fMRI Experimental Design
-- a Linear System Perspective

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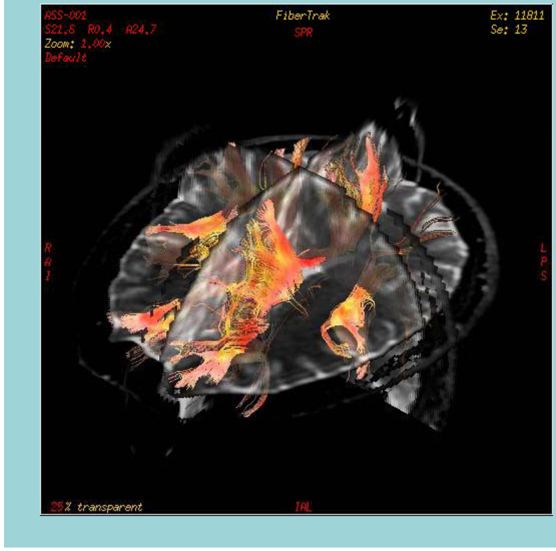
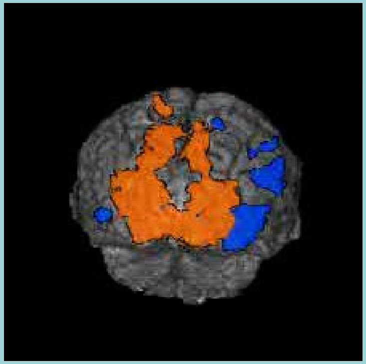
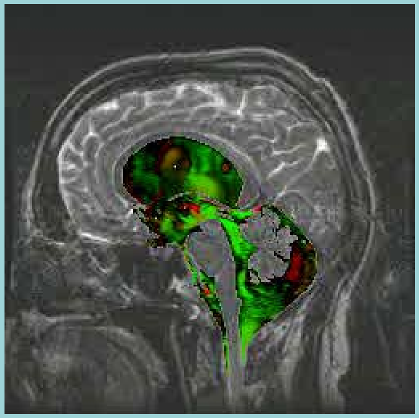
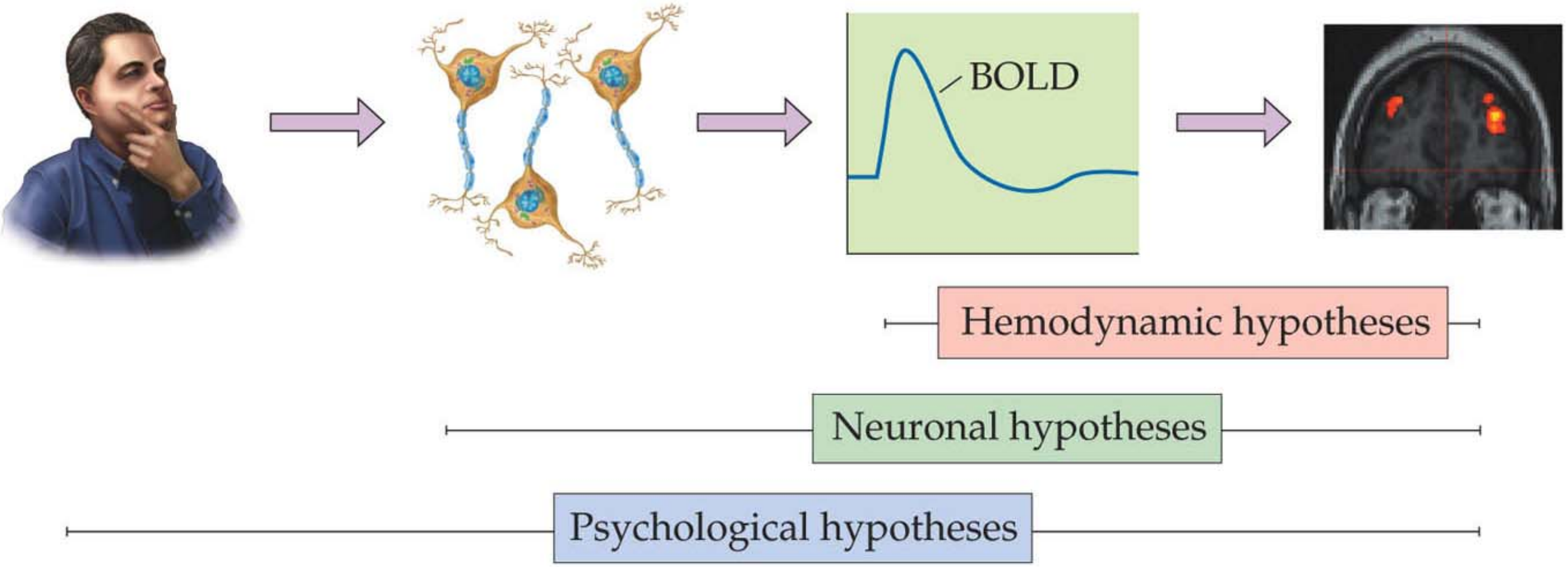








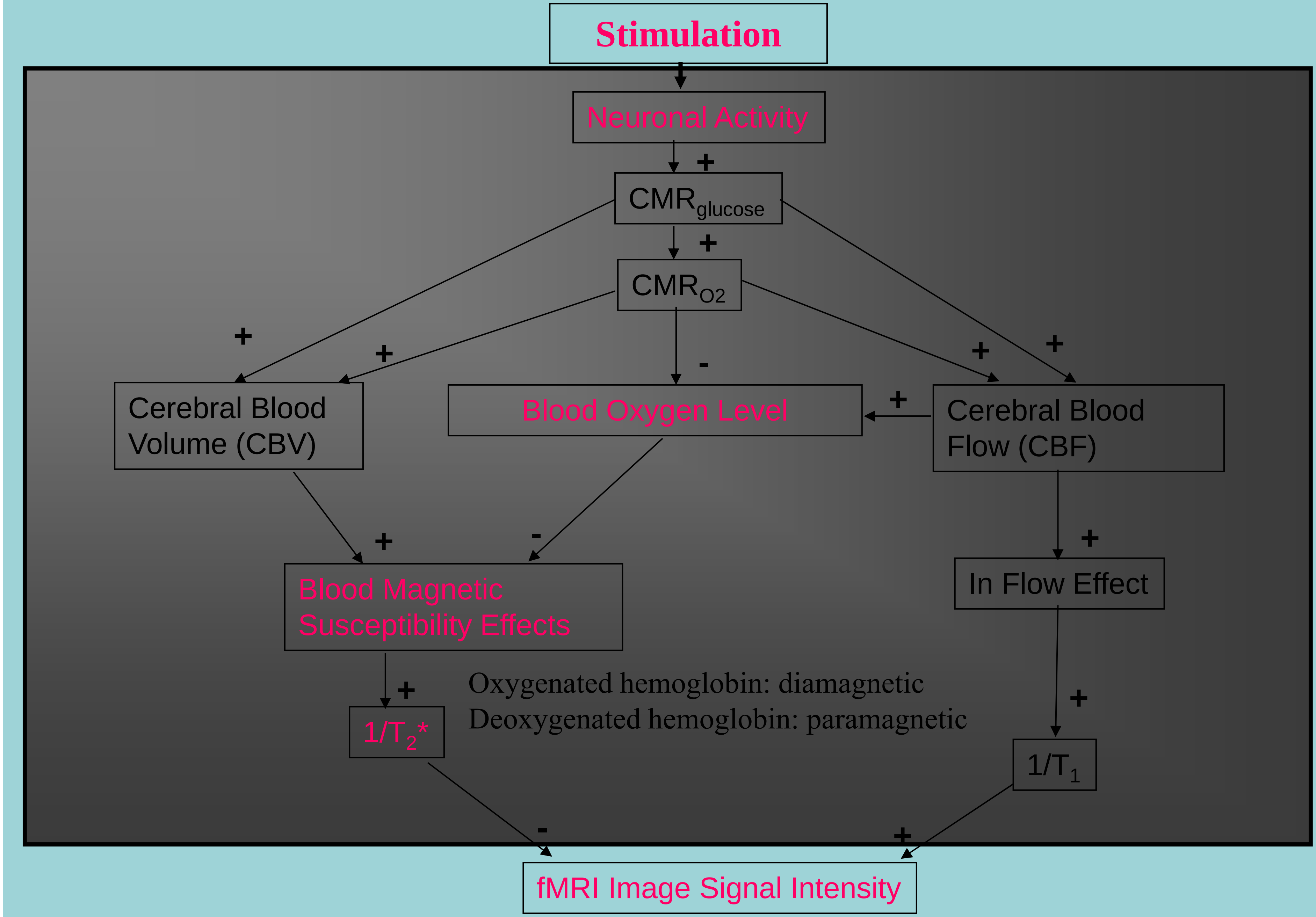
Hemodynamic hypotheses

Neuronal hypotheses

Psychological hypotheses

FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 11.3**

Mechanisms of BOLD (Blood Oxygen Level-Dependent) fMRI



Stimulation

Neuronal Activity

$CMR_{glucose}$

CMR_{O2}

Cerebral Blood Volume (CBV)

Blood Oxygen Level

Cerebral Blood Flow (CBF)

Blood Magnetic Susceptibility Effects

In Flow Effect

$1/T_2^*$

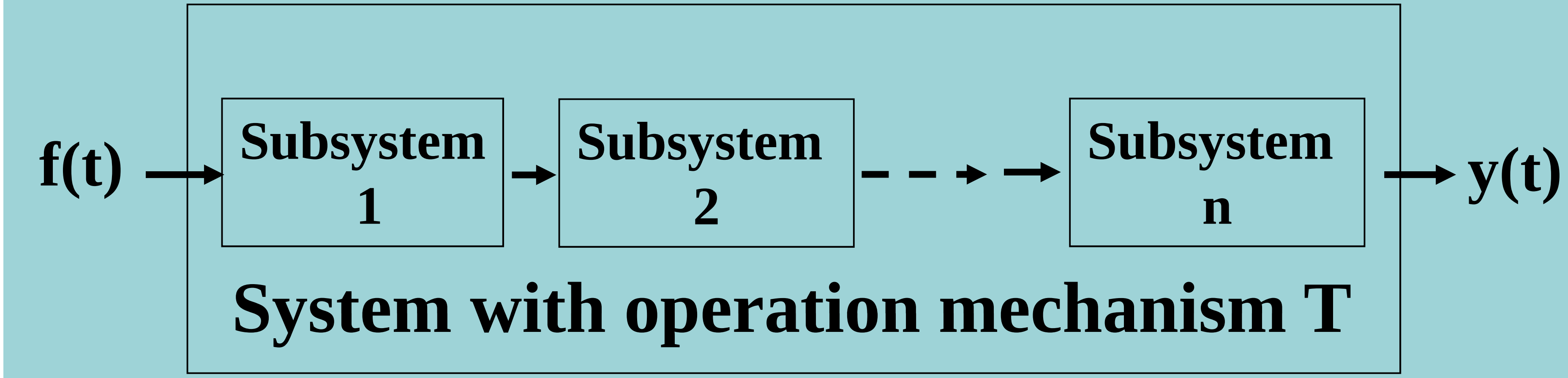
$1/T_1$

Oxygenated hemoglobin: diamagnetic

Deoxygenated hemoglobin: paramagnetic

fMRI Image Signal Intensity

Springer CS Jr, Patlak CS, Palyka I and Huang W. “Principles of susceptibility contrast-based functional MRI: …



f(t)

Subsystem 1

Subsystem 2

Subsystem n

y(t)

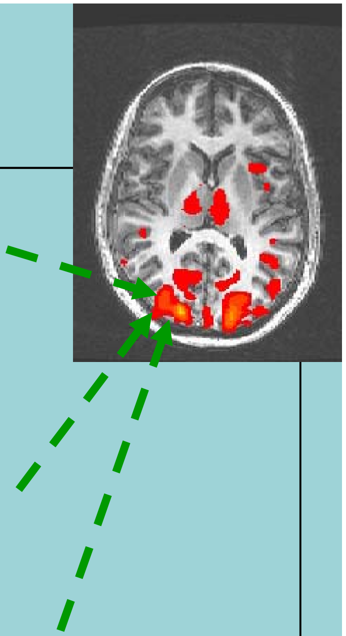
System with operation mechanism T

$$y(t) = T\{f(t)\}$$

(1) Find T => Event-related design

(2) Assume T' = T based on some model
Find expected y'(t) = T'{f(t)}
Compare y(t) and y'(t)
=> Block related design

Linear System



$$f(t) \longrightarrow \boxed{\text{System}} \longrightarrow y(t)$$

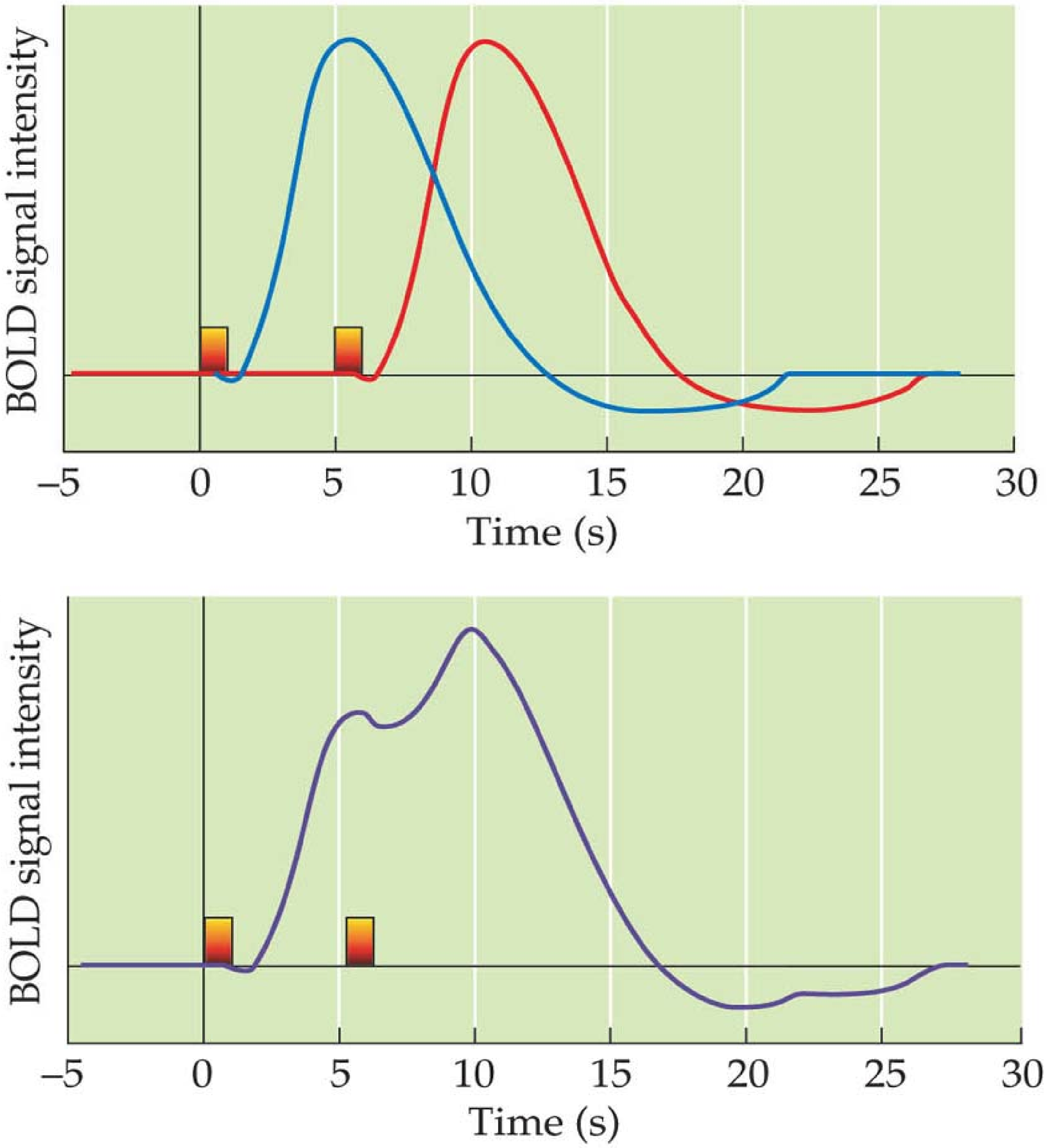
$$g(t) \longrightarrow \boxed{\text{System}} \longrightarrow z(t)$$

$$af(t) + bg(t) \longrightarrow \boxed{\text{System}} \longrightarrow ay(t) + bz(t)$$

$$f(t) \longrightarrow \boxed{\text{System}} \longrightarrow y(t)$$

$$f(t-t_0) \longrightarrow \boxed{\text{System}} \longrightarrow y(t-t_0)$$

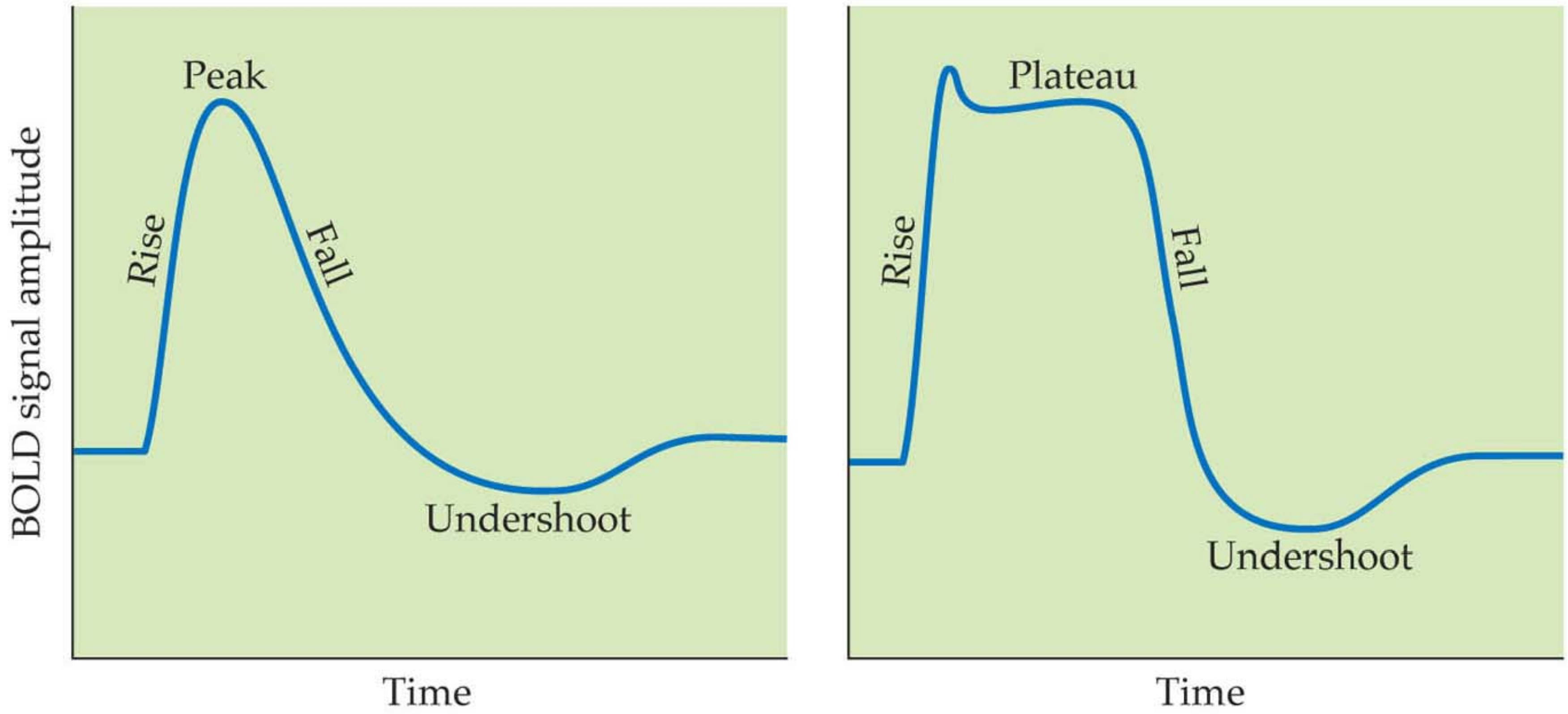
Linear Combination



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 8.16 (F

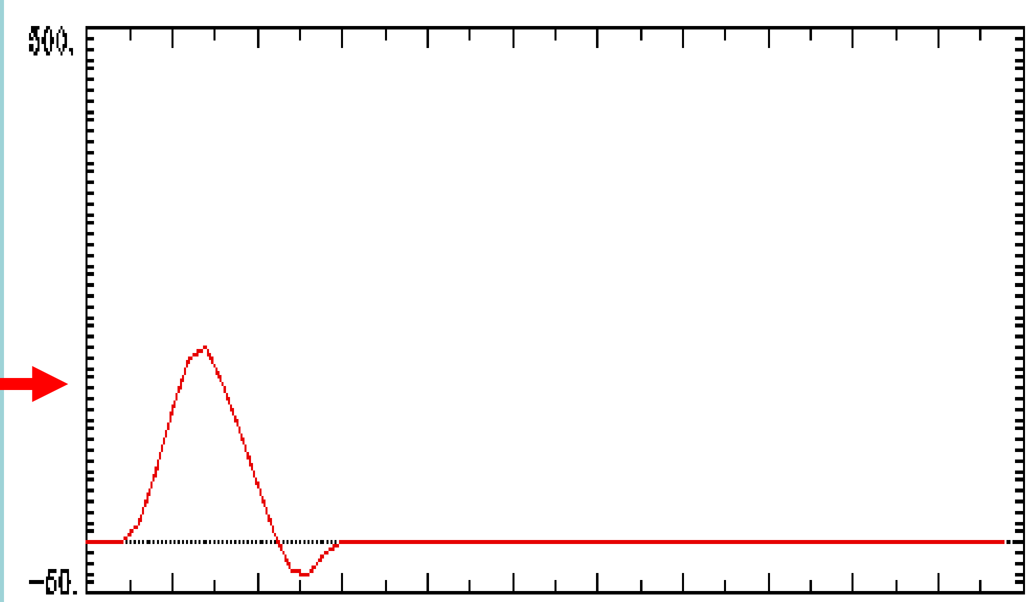
(A) A single short-duration event

(B) A block of multiple consecutive events



FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 7.15** © 2004 Sinauer Associates, Inc.

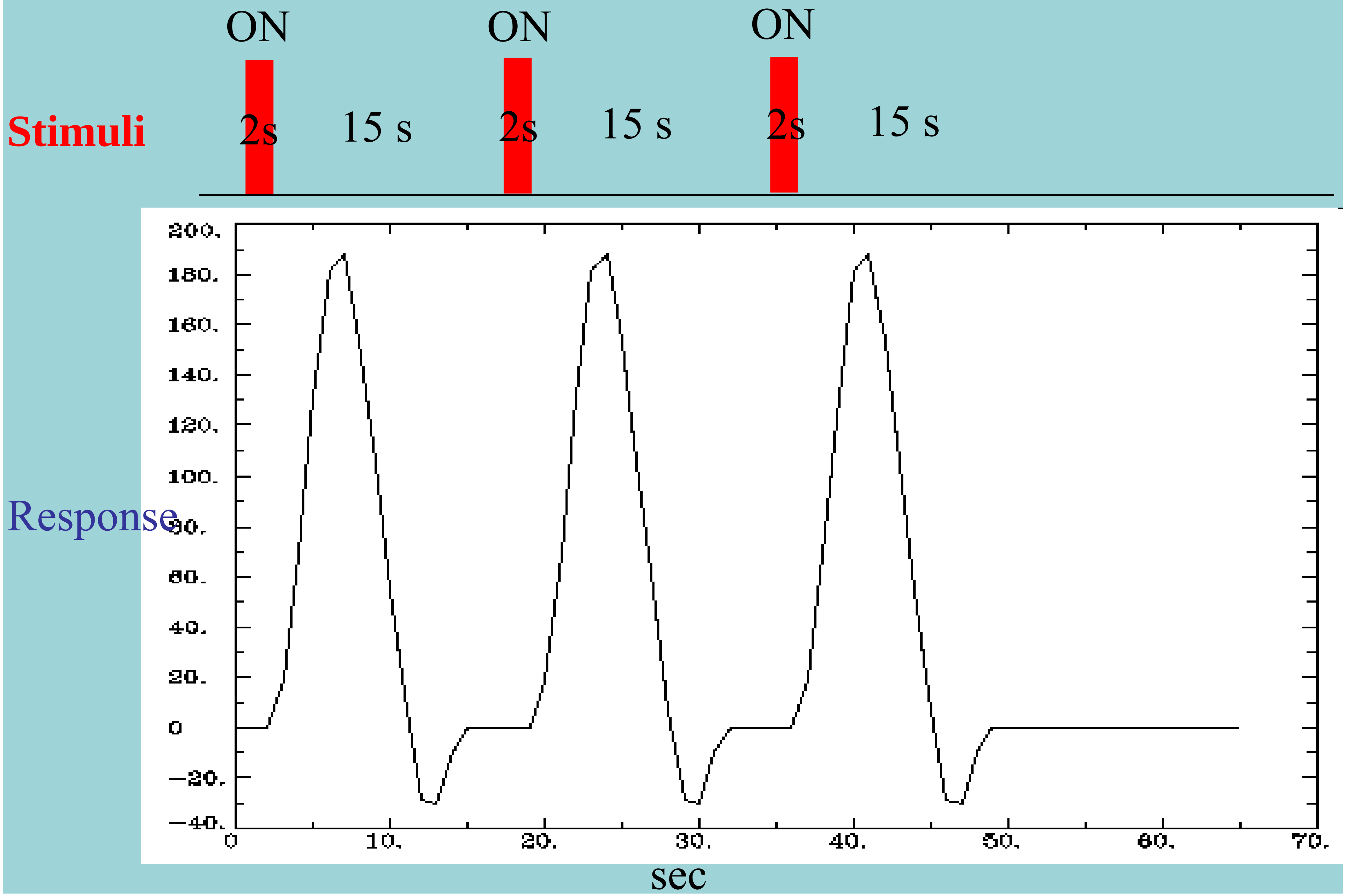
Present for 2 seconds



impulse → impulse response

$$\delta(t) \longrightarrow \boxed{\text{System}} \longrightarrow h(t)$$

Traditional (Slow) Event Related Design



Stimuli

ON 2s 15 s

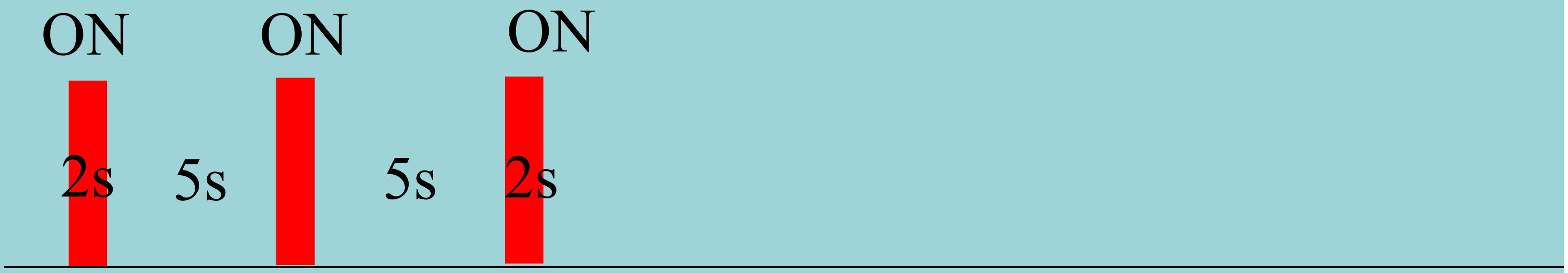
ON 2s 15 s

ON 2s 15 s

Response

sec

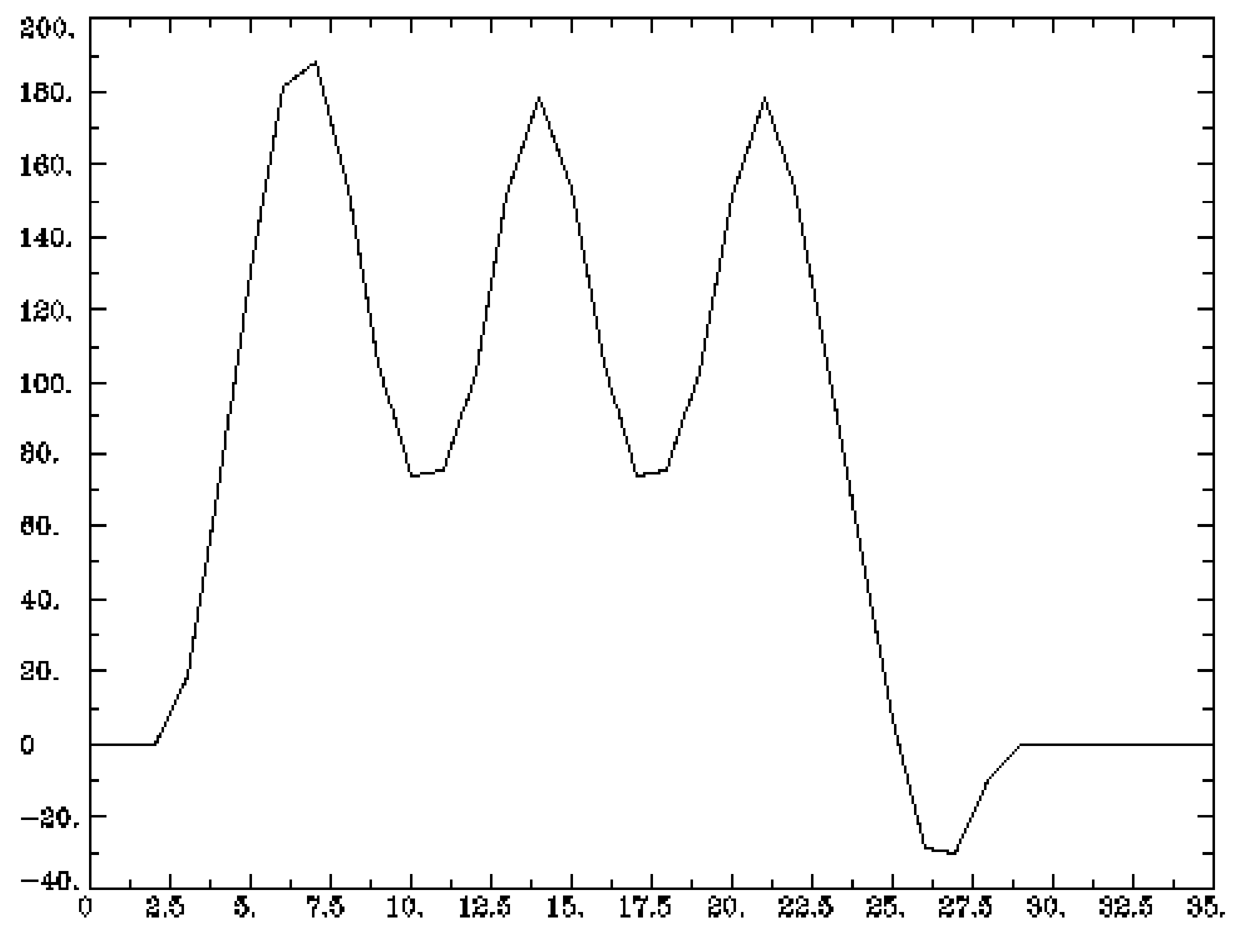
Stimuli



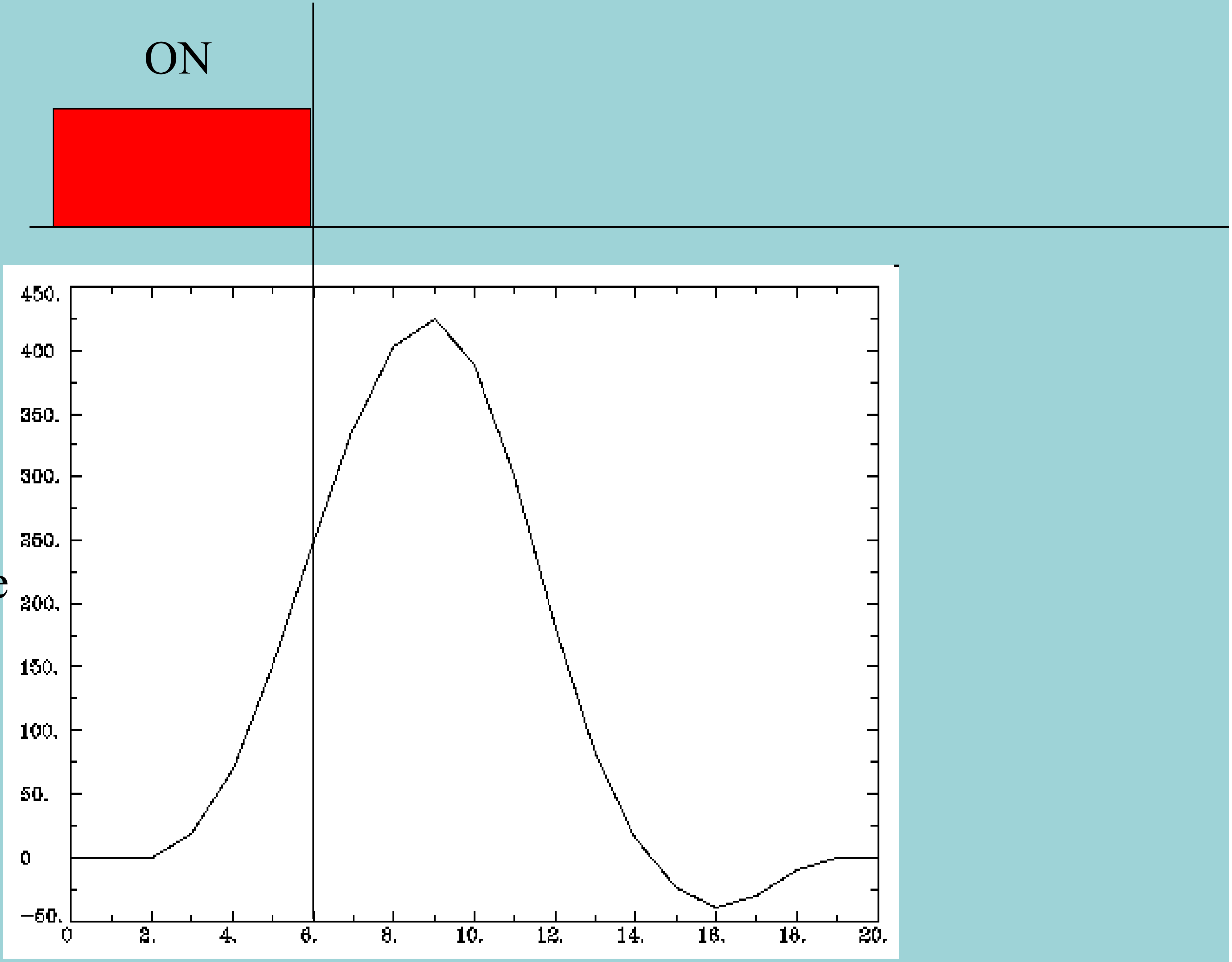
ON ON ON

2s 5s 5s 2s

Response



sec



ON

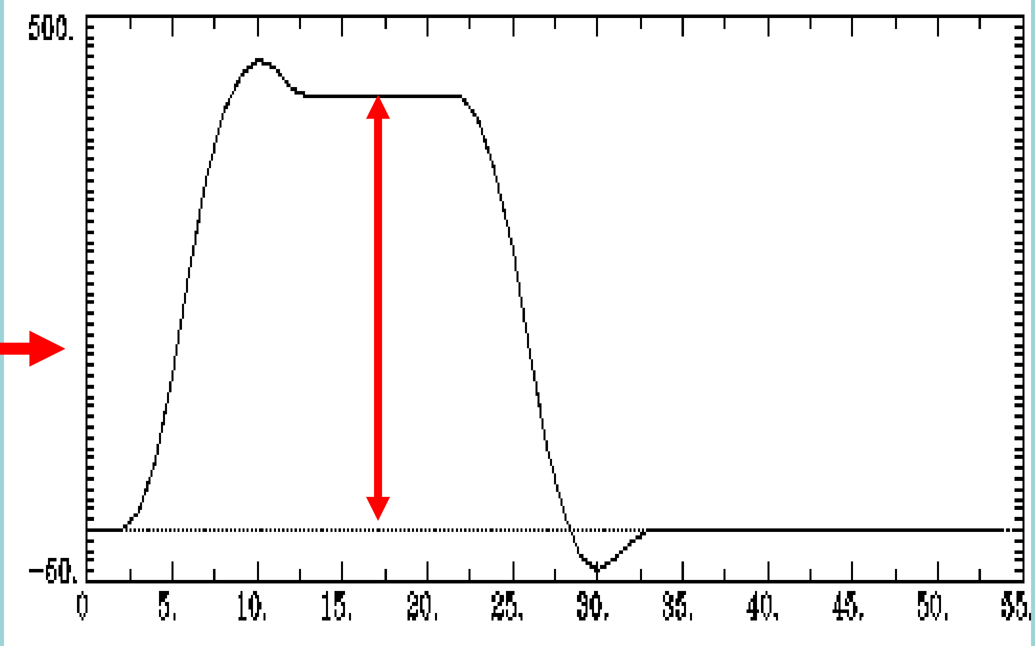
Stimuli

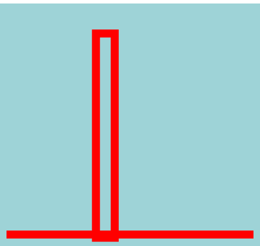
Response

Time

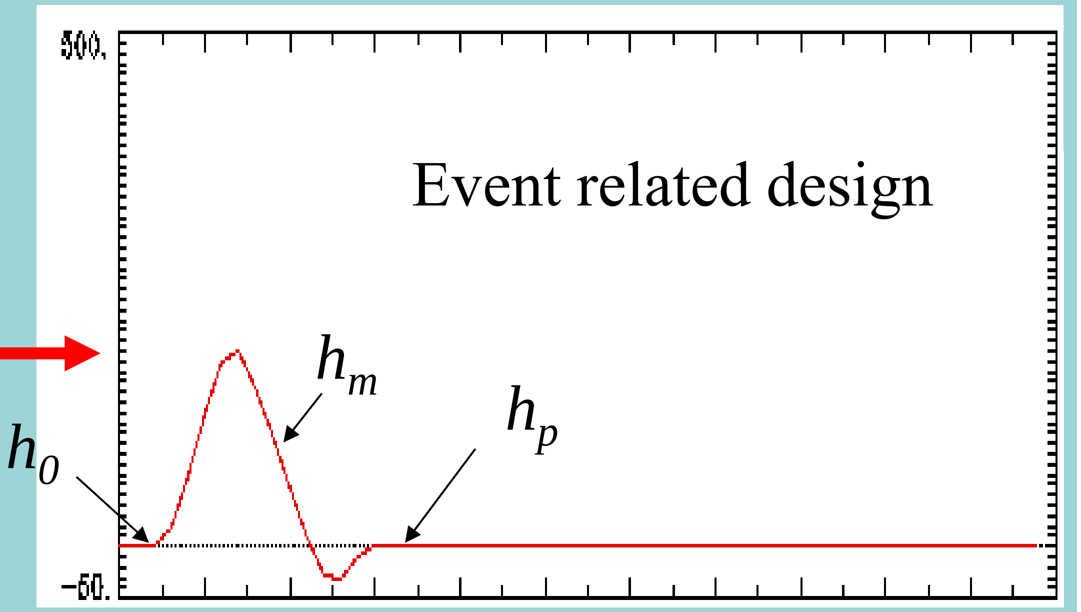
Block Design

Present 10 pictures
With 2 seconds each





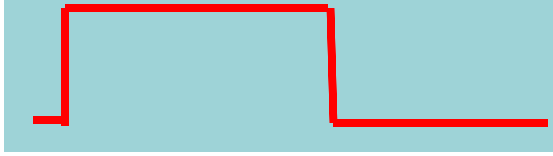
Present for 2 seconds

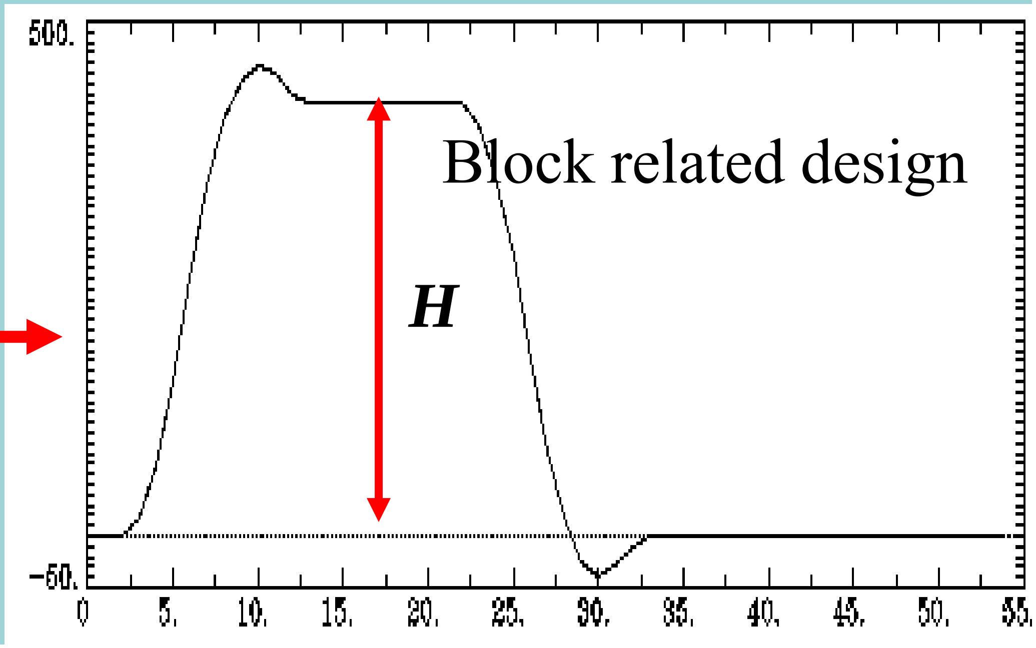


$$H \approx \sum_{m=0}^{p} h_m$$

$$\otimes$$

Present 10 pictures
With 2 seconds each





Rapid Event Related Design

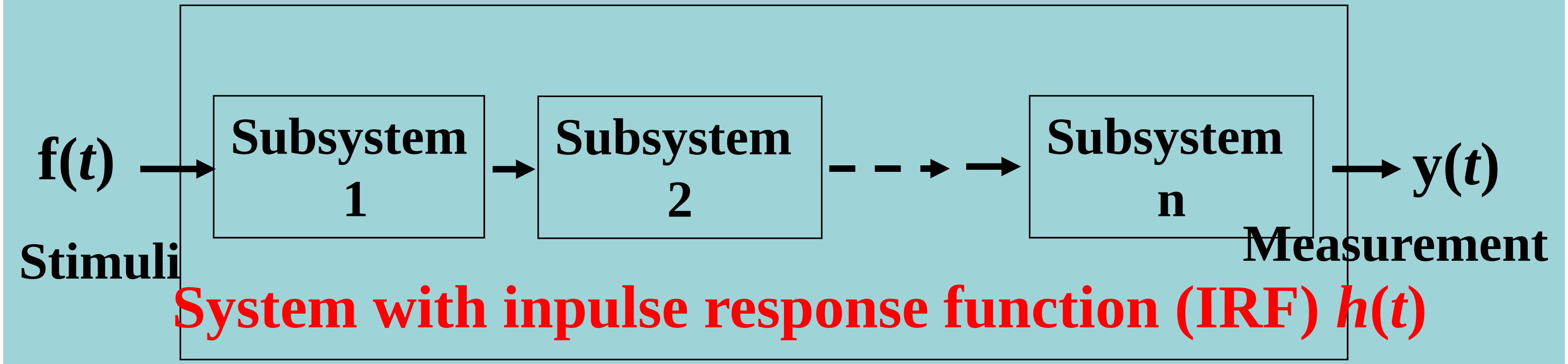
Randomizing the stimuli -> More real life

More stimuli per unit time comparing to traditional event related design -> time efficiency

Design flexibility -> more fun

Glover GH. Deconvolution of impulse response in event-related BOLD fMRI. Neuroimage. 1999;9:416-29.

Modeling of fMRI



f(*t*) → **Subsystem 1** → **Subsystem 2** - - → → **Subsystem n** → **y(*t*)**

Stimuli

Measurement

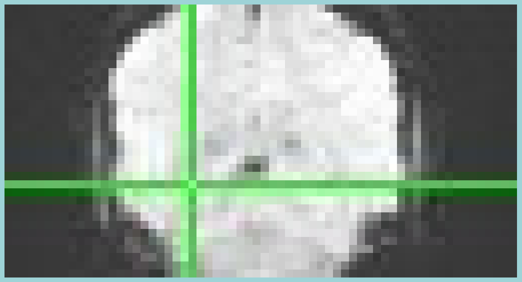
System with inpulse response function (IRF) *h*(*t*)

$$y(t) = f(t) \otimes h(t)$$ **+ noise (t)**

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

deconvolution

***h*(*t*)**



Continuous: $y(t) = f(t) \otimes h(t) = \int_0^t f(\tau) h(t-\tau) d\tau$

Discrete times: $y(n\Delta t) = \sum_{m=0}^{n} f(m\Delta t) h(n\Delta t - m\Delta t) \Delta t$

In short hand,

$$y_n = \sum_{m=0}^{n} f_m h_{n-m}$$

$$= \sum_{m=0}^{n} f_{n-m} h_m$$

Assume $h_m = 0$ for n ≥ p, then

$$y_n = \sum_{m=0}^{p} f_{n-m} h_m$$

Lathi BP. *Linear Systems and Signals*. Berkeley-Cambridge Press. 1992.

$$Z_n = \underbrace{\sum_{m=0}^{p} f_{n-m} h_m}_{y_n} + \varepsilon_n$$

measurement

Error

Including constant baseline + linear trend, the MR signal measured

$$Z_n = y_n + \beta_0 + \beta_1 n + \varepsilon_n$$
$$= \beta_0 + \beta_1 n + h_0 f_n + h_1 f_{n-1} + \cdots + h_p f_{n-p} + \varepsilon_n$$

For $n = p, p+1, \ldots, N-1$

Using the matrix notation,

$$Z = \begin{bmatrix} Z_p \\ Z_{p+1} \\ . \\ . \\ . \\ Z_{N-1} \end{bmatrix}, \qquad X = \begin{bmatrix} 1 & p & f_p & \dots & f_0 \\ 1 & p+1 & f_{p+1} & \dots & f_1 \\ . & . & . & . & . \\ . & . & . & . & . \\ . & . & . & . & . \\ 1 & N-1 & f_{N-1} & \underset{,}{\dots} & f_{N-p-1} \end{bmatrix}$$

$$\beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ h_0 \\ . \\ . \\ . \\ h_p \end{bmatrix} \qquad \varepsilon = \begin{bmatrix} \varepsilon_p \\ \varepsilon_{p+1} \\ . \\ . \\ . \\ \varepsilon_{N-1} \end{bmatrix}$$

$$\mathbf{Z} = \mathbf{X}\,\boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

The MR signal intensity at a voxel from a 7-min run

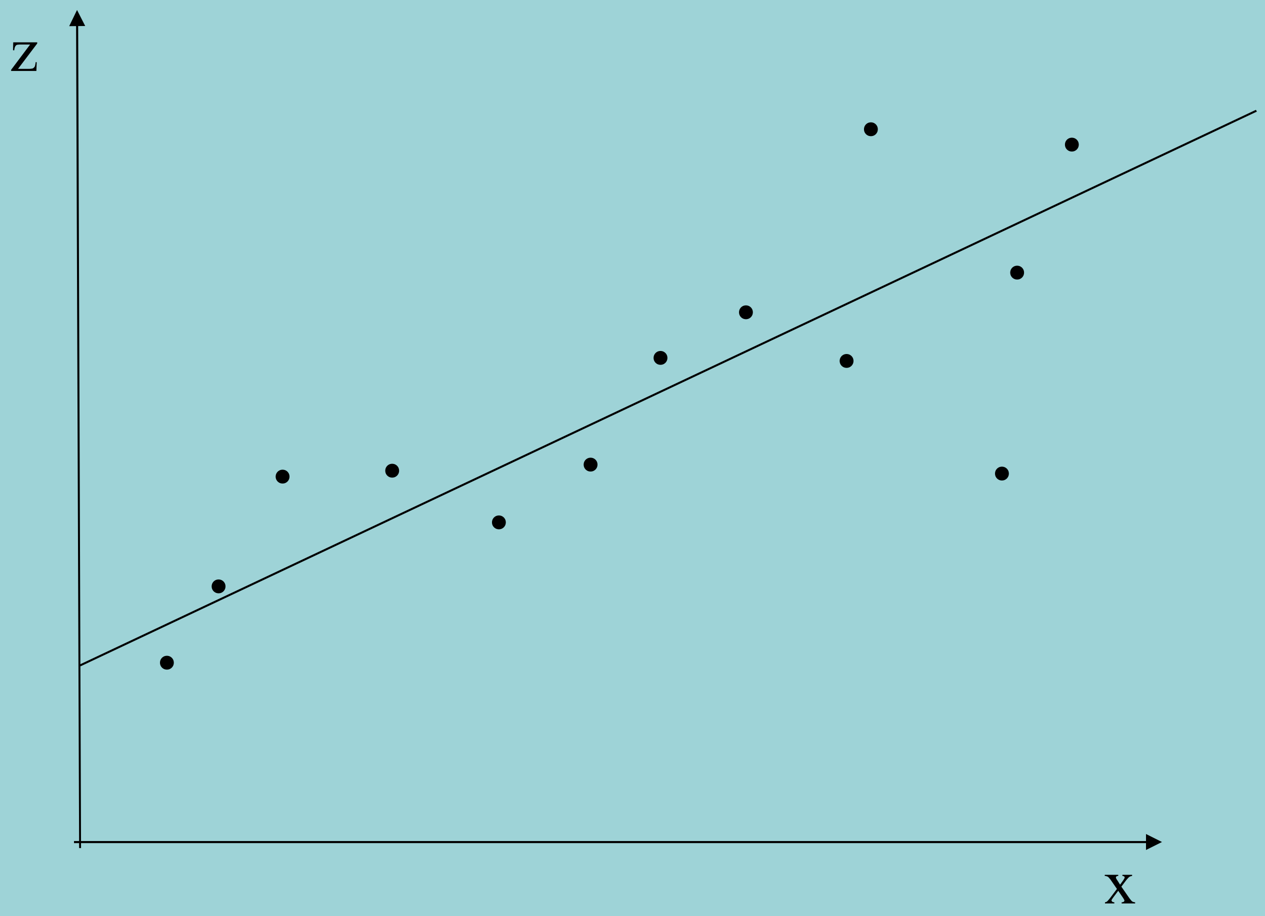
The design matrix (when the stimulus ON and OFF)

Baseline signal + linear trend + IRF

Error term

$$\hat{\beta} = \begin{bmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \\ \hat{h}_0 \\ . \\ . \\ . \\ \hat{h}_p \end{bmatrix} = (X^t X)^{-1} X^t Z$$

$Z = \beta_0 + k\ X + \text{Noise}$



Example

$$\begin{cases} a1x1 + b1x2 + c1x3 = 1 \\ a2x1 + b2x2 + c2x3 = 2 \\ a3x1 + b3x2 + c3x3 = 3 \end{cases}$$

$$\Downarrow$$

$$\begin{bmatrix} a1x1 + b1x2 + c1x3 \\ a2x1 + b2x2 + c2x3 \\ a3x1 + b3x2 + c3x3 \end{bmatrix} = \begin{bmatrix} 1 \\ 2 \\ 3 \end{bmatrix}$$

$$\swarrow$$

$$\begin{bmatrix} a1x1 + b1x2 + c1x3 \\ a2x1 + b2x2 + c2x3 \\ a3x1 + b3x2 + c3x3 \end{bmatrix} = \begin{bmatrix} a1 & b1 & c1 \\ a2 & b2 & c2 \\ a3 & b3 & c3 \end{bmatrix} \begin{bmatrix} x1 \\ x2 \\ x3 \end{bmatrix} \Rightarrow \begin{bmatrix} a1 & b1 & c1 \\ a2 & b2 & c2 \\ a3 & b3 & c3 \end{bmatrix} \begin{bmatrix} x1 \\ x2 \\ x3 \end{bmatrix} = \begin{bmatrix} 1 \\ 2 \\ 3 \end{bmatrix}$$

$$\mathbf{Z} = \mathbf{X}\,\boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

$$\hat{\beta} = \begin{bmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \\ \hat{h}_0 \\ . \\ . \\ . \\ \hat{h}_p \end{bmatrix} = \underbrace{(X^t X)^{-1}}_{} X^t Z$$

Design Evaluation:

(1)Multicollinearity issue

(2)Minimize error

Ward, B. (2002). *Deconvolution analysis of fMRI time series data*. Milwaukee, WI: Biophysics Research Institute, Medical College of Wisconsin.

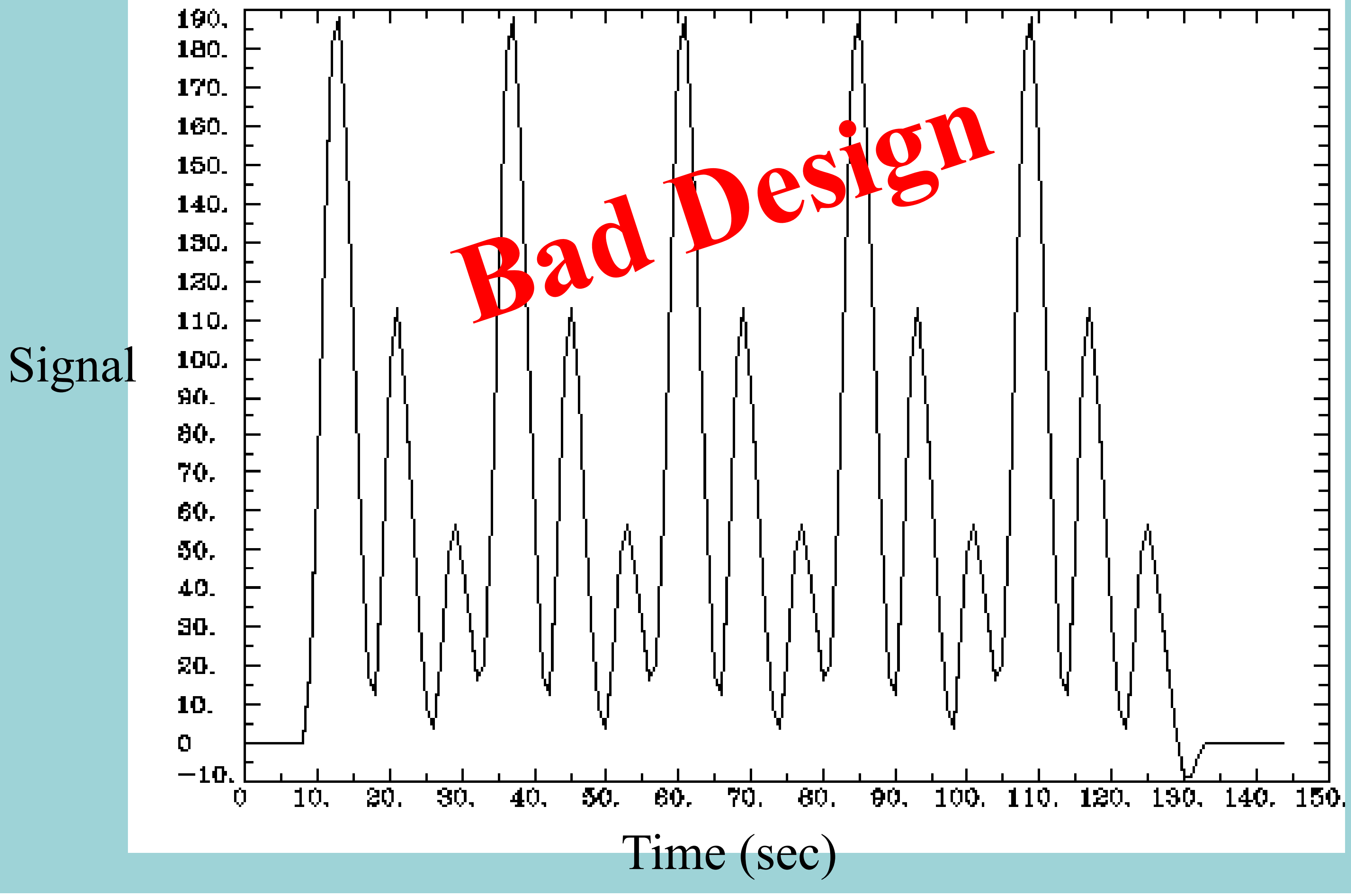
Analogy of Multicollinearity Issue

$$\begin{cases} X + Y + Z = 1 \\ 2\,X + 2\,Y + 2\,Z = 2 \\ 3\,X + 3\,Y + 3\,Z = 3 \end{cases} \longrightarrow \begin{cases} X + Y + Z = 1 \\ X + Y + Z = 1 \\ X + Y + Z = 1 \end{cases} \longrightarrow \text{Cannot Resolve } X, Y \text{ and } Z$$

$$\begin{cases} X + Y + Z = 1 \\ X + 3\,Y + Z = 2 \\ X + Y + 3\,Z = 3 \end{cases} \longrightarrow \text{Can resolve } X, Y \text{ and } Z$$

2 sec for each stimulus

--- $\overbrace{\text{6sec-}\textbf{A}\text{-6sec-}\textbf{B}\text{-6sec-}\textbf{C}}^{\text{Repeat}}$-6sec ----

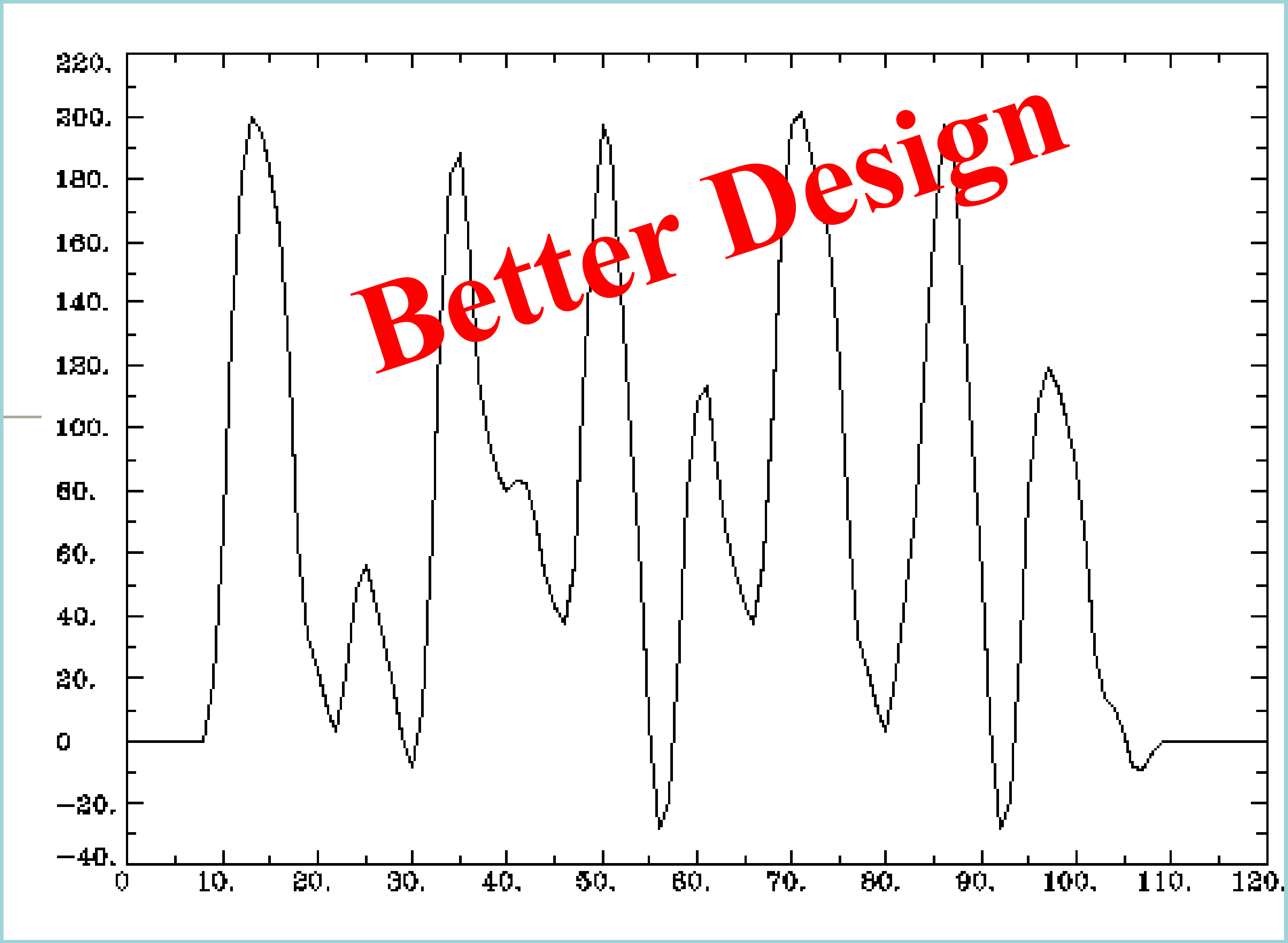


Bad Design

2 sec for each stimulus

Repeat with Various ISIs

--- 6sec-**A**-2sec-**B**-6sec-**C**-8sec-**A**-4sec-**B**-4sec-**C**-

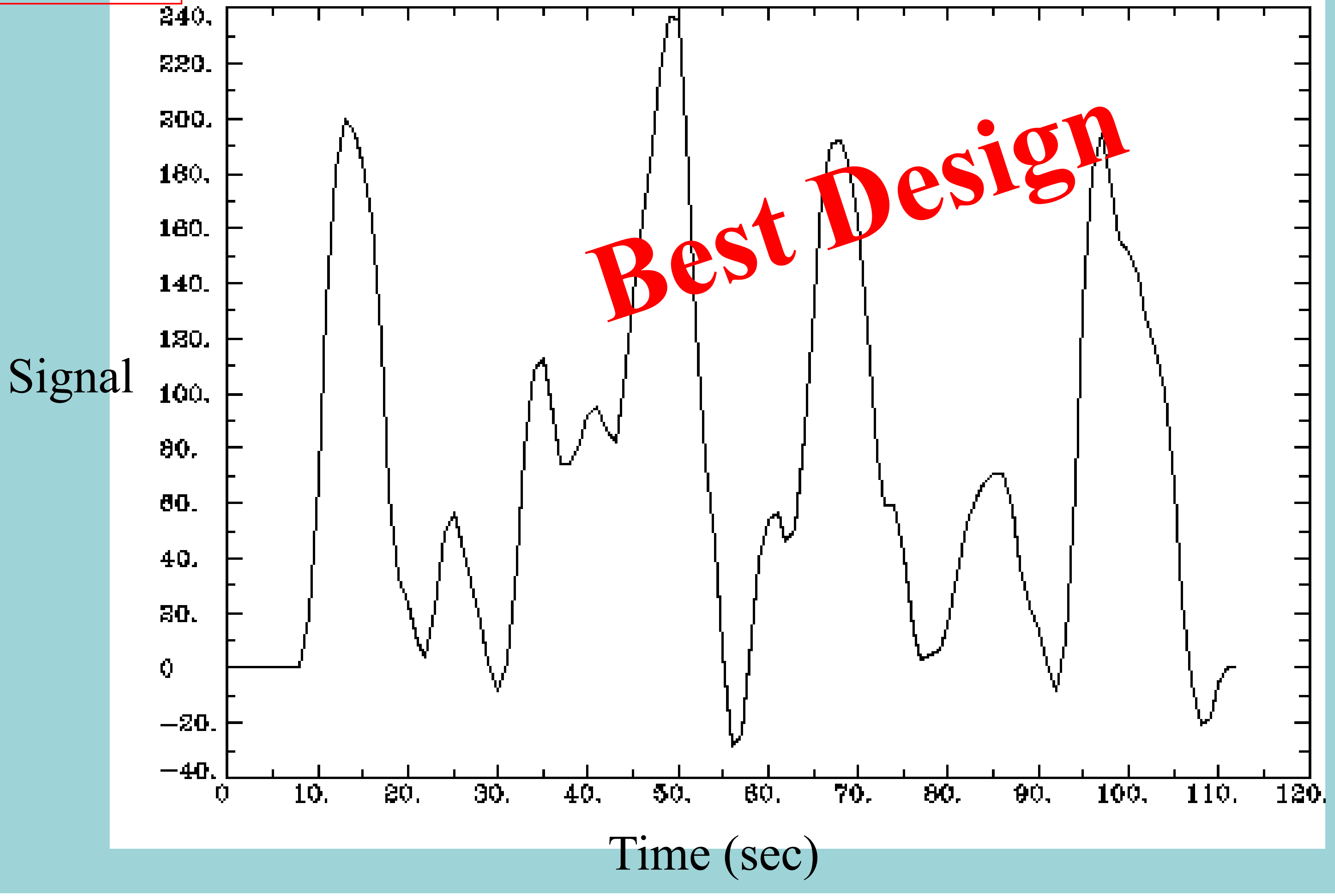


Better Design

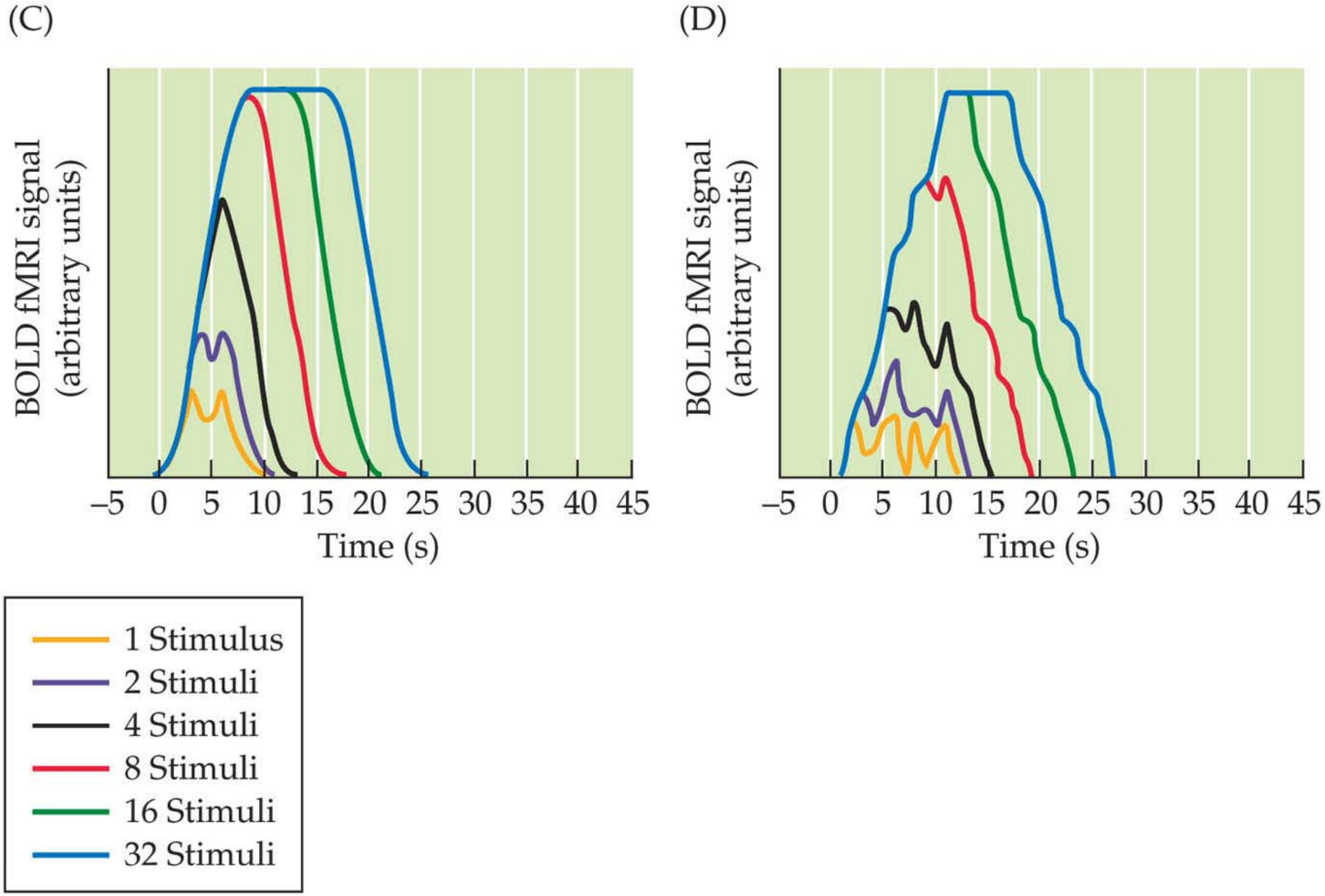
Repeat with Various ISIs and Random Order of Stimuli

2 sec for each stimulus

---6sec-**A**-2sec-**B**-6sec-**C**-8sec-**B**-4sec-**B**-4sec-**A**-2sec-**A**--



Best Design



***FUNCTIONAL MAGNETIC RESONANCE IMAGING,* Figure 11.11 (Part 2)**

Summary

Block Design

Advantage: Best for detection
Easy to implement paradigm
Relative immune to timing error

Traditional (Slow) Event Related Design:

Advantage: No assumption of linear system
Able to characterize IRF

Rapid Event Related Design:

Advantage: More life like
More time efficient
Flexible design
Able to characterize IRF

Hi, I enjoy to volunteer for an fMRI study !

Common Neuroimaging Data Analysis and Display Software

AFNI

FSL

FreeSurfer

SPM