Fractional Dynamical Model for Neurovascular Coupling

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Abstract— **The neurovascular coupling is a key mechanism linking the neural activity to the hemodynamic behavior. Modeling of this coupling is very important to understand the brain function but it is at the same time very complex due to the complexity of the involved phenomena. Many studies have reported a time delay between the neural activity and the cerebral blood flow, which has been described by adding a delay parameter in some of the existing models. An alternative approach is proposed in this paper, where a fractional system is used to model the neurovascular coupling. Thanks to its non-local property, a fractional derivative is suitable for modeling the phenomena with delay. The proposed model is coupled with the first version of the well-known balloon model, which relates the cerebral blood flow to the Blood Oxygen Level Dependent (BOLD) signal measured using functional Magnetic Resonance Imaging (fMRI). Through some numerical simulations, the properties of the fractional model are explained and some preliminary comparisons to a real BOLD data set are provided.**

I. INTRODUCTION

Over the past two decades, advances in neuroimaging have contributed to significant progress in neuroscience and have improved diagnosis and treatment of several neurological diseases. For example, functional magnetic resonance imaging (fMRI) has evolved as a technique for mapping brain activation and has attracted widespread interest in basic and clinical research and patient care. The fMRI technique works by detecting associated changes in blood flow and deoxyhemoglobin concentration in response to neural activity. It is a highly successful tool which does not involve radiation and is reproducible with good spatial resolution. Despite the efforts that have been devoted to understand the chain from neural activity to the measured fMRI signal, namely the Blood Oxygen Level Dependent (BOLD) signal, the physiological relationship is yet unclear and not fully explained.

Several linear and nonlinear models have been proposed to relate neural activity, BOLD signal, hemodynamic variables (Cerebral Blood Flow "CBF", Cerebral Blood Volume "CBV"), the concentration of deoxyhemoglobin, oxygen metabolism and glucose metabolism [1], [2], [3], [4]. The balloon model proposed by Buxton *et al.*, and its variants introduced by Friston *et al.* [2] belong to the nonlinear physiological models category. The initial version of the balloon model [1] gives the relation between the dynamics of CBV, deoxyhemoglobin content and BOLD signal, with the CBF considered as an input. In [2], Friston *et al.* related the CBF to the neural activity using a second order differential equation. The balloon model and its variants have been proposed to interpret the BOLD signal. However, recent studies have outlined the limitations of these models in the interpretation of the BOLD [6], suggesting the involvement of additional factors in the model. In this paper, we will focus on improving the neurovascular coupling model by introducing the fractional derivatives, suitable to handle delays.

A fractional derivative (FD) is a generalization of the traditional derivative to non-integer order. The interest in FD has grown considerably and it is now used in many fields of engineering and science [7], [8]. Due to its non-locality and memory properties, FD is a powerful tool for modeling physical phenomena involving memory effect. Many researchers have been interested in modeling and analyzing biomedical and biological systems using fractional calculus. For instance, Magin [9] showed that fractional calculus can be an interesting tool to model complex dynamics in bioengineering because it can provide a much better understanding of the dynamic processes that occur in biological tissues. In [10], it has been shown that fractional differentiation provides single neurons with a fundamental and general computation which can contribute to efficient information processing and stimulus anticipation. In addition, a fractional model was proposed to describe anomalous nuclear magnetic resonance (NMR) relaxation phenomenon [11].

This paper is organized as follows. Section II recalls some definitions of FD. Section III describes the main features of the BOLD signal. In section IV, a fractional model is provided for the neurovascular coupling. In section V, the performance of the FD balloon model is compared to the standard balloon model and also to a real event related data set. Section VI concludes the paper and outlines the future work.

II. PRELIMINARY

In this study, Grunwald-Letnikov (GL) definition [12] is used in the calculation of FD. The fractional derivative of a function f is given by

$$D_t^q f(t) = \lim_{h \to 0} \frac{1}{h^q} \sum_{i=0}^{\infty} c_i^{(q)} f(t-ih), \tag{1}$$

where h is the time step, q is the fractional order and $c_i^{(q)} (i = 0, 1, ...)$ are the binomial coefficients that can be computed using the following expression,

$$c_0^{(q)} = 1, c_i^{(q)} = \left(1 - \frac{1+q}{i}\right) c_{i-1}^{(q)}. \tag{2}$$

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978-1-4244-7929-0/14/$26.00 ©2014 IEEE

If we consider $n = \frac{t-a}{h}$, where a is a real constant, which expresses a limit value, we can write:

$$_aD_t^q f(t) = \lim_{h\to 0} \frac{1}{h^q} \sum_{i=0}^{[n]} c_i^{(q)} f(t - ih), \qquad (3)$$

where [.] refers to the integer part, a and t are the bounds of operation for $_aD_t^q f(t)$.

The discrete approximation formula of the q^{th} derivative at the points kh $(k = 1, 2, ...)$ has the following form:

$$_{(k-L_m/h)}D_{t_k}^q f(t) \approx h^{-q} \sum_{i=0}^{k} c_i^{(q)} f(t_{k-i}), \qquad (4)$$

where L_m is the "memory length".

Therefore, the general numerical solution of the fractional differential equation:

$$_aD_t^q y(t) = g(y(t), t),$$

is given by,

$$y(t_k) = g(y(t_k), t_k)h^q - \sum_{i=1}^{k} c_i^{(q)} y(t_{k-i}). \qquad (5)$$

III. Fractional derivatives and BOLD signal

The BOLD fMRI signal is the magnetic resonance imaging contrast of blood deoxyhemoglobin. It is considered as an indirect measure of the neural activity. Since its discovery in 1990 by Seiji Ogawa and his colleagues [17], it has attracted many researchers seeking the interpretation and analysis of this signal in order to extract information on the neural activity and the related hemodynamic response. Different studies have confirmed that the BOLD signal can be characterized by specific features as illustrated in Fig. 1 (extracted from [14]). A delay between the stimulus and CBF has been also reported in [5] and modeled by adding a delay parameter in the balloon model.

In this paper, we discuss the use of a fractional model to capture the different details of the BOLD signal. Fractional derivatives provide an interesting tool for modeling memory and hereditary properties of different phenomena. Hence, FDs are suitable for the characterization of delays. The idea is to use FD for the neurovascular coupling willing to improve the description of the BOLD signal. We hope that the introduction of FD will help to capture the main features of the signal such as the initial dip.

IV. Proposed fractional dynamical model

In this section, the damped oscillator that models the neurovascular coupling in Friston's variant of the balloon model [2] has been replaced by a fractional one. The overall fractional model is given by,

$$\begin{cases} D_t^{q_1} f(t) = s, \\ D_t^{q_2} s(t) = \epsilon u(t) - s/\tau_s - (f-1)/\tau_f, \\ \frac{dv(t)}{dt} = \frac{1}{\tau}(f - v^{\frac{1}{\alpha}}), \\ \frac{dq(t)}{dt} = \frac{1}{\tau}\left(f \frac{1-(1-E_0)^{\frac{1}{f}}}{E_0} - v^{1/\alpha}\frac{q}{v} \right), \\ y(t) = V_0\left(k_1(1-q) + k_2(1-\frac{q}{v}) + k_3(1-v)\right), \end{cases} \qquad (6)$$

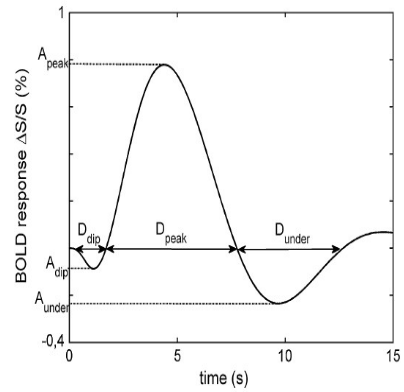

Fig. 1: Features of BOLD response as function of time. A_{type} and D_{type} represent the amplitude and the duration of $type$ which can be either the initial dip, principle peak or the post-stimulus undershoot [14].

where the state variables f, s, v and q are respectively CBF, flow inducing signal, CBV and deoxyhemoglobin content. The parameters of the model are the neural efficacy ϵ, the flow decay τ_s, the auto-regulation τ_f, the transit time τ, the stiffness α and oxygen extraction by the capillary bed at rest E_0. q_1 and q_2, such that $0 < q_1 \leq 1$ and $0 < q_2 \leq 1$ are fractional differentiation orders that will be discussed in the next section. V_0 is the blood volume fraction at rest. The parameters k_1, k_2 and k_3 depend on the scanner and are fixed for a $1.5T$ scanner and $TE = 40ms$ [1] to,

$$k_1 = 7E_0, \quad k_2 = 2, \quad k_3 = 2E_0 - 0.2. \qquad (7)$$

V. Numerical Results

A. Synthetic data

GL approximation (Eq. 5) has been used to solve the fractional differential equations in Matlab. The parameters used are from references [2] and [5] ($\epsilon = 0.2, \tau_s = 0.8, \tau_f = 0.4, \tau = 1, \alpha = 0.4, E_0 = 0.4, V_0 = 0.04$). The neural activity $u(t)$ is taken as a step function activated at $t = 0.2s$ and maintained until $t = 3s$. We propose to study the effect of fractional derivatives on the BOLD signal when the physiological parameters of the balloon are taken to be the same for both integer and fractional models. Three different cases are studied:

- Case I: $q_1 = 1$ and $0 < q_2 < 1$.
- Case II: $0 < q_1 < 1$ and $q_2 = 1$.
- Case III: $0 < q_1 < 1$ and $0 < q_2 < 1$.

The BOLD signal obtained in the three cases is compared to the one obtained with the standard balloon model (with integer-order).

Fig. 2 shows the BOLD signal in case I. The value of the peak and the post-stimulus undershoot of the BOLD signal are affected by variations in the fractional order q_2. Indeed, decreasing q_2 reduces the amplitude of the BOLD peak. It also results in a less marked and longer lasting undershoot. In Fig. 3, results of case II are illustrated. A smaller q_1

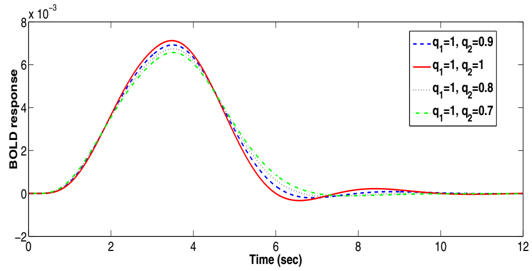

Fig. 2: BOLD response (case I versus standard integer order system).

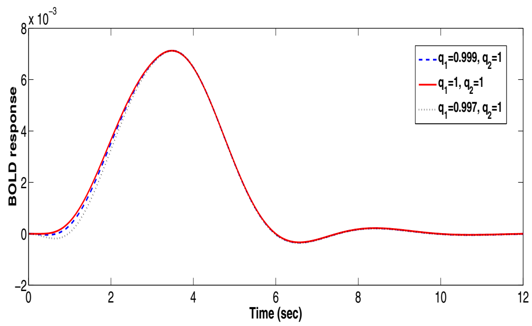

Fig. 3: BOLD response (case II versus standard integer order system).

allows an initial dip and increases the delay in the BOLD signal. In case III, combining the effect of both q_1 and q_2 results in a delayed BOLD response with a small initial dip and a reduced value of both the peak and the post-stimulus undershoot as illustrated in Fig. 4.

B. Experimental data

An event-related data set has been extracted from the SPM website (http://www.fil.ion.ucl.ac.uk/spm/data/face_rep/) corresponding to a study of the repetition priming for famous and non-famous faces [15]. The subject was presented with famous and non-famous faces against a checkerboard baseline. The faces were presented twice to study the effect of repetition, which gives a total of 4 events labeled: F1 (famous 1st presentation); F2 (famous 2nd presentation); N1 (non-famous 1st presentation); N2 (non famous 2nd presentation). The data set is pre-processed with the SPM8 toolbox to correct head motion and slice timing. Then, several processing steps were carried out to identify the regions with positive response to face presentation as per the analysis manual [16]. The event-related averaged response (peri-stimulus histogram, PSTH) for the N1 event was extracted at [39,-70,-14]. SPM toolbox also fits a linear combination of the canonical hemodynamic response function and its temporal first two derivatives to the real data, which is the dashed red line depicted in Fig. 5. In this study, we propose to fit the fractional model (Eq. 6) to this set of real data.

The fractional model given in Eq. 6 has been solved using GL approximation and has been compared to the experimental data set extracted from SPM website. In order to have comparable BOLD signals, the physiological parameters and

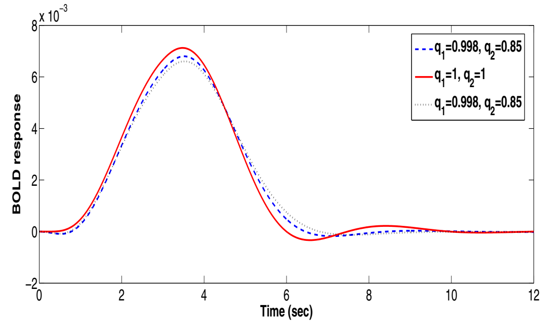

Fig. 4: BOLD response (case III versus standard integer order system).

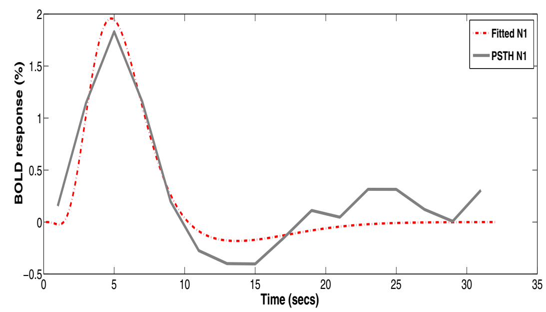

Fig. 5: Real event-related BOLD response. Fitted response (dashed) and peristimulus histograms (PSTH) for N1 event.

the input $u(t)$ of the balloon have been fixed to be the same for both fractional and first-order models. The parameters used for this part are; within their interval of possible values as reported in [14]; given by: $\epsilon = 0.2, \tau_s = 1.3, \tau_f = 2.2, \tau = 0.6, \alpha = 0.34, E_0 = 0.32, V_0 = 0.027$.

Fig. 6 illustrates a comparison between the first order derivative model, the proposed fractional model and the event-related data set extracted from SPM website. The results show that the three features classically used to characterize BOLD signal: the initial dip, the peak and the post-stimulus undershoot are better represented with the fractional order system.

In Fig. 7, a second set of fractional differentiation orders

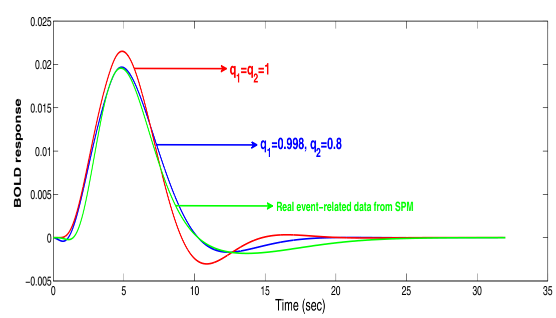

Fig. 6: BOLD responses. *Red line* corresponds to first order model, *blue line* corresponds to proposed fractional model. *Green line* corresponds to data extracted from SPM website.

is used. We observe that the time response is larger and the initial dip is more pronounced.

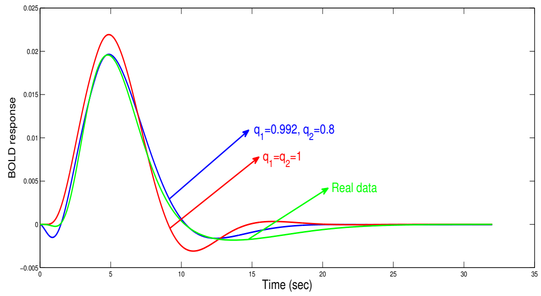

Fig. 7: BOLD responses. *Red line* corresponds to first order model, *blue line* corresponds to proposed fractional model. *Green line* corresponds to data extracted from SPM website.

VI. Conclusion

Mathematical modeling of the neurovascular coupling is important for the interpretation of the BOLD fMRI data. The existing models, including the well-known balloon, are limited in terms of BOLD signal interpretation. In this paper, the use of FD to model the neurovascular coupling has been investigated. The simulated BOLD signal of the fractional model has been compared to the BOLD signal issued using an integer-order model and also to a set of real data. The main findings of this study are:

- Fractional modeling of the relation between neural activity and CBF allows to better fit the BOLD signal.
- The fractional differentiation orders q_1 and q_2 help to adjust the simulated BOLD signal to include all the features. q_1 controls the initial dip and the time response (delay) while q_2 affects the duration of the undershoot and the amplitude of the peak of the BOLD signal.

In future work, more real data sets will be used to investigate and validate the model. Also, the identification of the fractional differentiation orders using real BOLD data will be studied.

VII. Acknowledgement

Research reported in this publication was supported by the King Abdullah University of Science and Technology (KAUST).

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