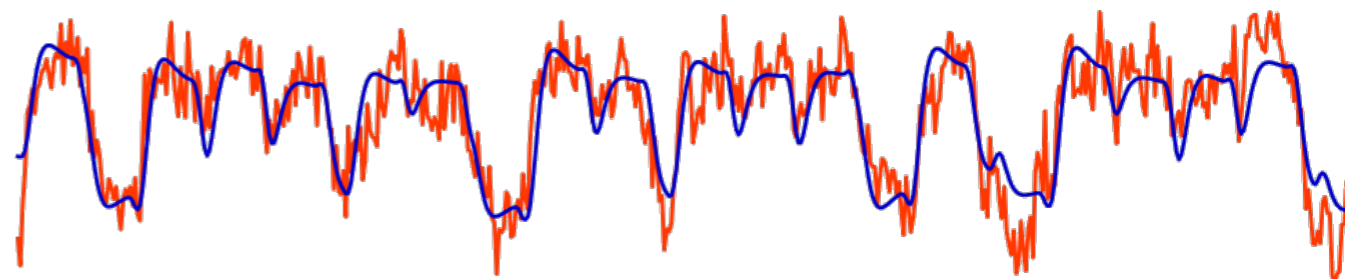




FMRI single subject analysis

- Overview
- Preprocessing
- **Setting up a GLM model**
- Contrasts and statistics

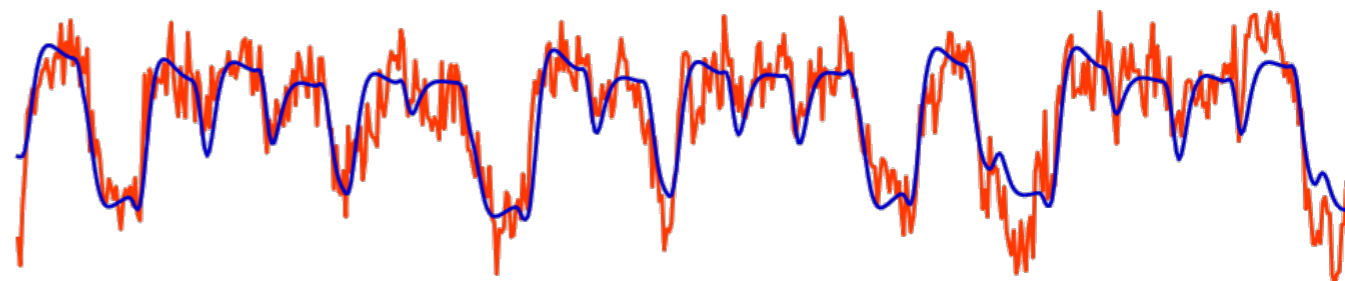
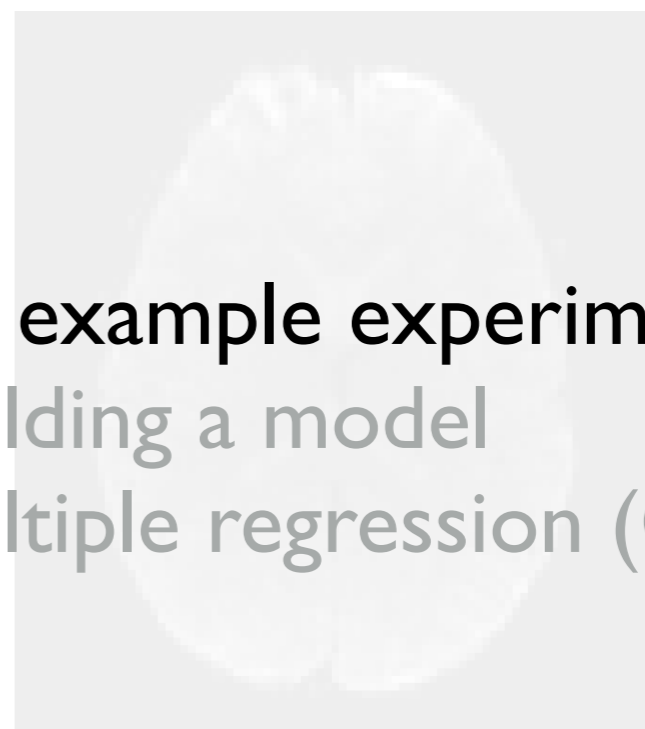




FMRI single subject analysis

- Overview
- Preprocessing
- **Setting up a GLM model**
- Contrasts and statistics

- **An example experiment**
- Building a model
- Multiple regression (GLM)

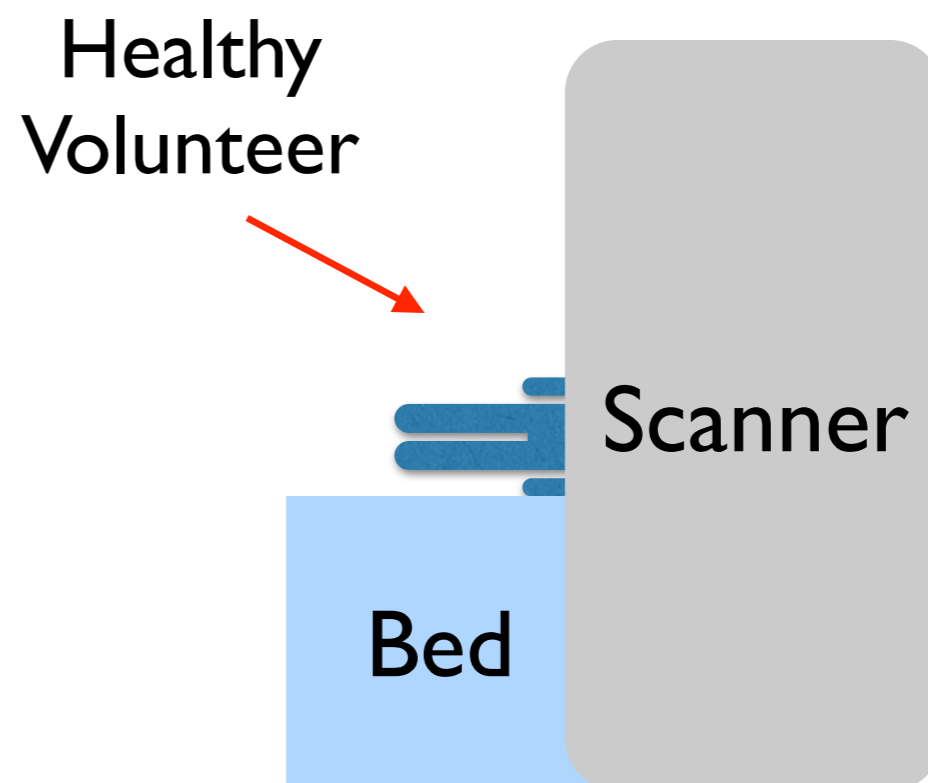
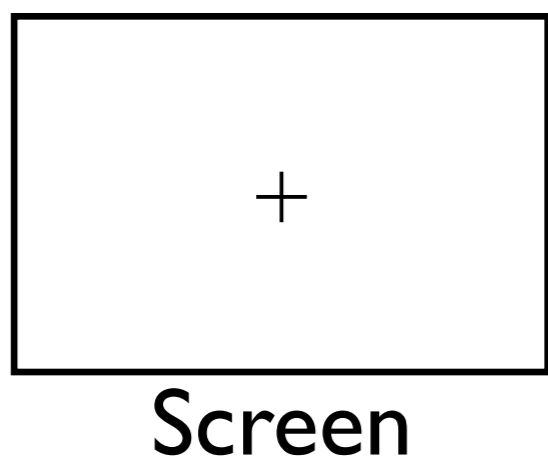




An example experiment

An fMRI adaptation of a classical PET experiment

- Three types of events
- 1st type: Word Generation



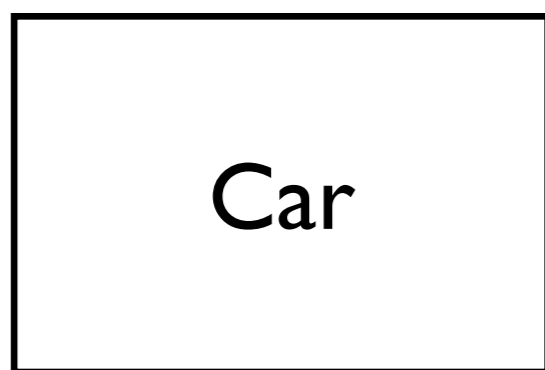


An example experiment

An fMRI adaptation of a classical PET experiment

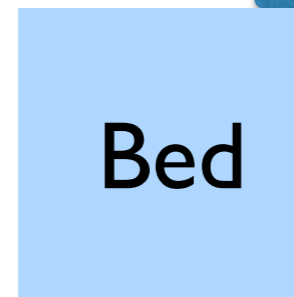
- Three types of events
- 1st type: Word Generation

Noun is presented



Screen

Healthy Volunteer



Bed

Verb is generated



Scanner



An example experiment

An fMRI adaptation of a classical PET experiment

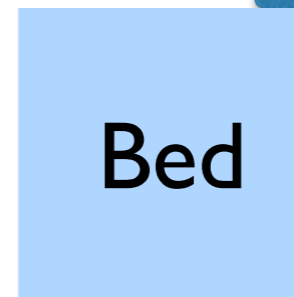
- Three types of events
- 1st type: Word Generation

Noun is presented



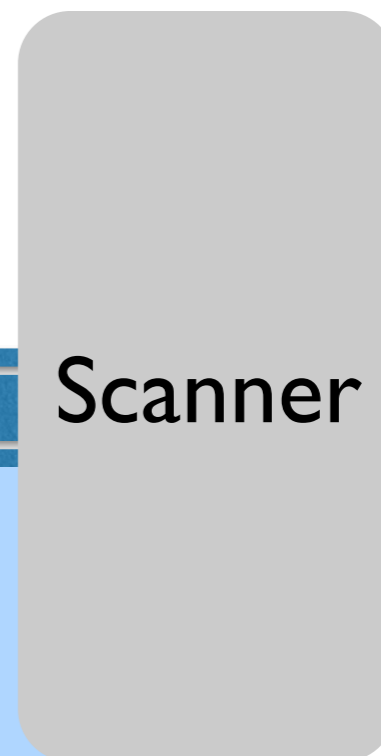
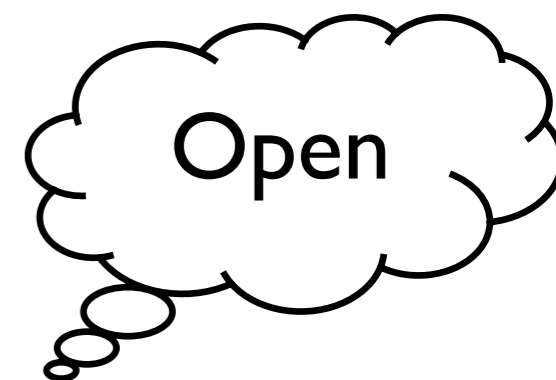
Screen

Healthy
Volunteer



Bed

Verb is generated



Scanner



An example experiment

An fMRI adaptation of a classical PET experiment

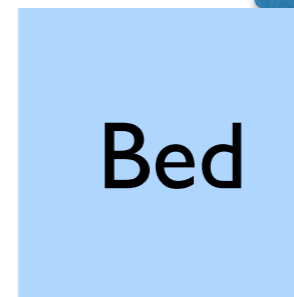
- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing

Verb is presented

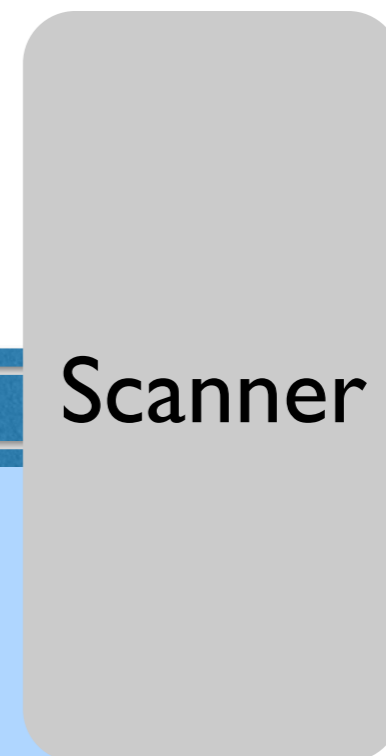


Screen

Healthy
Volunteer



Bed



Scanner

Verb is repeated



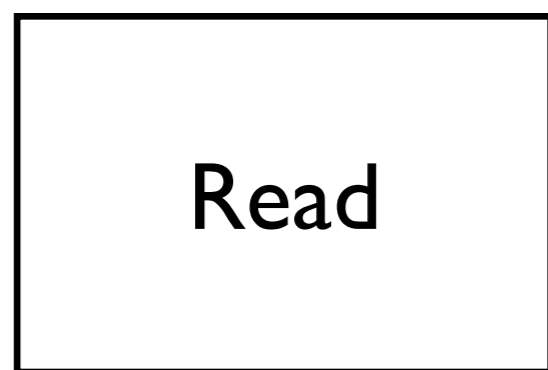


An example experiment

An fMRI adaptation of a classical PET experiment

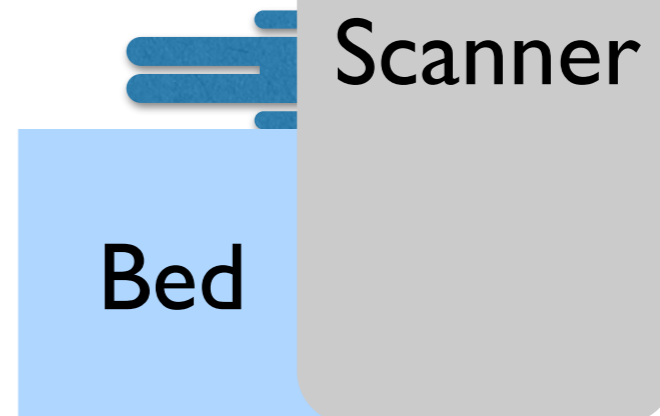
- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing

Verb is presented

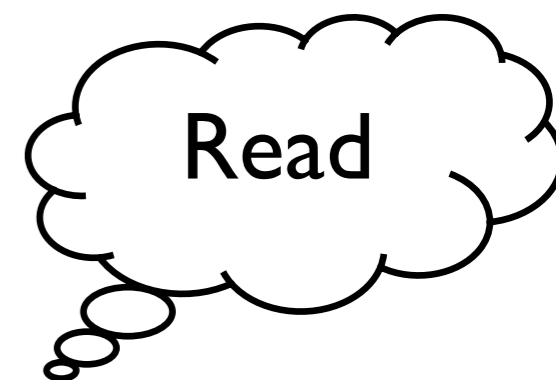


Screen

Healthy
Volunteer



Verb is repeated



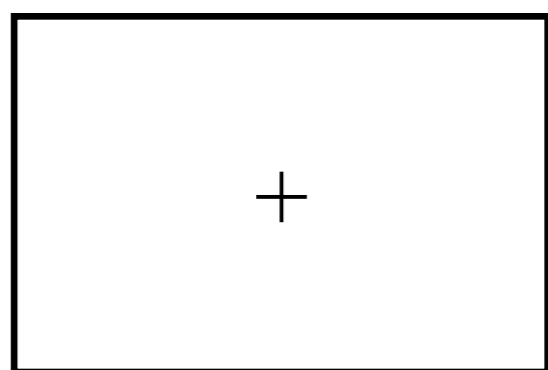


An example experiment

An fMRI adaptation of a classical PET experiment

- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing
- 3rd type: Null event

Crosshair is shown



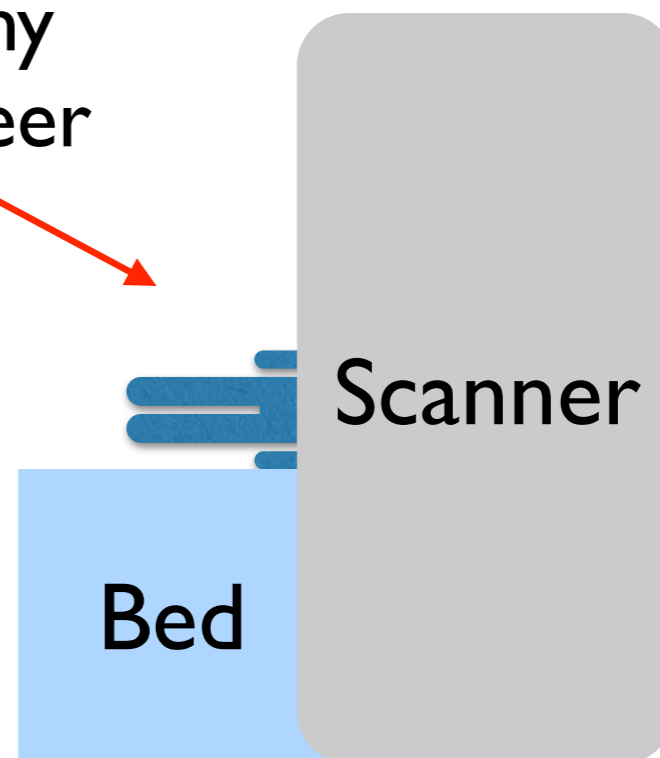
Screen

Healthy
Volunteer



Scanner

Bed



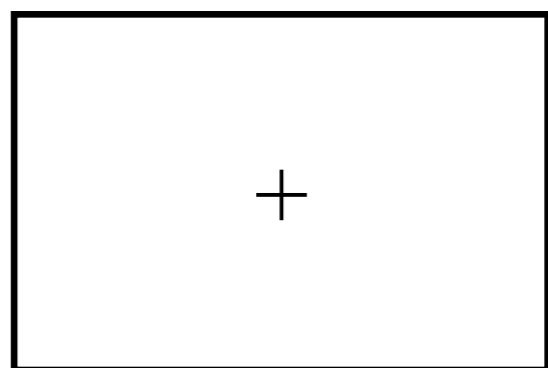


An example experiment

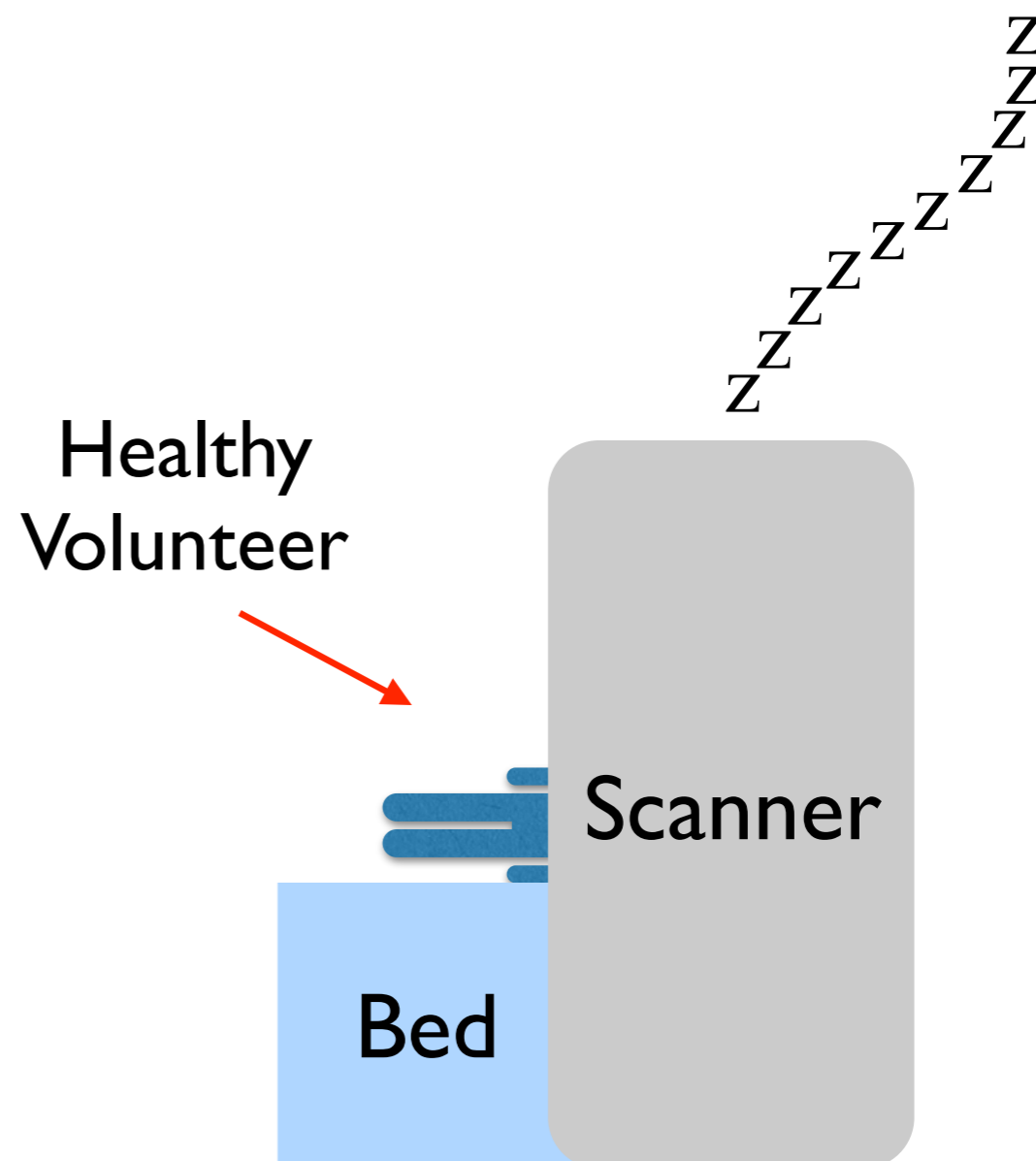
An fMRI adaptation of a classical PET experiment

- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing
- 3rd type: Null event

Crosshair is shown



Screen

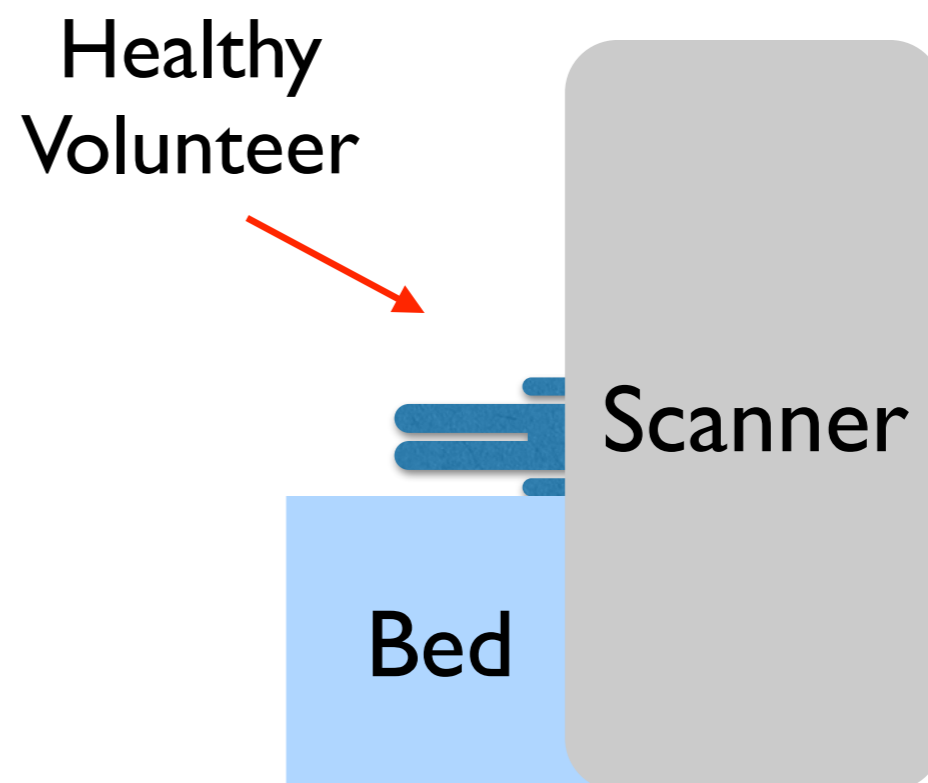
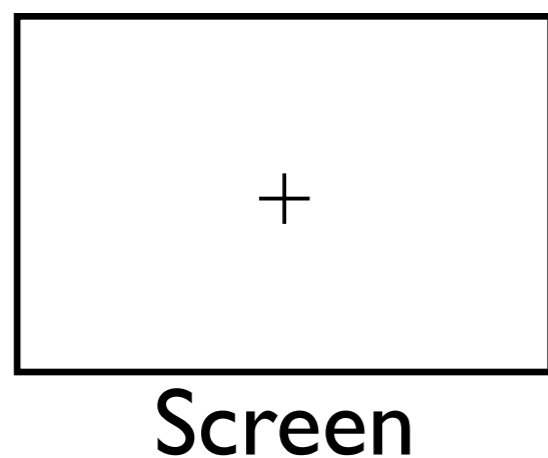




An example experiment

An fMRI adaptation of a classical PET experiment

- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing
- 3rd type: Null event
- 6 sec ISI, random order

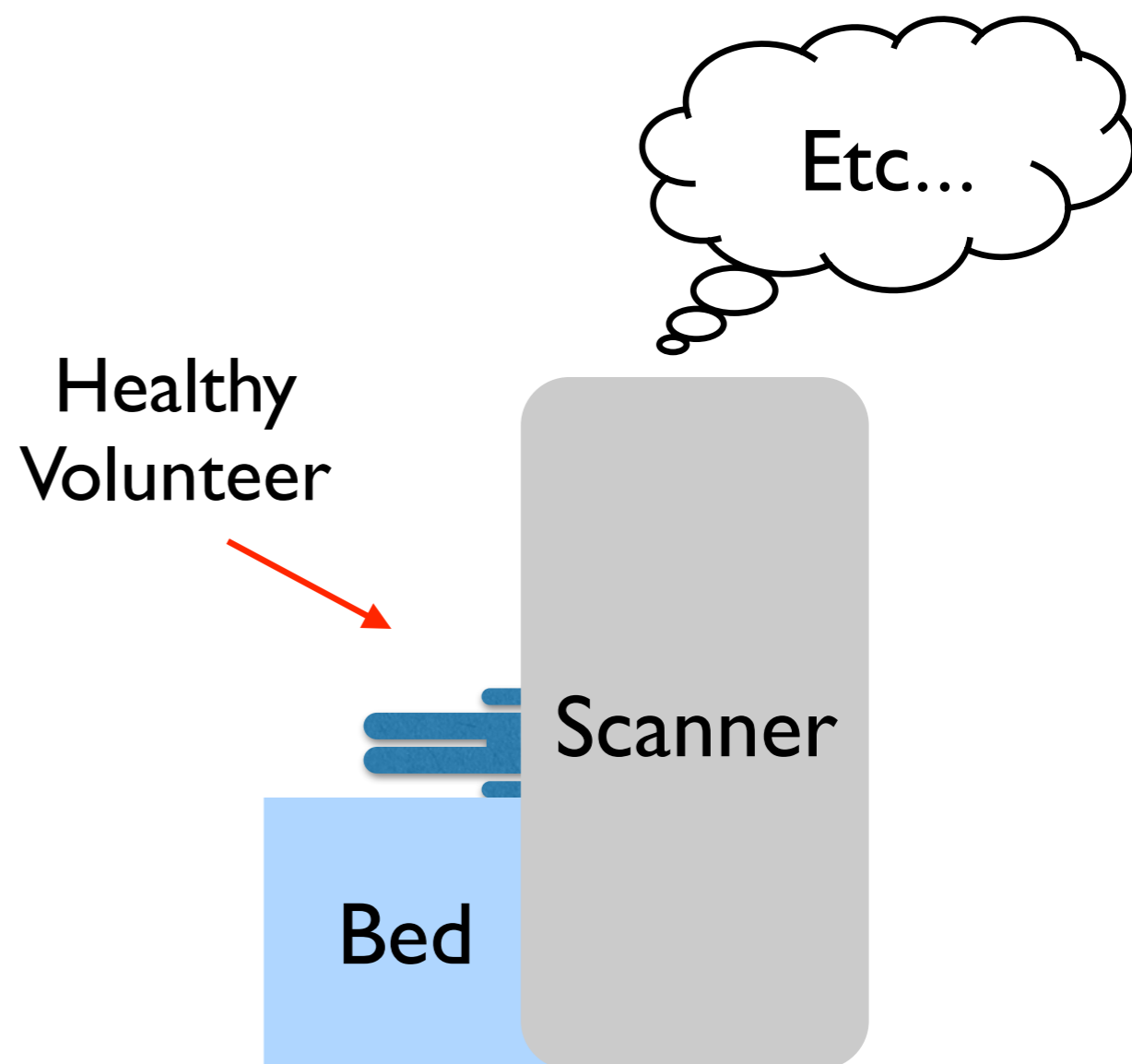
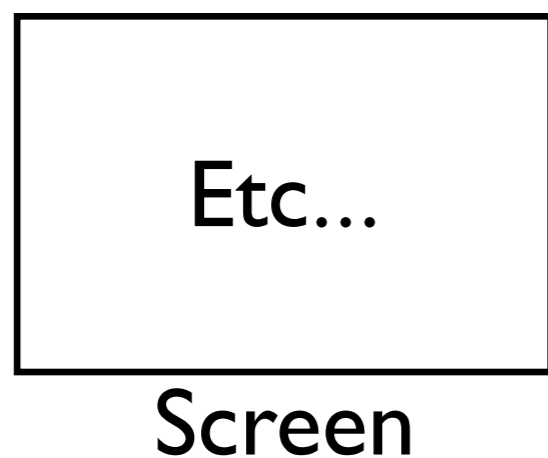




An example experiment

An fMRI adaptation of a classical PET experiment

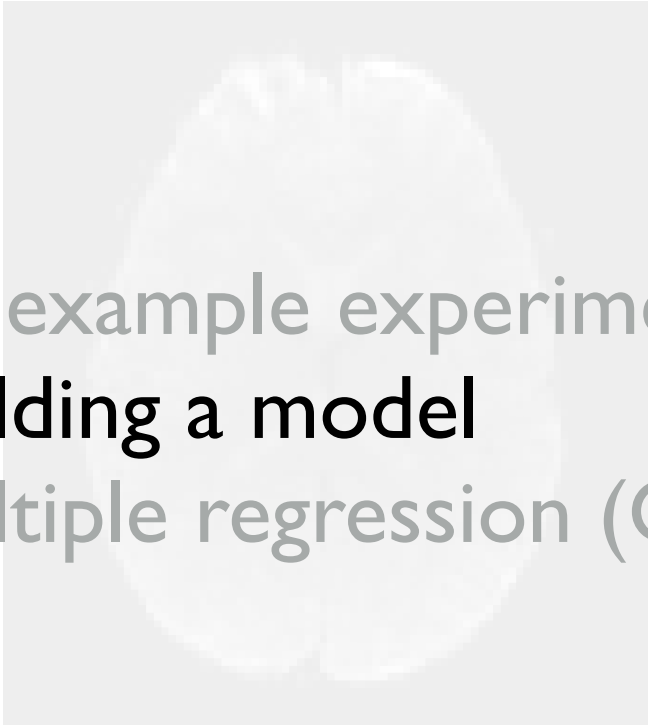
- Three types of events
- 1st type: Word Generation
- 2nd type: Word Shadowing
- 3rd type: Null event
- 6 sec ISI, random order
- For 24 events of each type

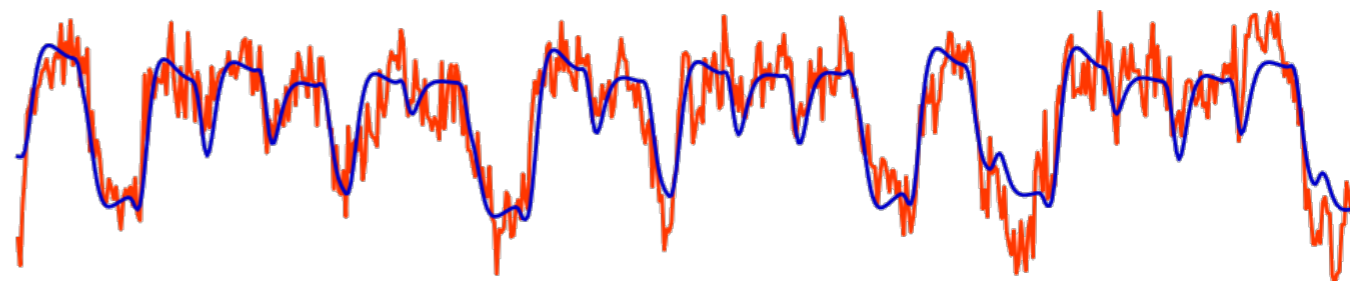




FMRI single subject analysis

- Overview
- Preprocessing
- **Setting up a GLM model**
- Contrasts and statistics

- 
- A grayscale axial slice of a human brain, showing the cerebral cortex and internal structures. It is positioned behind the text on the right side of the slide.
- An example experiment
 - **Building a model**
 - Multiple regression (GLM)





Building a model

Our task is now to build a model for that experiment

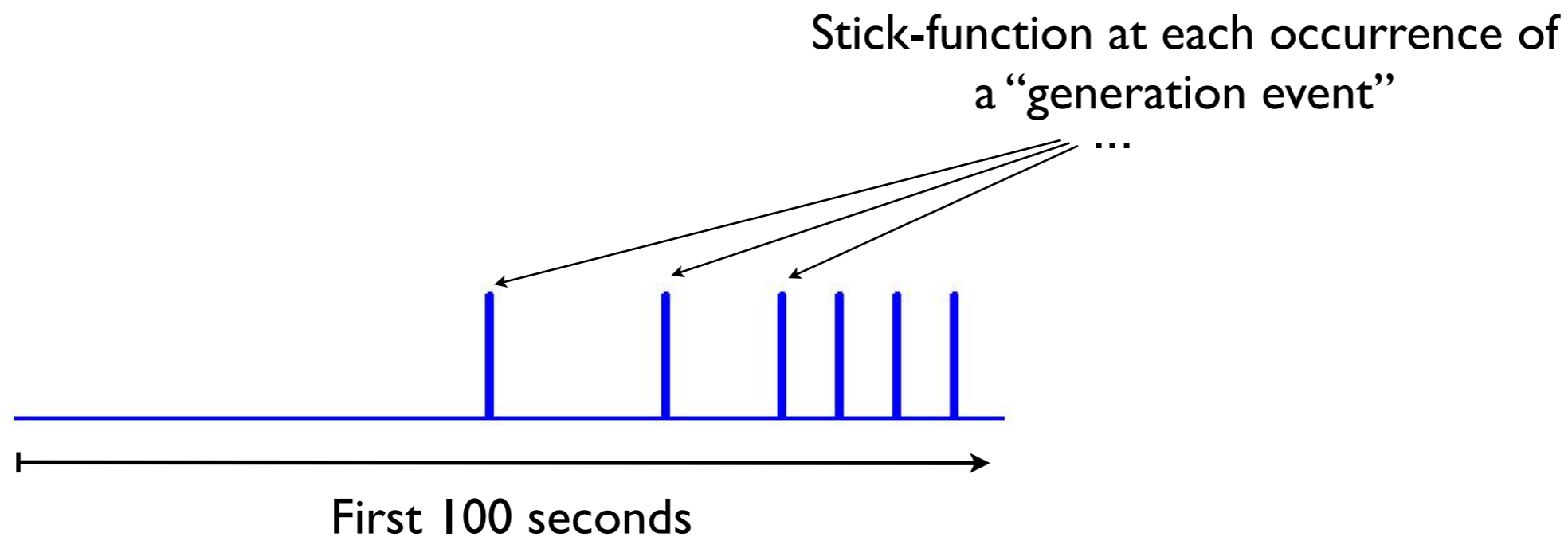
What is our predicted response to the word generation events?



Building a model

Our task is now to build a model for that experiment

What is our predicted response to the word generation events?



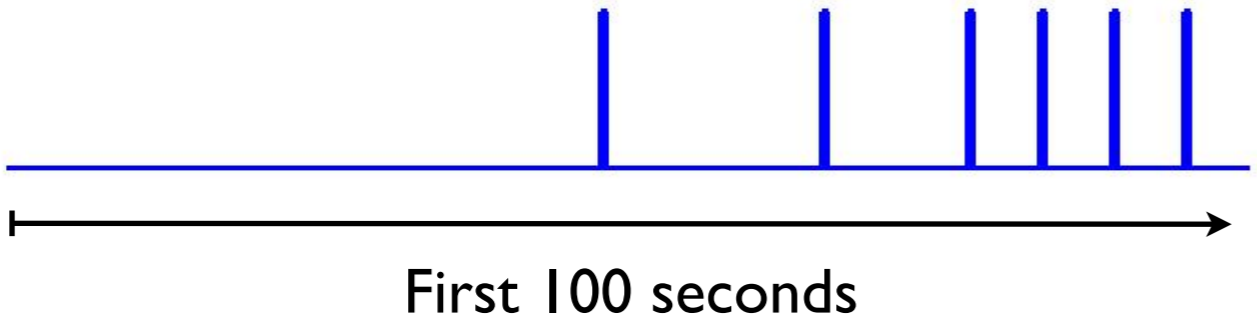
Well, hardly like this...



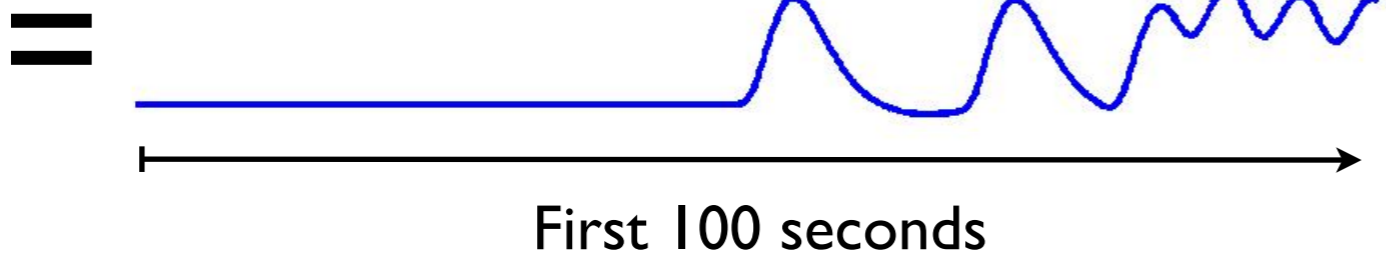
Building a model

Our task is now to build a model for that experiment

What is our predicted response to the word generation events?



$$\otimes \text{ HRF} =$$



predicted response

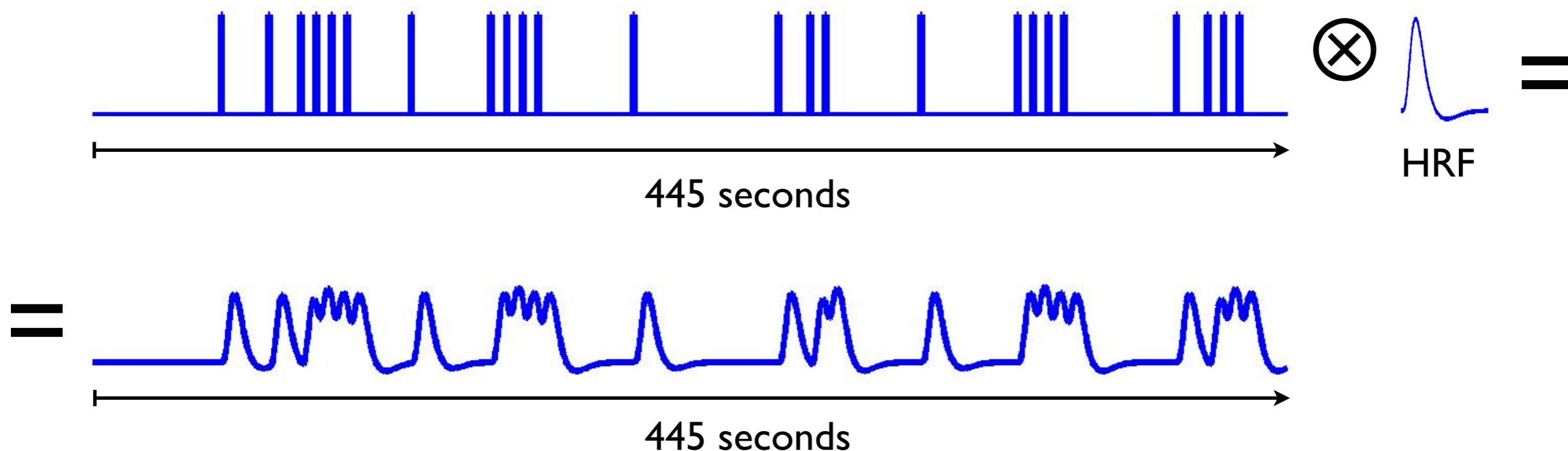
That looks better!



Building a model

Our task is now to build a model for that experiment

What is our predicted response to the word generation events?



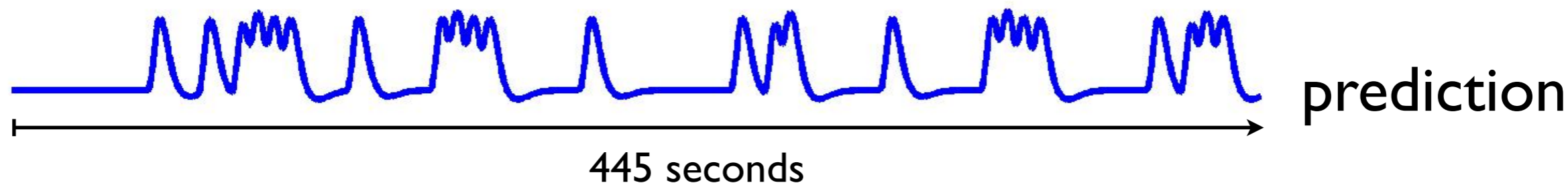
And this is the prediction for the whole time-series



Building a model

Our task is now to build a model for that experiment

What is our predicted response to the word generation events?



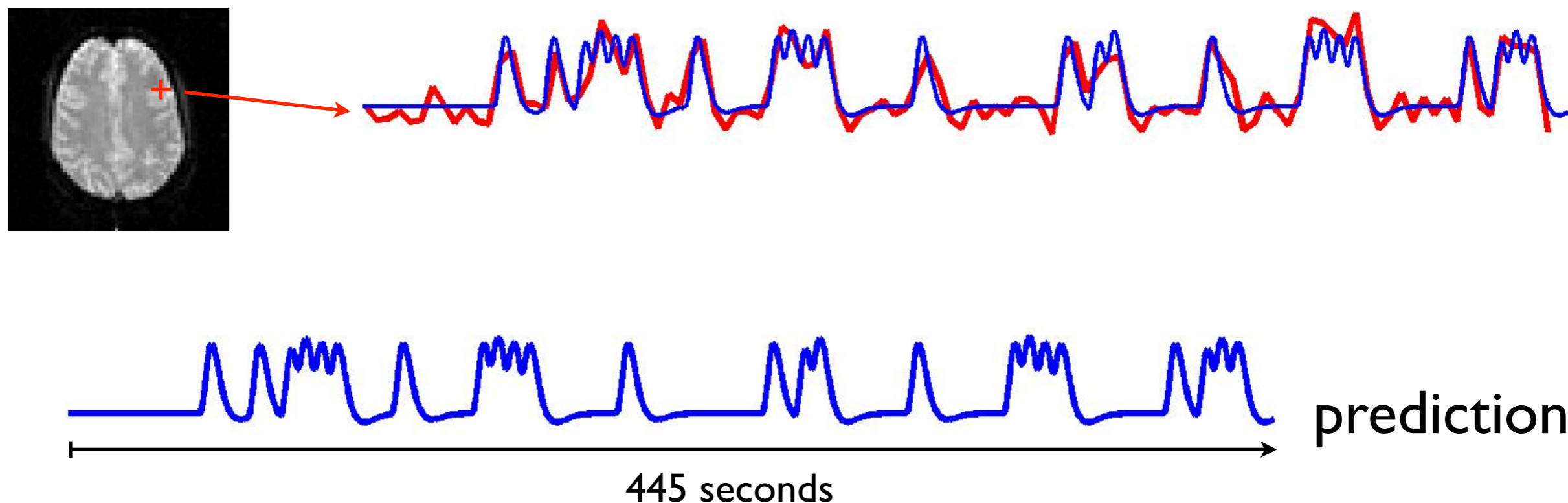
So, if we spot a time-series like this



Building a model

Our task is now to build a model for that experiment

What is our predicted response to the word generation events?



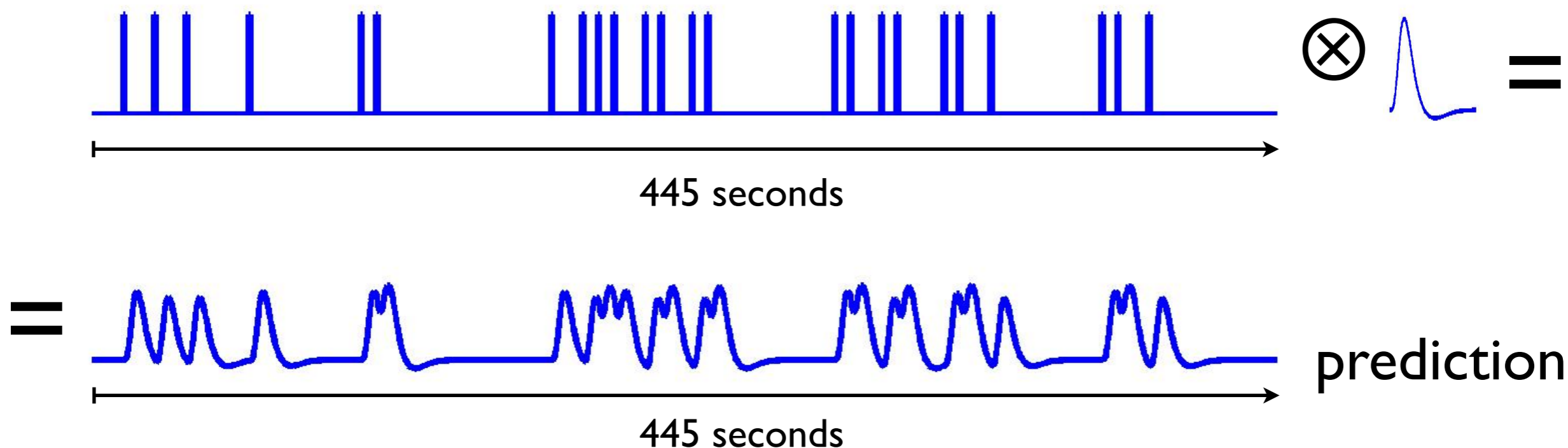
And then check it against our prediction
we can conclude that this voxel is into word generation



Building a model

Our task is now to build a model for that experiment

And we can do the same for the word shadowing events?



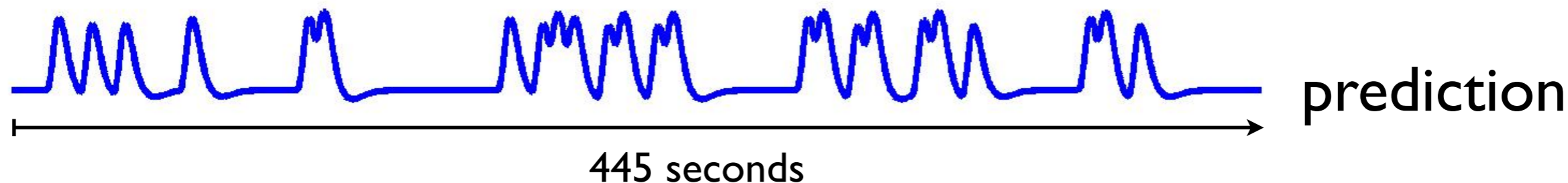
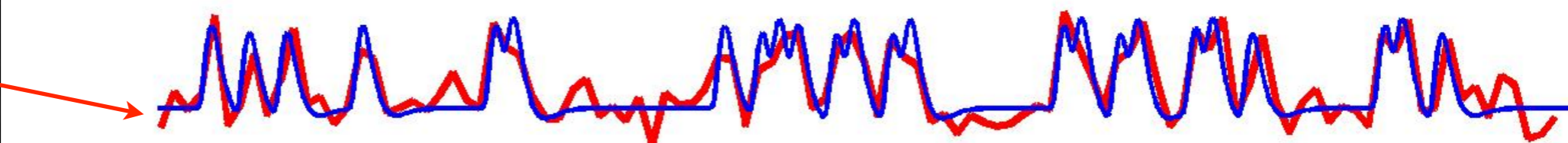
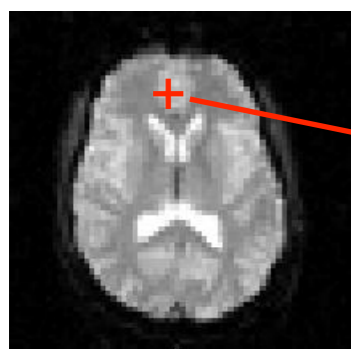
This time we used the onset times for the shadowing events to get the predicted brain response for those



Building a model

Our task is now to build a model for that experiment

And we can do the same for the word shadowing events?

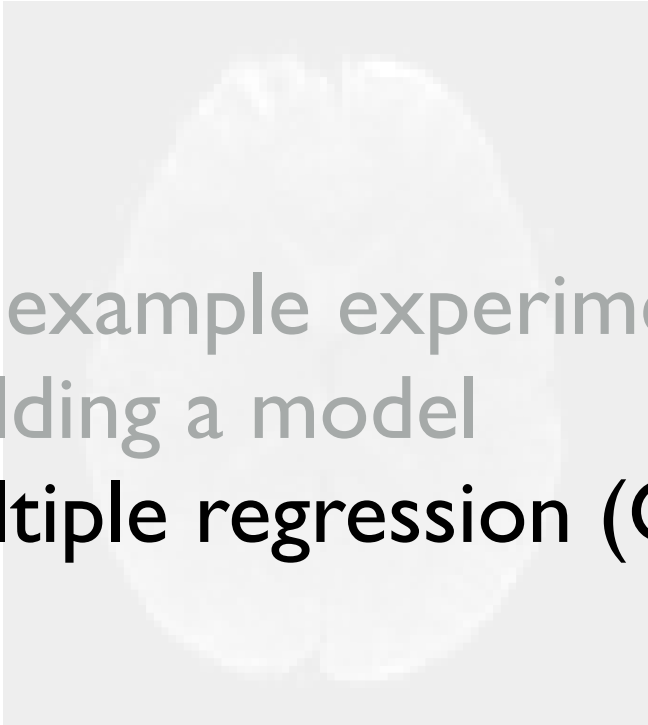


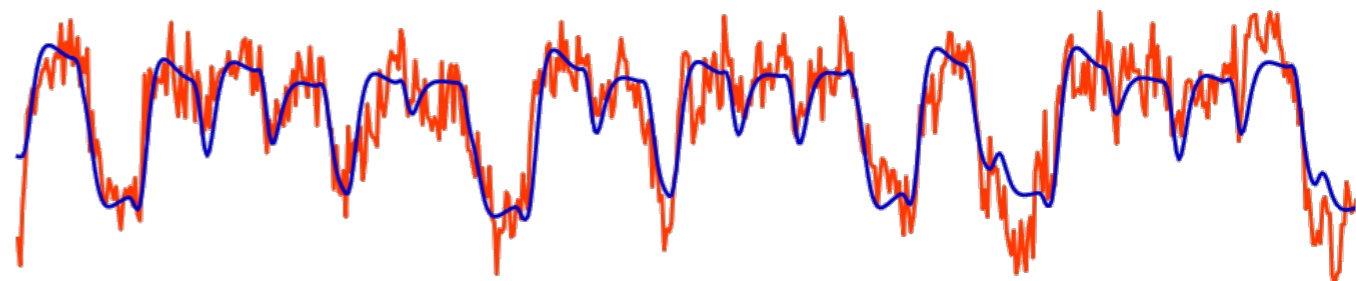
And we can look for voxels that match that



FMRI single subject analysis

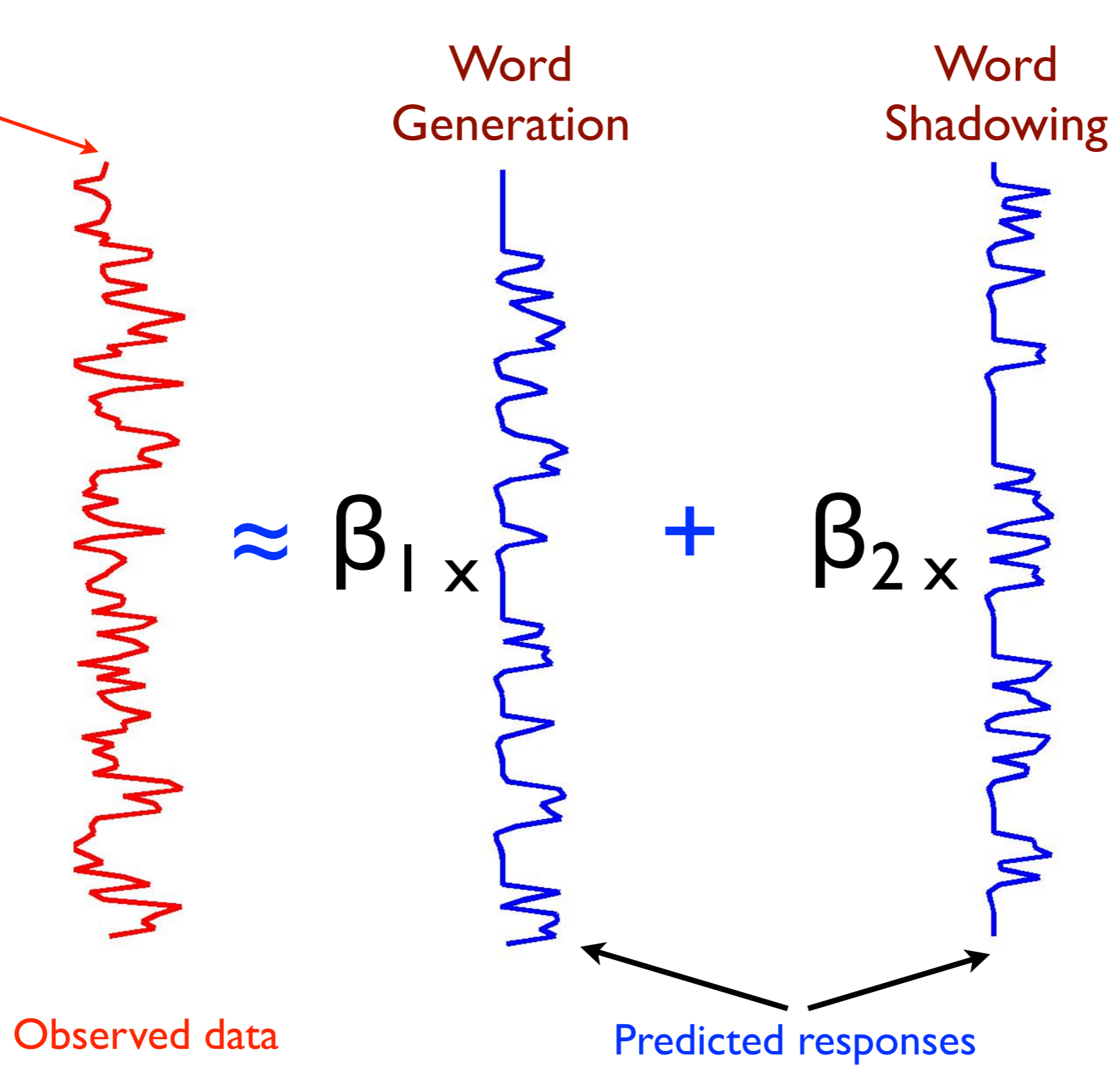
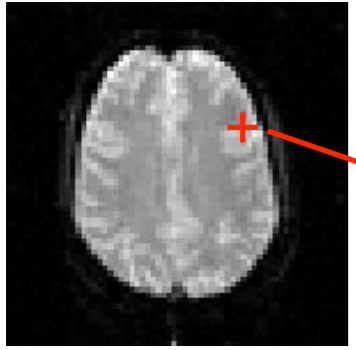
- Overview
- Preprocessing
- **Setting up a GLM model**
- Contrasts and statistics

- 
- A grayscale axial brain scan image is centered on the right side of the slide. It shows a cross-section of a human brain with some areas highlighted in white, likely representing regions of interest or activation.
- An example experiment
 - Building a model
 - **Multiple regression (GLM)**



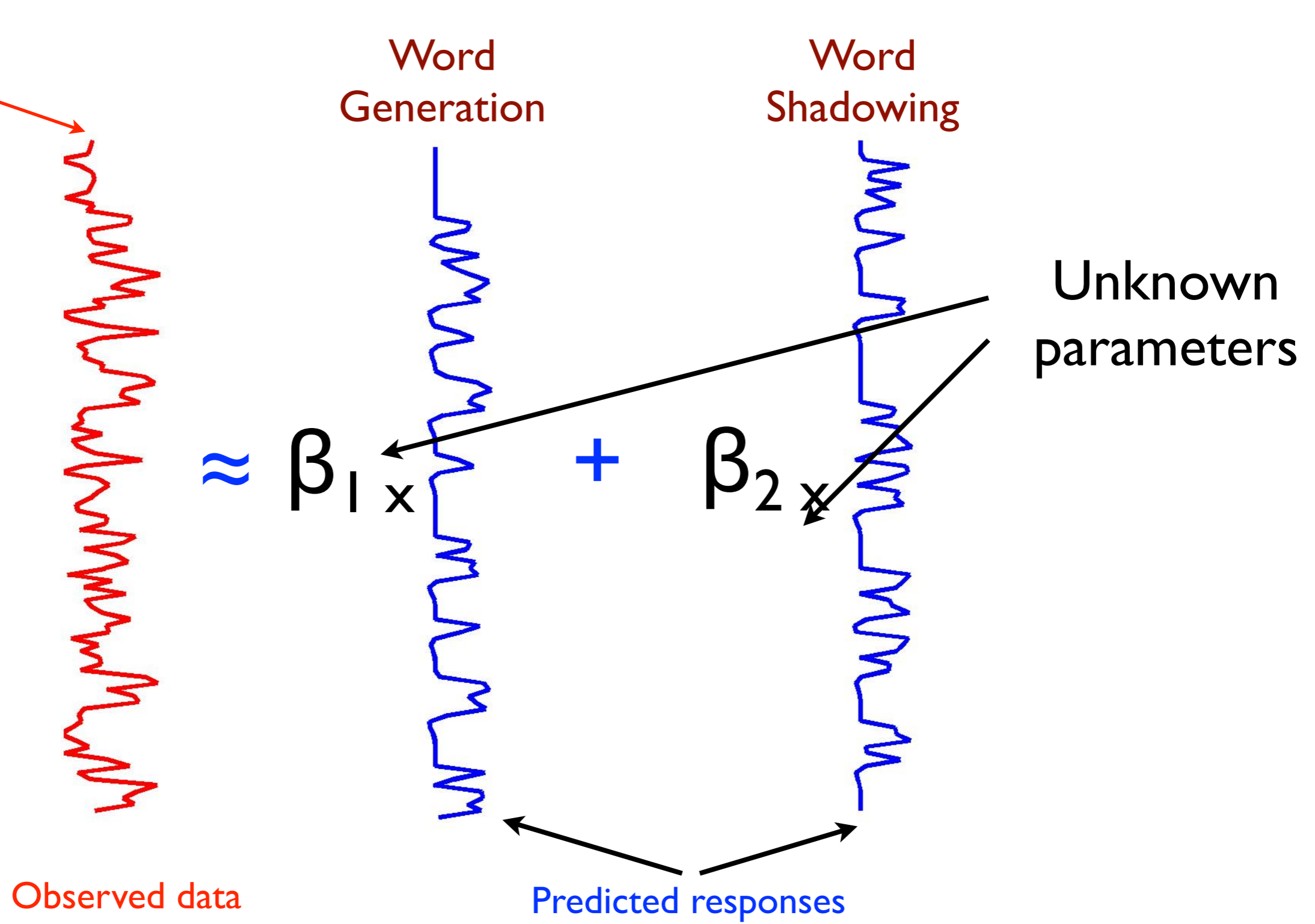
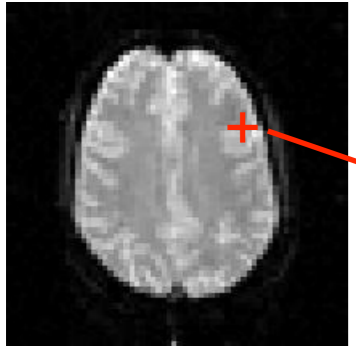


Formalising it: Multiple regression





Formalising it: Multiple regression

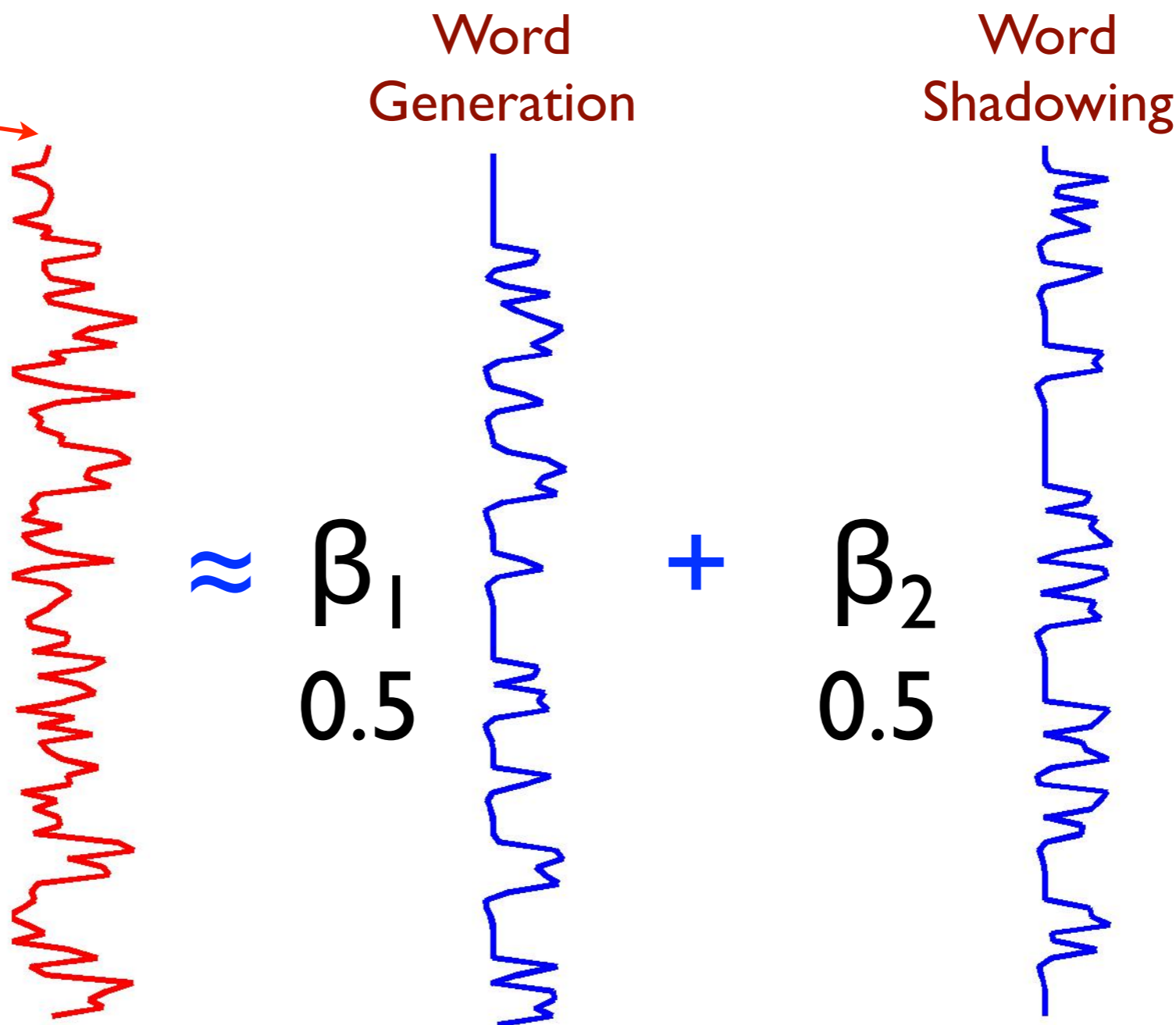
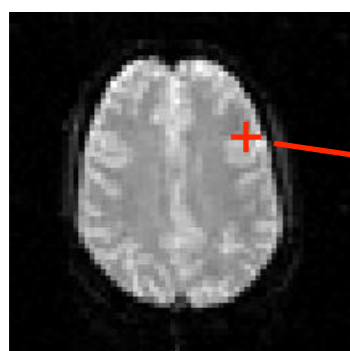




Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.



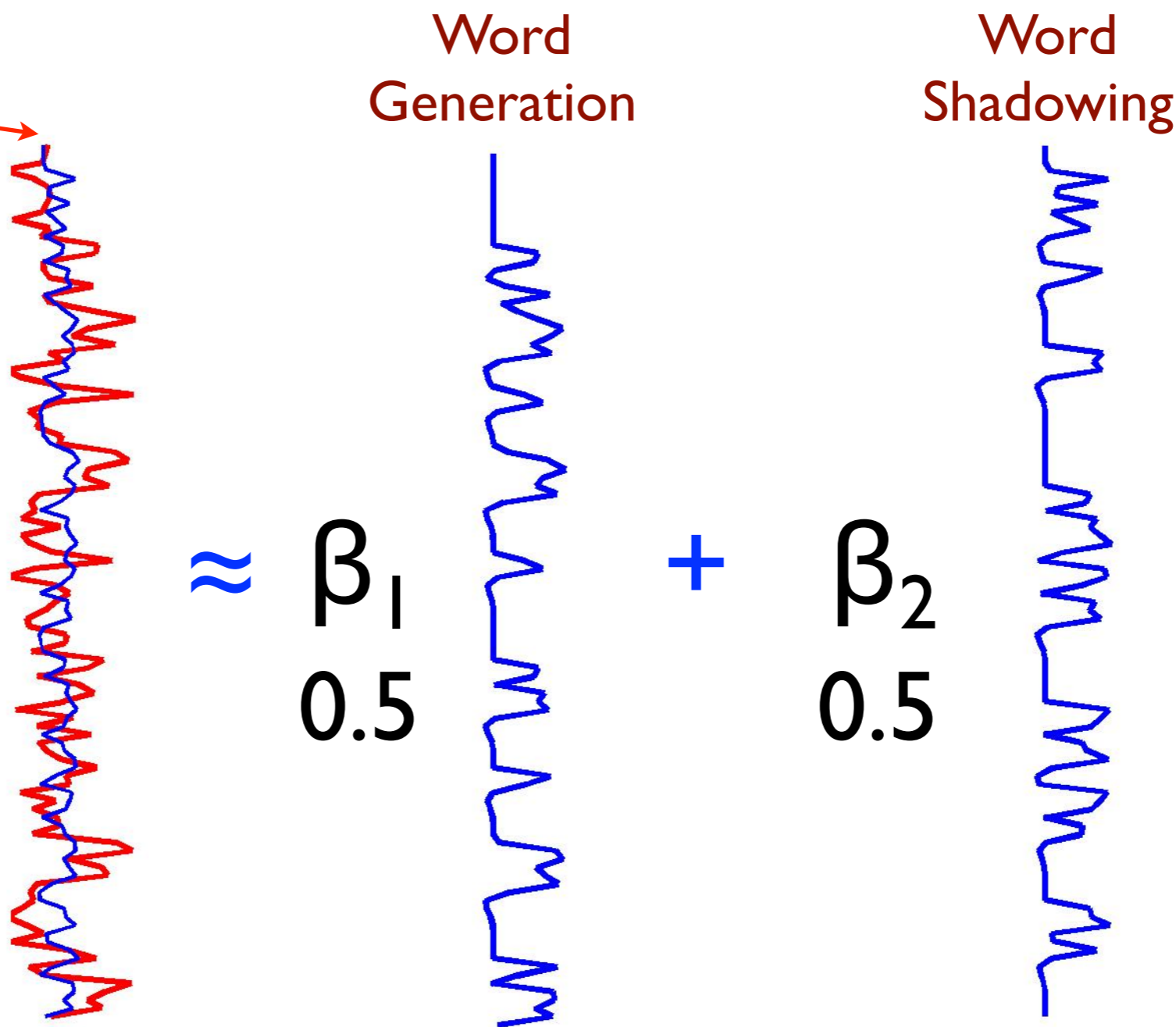
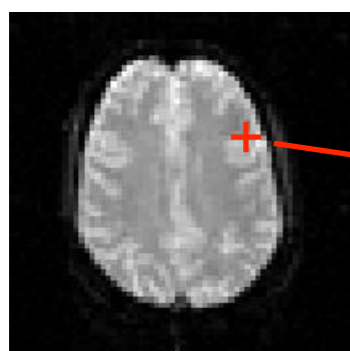
Let's try these parameter values



Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.



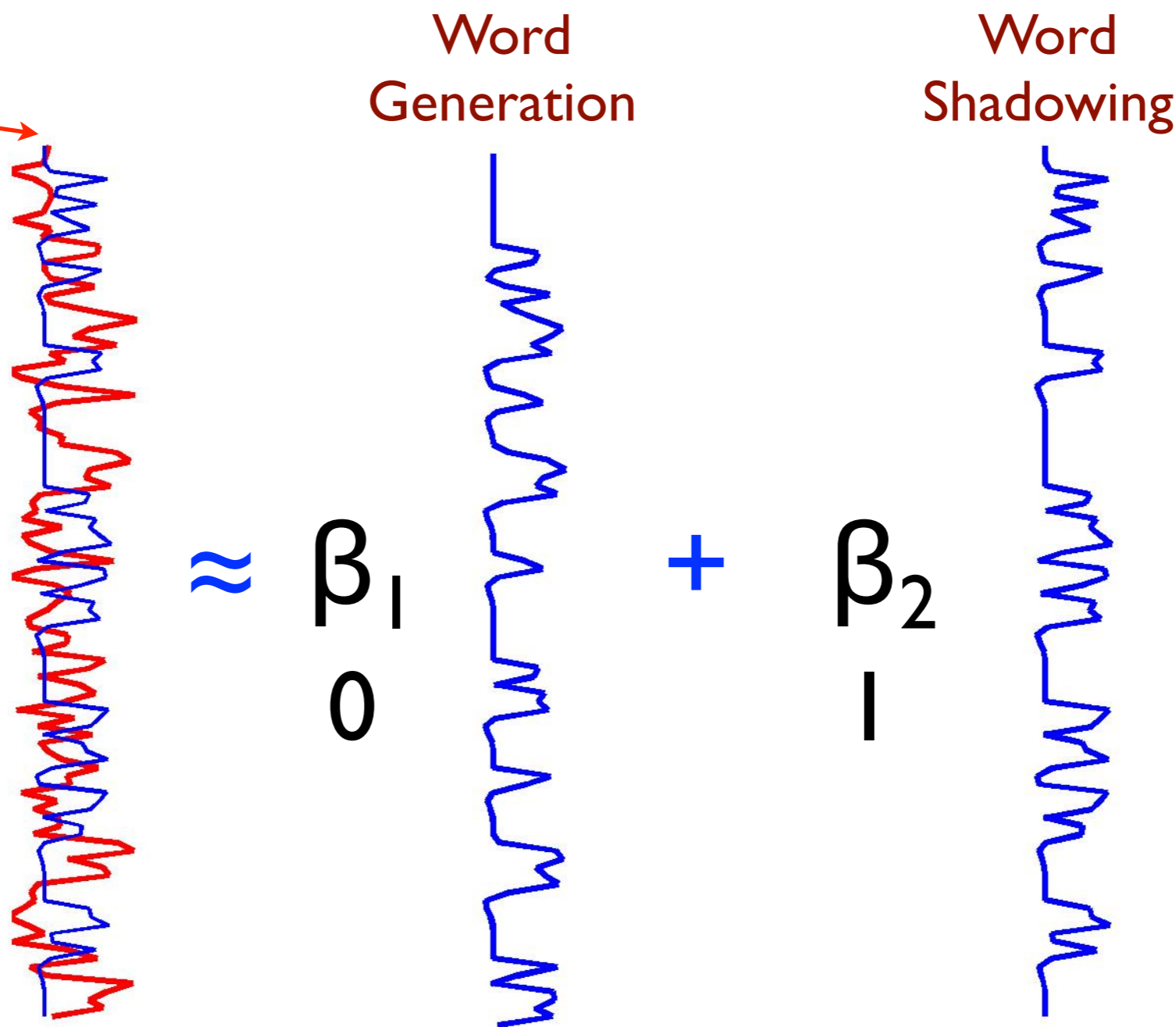
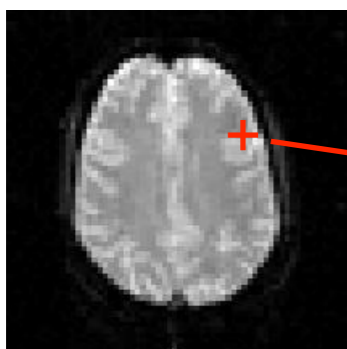
Hmm, not a great fit



Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.



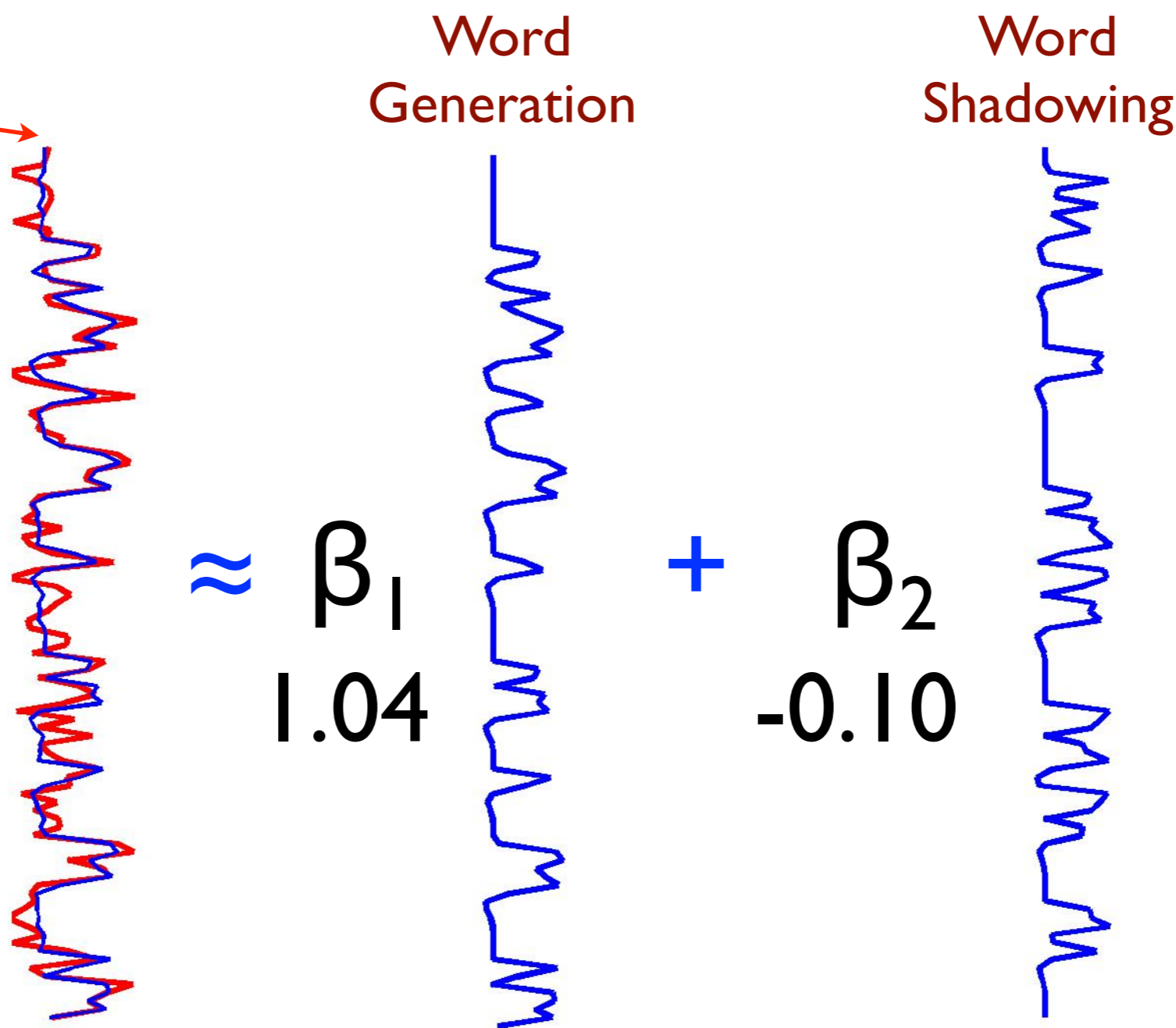
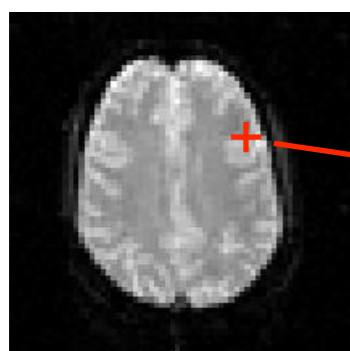
Oh dear, even worse



Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.



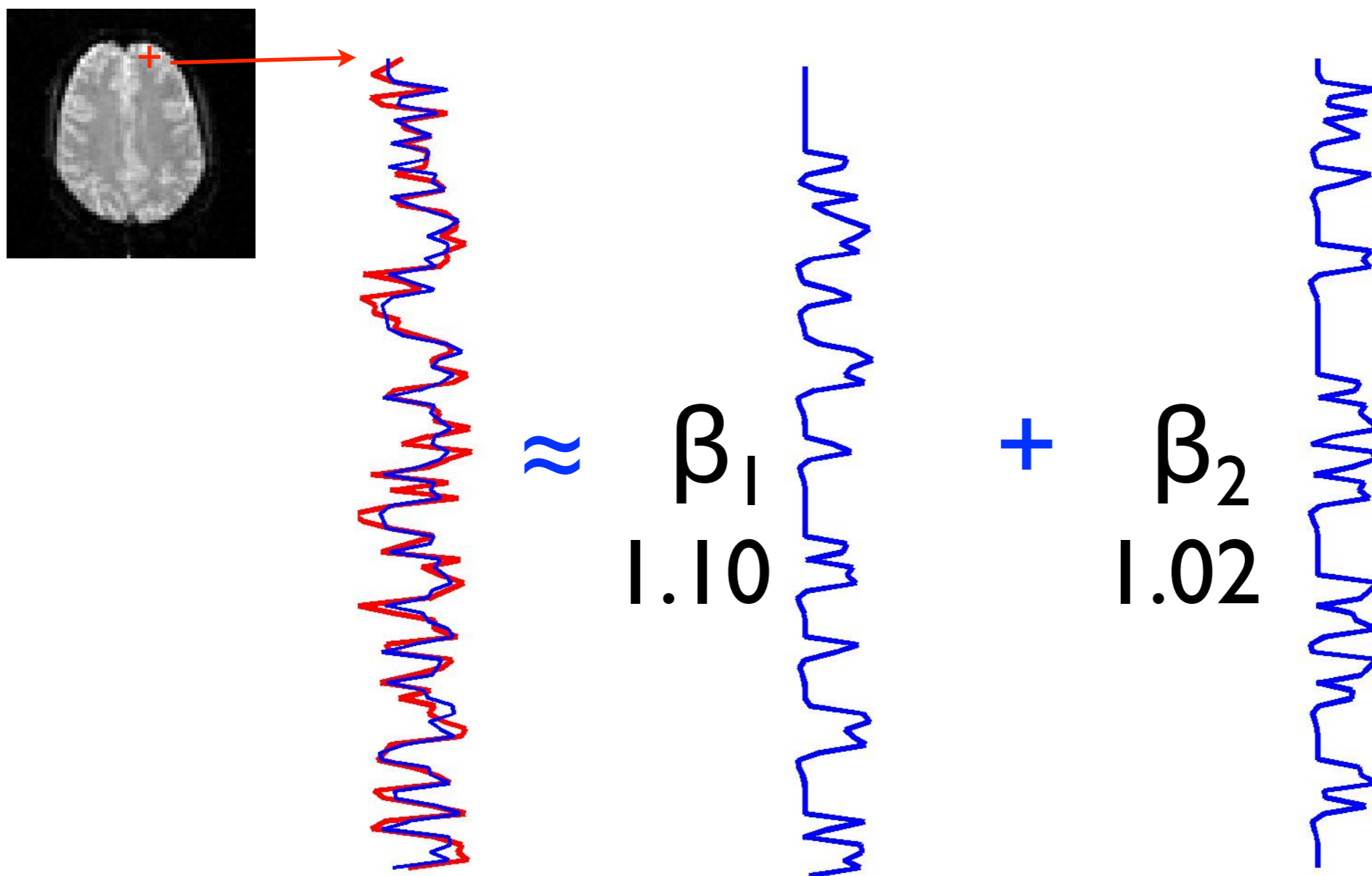
But that looks good



Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.



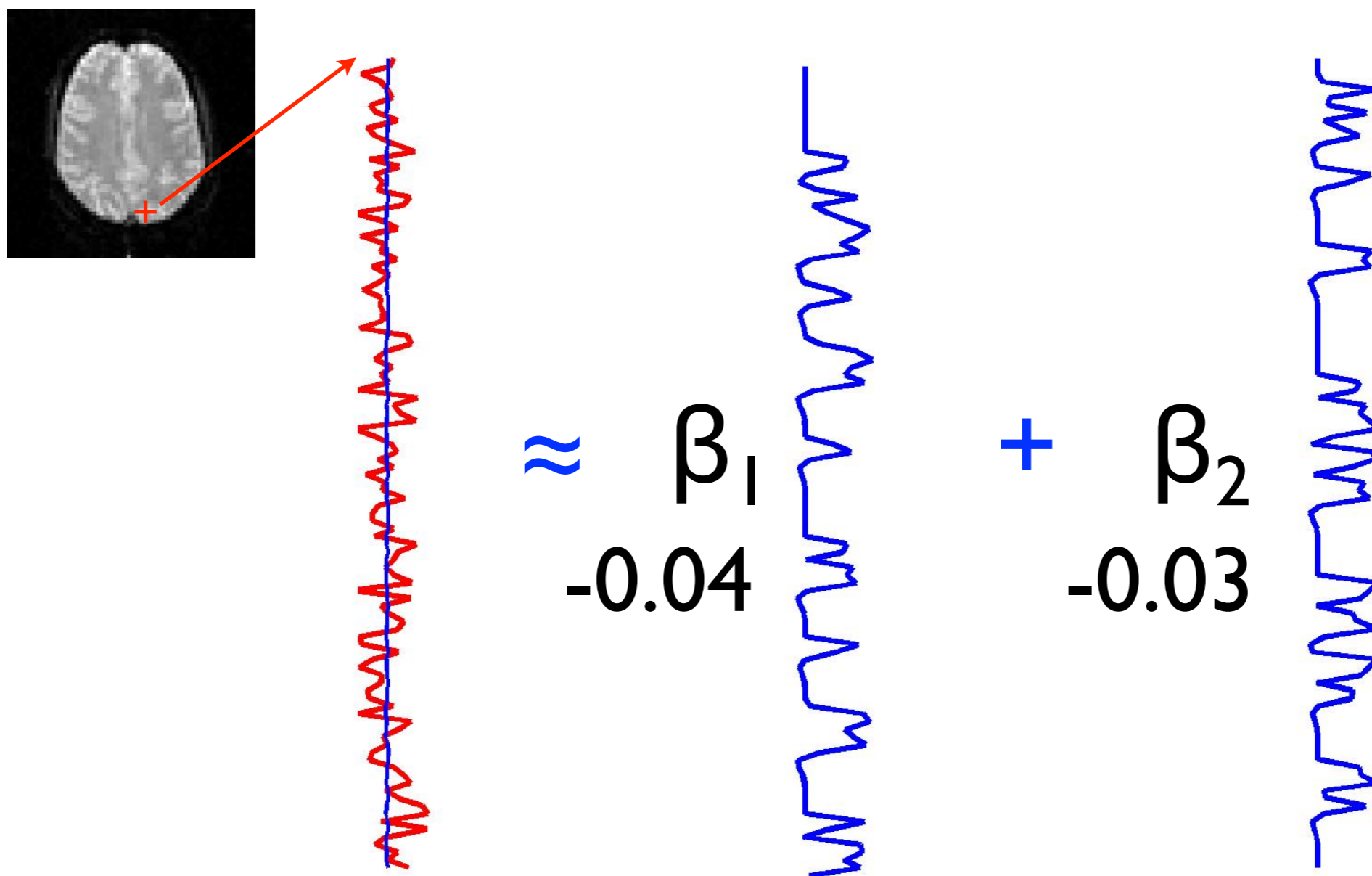
And different voxels yield different parameters



Estimation:

Finding the “best” parameter values

- The estimation entails finding the parameter values such that the linear combination “best” fits the data.

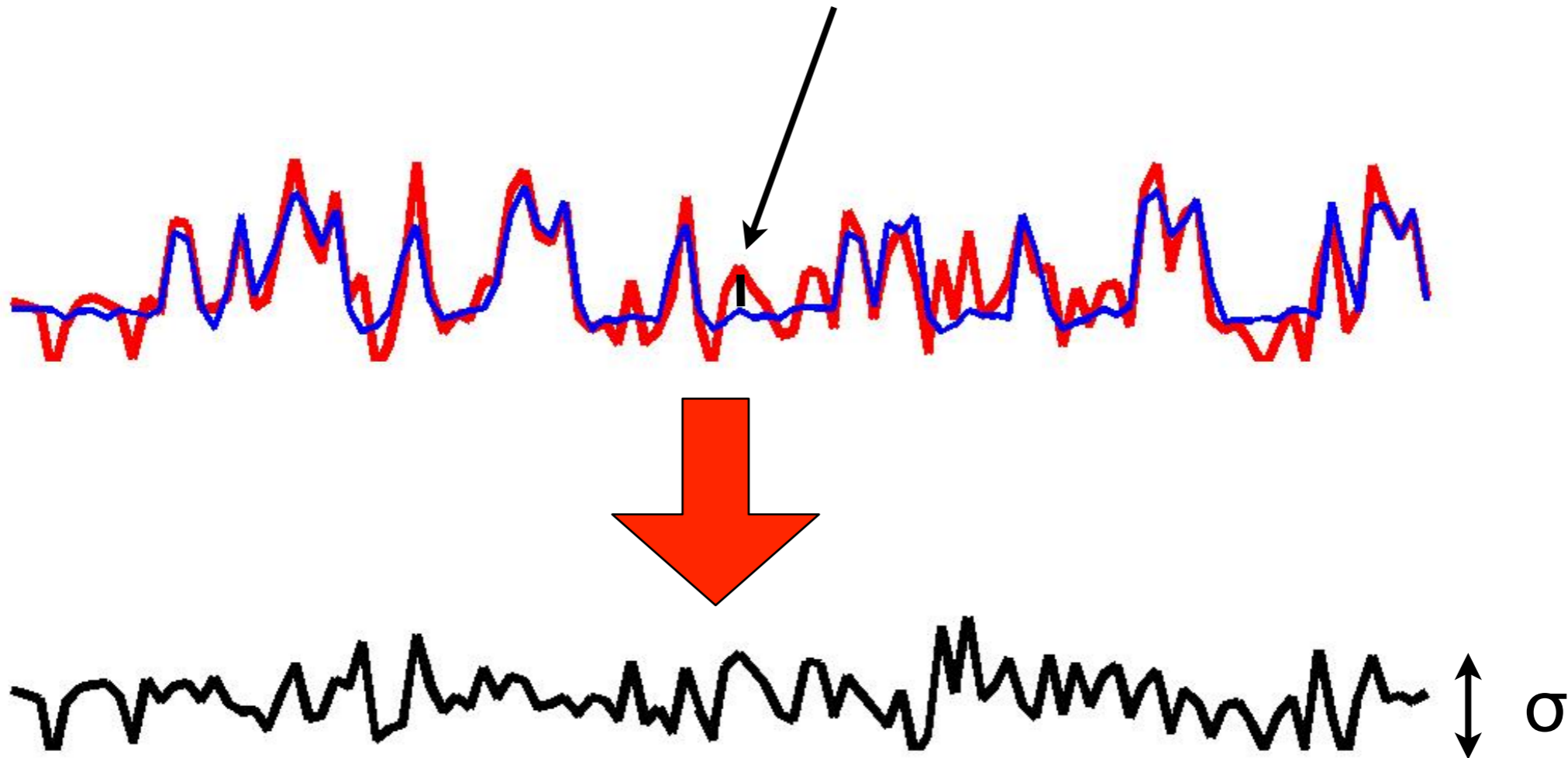


And different voxels yield different parameters



We can also estimate the residual error

Difference between data and best fit:



Residual error

Ortho View 1

fmri1: filtered_func_data
3D/4D volume

Opacity

R S I L A P
A
R L
P

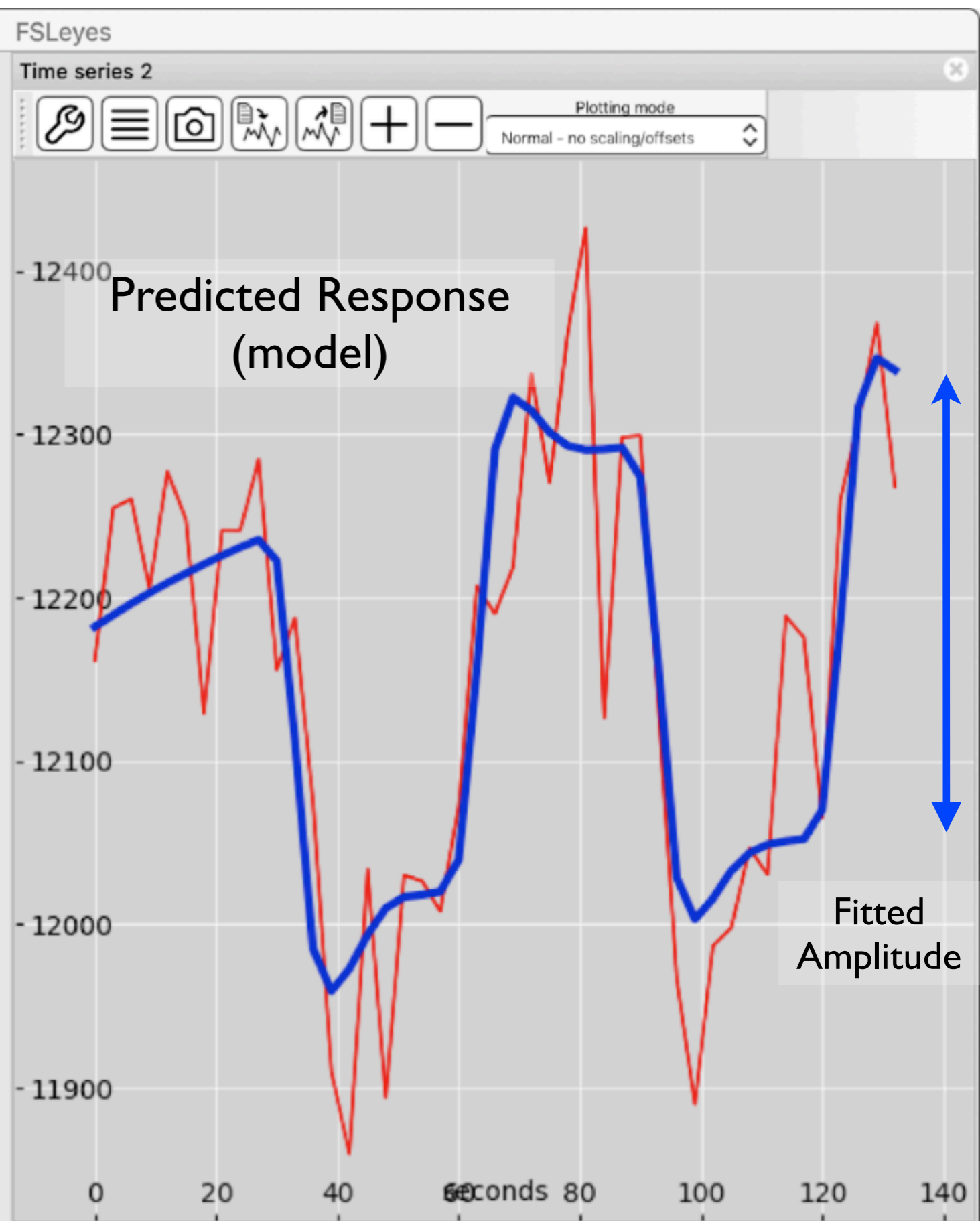
Location

Coordinates: Scanner anatomical

-116	29
36	9
18	3
	0

Volume

fmri1: filtered_func_data [29 9 3 0]: 12161.3359375



Ortho View 1

fmri1: filtered_func_data
3D/4D volume

Opacity

R S L A P
A
R L
P

Location

Coordinates: Scanner anatomical

-116
36
18

Volume

Voxel location

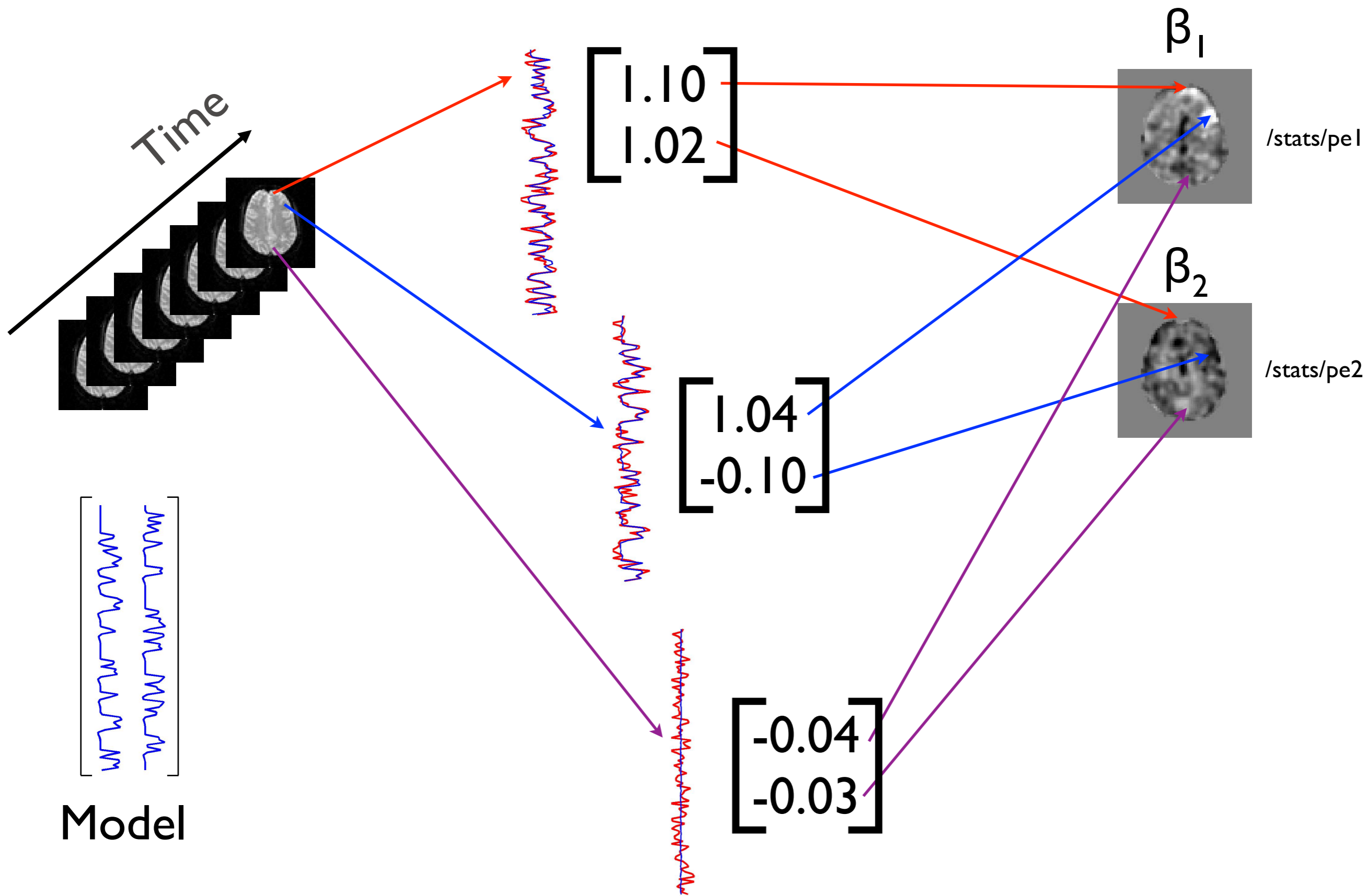
29
9
3
0

fmri1: filtered_func_data
[29 9 3 0]: 12161.3359375



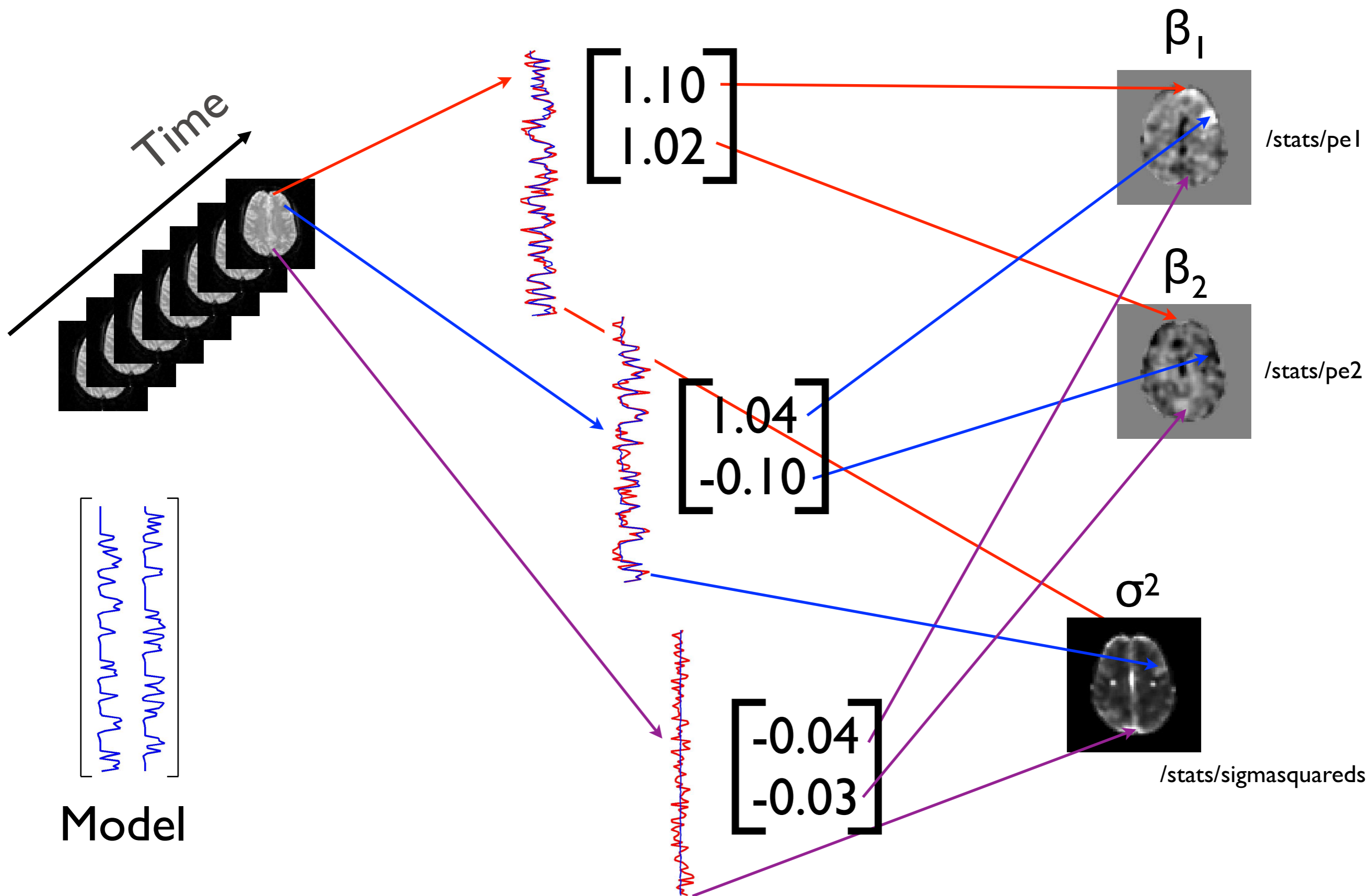


One model to fit them all



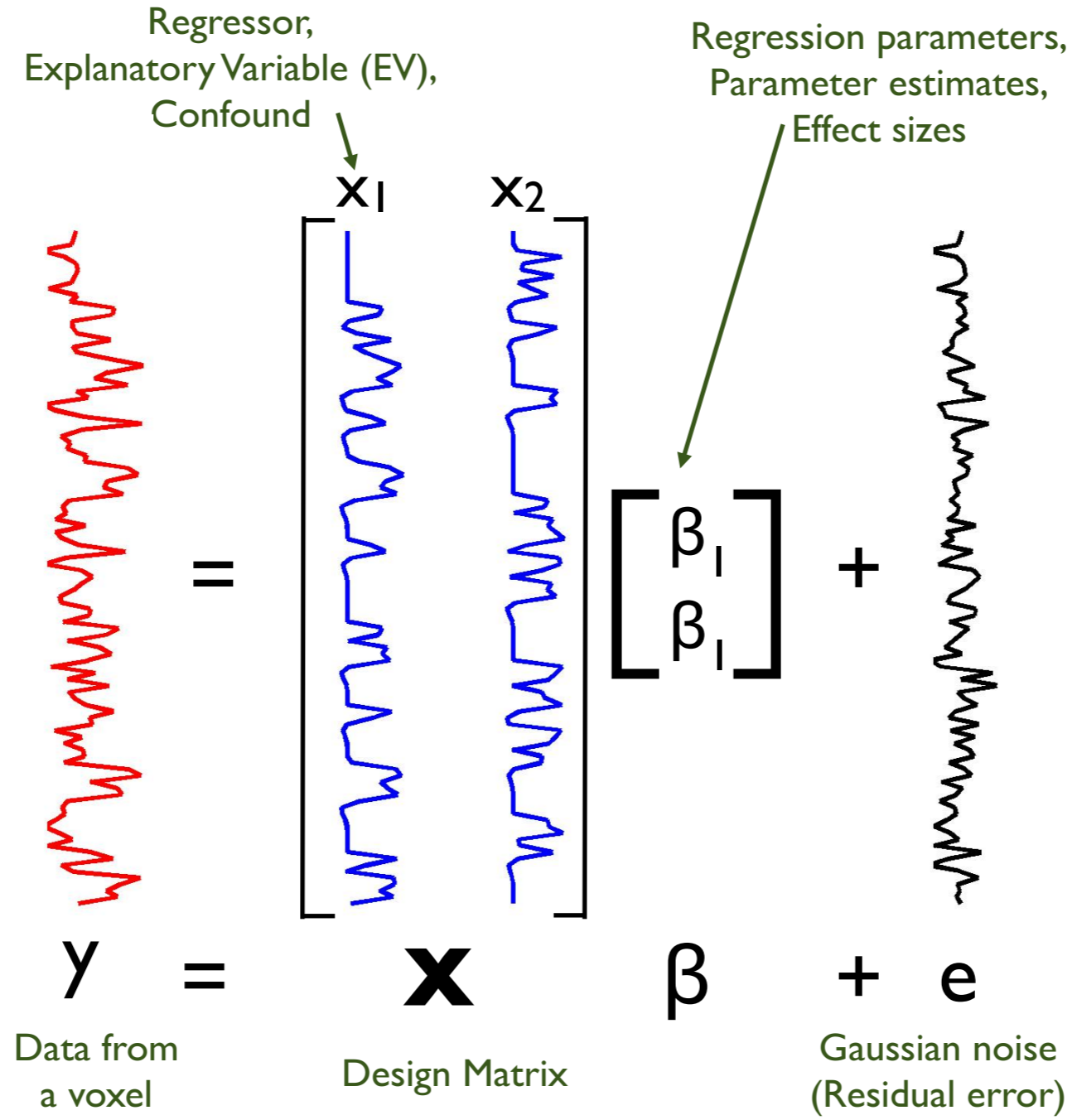


One model to fit them all





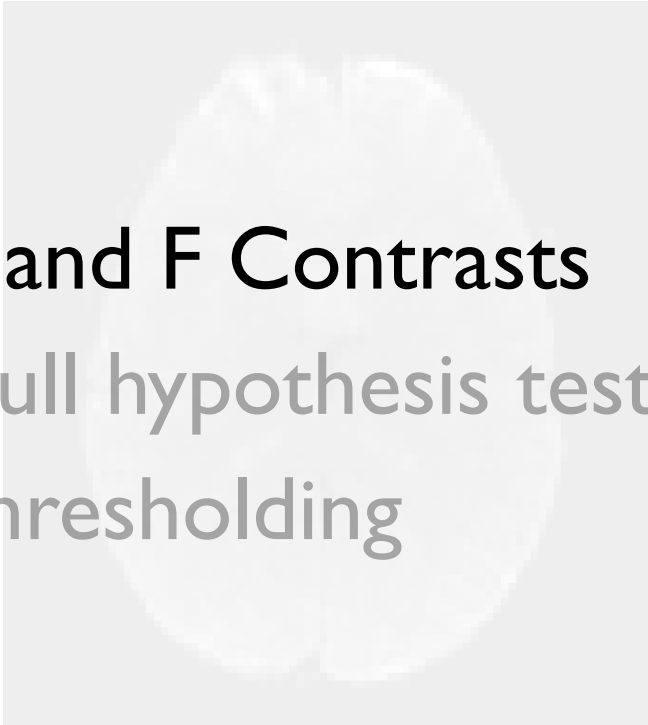
General Linear Model (GLM)

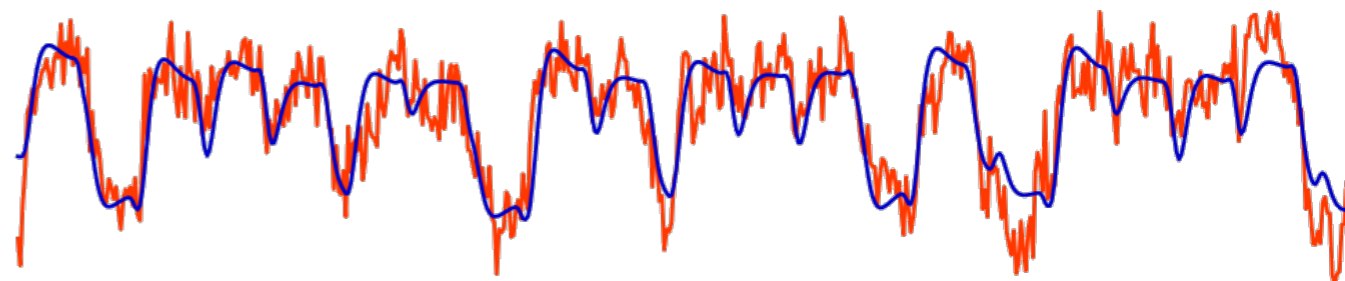




FMRI single subject analysis

- Overview
- Preprocessing
- Setting up a GLM model
- **Contrasts and statistics**

- 
- A grayscale axial slice of a human brain, showing the cerebral cortex and internal structures. It is positioned behind the text on the right side of the slide.
- **T and F Contrasts**
 - Null hypothesis testing
 - Thresholding





t-contrasts

- A contrast of parameter estimates (COPE) is a linear combination of PEs:

$$[1 \ 0]: \text{COPE} = 1 \times \beta_1 + 0 \times \beta_2 = \beta_1$$

$$[1 \ -1]: \text{COPE} = 1 \times \beta_1 + -1 \times \beta_2 = \beta_1 - \beta_2$$

- Test null hypothesis that COPE=0

t-statistic: $t = \frac{\text{COPE}}{\text{std}(\text{COPE})}$



t-contrasts

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})}$$

Higher COPE → higher t
Higher std(COPE) → lower t



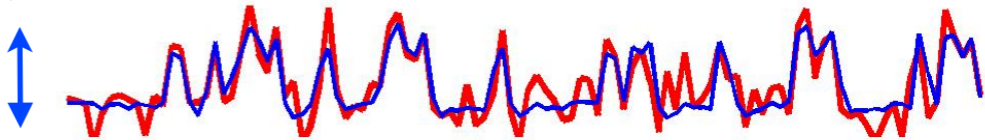
t-contrasts

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})}$$

Higher COPE → higher t
Higher std(COPE) → lower t

Depends on

Fitted amplitude
(βs in contrast)





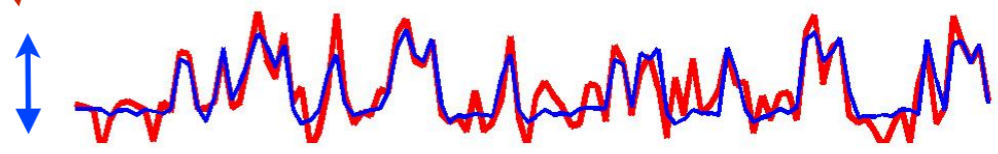
t-contrasts

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})}$$

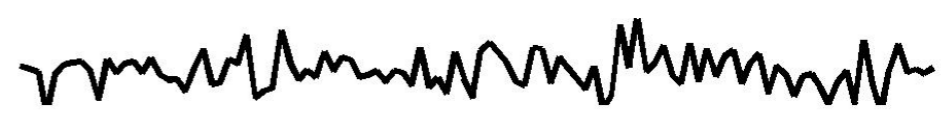
Higher COPE → higher t
Higher std(COPE) → lower t

Depends on

Fitted amplitude
(βs in contrast)



σ



Residual error

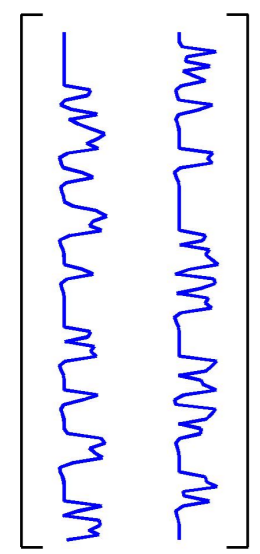


t-contrasts

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})}$$

Higher COPE → higher t
Higher std(COPE) → lower t

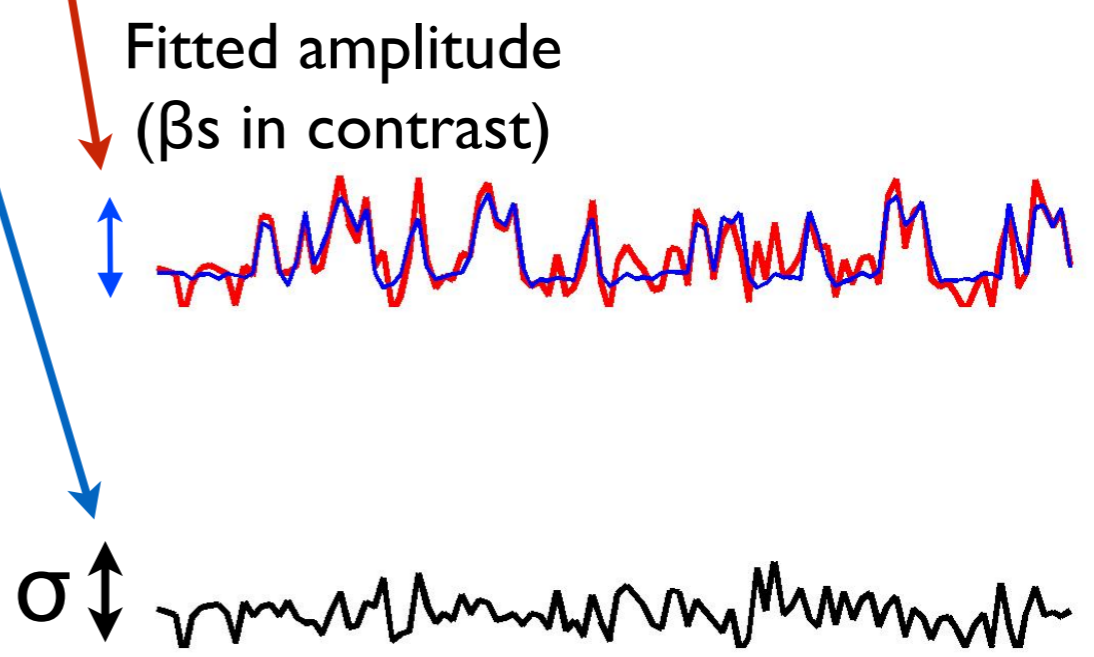
Depends on



The Model,

[1 0]

the Contrast,

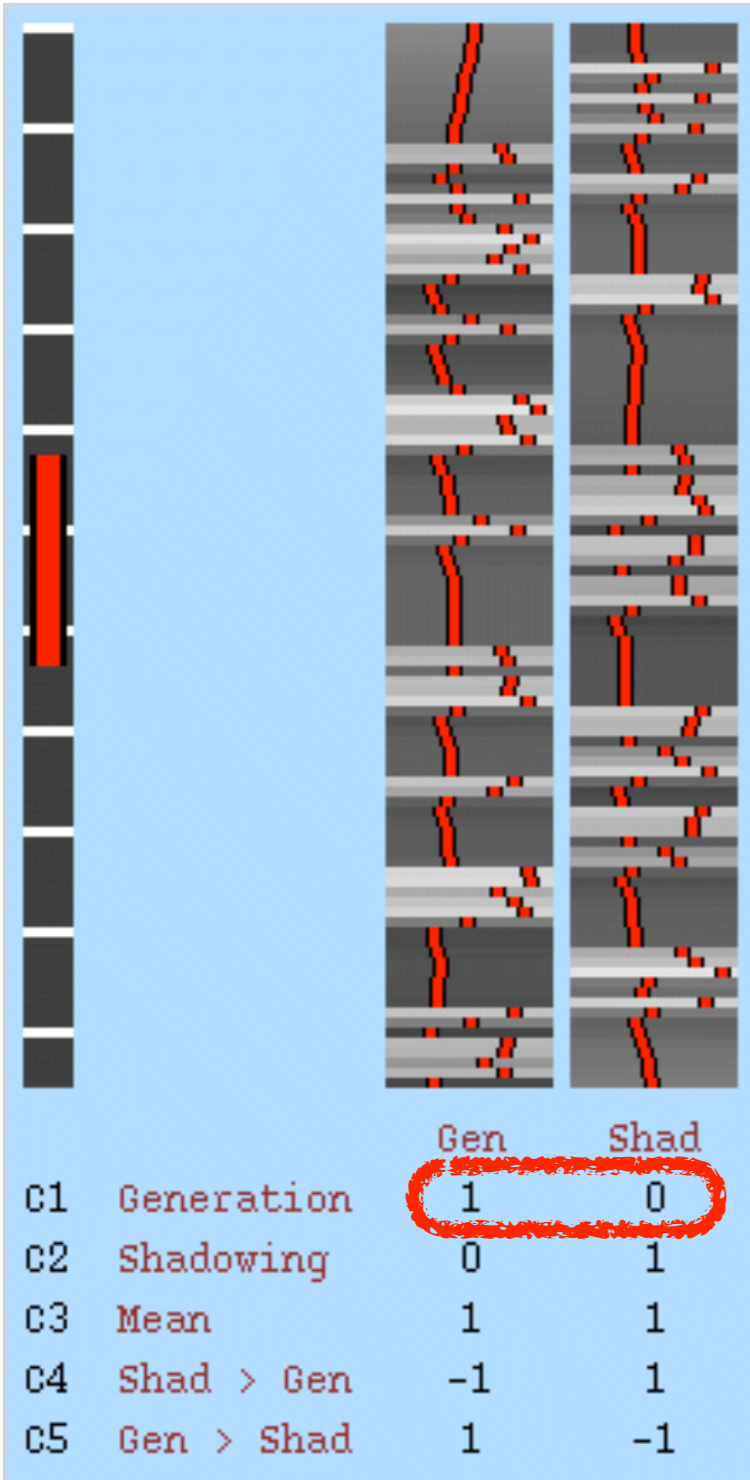


and the Residual error



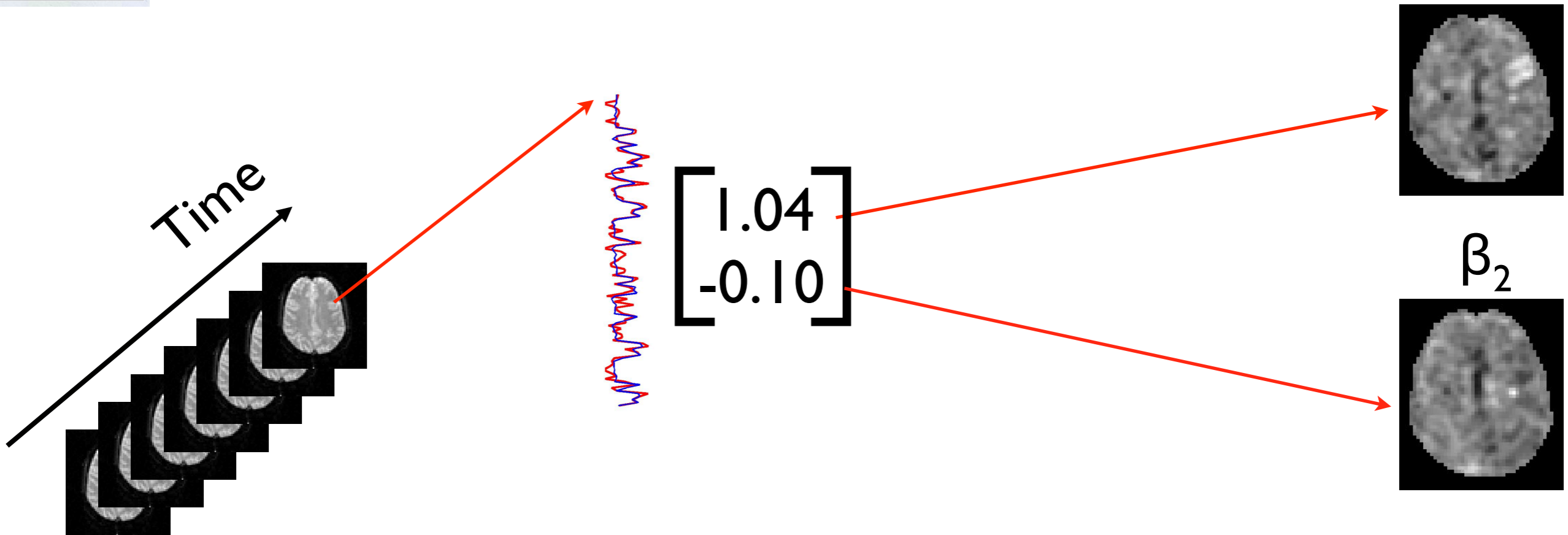
t-contrasts

- $[1\ 0]$: EV1 only (i.e. Generation vs rest)
- $[0\ 1]$: EV2 only (i.e. Shadowing vs rest)

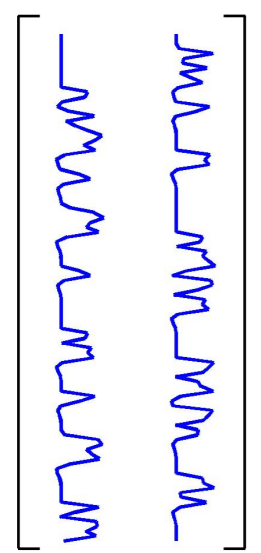




t-contrasts



Contrast weight vector: $[1 \ 0]$

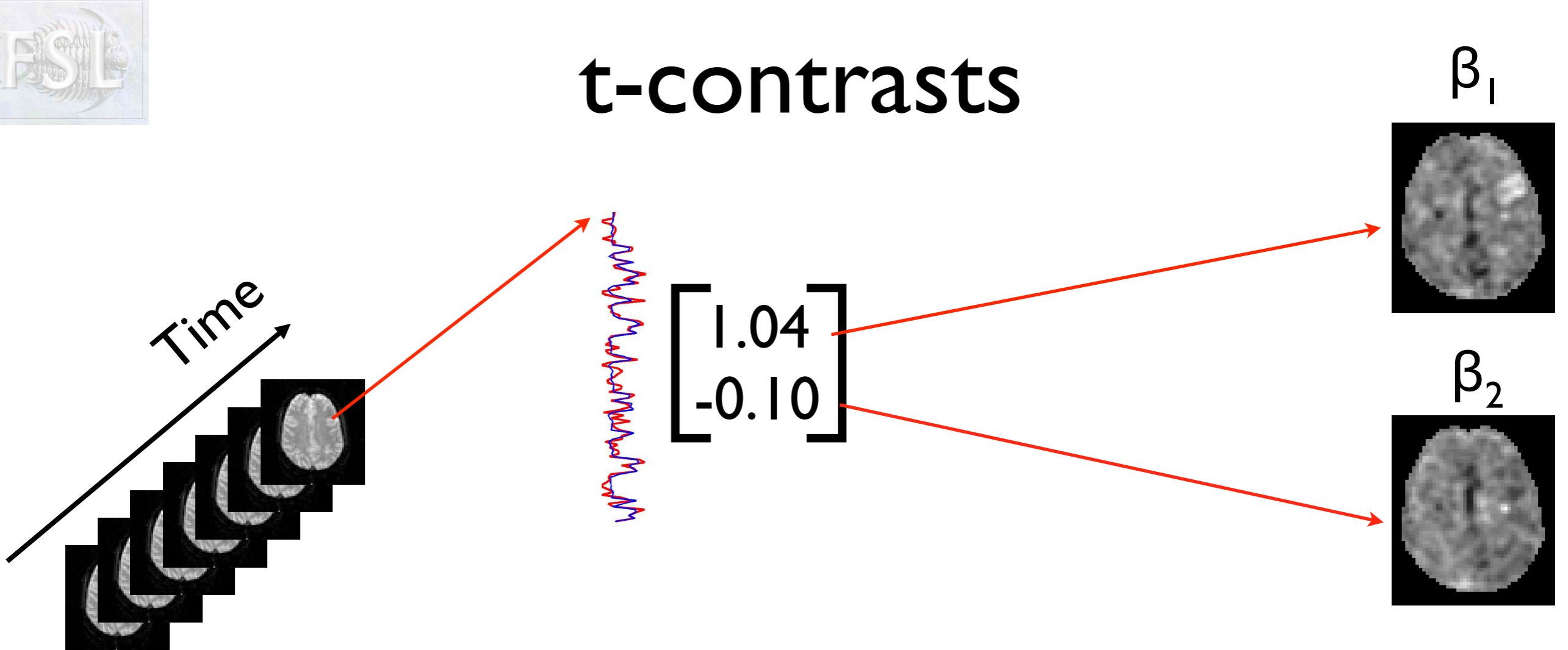


Model

Asks the question: Where do we need this regressor to model the data, i.e. what parts of the brain are used when seeing nouns and generating related verbs?

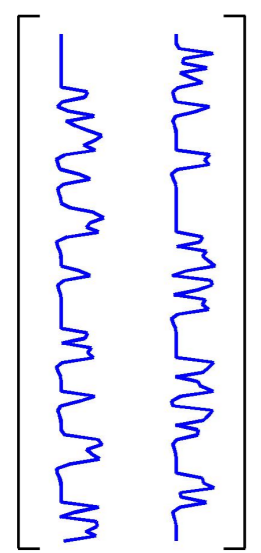


t-contrasts

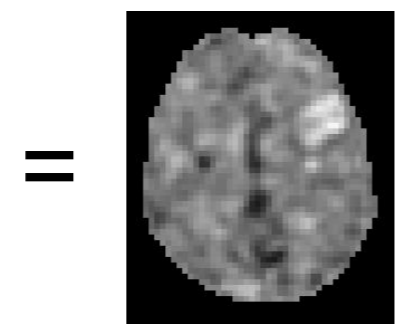


Contrast weight vector: $[1 \ 0]$

$$\begin{aligned}
 \text{COPE} &= 1 \times \hat{\beta}_1 + 0 \times \hat{\beta}_2 \\
 &= 1 \times 1.04 + 0 \times -0.1 \\
 &= 1.04
 \end{aligned}$$



Model

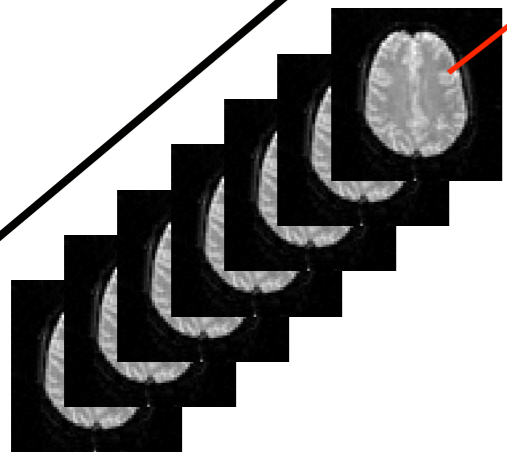


β_1

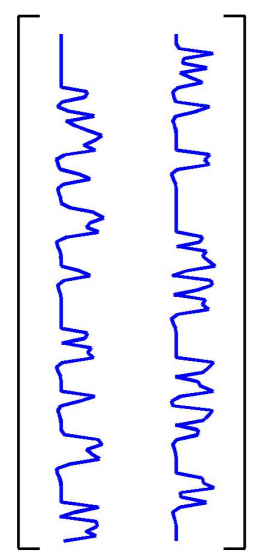
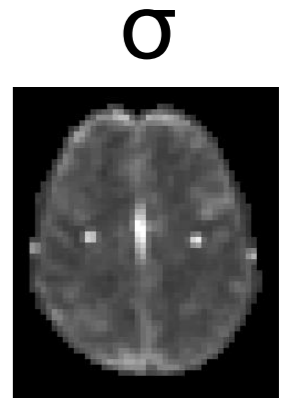
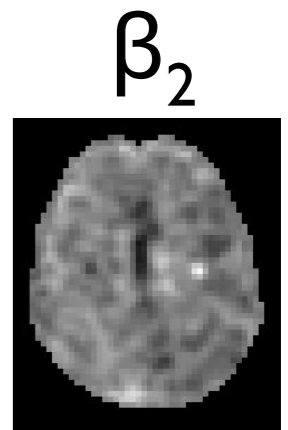
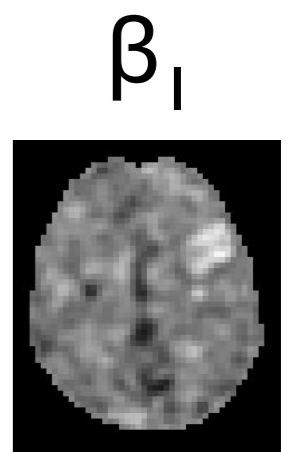


t-contrasts

Time



$$\begin{bmatrix} 1.04 \\ -0.10 \end{bmatrix}$$



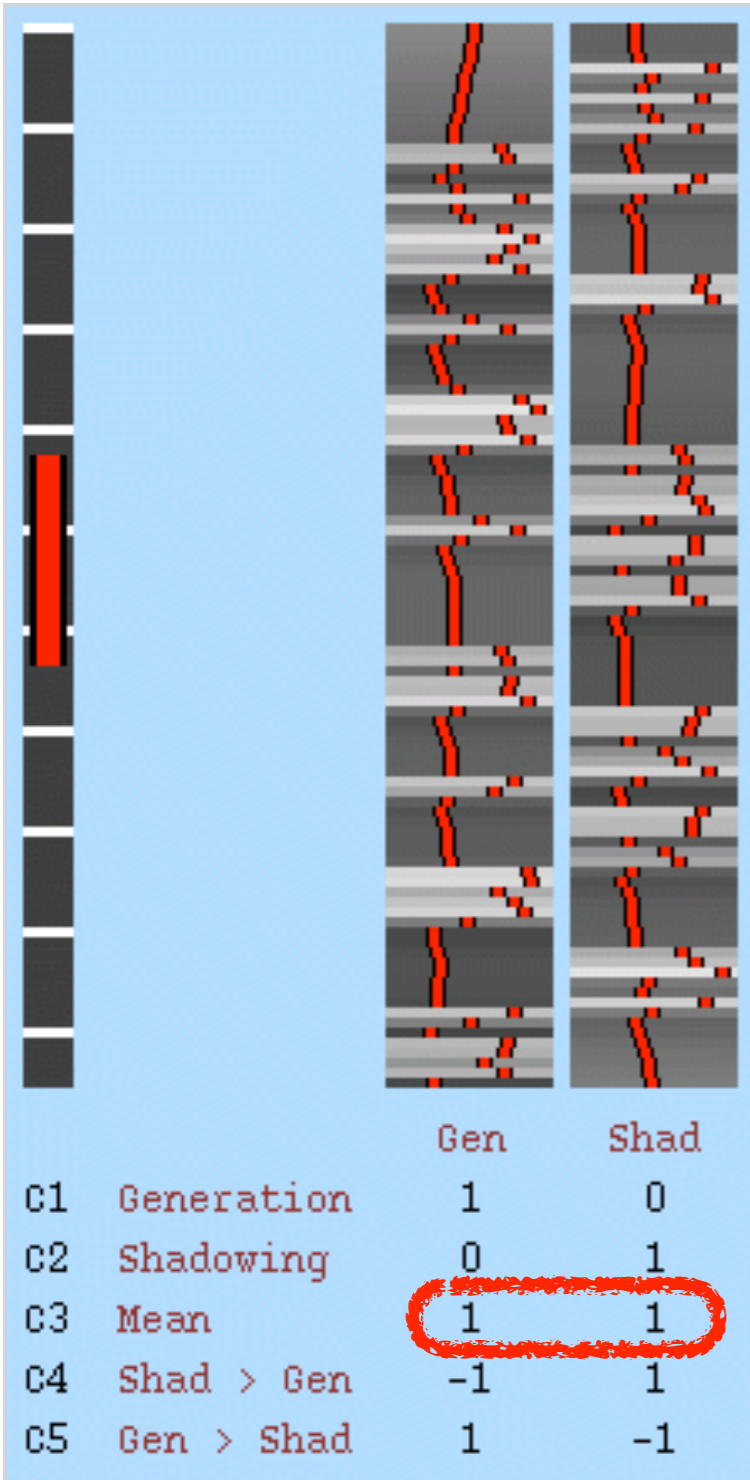
Model

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})} = \frac{\text{Brain slice } \beta_1}{\text{Brain slice } \sigma} = \text{Brain slice } \beta_2$$



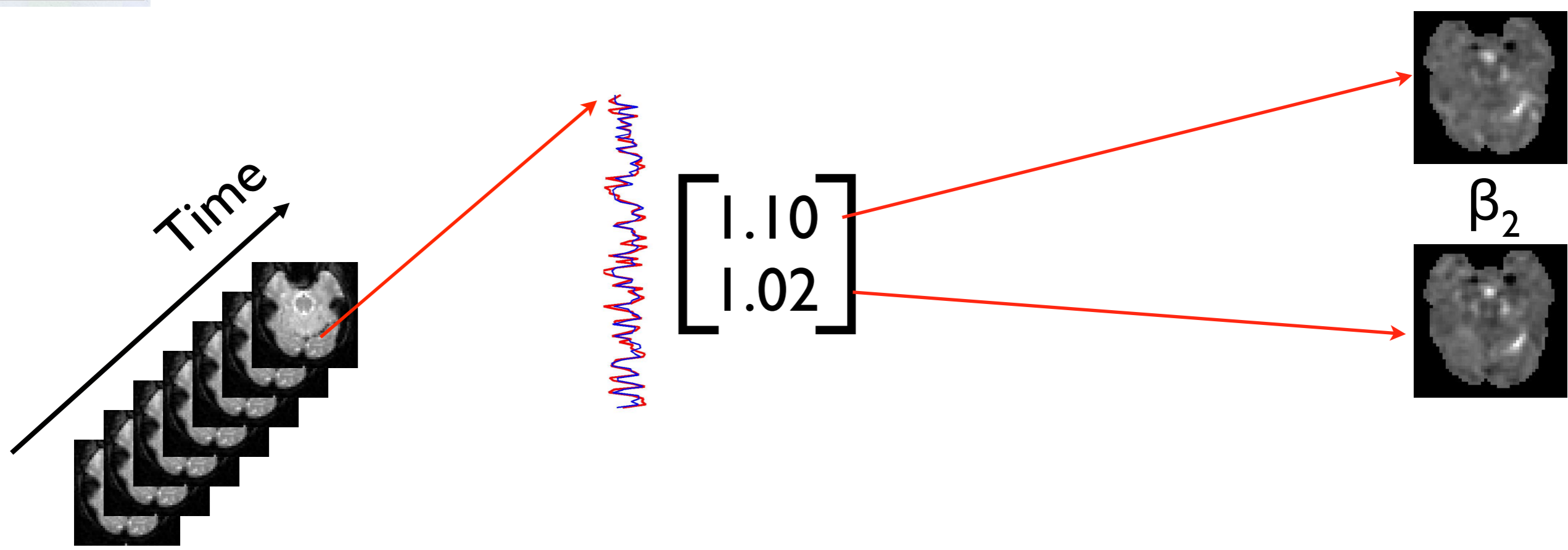
t-contrasts

- $[1\ 0]$: EV1 only (i.e. Generation vs rest)
- $[0\ 1]$: EV2 only (i.e. Shadowing vs rest)
- $[1\ 1]$: EV1 + EV2 (Mean activation)

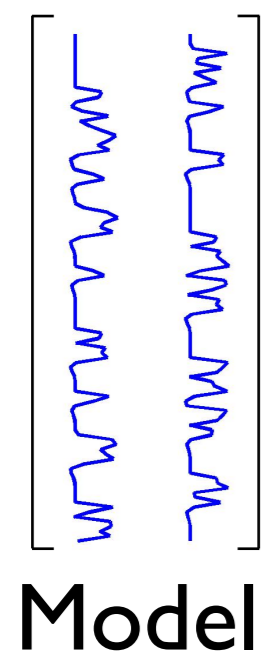




t-contrasts



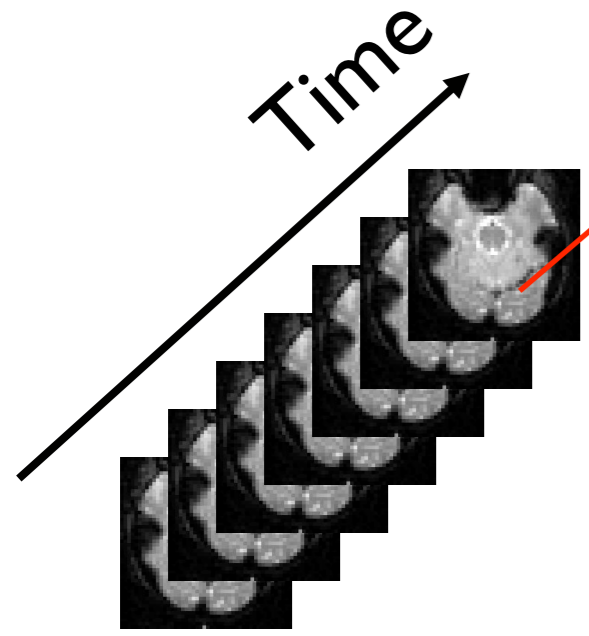
Contrast weight vector: $[1 \ 1]$
COPE = $1 \times 1.10 + 1 \times 1.02 = 2.12$



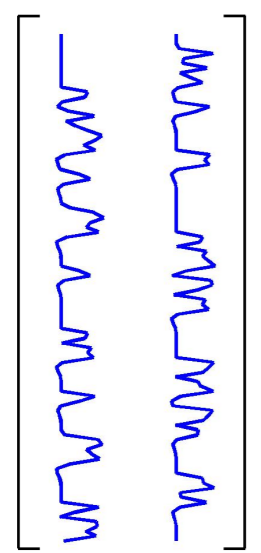
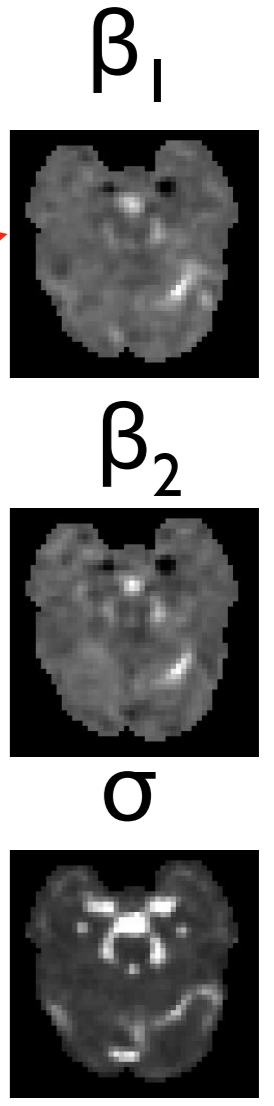
$$\text{COPE} = \beta_1 + \beta_2 = \text{[combined image]}$$



t-contrasts



$$\begin{bmatrix} 1.10 \\ 1.02 \end{bmatrix}$$



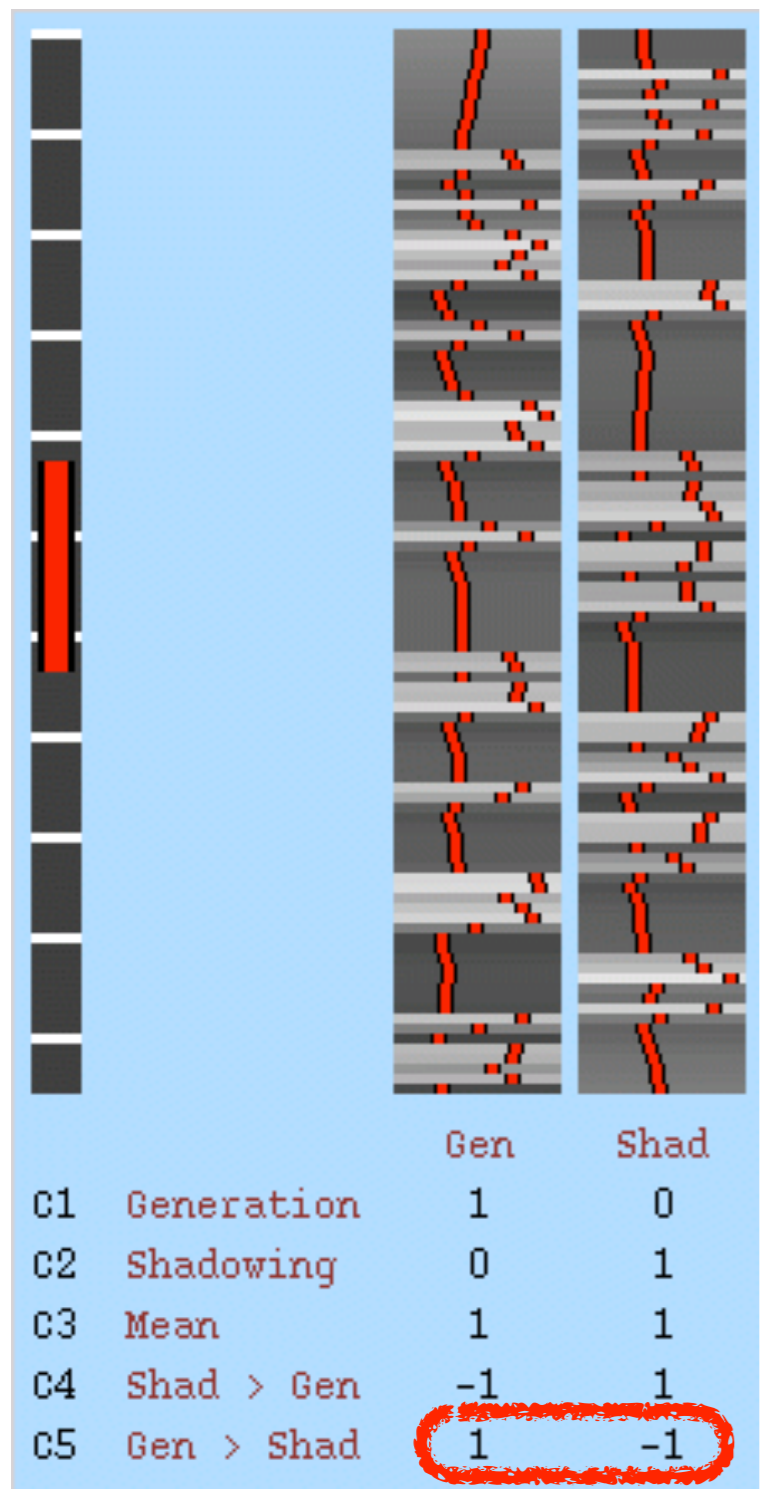
Model

$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})} = \frac{\text{Brain Slice 1}}{\text{Brain Slice 2}} = \text{Brain Slice 3}$$



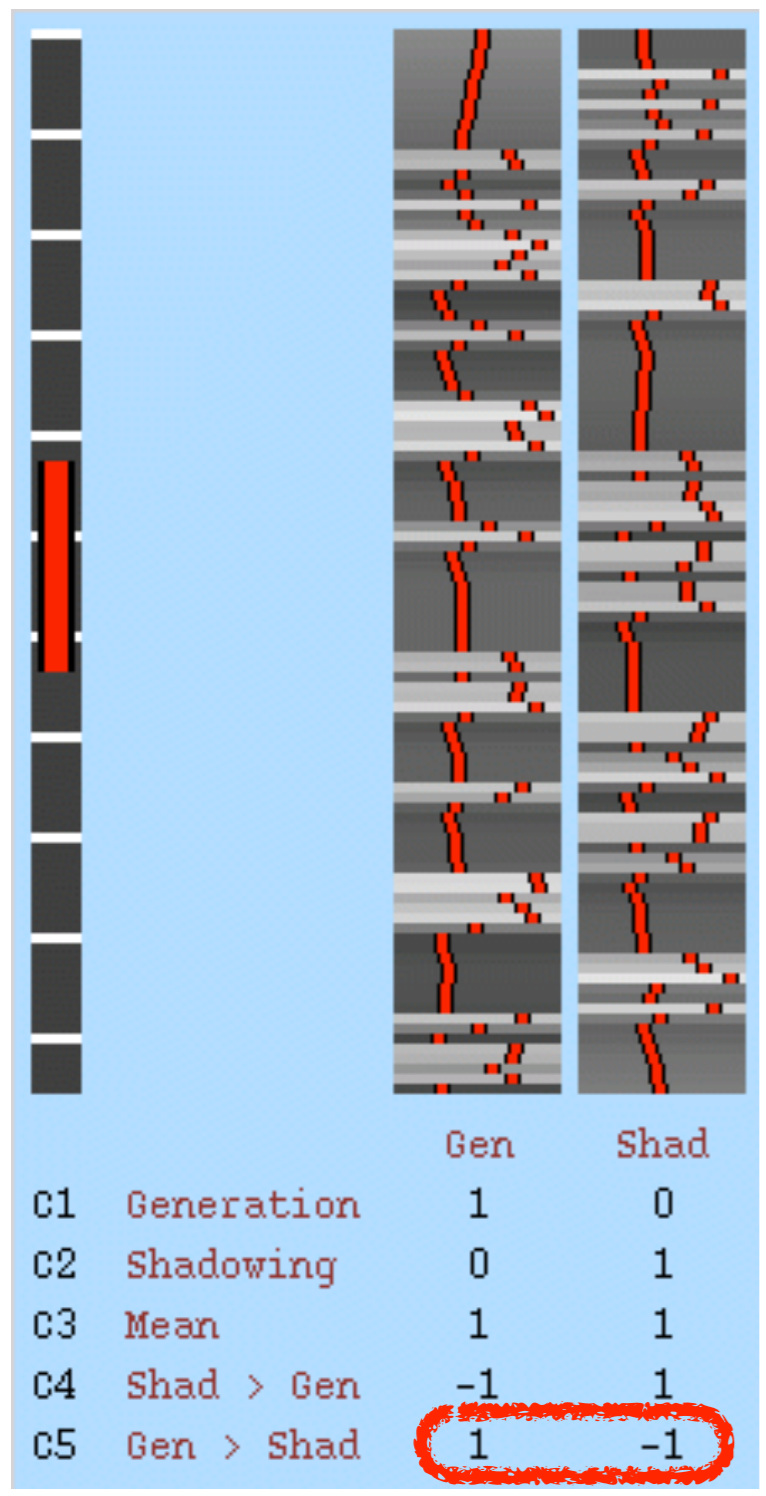
t-contrasts

- $[1\ 0]$: EV1 only (i.e. Generation vs rest)
- $[0\ 1]$: EV2 only (i.e. Shadowing vs rest)
- $[1\ 1]$: EV1 + EV2 (Mean activation)
- $[-1\ 1]$: EV2 - EV1 (More activated by Shadowing than Generation)
- $[1\ -1]$: EV1 - EV2 (More activated by Generation than Shadowing (*t*-tests are directional))





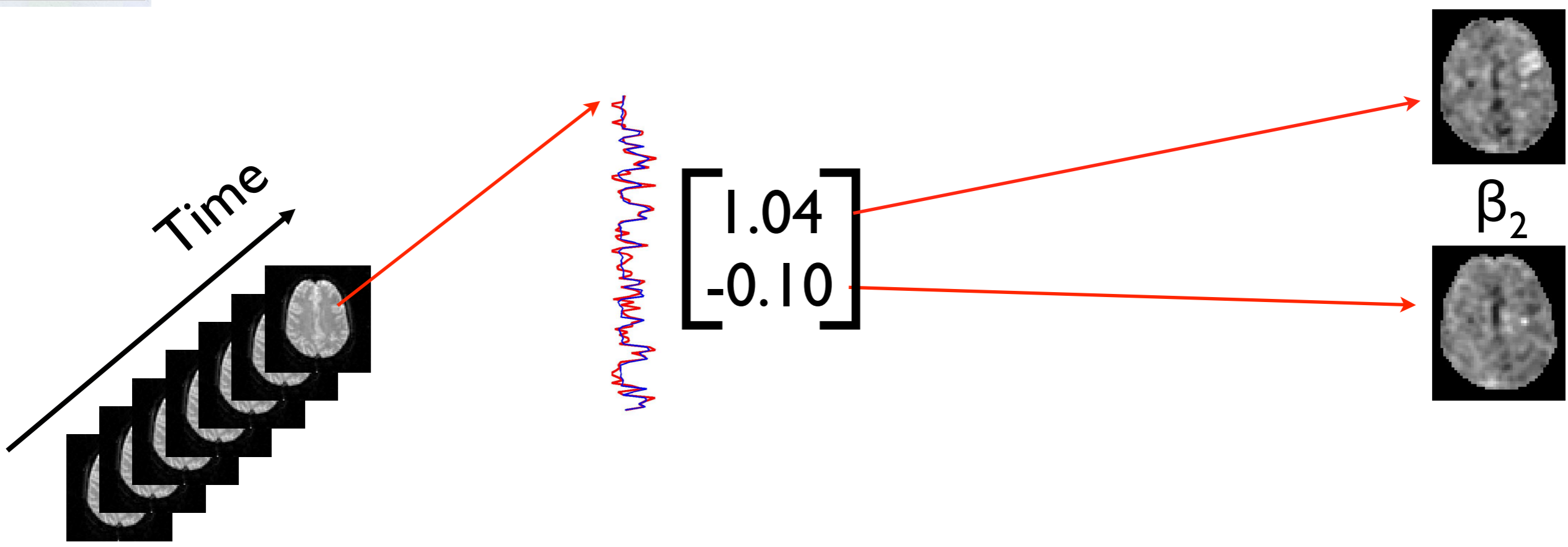
t-contrasts



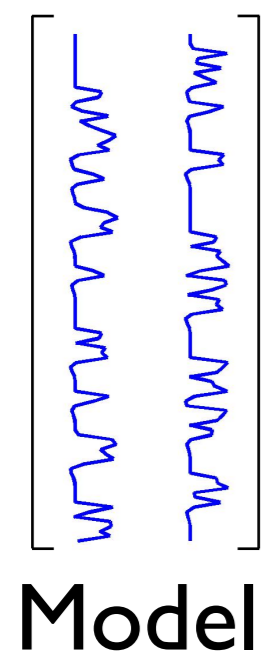
- $[1\ 0]$: EV1 only (i.e. Generation vs rest)
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t-contrasts



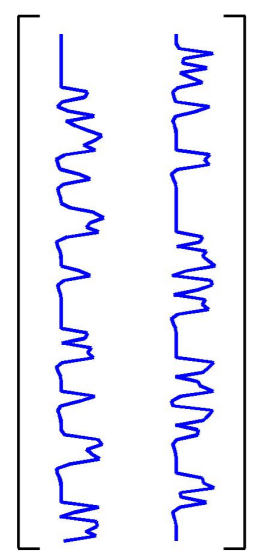
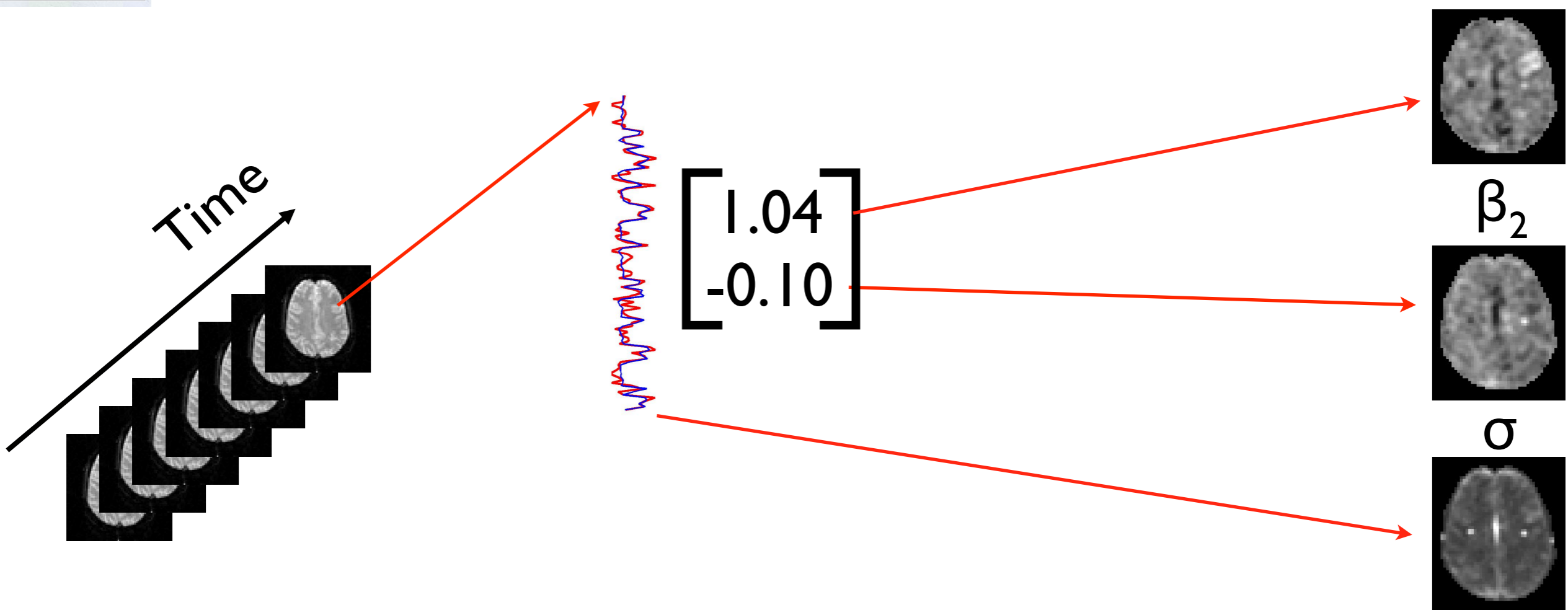
Contrast weight vector: $[1 \ -1]$
COPE = $1 \times 1.04 - 1 \times -0.10 = 1.14$



$$\text{COPE} = \beta_1 - \beta_2 = \text{[Resulting Brain Map]}$$



t-contrasts



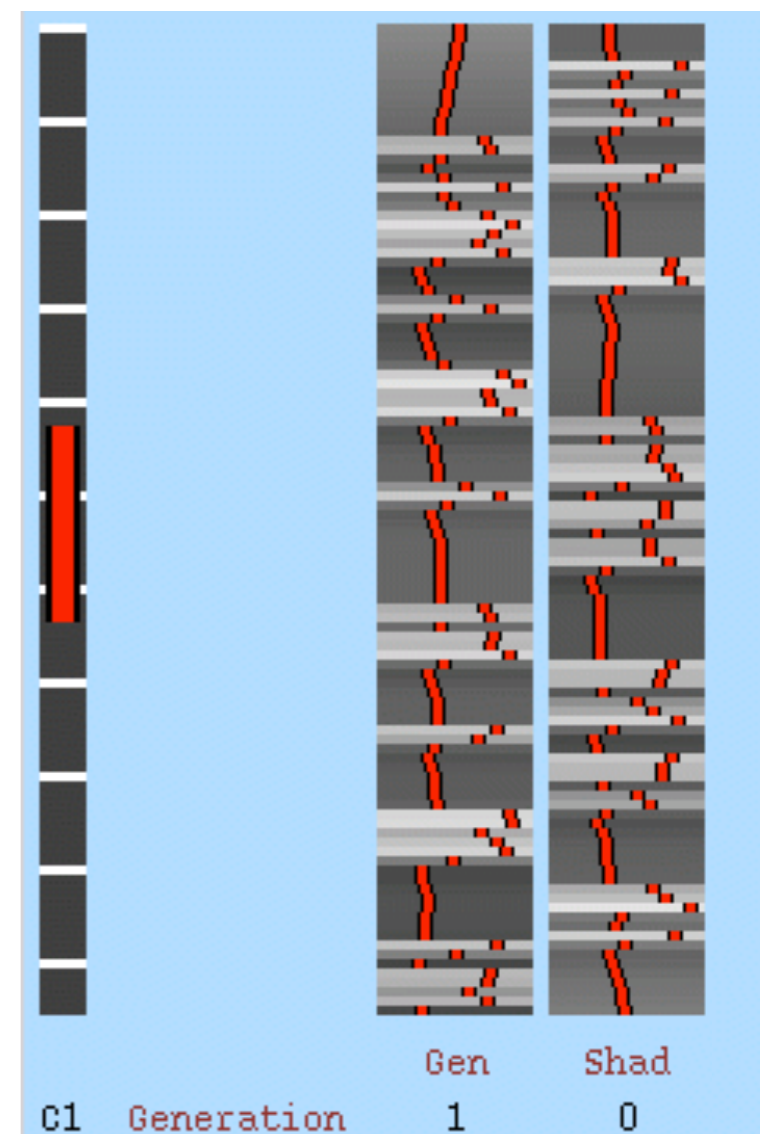
$$t = \frac{\text{COPE}}{\text{std}(\text{COPE})} = \frac{\text{Brain Map } \beta_1}{\text{Brain Map } \sigma} = \text{Brain Map } \beta_2$$



F-contrasts

We have two conditions:
Word Generation and Shadowing

We want to know:
Is there an activation to any condition?



First we ask: Is there activation to Generation?

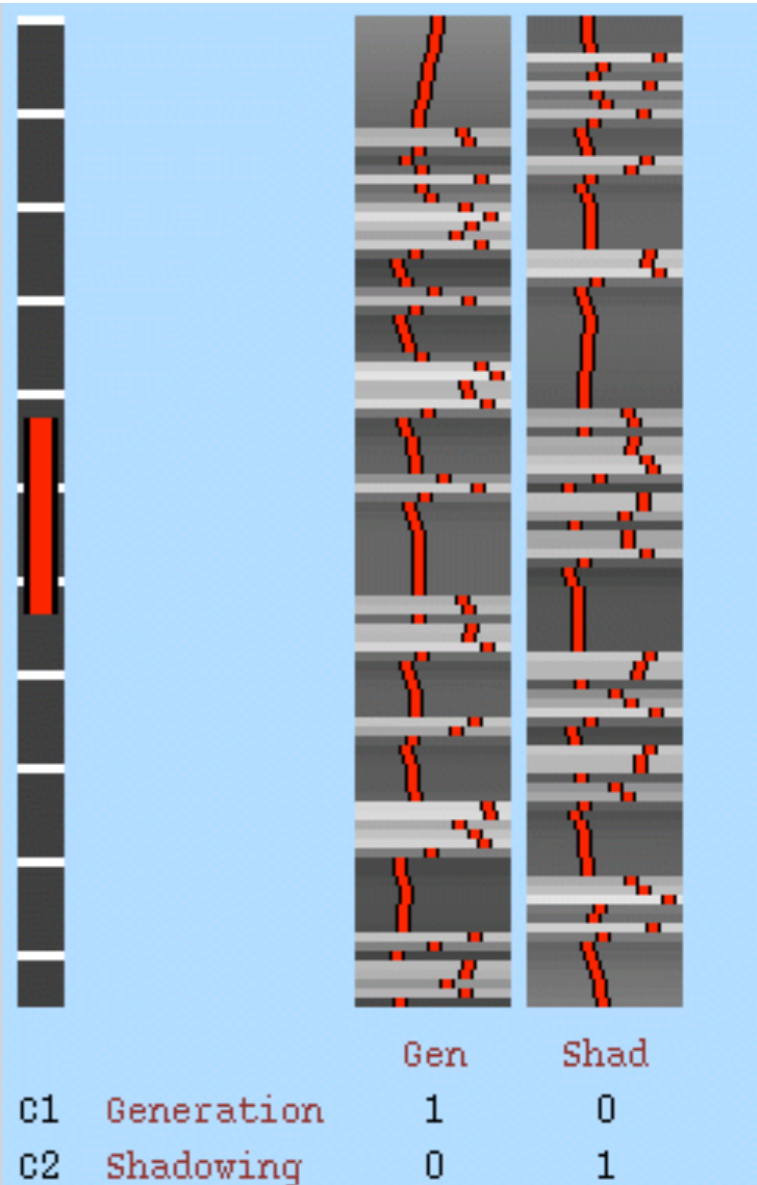
[1 0]



F-contrasts

We have two conditions:
Word Generation and Shadowing

We want to know:
Is there an activation to any condition?



Then we ask: Is there activation to Shadowing?

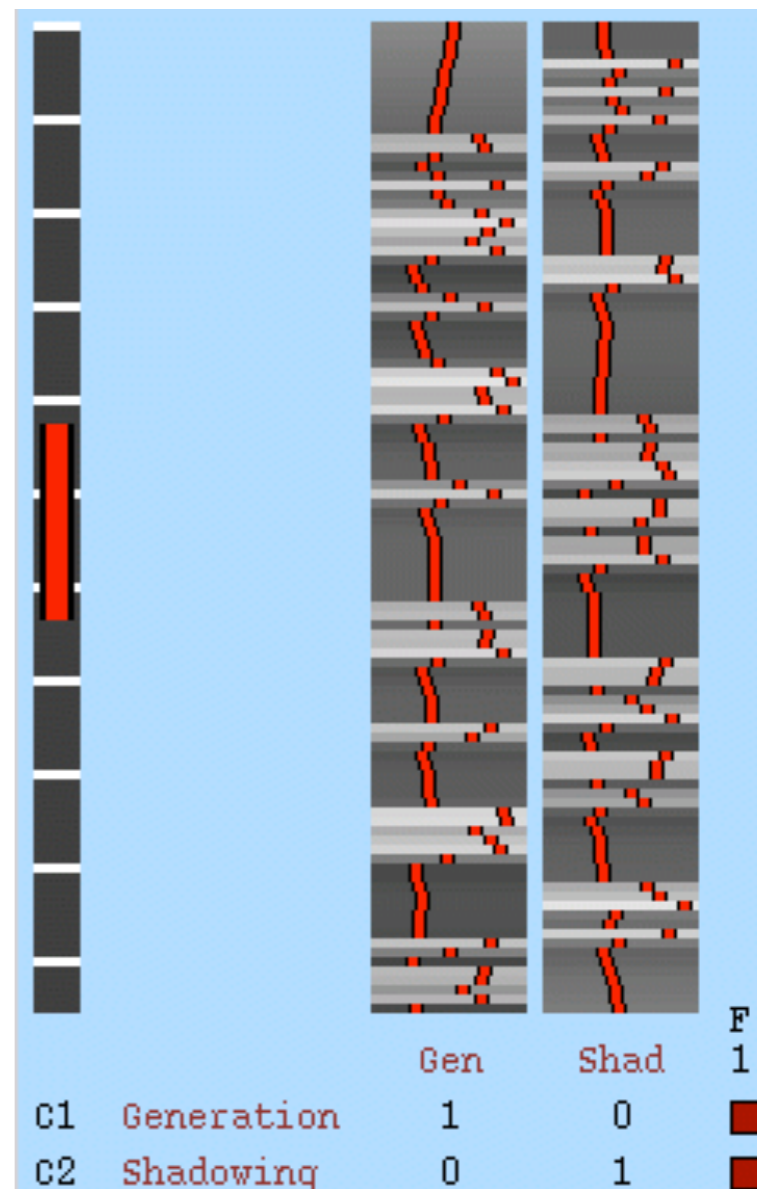
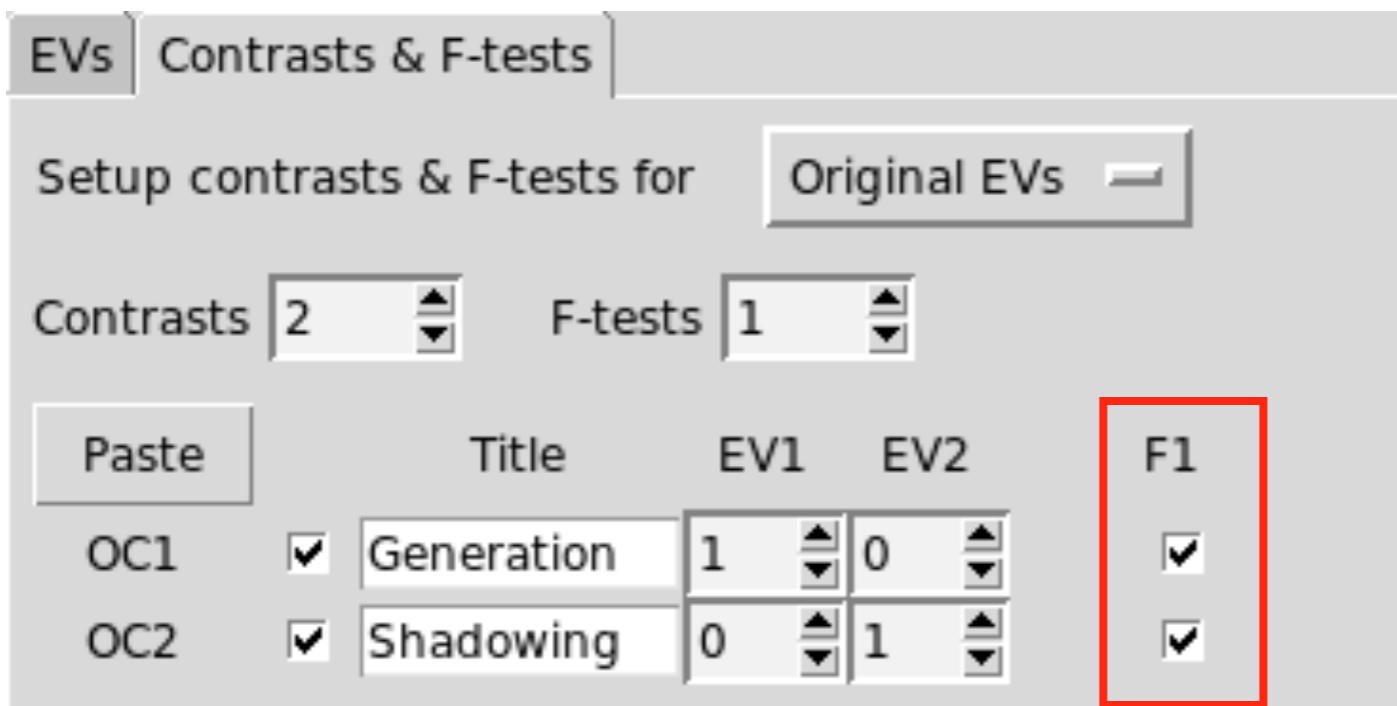
$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$



F-contrasts

We have two conditions:
Word Generation and Shadowing

We want to know:
Is there an activation to any condition?



Then we add the OR

$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$



F-contrasts

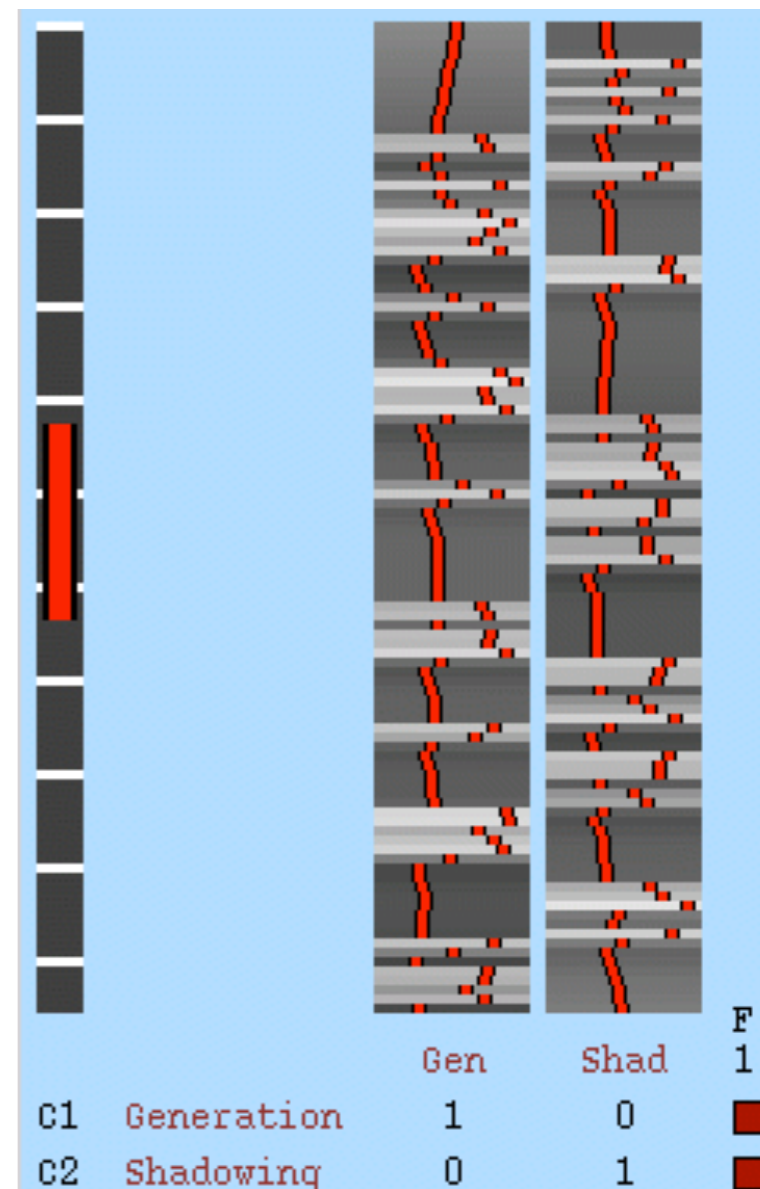
We have two conditions:
Word Generation and Shadowing

We want to know:
Is there an activation to any condition?

Is there an activation to any condition?

Is equivalent to:

Does any regressor explain the variance in the data?



Then we add the OR

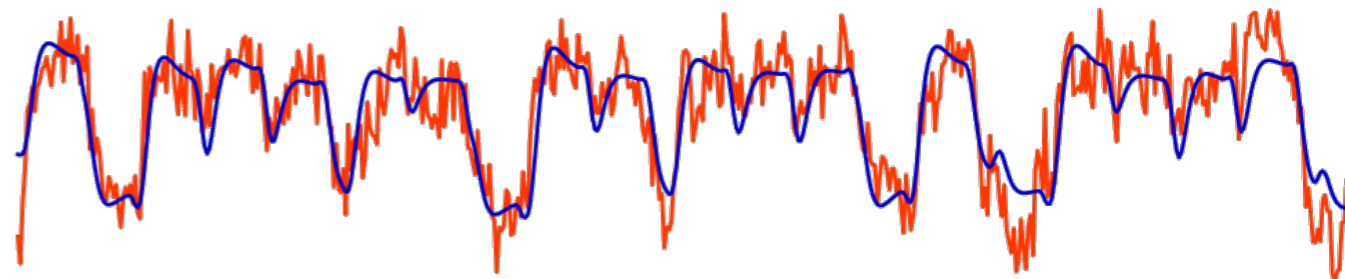
$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$



FMRI single subject analysis

- Overview
- Preprocessing
- Setting up a GLM model
- **Contrasts and statistics**

- 
- A grayscale axial brain slice is shown in the background of the right-hand list. It displays the internal structure of the brain, including the cerebral cortex and white matter.
- T and F Contrasts
 - **Null hypothesis testing**
 - Thresholding





Inferring Activity. Is β Non-zero?

- If β is non-zero then voxel is “active”
- We have estimated β 's from the best fit to the data
- BUT the data is noisy - so can we trust the estimated β 's??

t-statistic $t = \frac{\beta}{\text{std}(\beta)}$



Inferring Activity. Is β Non-zero?

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t-statistic $t = \frac{\hat{\beta}}{\text{std}(\beta)}$

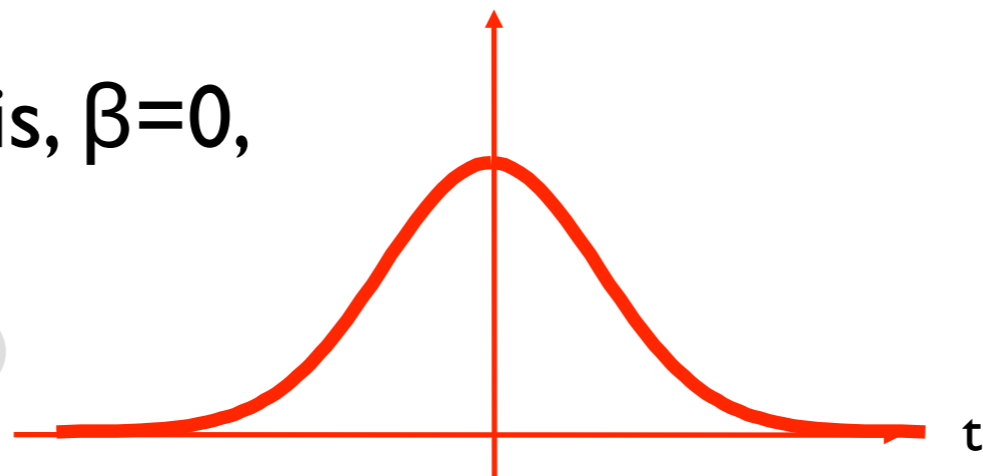


Null Hypothesis Testing

t-statistic: $t = \frac{\hat{\beta}}{\text{std}(\hat{\beta})}$

Under null hypothesis, $\beta=0$,
t is t-distributed

(what are the chances of that?)

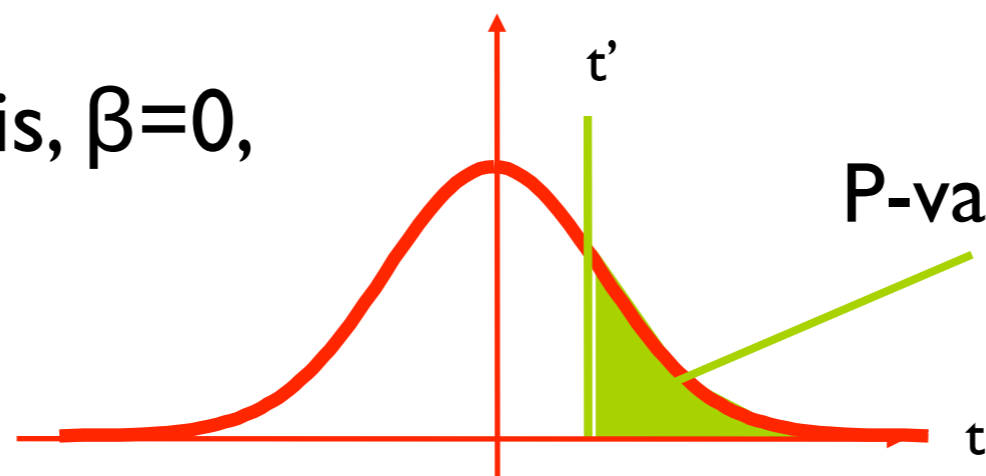




Null Hypothesis Testing

t-statistic: $t = \frac{\hat{\beta}}{\text{std}(\hat{\beta})}$

Under null hypothesis, $\beta=0$,
 t is t-distributed



P-value = $p(t > t' \mid \beta = 0)$

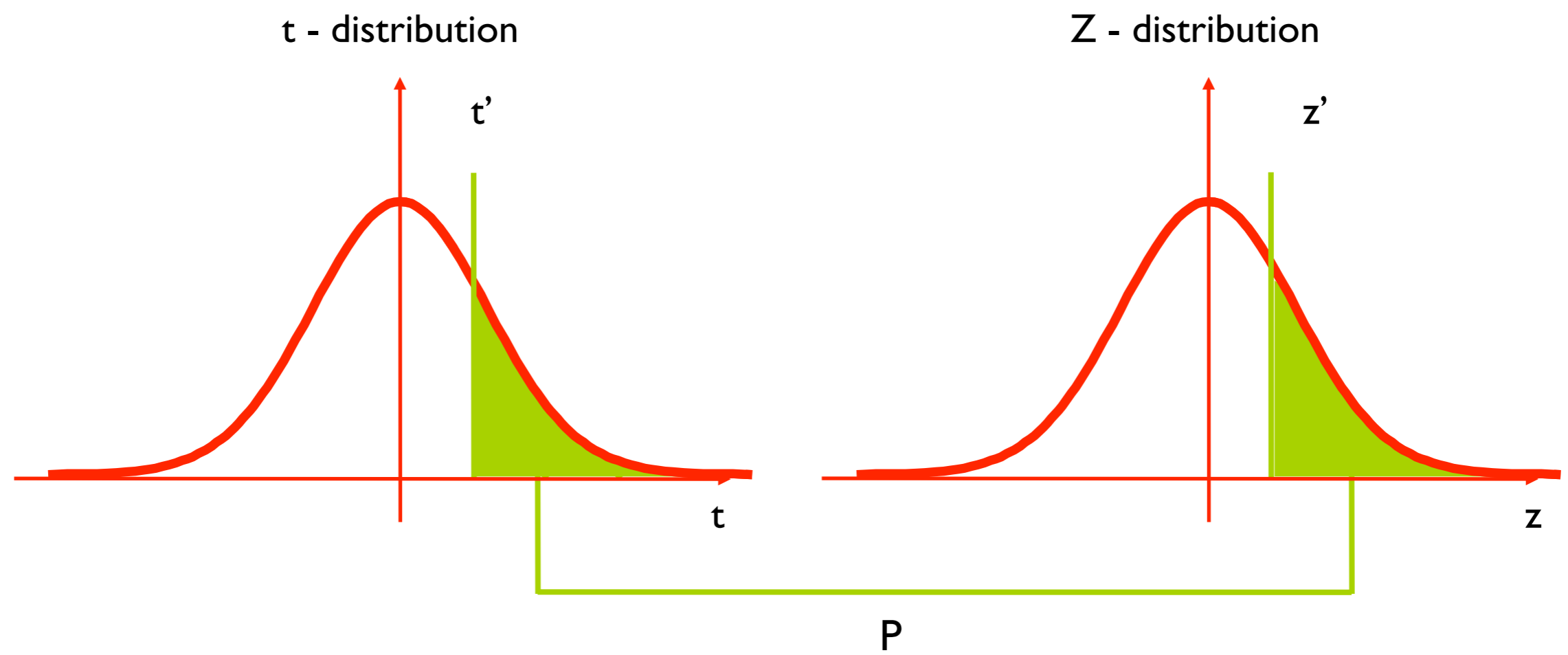
Small P-Value = null hypothesis unlikely

If P-Value < P-threshold then voxel is “active”

P-threshold corresponds to False Positive Rate (FPR)



T to P to Z



FEAT performs spatial inference on z statistic maps

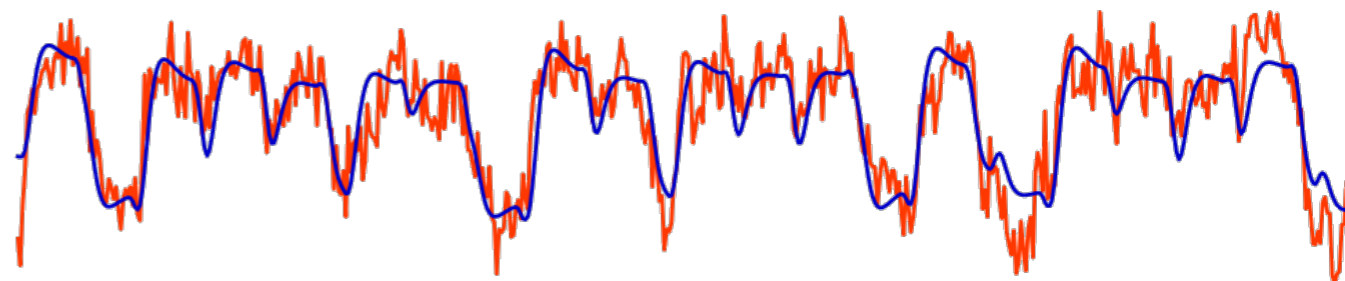
Therefore, we convert t statistics to z statistics by equating probabilities under the tails of the distributions ($t' \rightarrow p \rightarrow z'$)



FMRI single subject analysis

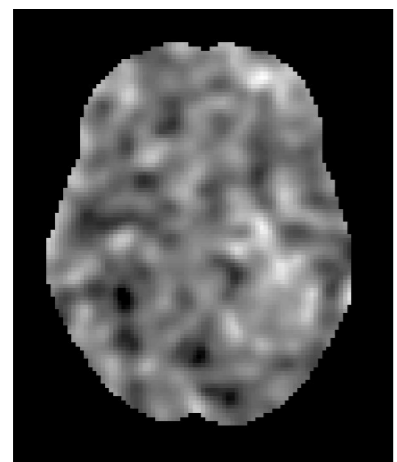
- Overview
- Preprocessing
- Setting up a GLM model
- **Contrasts and statistics**

- 
- A grayscale axial brain scan image is centered on the right side of the slide. It shows a cross-section of a human brain with some areas highlighted in white, likely representing regions of interest or statistical significance.
- T and F Contrasts
 - Null hypothesis testing
 - **Thresholding**

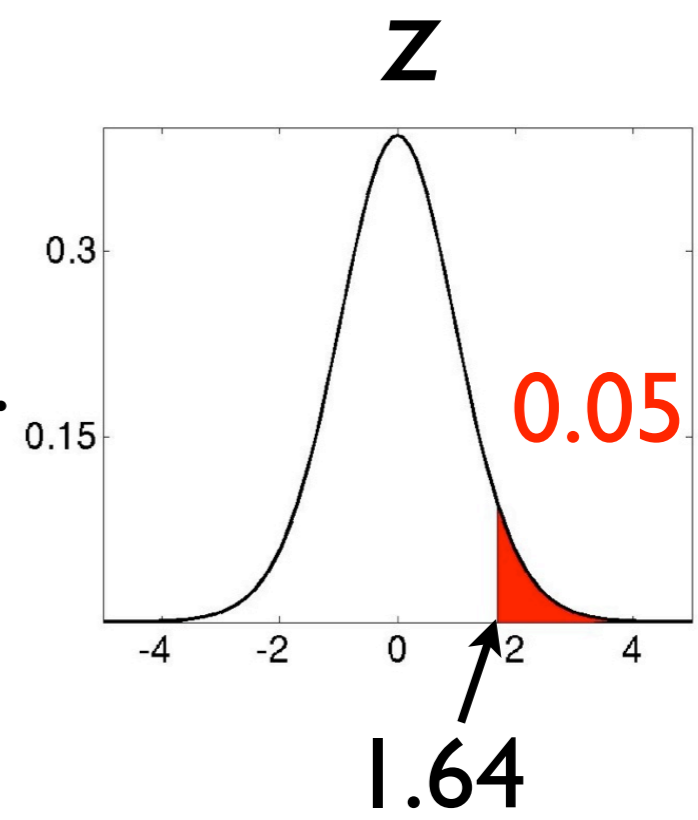




What happens when we apply “standard” statistical testing to imaging data?



z-map where each voxel $\sim N$.
Null-hypothesis true everywhere, i.e.
NO ACTIVATIONS



z-map
thresholded at
1.64



16 clusters
288 voxels
~5.5% of the voxels

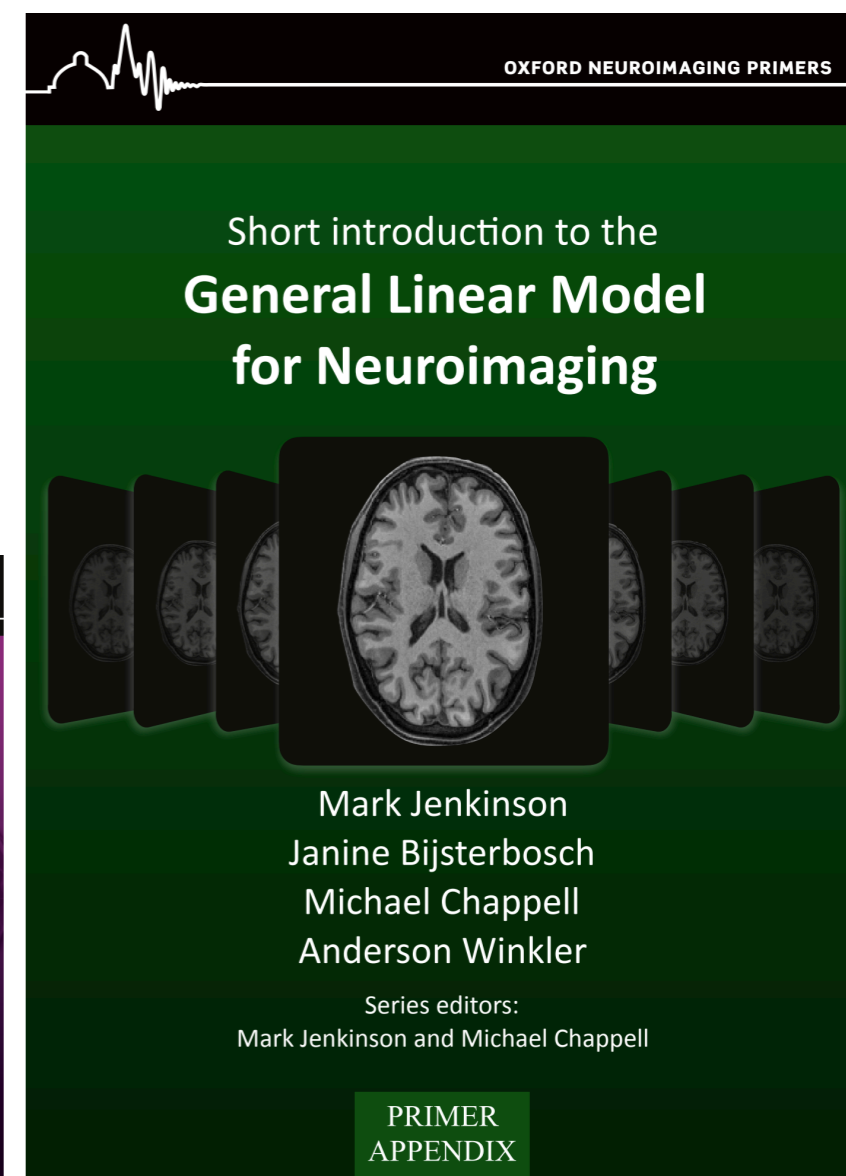
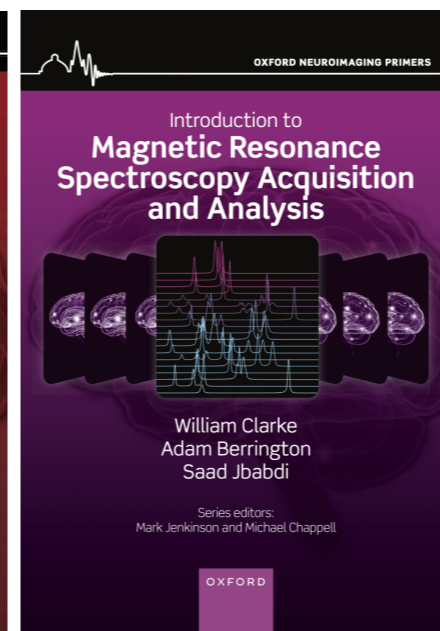
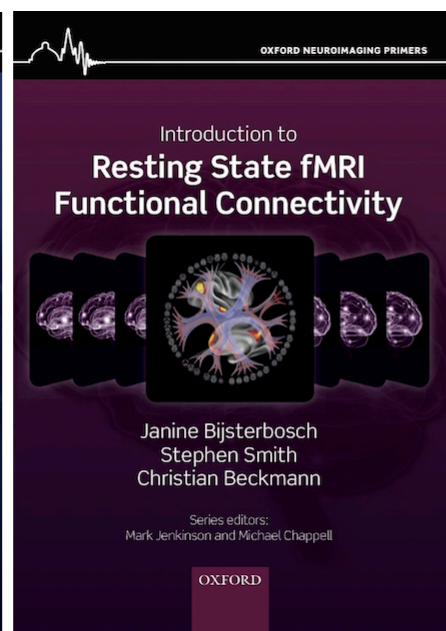
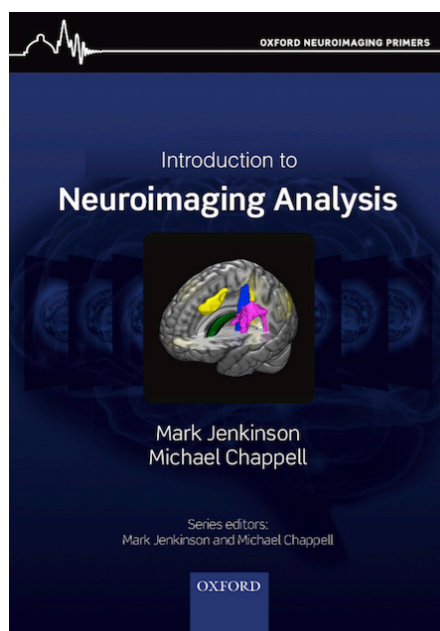
That's a LOT of false positives



Free online appendix

Oxford Neuroimaging Primers

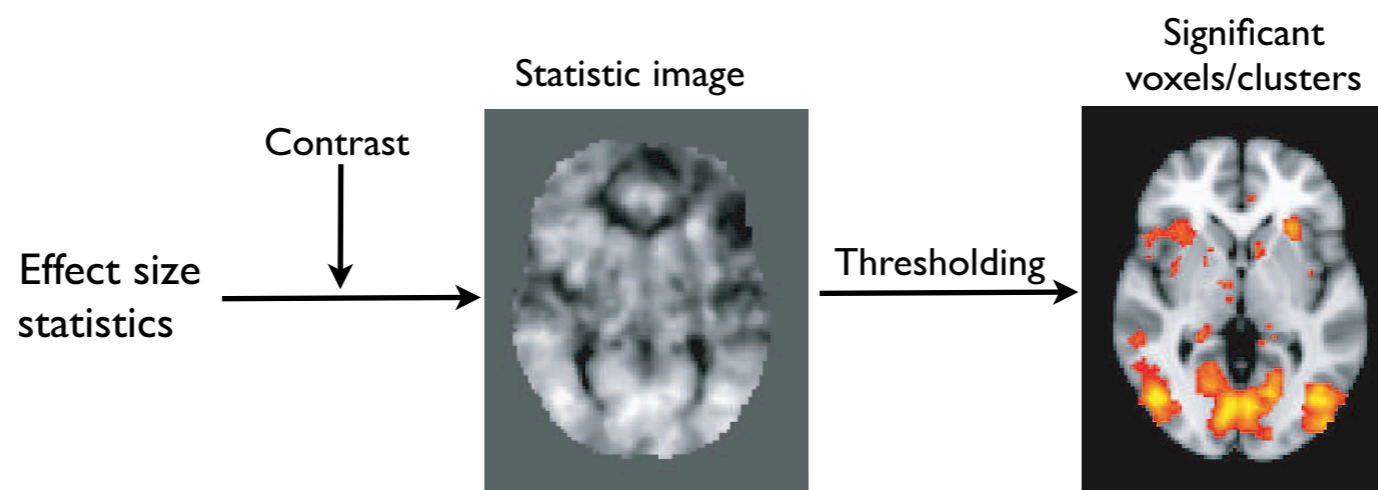
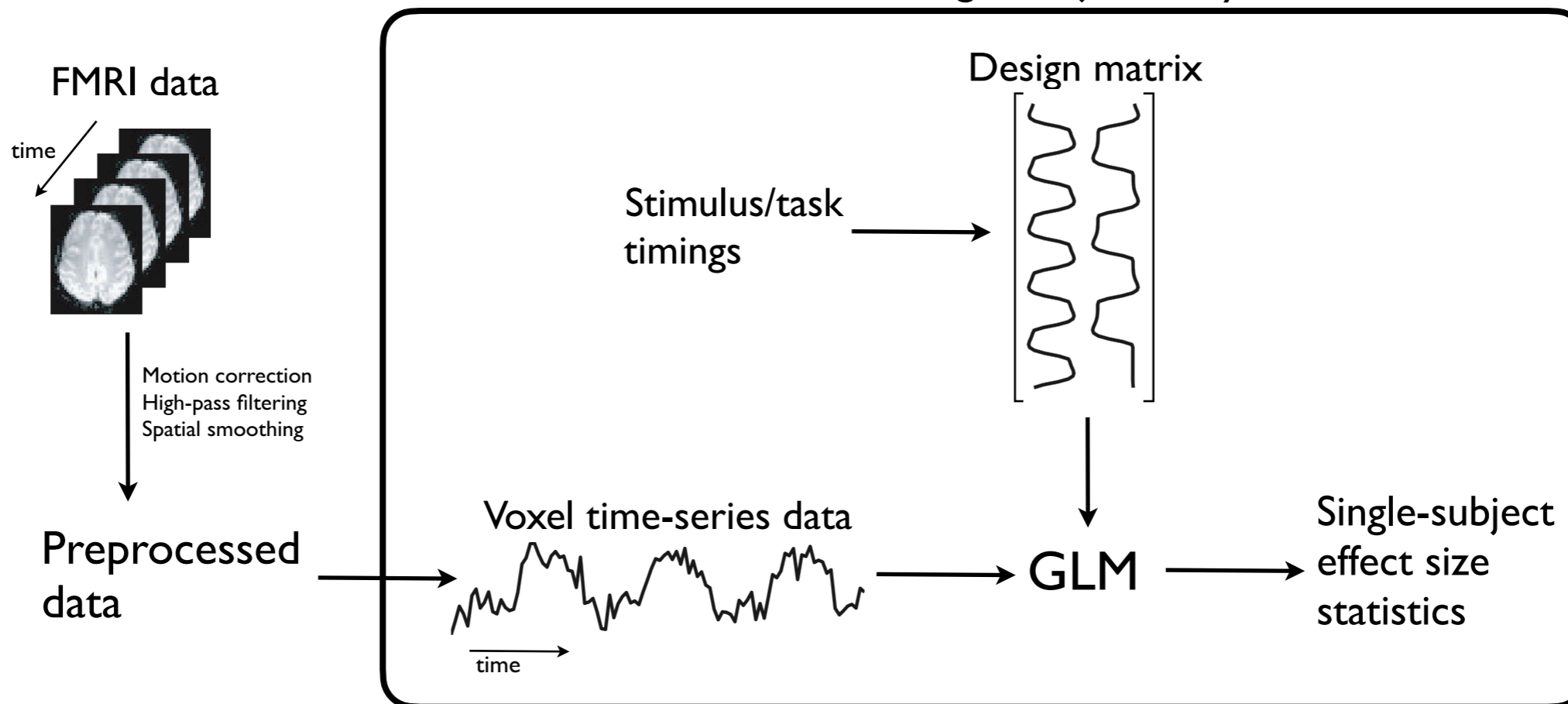
<https://www.fmrib.ox.ac.uk/primers/appendices/glm.pdf>



FMRI single subject analysis

That's all folks!

Voxel-wise single-subject analysis

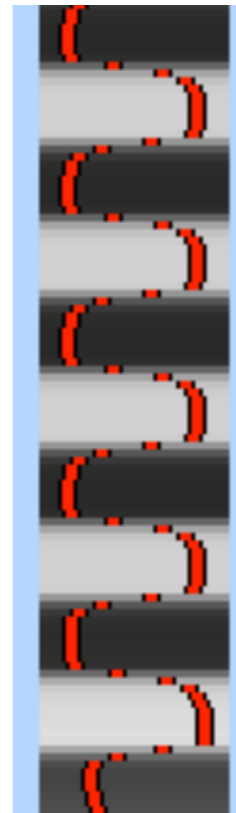




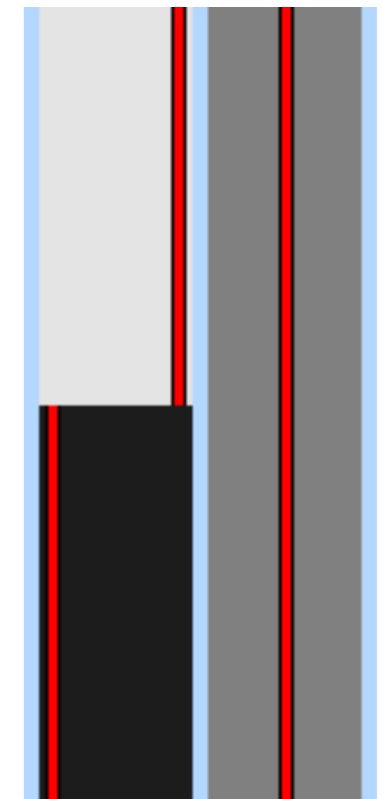
“Demeaning” and the GLM

- The mean value is uninteresting in an fMRI session
- There are two equivalent options:
 1. remove the mean from the data and don't model it
 2. put a term into the model to account for the mean

option #1



option #2



In FSL we use option #1 for first-level analyses and #2 for higher-level analyses

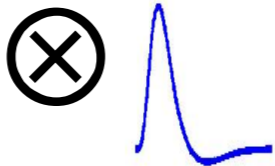
A consequence is that the baseline condition in first-level analysis is **NOT** explicitly modelled (in FSL)



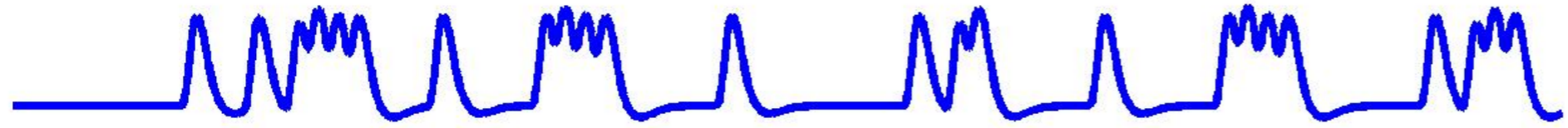
Slight detour: Making regressors



Event timings at “high” resolution



Convolve with HRF



Predictions at “high” resolution



Sub-sample at T_R of experiment



Regressor



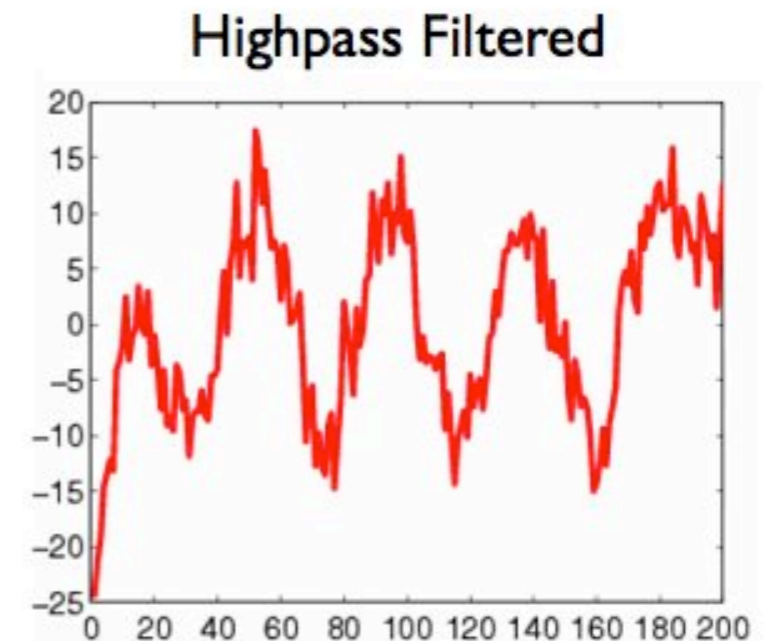
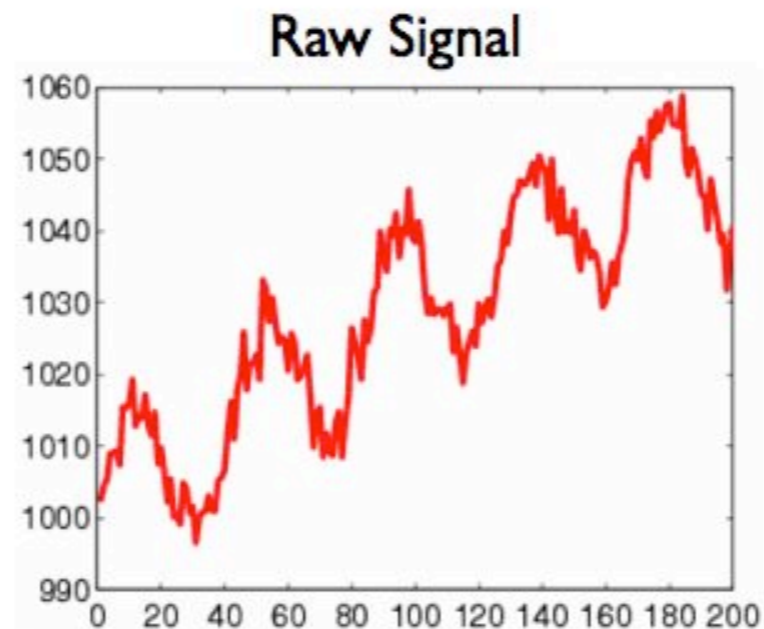
Choosing High-Pass Filter Cut-off

- Can use FEAT to determine a good cut-off value

Remember
highpass filtering?



Temporal Filtering: Highpass



- Removes low frequency signals, including linear trend
- Must choose cutoff frequency carefully (lower than frequencies of interest = longer period)

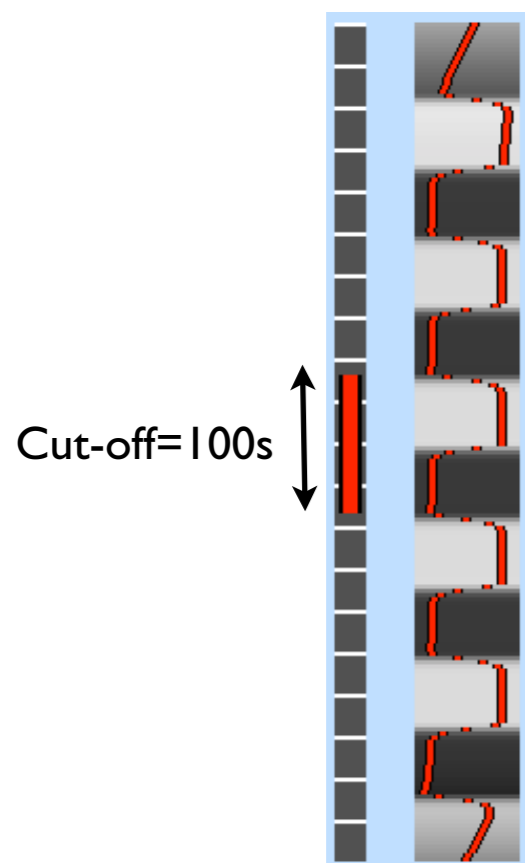


Choosing High-Pass Filter Cut-off

- Can use FEAT to determine a good cut-off value
- **OR**
- Set by hand, but make sure model is not badly affected

Example: Boxcar EV with period

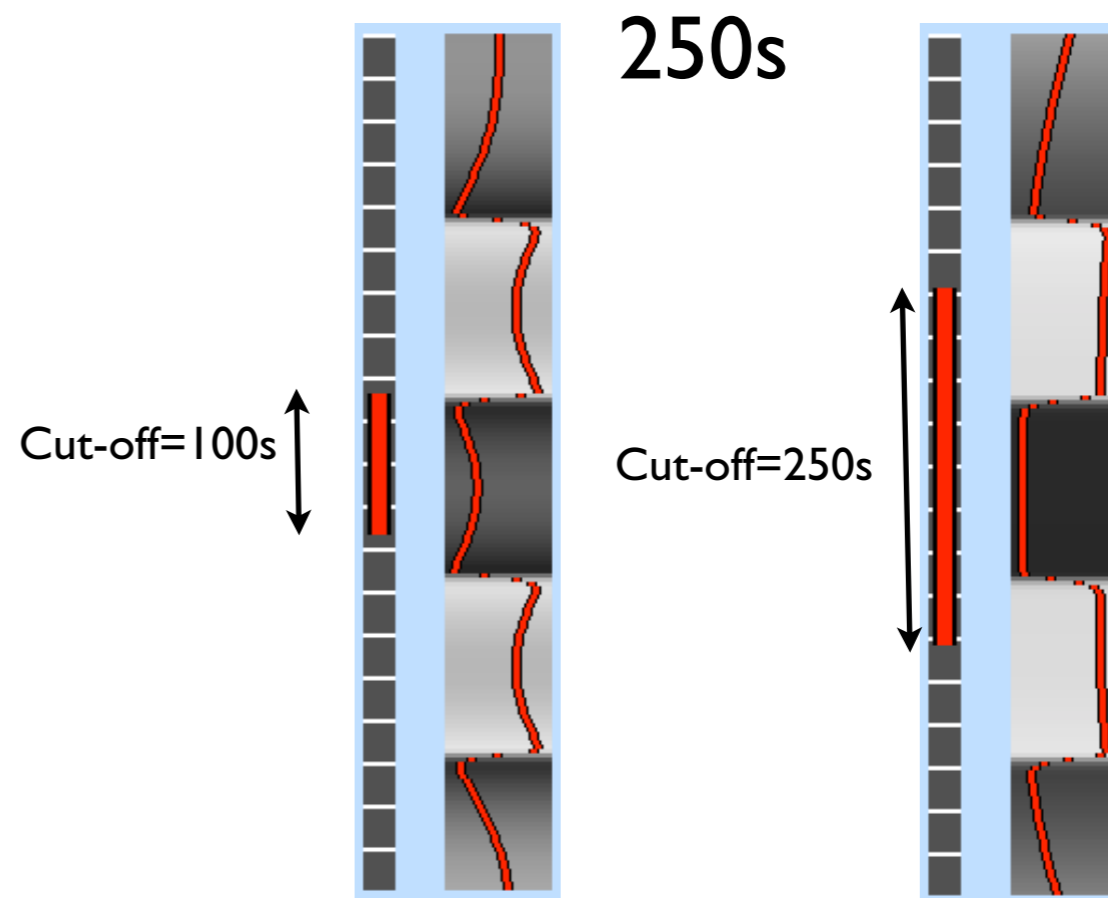
100s



Negligible effect on EV, so use cut-off of 100s

Example: Boxcar with period

250s

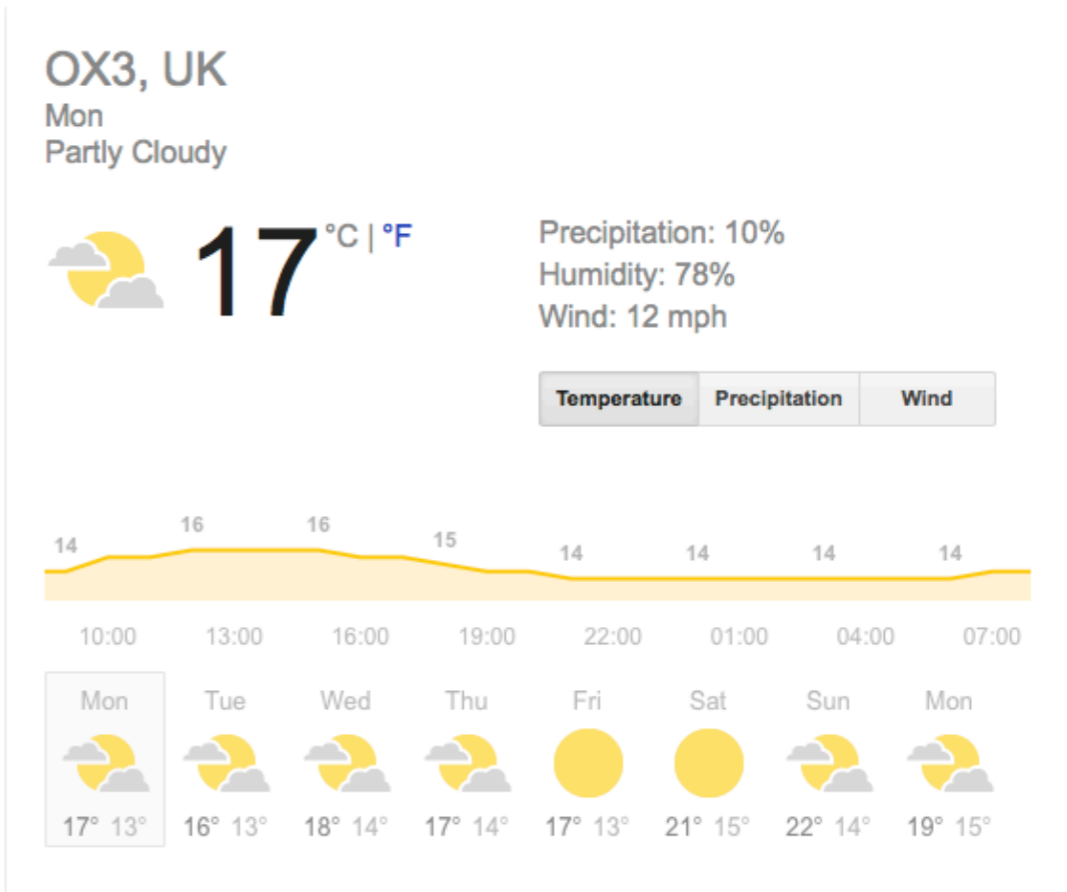


Substantial effect on EV, so need longer cut-off

Negligible effect on EV, so use cut-off of 250s



Non-independent/Autocorrelation/ Coloured FMRI noise



Uncorrected, this causes:

- biased stats (increased false positives)
- decreased sensitivity

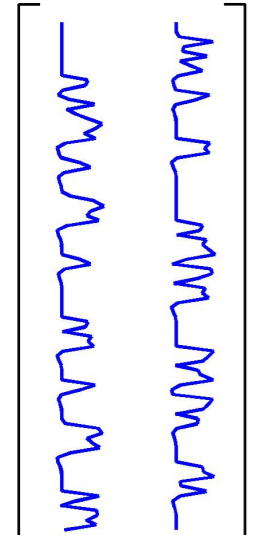
FSL fixes it for you in FEAT!

Cannot use randomise (see later) because of autocorrelation

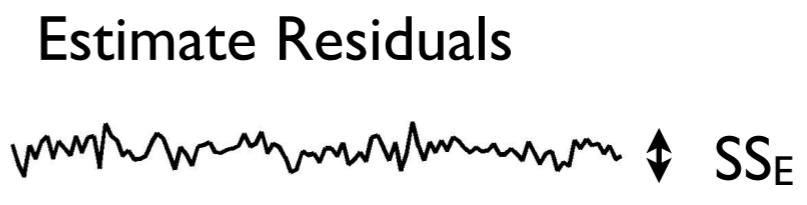
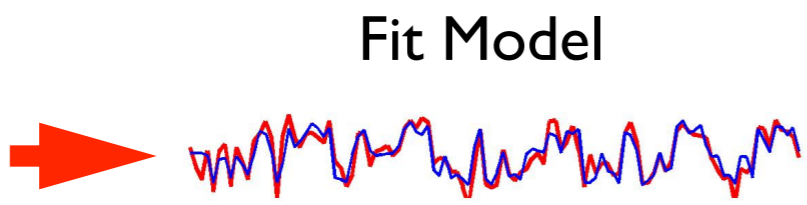


F-contrasts

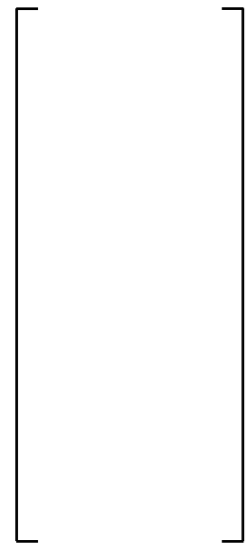
$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$



Full Model



$$F = \frac{SS_R - SS_E}{SS_E} = \frac{\text{↑} - \text{↑}}{\text{↑}}$$



Reduced Model

