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Identification of Nonlinear fMRI Models Using Auxiliary Particle Filter and Kernel Smoothing Method

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Abstract—**Hemodynamic models have a high potential in application to understanding the functional differences of the brain. However, full system identification with respect to model fitting to actual functional magnetic resonance imaging (fMRI) data is practically difficult and is still an active area of research. We present a simulation based Bayesian approach for nonlinear model based analysis of the fMRI data. The idea is to do a joint state and parameter estimation within a general filtering framework. One advantage of using Bayesian methods is that they provide a complete description of the posterior distribution, not just a single point estimate. We use an Auxiliary Particle Filter adjoined with a kernel smoothing approach to address this joint estimation problem.**

I. Introduction

Functional Magnetic Resonance Imaging (fMRI) is an imaging modality which dominantly measures the Blood oxygenation level dependent (BOLD) effect, which is as an end result of the neural activity of the brain. The dynamics which arises due to the neural activity is collectively referred to as the hemodynamic response and many attempts have been made to model this physiological chain of activities. As a result the first convincing model (Balloon model) is proposed in [1], and also has been completed and enhanced by work in [2][3].

There are many instances reported in literature on analysis of experimental fMRI data using the Balloon model [4][5][6]. However, at present there is no ideal solution for the identification of the Balloon model. Several previously published work [7][8] has shown that the parameters of the BOLD model is unidentifiable. The work in [8] carries out a sensitivity analysis which shows this while the work in [7] estimates the correlation of the parameters using the joint posterior distributions estimated by a Particle Filter (PF).

The poor identifiability of the model makes it difficult to conclude on an optimal estimation technique, furthermore demands for a complete estimation based on their joint posterior probability. Thus, although point estimates of the parameters are preferred, due to the unidentifiable nature of the physiological parameters more descriptive estimation is required. The Balloon model has an input-state-output formulation and is well suited to use with posterior based Bayesian estimation techniques for fMRI data analysis. The work presented in this paper thus investigates the applicability of a novel Sequential Monte Carlo (SMC) based joint posterior probability estimation technique.

State space linearization approaches has been used in the joint estimation of the Balloon model parameters in the work presented in [4]. They use a local linearization filter in the Kalman filter methodology. Other than linearized filter approaches, nonlinear filtering strategies have been applied for the estimation of the states and parameters from the BOLD responses. The work in [6] applies an unscented kalman filter (UKF) methodology for fMRI data analysis.

There are several work related to parameter estimation of the Balloon model in literature via the use of PF’s.The first application of PF’s to the extended Balloon model is presented in [5]. In their work they use a PF for the state estimation and an offline maximum likelihood approach for the parameter estimation. The work presented in [9] discusses the estimation problem but with weight to advances in PF, not in the interest of fMRI data fitting, also they consider the hemodynamic parameters as known. Work in [7] uses an intact PF implementation for both state plus parameter estimation, however they do not consider a stochastic version of the Balloon model.

State filtering in nonlinear models similar to the Balloon model formulation is a well-studied issue. However, joint estimation of states and parameters of the model is still under extensive research. Thus as to cater the requirement of estimating joint posteriors within a robust filtering framework we present an alternate to the methods used in [7]. We propose to use an Auxiliary PF, a variant of the generic PF and an adjoined kernel smoothing approach.

The rest of the paper is organized as follows. Section 2 describes the Balloon model equations. We also describe an accurate link between the input stimulus and the neural activity which is the input to the Balloon model. Further the stochastic formulation of the full model is discussed. In Section 3 the Bayesian estimation and the proposed Auxiliary PF method with the kernel smoothing approach is presented. The simulated results, to evaluate the performance of the proposed method are presented in Section 4. Section 5 outlines the conclusions of the paper.

II. Single Region model

A. Neuronal Model

The general formulation for the neural interactions (connectivity) is given in [10] as a bilinear state equation given by,

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$$\dot{z}_t \approx \left(A + \sum_{j=1}^{M} u_t^j B^j \right) z_t + C u_t \quad (1)$$

where A is the intrinsic coupling matrix, C extrinsic coupling matrix, B^j matrix contains modulation of connectivity, $z$the neural activity, u the stimulus input and u^j the modulation inputs with M the number of modulatory inputs. The subscript t always denotes a time point. Thus for a single region, excluding the bilinear terms simplifies to,

$$\dot{z}_t \approx a z_t + c u_t \quad (2)$$

Where a is the self-connectivity, set to -1for stable operation conditions and c the input connectivity strength. This is the model adopted in this paper.

B. Hemodynamic Model

Here, we use the first compelling version of the hemodynamic forward model proposed in [1], namely the Balloon model, supplemented with a damped oscillator to model the blood flow in [2]. The input to the model is treated as the neural activity from (2) [3].The full path of the model describes the dynamics of the normalised cerebral blood flow f, the normalised flow inducing signal s, the normalised blood volume v and the normalised deoxyhemoglobin content q with ordinary differential equations*;*

$$\dot{s}_t = z_t - \frac{1}{\tau_s} s_t - \frac{1}{\tau_f}(f_t - 1) \quad (3)$$

$$\dot{f}_t = s_t \quad (4)$$

$$\dot{v}_t = \frac{1}{\tau_0}\left(f_t - v_t^{1/\alpha}\right) \quad (5)$$

$$\dot{q}_t = \frac{1}{\tau_0}\left(\frac{f_t\left(1-(1-E_0)^{1/f_t}\right)}{E_0} - \frac{q_t}{v_t^{1-1/\alpha}}\right) \quad (6)$$

The BOLD signal y as given in [11] is,

$$y_t = V_0\left(a_1(1-q_t) - a_2(1-v_t)\right) \quad (7)$$

The model parameters are the transit time through the balloon τ_0, the signal decay time constant τ_s, the autoregulatory time constant τ_f, the stiffness parameter α, the baseline blood volume V_0, resting state oxygen extraction E_0, and the BOLD signal parameters a_1 and a_2.

The above equations (2)-(6) can be given in a general form of a continues time stochastic nonlinear system including uncertainly in the system evolution and additive measurement and instrumental noise e_t,

$$dx_t = f(x_t, u_t, \theta)dt + BdW \quad (8)$$

$$y_t = g(x_t, \theta) + e_t e_t \sim N(0, \sigma_e^2) \quad (9)$$

where$x_t = [z_t, s_t, f_t, v_t, q_t]$ are the unobserved states of the system, $\theta = [c, \tau_s, \tau_f, \tau_0, \alpha, E_0, V_0]$ the neural and hemodynamic parameters, dW is an increment of a wiener process and B is a weighting matrix. $N(\mu, \sigma^2)$ denotes a Normal distribution with mean μ and variance σ^2.

In order to implement the above system and to apply in a general filtering framework we use a time discretization of equation (8) using a simple first order Euler-Maruyama scheme [12]. The resulting state equation is,

$$x_{t+\Delta t} = x_t + f(x_t, u_t, \theta)\Delta t + B\Delta W_t \quad (10)$$

where $\Delta W_t \sim N(0, \Delta t I)$, in this case I is a 5 X 5 identity matrix.

III. PARTICLE FILTER FOR JOINT ESTIMATION

In a probabilistic context the state transition equation (10) and observation equation (9) can be respectively given as;

$$x_t \sim p(x_t|x_{t-1}) = N(x_t + f(x_t, u_t, \theta)\Delta t, \Delta t BB^T) \quad (11)$$

$$y_t \sim p(y_t|x_t) = N(g(x_t, \theta), \sigma_e^2) \quad (12)$$

In the context of Bayesian estimation the solution to an estimation problem is given by the *a posteriori* density $p(x_t|Y_t)$i.e. a posteriori density estimation of a variable at a specific time given all the measurements /observations up to that time point$Y_t = [y_1, y_2, \ldots, y_t]$.

The PF is an alternative to approximate Kalman filtering for nonlinear systems. PF's are Bayesian filters approximating the probability density functions (PDF) with a set of weighted particles [13][14]; $\{x_t^i, w_t^i\}$ where $i = 1,2, \ldots, m$ and m is the no of particles. The particles and associated weights are updates recursively at both the time update and measurement update. With the weights normalized such that $\sum_{i=1}^{m} w_t^i = 1$, the posterior density is approximated as,

$$p(x_t|Y_t) \approx \sum_{i=1}^{m} w_t^i\, \delta\left(x_t - x_t^i\right) \quad (13)$$

where $\delta(x)$ is the Dirac delta function. Usually the samples x_t^i cannot be sampled from the posterior directly. Thus we sample directly from an *importance function* as detailed in [13], where w_t^i are now the importance weights. We omit a comprehensive discussion on PF's in the paper, which can be found in [13] [14] in great detail.

The PF has several variants such as Sequential Importance sampling (SIS), sampling importance resampling (SIR) [15], Auxiliary sampling importance resampling (ASIR) and regularized particle filter (RPF). To counteract the drawbacks in SIR algorithm, the work in [16] introduce ASIR constructing proposals that better correspond to the true posterior distribution. In the work presented in the paper we use an ASIR filter for the joint estimation of states and parameters.

In order to fully identify the system we need to estimate the hidden states $x_t$plus the static parameters θ of the single region fMRI model. In the case where the fixed parameters are unknown thejoint posterior is given as;

$$p(x_{t+1}, \theta|Y_{t+1}) \propto p(y_{t+1}|x_{t+1}, \theta)p(x_{t+1}|\theta, Y_t)p(\theta|Y_t) \quad (14)$$

We deal with thejoint estimation through theuse of an augmented state vector$\emptyset_t = [x_t, \theta_t]^T$. The superscript T denotes the transpose of the vector. The basic idea of the ASIR is to introducesample auxiliary variable, k, which is the index of the particles at time t. By augmenting the filtering distribution with this additional auxiliary variable, ASIRs consider the target jointdistribution;

$$p(\emptyset_{t+1}, i|Y_{t+1}) \propto p(y_{t+1}|\emptyset_{t+1})w_t^i p(\emptyset_{t+1}|\emptyset_t^i) \quad (15)$$

Thus the APF has to generate samples from$p(\emptyset_{t+1}, i|Y_{t+1})$ and drop the index to generate the required samples from $p(\emptyset_{t+1}|Y_{t+1})$. To generate samples $\{\emptyset_{t+1}^{(k)}, i_k\}$ the ASIR uses importance sampling with an importance density of the form $(\emptyset_{t+1}, i|Y_{t+1}) \propto p(y_{t+1}|\mu_{t+1}^i)p(\emptyset_{t+1}|\emptyset_t^i)w_t^i$, where μ_{t+1}^i is a measure associated with the density $p(\emptyset_{t+1}|\emptyset_t^i)$ such as the mean, mode or a sample.

However, the non-dynamics of the parameters will create degeneracy. Adding artificial dynamics through a random walk model of the parameters is a good option [14] although this will result in an artificial loss of information. However instead of the random walk modeling for parameters, we use a kernel smoothing approach in which the latter issue is avoided.

If the posterior parameter samples and weights $\{\theta_t^i, w_t^i\}$ are available at time t the parameter posteriors are now given by,

$$p(\theta_{t+1}|Y_t) \approx \sum_{i=1}^{m} w_t^i N(\theta_{t+1}|m_t^i, h^2 V_t) \quad (16)$$

where h is the kernel smoothing factor with $0 < h < 1$ and m_t^i's are the kernel location, specified by a shrinkage rule that forces the particles to be close to their mean $m_t^i = (\sqrt{1-h^2})\theta_t^i + (1-\sqrt{1-h^2})\bar{\theta}_t$, with $\bar{\theta}_t$ and V_t are the monte carlo mean and the monte carlo variance of the samples respectively. This approach is applied in [17] as an extended version of the ASIR in treatment of static model parameters. The extended ASIR with the kernel smoothing is outlined in Table I.

Table I: ASIR with Kernel Smoothing

1. **FOR** $i = 1 \ to \ m$ **Calculate**

$$\mu_{t+1}^i \sim p(x_{t+1}|x_t^i)$$
$$m_t^i = \left(\sqrt{1-h^2}\right)\theta_t^i + \left(1-\sqrt{1-h^2}\right)\bar{\theta}_t$$

2. **Calculate the first stage normalized weights**

$$w_{t+1}^{1,i} = \frac{p(y_{t+1}|\mu_{t+1}^i, m_t^i)w_t^i}{\sum_{i=1}^m (p(y_{t+1}|\mu_{t+1}^i, m_t^i)w_t^i)}$$

3. **Resample the indices which generate** $\{i^{(k)}\}_{k=1}^m$ **using** $\{\mu_{t+1}^i, w_{t+1}^{1,i}\}$.
4. **Forward sample**

Draw $\theta_{t+1}^{i(k)} \sim N\left(\theta_{t+1}|m_t^{i(k)}, h^2 V_t\right)$

Draw $x_{t+1}^{i(k)} \sim p\left(x_{t+1}|x_t^{i(k)}, \ \theta_{t+1}^{i(k)}\right)$

5. **Calculate the second stage weights**

$$w_{t+1}^{2,k} \propto \frac{p\left(y_{t+1}|x_{t+1}^{i(k)}, \theta_{t+1}^{i(k)}\right)}{p\left(y_{t+1}|\mu_{t+1}^{i(k)}, m_t^{i(k)}\right)}$$

6. **Calculate the stage two normalized weights.**

IV. SIMULATION RESULTS

As there is no ground truth data available with fMRI data the proposed method is evaluated by using simulated data. In order to generatethe simulation data we integrate the non-linear system of stochastic differential equations (10) using sampling rate of 0.1s. However, resampling and reweighting is performed only at those integration points where the measurements are available. In the present work we consider a typical fMRI repetition time (TR) of 2s.

However, due to the poor identifiability of the model, fixing some parameters as proposed in literature [8] is a good precaution at the stage of model parameterization. As the main target of this work is to provide an alternate robust platform for joint estimation of the Balloon model parameters, we do not discuss the issues relating to correlations of the parameters. For demonstrating the performance of the proposed method we only estimate the parameters c, τ_s, τ_f and τ_0.

For the synthetic data generation, we use the mean values reported in [2], for fixed parametersas$\alpha = 0.33, E_0 = 0.34, V_0 = 0.02$. Also $a_1 = 3.4$ and $a_2 = 1.0$ [10]. The data is generated with values $c = 0.5, \tau_s = 2, \tau_f = 1.67, \tau_0 = 1.3$. The ASIR is initialized with the priors given in Table 2 as reported in [2][10].

We first generate data for an on/off block input shown in Fig. 1(a).The noise levels (low noise) were set to $\sigma_e^2 = 1 \times 10^{-4}$ and $B = [0.01\ 0\ 0\ 0\ 0]^T$.Fig. 1(b) shows the simulated BOLD signal and the reconstructed BOLD signal while Fig. 1(c) shows the estimated neural signal. Fig. 2 shows the convergence of the mean of the estimated posterior distribution during the estimation. Table II gives the final posterior of the parameters. The accuracy of the joint estimation is evident with the state estimates closely agreeing with the true values and joint estimation gives robust parameter estimates with low variance in the posterior. The proposed joint scheme used only 1000 particles and used $h = 0.1$.

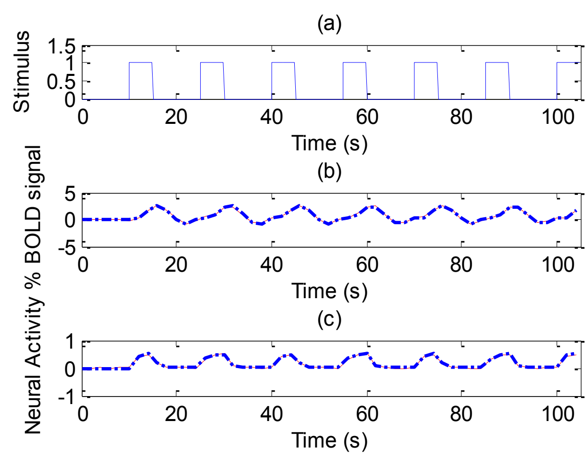

Figure 1. (a) Input stimulus (b) Simulated (solid red) and reconstructed BOLD signal (dashed blue) (c) Simulated and estimated neural activity.

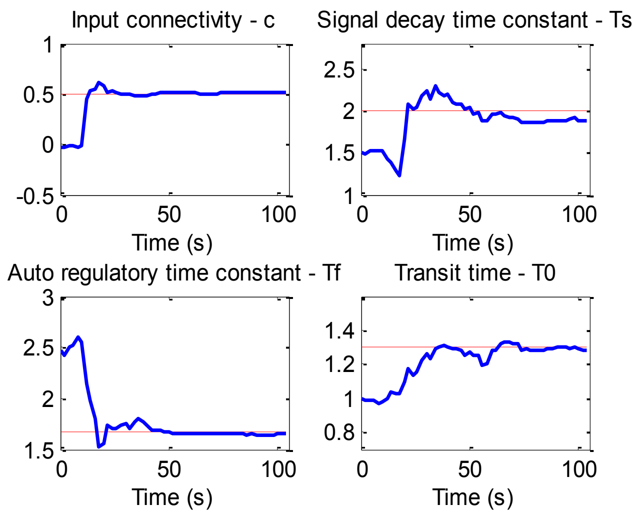

Figure 2. The parameter convergence for block input of Fig. 1(a) (blue) and Simulated values of parameters (red).

In order to evaluate the sensitivity of the method to variations in noise, another data set was generated by setting $\sigma_e^2 = 1 \times 10^{-2}$ and $B = [0.1\ 0\ 0\ 0\ 0]^T$(high noise) for the same block input of Fig. 1(a). It was observed that the time for convergence was still around 60-70 seconds as in the previous low noise case. Table III gives the converged estimates at six different runs with different particle initializations of the ASIR. Last row of Table III gives the average of the parameter estimations. Except for parameter τ_s the other parameters have a discrepancy from the simulated values. This is clearly due to the high noise present in the data.

Thirdly, in order to evaluate the sensitivity of the method to different experimental inputs (stimulations) we generated data using an event related stimulus shown in Fig. 3(a). The noise levels were set to the values of the low noise case of the block input. The estimated neural activity using the joint estimation is shown in Fig. 3(b), and it is very close to the simulated true neural activity. The recursive variation of the mean of the estimated posterior is shown in Fig. 4. The parameters converged faster, within the 20-40 seconds compared to the block input case.

The results show that the ASIR with the Kernel smoothing performs reasonably well under different experimental conditions, providing a robust platform for fMRI data analysis.

Table II. Prior density and Estimated Posterior density of model Parameters

Parameter	Prior	Posterior
c	$N\sim(0,0.25)$	$N\sim(0.506,0.0184)$
τ_0	$N\sim(0.98,0.25)$	$N\sim(1.2952,0.0572)$
τ_s	$N\sim(1.54,0.25)$	$N\sim(1.89,0.0113)$
τ_f	$N\sim(2.46,0.25)$	$N\sim(1.646,0.0146)$

Table III. Estimated Posterior density of model Parameters at high noise levels in the simulated data for different runs

Run	c	τ_s	τ_f	τ_0
1	0.4906	1.9988	1.5649	1.2200
2	0.3786	2.0627	1.8681	1.0220
3	0.3485	1.8713	2.0288	0.8211
4	0.3982	1.9429	1.8328	1.0038
5	0.4317	1.9194	1.8786	1.0542
6	0.4179	2.2139	1.7126	1.2252
Mean	***0.4109***	***2.0015***	***1.8143***	***1.0577***

V. Conclusion

In conclusion we propose a new method for jointstate/parameter estimation of nonlinear fMRI models by usinga kernel smoothing method with the ASIR.The most common method used for fMRI data analysis is the General Linear Model (GLM). The GLM is the best method when it comes to activation studies [5], as the nonlinear model based analysis has been unable to show significant differences in the activation mapscompared to the GLM [8] created activation maps, while also is computationally much expensive.On the other hand, the nonlinear models involve physiologically plausible parameters that capture a better temporal characterization of the BOLD signal. So, in more advanced fMRI data analysis, nonlinear models serve an important role in understanding the brain functionality.

Amongst the available nonlinear methods for fMRI analysis, particle filters have gained a lot of attention during the past few years [5][7][9], due to its excellent performance in the highly nonlinear domain [13]. Our work highlights the applicability of an alternate to the SIR particle filter used in the above approaches. Being an online state/parameter estimation algorithm, our approach saves computing time compared to the offline maximum likelihood based parameter estimation methods proposed in [5].

Results show accurate joint estimates of states and parameters with less computational requirements (only 1000 particles). Even with a high TR still the proposed method performs robustly and the parameters converge relatively quickly compared to the typical experimental times of the fMRI experiments. With suitable parameterization that does not compromise the effectiveness of the model and with the knowledge of priors, proposed Bayesian framework is well suited for the model based analysis of fMRI data.

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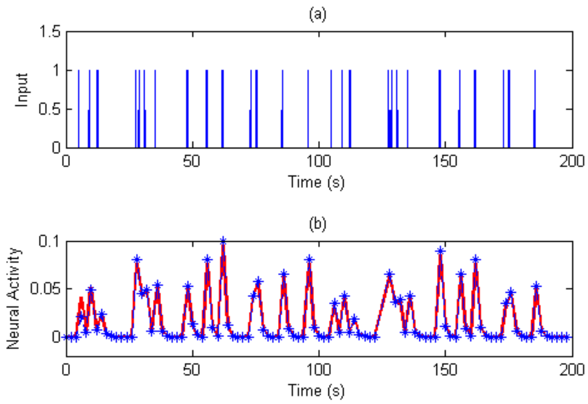

Figure3. (a) Event related Input stimulus (b) Simulated (red) and estimated neural activity (dashed blue).

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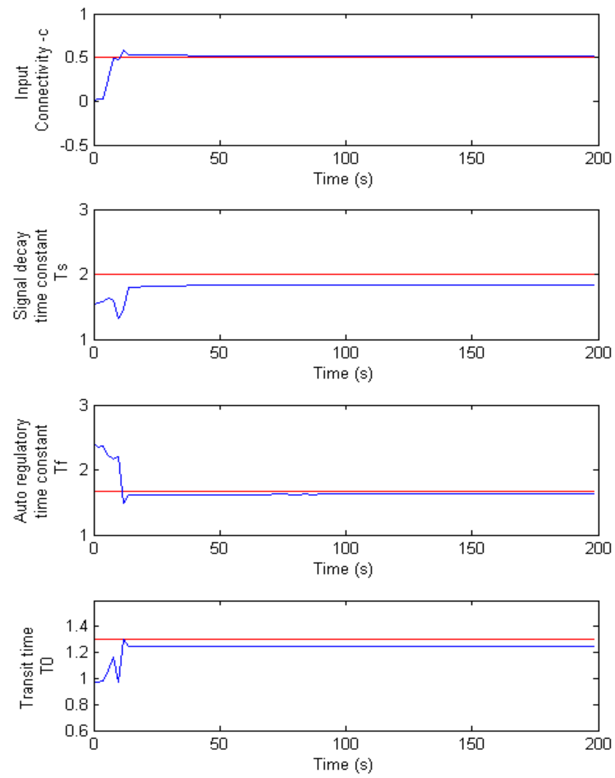

Figure 4. Parameter convergence for event related input (blue) and Simulated values of parameters (red).

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