GLM for fMRI analysis

12.9.2023 Kerttu Seppälä
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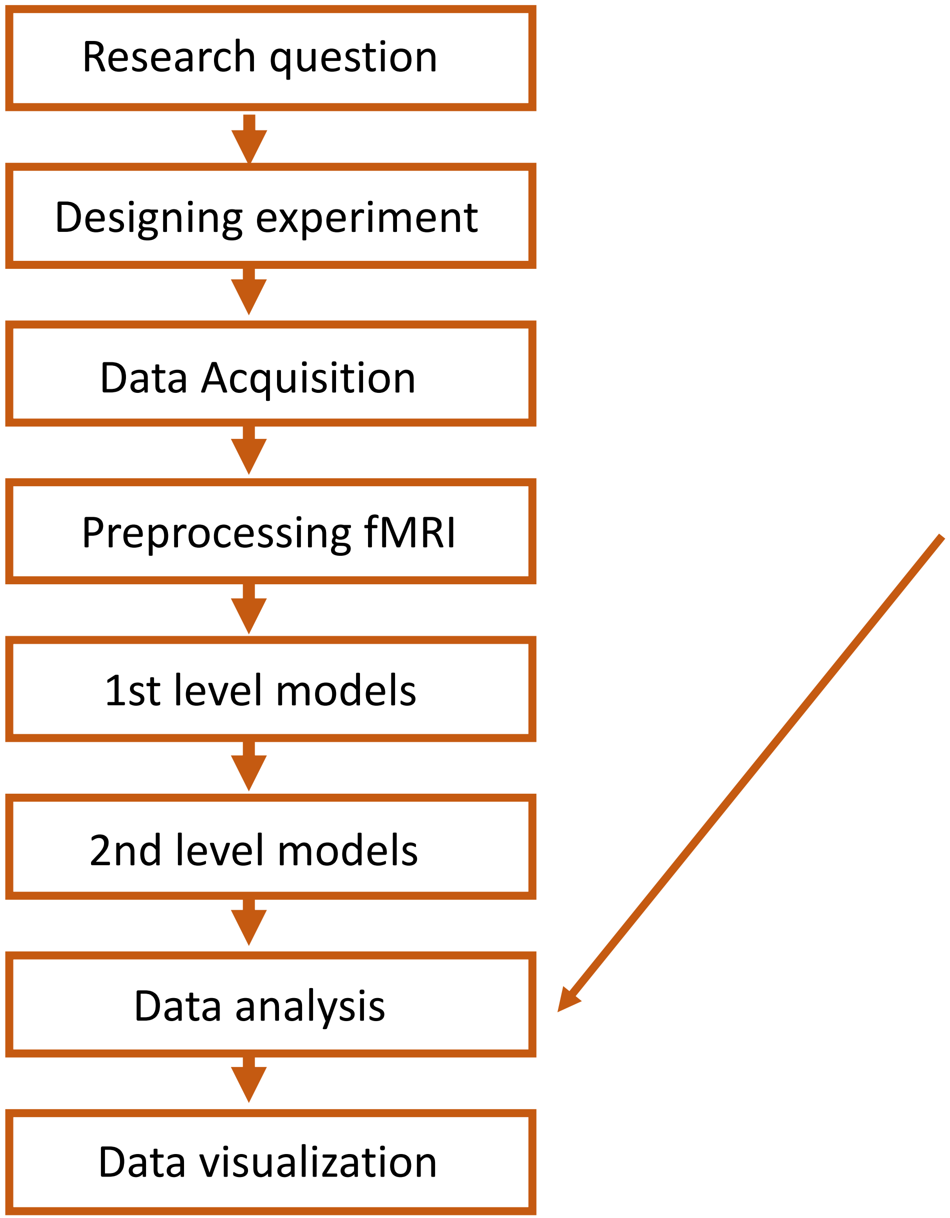
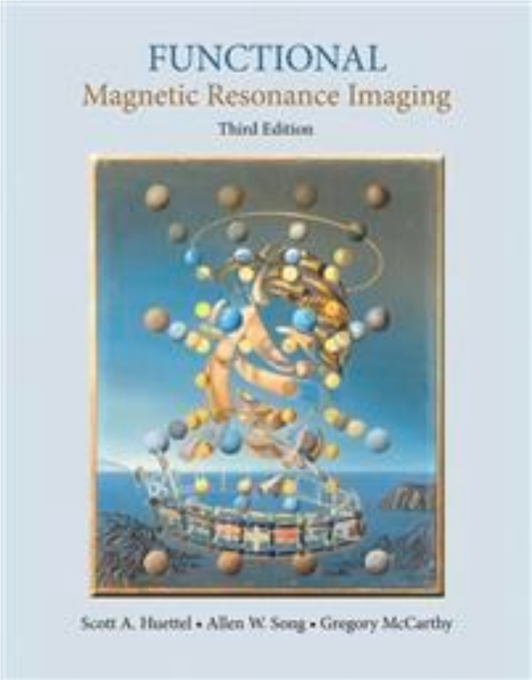
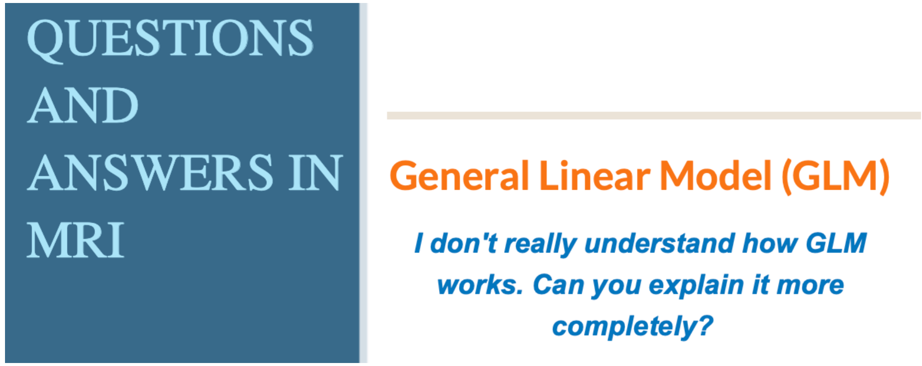


8:30–9:15	Physiology of the BOLD signal and T2* image acquisition
9:15–10:00	Experimental designs for fMRI
10:00–10:45	Preprocessing with fMRIprep
10:45–12:00	Lunch break
12:00–12:45	**General Linear Model**
12:45–13:30	First level models for fMRI
13:30–13:45	Coffee break
13:45–14:30	Second level models for fMRI
14:30–15:15	Region of interest analysis
15:15–16:00	Data visualization



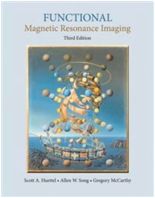
Huettel Scott A., Song Allen W., McCarthy Gregory: Functional Magnetic Resonance Imaging, 2014, Oxford University Press Inc



https://mriquestions.com/general-linear-model.html

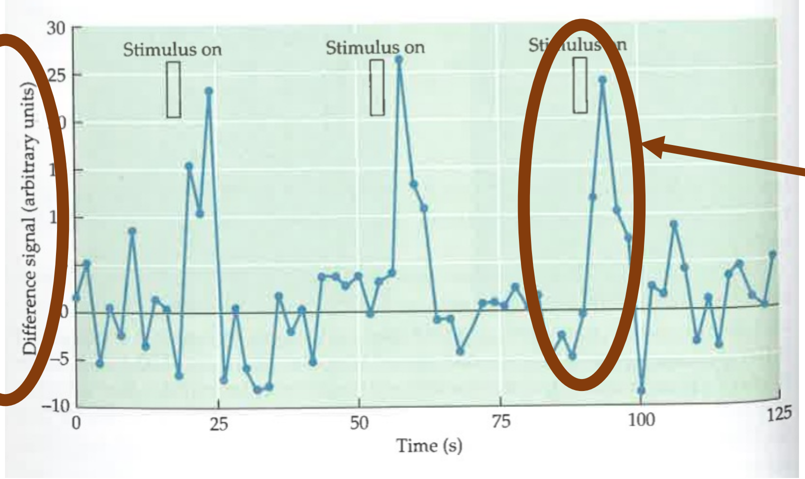
http://www.newbi4fmri.com/tutorial-3-glm

Recap: The Actual Measured Signal



Changes in BOLD activation after presenting single event stimuli for subject from a voxel

Arbitary Units



Notice also the delay after the stimulus and before the peak

Fig. 7.9

Example of BOLD hemodynamic response to a hand squeezing task

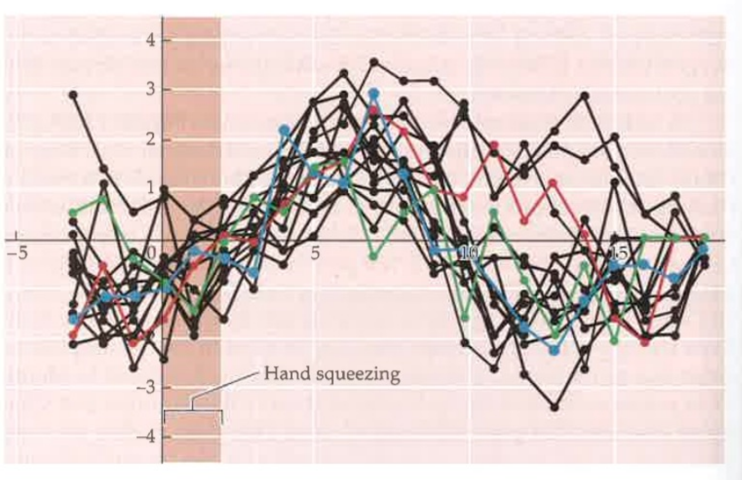


Fig. 7.12

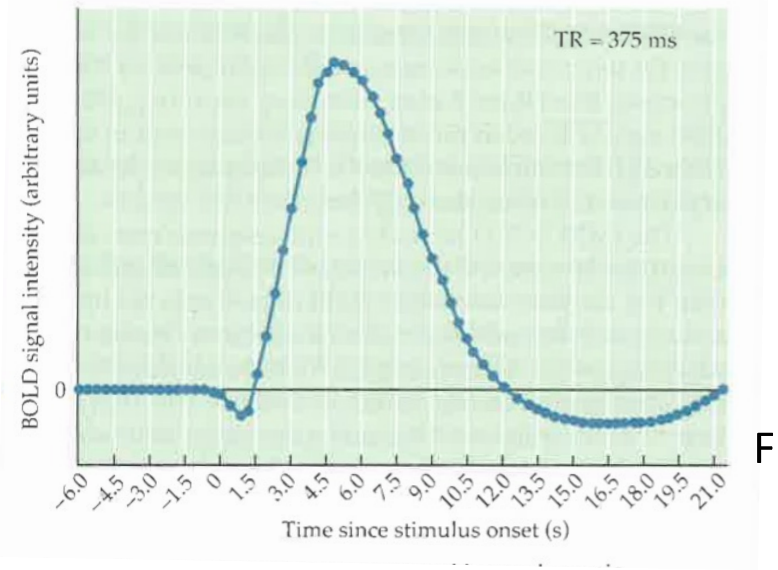
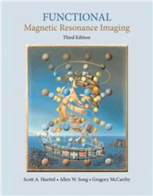


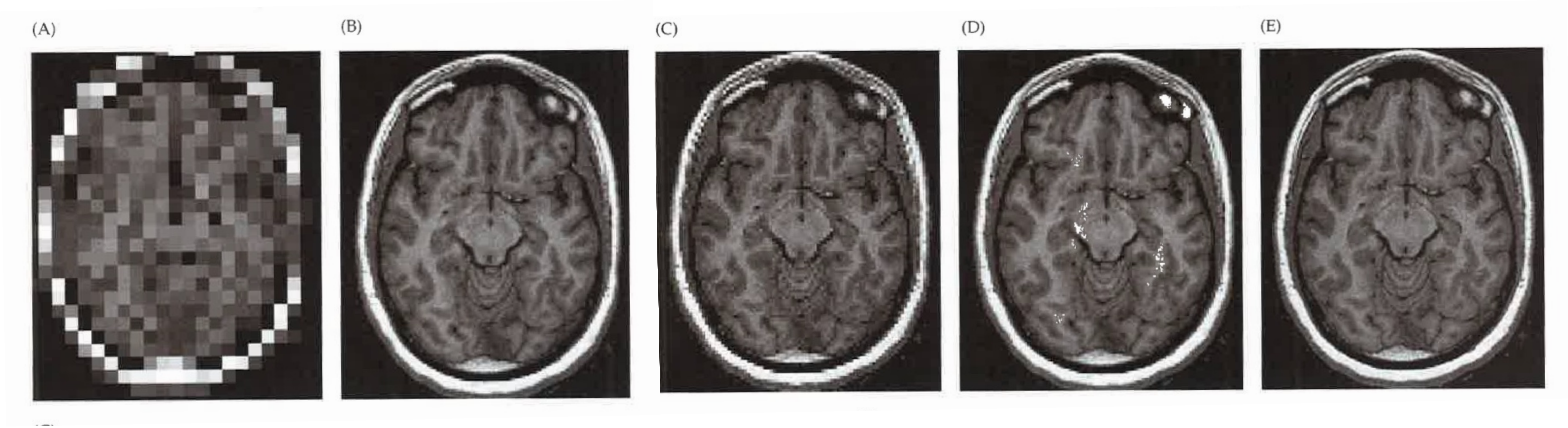
Fig. 7.20

Spatial Resolution



- Spatial Resolution: Ability to distinguish different locations within an image

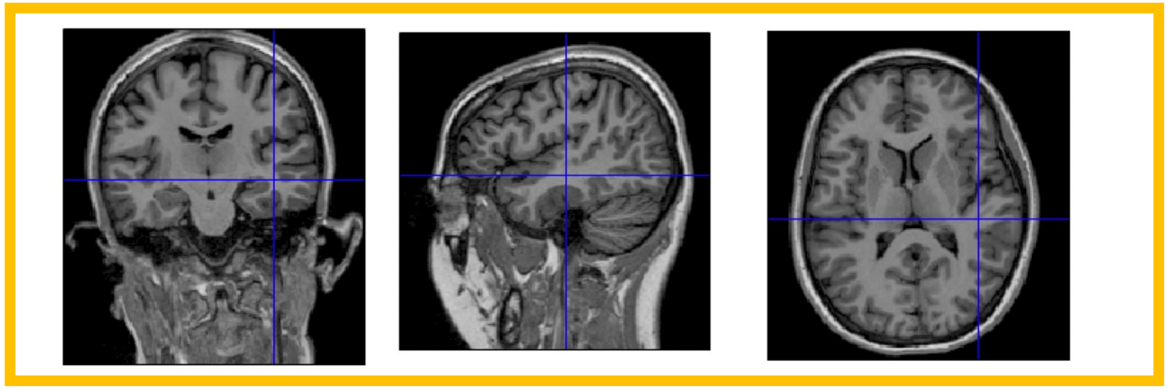
Figure 1.7 The human brain at different spatial resolutions. Spatial resolution refers to the ability to resolve small differences in an image. In general, we can define spatial resolution based on the size of the elements (i.e., voxels) used to construct the image. The images shown here present the same brain sampled at five different element sizes: 8 mm (A); 4 mm (B); 2 mm (C); 1.5 mm (D); and 1 mm (E). Note that the gray–white structure is well represented in the latter three images, all of which were produced using element sizes that were less than half the typical gray matter thickness of 5 mm.



Spatial Resolution 2

- Structural images voxels maybe
  1 x 1 x 1 mm
- Functional images voxels maybe
  3 x 3 x 3 mm (depends on the question)
- BOLD signal is direct measure of the amount of deoxyhemoglobin in a voxel
- Partial volume effects: combination of different tissue types within a voxel (effect from large arteries / small capillaries)
- → Spatial smoothing for statistics and better signal-to-noise ratio

MRI



fMRI

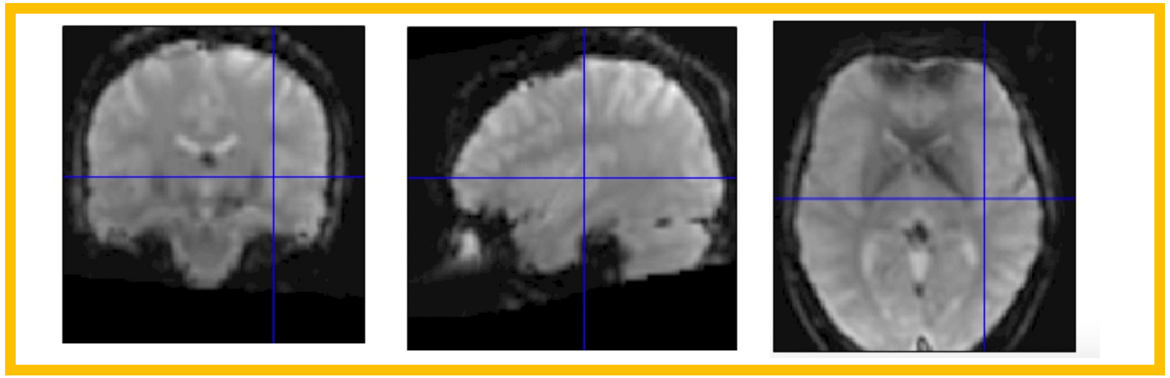
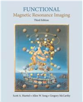
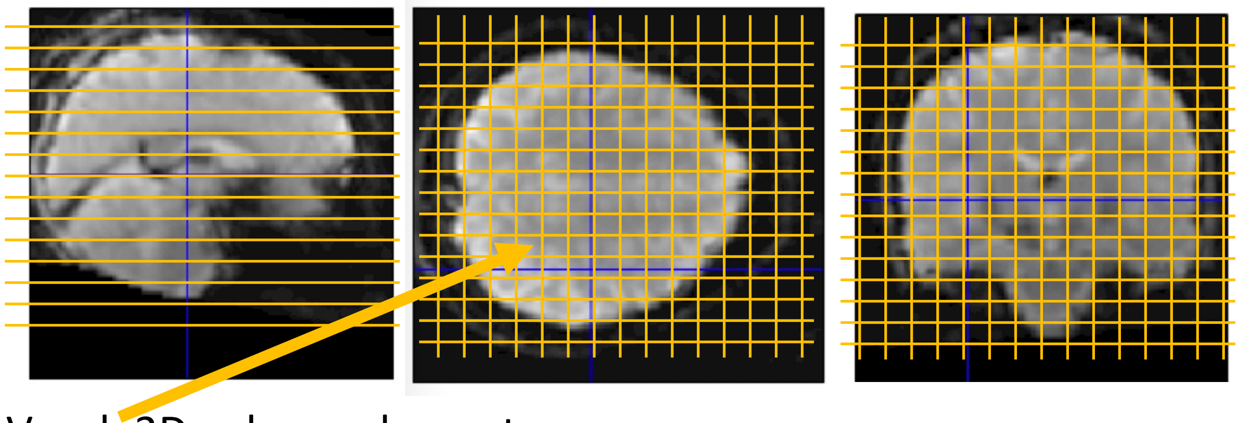
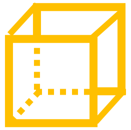


Table 7.1 Spatial Scales in the Human Brain

Structure	Scale (mm)
Brain	100
Gyri	10
Dominance column	1
Neuron	0.01
Synapse	0.001
Ion channel	0.00001







Voxel: 3D volume element

30 slices, 64 x 64 voxels per slice → 122800 voxels

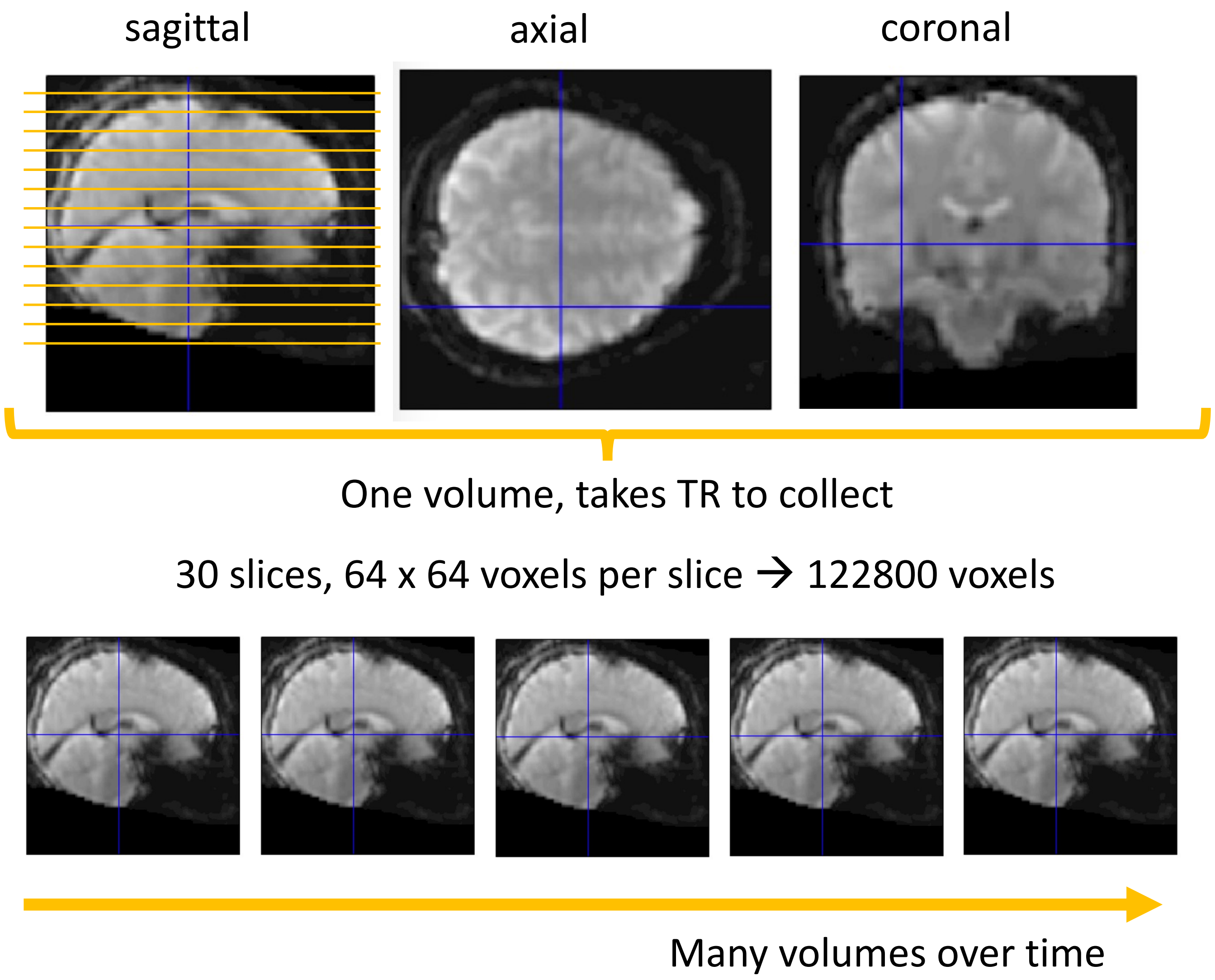
Temporal Resolution

- Determined by TR and by limitations of vascular system
  - TR = time of repetition (time for a volume)
  - HDR rises and falls within 10-15 s
  - Duration of the stimulus does not necessarily correspond with duration of neuronal activity

- fMRI is slow
  - neuronal activity is short < 1s
  - no snapshot of neuronal activity but an estimate of slower changes in vascular system

- Good TR?
  - Depending on the experiment (0,5 s – 3 s)
  - Smaller TR

    → more accurate estimation of HDR shape;
    not necessary effect on amplitude



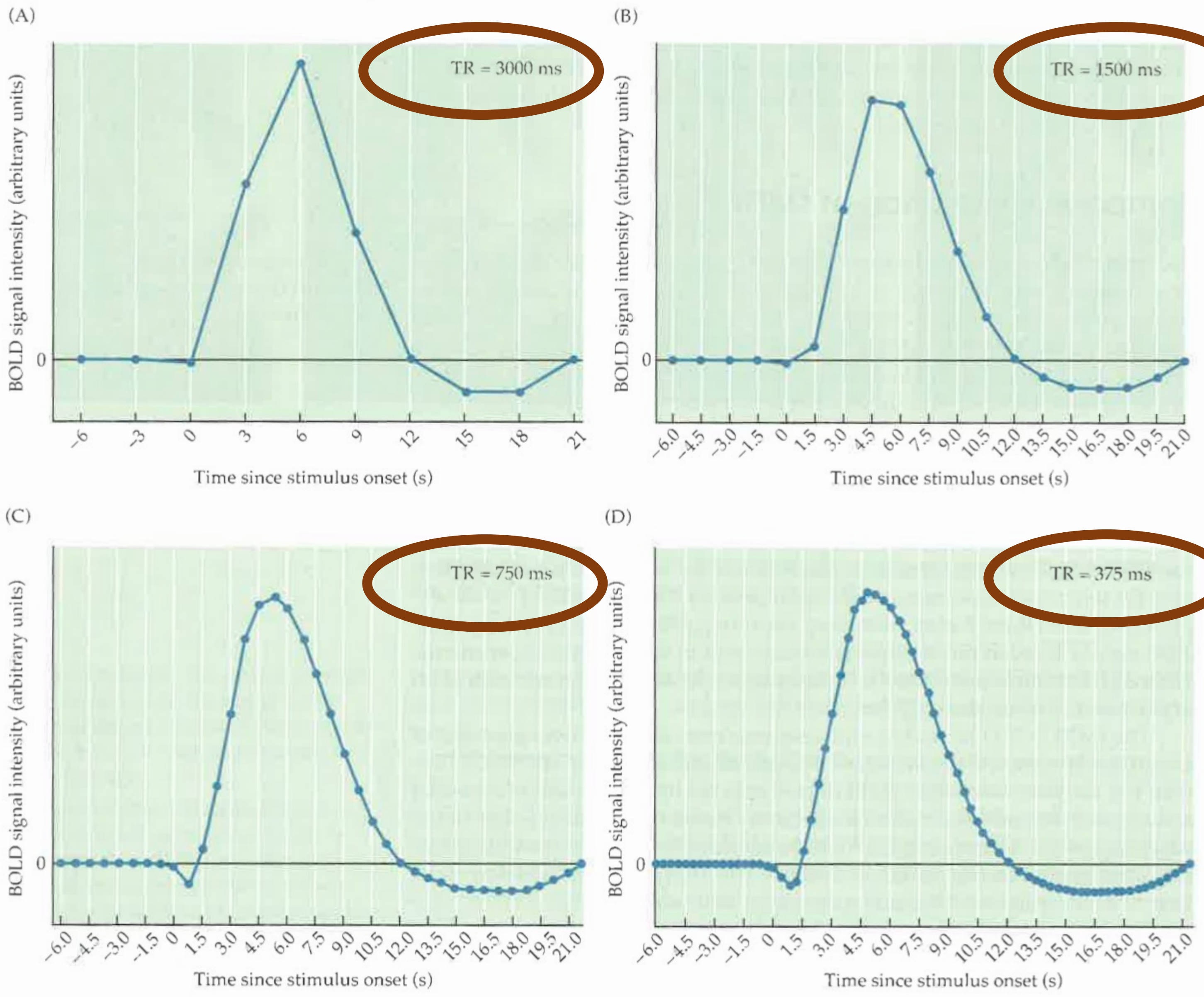
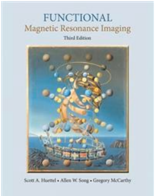
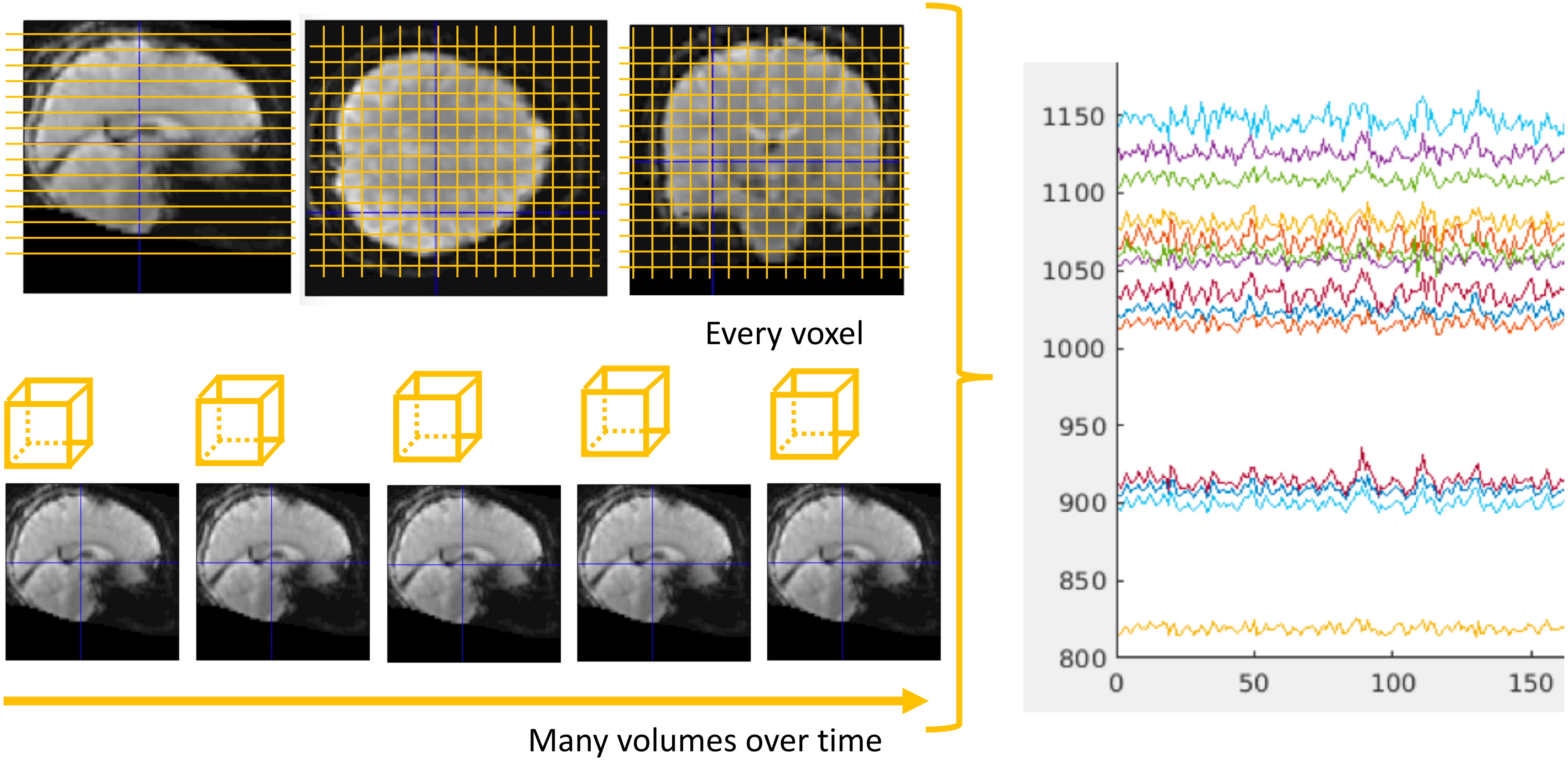


Figure 7.20 Effects of sampling rate (TR) on the measured hemodynamic response. In each figure, an idealized hemodynamic response is sampled at a different rate.

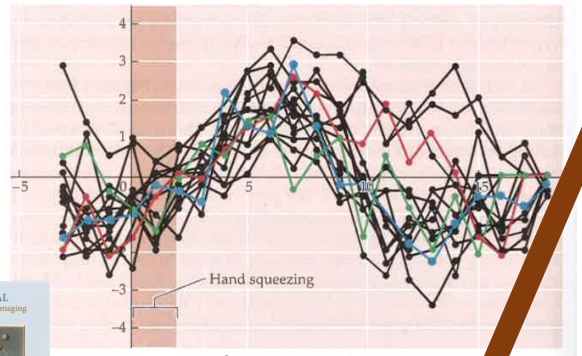


Timeseries



Every voxel
Many volumes over time
1150
1100
1050
1000
950
900
850
800
0
50
100
150

?



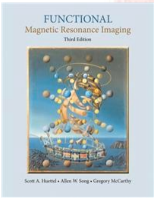


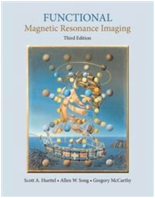
Fig. 7.12

Supplementary Figure 2. The relationship between experienced fear and neural activity for Conjuring 2.

Fear ratings were convolved with a hemodynamic response function and entered as a regressor into a GLM analysis with a high-pass filter of 256s (uncorrected $p = 0.001$).

Hudson et al. "Dissociable neural systems for unconditioned acute and sustained fear", NeuroImage, Vol 216, 2020.

Linearity of the Hemodynamic Response



Linear system

- System: for a given input the system will respond with same output

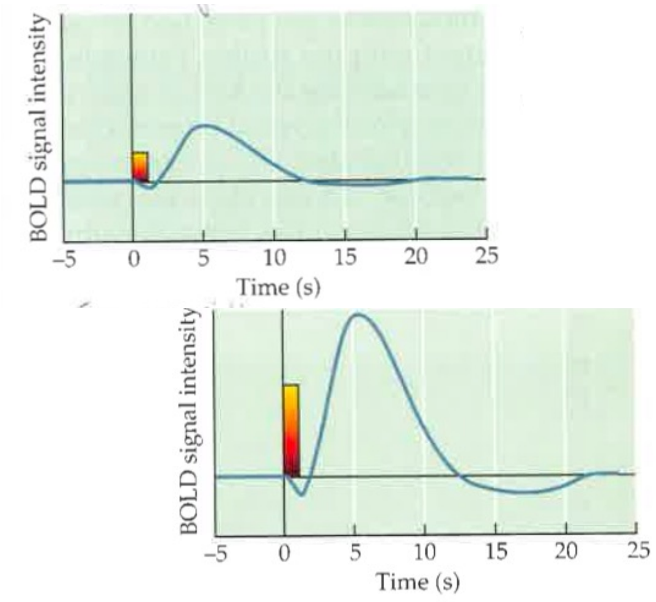
- Input: neuronal activity is a short-duration input
- Output: HDR

Principles of linear system

1) Scaling + 2) Superposition

1) Scaling

- The magnitude (amplitude) of the system output must one proportional to the system input
- Test condition and control condition:
  - neuronal activity in task required twice as much of work as in rest condition, so the amplitude of HDR is more in activation than in rest
  - if no interference, the brain areas are not activating so



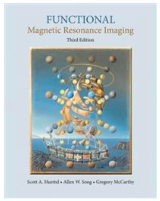
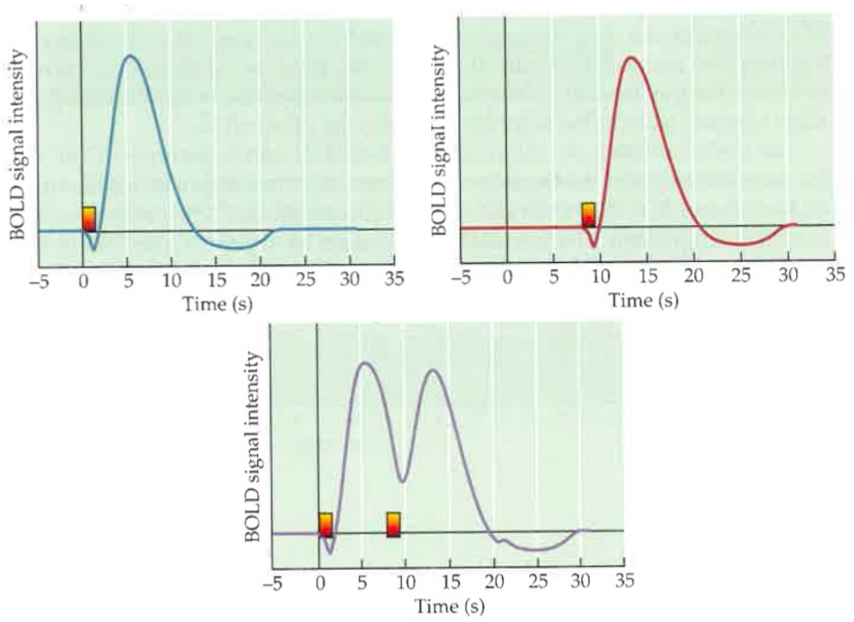
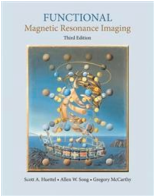


Fig 7.28

2) Superposition

- Total response to a set of imputes is equivalent to the summation of the independent responses to the inputs
- 1 event creates 1 HDR, 2 events create combined response equal to two individual responses added together





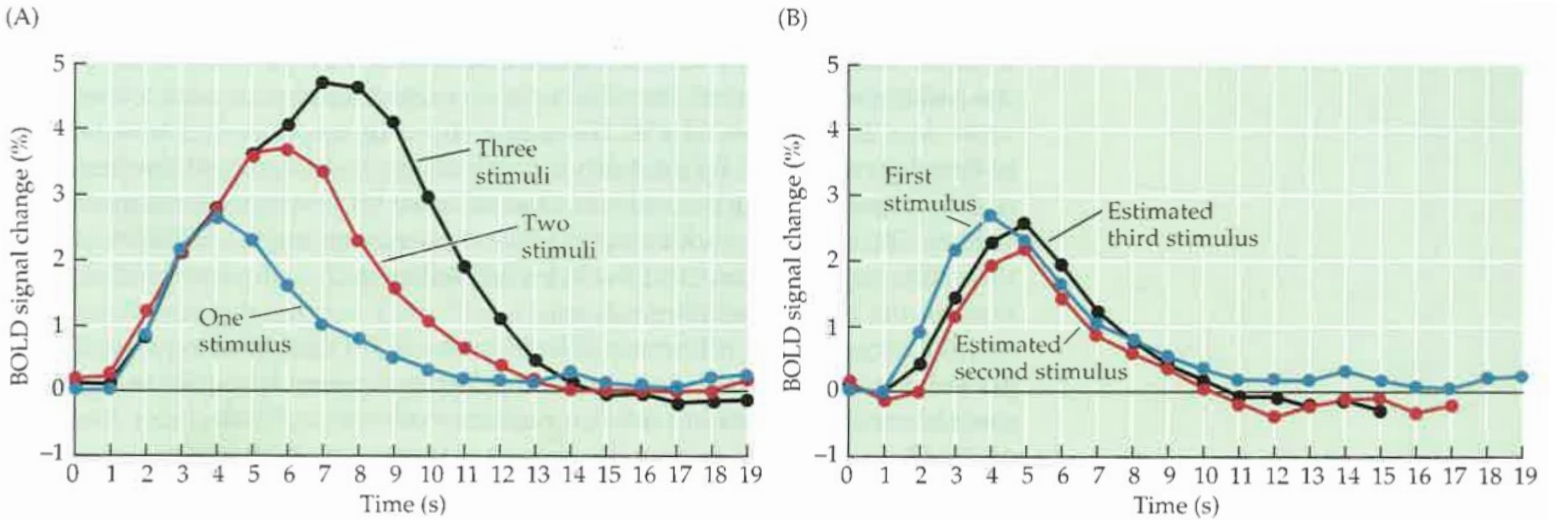
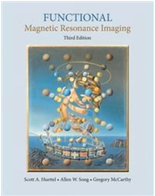


Figure 7.29 Linear addition of hemodynamic responses to individual stimulus events. (A) The hemodynamic responses evoked by presentation of one, two, or three identical stimuli (short-duration visual flashes) at short interstimulus intervals were measured. Shown here are data from a 2-s interval. The total hemodynamic response increased in a regular fashion as the number of stimuli in a trial increased. (B) By subtracting the one-stimulus trial from the two-stimulus trial and subtracting the two-stimulus trial from the three-stimulus trial, the contributions of the second and third stimuli in a trial were estimated. The responses to the second and third stimuli were generally similar to the response to the first stimulus, suggesting that the BOLD response scales in a roughly linear fashion. (From Dale and Buckner, 1997.)

Limitations in Linearity of HDR



- Limitation: short stimuli intervals create more deviation in HDR

→ less linear system, BUT more data and more statistical power

- Limitation coming from refractory period: a time period following the presentation of a stimulus during which subsequent stimuli evoke a reduced response, around 6 s

→ refractory period differs between the brain areas

→ However, offers possibility for further studies in brain science, but requires advanced modelling

GLM for fMRI

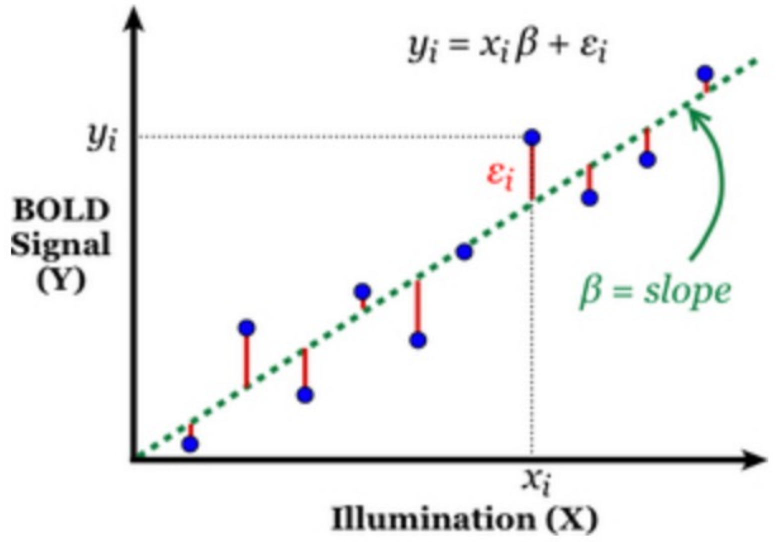
QUESTIONS AND ANSWERS IN MRI

General Linear Model (GLM)

I don't really understand how GLM works. Can you explain it more completely?

General Linear Model

- Because the system is linear, the modelling can be linear



Simplified linear regression example, adapted from data of Hansen et al (2004)

http://mriquestions.com/general-linear-model.html

$$y = \beta X + \varepsilon$$

Y = measured signal (BOLD)
X = the stimuli for the subject

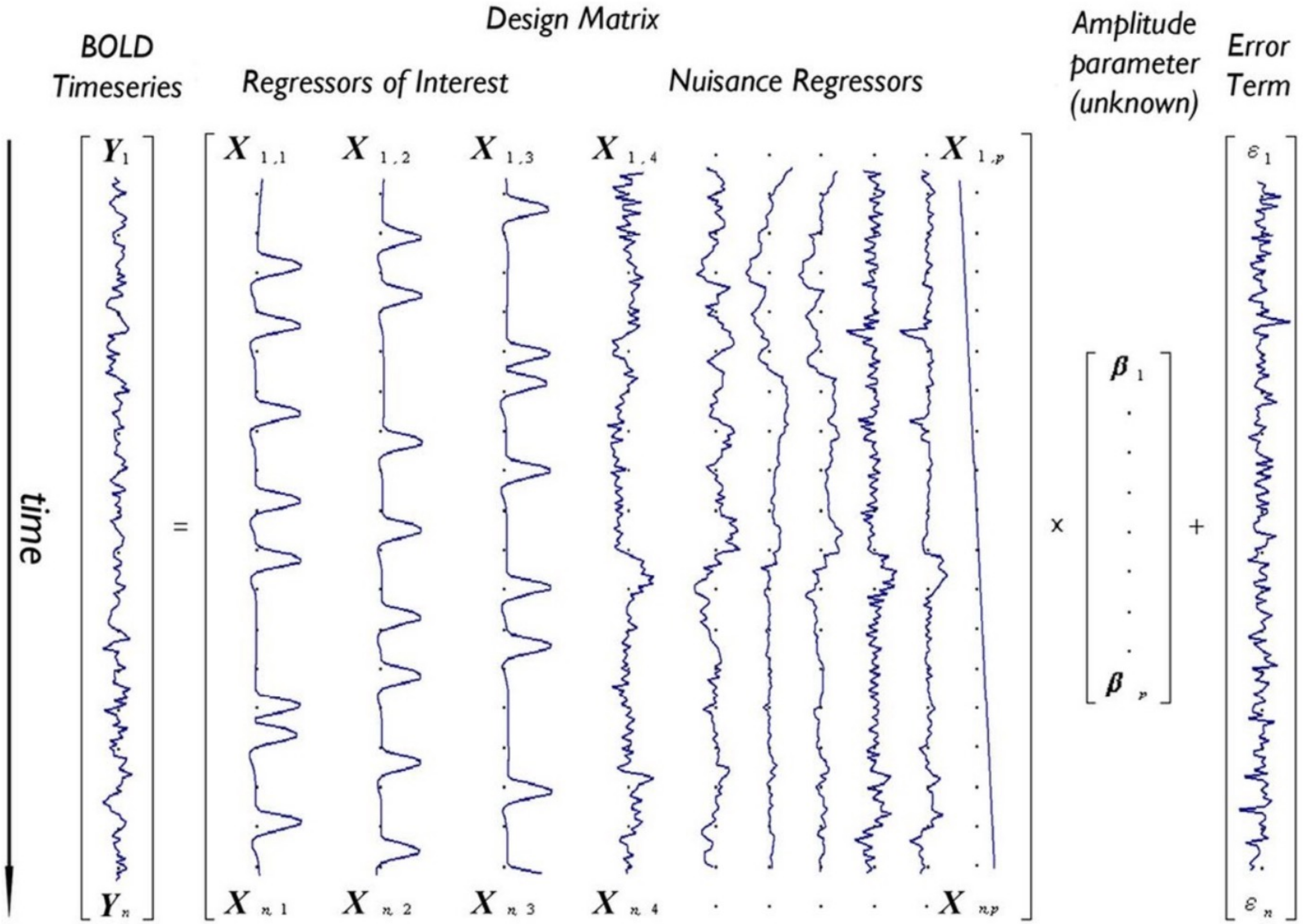
Because the system is linear, we hope that modelling it as such will explain the brain activity found, so:

B = find the best ones that leaves the error minimized
E = error

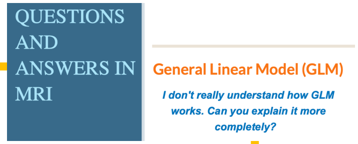
So: **1)** create a **model**, **2) fit** the model with the data and **3)** do the **statistical** tests → beautiful activation maps and pictures

$$\begin{aligned} y_1 &= x_1\beta + \varepsilon_1 \\ y_2 &= x_2\beta + \varepsilon_2 \\ y_3 &= x_3\beta + \varepsilon_3 \\ &\vdots \\ y_n &= x_n\beta + \varepsilon_n \end{aligned} \rightarrow \begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ \vdots \\ x_n \end{bmatrix} [\beta] + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \\ \vdots \\ \varepsilon_n \end{bmatrix} \rightarrow \mathbf{Y} = \mathbf{X}\beta + \boldsymbol{\varepsilon}$$

Y and **ε** a single voxel at successive time points (*i* = *1* to *n*).



Depiction of the General Linear Model (GLM) for a voxel with time-series **Y** predicted by a design matrix **X** including 10 effects (three regressors of interest – e.g., tasks A,B,C – and seven nuisance regressors – e.g., six motion parameters and one linear drift). Calculated weighting factors ($\beta_1 - \beta_{10}$) corresponding to each regressor are placed in amplitude vector **β** while column vector **ε** contains calculated error terms (ε_i) for the model corresponding to each time point *i*. (From Monti, 2011, under CC BY license)

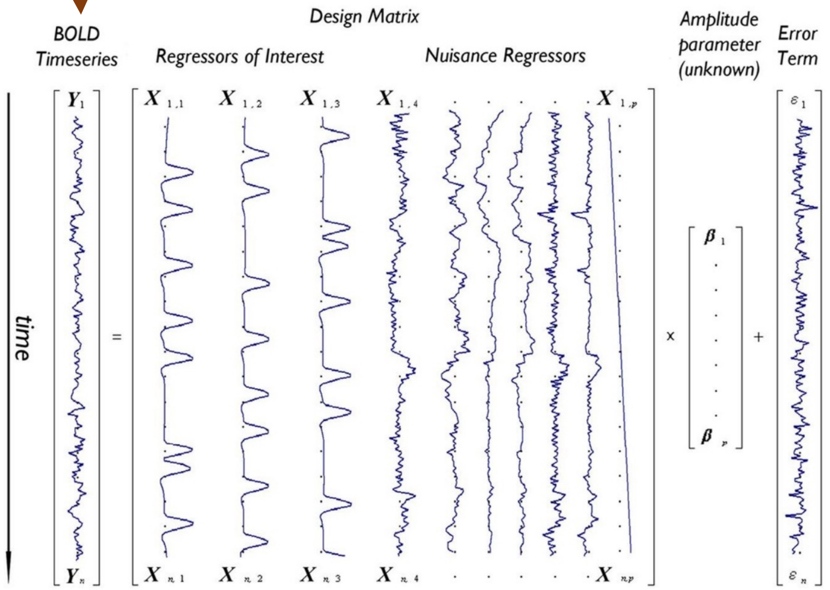


”Stated in words, the GLM says that **Y** (the measured fMRI signal from a single voxel as a function of time) can be expressed as the sum of one or more experimental design variables (**X**), each multiplied by a weighting factor (***β***), plus random error (**ε**)”

http://mriquestions.com/general-linear-model.html

$$\begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ \vdots \\ x_n \end{bmatrix} [\beta] + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

$y = \beta X + \varepsilon$: data



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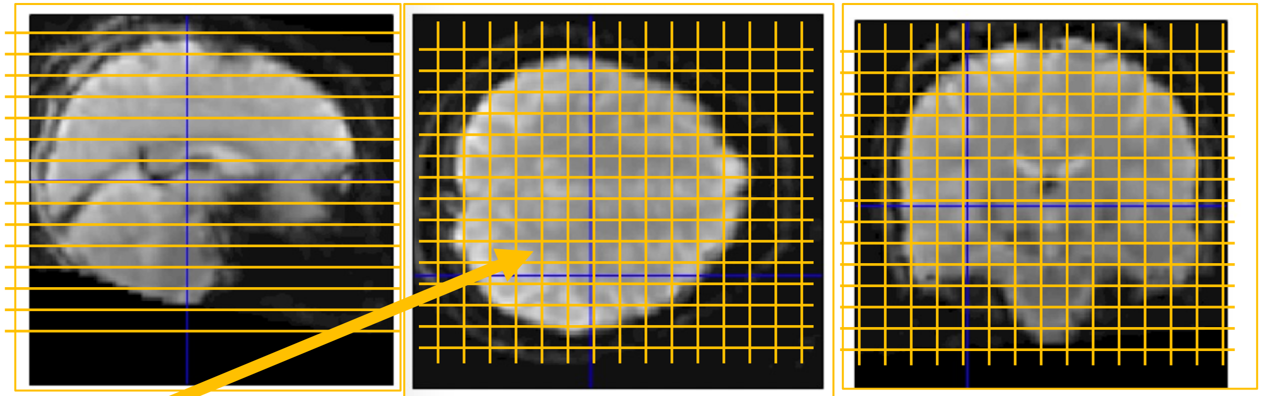

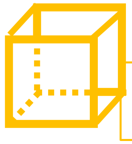

Voxel: 3D volume element

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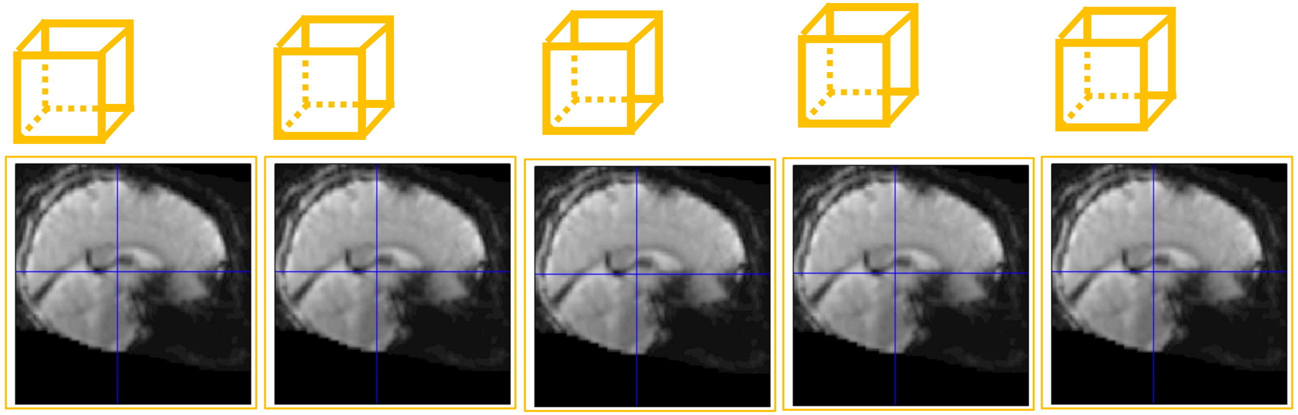
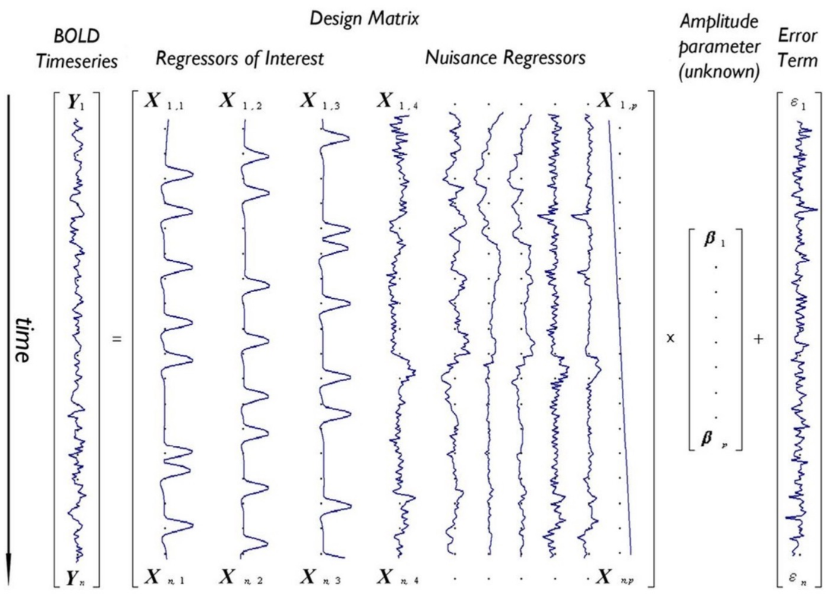


The same voxel imaged at each TR → Timeserie

$\boldsymbol{y} = \beta X + \varepsilon$: regressors



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Essential regressors

- Expectation shape of the *HRF*, if a voxel of interest gets activated during to a stimulus
- Time runs from top to down
- Must be independent from each others (can't explain the same variance)

Nuisance regressors

- Factors that confound the analysis but not interesting by themselves
  - Head movement
  - Scanner drifts
  - Physiological signals (heart)
- Helps with the GLM:
  - Reduce the amount of error
  - Improves validity of the GLM (model assumes the residuals being independend and identically distributed as Gaussian noise)

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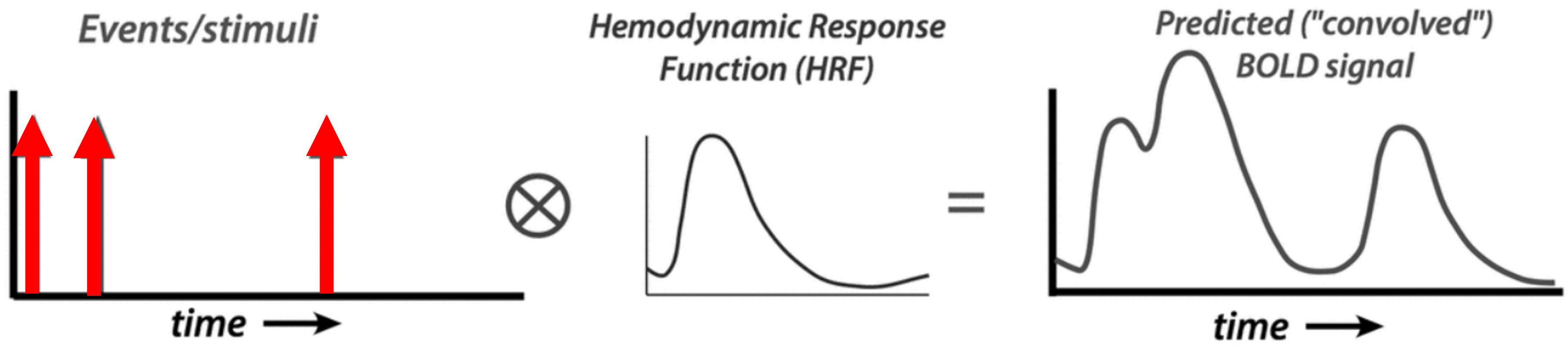
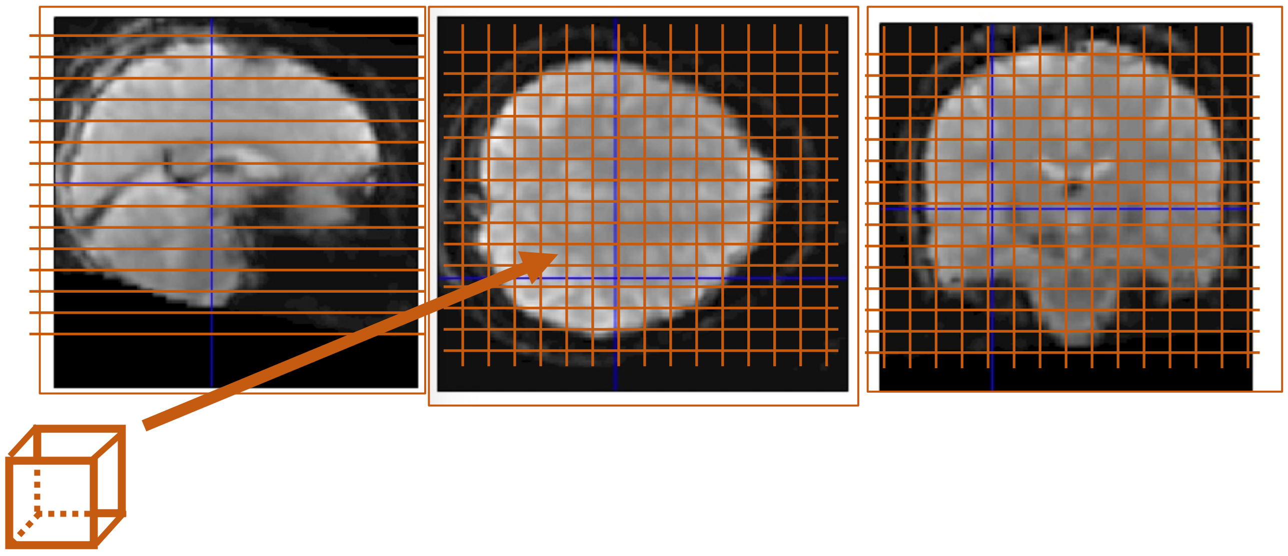
$y = \beta X + \varepsilon$: regressors



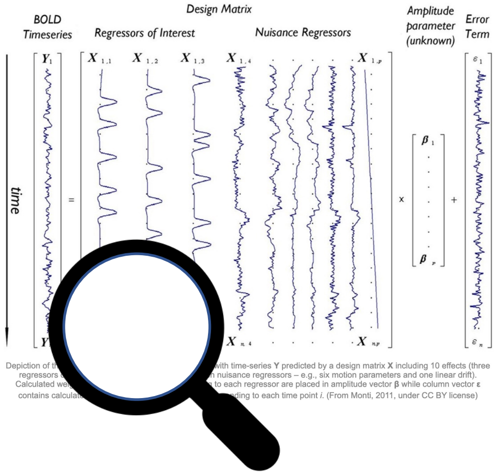
Simuli
A (bright light)
B (medium bright light)
C (not bright light)

- Red arrows above points timing for A

→ Might find a voxel showing HRF as illustrated in the visual cortex



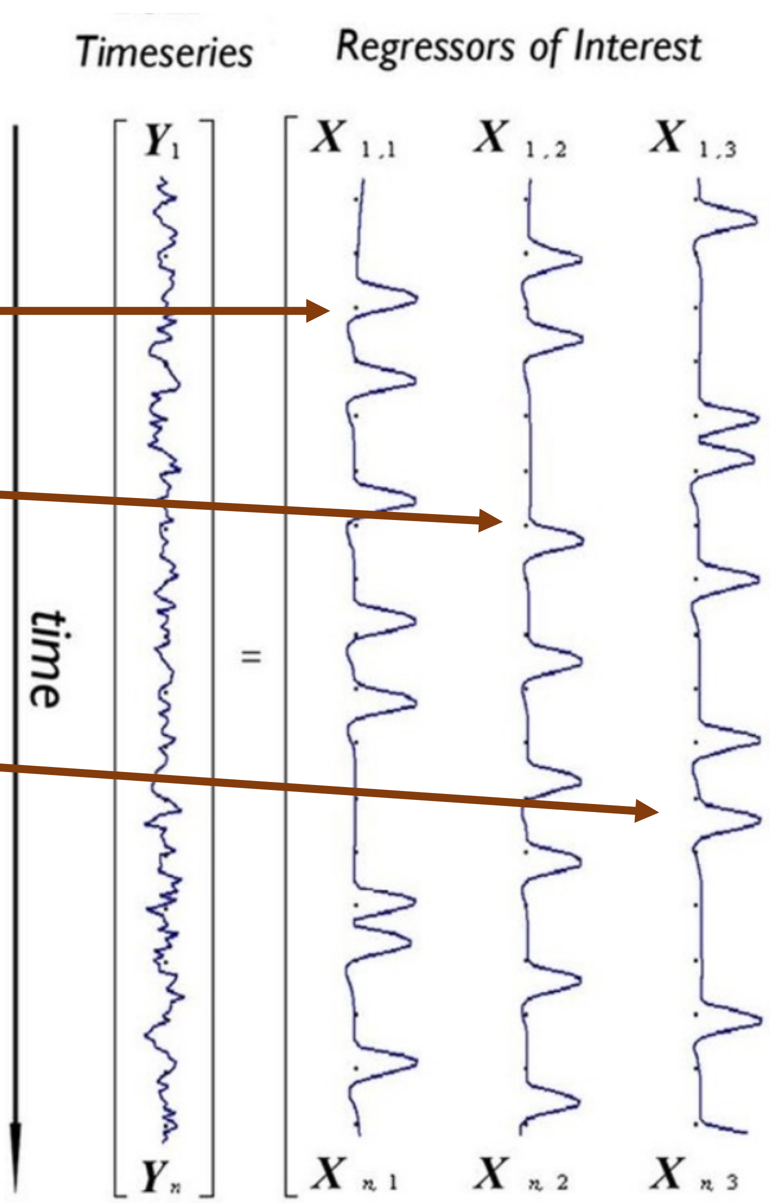
$y = \beta X + \varepsilon$: regressors

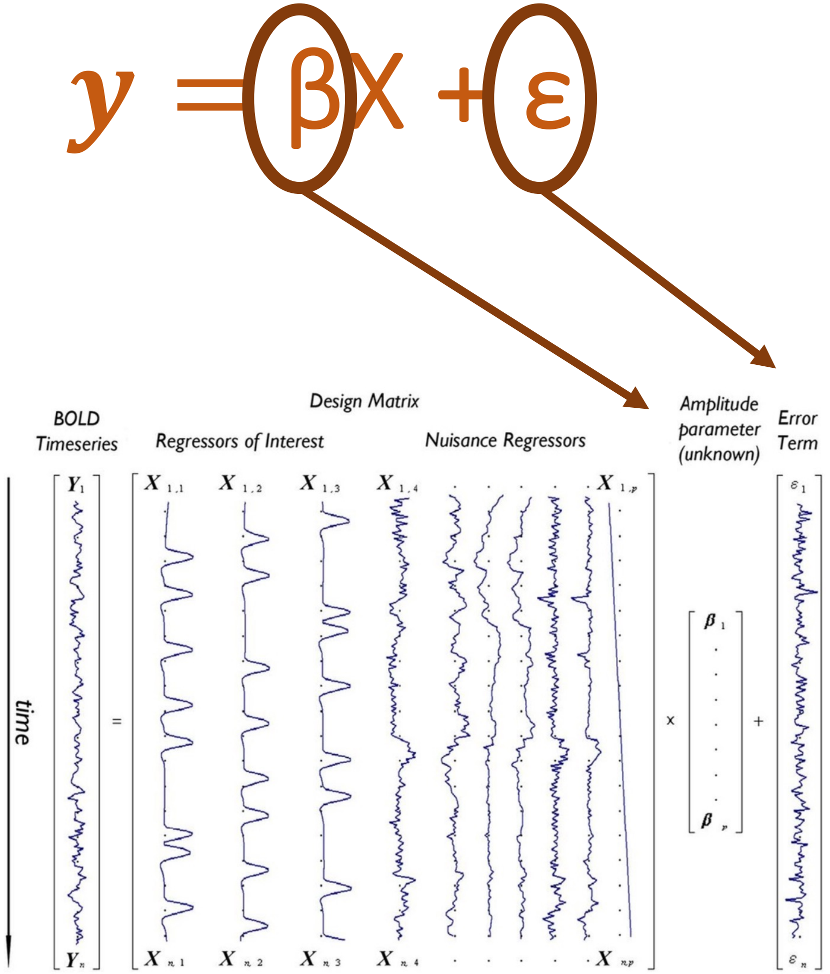


Stimulus A on

Stimulus B on

Stimulus C on





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- **ε** = error
- Aim to be mimized (patient trainingn, scanner optimization, preprocessing, modeling….)

- ***β*** *and* **ε** vectors are computed

→ Statistical testing for hypothesis

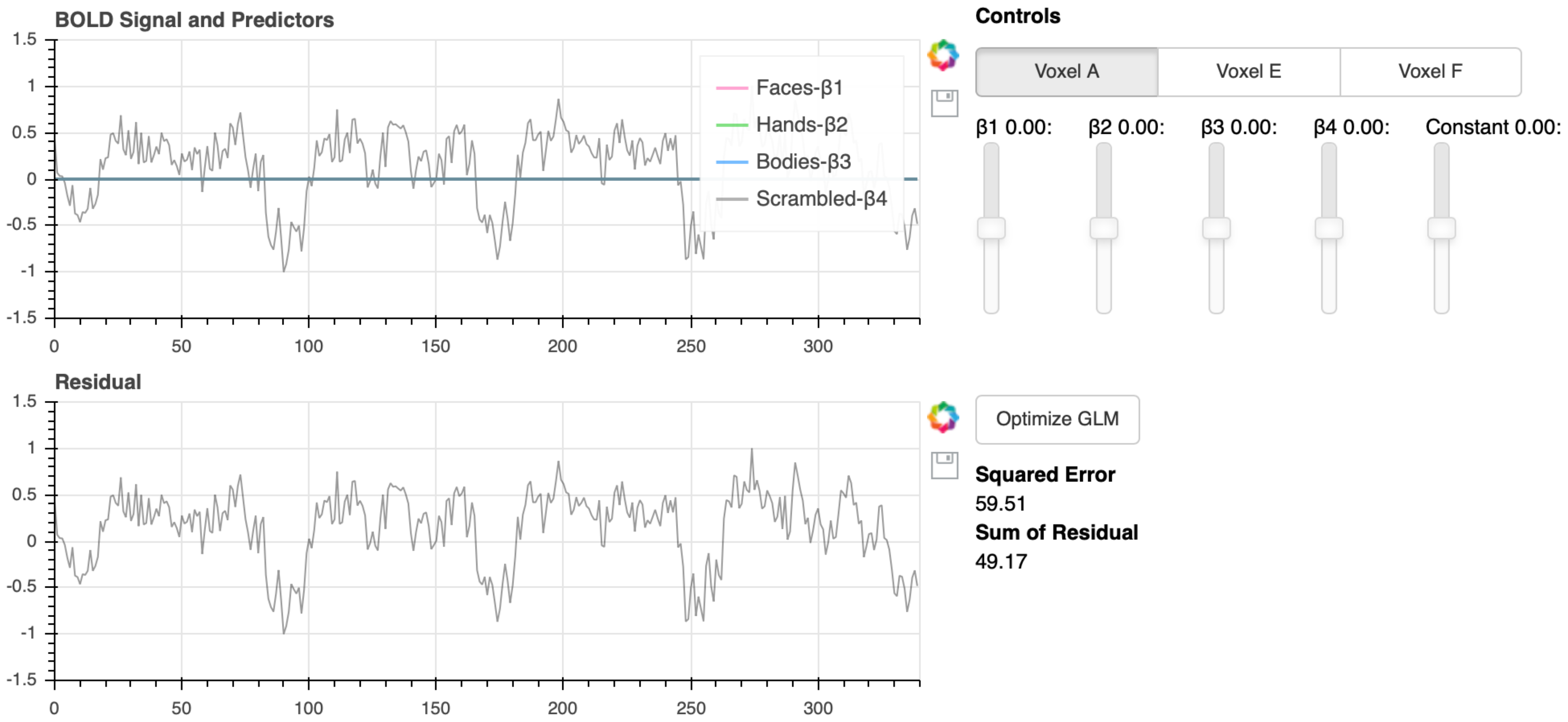
→ ***Statistical Parametric Map (SPM)*** or ***Posterior Probability Map (PPM)***

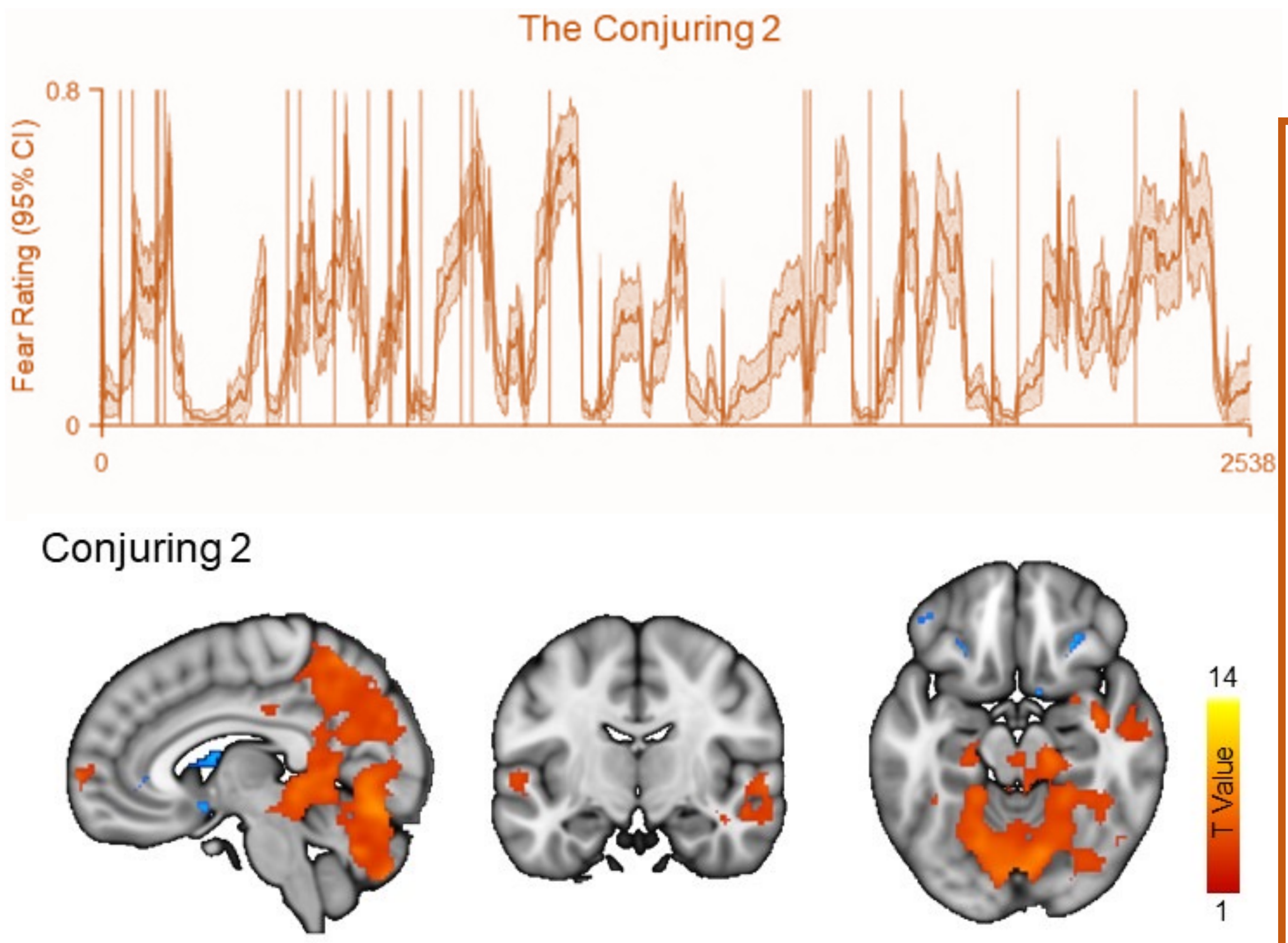
NEWBI 4 fMRI

Neuroimaging Web-Based Instruction for fMRI

http://129.100.119.110:22028/GLM-LocalizerPred

http://www.newbi4fmri.com/tutorial-3-glm



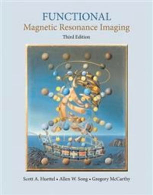


Supplementary Figure 2. The relationship between experienced fear and neural activity for Conjuring 2.

Fear ratings were convolved with a hemodynamic response function and entered as a regressor into a GLM analysis with a high-pass filter of 256s (uncorrected $p = 0.001$).

Hudson et al. "Dissociable neural systems for unconditioned acute and sustained fear", NeuroImage, Vol 216, 2020.

Limitations and Assumptions



- Hemodynamic response might differ across the brain areas but the model is the same for each voxel (betas calculated separately)

- Model assumes that noise varies with a normal distribution in each voxel in each time point (differs greatly close to large arteries)

- Model assumes also independent statistical test for each voxel (adjacent voxels have similar properties)

Summary

- **Linear System**: for a given input the system will respond with same output
- **GLM**: General linear model

$$y = \beta X + \varepsilon$$

- ”Stated in words, the GLM says that **Y** (the measured fMRI signal from a single voxel as a function of time) can be expressed as the sum of one or more experimental design variables (**X**), each multiplied by a weighting factor (**β**), plus random error (**ε**)”

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Question Time!