Modeling the Temporal Dynamics of the Positive and Negative BOLD Response

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Introduction
It has been shown that the positive and negative transient blood oxygenation level dependent (BOLD) responses exhibit significantly different temporal dynamics [1]. As compared to the positive BOLD responses, the negative BOLD responses exhibited greater faster rise times, increased peak amplitudes, and a less pronounced post-stimulus undershoot [1]. Previous studies suggested that the differences were possibly associated to various nonlinear hemodynamic factors [1][2]. In this work, we examine the dynamics of the positive and negative BOLD responses using an arteriolar compliance model of the cerebral blood flow response (CBF) [3] coupled with a Balloon model of the venous compartment [4]. The model simulations suggest that the observed differences may be a result of the varying contribution of smooth muscle compliance during increases and decreases of neural activity.

Theory
In the arteriolar compliance model of the CBF response to neural stimulus [3], a neurally driven vasoactive agent modulates the arteriolar muscle compliance, which is proportional to muscle tone. Changes in total arteriolar compliance then lead to changes in vessel radius and CBF. The total stress is modeled as the combination of the stress in the active component representing smooth muscle and a passive component representing connective tissue and is represented in figure 1a. This results in the depicted nonlinear relation between radius and smooth muscle compliance in figure 1b. The effective gain, represented as the rate of change of radius with respect to the rate of change of muscle compliance, is shown in figure 1c). During negative stimuli, the gain increases over the course of deactivation whereas it is continually decreasing during positive activation. Based on the relationship between effective gain and normalized radius presented in figure 1c), the expected response to a negative stimulus would be larger than the response to a positive stimulus of equal amplitude.

Methods
Simulations were performed using an arteriolar compliance model coupled with the Balloon model with viscoelastic effects and the nominal parameters described in [3]. The input to the model was a 3 second stimulus similar to that in [1], representing a term proportional to the change in neural activity. The stimulus in [1] consisted of 25% visual contrast for 60 seconds followed by 3 second contrasts that were either two octaves above (positive) or below (negative). The expected neural input was assumed identical for both the positive and negative stimuli but with an inverted sign.

Results and Discussion
Figure 2 shows the simulated positive response and the negative response (inverted for comparison). The results show good qualitative agreement with the reported dynamics of [1], displayed as an insert in figure 2. The negative response has a faster rise time, narrower width, and a faster resolving post stimulus undershoot. The longer initial delay of the negative response is a result of the differing viscoelastic time constants for inflation and deflation[3][5]. Our simulations demonstrate that the reported difference between positive and negative BOLD may be explained by the varying contribution of the smooth muscle compliance during increasing and decreasing neural activity.

References