A model of power spectral density in cortical EEG, for the study of cortical connectivity

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Abstract

Neural mass models have been used for many years to study the dynamics of neural groups, or of entire cortical areas, in a simple and computationally inexpensive way. In this paper, we modified a model proposed by Wendling et al. [6] to analyze EEG power density in some cortical areas during a simple task (finger movement). The work consists of three subsequent stages: 1) in the first we performed a sensitivity analysis of the main model parameters (i.e., strength of inhibitory and excitatory synapses and their time constants) and evaluated their role in affecting power spectral density (PSD). This analysis confirmed the possibility to simulate various EEG rhythms by modifying just the strength and time constants of a few synapses. However, a single neural mass model produces a narrow frequency band, which cannot mimic the overall complexity of EEG in an entire cortical area. 2) Hence, in the second stage we built a model of a region of interest (ROI) by combining three neural mass models arranged in parallel. With this model, and using an automatic fitting procedure to establish parameter values, we carefully reproduced the PSD of cortical EEG in six ROIs during finger movement. Cortical EEGs were computed with an inverse propagation model, starting from measurement performed with 128 electrodes on the scalp. 3) In the third stage, we simulated how PSD in some ROIs can be modified, as a consequence of some hypothetical functional connectivity among the regions.

Results show that the proposed model is able to mimic PSD of cortical activity acting on a few parameters only. The pattern of power spectra, however, is significantly modified by a functional connectivity among the ROIs.

Knowledge obtained from the model may be exploited to derive information on functional connectivity, starting from non-invasive EEG measurements.

Keywords: neural models, brain connectivity, intracerebral EEG.

1 Introduction

Cognitive functions are the result of the interaction among several cortical regions in the brain, each dedicated to specific functions. Hence, differences in brain activation among different tasks, or among different subjects in the same task, may derive both from a diversity in the dynamics of the cortical regions involved and in their synaptic connections. In other words, similarly activated regions may produce different responses due to variations in their structure and/or in their functional connectivity. The use of mathematical models and computer simulation techniques has been frequently advocated to help the analysis of this problem [1, 2]. Indeed, various mathematical models have been proposed during the past decades to simulate neural signals, with different purposes and at different levels of detail. Among the others, "neural mass 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. These models were first developed in the mid seventies [3, 4], and subsequently improved and extended by Jansen and Rit [5] and Wendling et al. [6]. However, just a few studies deal with the problem of simulation of the entire frequency content in a cortical region of interest (ROI) during a real task, or with simulation of functional connectivity among different ROIs [7-9].

The aim of this work is to utilize a neural model, consisting of several populations arranged in parallel, in order to simulate EEG activity in several regions of interest (ROI) during a simple cognitive task. Two main objectives are pursued. First, we wish to analyse whether a model, based on several populations arranged in parallel, is able to reproduce the frequency content of real cortical EEG signals in different ROIs, by assigning just a few parameters via a simple best fitting procedure. Subsequently, we wish to analyze the effect of different patterns of connectivity among ROIs, via a sensitivity analysis on the parameters specifying this connectivity. Hence, the second objective is to reach a deeper insight into how EEG activity is affected by the reciprocal connections among cortical regions, and whether this connectivity may be recovered from analysis of EEG activity only.

In perspective, the final aim is to arrive at realistic models of cortical activities, which can be used to simulate and decipher EEG and to summarize data from different neuroimaging techniques during cognitive tasks.

2 Model description

First, we will describe the model of a single neural population. Subsequently, the model of an overall region of interest will be introduced, and the problem of connectivity will be dealt with.

The model of a single population was obtained by modifying equations proposed by Wendling et al. [6]. In this model cortical activity derives from the interaction among four neural groups: pyramidal cells, excitatory interneurons, inhibitory interneurons with slow synaptic kinetics, and inhibitory interneurons with faster synaptic kinetics (see Fig. 1).

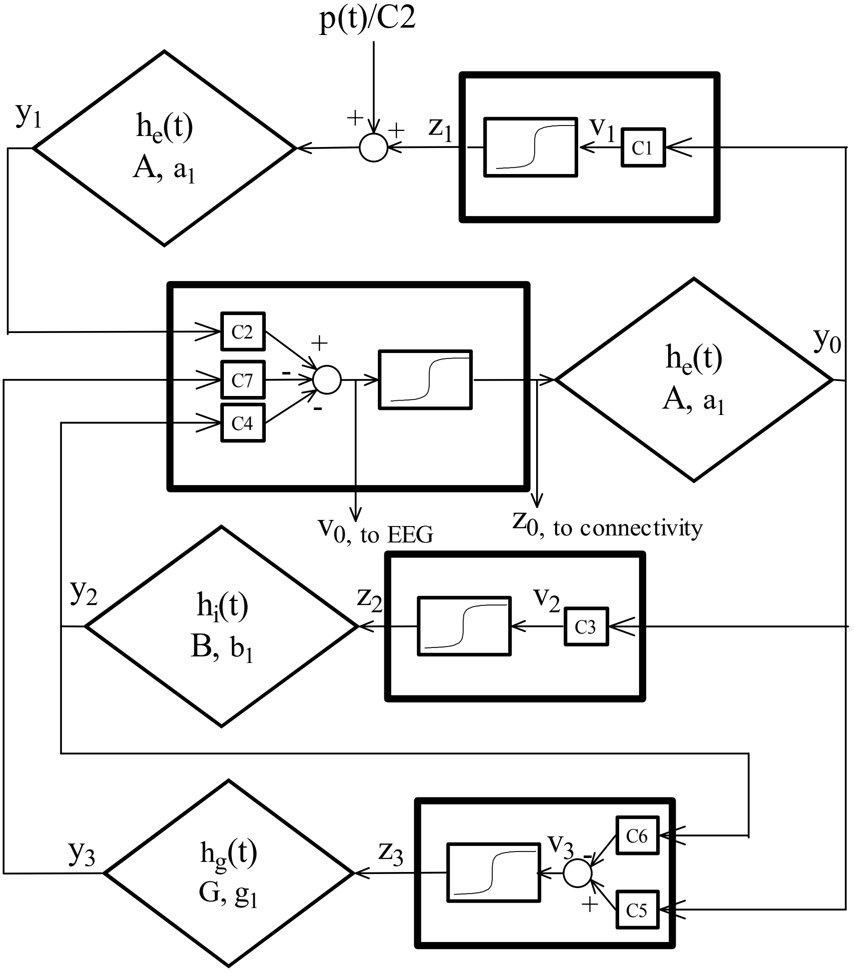

Figure 1: Layout of a single population model.

Each neural group receives average postsynaptic membrane potentials from the other groups, and converts the average membrane potential into an average density of spikes fired by the neurons. This conversion is simulated via a static sigmoidal relationship. The effect of the synapses is described via second order linear transfer functions, which convert the presynaptic spike density into the postsynaptic membrane potentials. Three different kind of synapses, with impulse response h_e, h_i and h_g, (see Fig. 1), 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, respectively. According to Fig. 1, model equations can be written as follows:

Pyramidal neurons

$$\frac{dy_0(t)}{dt} = y_5(t)$$

$$\frac{dy_5(t)}{dt} = A \cdot a_1 \cdot z_0(t) - 2 \cdot a_1 \cdot y_5(t) - a_1^2 \cdot y_0(t)$$

$$z_0(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_0)}}$$

$$v_0(t) = \mathrm{C}_2 \cdot \mathrm{y}_1(\mathrm{t}) \text{-} \mathrm{C}_4 \cdot \mathrm{y}_2(\mathrm{t}) \text{-} \mathrm{C}_7 \cdot \mathrm{y}_3(t)$$

Excitatory interneurons

$$\frac{dy_1(t)}{dt} = y_6(t)$$

$$\frac{dy_6(t)}{dt} = A \cdot a_1 \cdot (z_1(t) + \frac{p(t)}{C_2}) - 2 \cdot a_1 \cdot y_6(t) - a_1^2 \cdot y_1(t)$$

$$z_1(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_1)}}$$

$$v_1(t) = \mathrm{C}_1 \cdot \mathrm{y}_0(\mathrm{t})$$

Slow inhibitory interneurons

$$\frac{dy_2(t)}{dt} = y_7(t)$$

$$\frac{dy_7(t)}{dt} = B \cdot b_1 \cdot z_2(t) - 2 \cdot b_1 \cdot y_7(t) - b_1^2 \cdot y_2(t)$$

$$z_2(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_2)}}$$

$$v_2(t) = \mathrm{C}_3 \cdot \mathrm{y}_0(\mathrm{t})$$

Fast inhibitory interneurons

$$\frac{dy_3(t)}{dt} = y_8(t)$$

$$\frac{dy_8(t)}{dt} = G \cdot g_1 \cdot z_3(t) - 2 \cdot g_1 \cdot y_8(t) - g_1^2 \cdot y_3(t)$$

$$z_3(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_3)}}$$

$$v_3(t) = \mathrm{C}_5 \cdot \mathrm{y}_0(\mathrm{t}) - \mathrm{C}_6 \cdot y_2(t)$$

In these equations, the symbols v_i represent the average membrane potential *(i* = 0, 1, 2, 3 for the four groups). These are the input for the sigmoid function which converts it into the spikes (z_i, i = 0, 1, 2, 3) fired by the neurons. Then, this output enters into the synapses (excitatory, slow inhibitory or fast inhibitory), represented via the second order linear functions. Each synapse is described by a synaptic gain (*A, B, G* for the excitatory, slow inhibitory and fast inhibitory synapses, respectively) and a time constant (the reciprocal of a_1, b_1, g_1

respectively). The outputs of these equations, which can be excitatory, slow inhibitory or fast inhibitory, represent the postsynaptic membrane potential (y_i, $i = 0, 1, 2, 3$). Interactions among neurons are represented via seven connectivity constants (C_i). Finally, *p(t)* represents a Gaussian white noise with assigned mean value and variance, which describes the overall density of action potentials coming from other regions. This term will be modified to simulate connectivity among different ROIs.

The previous model was used to simulate a single population, the dynamic of which ensues from the interactions of the four neural subgroups. As shown below, however, a single population can produce just a single rhythm, i.e., it is unable to simulate the entire frequency content of a real EEG. For this reason, the model of an overall ROI has been constructed by using three populations arranged in parallel. Each population is characterized by different values of time constants (i.e., of parameters a_1, b_1, g_1) and so can produce a different rhythm. The cortical EEG of a ROI is obtained as the mean value of the membrane potentials of pyramidal neurons in the three populations (i.e., averaging quantity v_0).

Finally, in order to simulate connectivity among different regions, we assume that each ROI can send its spike rate to other ROIs. Hence, output of each ROI is computed as the mean value of the spike rate of pyramidal neurons in the three populations (i.e., quantity z_0 in the previous equations). This quantity is sent to the input of populations in other ROIs (i.e., it is summed to quantities *p(t)*) via a pure delay and a gain constant. An example of connectivity among ROIs is illustrated in Fig. 2. In the present study, all time delays among ROIs have been taken equal to 10 ms. The gain factors have been assigned different values, in order to simulate various patterns of connectivity and analyze their influence on the EEG of the downstream region.

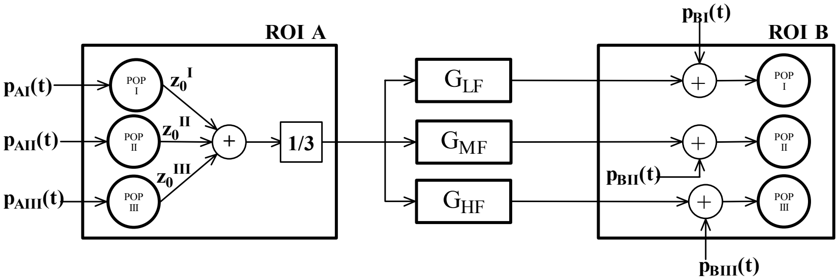

Figure 2: Example of connectivity between two ROIs.

3 Results

First, we analyzed the model of a single population described above. To this end, we performed a sensitivity analysis of the main model parameters and evaluated their role in affecting power spectral density (PSD). This analysis confirmed the possibility to simulate different EEG rhythms, by modifying just the strength and time constants of synapses. In particular, the sensitivity analysis shows that a single neural population model can reproduce just a narrow frequency band. The position of this band can be moved from low-frequency (α rhythm) to high frequency (γ rhythm) by acting only on the gains and time constants. Some examples are illustrated in Fig.3.

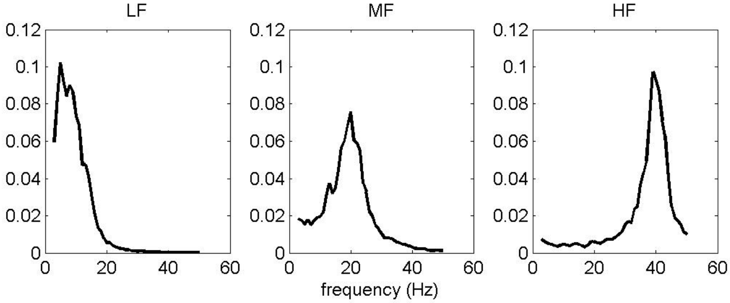

Figure 3: Dependence of power spectral density (PSD) upon the parameters A, B, G (strength of inhibitory and excitatory synapses) and a_1,b_1,g_1, (inverse of time constants). The single neural population model can produce a narrow frequency band, which moves from low frequency (LF), to medium frequency (MF) and high frequency (HF). The parameters used are: LF parameters: A=4.5 B=5 G=25 a_1=40 b_1=20 g_1=300. MF parameters: A=7 B=6 G=60 a_1=85 b_1=30 g_1=350. HF parameters: A=7 B=4.5 G=90 a_1=110 b_1=40 g_1=790.

The previous analysis demonstrate that this model cannot reproduce the overall complexity of EEG in an entire cortical area. So, the second step of our research was to build a model of a ROI, by adding three neural populations in parallel (see Fig. 2). With this model, there is the possibility to obtain a power density spectrum made up of three different bands. In order to verify the capacity of this model to mimic the entire frequency content of a ROI, the model has been fitted to real cortical EEG obtained in six different ROIs during a simple task (finger movement). Cortical EEGs were computed with an inverse propagation model, starting from measurement performed on the scalp with 128 electrodes [10]. The best fitting has been achieved by means of an automatic algorithm which minimizes a least square cost function of the difference between model PSD and real PSD. Parameters used during the minimization are the synaptic gains of each population, whereas time constants were assigned fixed values equal to those used in Fig. 3 for the three populations. All spectra have been normalized to have unitary area between 2 Hz and 50 Hz. The results of the best fitting procedures are reported in Fig. 4.

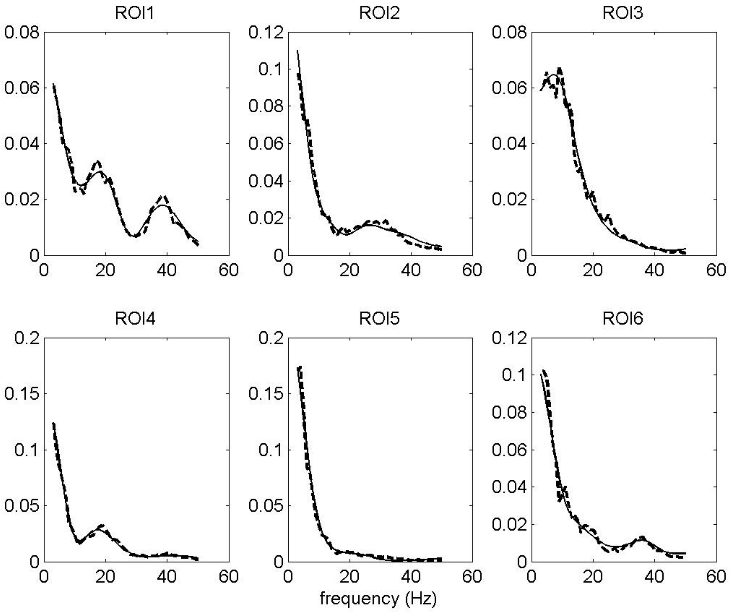

Figure 4: Fitting of experimental signals from six regions of interest (ROI). The model used for the automatic fitting procedure was obtained by arranging three single population models in parallel. Dashed line is used for signals simulated by the model of a ROI. Continuous line is used for experimental signals. The three populations in each ROI have the same time constants used in Fig. 3 to simulate LF, MF and HF bands, and differ as to the value of synapses.

In the third stage, we investigated the connectivity among three simulated cortical areas, to understand how connectivity can modify the PSD. With the model described before, we simulated three ROIs (named ROI A, ROI B, ROI C), having the same synaptic parameters but with different input noise. In particular, in the example below we used the same parameters as in ROI1 of Fig. 4, since this ROI, if suitably stimulated by the input noise, can produce rhythms in all frequency bands. ROI A receives a significant input noise, *p(t)*, just in the first population, hence it exhibits significant activity, but a spectrum similar to that of ROI3 in Fig. 4. ROI B and ROI C were identical as ROI A, but we assumed that they receive just negligible input noise in all populations, hence show mild activity. This basic situation signifies that ROI A receive significant activation from the external environment, whereas ROI B and ROI C are almost silent. Starting from this situation, we introduced various connectivity patterns from ROI A to ROI B and ROI C. Two examples are reported in Fig. 5. For these simulations we imagined two hypothetical patterns of functional connectivity among the three ROIs. In the first, ROI A affects both the MF and HF populations in ROI B, while ROI C is almost silent. In the second, ROI A affects the MF population in ROI B, while ROI B affects both MF and HF populations in ROI C. Results show that connectivity is reflected in evident peaks in the PSD.

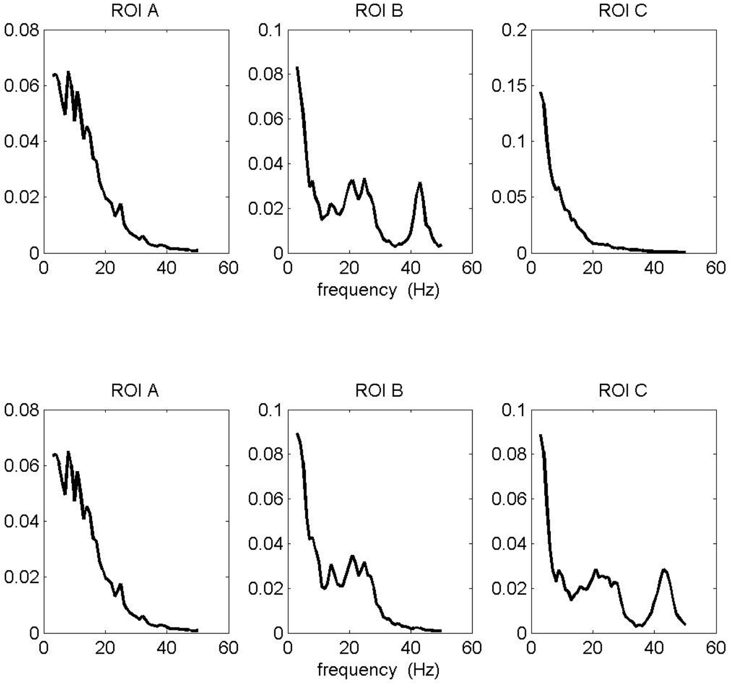

Figure 5: Examples of hypothetical connectivity among three regions, simulated by the model of a ROI described before. In the first case the coupling moves from the first region (ROI A) to the second one (ROI B) with a MF connectivity strength of 10 and a HF connectivity strength of 10. In the second case the coupling moves from the first region (ROI A) to the second one (ROI B) with a MF connectivity strength of 10, and from the second region (ROI B) to the third one (ROI C) with a MF connectivity strength of 50, and a HF connectivity strength of 50. Connectivity causes evident peaks in the ROIs.

4 Discussion

The main objective of this work was to use a neural mass model, recently proposed by Wendling et al. [6], in order to simulate electrical activity in cortical regions during a simple cognitive task. The use of this type of models can find several important applications in the neurophysiological and neuroimaging fields. It is generally assumed that signals measured in electroencephalography

(EEG) or magnetoencephalography (MEG) contain important information on behavioural states, which are reflected in different rhythms and in the frequency spectral distribution. The exact neurophysiological mechanisms involved, however, and their role in cognitive functions are still far from being assessed.

In general, the aetiology of EEG/MEG rhythms may depend on two fundamental aspects: the interaction of different neural populations in the same cortical area (i.e., interaction among excitatory and inhibitory cells, which may induce rhythms at a given frequency) and the pattern of connectivity among remote regions. Although neural mass models have frequently been used in past years, starting from the mid-seventies [3, 4], just a few studies analysed the effect of intra-region synapses, and/or of the connectivity patterns on the EEG frequency content. As to the first aspect, models have been used to simulate alpha rhythms [5], dynamics in the olphactory cortex [11], or paradoxical epileptic discharges [6]. In particular, Wendling et al. [6] demonstrated that different kinds of realistic activities, from interictal to fast ictal, can be obtained acting on a few parameters describing synaptic strength. As to the second point, David and Friston [9] analyzed the changes in power spectrum resulting from simple connectivity patterns among two ROIs, each simulated via a neural mass model of two parallel populations. This recent paper provides a first attempt to characterize how interactions among different ROIs are reflected in MEG/EEG oscillations, and it represents a first step toward a theoretical analysis of indices for nonlinear coupling. However, an important aspect that was not addressed in that study is how the model can be used to fit real data.

The present paper moves in the same direction as the paper by David and Friston [9] but extends and improves it as to two major issues. First, we demonstrated that a model, including three neural populations arranged in parallel (named low-frequency, LF, medium frequency, MF, and high frequency, HF) can actually fit real data, by means of an automatic minimization procedure. An important point of this fitting procedure is that the time constants are characteristics of the three populations, i.e., they do not change from one ROI to the next. Only parameters describing the synaptic gains have been adapted to fit individual ROIs. The previous procedure, however, exhibits a fundamental drawback, i.e., individual ROIs are treated as separate entities, which receive an input noise and differ in their internal synaptic links. By contrast, cognitive tasks are the result of functional connections among different regions. Experimental studies suggest that EEG/MEG activity reflects connections among strongly coupled distant cortical areas [12, 13]. Analysis of functional connectivity is becoming a fundamental issue in recent neuroimaging literature [1, 2]. Hence, in the last part of this work we analysed the effect of some connectivity patterns on PSD. In performing these simulations we considered three identical ROIs, which can generate just low-frequency spectra, and receive different input noise. A first strongly activated ROI sends its output signal (in term of spike density) to other two poorly activated regions, causing their excitation and the appearance of new frequencies in the power spectrum. It is worth noting that our simulations are more complex than those presented in David and Friston [9] since they imply different connectivity in the LF, MF and HF ranges (i.e., connectivity may differ depending on the frequency range considered). This allows the appearance of new rhythms in the downstream region, which were not present upstream.

Finally, we wish to discuss the main limitations of this study. First, in this work we did not tested the effect of recurrent connections, i.e., connections including feedback loops among regions. They may important to induce synchronization among rhythms. Second, we did not try to fit interconnected regions to real data. These aspects will be the target of future work.

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