



MRC Cognition
and Brain
Sciences Unit



UNIVERSITY OF
CAMBRIDGE

fMRI analysis



GitHub

https://github.com/dcdace/fMRI_training

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[Datza]



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Winter, 2023



Environment



Data
Organise & Manage



Pre-process

Analyse

Faces vs Scrambled
images are processed
differently in the brain

Design an experiment



Data

Stimuli
Timing

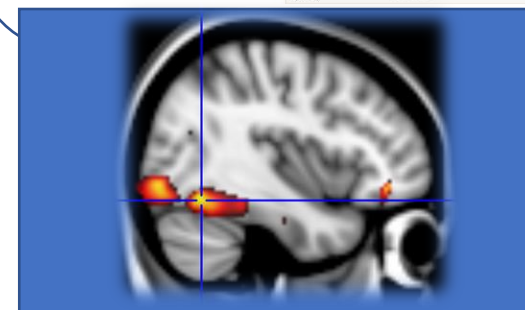
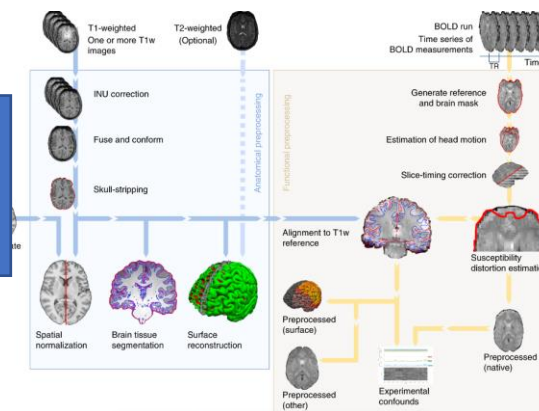
Collect the MRI data



Data

Anatomical image
Functional images
Event details

Pre-process & Analyse



fMRI Analysis

The General Linear Model (GLM)

Largely based on Idan Blank's materials

https://cbmm.mit.edu/videos?field_video_grouping_tid%5B%5D=770

Finding a **Face** area in the brain

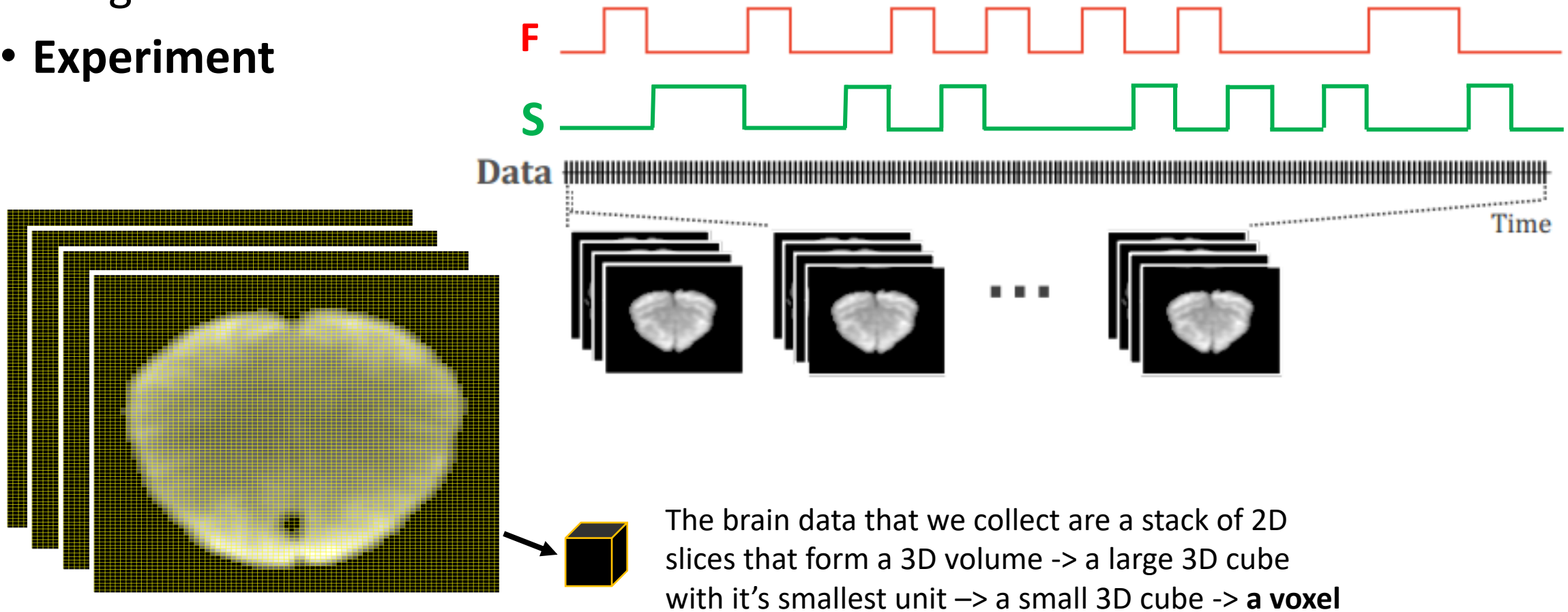
Which brain regions are engaged when people look at faces



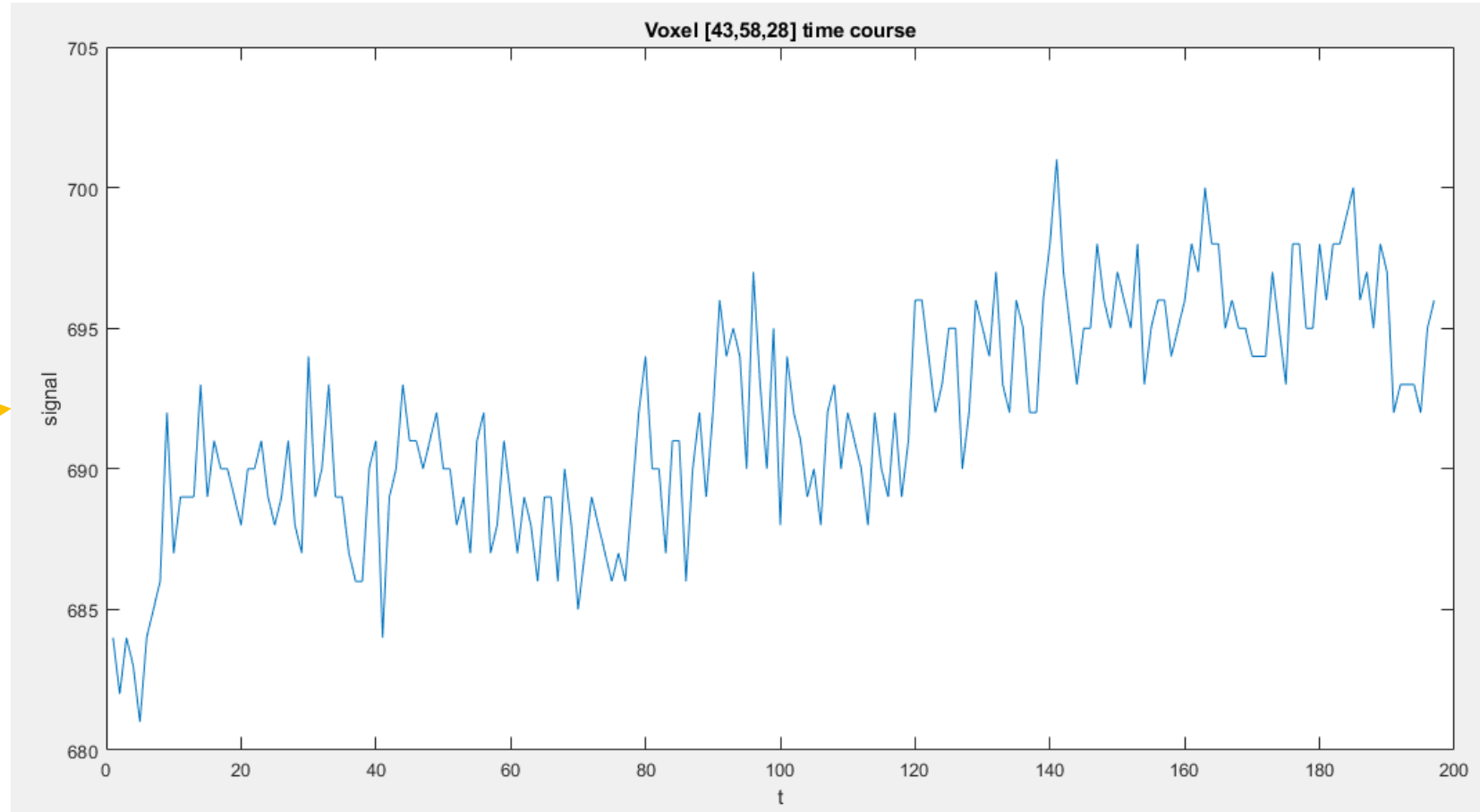
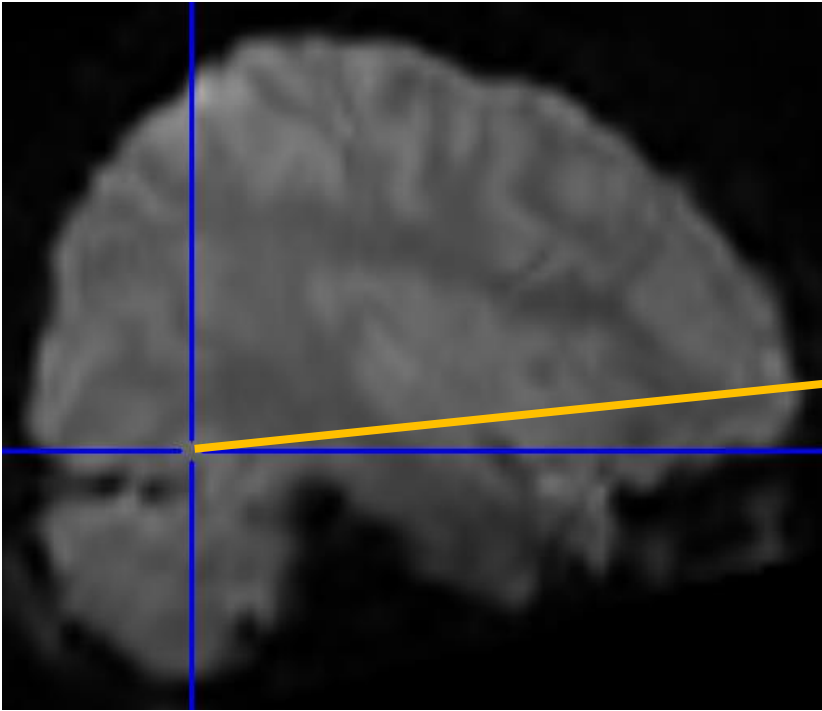
- With fMRI the meaningful questions are questions that **compare two conditions**
 - We need some sort of control condition → **Scrambled** condition
- Which brain regions respond more to looking at **face** images than **scrambled** images
 - The control question hopefully help to **wash out all the regions we are not interested in**. Because regions that we are NOT interested in should activate both conditions to the same extend (e.g. visual areas)

The structure of our data

- **Question:** Which brain regions respond more to **face** images than to **scrambled** images
- **Experiment**



Voxel time course

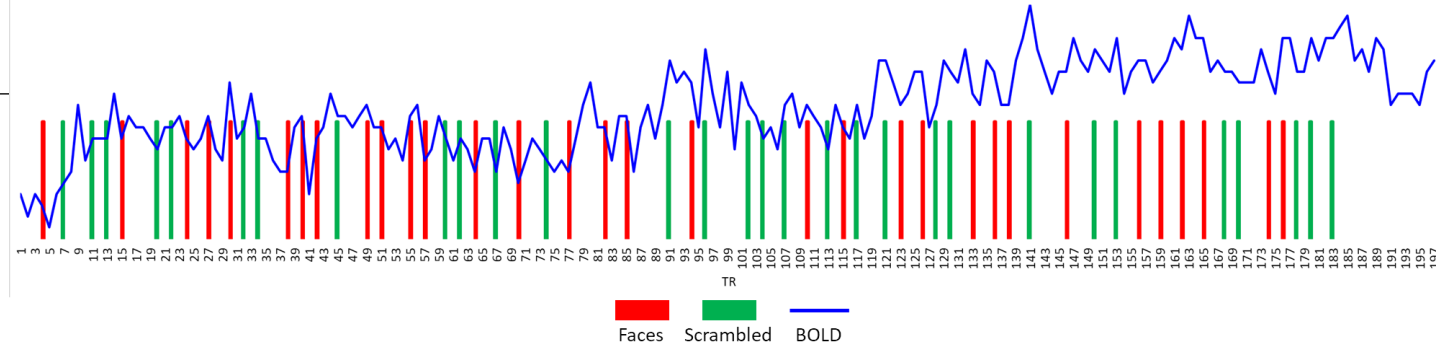


Question: Which brain regions respond more to **face** images than to **scrambled** images

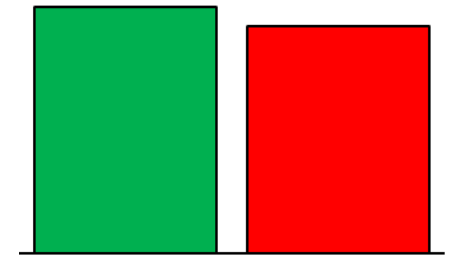
- Event onsets and BOLD signal in a sample voxel
- **How do we analyse this?**



Question: Which brain regions respond more to **face** images than to **scrambled** images



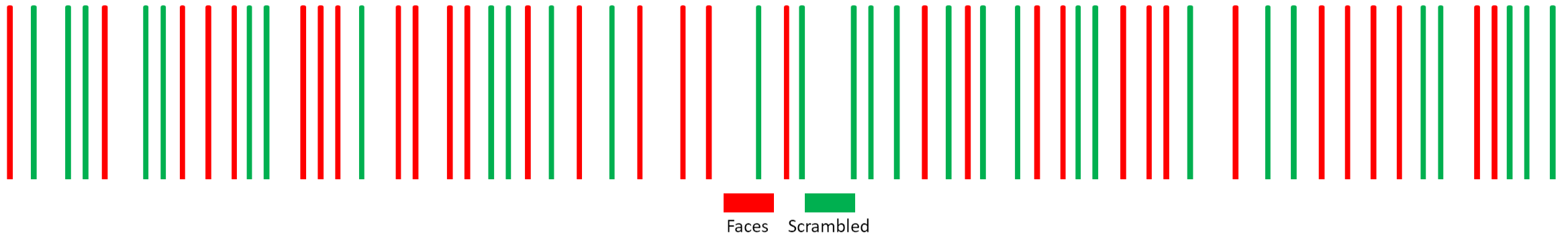
- A raw BOLD signal is noisy
- Let's start with an intuitive way, and that's how people started to analyse fMRI data
- **Analysis:** an intuitive approach
 1. For each voxel, look at its signal time-series (activity across time)
 2. Average the signal across volumes that were collected while participants were looking at **Faces**
 - Mean **Faces** = 691.92, Mean **Scrambled** = 692.35, **F-S** = -0.43



Why does the averaging method does not work?

Question: Which brain regions respond more to **face** images than to **scrambled** images

- **Stimuli**



- **Neural activity**

- Starts briefly after the onset of the stimulus

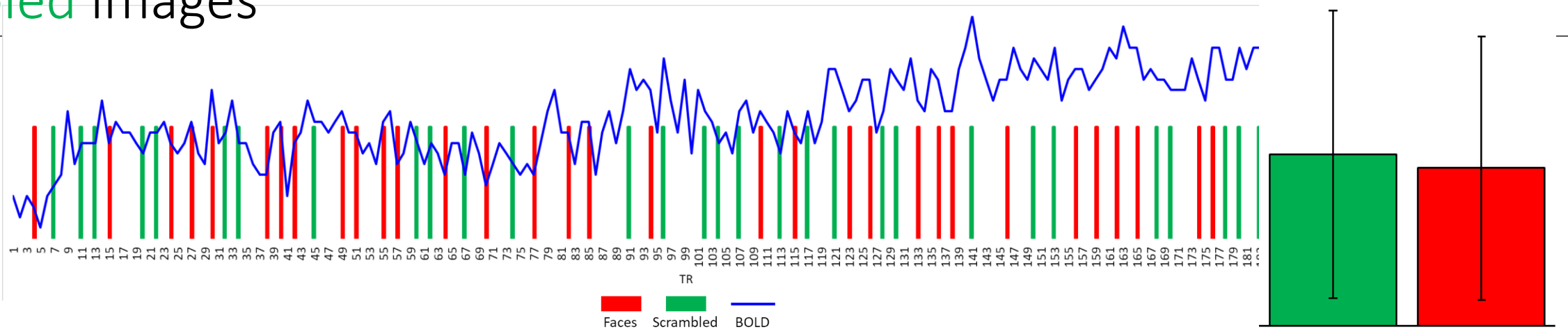
- **BOLD signal** (not a direct measure of neural activity)

- When neurons are active, the fMRI BOLD signal will rise _____

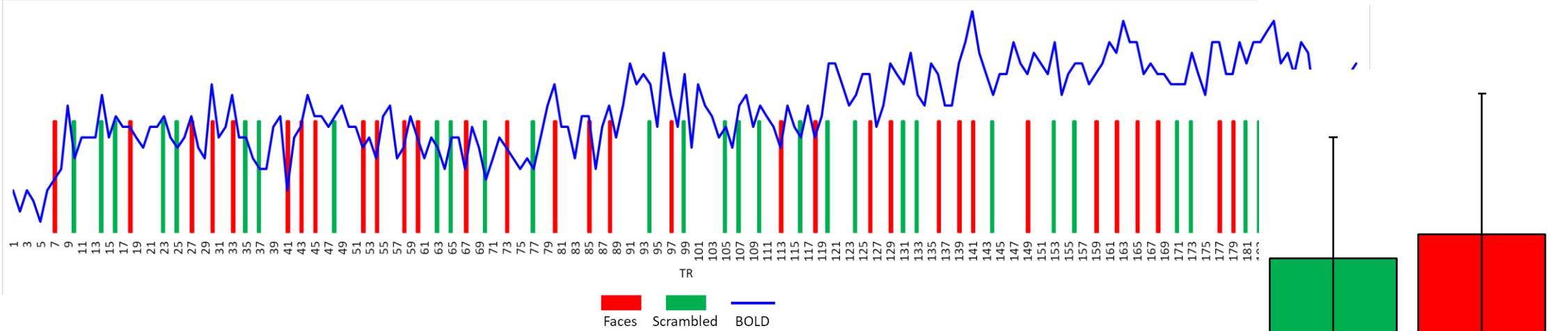
- A. Immediately
- B. 1-3 seconds after the neural activity
- C. 6-12 seconds after the neural activity
- D. 25-30 seconds after the neural activity

We were averaging the wrong points! The points in time when the 'Face area' would respond are actually little later than the onset of the stimulus; about 6-12 s later than the onset.

Question: Which brain regions respond more to **face** images than to **scrambled** images



+6s shift

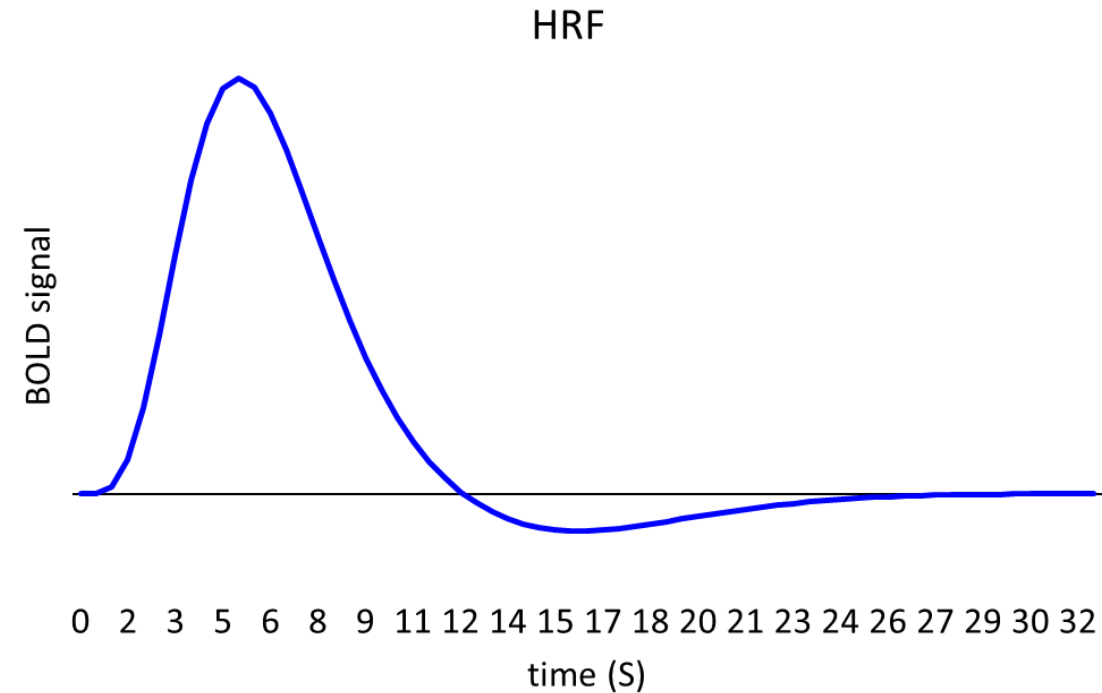


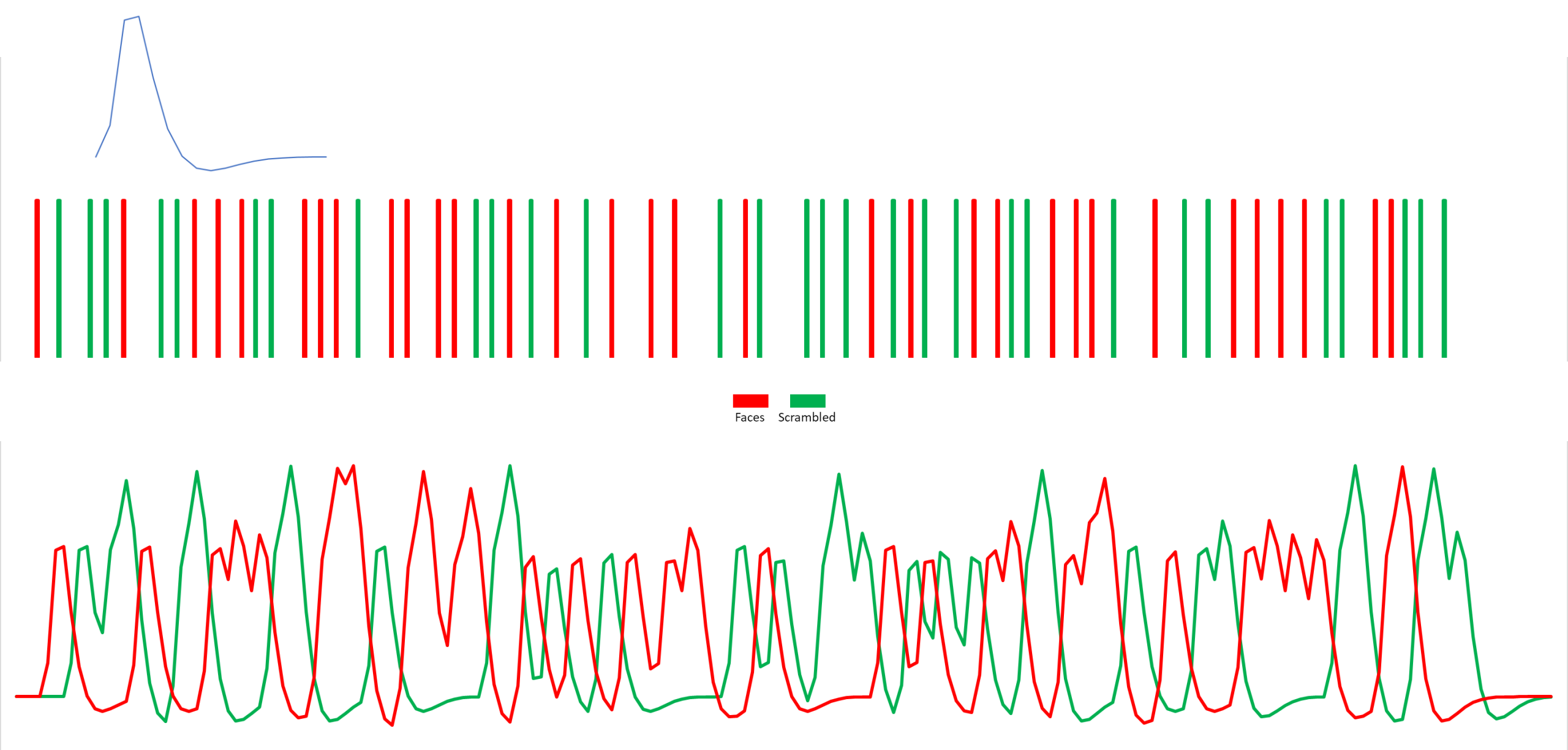
Looks slightly better, but still not working!

Bold signal does not change from 0 to 1 (on or off)!

Question: Which brain regions respond more to **face** images than to **scrambled** images

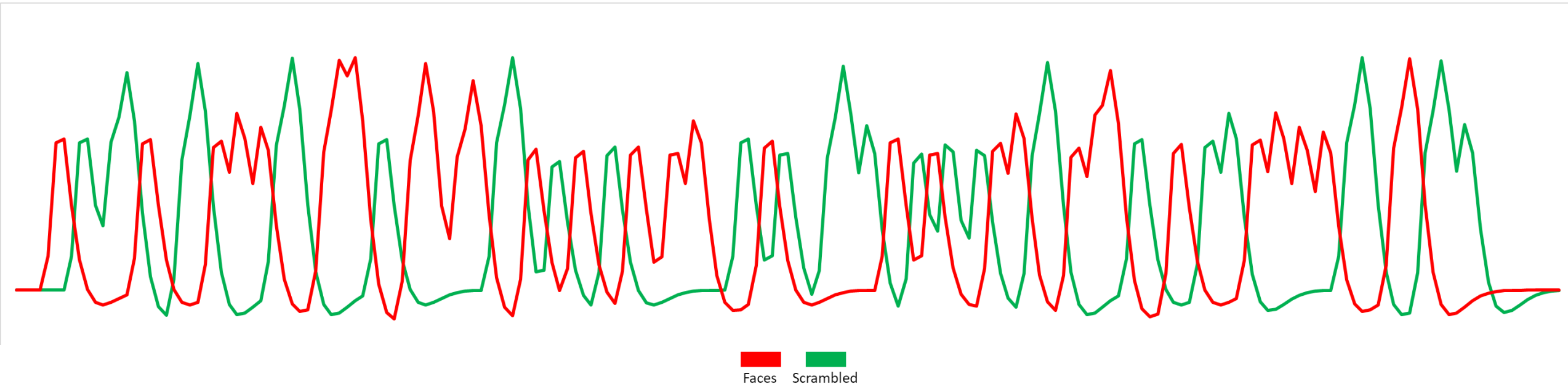
- The haemodynamic response function looks like this
- It is not binary, but smooth
- We need to make our prediction to look more like this
- How do we do that? This is done by mathematical process called **convolution**
- It is filtering the **signal to look more like this shape**





These are our BOLD predictions. **This is how we should expect our signal to look like!**

Question: Which brain regions respond more to **face** images than to **scrambled** images

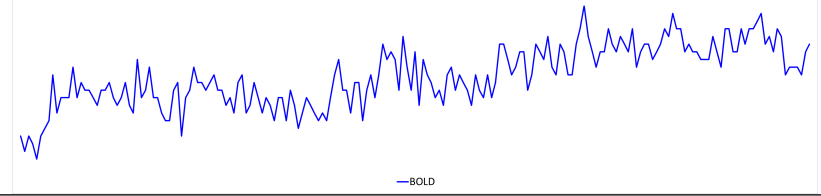


The time series of a voxel that responds more to **Faces** than to **Scrambled** should look like a combination of the two signals above, with **Faces** having more weight than **Scrambled**.



- **Which points should we average?**
- Averaging does not seem to be the best idea anymore.
- We need a more principled solution, not an arbitrary choice of points!
- Voxels in the 'Face area' should respond **a lot to Faces**, but very little to **Scrambled** images.

(de)Constructing the BOLD signal



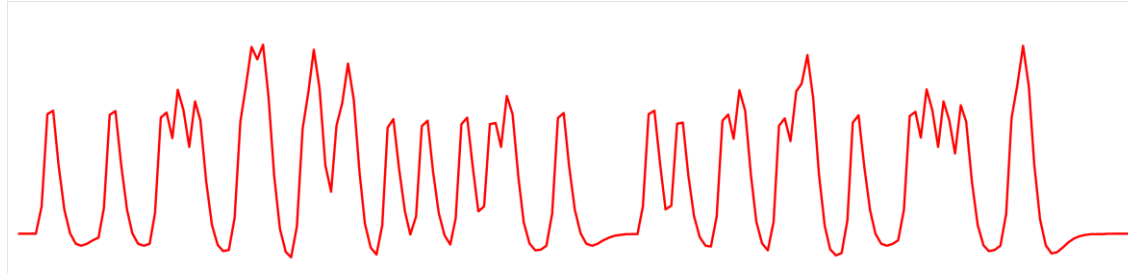
- We can approximate the signal time-series of a voxel by **combining these 3 signals**:

- Baseline signal:

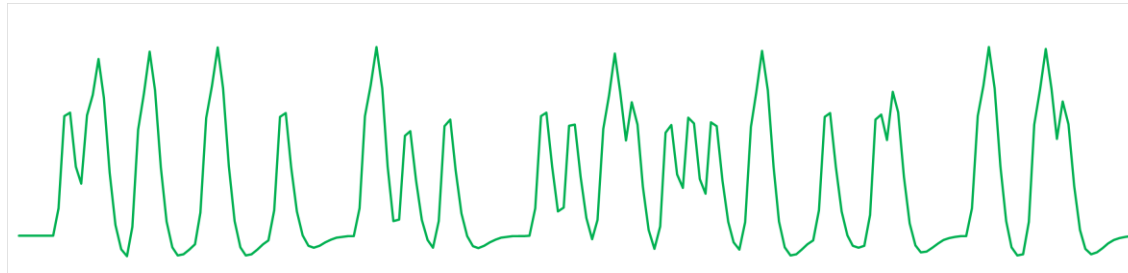
- an average activity in that voxel when you are doing nothing



- Response to **Faces**:



- Response to **Scrambled**:



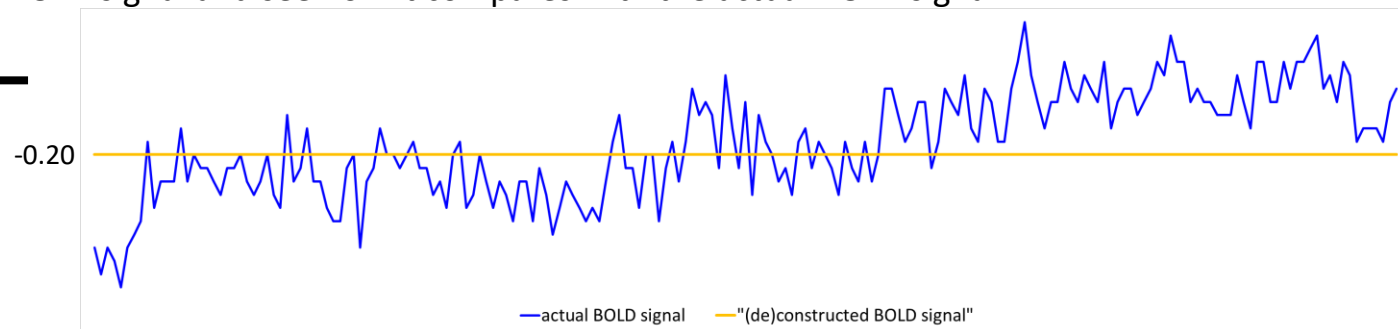
(de)Constructing the BOLD signal

The true BOLD signal

Deconstructed BOLD signal

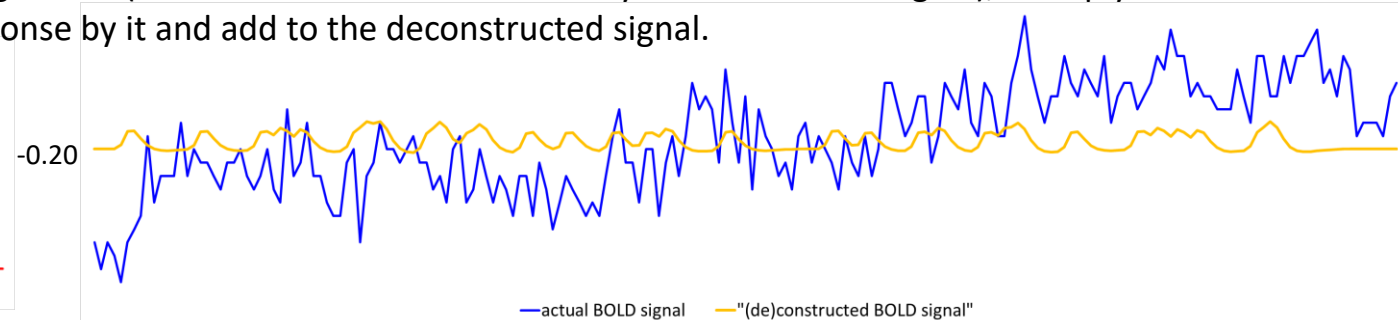
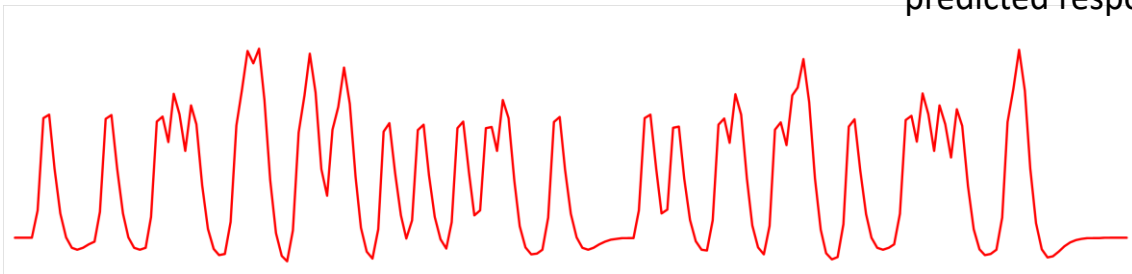
1. Let's say the average signal at baseline was -0.2. We add this baseline measure to our deconstructed BOLD signal and see how it compares with the actual BOLD signal.

Baseline -0.20



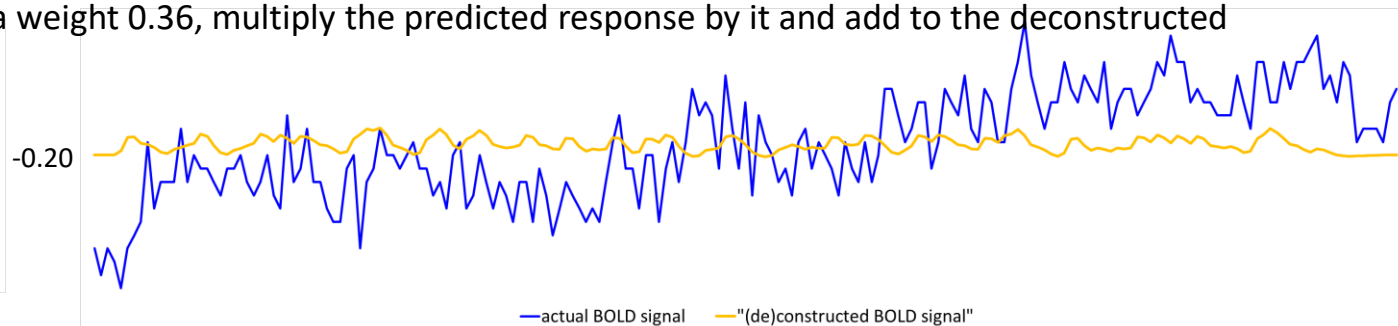
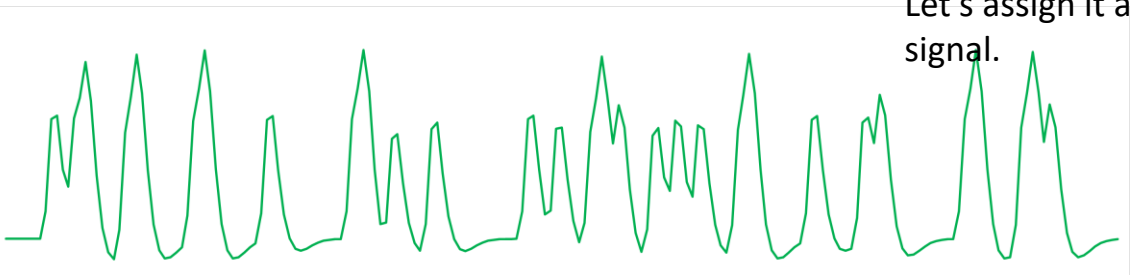
2. We predict that in this voxel **Faces** condition contributes quite a lot to the true BOLD signal. Let's assign it a weight 0.89 (we will find out later how exactly we find these weights), multiply the predicted response by it and add to the deconstructed signal.

+ **Faces** 0.89



3. We predict that in this voxel **Scrambled** condition has little contribution to the true BOLD signal. Let's assign it a weight 0.36, multiply the predicted response by it and add to the deconstructed signal.

+ **Scrambled** 0.36

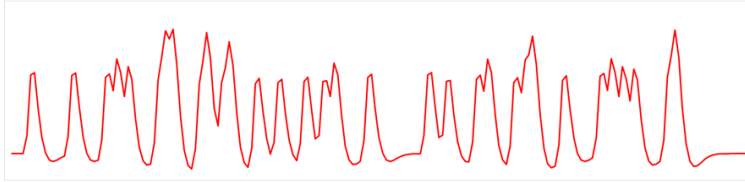


(de)Constructing the BOLD signal

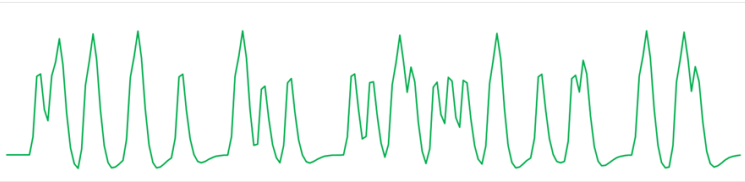
The true BOLD signal
Deconstructed BOLD signal

Baseline * -0.20

+ **Faces** * 0.89



+ **Scrambled** * 0.36

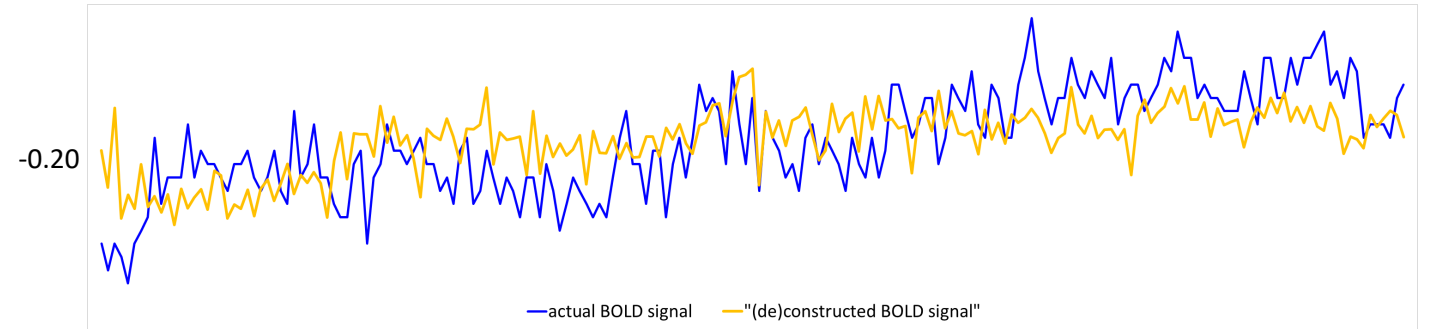
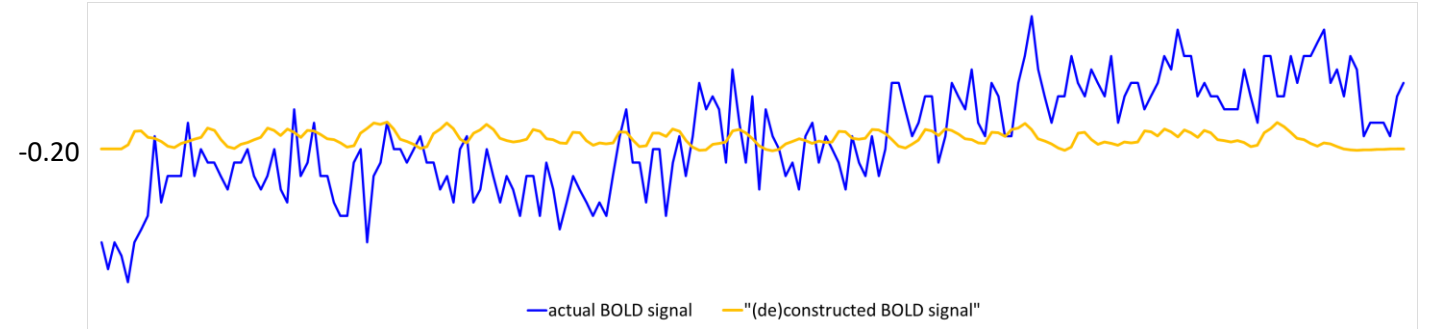


+

Let's assign some weights and add the **6 movement parameters (mp)** to the deconstructed signal.

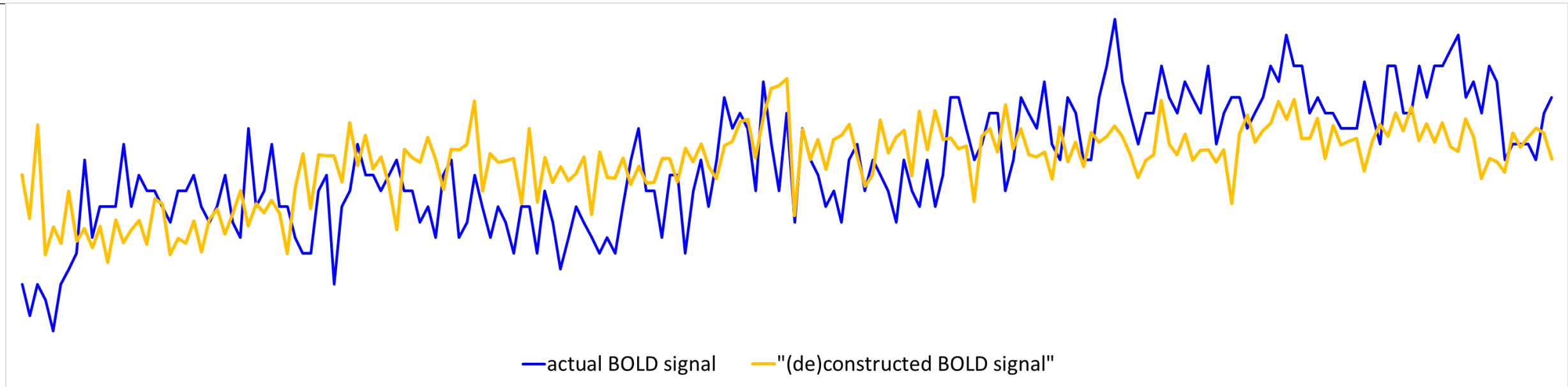
Participant's movement parameters

mp1-0.30 +
mp2-0.13 +
mp3 0.33 +
mp4 0.21 +
mp5-0.01 +
mp6 0.64 +



The deconstructed signal matches the true signal much better now!

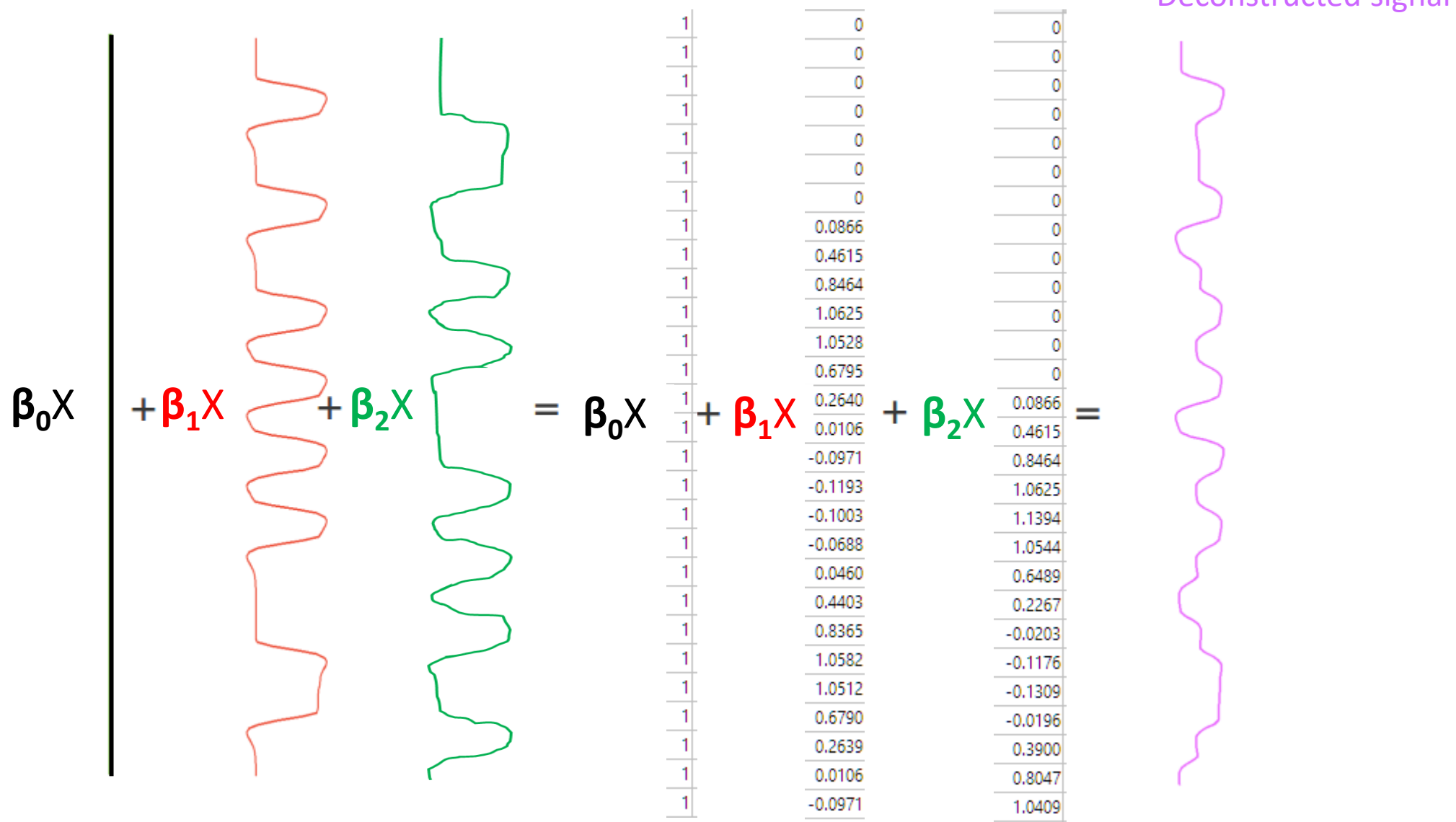
(de)Constructing the BOLD signal



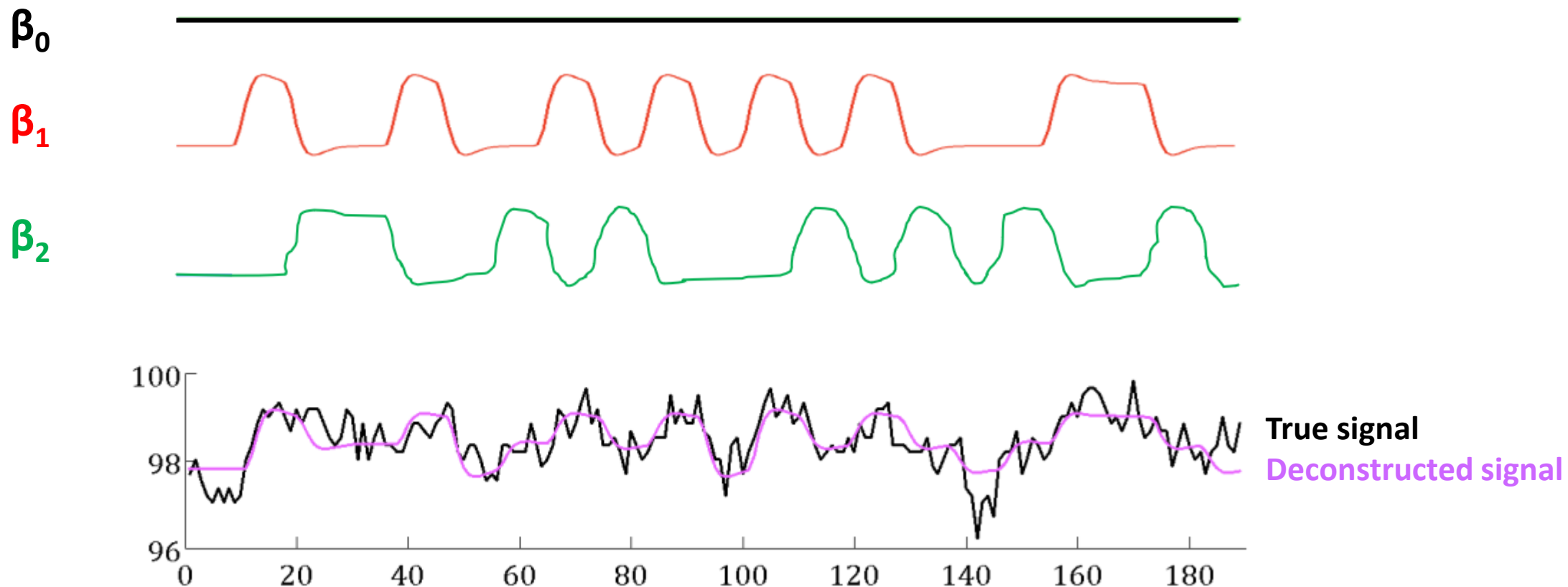
- These signals that we use to construct the approximation are called **predictors**
- One predictor predicts a **constant response**, just **baseline**
- Another predictor predicts how you should **respond to the task**
- Each predictor is associated with a weight called a **beta-weight**
- To create a **linear combination** of predictors, which **approximates a true signal**, we multiply each predictor by its beta-weight and then sum the results.

(de)Constructing the BOLD signal

These signals are just columns (arrays) of numbers stored in a matrix.

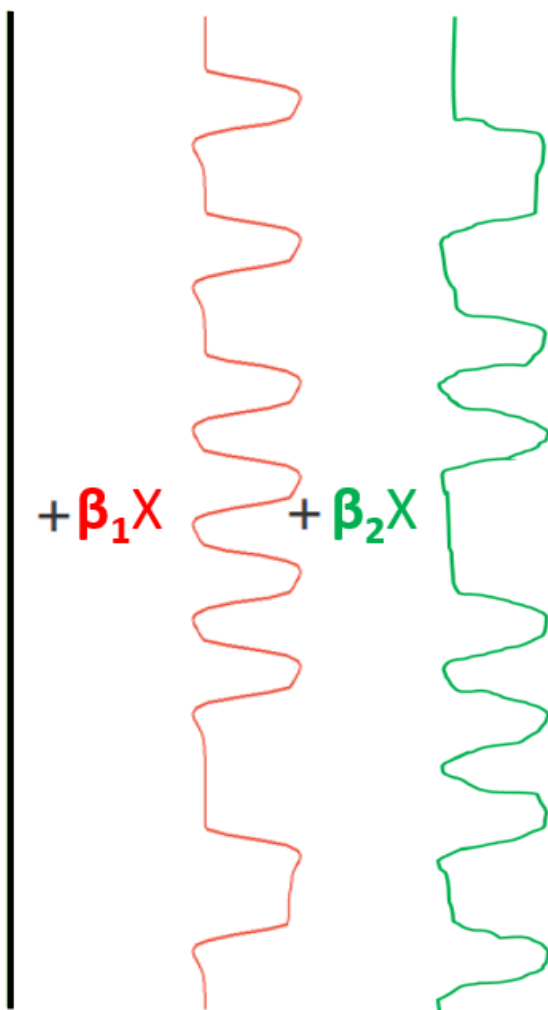


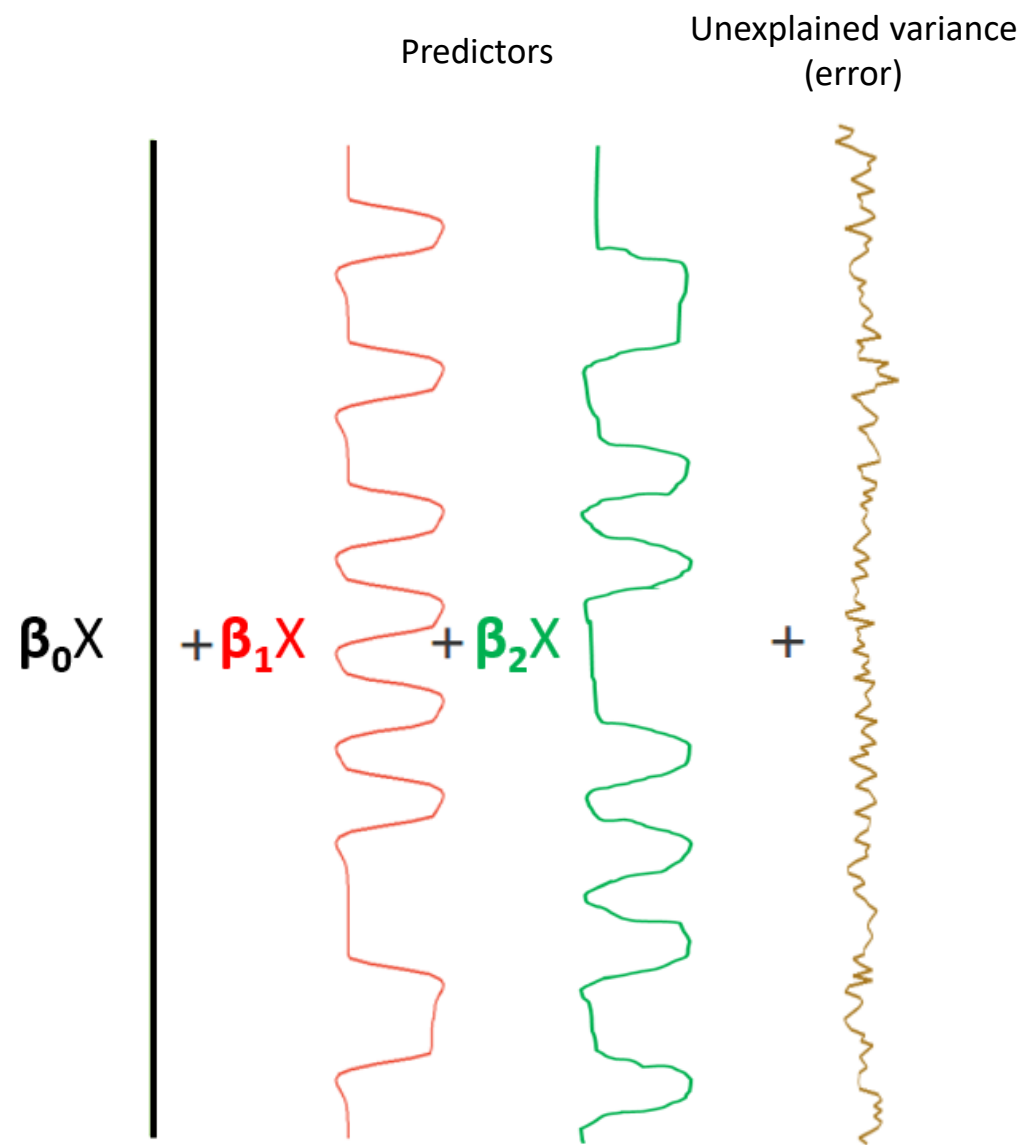
(de)Constructing the BOLD signal

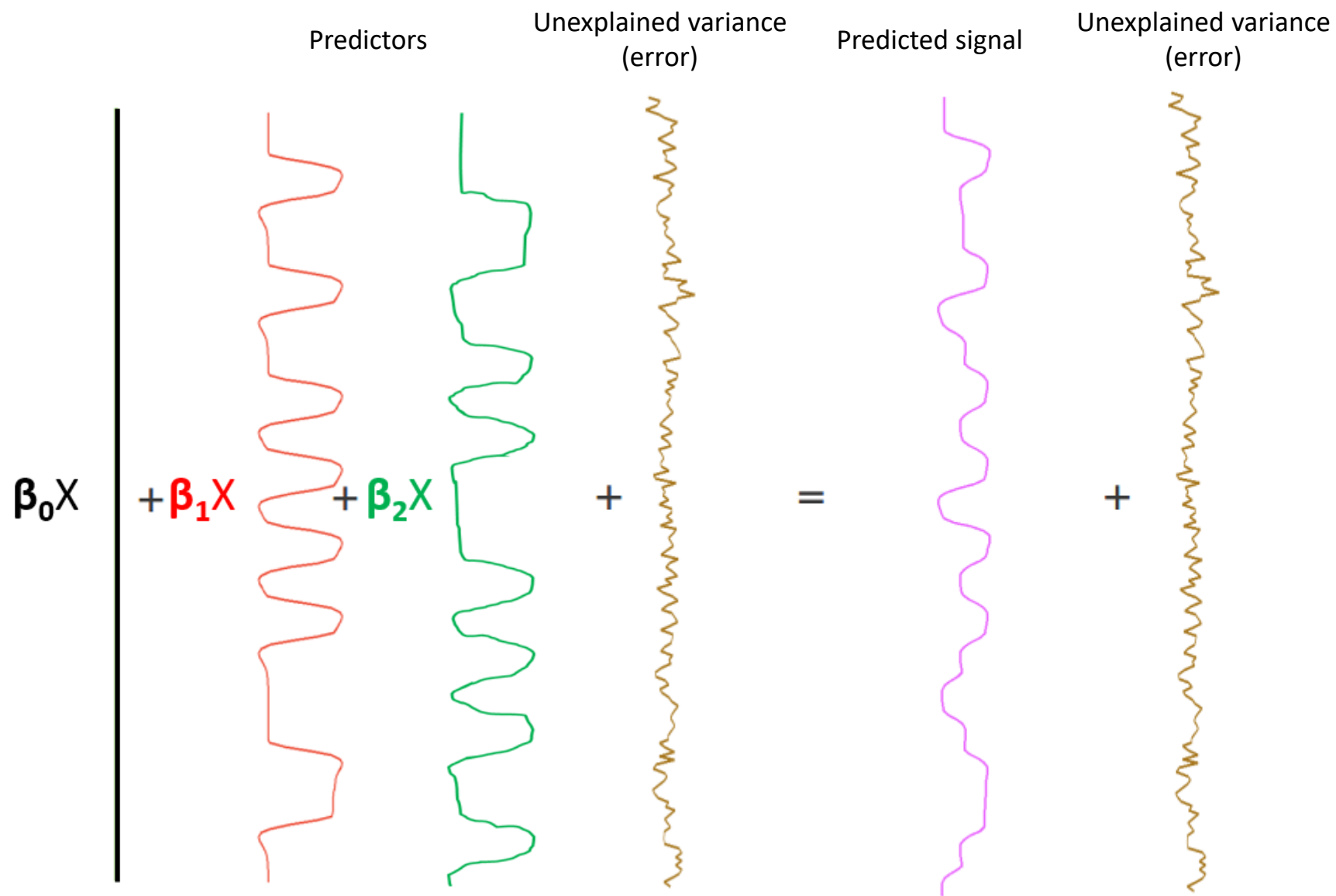


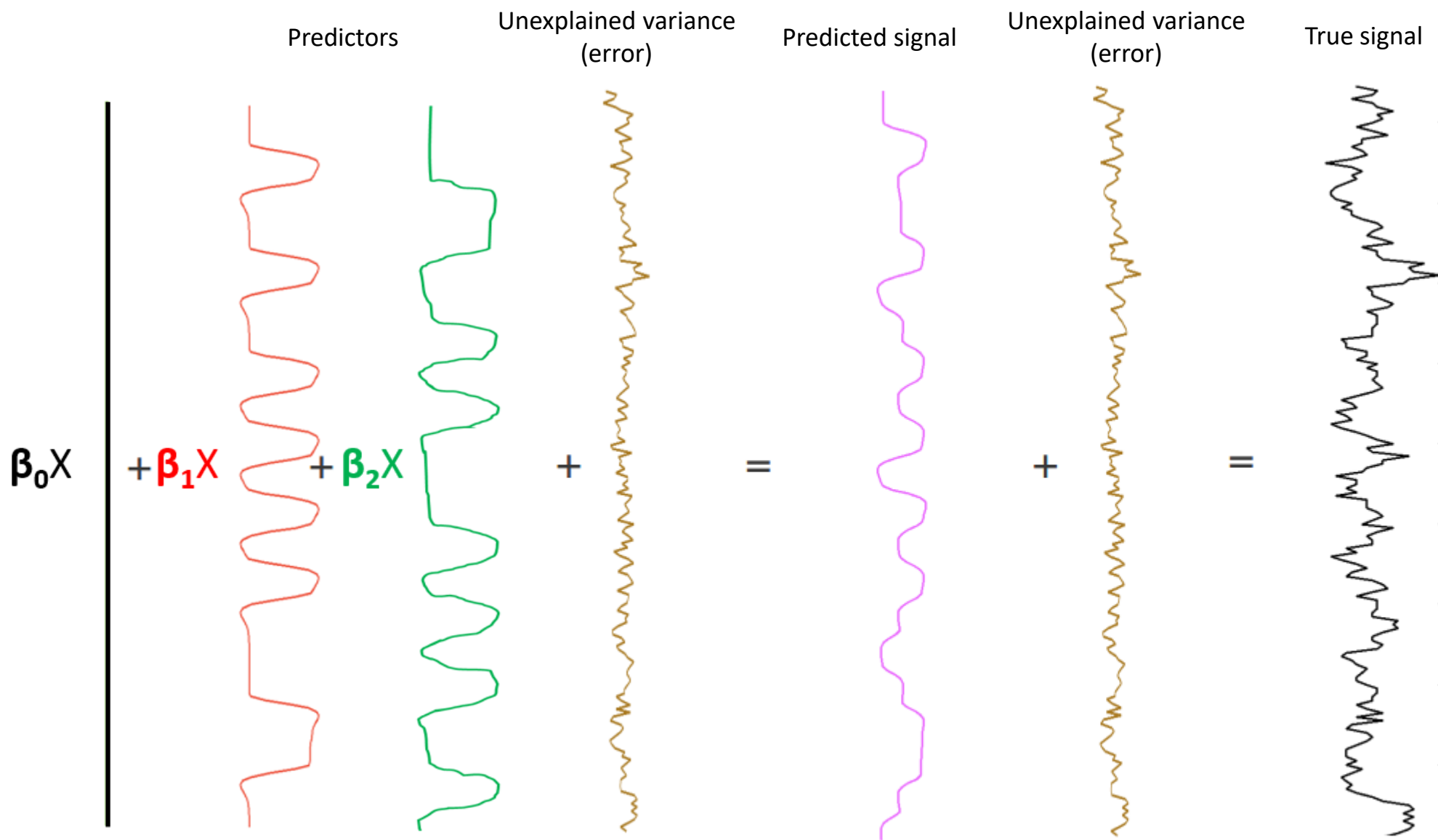
For every time point: **signal(t)** – **prediction(t)** = **error(t)**

Predictors

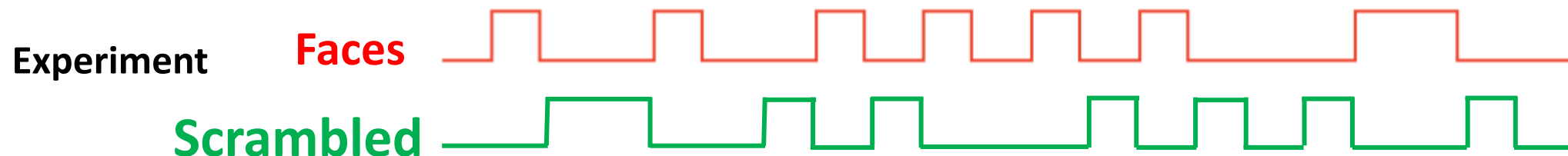
$$\beta_0 X + \beta_1 X + \beta_2 X$$








(de)Constructing the BOLD signal

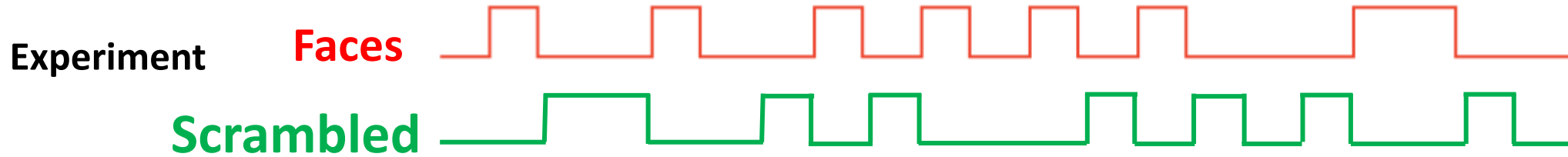


Analysis: the approach that works

- Find the **beta-weights** that best approximate the voxel's signal time-series.
The best approximation is the one with the least errors
- Compare the beta-weights for estimated response to **Faces** to beta-weights for estimated response to **Scrambled**

$$\begin{aligned} \text{BOLD signal} &= \text{task-related activity changes} + \text{noise (other changes)} \\ &\quad \text{explained variation} \quad \quad \quad \text{unexplained variation} \\ &= \text{Linear combination of predictors} + \text{errors} \\ &\quad \text{(deconstructed signal)} \end{aligned}$$

(de)Constructing the BOLD signal



Analysis: the approach that works

- Find the beta-weights that best approximate the voxel's signal time-series.
The best approximation is the one with the least errors
- Compare the beta-weights for estimated response to **Faces** to beta-weights for estimated response to **Scrambled**

To find beta-weights, we use **General Linear Model (GLM)**

How to find betas: GLM $Y = X\beta + \varepsilon$

$$\text{BOLD signal} = \underbrace{X \beta}_{\substack{\text{explained variation} \\ \text{task-related activity changes}}} + \underbrace{\varepsilon}_{\substack{\text{unexplained variation} \\ \text{noise (other changes)}}}$$

- **What we know?**
 - **BOLD signal**: we collect this from the brain (functional data)
 - **X**: the design matrix (each column is a predictor that we built ourselves)
- **What we want to find?**
 - **b**: vector of beta-weights (one weight for predictor in X) that give the best approximation of the BOLD signal
- **How we find it?**
 - By **minimising the sum of squared errors**. In practice, the **GLM** has a formula, which guarantees to find these beta-weights

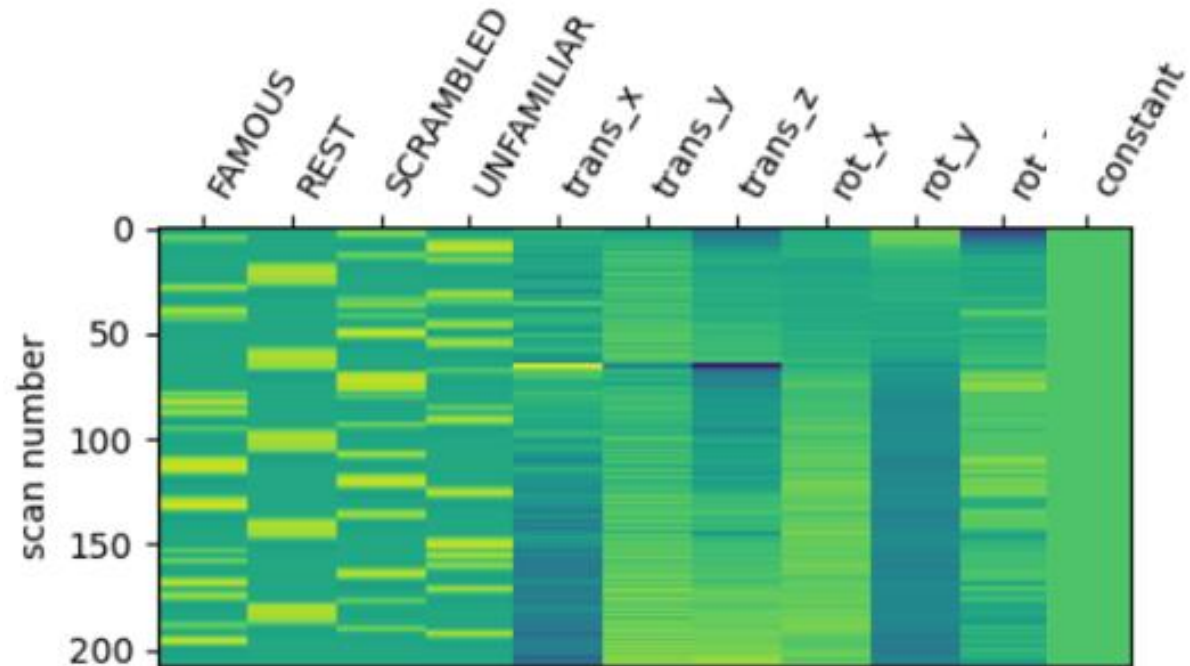
How to find betas: GLM $Y = X\beta + \varepsilon$

- Any predictor that can help approximate the BOLD signal will decrease the **Sum of Squared Errors**
- Therefore, we include additional predictors:
 - The 6 head-motion parameters

An example design matrix.

Each column is a predictor:

- events
- 6 movement parameters
- constant



Multiple regression, to find beta-weights

voxel	S	F	rp1	rp2	rp3	rp4	rp5	rp6
-1.98409	0	0	0.744	-0.968	-0.815	-0.263	2.13	-0.0816
-2.49237	0	0	1.15	-0.399	-1.42	-0.365	1.95	0.0903
-1.98409	0	0	-1.33	0.482	-1.81	-0.729	0.666	-0.304
-2.23823	0	0	2.11	0.35	-1.81	-0.748	0.177	-0.157
-2.74651	0	0.0865661	1.49	0.722	-1.99	-0.63	-0.0958	-0.202
-1.98409	0	0.374888	2.35	1.17	-1.98	-0.718	0.0911	-0.509
-1.72996	0	0.384923	0.989	-0.953	-2.12	-1.12	-0.369	-0.378
-1.47582	0.0865661	0.216117	2.11	1.49	-2	-1.41	-0.556	-0.0755

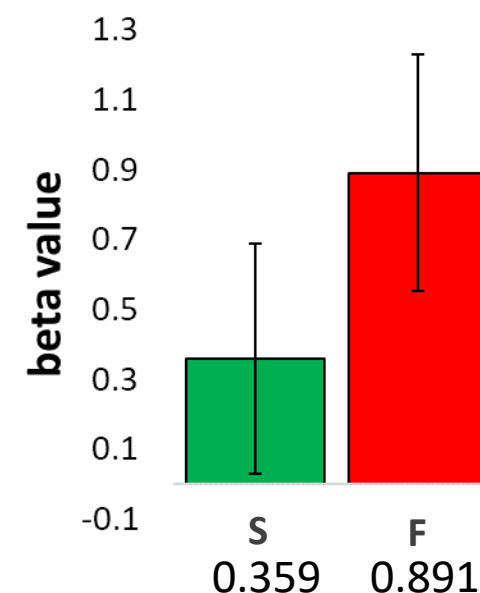
Dependent: voxel1

Method: Enter

Covariates: S, F, rp1, rp2, rp3, rp4

Coefficients

Model		Unstandardized	Standard Error	Standardized	t	p
1	intercept	-0.199	0.106		-1.877	0.062
	S	0.359	0.329	0.070	1.091	0.277
	F	0.891	0.338	0.171	2.637	0.009
	rp1	-0.302	0.077	-0.302	-3.916	< .001
	rp2	-0.129	0.051	-0.129	-2.544	0.012
	rp3	0.326	0.063	0.327	5.223	< .001
	rp4	0.210	0.074	0.210	2.829	0.005
	rp5	-0.008	0.059	-0.008	-0.135	0.893
	rp6	0.643	0.064	0.643	9.978	< .001



A comparison of beta-weights is called a **contrast**.

Formally, a contrast is a vector indicating which beta-weights we are testing. $\beta(F) - \beta(S)$: $[-1 \ 1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0]$ $-0.359 + 0.891 = 0.532$

How to find betas: GLM

1. **Extract the signal time-series** from a given voxel
2. Create a **design matrix** (predictors)
3. **Run GLM** (the signal and your design matrix are the inputs) to **find beta-weights** that best approximate the true signal
4. Define your **contrast** and test it
5. Repeat for **all voxels**
 - Produces
 - An image file for each predictor with beta values for each voxel: **beta-maps**
 - An image file with contrast values for each voxel: **contrast-maps**
 - An image file with contrast-specific t-values for each voxel: **t-maps**

First-level analysis: model specification

```
fmri_glm = FirstLevelModel(  
    t_r = TR,  
    slice_time_ref = TR/2,  
    hrf_model = 'spm',  
    drift_model = 'Cosine',  
    high_pass = 1./128,  
    smoothing_fwhm = 6,  
    noise_model = 'ar1'  
)
```

- **t_r**, Repetition Time (TR)
- **slice_time_ref**: This parameter indicates the time of the reference slice used in the slice timing pre-processing step
- **hrf_model**: defines the HRF model to be used
- **drift_model**: specifies the desired drift model for the design matrices. It can be 'polynomial', 'cosine' or None. Default = 'cosine'.
- **high_pass**: specifies the cut frequency of the high-pass filter in Hz for the design matrices. Used only if drift_model is 'cosine'. Default=0.01 (1/128, as in SPM). Slow signal drifts with a period longer than 128 s will be removed. It is a way to remove possible confounds.
- **smoothing_fwhm**: the full-width at half maximum in millimeters of the spatial smoothing to apply to the signal (smoothing was not done in fMRIPrep!).
- **noise_model**: {'ar1', 'ols'} The temporal variance model. Default='ar1'. Accounting for serial correlations in fMRI time series due to aliased biorhythms and unmodelled neuronal activity. Accounts for non-independency in the BOLD response.

First-level analysis: model specification

The screenshot shows the 'Help on: fMRI model specification' window. It contains a list of parameters and their values. Red arrows point from text boxes to specific parameters in the window.

Annotations:

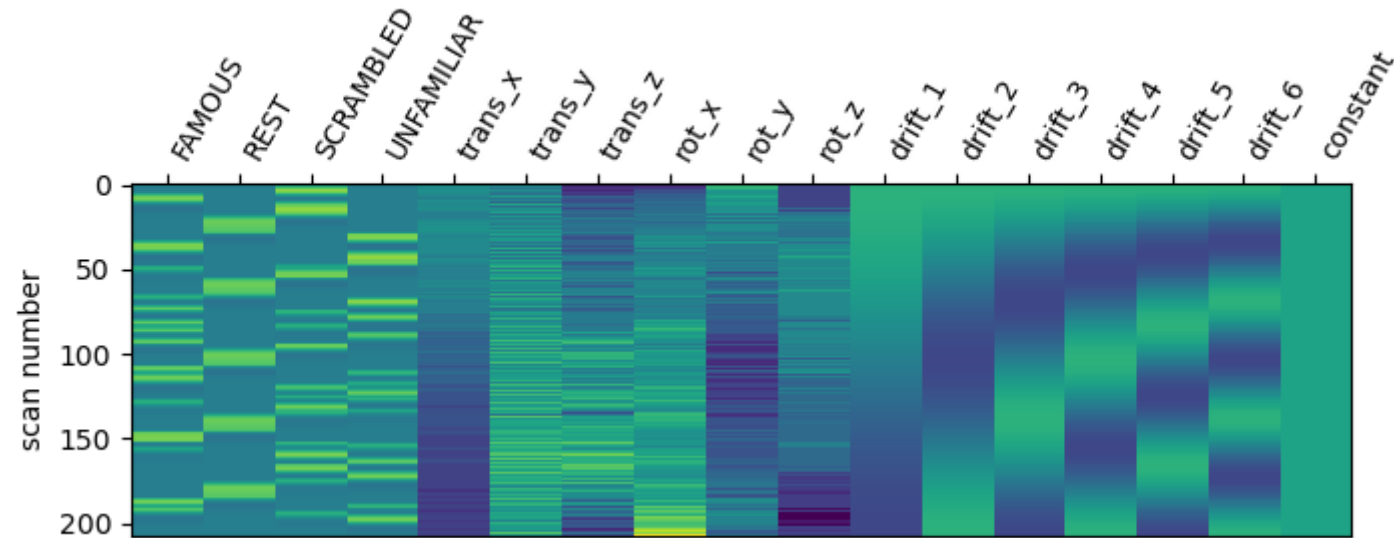
- The pre-processed files for this session** points to **Scans** (207 files).
- Event onsets and duration** points to **Multiple conditions** (...\\TNT1\\s01_run1_onsets.mat).
- Movement parameters** points to **High-pass filter** (128).
- Slow signal drifts with a period longer than 128 s will be removed. It is a way to remove possible confounds.** points to **High-pass filter** (128).
- Accounting for serial correlations in fMRI time series due to aliased biorhythms and unmodelled neuronal activity. Accounts for non-independency in the BOLD response.** points to **Serial correlations** (AR(1)).

Parameter values:

- Directory: ...\\FirstLevel\\stats\\model01\\s01
- Timing parameters
 - Units for design: Seconds
 - Inter-scan interval: 2 (labeled **TR**)
 - Microtime resolution: 31
 - Microtime onset: 15
- Data & Design
 - Subject/Session
 - Scans: 207 files
 - Conditions
 - Multiple conditions: ...\\TNT1\\s01_run1_onsets.mat
 - Regressors
 - Multiple regressors: ...\\1_006_TNT1_pace_0001.txt
 - High-pass filter: 128
 - Subject/Session
 - Scans: 204 files
 - Conditions
 - Multiple conditions: ...\\TNT2\\s01_run2_onsets.mat
 - Regressors
 - Multiple regressors: ...\\1_008_TNT2_pace_0001.txt
 - High-pass filter: 128
- Factorial design
- Basis Functions
 - Canonical HRF
 - Model derivatives: No derivatives
- Model Interactions (Volterra): Do not model Interactions
- Global normalisation: None
- Masking threshold: 0.8
- Explicit mask
- Serial correlations: AR(1)

First-level analysis: design matrix and contrasts

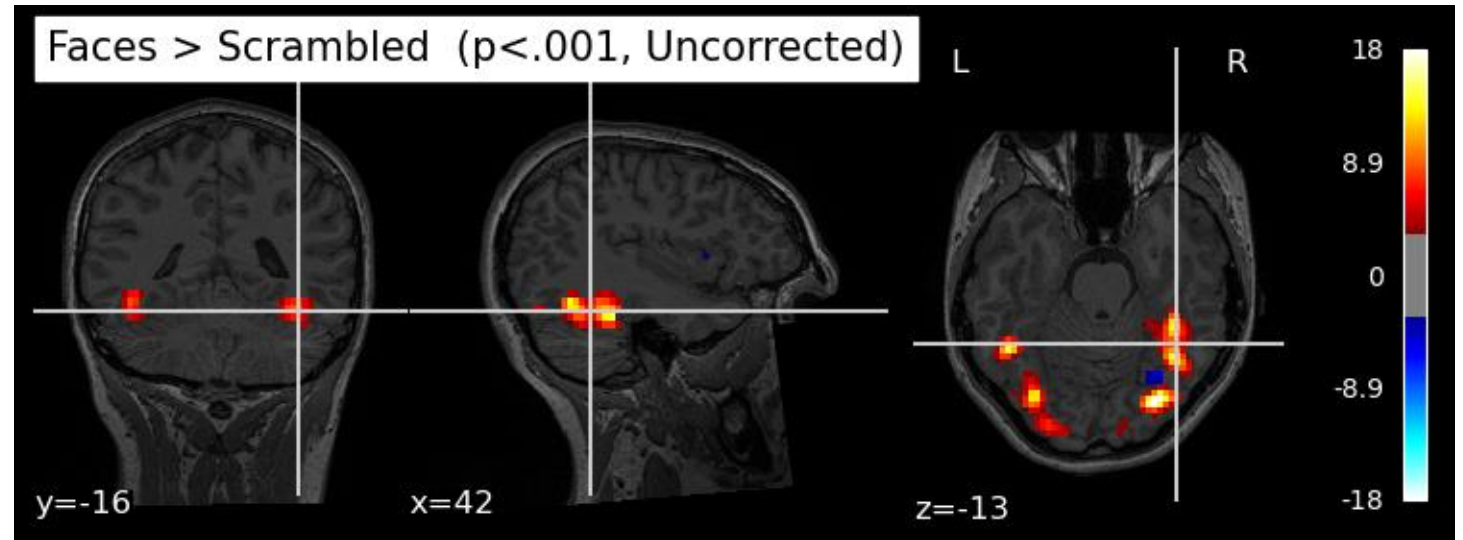
Design matrix for run 1



```
contrasts = {'Famous_Unfamiliar': pad_vector([1, 0, 0, -1], n_columns),
            'Unfamiliar_Famous': pad_vector([-1, 0, 0, 1], n_columns),
            'Faces_Scrambled': pad_vector([1, 0, -2, 1], n_columns),
            'Scrambled_Faces': pad_vector([-1, 0, 2, -1], n_columns),
            'EffectsOfInterest': np.eye(n_columns)[[0,2,3]]}
```

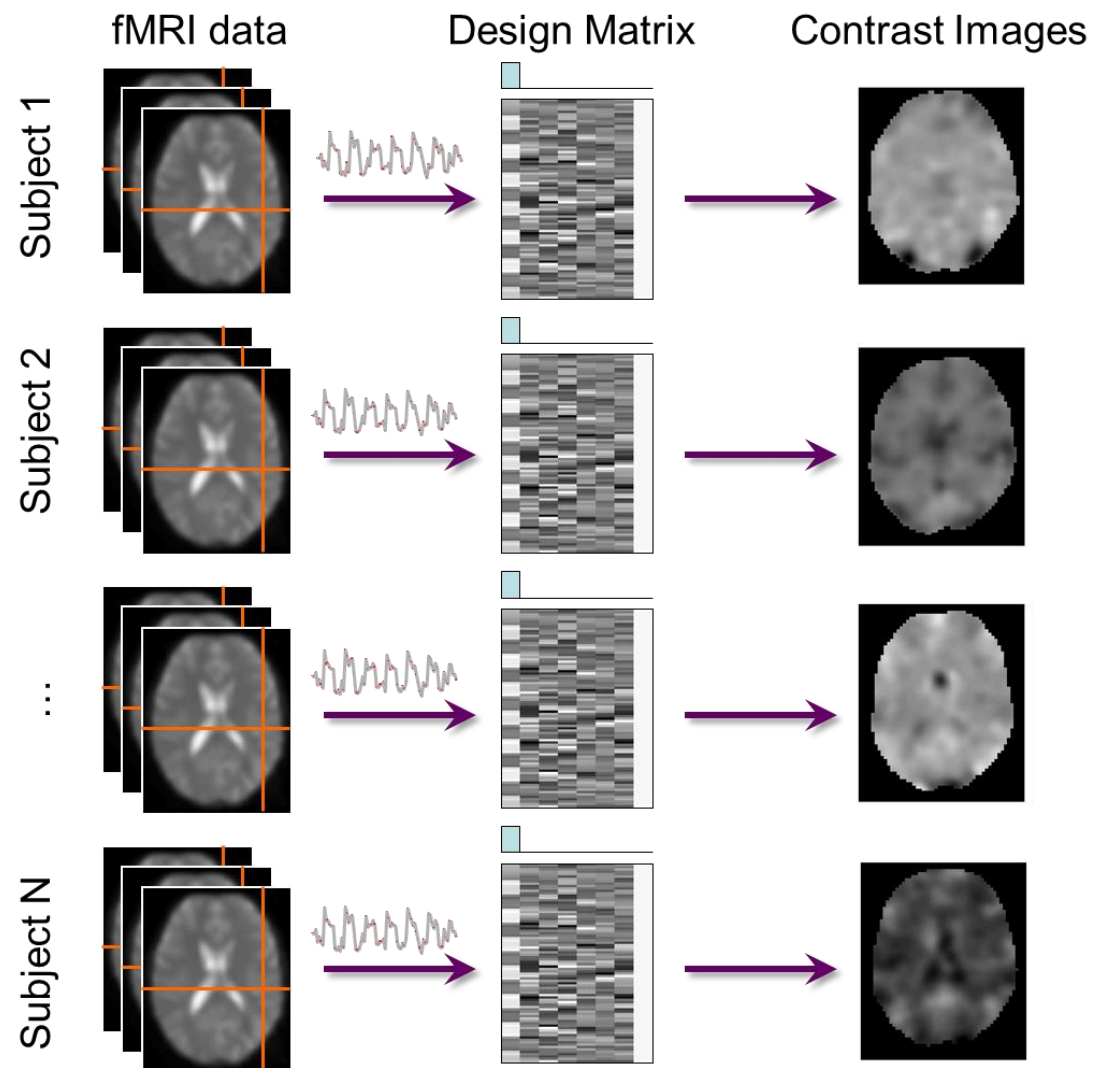
Faces > Scrambled

Statistical brain map (z-map)
of regions showing significant
positive difference between
Faces and **Scrambled**



First-level analysis

- Run the GLM for each subject



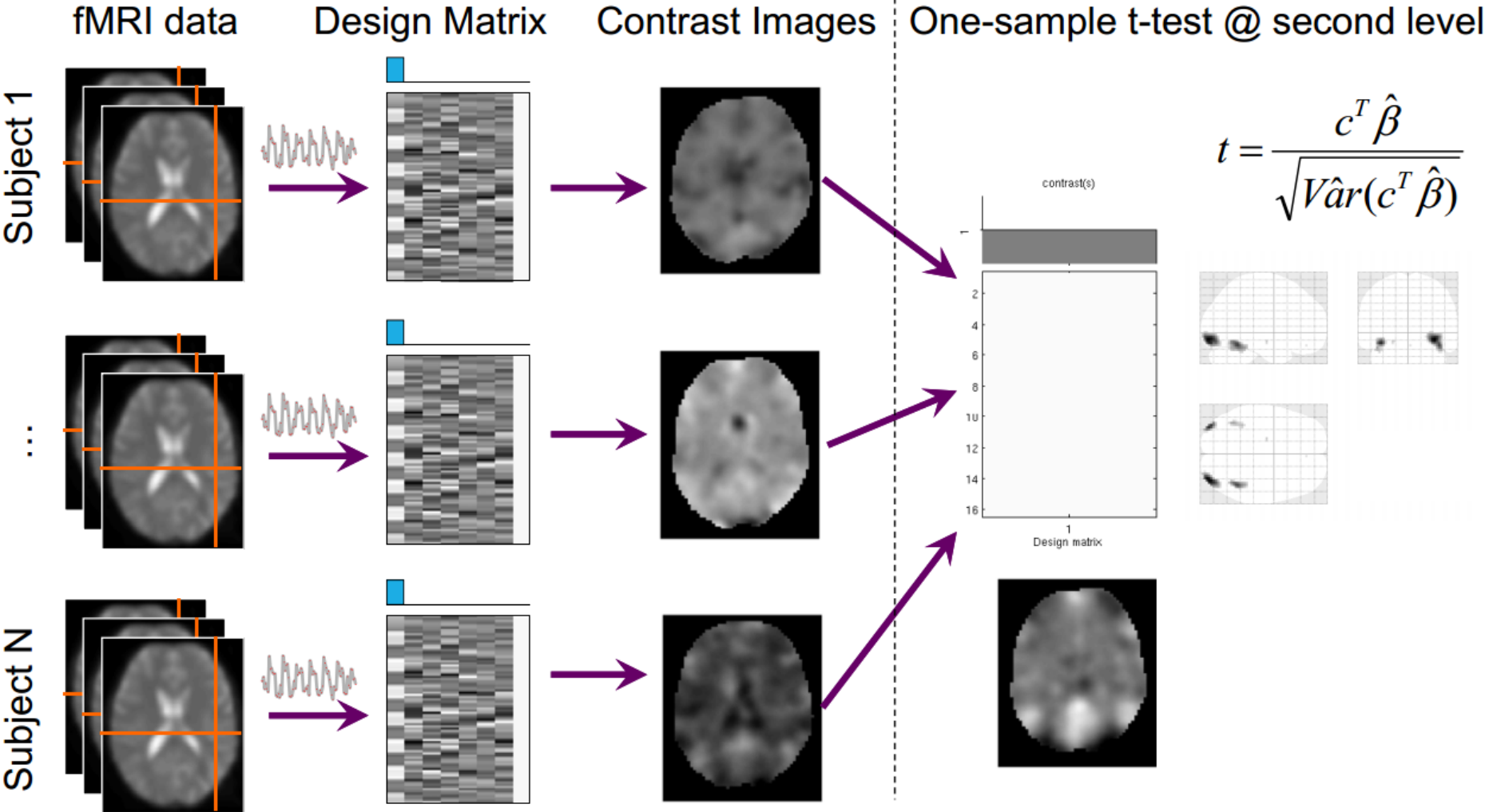
Group level (2nd level) analysis is across subjects

- Which voxels are showing a significant activation differences between our conditions consistently **within a group**
 - Average contrast effect across sample (e.g., one-sample t-test)
- Importantly, all subject brains need to be in common space, e.g. MNI, to perform voxel-wise group analyses
 - That was achieved by the **Normalisation step** in pre-processing

Summary statistics, Random effects approach

First level

Second level



$$t = \frac{c^T \hat{\beta}}{\sqrt{V\hat{ar}(c^T \hat{\beta})}}$$

It is still a GLM model, and we get group level beta estimates!

$$Y_{\text{group}} = X_{\text{group}} \beta_{\text{group}} + \epsilon_{\text{group}}$$

Stats tests at the 2nd level

- Condense where possible
 - If a factor can be collapsed through a contrast at the 1st level, do so and use the simplest possible 2nd level model
 - T-tests at the 2nd level are preferred
 - Avoids need to estimate non-sphericity to account for within-subject correlations across repeated measures
 - Generally more accurate estimation of error
- However, if more than 2 factors or levels exist, a single t-contrast cannot capture the main effects and interactions
 - 2nd level ANOVA will be necessary

Stats tests at the 2nd level

SPM RECIPE		
Design	1 st Level	2 nd Level
1 group, 1 factor, 2 levels	A1 – A2	One-sample t-test
1 group, 1 factor, 2+ levels	A1, A2, ..., A _n	One-way ANOVA (within-subjects)
1 group, 2 factors, 2 levels each	(A1B1+A1B2)-(A2B1+A2B2): ME A (A1B1+A2B1)-(A1B2+A2B2): ME B (A1B1+A2B2)-(A1B2+A2B1): A x B	One-sample t-tests
1 group, 2+ factors/2+ levels	Multiple contrasts for each ME and interaction	One-way ANOVA
2 groups, 1 factor, 2 levels	A1 – A2	Two-sample t-test
2 groups, 1 factors, 2+ levels	A1, A2, ..., A _n	Two-way ANOVA (mixed)
2 groups, 2 factors, 2 levels each	(A1B1+A1B2)-(A2B1+A2B2): ME A (A1B1+A2B1)-(A1B2+A2B2): ME B (A1B1+A2B2)-(A1B2+A2B1): A x B	Two-sample t-tests
2 groups, 2+ factors/2+ levels	Multiple contrasts for each ME and interaction	Two-way ANOVA

Hypothesis

Design an experiment



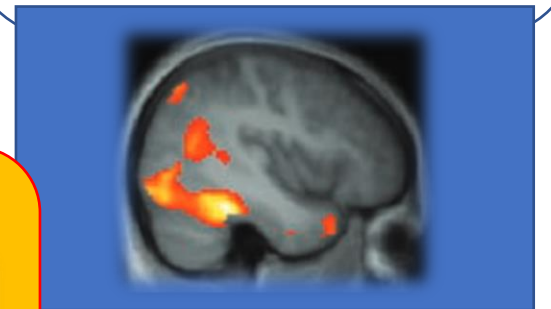
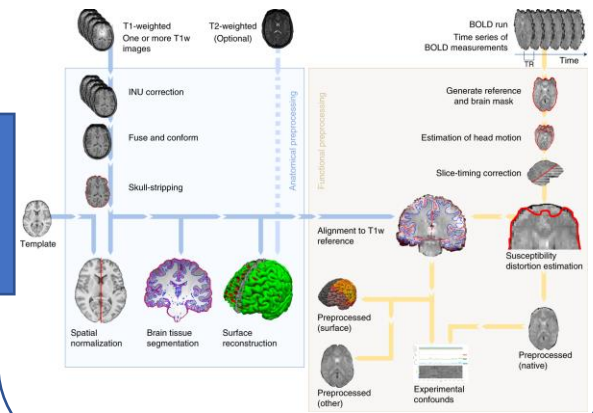
Stimuli
Timing

Collect the data



Anatomical image
Functional images
Event details

Pre-process & Analyse



The final push





Environment



Data Organise & Manage



Pre-process



Analyse

Report

Sharing & Reporting



- Share your **code** and notebooks on GitHub



- Make it **citable** with Zenodo
 - <https://docs.github.com/en/repositories/archiving-a-github-repository/referencing-and-citing-content>



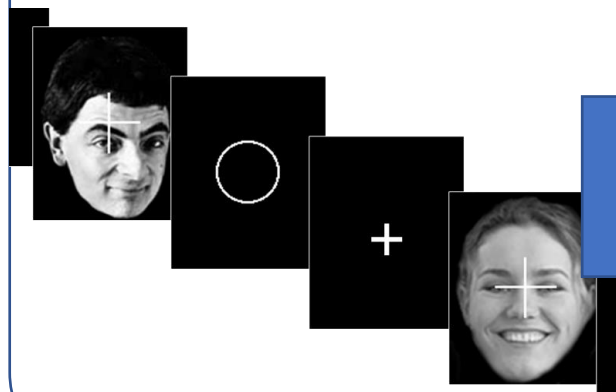
- If you have consent from participants, share the **BIDS data** on OpenNeuro. Before sharing, 'deface' the T1w images



- Add your **contrast maps** to NeuroVault

Famous vs Unfamiliar
faces are processed
differently in the brain

Design an experiment



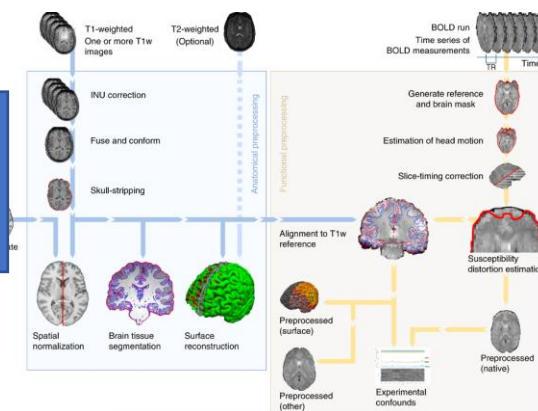
Stimuli
Timing

Collect the MRI data

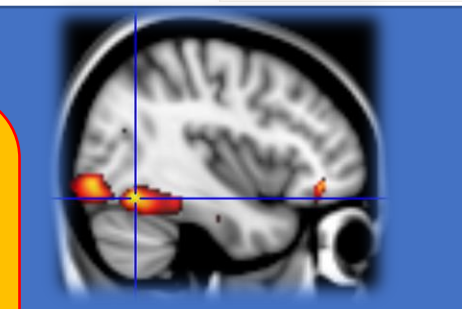


Anatomical image
Functional images
Event details

Pre-process & Analyse



The final push





Statistical analysis with Nilearn

https://github.com/dcdace/fMRI_training



Hands-On_03_Subject-Level-Analysis.ipynb

Hands-On_04_Group-Level-Analysis.ipynb