`TrapFit` background
Jurriaan Barkeij Wolf
updated October 25, 2016

1 Rationale

Many brain pathologies manifest with some degree of vascular dysfunction. Blood-oxygen-level dependent (BOLD) functional magnetic resonance imaging (fMRI) is frequently used to investigate the brain's haemodynamic response to stimuli. `TrapFit` allows an investigator to derive several parameters relevant to vascular physiology from block-design stimulus experiments. It works by generating a crude, trapezoid-shaped approximation of the haemodynamic response function from a BOLD timeseries so that the time-to-peak, time-to-baseline and amplitude of the response can be calculated. It is based primarily on the method described by Dumas et al.[1], with some modifications. Many of the methodological considerations discussed in that paper are also applicable for this method. If you want to cite this method, please consider citing the Dumas paper but be sure to consider the differences between the approaches.

2 Procedure

Take the average BOLD time series of your region of interest. The data used for this example were acquired during a block design visual stimulus experiment ($ArArAr$), but the approach can in principle also be used for different block designs. These data were already preprocessed using the *FEAT*-tool from the *FSL[2].*

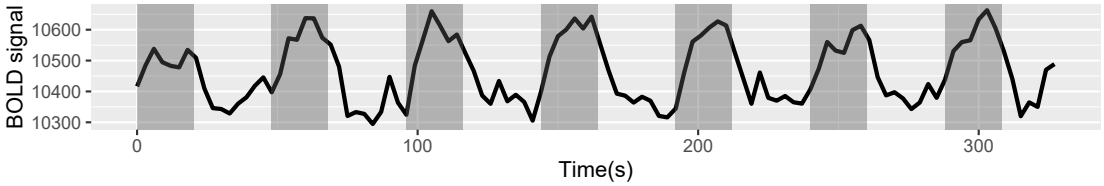


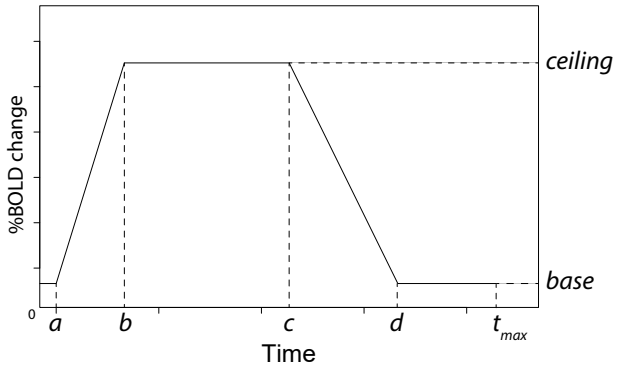
Figure 1: The shaded area denotes a stimulus 'on' period.

Stepwise:

1. Cut up the timeseries into blocks (block = stimulus + rest)
2. Optional: discard blocks with a Coefficient of Variation above a specified threshold (outliers).
3. Transform the data into %BOLD change by using the mean value of the entire timeseries (of *of all non-outlier blocks).*
4. Add the smallest %BOLD change value of the entire timeseries to effectively raise the data above zero for more convenient analysis.
5. Calculate the mean timeseries by taking the mean %BOLD change value of all blocks at each timepoint. The mean timeseries is only used to simplify visual evaluation of fit quality.
6. Calculate appropriate starting values for the trapezoid curve fitting procedure.
7. Fit the trapezoid curve to the data by minimizing the least-squares criterion.
8. Calculate physiologically relevant parameters from the fit values.

Curve fitting procedure:

The trapezoid function:



$$f(t,\theta) = \begin{cases} base & \text{if } 0 \leq t < a \\ base + (1 - \frac{b-t}{b-a})(ceiling - base) & \text{if } a \leq t < b \\ ceiling & \text{if } b \leq t < c \\ base + (\frac{d-t}{d-c})(ceiling - base) & \text{if } c \leq t \leq d \\ base & \text{if } t > d \end{cases} \tag{1}$$

Where:

$$\theta = \big[a, b, c, d, base, ceiling\big]$$

Subject tot the following linear constraints:

$$0 \geq a < b < c < d < t_{max}$$

To find the optimal values for θ, the residual Sum-of-Squares criterion is minimized. As this is a nonlinear problem, the Broyden–Fletcher–Goldfarb–Shanno (BFGS) method, an iterative numerical algorithm, is used. The %BOLD change data vector of size n is denoted by y.

$$RSS_f(\theta) = \sum_{i=1}^{n} (y_i - f(t_i, \theta))^2 \tag{2}$$

The gradient of $RSS_f(\theta)$ is approximated using the central difference formula for use with the BFGS algorithm.

$$RSS'_f(\theta) \approx \frac{RSS_f(\theta + h) - RSS_f(\theta - h)}{2h} \tag{3}$$

Where h is the smallest floating point number that the system can handle.

Extract Physiological Parameters

When the optimal value for θ is found, the time-to-peak (TTP), time-to-baseline (TTB), and amplitude can be calculated as follows:

$$TTP = b - a$$
$$TTB = d - c$$
$$Amplitude = ceiling - base$$

Implementation Details

The curve fitting procedure is performed using the BFGS algorithm implemented in the *R*-function `constrOptim`. The constraints are passed to this function such that the feasible region is defined by:

$$\begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 \end{bmatrix} \times \begin{bmatrix} a \\ b \\ c \\ d \\ base \\ ceiling \end{bmatrix} - \begin{bmatrix} 0 \\ 0.1 \\ 0.1 \\ 0.1 \\ -t_{max} \end{bmatrix} >= 0$$

Note that a distance of 0.1 seconds is enforced between each of the breakpoints a,b,c,d to ensure none of them overlap.

3 Example Results

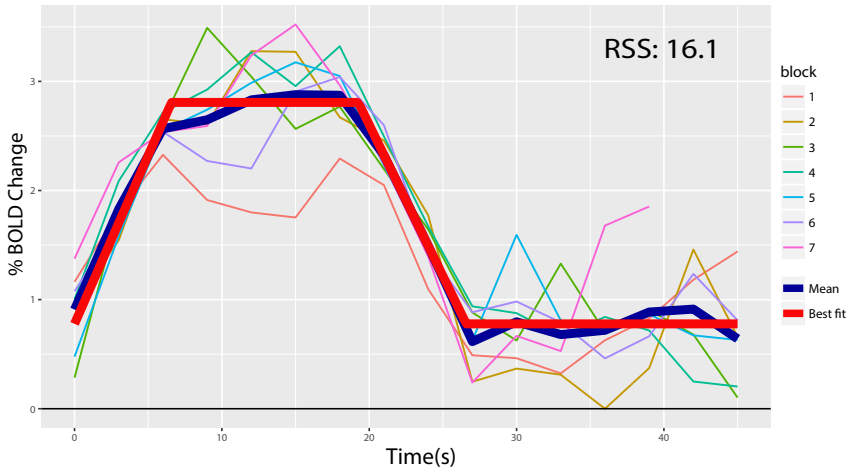


Figure 2: An example of a successful fit.

	a	b	c	d	baseline	ceiling	RSS	$TTB_{(s)}$	$TTP_{(s)}$	amplitude
subj1	0.16	2.03	9.73	30.24	1.04	2.30	28.96	20.50	1.88	1.26
subj2	0.63	5.87	25.55	30.69	0.50	0.90	6.54	5.14	5.24	0.39
subj3	1.58	2.72	21.79	26.74	2.01	2.81	67.96	4.95	1.14	0.80
subj4	0.00	6.35	17.57	32.25	1.01	2.57	18.53	14.68	6.35	1.56
subj5	5.23	14.79	22.70	42.88	0.59	1.33	9.07	20.18	9.56	0.74
subj6	0.00	6.58	19.26	26.58	0.78	2.81	16.56	7.32	6.58	2.03

Example output data. The baseline, ceiling and amplitude parameters are in units of %BOLD change. TTB: time-to-baseline, TTP: time-to-peak.

References

[1] Andrew Dumas, Gregory A Dierksen, M Edip Gurol, Amy Halpin, Sergi Martinez-Ramirez, Kristin Schwab, Jonathan Rosand, Anand Viswanathan, David H Salat, Jonathan R Polimeni, et al. Functional magnetic resonance imaging detection of vascular reactivity in cerebral amyloid angiopathy. *Annals of neurology*, 72(1):76–81, 2012.

[2] Mark Jenkinson, Christian F Beckmann, Timothy EJ Behrens, Mark W Woolrich, and Stephen M Smith. Fsl. *Neuroimage*, 62(2):782–790, 2012.