

A model of rhythm generation and functional connectivity during a simple motor task: preliminary validation with real scalp EEG data

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Abstract. A simple original model of five interconnected neural populations is used to investigate the origin of EEG rhythms in the cerebral cortex during a simple motor task. The model considers three regions of interest (the cingulate cortex, the primary motor cortex and the supplementary motor cortex), each oscillating with a medium-frequency rhythm, and two additional remote regions (without a clear anatomical counterpart) able to induce alpha and gamma rhythms. The model has been fitted (in terms of power spectral density, PSD, and coherences among populations) to real EEG data measured on the scalp on a volunteer during a right foot movement task and then propagated to the cortex. The estimated parameters include the connectivity weights among the populations, and the time constants of intra-area excitatory synapses. Results show that the model is able to simulate the occurrence of multiple PSD peaks in the three examined regions quite well, at the same time providing realistic values of coherence. It can be useful to gain a deeper insight into the functional connectivity links occurring among brain regions during simple tasks, and provide artificial data for testing existing algorithms. Virtues and possible limitations of the method are discussed, and lines for future research pointed out.

Keywords: Neural mass models; Parameter estimation; Functional connectivity; EEG rhythms; EEG coherences; Motor tasks

1. Introduction

Analysis of functional connectivity between different brain areas during the execution of motor or cognitive tasks has become a fundamental problem in computational neuroscience, which may have important theoretical and practical consequences. The problem is of the greatest value to deepen the present basic neurophysiological knowledge, while practical outcomes may be concerned with rehabilitation of patients with brain lesions, brain-computer interface and the design of innovative prostheses for driving voluntary movements.

Actually execution of a motor task, and the consequent changes in cortical electrical activity and EEG, are thought to be realized by the interaction among different regions of the brain, which are mutually connected and interact in complex non-linear ways. Functional connectivity is usually analyzed from electromagnetic measurement (such as scalp EEG or MEG) and using sophisticated processing algorithms [Astolfi et al., 2005; Astolfi et al., 2006; Astolfi et al., 2007]. These techniques, however, are generally based on linear assumptions, whereas neural processing is intrinsically non-linear. Furthermore, data are generally corrupted by noise, which may affect algorithms for brain connectivity estimation in a complex and often unpredictable way. The use of mathematical models and computer simulation techniques has been advocated to help the analysis of this information, to favor the conceptualization of knowledge, and the formulation of coherent and comprehensive theories [Horwitz et al., 1999; Horwitz et al., 2000]. Furthermore, computer models can provide artificial data, which may be used as input to test the accuracy and reliability of information processing algorithms.

Various mathematical models have been proposed during the past decades to simulate neural signals. These models can be subdivided into two main classes: detailed models, which try to reproduce dynamics of single neurons, or simplified models, in which neurons are reproduced at a population level [Whittington et al., 2000]. The complexity of neural networks which generate EEG/MEG makes the second approach more useful. Population models mimic the activity of entire neural groups, via the feedback arrangement of excitatory and inhibitory populations; this interaction induces rhythmic patterns similar to those observed in EEG recordings. Neural mass-models of cortical columns, particularly useful to simulate realistic EEG signals, were developed by Lopes da Silva et al. [Lopes da Silva et al., 1976] and by Freeman [Freeman, 1978] in the mid seventies, and subsequently improved and extended by Jansen and Rit [Jansen and Rit, 1995] and Wendling et al. [Wendling et al., 2002]. These models have been used to simulate alpha rhythms [Jansen and Rit, 1995], dynamics in the olfactory cortex [Freeman, 1987], or paradoxical epileptic discharges [Wendling et al., 2000; Wendling et al., 2002]. However, just a few studies deal with the problem of simulation of functional connectivity among different regions of interest (ROIs), and on dependence of cortical EEG on connectivity patterns [David and Friston, 2003; Sotero et al., 2007].

In recent years, we developed original neural mass models to simulate realistic EEG power spectral densities in some regions of the cortex during simple motor tasks, by acting just on a few model parameters which describe synaptic kinetics in the main regions and the connectivity among them [Zavaglia et al., 2006; Ursino et al., 2007]. Furthermore, the model was used to identify simple connectivity circuits able to explain the EEG tracings in the scalp [Ursino et al., 2007].

Aim of this work is to extend and improve the previous model for simulating EEGs power spectral densities, and to propose its use for the estimation of connectivity relationships among ROIs from high-resolution EEG data taken on the scalp. Two main improvements are gained compared with previous recent works: i) we use a simpler model of a single ROI, which allows simulation of EEGs power spectral densities with a smaller number of parameters and hypotheses; ii) parameters of brain connectivity are estimated, in a few exemplary cases, by accounting not only for the rhythms generated in the different ROIs and their relative power density, but also for some aspects of cross-power spectral density and coherence among regions.

The method is first presented in a synthetic form. Subsequently, some results, concerning a simple motor task (right foot movement) are shown. The discussion underlines the main virtues and limitations of the proposed method and points out the main aspects for future research.

2. Material and Methods

2.1. Model of a single population

The model of a single population was obtained by modifying equations proposed by Wendling et al. [Wendling et al., 2002]. It consists of four neural groups which communicate via excitatory and inhibitory synapses: pyramidal cells, excitatory interneurons, inhibitory interneurons with slow synaptic kinetics, and inhibitory interneurons with faster synaptic kinetics. Each neural group receives an average postsynaptic membrane potential from the other groups, and converts the average membrane potential into an average density of spikes fired by the neurons. Three different kinds of synapses are used to describe the synaptic effect of excitatory neurons (both pyramidal cells and excitatory interneurons), of slow inhibitory interneurons and of fast inhibitory interneurons. Each synapse is simulated by an average gain (A , B , G for the excitatory, slow inhibitory and fast inhibitory synapses, respectively) and a time constant (in the model, the reciprocal of these time constants is denoted as a_I , b_I and g_I , respectively). The input to the model (named $p(t)$) excites pyramidal neurons, and represents all exogenous contributions, both excitation coming from external sources and the density of action potentials coming from other connected regions. Model equations are described in detail in a previous work [Zavaglia et al., 2006], hence are not reported here for the sake of brevity.

2.2. Model of connectivity among populations

In order to study how the different populations interact, we then considered a model composed of N populations (in the present work $N = 5$), which are interconnected through long-range excitatory connections. These connections can include both feed forward and feedback links among populations, with different weights. To simulate connectivity, we assumed that the average spike density of pyramidal neurons (z_0) affects the target population via a weight factor, W , and a time delay, T . This is achieved by modifying the input quantity $p(t)$ of the target population. In the following, in order to deal

with several populations simultaneously, we will use the subscripts i (or j) to denote a quantity which belongs to the i th (or j th) population.

Hence, the input $p_i(t)$ to the i th population can be computed as follows

$$p_i(t) = n_i(t) + \sum_j W_{ij} z_{0,j}(t - T) \quad (1)$$

where W_{ij} is the weight of the synaptic link from the j th (pre-synaptic) population to i th (post-synaptic) population, T is the time delay (assumed equal for all synapses), $n_i(t)$ represents a gaussian white noise with mean value m_i and standard deviation σ_i , and the sum in the right hand member of Eq. 1 is extended to all populations, j , which target into the population i .

2.3 Acquisition of experimental data

The experiment took place in the laboratories of the Santa Lucia Foundation, Rome, after the informed consent was obtained. The subject was comfortably seated in an armchair with both arms relaxed, in an electrically shielded, dimly lit room. He was asked to perform a brisk protrusion of the lips (lip pursing) while he was performing a right foot movement. A 58-channel EEG system (BrainAmp, Brainproducts GmbH, Germany) was used to record electrical potentials by means of an electrode cap, accordingly to an extension of the 10-20 international system. A/D sampling rate was 200 Hz. During motor task, subject was instructed to avoid eye blinks, swallowing or any movement other than the required foot movements. A 3-shell Boundary Element Model (BEM) of the head was used to estimate the cortical current density (CCD) distribution in some regions of interest (ROI) of the cortex (*the cingulate cortex* (CMA_L), *the primary motor area* (M1F_L), and *the supplementary motor area* (SMAp_L)) starting from activity measured on the scalp. The procedure used is described in previous works [Babiloni et al., 2005; Zavaglia et al., 2006; Ursino et al., 2007]. From the CCD, the average estimated cortical activity in the region has then been evaluated. The latter has been successively subjected to spectral analysis in order to produce the spectra used for the estimation of the model parameters.

2.4. The model of the motor task

Simulations performed in a previous paper [Zavaglia et al., 2007] demonstrate that a single population model, stimulated with input white noise, produces just a unimodal spectrum (i.e., a spectrum with a single well defined peak). The position of the peak primarily depends on the synaptic kinetics (i.e., on parameters a_I , b_I and g_I). However, a single population can oscillate with different simultaneous rhythms, provided that some of these rhythms come from external sources (for instance, from remote regions).

According to these results, we assumed that the main populations which participate to the motor task (i.e., *the cingulate cortex*, *the primary motor area* and *the supplementary motor area*) exhibits an internal kinetics, corresponding to a rhythms in the medium frequency range (beta band, 12-30 Hz) but they also receive a low-frequency rhythm (in the alpha band (4-12 Hz)). The latter may come from subcortical region (like the thalamus) or from other regions in the cortex (like occipital lobes) not directly investigated here. Furthermore, we assumed that the cingulate cortex may also receive a high-frequency rhythm (greater than 30 Hz, gamma range) and, in turn, can affect this rhythm. In fact, a gamma rhythm is considered essential for binding information among different regions, and for high-level information processing.

The model is thus implemented through the connectivity pattern shown in Fig. 1, which is composed of five interconnected populations with different synaptic kinetics. The populations POP LF and POP HF exhibit an intrinsic rhythm at low and high frequency respectively. The other three populations (POP 1, POP 2 and POP 3) exhibit an intrinsic rhythm at medium frequency and simulate the cingulate cortex (ROI1), the primary motor area (ROI2) and the supplementary motor area (ROI3), respectively. The corresponding values of parameters are described in detail in previous works [Zavaglia et al., 2006; Zavaglia et al., 2007] hence are not reported here for the sake of brevity.

In the present model, we assumed that POP LF receives a significant white noise and activates the other populations, but does not receive any connectivity from them. On the contrary, POP HF, POP1, POP2 and POP3 receive a negligible Gaussian white noise but can be activated by connections from all other populations as in Fig. 1. Hence, the motor command originates from region LF, and spreads toward the cingulate cortex. The latter, in turn, recruits a high-frequency rhythm, and drive the primary and supplementary motor areas. The latter are linked via a feedback loop.

2.5. Fitting procedure

In order to verify the ability of the model to mimic experimental data, the model has been fitted to real spectra computed in the cingulate cortex (ROI1), the primary motor area (ROI2) and the supplementary motor area (ROI3) during a right foot movement task in one normal subjects (two trials, see section 2.3). The fitting was performed with an automatic procedure, by minimizing a least square criterion function of the difference between model and real data. Parameters estimated for the minimization are the connection strengths among populations (W_{1L} , W_{1H} , W_{H1} , W_{23} , W_{32} , W_{2L} , W_{3L} , W_{21} , W_{31}) and the time constant of excitatory synapses in the five populations (inversely related to a_1^L , a_1^H , a_1^1 , a_1^2 and a_1^3). The information used for building the criterion function includes the PSD in the range 4-50 Hz (evaluated with a frequency step = 1Hz) and the coherence among the population, ROI1-ROI2, ROI1-ROI3 and ROI2-ROI3 evaluated at the frequencies of peaks in the PSD of ROI1. In fact, according to the model (Fig. 1) the cingulate cortex drives the supplementary and primary motor areas.

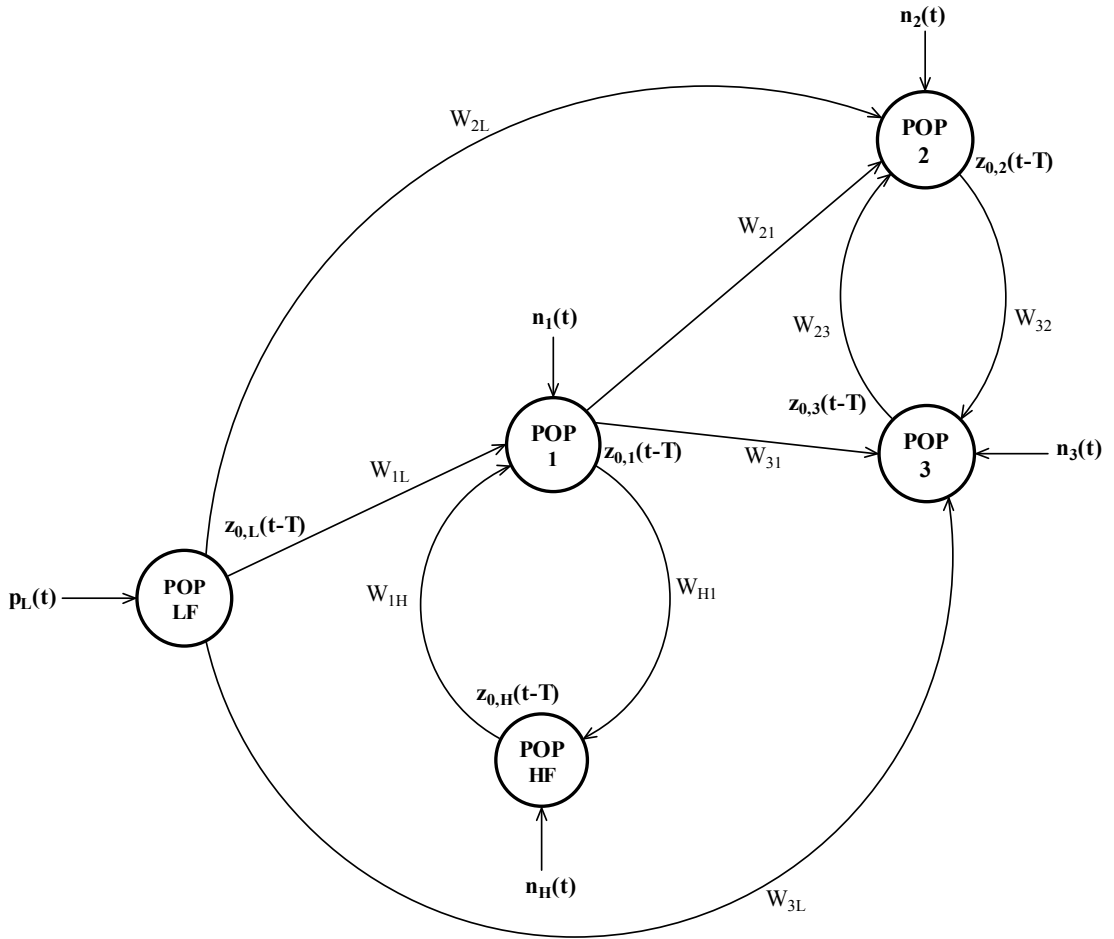


Figure 1. Example of connectivity among five populations, according to the present model. The populations POP LF and POP HF exhibit intrinsic rhythms at low and high frequency respectively; POP1, POP 2 and POP 3 exhibit intrinsic rhythms at medium frequency.

3. Results

The results on the comparison between model and real PSDs, and between model and real coherence, obtained in two trials of one healthy subject are shown in Figs. 2 and 3. The corresponding values of the parameters are reported in Table 1. Results show that the model is able to simulate real PSDs quite well in both examined cases and that the parameter values are quite repetitive within the subject. The results obtained with the coherence are encouraging and could be useful to establish causal relationships among remote cortical regions connected during a task. However, it should be noted that the model overestimates the coherence between RO1 and RO12, while it underestimates coherences between RO13 and the other two regions.

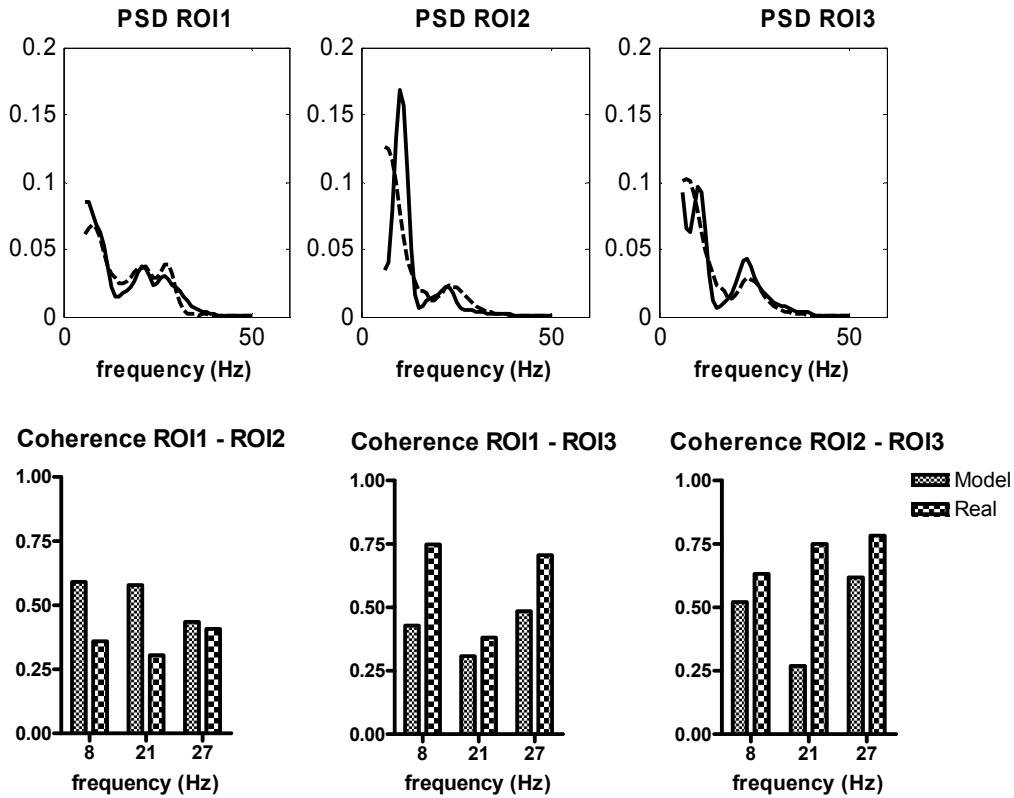


Figure 2. Example of model fitting to three real power spectral densities (upper panels), belonging to cingulated cortex (RO11), primary motor cortex (RO12) and supplementary motor cortex (RO13) in one subject (trial1). The fitting has been achieved by estimating the connection strengths among populations and the time constant of excitatory synapses in the five populations of Fig.1. The values for mean and variance of the noise are: $m_L=0$, $m_H=-50$, $m_I=-50$, $m_2=-50$, $m_3=-50$ and $(\sigma_L)^2=(\sigma_H)^2=(\sigma_I)^2$ $(\sigma_2)^2=(\sigma_3)^2=20$. Continuous lines represent experimental Power Spectral Densities, while dashed lines are model ones. Estimated parameters are shown in Table 1. The three lower panels represent the comparison between model and real coherence computed at the frequency of the peaks of RO11.

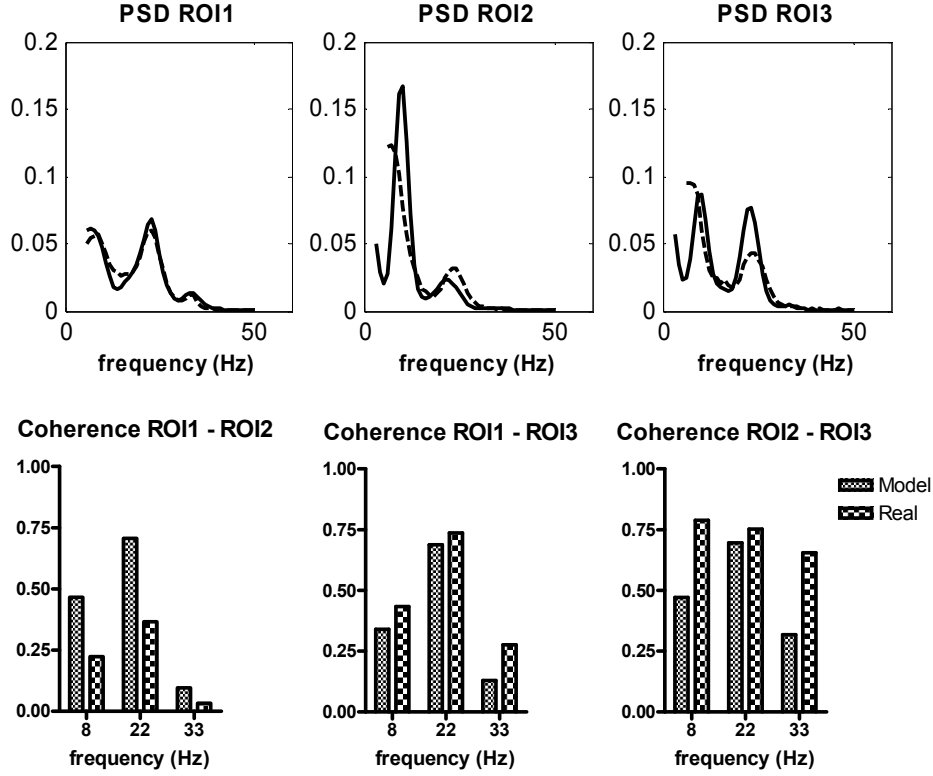


Figure 3. Example of model fitting to three real power spectral densities (upper panels), belonging to cingulate cortex (ROI1), primary motor cortex (ROI2) and supplementary motor cortex (ROI3) in one subject (trial2). The fitting has been achieved by estimating the connection strengths among populations and the time constant of excitatory synapses in the five populations of Fig.1. The values for mean and variance of the noise are: $m_L=0$, $m_H=-50$, $m_I=-50$, $m_2=-50$, $m_3=-50$ and $(\sigma_L)^2=(\sigma_H)^2=(\sigma_I)^2$ $(\sigma_2)^2=(\sigma_3)^2=20$. Continuous lines represent experimental Power Spectral Densities, while dashed lines are model ones. Estimated parameters are shown in Table 1. The three lower panels represent the comparison between model and real coherence computed at the frequency of the peaks of ROI1.

	W_{IL}	W_{HI}	W_{IH}	a_I^L	a_I^I	a_I^H
TRIAL1	100.0	86.0	25.0	20.5	70.0	42.0
TRIAL2	84.0	86.0	15.0	20.5	75.0	63.5

	W_{21}	W_{31}	W_{23}	W_{32}	W_{2L}	W_{3L}	a_I^2	a_I^3
TRIAL 1	1.0	10.0	18.0	5.0	91.7	80.0	75.0	80.0
TRIAL 2	1.0	47.0	11.0	0.0	96.0	47.0	78.0	83.4

Table 1.

Estimated parameters for the cingulate cortex, primary motor cortex and supplementary motor cortex in one subject (two trials) during a right foot movement task.
(Parameter a_I is in s^{-1})

4. Discussion

In the present work, a simple original model of five interconnected neural populations has been used to investigate the origin of EEG rhythms in the cerebral cortex during a simple motor task, and to point out the possible connectivity patterns linking the cingulate cortex, the primary motor area and the supplementary motor area. The main basic idea of our model is that each region receives a low-frequency rhythms from a common remote region (maybe the thalamus, and/or an occipital region). Moreover, the cingulate cortex drives the other two regions and is also involved in the synchronisation of a gamma rhythm with other areas in the brain. Indeed, the gamma rhythm is frequently involved in high mental activity. Then, we tested the possibility that the simple proposed schema is able to simulate real power spectra in the cortex, and to account for some aspects of the observed coherence among EEGs, by acting just on a few parameters which represent the strength of inter-area connections and the kinetics of excitatory synapses inside the regions.

The results are encouraging, both for what concerns the presence of multiple rhythms in the same region, the repeatability of parameter values in the same subject, and the coherence among EEG signals. However, some differences can be observed among model and real coherences. In particular, looking at Figs. 2 and 3, one can observe that the model generally overestimates the coherence between population 1 (the cingulate cortex) and the population 2 (the primary motor cortex), while it underestimates the coherences of the cingulate cortex and primary motor cortex with the supplementary motor cortex. The significance of these differences deserves further analysis.

The model may have several possible applications. First, it may be useful in neurophysiology to help understanding the functional links among the regions involved in a task and, in perspective, to analyze the changes in connectivity occurring during the temporal prosecution of a task, or as a consequence of an input change or a pharmacological treatment. Furthermore, the model may also be useful to investigate differences in functional connectivity and EEG rhythms generation between control subjects and paraplegic patients. These differences may be exploited in the computer-interface problem. The model may also be valuable to generate artificial cortical EEG data, with a pre-assigned pattern of connectivity. These data, propagated to the scalp according to anatomical knowledge, and corrupted with noise, may be used to test the accuracy and performances of the algorithms (such as the directed coherence or the partial directed coherence) commonly employed to derive connectivity from scalp EEG.

The present results, however, are just preliminary, and several additional steps should be performed to expand model applicability for the study of neural integration during motor tasks. A first important step is to perform a sensitivity analysis on model parameters, to discover which among the estimated parameters can be detected with sufficient accuracy based on available data, and which parameters should be considered with caution. A further important point is to improve the analysis of coherence and perhaps, replace the use of this index with other indices more suitable for the interpretation of non-linear systems. Indeed, power spectral density and coherence (i.e., cross spectra) are commonly used to estimate transfer functions in linear systems. Other indices (such as bi-spectra), explicitly conceived to investigate interactions between non-linear systems, may be utilized in future works within the present automatic estimation procedure. Finally, it might be interesting in future works to encompass more detailed anatomical and/or physiological knowledge into the present model. This knowledge may be essential to account for a greater number of ROIs in the description of brain integration during the motor task, at the same time establishing some constraints on parameter values and on model structure, which may drive the estimation procedure. Indeed, one of the main problems in the present estimation procedure is the large number of parameters simultaneously involved, which precludes the possibility to incorporate a greater number of regions without enforcing some limitations in the parameter space.

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