# A Model for the Muscle Functional MRI Signal Intensity Time Course

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## Introduction

Muscle functional MRI (mfMRI) reflects the metabolic and hemodynamic responses of muscles to exercise (1-3). While it would be useful to understand the independent contribution of each variable, it is difficult to manipulate them in isolation *in vivo*. In this study we used a computer model of neuromuscular function to study how metabolic and hemodynamic variables influence the mfMRI signal intensity (SI) time course.

## Methods

*Neuromuscular Model* A 2 min isometric contraction of the anterior tibialis (AT) was modeled using a 150×150 matrix of muscle fibers organized into 56 motor units. The fiber type composition was 70% slow oxidative (SO), 25% fast oxidative glycolytic (FOG) and 5% fast glycolytic (FG) (4). Motor units were recruited and their discharge frequency increased until a specified percentage of maximum voluntary contraction (MVC) was achieved. Intensity-dependent and fiber type-specific responses were modeled in the intracellular (lactate and $P_i$ accumulation, volume increase, pH decrease); interstitial (lactate accumulation, volume increase); and vascular (capillary recruitment, oxygen extraction) spaces. The time courses were modeled using appropriate assumptions about the time to onset and time constants for each event (5, 6).

*Calculation of NMR Responses* In each tissue compartment, initial values were assumed for the rates of longitudinal ($1/T_1$) and transverse ($1/T_2$) relaxation. During exercise, $1/T_1$ was assumed not to change in any compartment. In the intracellular and interstitial spaces, $1/T_2$ changes were assumed to depend linearly on volume and pH changes (1-3). In the vasculature, $1/T_2$ changes were calculated using published relationships between it and the fractional oxyhemoglobin saturation ($Y$; 7). SI was calculated for single-slice, spin-echo, echo-planar images (TR/TE=4000/35 ms).

*Experimental Trials* The modeled mfMRI SI time course was compared to published mfMRI data obtained using sustained isometric dorsiflexion performed at 40% MVC (8). To test the effect of metabolic responses on the mfMRI time course, the percentage of SO fibers was changed from 70% (control) to 25% and 95%; the percentage of FG fibers was always 5%. To test the influence of blood oxygenation level dependent (BOLD) contrast, the final values for $Y$ were varied from 0.45 (control) to 0.60 and 0.30. In all cases, six fully independent and randomized model trials were performed; mean and standard deviation were calculated.

## Results and Discussion

Figure 1A shows the modeled (solid line) and experimental (circles) mfMRI time courses for isometric dorsiflexion performed at 40% MVC. The corresponding residual errors are shown in Figure 1B.

Figure 1C shows the predicted effect of muscle fiber type (and therefore the extent of anaerobic metabolism) on the mfMRI SI time course; these results are consistent with the conclusions of Prior et al (1) and imply that the effect of anaerobic metabolism on the mfMRI time course is greatest at long exercise durations. Figure 1D shows the effect of blood oxygenation on the mfMRI SI; the greatest relative effect occurs during the early portion of the time course.

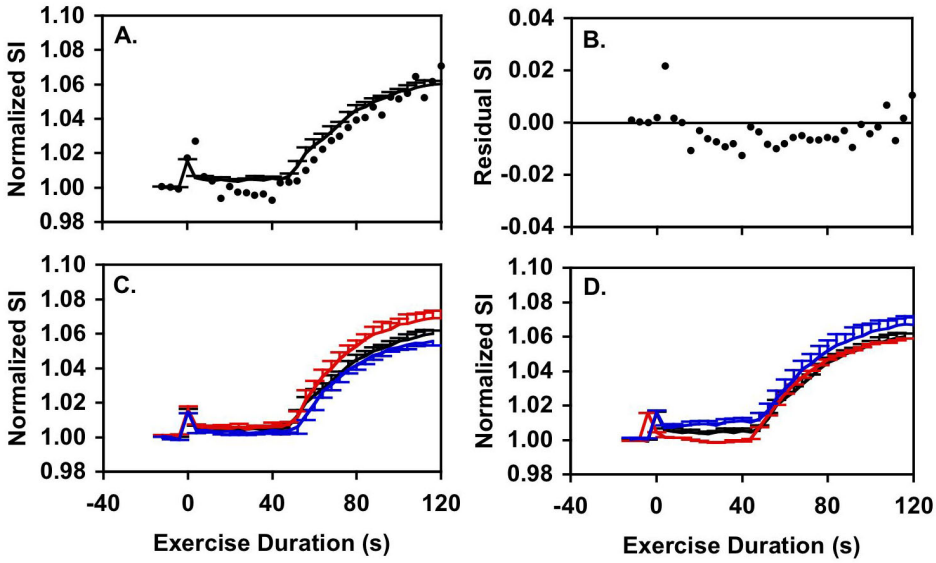


**Figure 1.** *Panel A:* Modeled (solid line) and experimental (points) mfMRI time series. *Panel B*: Residual plot of the data in panel A. *Panel C*: Effects of high (blue), control (black), and low (red) SO fiber percentage on the mfMRI time series. *Panel D:* Effects of decreased (blue), control (black), and increased (red) oxygen extraction on the mfMRI time series. Mean and SD are shown for all data.

## Conclusions

We used a computer model to examine time-dependent contributions of metabolic and hemodynamic processes to the mfMRI time series. Oxygen extraction has the greatest relative impact on the mfMRI signal at short exercise durations, while anaerobic metabolic responses are most important at long exercise durations. The observation that the largest residual errors occurred at short and intermediate exercise durations indicates the need for an improved understanding of how BOLD contrast contributes to the mfMRI time course.

## References

1. Prior BM et al. *J Appl Physiol* 2001;90:615-23.
2. Meyer RA, et al. *NMR Biomed* 2001;14;199-203.
3. Damon BM, et al. *Magn Reson Med* 2002;47;14-23.
4. Johnson MA, et al. *J Neurol Sci*. 1973;18:111-29.
5. Conley KE, et al. *Am J Physiol* 1997;273:C306-15.
6. Hicks A, et al. *Can J Appl Physiol* 1999;24:216-30.
7. Spees WM, et al. *Magn Reson Med* 2001;45:533-42.
8. Damon, BM, et al. *J Appl Physiol* 2003;95;1287-1296.