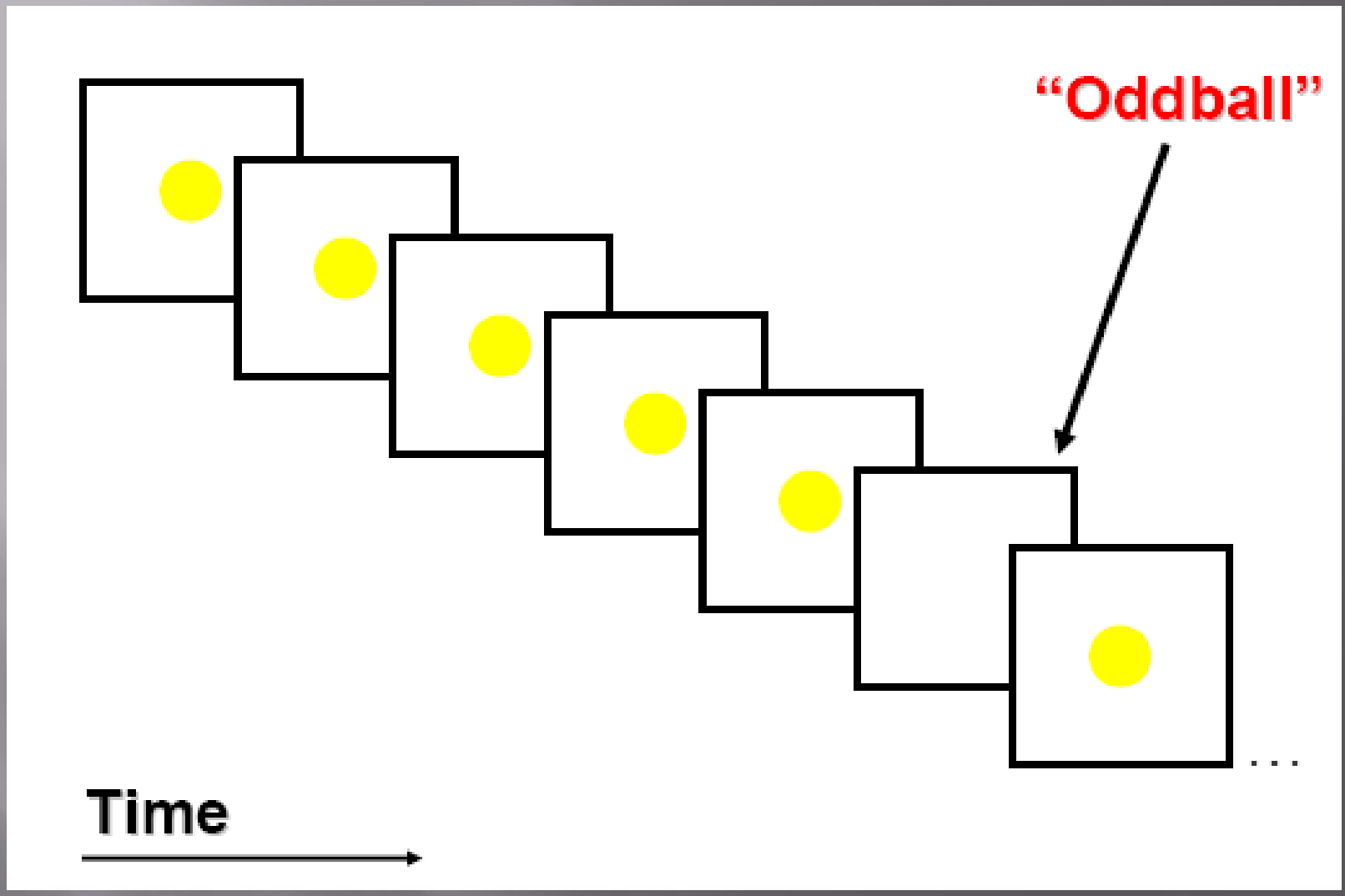
2. **Post hoc / subjective classification of trials** *e.g, according to subsequent memory (Gonsalves & Paller 2000)*

3. **Some events can only be indicated by subject (in time)**

   e.g, spontaneous perceptual changes (Kleinschmidt et al 1998)

4. **Some trials cannot be blocked due to stimulus context or interactions**

   e.g, "oddball" designs (Clark et al., 2000)


"Oddball"
...
Time

Modeling block designs: epochs vs events

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

Modeling block designs: epochs vs events

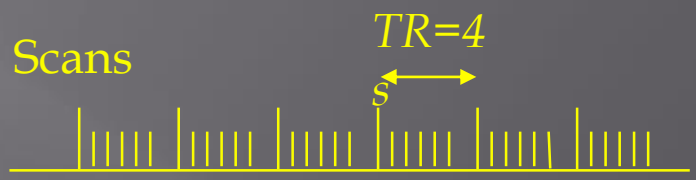
- Epochs are periods of sustained stimulation

Modeling block designs: epochs vs events

- **Events are impulses (delta-functions)**

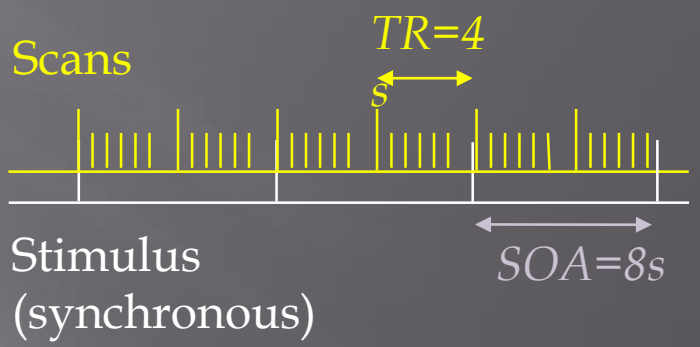
Timing Issues

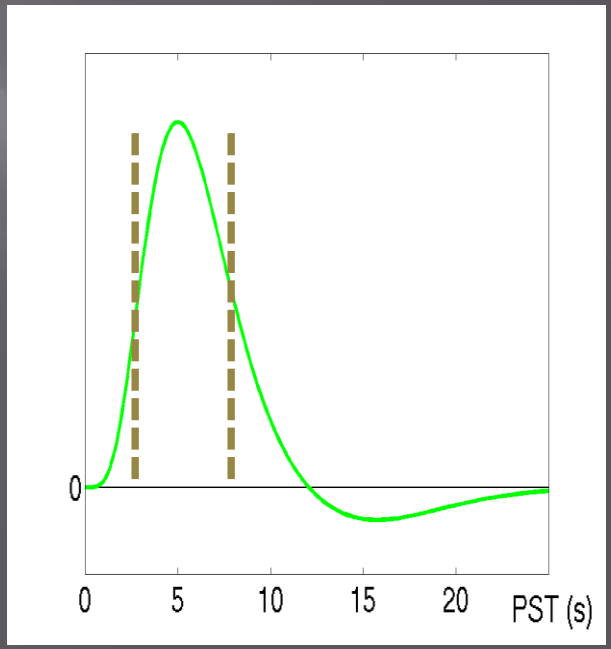
- Typical TR for 60 slice EPI at 3mm spacing is ~ 4s



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

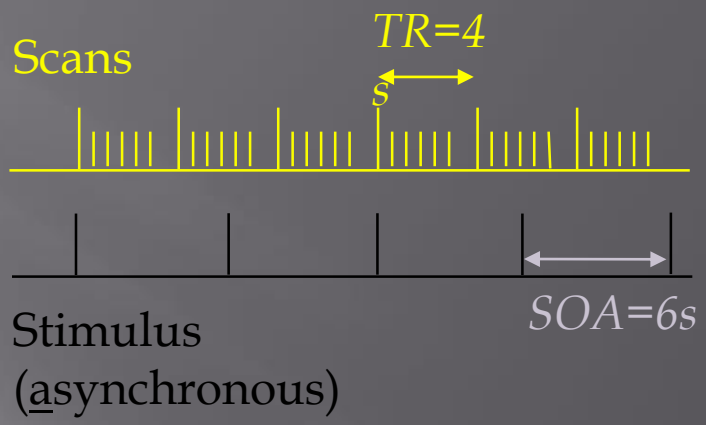


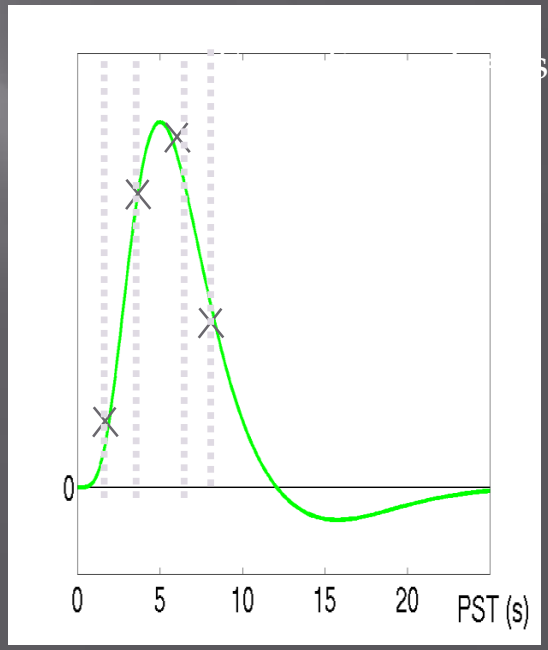


Timing Issues

- 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*



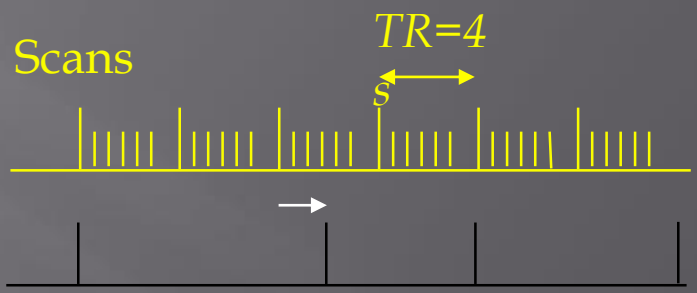


Timing Issues

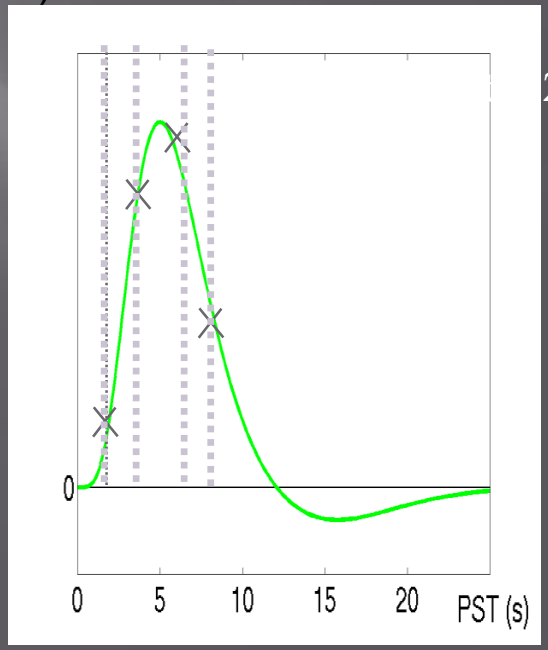
- Typical TR for 48 slice EPI at 3mm spacing is ~ 4s
- Sampling at [0,4,8,12…] post-stimulus may miss peak signal
- Higher effective sampling by:

1. Asynchrony
   e.g., *SOA=1.5TR*

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



Stimulus (random jitter)



fMRI Designs and Efficiency

- 1- Choose your design and task according to your Hypothetic topic
- 2- consider:
  - Block design for Detection
  - Event-related design for Estimation
  - Mixed design for Estimation of events during different ‘states’
- 3- Think ‘frequency’, ‘decorrelation’, and ‘sequence order’

fMRI Designs and Efficiency

Optimize the covariance matrix = increase the variability

- $Y = X\beta + e$ (data=model*reg coef + error)
- $\hat{\beta} = (X^T X)^{-1} X^T Y$ (we search β)

- $\gamma = C\hat{\beta}$ (contrast = combination of $\hat{\beta}$)
- $t = \gamma / (\text{std} * \text{sqrt}(C (X^T X)^{-1} C^T))$ (usual t-test effect / error)

'noise' variance and design variance