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Research Article

Improvement of CSCKS approach for solving hemodynamic model by using fMRI images.

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Abstract

The hemodynamic model describes the blood flow mechanisms as well as the coupling between the metabolic and neuronal activities in a voxel on the human brain. The solution and deconvolution for identifying dynamical variables, biophysical parameters, and hidden states of this hemodynamic model is a researchable work. In order to solve the hemodynamic model parameters, hidden states, and estimate blood oxygen level dependent (BOLD) signal from fMRI images, there are three popular methods in brain imaging field. First method, dynamic expectation maximization (DEM) is a routine algorithm of inverting hemodynamic model. Second method, square root cubature kalman filtering and smoothing (SCKF-SCKS) based on the cubature kalman filter (CKF). Third method, the recently introduced confounds SCKF-SCKS (CSCKF-CSCKS) is modified model of the second method and worked at low interference factors. In this paper, the improvement of CSCKS algorithm are provided due to some major problems in traditional algorithm and obviously removes problems to get better results. The improved CSCKS algorithm estimates hemodynamic model parameters that are 89% close to real value, whereas the traditional CSCKS and DEM algorithms estimate parameters that are 82% and 53% close to real value, respectively. To compare the BOLD responses, a new parameter named power spectral density (PSD) is measured in this research work, which shows that the new CSCKS method produce the minimum BOLD signal strength 10^{-11}dB at 3220Hz frequency, whereas SCKS and DEM methods shows 10^{-14}dB at 3020 Hz and 10^{-16} dB at 2980 Hz frequency, respectively. This proves the ability of improved CSCKS method is to solve the hemodynamic model perfectly than that of others.

Keywords: Cubature kalman filter; blood oxygen level dependent signal; hemodynamic model; functional magnetic resonance imaging.

1. Introduction

The functional magnetic resonance imaging (fMRI) uses a magnetic field to assess the blood flow in our brain, as the hemoglobin of blood is made up of magnetic elements. Blood flow of our brain is a dynamic process; neurons are driven by various synaptic activities of human body, causing hemodynamic responses in our brain and so producing BOLD signals. Buxton and his team [1-3] presented a single region of the brain associated with Balloon-windkessel model in 1998, which is nearly identical to the existing hemodynamic models, consists of a set of differential equations [Eq. (1) - (7)]. These differential equations characterize the relationship between the various components of the

hemodynamic model, and we can see from them that the hemodynamic model has a nonlinear property, which is a very important and interesting point to represent the entire scenario in a single voxel and the nature of blood flow in our brain. Model fitting to raw data is a validation procedure, and there are numerous models fitting algorithms in hemodynamic models, which estimate the accurate input, hidden states, and parameters of the proposed model, all of which are useful in uncovering our enigmatic brain.

This article compares and contrasts various model fitting methods with propose model fitting method. Among those, DEM of J. K. Friston and his team **[**5, 6], SCKS of Martin Havlicek and his team [7], and CSCKS of Mingzhi Lu and his team [9, 12**]** are the three noteworthy models fitting algorithm published in 2008, 2011, and 2021, respectively. Because of its dynamical expectation maximization techniques, the DEM model fitting method took longer to fit data with a model. If we utilize attention to visual motion data in the DEM fitting approach, it takes 92.39 seconds to complete the iteration process for a single brain region by performing seventeen E-steps. The SCKS model fitting approach can't estimate the coefficients of low frequency interference factors, and the recently introduced CSCKS model fitting method estimate model parameters effectively when low interference factors are taken into account. The proposed improved CSCKS algorithm performed well in low, medium, and high frequency interference factors, as well as accurately estimating hidden states, and took 72.32 seconds to complete its iteration operations, which is 21.72% faster than the DEM method. In this article, the improvement of CSCKS algorithm are provided due to some major problems in traditional algorithm and obviously remove problems to get better results. The new CSCKS algorithm estimates hemodynamic model parameters that are 89% close to real value, whereas the traditional CSCKS and DEM algorithms estimate parameters that are 82% and 53% close to real value, respectively. To compare the BOLD response, the power spectral density (PSD) determining algorithms are first time included in the proposed algorithm, which shows that CSCKS method produce the minimum BOLD signal strength 10^{-11}dB at 3220Hz frequency, whereas SCKS and DEM methods shows 10^{-14}dB at 3020 Hz and 10^{-16} dB at 2980 Hz frequency, respectively.

2. Materials and methods

The fMRI machine acquires raw images from the human brain, which are then processed by image processing software SPM to produce data, which is then fitted to a hemodynamic model, and the BOLD signal is estimated at the end of the process. First, we used a 3tesla fMRI scanner to scan 360 pictures. Christian Buchel [4**]** describes the image capture procedure, the patient's physical description, and the fMRI machine parameters in general. Second, we utilized image processing software called statistical parametric mapping (SPM) that is integrated with MATLAB to extract statistical data in required format that represented the existence of blood activation and metabolic function in the brain. Third, we used inverse process by using improve CSCKS method and determine models parameters, hidden states. Model fitting and BOLD signal extraction are critical in discovering our brain.

2.1 Image acquisition process

The image acquisition related experimental design and all parameter settings of this acquisition processes are broadly and detailed described in Christian Buchel article [4] and the acquired raw images related zip file is available in an open access SPM website named attention to visual motion data set. This archive contains 360 images of the human brain.

2.2 Data acquisition process

The raw images have utilized to produce a mat file according to the instructions described in the chapter 35 on the SPM12 manual **[11]**. The extracted mat files have then employed in the DEM, SCKS, CSCKS, and improve CSCKS algorithms to determine parameters, hidden states, and power spectral density (PSD) for analysis.

2.3 Hemodynamic model description

Fig.1 depicts the basic concepts of hemodynamic model. The modified Balloon-windkessel model which is illustrated in the following figure can be considered as consisting of five sub-systems linking: (1) neural activity to changes in blood flow; (2) changes in blood flow to oxygen delivery to tissue **[1]**; (3) changes in blood flow to the changes in blood volume and venous outflow **[2, 9]**; (4) changes in blood flow, volume and oxygen extraction fraction to changes in deoxy-hemoglobin, and finally; (5) changes in volume and deoxy-

hemoglobin to the BOLD response. The complete hemodynamic model relating input synaptic activity u(t) to BOLD signal y(t) is described by the set of characteristic equations listed below**[Eq. (1) – (7)]**.The nonlinear property of the BOLD contrast presented by (7), which is created from venous volume v and deoxy-hemoglobin quantity q, is the most important aspect of the hemodynamic model.

$$\dot{s} = \varepsilon u(t) - \frac{S}{T_s} - \frac{(f_{in} - 1)}{T_f} \quad (1)$$

$$\dot{f_{in}} = s \quad (2)$$

$$E(f_{in}, E_0) = 1 - (1 - E_0)^{1/f_{in}} \quad (3)$$

$$\tau_0 \dot{q} = f_{in} \frac{E(f_{in}, E_0)}{E_0} - f_{out}(v) \frac{q}{v} \quad (4)$$

$$f_{out}(v) = v^{1/\alpha} \quad (5)$$

$$\tau_0 \dot{v} = f_{in} - f_{out}(v) \quad (6)$$

$$y(t) = V_0(7E_0(1 - q) + 2\left(1 - \frac{q}{v}\right) + (2E_0 - 0.2)(1 - v)) \quad (7)$$

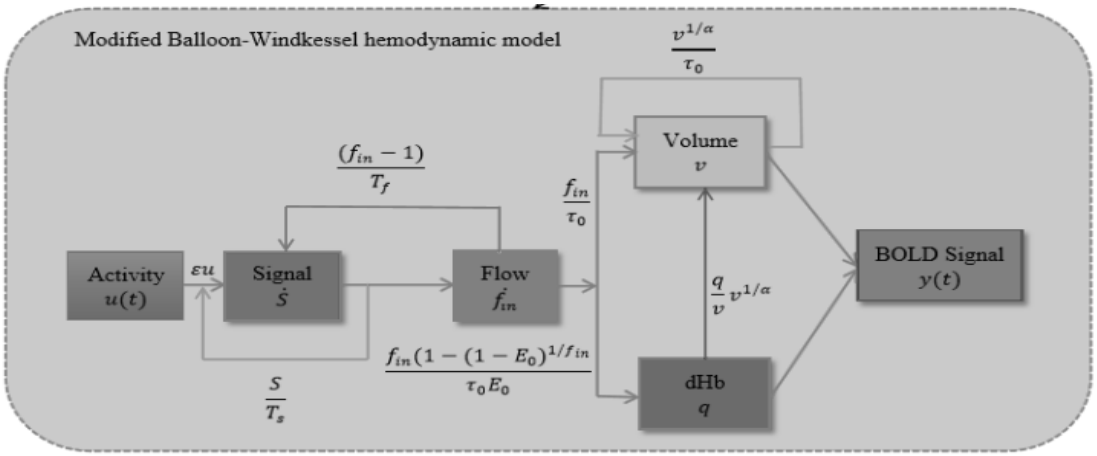

Fig.1: Graphical representation of hemodynamic model used in this paper. This is a modification of original Balloon model proposed by Richard B. Buxton **[2]**

2.4 Model fitting methods

Model fitting algorithms have evolved to solve a specific problem and reduce BOLD contrast. This development is progressing day by day in order to tackle a better problem. Inverting the hemodynamic model with the DEM algorithm is a common practice. There are three steps in the DEM algorithm: D, E, and M [5]. The SCKS method is based on the proposed kalman filter technique. First, the algorithm performs forward filtering, followed by backward filtering using the RTS smoothing algorithm [6]. In hemodynamic models that include low frequency interference effects, the SCKS approach is unable to estimate their coefficients. On the other hand, the CSCKS method integrates system state and filter theory in a cubature kalman filter algorithm is to determine accurately the low frequency interference factors but not able to estimate parameters as closed real value. For this the improvement of CSCKS is needed to determine parameters estimation as close to real value. In CSCKS method, model related characteristic differential equations [Eq. (1) – (6)] can be modified and described as the following state equations-

$$\dot{s} = \dot{z} - ks - \gamma(f - 1) \quad (8)$$

$$\dot{f} = s \tag{9}$$

$$\tau\dot{v} = \dot{f} - v^{\frac{1}{\alpha}} \tag{10}$$

$$\tau\dot{q} = f\frac{E(F,q)}{q} - v^{\frac{1}{\alpha}}\frac{q}{v} \tag{11}$$

Where, the newly introduced parameters $\dot{z}$, γ, k represents the hidden state, the rate of flow dependent elimination, the rate of signal decay, respectively. From Eq. (1) - (11), we can now derive the general form of the improve CSCKS and also describe the same things in these cases of our existing algorithms –

DEM
$$\begin{cases} \dot{x}(t) = f(x, u(t)) \\ y(t) = \lambda(x(t)) \end{cases} \tag{12}$$

SCKS
$$\begin{cases} \dot{z} = h(z, u, \theta) + p \\ y = \eta(z) + r \end{cases} \tag{13}$$

CSCKS
$$\begin{cases} \dot{z} = h(z, u, \theta) + p \\ y = \eta(z) + X\beta + r \end{cases} \tag{14}$$

Improve CSCKS
$$\begin{cases} \dot{z} = h(z, u, \theta) + p \\ y = \eta(z) + (X1 + X2 + X3)\beta + r \end{cases} \tag{15}$$

The DEM method uses model describing state equations to represent the model synaptic activity to the observed BOLD signal without estimating the hidden states of a model. The SCKS method, in the first time, describes the hidden states with its noises. Here, p and r presents white Gaussian noise of the hidden states. The CSCKS method considers confounds of the low frequency interference factors and estimate the coefficients of its. Our proposed improvement of CSCKS method considers all types of frequency interference factors and estimate all coefficients of related in its. Although there are no significant differences between CSCKS and proposed CSCKS methods for the sake of simplicity, the actual filter description and initialization of the filter reveals that the improve CSCKS approach is more sophisticated and produces more accurate results than CSCKS. The DEM, SCKS, and CSCKS algorithm have been broadly described in **[5, 6]**, and **[7]**,**[12]**, respectively. Where, X1, X2, X3, β, θ are low, medium and high frequency interference factors, coefficients of related interference factors, biophysical parameter, respectively. The biophysical parameter $\theta = \{k, \chi, \tau, \alpha, \varphi, \sigma, \epsilon\}$ is described the model characteristic.

2.5 The improvement of CSCKS algorithm

The projected estimate vector of state, predicted error covariance matrix, innovation covariance matrix, and cross-covariance matrix involved in the existing CSCKS algorithm must be re-derived due to the current high interference factors in confounds. To estimate model parameters, the approach employs a CKF filter, which is separated into three steps: filter initialization, forward filtering, and backward smoothing. A time update step and a measurement update step can be added to forward filtering. The forward filtering and backward smoothing steps of the existing CSCKS method have been kept unchanged in our proposed improve CSCKS method, but the filter initialization step has been revised and redesigned to satisfy the required new criteria. We'll go over each of them in detail below. First, we initialize the filter, where we construct the augmented form of state vector described in **[Eq. (16)]**, Where, $x_0, \theta_0, \beta_{0|j\,(h,m,l)}$ denote the estimated values of the hidden states x, biophysical parameters θ, and coefficients β of confounds at time zero, respectively. Here, the coefficients of confounds are three types – high, medium, and low contains interference factors. $0_p, 0_s, 0_v, 0_m$ are all zero vectors and denote the values of corresponding dynamic noises p, s, v, and m of x, $\theta, \beta,$ and y at time zero.

$$\hat{x}_0^a = E[x_0^a] = \left[\hat{x}_0^T, 0, 0, 0, 0\right]^T = \left[x_0, \theta_0, \beta_{0|h}, \beta_{0|m}, \beta_{0|l}, 0_p, 0_s, 0_v, 0_m\right]^T \quad (16)$$

$$S_0^a = \text{chol}\left(E[(x_0^a - \hat{x}_0^a)(x_0^a - \hat{x}_0^a)^T]\right) = \text{diag}(S_0, S_p, S_s, S_v, S_m) \quad (17)$$

$$\chi_{i,j-1|t-1}^a = S_{t-1|t-1}^a \xi_t + \widehat{\chi_{t-1|t-1}^a} \quad (18)$$

$$\chi_{i,t|t-1}^{x,u,\theta} = F\left(\chi_{i,t-1|t-1}^{a(x)}, \chi_{i,t-1|t-1}^{a(u)}, \chi_{i,t-1|t-1}^{a(\theta)}\right) + \chi_{i,t-1|t-1}^{a(q,y,w)} \quad (19)$$

$$Y_{i,t|t-1} = g(\chi_{i,t-1|t-1}^{x}, \chi_{i,t-1|t-1}^{u}, \chi_{i,t-1|t-1}^{\theta}) + \chi_{i,t-1|t-1}^{a(r)} \quad (20)$$

$$P_{xy,t|t-1} = X_{t|t-1} Y_{t|t-1}^T \quad (21)$$

$$K_t = (P_{xy,t|t-1} / S_{xy,t|t-1}^T) / S_{xy,t|t-1} \quad (22)$$

Next, the initial square root of the corresponding error-covariance matrix is assigned to [Eq. (17)]. Firstly, we calculate the computational summation by an integration processes using the above mentioned state vector described in [Eq. (18)].Then, we are able to calculate the spread of the cubature point symbolized Greek small latter chi which is described by the following equation [Eq. (19)]. Then, we began to calculate the estimate error covariance by using spread equation and able to find out the following predicted value described in [Eq. (20)]. Finally, we are able to calculate kalman power and the gain of the state vector which are used to determine the filtered estimation of the given state vector. The kalman power and gain are described by the following equations [Eq. (21), (22)]. During program executions in MATLAB, the whole processes executes until the last fMRI images is to used and simulate biophysical parameters.

3. Result and discussion

With the use of typical toolbox of DEM, SCKS, CSCKS and the proposed improve CSCKS are applied to data set and observe the simulation results obtained from them. Our observations are divided into hidden states estimate, parameters estimation and analysis of power spectral density of BOLD response. The coding and algorithm process of CSCKS has been performed in MATLAB R2020b integrated with SPM12 version software. In order to evaluate the performance of the improved CSCKS algorithm, we have to compare CSCKS with DEM and SCKS algorithms. The DEM and SCKS algorithms would be seen details in the Toolbox directory of spm12 software named MATLAB files spm_sck.m and spm_DEM.m. In summary, we used 360 fMRI images to make real BOLD signal by using SPM12 software and we also applied four algorithms, DEM, SCKS, CSCKS and improved CSCKS to perform inverse process of BOLD signal for determining hemodynamic model parameters, hidden states, and PSD in this experiment. The parameters and initial conditions settings of our proposed CSCKS are described in **Table.1**. We have solved the proposed model by Taylor series expansion using the processes equations [Eq. (1) - (6)] described in materials and methods section. We also measure the BOLD response for the model inversion CSCKS approach by using the observation equation [Eq. (7)] from the state variables cerebral blood volume and deoxy-hemoglobin content. We have demonstrated the estimated BOLD response in **Fig.2** for the designed multi pulse square input signal.

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Table.1: Parameters and initial conditions settings of improved CSCKS algorithm [8].

Parameters settings	**Descriptions**	**Remarks**
$x_{0\|0} = [0,0,0,0]$	State vector	Initial conditions
$\theta_0 = [0.65, 0.41, 0.98, 0.32, 0.34, 0.02, 0.5]$	Model parameters	True value
$\theta = [\theta_1, \theta_2, \theta_3, \theta_4]$	Model parameters	
$\beta_{0\|0} = [0,0,0,0,0,0]$	Noice matrix	Initial conditions
$\beta = [2.4, -0.4, 1.0, -0.8, 0.6, 0.2]/0.5$	Noice matrix	In data generation
$Q_{x\|0}$ = diag $[10^{-2}, 10^{-2}, 10^{-2}, 10^{-2}]$	Error covariance matrix	
$Q_{\beta\|0}$ = diag $[10^{-3}, 10^{-3}, 10^{-3}, 10^{-3}, 10^{-3}, 10^{-3}]$	Error covariance matrix	
$Q_{\theta\|0}$ = diag $[10^{-20}, 10^{-20}, 10^{-20}, 10^{-20}]$	Error covariance matrix	
Q_p = diag $[10^{-6}, 10^{-6}, 10^{-6}, 10^{-6}]$	Covariance Matrix	
Q_s = diag $[10^{-4}, 10^{-4}, 10^{-3}]$	Covariance Matrix	
Q_v = diag $[10^{-4}, 10^{-4}, 10^{-4}, 10^{-4}, 10^{-4}, 10^{-4}]$	Covariance Matrix	
Q_m = diag $[10^{-3}]$	Covariance Matrix	
Δt = 0.2 second	Integration step	
$f_s = 10\ kHz$	Reference frequecy	For PSD

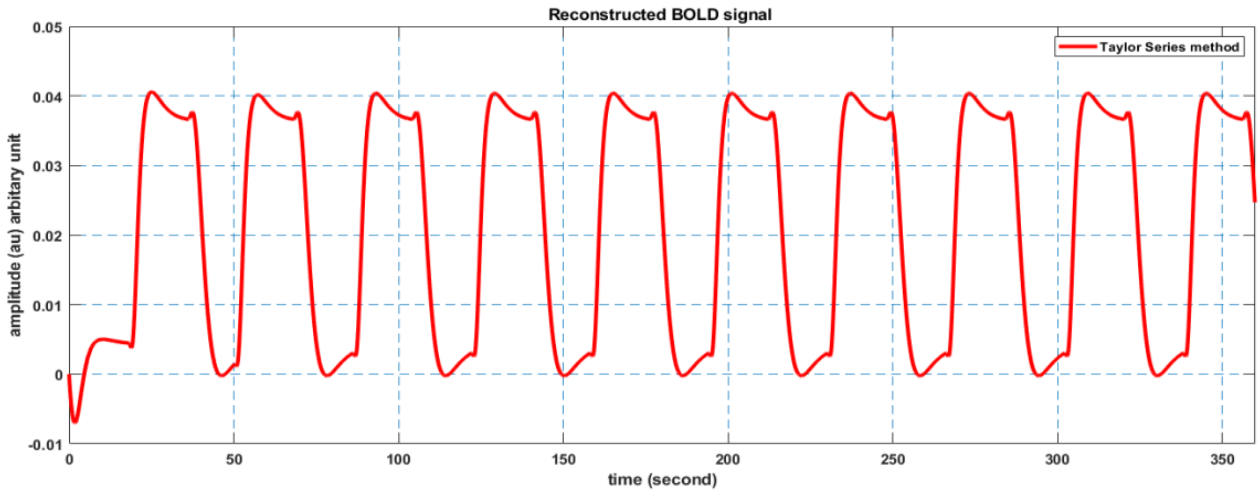

Fig.2: Reconstructed BOLD signal.

Fig.3 shows the estimated results of hidden states, the estimated curves of various algorithms at time point 6-7, 22-24, 34-35, 38-39, 47-48, and 62-64 are coincides to each other and rest of time the estimated curves are deviated from each other maintained a numerical relationship. The coincides of 6-7, 22-24 time points are much more consisted than 34-35, 47-48 time points. On the other hands, the deviation lengths of 9-22, 25-33 time points are much more looped than that of 35-38, 39-47 time points. This observations state that at these two times the slices area of the human brain is busy any task and after that time, the human take rest to attend further actions. The deviation of new CSCKS estimated curves (red curves) are much more closed to the true estimated curves (black curves) than that of CSCKS, SCKS, and DEM estimated magenta, cyan and green curves, respectively, except the DEM (S1) curve. If we closely observed that the deviation pattern of DEM (S1) curve is unstable at time point 10-20, at this time duration, the DEM (S1) curve is suddenly ups and downs. For this reason, the DEM algorithm cannot estimate the accurate scenario of hidden

states. The deviation in arbitrary unit (au) of 9-22 time points are 0.14 for true value, 0.125 for new CSCKS (89% similarity with true value), 0.115 for CSCKS (82% similarity with true value), 0.05 for SCKS (36% similarity with true value). The new CSCKS algorithm is to estimate hidden states 7%, 53% more accurate than that of CSCKS, SCKS algorithms, respectively. So, it is clear from the **Fig.3** that the performance of new CSCKS algorithm is more accurate to determine hidden states than that of others algorithms.

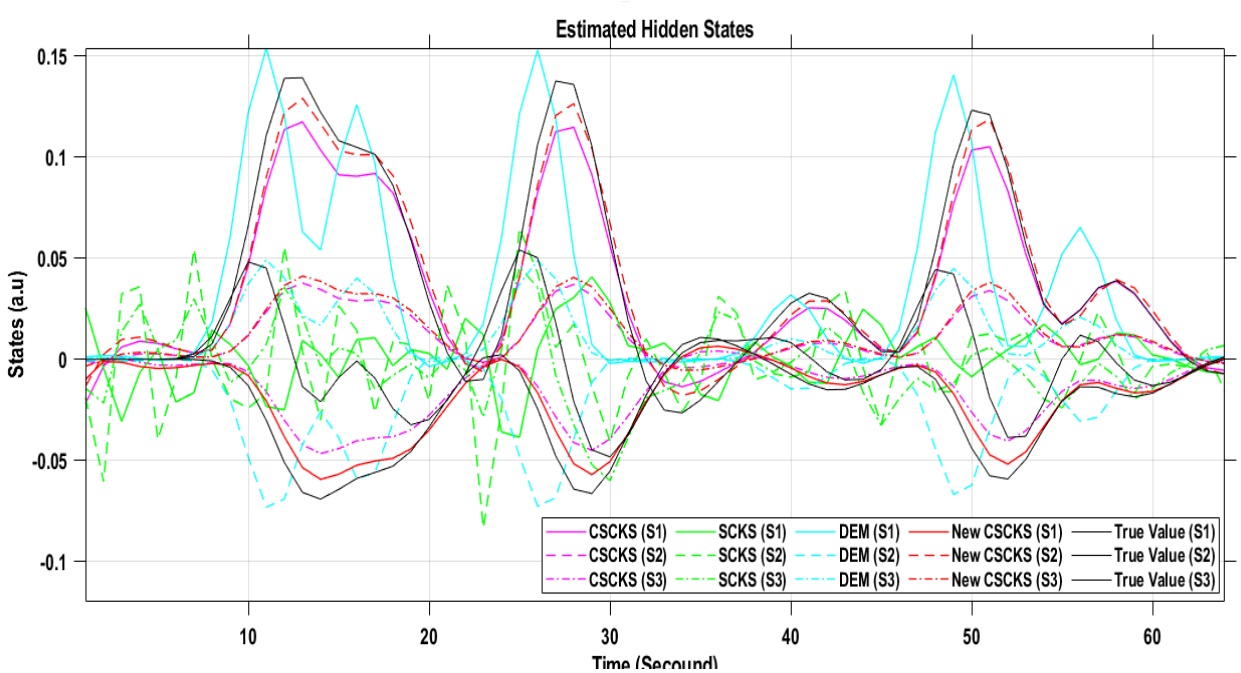

Fig.3: The simulation result of hidden states at $\Delta t = 0.2$ Second in case of DEM, SCKS, CSCKS and New CSCKS.

Fig.4 shows the estimated results of model parameters – rate of signal decay K (θ_1), rate of flow dependent elimination χ (θ_2), and resting oxygen extraction fraction λ (θ_3) at integration step Δt 0.2 second in case of DEM, CSCKS, and new CSCKS algorithms. The estimated result of signal decay is 99%, 94%, and 86% similar with true value (signal decay 0.65) compare with new CSCKS (signal decay 0.6526), DEM (signal decay 0.6146), and CSCKS (signal decay 0.7408)algorithm, respectively. The flow dependent elimination and resting oxygen extraction fraction are also more similar with true value within new CSCKS algorithm than that of others.

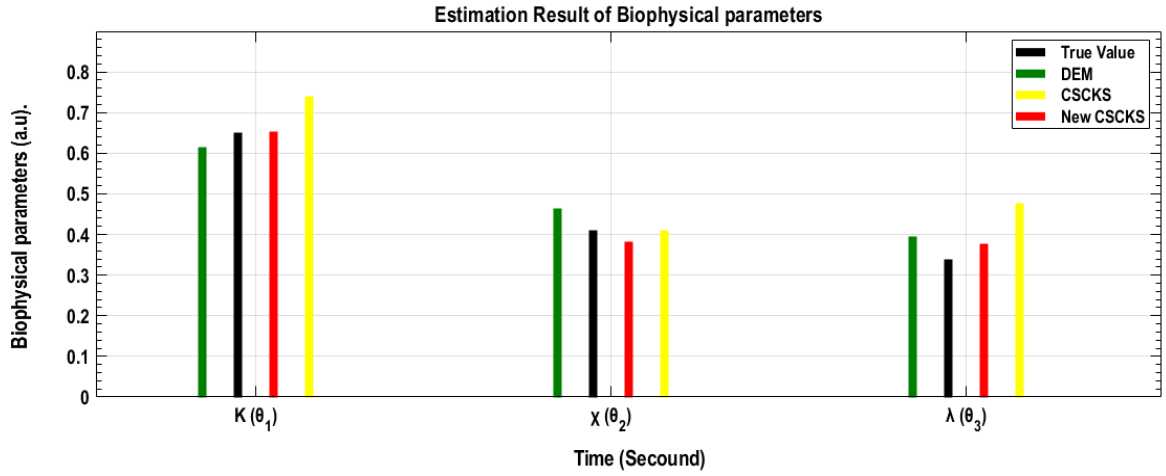

Fig.4: Estimated result of biophysical parameters.

Fig.5 shows the estimated results of PSD of BOLD response. In this estimation process; we consider reference frequency 10 kHz. The estimated result shows that the minimum BOLD signal strength of new CSCKS and CSCKS algorithm are almost same, 10^{-11} dB at 3220Hz(Nominal frequency 0.322), whereas the SCKS and DEM algorithm shows the estimated PSD 10^{-14} dB at 3020 Hz (Nominal frequency 0.3020), 10^{-16} dB at 2980 Hz (Nominal frequency 0.2980), respectively. So, it is clear from the information that the strength of BOLD signal response of CSCKS method is more than that of SCKS and DEM method.

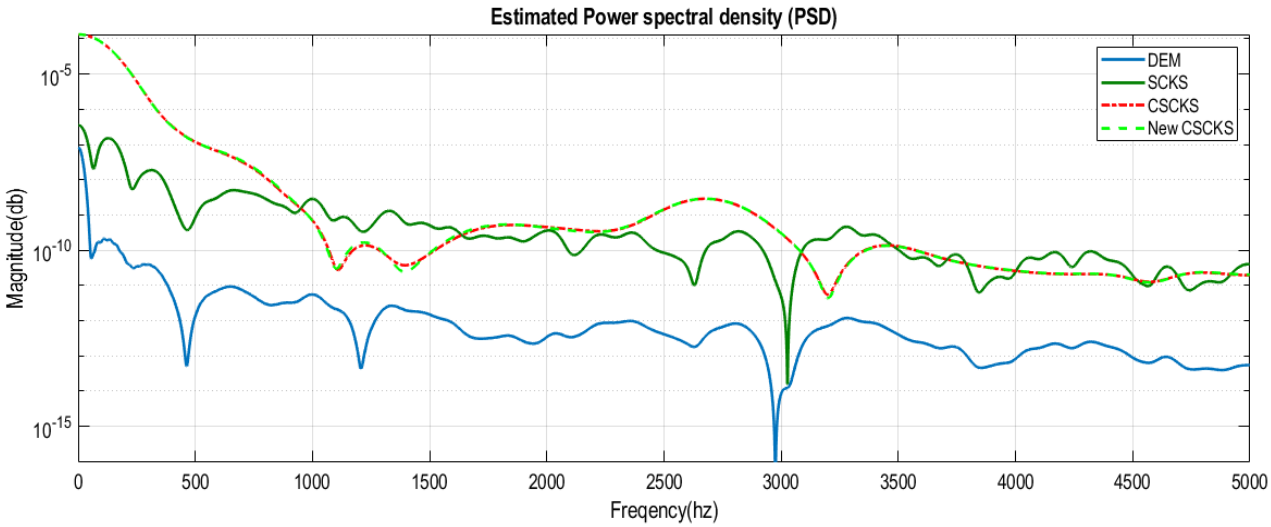

Fig.5: The simulation result of PSD of BOLD signal in case of DEM, SCKS, CSCKS and New CSCKS.

4. Conclusion

The improved CSCKS method is able to simulate in all frequency interference factors with any confounds and able to make hidden states, model parameters, PSD of BOLD response more accurately than that of existing methods. We can figure out the unknown stimulus that is created in our brain as a result of human activity by applying the inverse de-convolution method. In this method, genuine BOLD contrast is used, as determined by fMRI images. The improved CSCKS method is more accessible for reliably de-convolution BOLD signal. Our new CSCKS algorithm is to estimate hidden states of hemodynamic model more 7% accurate than that of existing methods.

5. Acknowledgement

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6. Conflict of interest

We declare that we have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

7. Funding

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8. Authors' contribution

The overall model design, data collection as well as the simulation of the proposed model was performed by the corresponding author Md. Roni Islam. Another author Md. Biplob Hossain contributed to write the paper and to draw some output figures.

9. Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

10. Data Availability Statement

The data was acquired raw images related zip file is available in an open access SPM website. The links of attention dataset are (https://www.fil.ion.ucl.ac.uk/spm/data/attention/) .

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