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A novel approach to calibrate the hemodynamic model using functional Magnetic Resonance Imaging (fMRI) measurements

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HIGHLIGHTS

- An efficient solution methodology for estimating the parameters of the brain response model is proposed.
- This method distinguishes itself from existing calibrating techniques by employing intelligently (a) the Newton algorithm, (b) a Tikhonov regularization approach, and (c) a Kalman filtering procedure.
- Both synthetic and real fMRI measurements were used to assess the performance of this method.
- The fast convergence, the accuracy, and the robustness to the noise effect of this method are clearly demonstrated by the reported numerical results.
- This method outperforms existing methods.

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ABSTRACT

Background: The calibration of the hemodynamic model that describes changes in blood flow and blood oxygenation during brain activation is a crucial step for successfully monitoring and possibly predicting brain activity. This in turn has the potential to provide diagnosis and treatment of brain diseases in early stages.
New method: We propose an efficient numerical procedure for calibrating the hemodynamic model using some fMRI measurements. The proposed solution methodology is a regularized iterative method equipped with a Kalman filtering-type procedure. The Newton component of the proposed method addresses the nonlinear aspect of the problem. The regularization feature is used to ensure the stability of the algorithm. The Kalman filter procedure is incorporated here to address the noise in the data.
Results: Numerical results obtained with synthetic data as well as with real fMRI measurements are presented to illustrate the accuracy, robustness to the noise, and the cost-effectiveness of the proposed method.
Comparison with existing method(s): We present numerical results that clearly demonstrate that the proposed method outperforms the Cubature Kalman Filter (CKF), one of the most prominent existing numerical methods.
Conclusion: We have designed an iterative numerical technique, called the TNM-CKF algorithm, for calibrating the mathematical model that describes the single-event related brain response when fMRI measurements are given. The method appears to be highly accurate and effective in reconstructing the BOLD signal even when the measurements are tainted with high noise level (as high as 30%).
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1. Introduction

Since its advent in the early 1990s, functional Magnetic Resonance Imaging (fMRI) has proven to be a powerful noninvasive tool for providing three-dimensional images of the brain per unit of time, which allows physicians to detect the activated regions in the brain. The principle of fMRI is relatively simple: it is a Magnetic Resonance Imaging (MRI) procedure imaging the brain over time. More specifically, it measures the brain activity by detecting associated changes in blood flow and produces three-dimensional images of the brain based on the Blood Oxygenation Level Dependent (BOLD) contrast (Huettel, 2008). Indeed, the BOLD signal is triggered by the variations of both the cerebral blood flow (CBF) and the cerebral metabolic rate of oxygen ($CMRO_2$). The BOLD

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signal reflects the decrease in the deoxyhemoglobin concentration at the site of the neural activity (Ogawa et al., 1990, 1993).

Expressing the observed phenomena of the BOLD signal as the output of a mathematical model remains one of the most outstanding issues. Two main approaches have been so far adopted to address this issue: the General Linear Modeling (GLM) and the nonlinear biophysical modeling frameworks. In the GLM approach, statistical analysis tools are used to assess the convolution of the neural activity signal with a predefined convolution kernel called the Hemodynamic Response Function (HRF). Several basis functions have been used to represent HRF including Poisson functions (Friston et al., 1994), Gaussian functions (Rajapakse et al., 1998), Gamma functions (Friston et al., 1998; Ciuciu et al., 2003), and inverse Logit functions (Lindquist and Wager, 2005). However, this class of methods is blind to the physiological aspects that underlie the BOLD transients and has the main drawback of excluding the nonlinear effects of the BOLD, as shown in Buxton and Frank (1997), Buxton et al. (1998), Friston et al. (1998, 1999). Due to these shortfalls, nonlinear biophysical modeling approaches emerged with the pioneer work of Buxton et al. (1998). Their model acknowledges – for the first time – the dependence of the BOLD signal on the variations of the normalized cerebral blood flow, volume, and deoxyhemoglobin content. Mandeville et al. (1999) modified the suggested model by considering the venous compartment's structure as a Balloon in which the stimulus, which induces a local neuronal activity, leads to an increase in blood flow (Mandeville et al., 1999). However, the pathway to the latter phenomenon was not specified. Note that since this increase exceeds $CMRO_2$, it then reduces the concentration of deoxyhemoglobin, which in turn results in an increase in the magnetic resonance signal. The missing relationship between the neural activity and CBF dynamics was introduced for the first time in Friston et al. (2000). More specifically, assuming that the synaptic activity and the regional CBF are linearly dependent, the neurovascular coupling between the neuronal activity and CBF has been described with a linear second order differential equation. We must point out that mathematical models which take into account metabolic effect such that the glucose variations, have been also proposed in attempt to better describe the brain activity (see, e.g., Sotero and Trujillo-Barreto, 2007).

The construction of such a reliable nonlinear biophysical model, called the Hemodynamic Model (HDM), has raised the challenging question of determining or accurately estimating the biophysiological parameters, the hidden states, and ultimately the neural activity. To the best of our knowledge, the first important attempt was made by Friston et al. (2000) who proposed a deterministic approach based on Volterra Kernel-type expansion to characterize the hemodynamic response. The bayesian framework was introduced in Friston (2002) so that the restriction induced by the use of temporal basis was replaced by Gaussian priors on the parameters. In addition, the nonlinear dynamic equation was also approximated using a bilinear equation to facilitate the likelihood maximization. Furthermore, in order to account for physiological noise, a Wiener process was added to the dynamics equation of the model proposed in Riera et al. (2004). More specifically, a Local Linearization Filter (LLF) based on a truncated Ito-Taylor expansion of the dynamics equation was employed to estimate both the state and the parameters of the Balloon model. It is interesting to note that the proposed approach uses a fixed number of radial basis functions to approximate the neural activity. Other attempts have been made to infer model states and parameters using similar filtering approaches with various but limited successes. Examples of such approaches include the iterative extended Kalman filtering method coupled with simplex search method (Deneux and Faugeras, 2006), the particle filtering method (Johnston et al., 2008), the particle smoothing method (Murray and Storkey, 2007), and the unscented Kalman filtering method (Hu et al., 2009). Note that all these methods employ different strategies to add the prior knowledge that makes the estimation problem well-posed in the stability sense (see, e.g., Hadamard, 1923). For example, radial basis functions were adapted to express the input in Riera et al. (2004), whereas Gaussian priors were used for the parameters in Havlicek et al. (2011). These small prior variances are needed to overcome the identifiability issues of some parameters. A nonlinear neural network method has also been used in Karam et al. (2014) for the estimation of the states and input, and observer techniques have been tested for state and input estimation in Laleg-Kirati et al. (2013), Zayane-Aissa and Laleg-Kirati (2014). The Cubature Kalman Filter (CKF) appears to be among the most prominent parameter estimation techniques. The CKF method was originally designed by Arasaratnam and Haykin (2009) for solving nonlinear state estimation problems such as tracking a maneuvering aircraft. It was later applied by Havlicek et al. (2011) to estimate the parameters of the Balloon model. The success of CKF in accurately estimating the parameters was however accomplished when applying this procedure in a pre-asymptotic convergence region, that is, when the values of initial guess of the parameters are the sought-after values tainted with a low noise level. In the absence of a priori knowledge on the parameters' values, which is the case in practice since these values are not measurable, the CKF procedure fails dramatically to estimate these parameters with a reasonable accuracy level, as demonstrated in this paper (see Fig. 4 in Section 4.1.1). Given that, the quest for efficiently and accurately estimating the model parameters remains an ongoing effort of pressing importance.

We propose a new solution methodology for efficiently solving the problem of calibrating the Hemodynamic Model (HDM) (Friston et al., 1999) when BOLD signal measurements are given. This problem is formulated as an inverse problem that falls in the category of parameter identification of a dynamical system. It is a nonlinear and ill-posed problem in the sense of Hadamard (1923). For this reason, we propose a regularized Newton method equipped with a Kalman filtering type procedure. The Newton component of the proposed algorithm addresses the nonlinear aspect of the problem. The regularization feature is used to ensure the stability of the algorithm. The Kalman filter procedure is the Cubature Kalman Filter (CKF) (Havlicek et al., 2011). It is incorporated here to address the noise in the data. We have conducted a numerical investigation using synthetic data tainted with various noise levels to assess the performance of the proposed method. We present results to illustrate the potential of the proposed solution methodology to accurately and efficiently estimate the biophysiological parameters. These results clearly indicate that the proposed method outperforms the Cubature Kalman Filter (CKF) (Havlicek et al., 2011), and significantly extends the range of satisfactory convergence. Finally, we also present model calibration results obtained when using real fMRI measurements corresponding to two paradigms: a face repetition stimulus (The FIL Methods Group, 2013) and a finger tapping stimulus (Karam et al., 2014).

The remainder of this paper is organized as follows. We specify in Section 2 the nomenclature and assumptions used in this paper and we state the hemodynamic model as well as the corresponding inverse problem. Section 3 is devoted to the description of the proposed solution methodology. In Section 4, we present numerical results obtained by using both synthetic data and real fMRI measurements. Concluding remarks are presented in Section 5.

2. Problem statement

2.1. Nomenclature and assumptions

Throughout this paper, we adopt the following notations and assumptions: