Modeling the Hemodynamic Response Function using Inverse Logit Functions

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INTRODUCTION

Linear and nonlinear statistical models of fMRI data simultaneously incorporate information about the shape, timing, and magnitude of task-evoked hemodynamic responses. Most brain research to date has focused on the magnitude of evoked activation, however, there is increasing interest in measuring onset and peak latency and duration of evoked fMRI responses.

In this work, we focus on the estimation of response height (H), time-to-peak (T), and full-width at half-max (W) as potential measures of response magnitude, latency, and duration. Although there are many ways to estimate such parameters, we suggest three criteria for optimal estimation:

(i) the relationship between parameter estimates and neural activity must be as transparent as possible,

(ii) parameter estimates should be independent of one another, so that true differences in one parameter are not confused for apparent differences in other parameters,and

(iii) statistical power should be maximized.

In this work, we introduce a new modeling technique designed to achieve these criteria. In simulations based on real fMRI data, we compare this technique, which is based on the superposition of three inverse logit functions (IL), with several other popular methods.

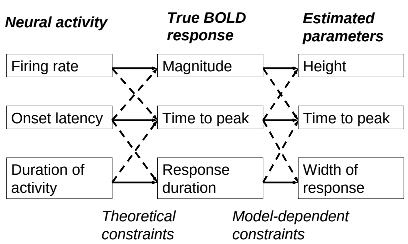


Figure 1: Relationship between neural activity, evoked changes in the BOLD response, and estimated parameters. Solid lines indicate expected relationships, and dashed lines indicate relationships that, if they exist, create problems in interpreting estimated parameters. For task-induced changes in estimated time-to-peak to be interpretable in terms of the latency of neural firing, for example, estimated time-to-peak must vary only as a function of changes in neural firing onsets, not firing rate or duration. The relationship between neural activity and true BOLD responses determines the *theoretical* limits on how interpretable the parameter estimates are. The relationship between true BOLD changes and estimated BOLD changes using a model introduce additional model-dependent constraints on the interpretability of parameter estimates.

METHODS

In this section we introduce a method for modeling the hemodynamic response function (HRF), based on the superposition of 3 inverse logit (IL) functions, and compare it with four other popular techniques — a non-linear fit on two gamma functions (NL), the canonical HRF + temporal derivative (TD), a finite impulse response basis set (FIR), and the canonical SPM HRF (Gam) — in simulations based on empirical fMRI data.

The Inverse Logit Model

The inverse logit function is defined as,

$$L(x) = \left(1 + e^{-x}\right)^{-1}$$

It is an increasing function of x, which takes the values 0 and 1 in the limits. In addition $L(0)=0.5$. (See Fig. 1a. For an example)

To derive a model for the HRF we use a superposition of three separate inverse logit functions. The first describes the rise following activation, the second the subsequent decrease and undershoot, while the third describes the stabilization of the HRF. Our model can therefore be written in the following form:

$$h(t\,|\,\theta) = \delta_1 L\big((t-T_1)/D_1\big) + \delta_2 L\big((t-T_2)/D_2\big) + \delta_3 L\big((t-T_3)/D_3\big)$$

In this particular model *h* will be based on nine variable parameters:

$$\theta = (\delta_1, T_1, D_1, \delta_2, T_2, D_2, \delta_3, T_3, D_3)$$

The δ parameters control the direction and amplitude of the curve, the *T* parameter shift the center of the function and the *D* parameters control the angle of the slope. In our implementation we constrain *h* to be zero at $t=0$ and T_{max}. By applying these two constraints we obtain a model with 7 variable parameters.

In applying this method to actual data, we seek to find the parameters which minimize the sum of squared deviations between the model and the data. Fig. 2a–c shows an example of how varying the parameters can control the shape of the function. By superimposing these three curves we obtain the function depicted in Fig. 2d, which shows an example of an IL fit (solid line) to an empirical HRF (dashed line). Note that this function efficiently captures the major details typically present in the HR function.

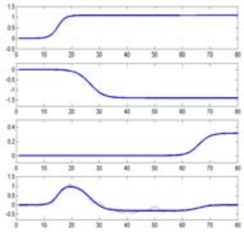
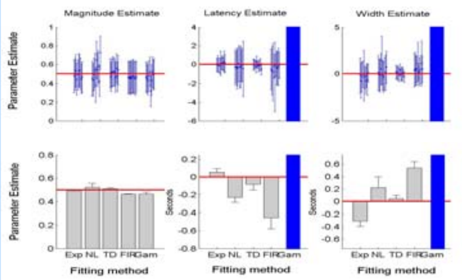


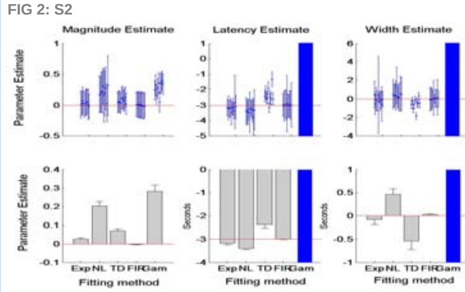
Figure 2. The functions $\delta L(A(T-t))$ with parameters: (A) δ=1.0, T=15 and A=0.75, (B) δ=-1.3, T=27 and A=0.4 and (C) δ=0.3, T=66 and A=0.5. (D) The three functions in (A)-(C) superimposed (bold line) together with actual HRF function (Dotted line).

FIG 1: S1



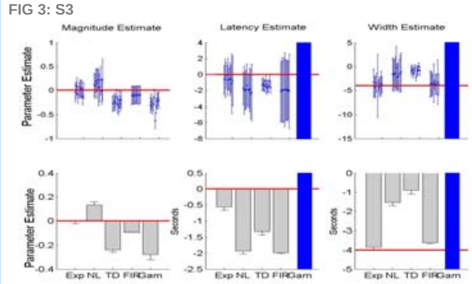
	H	L	W	H	L	W
IL	0.9993	4.7281	5.1812	0.5068	4.6722	5.4882
NL	0.9461	4.9180	4.5268	0.4229	5.1465	4.3002
TD	0.9952	4.8641	4.5236	0.4859	4.9456	4.4780
FIR	1.0116	5.0860	4.9078	0.5479	5.5385	4.3674
Gam	0.9401	5.5000	5.5000	0.4776	5.5000	5.5000
True	**1.0000**	**5.0000**	**5.0000**	**0.5000**	**5.0000**	**5.0000**

FIG 2: S2



	H	L	W	H	L	W
IL	1.0019	4.6831	5.2412	0.9776	7.8682	5.3251
NL	0.9723	4.6631	4.4406	0.7706	8.0635	3.9813
TD	0.9700	4.8016	4.4446	0.9003	7.1894	4.9835
FIR	1.0114	5.0756	4.9192	1.0142	8.0786	4.8996
Gam	0.9887	5.5000	5.5000	0.7074	5.5000	5.5000
True	**1.0000**	**5.0000**	**5.0000**	**1.0000**	**8.0000**	**5.0000**

FIG 3: S3



	H	L	W	H	L	W
IL	1.0069	4.7005	5.1059	1.0104	5.2568	8.9666
NL	0.9476	4.6632	4.5472	0.8157	6.5994	6.0840
TD	1.0016	4.7811	4.4341	1.2410	6.1079	5.3303
FIR	1.0092	5.0823	4.9243	1.1023	7.0621	8.5430
Gam	0.9786	5.5000	5.5000	1.2573	5.5000	5.5000
True	**1.0000**	**5.0000**	**5.0000**	**0.5000**	**5.0000**	**9.0000**

Figures 3-5. Results of simulations (S1)-(S3). Top panels: the true effects are shown by horizontal lines (red), and means and error bars for each of the 10 "participants" are shown by vertical lines. Bottom panels: the between subject means and standard errors are shown. The tables under each figure show the average height (H), latency (L) and width (W) for HRF A and B (left and right columns respectively) over all "participants" and repetitions for each of the five models together with the true values.

Simulation Study

The simulations are based on actual HRFs, obtained from a visual-motor task, measured on a group of 10 participants. We began by constructing stimulus functions for 6-minute runs of randomly intermixed event types (A & B), occurring at random intervals of length 2-18 seconds. Assuming a linear time invariant system, the stimulus functions were convolved with the empirically derived HRFs, and AR(1) noise was added to the resulting time course. The HRFs for A and B were modified prior to creating the time course in order to create three kinds of "true" effects an A – B amplitude difference, time-to-peak difference, and duration difference. In total we ran 3 types of simulations:

(S1) The HRF corresponding to event B has half of the amplitude of the HRF corresponding to event A.

(S2) The HRF corresponding to event B has a 3 s delay in rise time compared to HRF A.

(S3) The width of HRF B is increased by 4 s compared to HRF A.

Each of these three simulations were performed using the HRF corresponding to each of the 10 participants as HRF A. For each participant the process was repeated 1000 times using different simulated AR(1) noise in each repetition. For each simulation type and subject we estimated the difference in amplitude between HRF A and B, the time-to-peak difference, and the duration difference for each of the 1000 repetitions in order to test the efficiency and robustness of the model fits. We tested the ability of each type of model to recover these "true" effects, and the tendency of each method to confuse one effect (e.g., time-to-peak) with another (e.g., magnitude).

RESULTS

In Figs 3-5 the results are shown for the three simulation types. In the top panel of each figure, the true effects are shown by horizontal lines, and means and error bars for each of the 10 "participants" are shown by the vertical lines. In the bottom panels the between subject means and standard errors are shown. Tables 1-3 show the average magnitude (M), latency (L) and width (W) over the "participants" and repetitions for each of the five models and for comparison purposes the true values. Figure 6 shows a typical fit for each model and each simulation type. The IL model achieves the best overall balance between parameter interpretability and power. The FIR model was the next best choice, with gains in power at some cost to parameter independence.

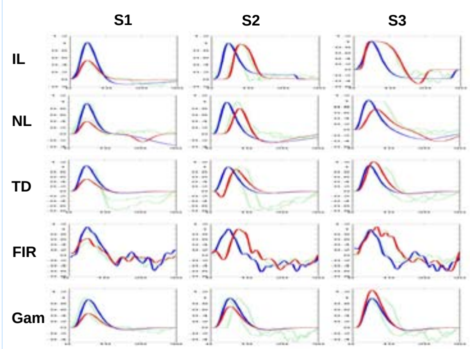


Figure 6: Typical fits for IL, NL, TD, FIR and Gam (Rows 1-5 respectively) for simulations S1, S2 and S3 (Columns 1-3 respectively). The actual HRF are shown in green.

DISCUSSION

In this work, we introduce a new technique for modeling the HRF, based on the superposition of three inverse logit functions (IL). In simulations based on actual HRFs measured in a group of 10 participants, we compare the performance of this model to four other popular choices of basis functions. We show that the IL model can capture magnitude, delay, and duration of activation with less error than the other methods tested, and provides a promising way to flexibly but powerfully test the magnitude and timing of activation across experimental conditions.

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