Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Assessment of Effective Connectivity among Cortical Regions based on a Neural Mass Model

M. Zavaglia[1], L. Astolfi[2], F. Babiloni[2] and M. Ursino[1]

1- Department of Electronics, Computer Science, and Systems, University of Bologna, Cesena, Italy
2- Department of Human Physiology and Pharmacology, University "La Sapienza", Roma, Italy

Abstract—**Assessment of brain connectivity among different brain areas during cognitive or motor tasks is a crucial problem in neuroscience today. Aim of this work is to use a neural mass model to assess the effect of various connectivity patterns in the power spectral density (PSD) of cortical EEG, and investigate the possibility to derive connectivity circuits from real EEG data. To this end, a model of an individual region of interest (ROI) has been built as the parallel arrangement of three populations, each described as in [1].**

The present study suggests that the model can be used as a simulation tool, able to produce reliable intracortical EEG signals. Moreover, it can be used to look for simple connectivity circuits, able to explain the main features of observed cortical PSD. These results may open new prospective in the use of neurophysiological models, instead of empirical models, to assess effective connectivity from neuroimaging information.

I. INTRODUCTION

BRAIN processing, even during simple cognitive tasks, is the result of the interaction among several cortical regions, which are reciprocally interconnected and functionally integrated. In this context, a crucial role in the neurophysiology is played by the concept of brain connectivity. Knowledge of connectivity is considered essential today to understand how the brain works, and to assess the role of different regions in the achievement of specific cognitive functions.

An interesting new opportunity, still at the pioneering stage, consists in the use of neurophysiological models (i.e., models based on biology) to derive effective connectivity from real data. These models may be useful to establish causal relationships among remote cortical regions, to gain a deeper insight into the underlying neural processes, and to establish some basic mechanisms for signal generation (including non-linearities).

Particularly useful are the so-called "neural mass" models, in which the activity of entire neural populations are described using just a few state variables. Such models may include Wilson-Cowan oscillators [2], [3] which have been frequently employed to analyze synchronization among neural groups. More sophisticate neural mass-models of cortical columns were developed by Wendling and Jansen and Rit ([1], [4]). Although these models have been used to simulate particular features of EEG, such as alpha rhythms [4], oscillations and synchronisation in the γ-band [3], dynamics in the olphactory cortex [5], or epileptic patterns [1], [6], only a few studies used these models to study and assess effective connectivity among several ROIs participating to the same task [7], [8].

The present study continues on the same route, with the aim of using a neural mass model [1] to infer connectivity from data. Three main objectives are pursued. First, we wish to build a neural mass model able to mimic the frequency content of real EEG spectra, with a good compromise between accuracy and complexity. Second, we wish to investigate the effect of different patterns of connectivity among ROIs (each described via the previous model), by using a sensitivity analysis on the parameters specifying this connectivity. Hence, the second objective is to reach a deeper understanding of how EEG spectra are affected by connections among ROIs. Third, we investigate which patterns of connectivity among ROIs can be derived, by using a best fitting procedure between model and data. To this end, high-resolution EEG activity measured on the scalp is propagated to the cortex with a realistic back-propagation model [9], in order to generate reliable cortical EEGs during a motor task. The best fitting procedure tries to minimize the square difference between model spectra and real ones, using the strengths of connectivity as estimated parameters.

Results show that the proposed neural mass model can be used to interpret real data, to simulate realistic EEG spectra, and to infer a connectivity circuit. To our knowledge, this is the first attempt to estimate connectivity, using a neurophysiological model fitted to real data. Although the results obtained are clearly preliminary, and still require further validation, they may open a promising route in the problem of effective connectivity estimation via physiological models.

II. METHOD

Mathematical model

Model of a single population - The model of a single population was obtained by modifying equations proposed by Wendling et al. [1]. In this model cortical activity derives from the interaction among four neural groups: pyramidal cells, excitatory interneurons, inhibitory interneurons with

1-4244-0033-3/06/$20.00 ©2006 IEEE.

slow synaptic kinetics, and inhibitory interneurons with faster synaptic kinetics (see Fig. 1).

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. 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 potential. Three different kinds 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

$$\frac{dy_0(t)}{dt} = y_5(t) \tag{1}$$

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

$$z_0(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_0)}} \tag{3}$$

$$v_0(t) = C_2 \cdot y_1(t) - C_4 \cdot y_2(t) - C_7 \cdot y_3(t) \tag{4}$$

Excitatory interneurons

$$\frac{dy_1(t)}{dt} = y_6(t) \tag{5}$$

$$\frac{dy_6(t)}{dt} = A \cdot a_1 \cdot (z_1(t) + \frac{p(t)}{C_2}) - 2 \cdot a_1 \cdot y_6(t) - a_1^2 \cdot y_1(t) \tag{6}$$

$$z_1(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_1)}} \tag{7}$$

$$v_1(t) = C_1 \cdot y_0(t) \tag{8}$$

Slow inhibitory interneurons

$$\frac{dy_2(t)}{dt} = y_7(t) \tag{9}$$

$$\frac{dy_7(t)}{dt} = B \cdot b_1 \cdot z_2(t) - 2 \cdot b_1 \cdot y_7(t) - b_1^2 \cdot y_2(t) \tag{10}$$

$$z_2(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_2)}} \tag{11}$$

$$v_2(t) = C_3 \cdot y_0(t) \tag{12}$$

Fast inhibitory interneurons

$$\frac{dy_3(t)}{dt} = y_8(t) \tag{13}$$

$$\frac{dy_8(t)}{dt} = G \cdot g_1 \cdot z_3(t) - 2 \cdot g_1 \cdot y_8(t) - g_1^2 \cdot y_3(t) \tag{14}$$

$$z_3(t) = \frac{(2 \cdot e_0)}{1 + e^{r \cdot (s_0 - v_3)}} \tag{15}$$

$$v_3(t) = C_5 \cdot y_0(t) - C_6 \cdot y_2(t) \tag{16}$$

In these equations, the symbols v_i represent the average membrane potentials *(i* = 0, 1, 2, 3 for the four groups). These are the input for the sigmoid function which converts them into the spikes (z_i, i = 0, 1, 2, 3) fired by the neurons. Then, these outputs enter 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 and g_1, respectively). The outputs of these equations, which can be excitatory, slow inhibitory or fast inhibitory, represent the postsynaptic membrane potentials (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.

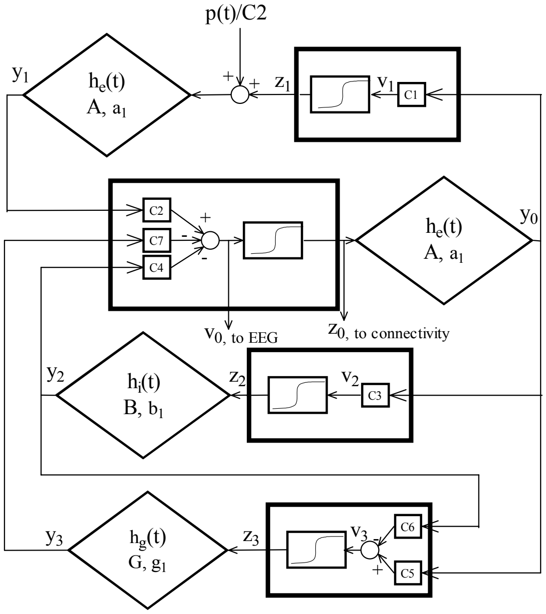

Fig. 1. Layout of a single population model

Model of a region of interest (ROI) - 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 in David et al. [7] and in our simulations however, a single neural mass model produces a narrow frequency band, which can be finely adjusted, but cannot mimic the overall complexity of EEG in an entire cortical area. 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 output quantities of each ROI (in terms of average membrane potential, $v_{out}(t)$, and average spike density, $z_{out}(t)$), are computed as the mean values of the same quantities in the three populations (see Fig. 2).

Parameters in the three populations have been chosen to obtain peaks in the theta and alpha band (4-12 Hz), in the beta band (12-30 Hz) and in the gamma band (greater than 30 Hz), respectively.

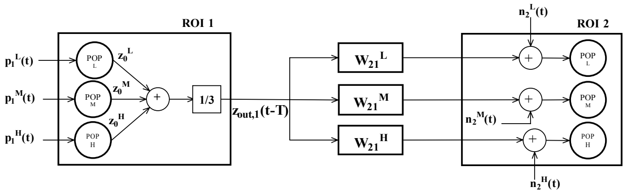

Fig. 2. Example of connectivity between two ROIs

Model of connectivity among ROIs - To simulate connectivity, we assumed that the average spike density of pyramidal neurons (i.e., the quantity $z_{out}(t)$) affects excitatory interneurons in the target region via a weight factor, *W*, and a time delay, *T*. This is achieved by modifying the quantity $p(t)$ in (6). In the following, in order to deal with several ROIs simultaneously, we will use the subscripts *i* (or *j*) to denote a quantity which belongs to the ith (or jth) ROI, while the superscript *k* will be used to denote the kth population (low, medium or high frequency) in the same ROI.

Hence, the input $p_i^k(t)$ to the kth population in the ith ROI can be computed as follows

$$p_i^k(t) = n_i^k(t) + \sum_j W_{ij}^k z_{out,j}(t-T) \qquad \text{k} = \text{L, M, H} \tag{17}$$

where W_{ij}^k is the weight of the synaptic link from the jth (pre-synaptic) ROI to the kth population of the ith (post-synaptic) ROI, T is the time delay (assumed equal for all synapses), $n_i^k(t)$ represents a gaussain white noise with mean value m_i^k and standard deviation σ_i^k, and the sum in the right hand member of (17) is extended to all ROIs, *j*, which target into the ROI *i*.

An example of connectivity among two ROIs is illustrated in Fig. 2. In the present study, all time delays among ROIs have been taken equal to 10 ms. The weights have been assigned different values, in order to simulate various patterns of connectivity and analyze their influence on the EEG of the downstream region.

III. RESULTS

A first group of simulations has been performed to analyze how the peaks of the EEG spectrum, caused by activity in the individual populations, can be affected by the ratio between inhibition and excitation. This preliminary analysis is important to understand whether the model is able to mimic reliable spectral patterns, characterized by different rhythms, by acting on its input and on excitation/inhibition ratio of synapses.

As shown in Fig. 3, a single population produces a signal with a narrow frequency band, at low, medium or high frequency (LF, MF, HF), depending on time constants of synapses. Subtle adjustments in the position of the peak generated by each population can be obtained by modifying the average gain of excitatory vs. inhibitory synapses. Analysis of cortical EEGs during motor tasks revealed the presence of two or three peaks in the frequency spectrum. An EEG spectrum with three peaks is obtained using the parallel arrangement depicted in Fig. 2.

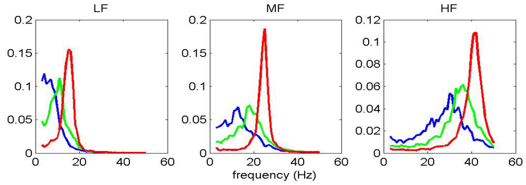

Fig. 3. Three populations (LF, MF, HF) which build a ROI, simulated with a gaussian white noise as input. Example of how the position of the peak generated by each population can be finely tuned, by acting on the average gain of fast inhibitory synapses.

A second set of simulations has been performed to analyze how the PSD spectrum of a ROI can be modified by the connections among ROIs. To this end, we constructed a network of three ROIs, and we studied how their power spectral densities can be modified by the pattern of connectivity among them. In particular, we assumed that the first ROI (subscript i = 1) receives significant input noise but does not receive connections from the other regions. Parameters of the input noise (mean values and variances) have been chosen to mimic the power spectral density measured in the region 5L of Broadman (left superior parietal cortex) during 0.6s of right finger movement. By contrast, we assumed that the other two ROIs (i = 2, 3) receive negligible excitation and are activated mainly as a consequence of connections from the other regions. The previous assumptions are justified by the observation that, during the performed motor task, there is an anticipatory function that is usually promoted by the superior parietal cortex in humans, here represented by the ROI 1.

Three simple examples of how feedforward connectivity can modify the EEG power spectral density in ROIs 2 and 3 are displayed in Fig. 4. This figure illustrates that the pattern of connectivity is reflected into evident and well-detectable changes in the EEG spectrum.

The last step in our study concerns estimation of parameters W_{ij}^k in (17), and of the excitation/inhibition ratio, starting from real data. These data concern cortical EEG in several ROIs obtained, during a right finger movement task, starting from measurements performed on the scalp with 96 electrodes, and using an inverse propagation algorithm [9].

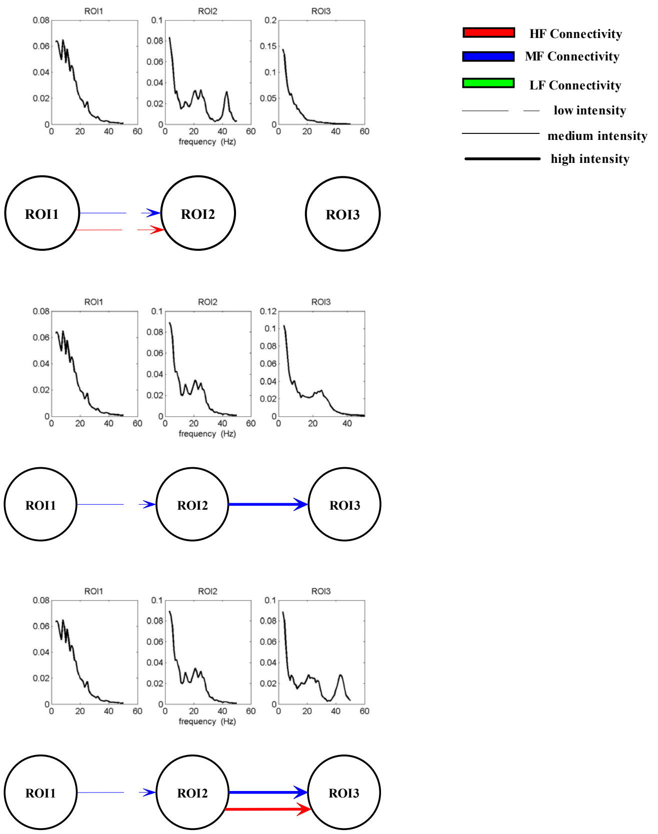

Fig. 4. Three examples of hypothetical feedforward connectivity among 3 ROIs, simulated by the connectivity model described before. Connectivity causes evident peaks in the power spectral density of the ROIs.

Best fitting has been achieved by minimizing a least square criterion function of the difference between model and experimental power spectral density, in the range 3-50 Hz with a resolution of 1 Hz. We considered only three regions in the brain (5L, 6AL, 46L according to Broadman classification) and so three corresponding ROIs in the model; this choice is justified by the necessity to maintain a moderate level of complexity in this initial study, and by the observation that these ROIs may represent the regions of the left hemisphere mainly concerned with the right finger movement task. In performing the minimization algorithm we assumed that ROI 1, representative of experimental ROI 5L, does not receive any connection from the other regions, but receives a significant input noise, whereas the ROI 2 and ROI 3, which are considered representative of experimental regions ROI 6AL and ROI 46L, receive negligible input noise but may receive all possible connections from the other ROIs, including self connections. The previous choice is the same adopted in the simulations of Fig. 4, i.e., region ROI 1 receives most of the external stimulus which triggers the motor task, and drives the other two regions. The latter may further modulate their activity by recurrent connections.

Unknown parameters for the algorithm are all connectivity weights W_{ij}^{k}, with i = 2, 3, j = 1, 2, 3, and k = L, M, H and the excitation/inhibition ratio of synapses of each population of ROI 2 (6AL) and ROI 3 (46L). The total number of estimate parameters is 24.

Results obtained by the minimization algorithm are presented in Fig. 5, where a block diagram of the estimated connections is also shown. It is noticeable that just 6 connections weights are significantly different from zero at the termination of the algorithm. All other connections, including all self connections, assume negligible values. The algorithm suggests the presence of a feedforward connection from ROI 1 (5L) to ROI 2 (6AL) at low frequencies, and from ROI 1 (5L) to ROI 3 (46L) at high frequencies. Moreover, the algorithm puts in evidence the presence of significant recurrent connections between ROI 2 (6AL) and ROI 3 (46L): from ROI 2 (6AL) to ROI 3 (46L) at medium and high frequencies, and from ROI 3 (46L) to ROI2 (6AL) at low and high frequencies. Although the present results are just preliminary, they show that power spectral density can be mimicked using a simple circuit simulating effective connectivity. The same algorithm has been applied to a second subject performing the same task, obtaining quite similar values of estimated parameters.

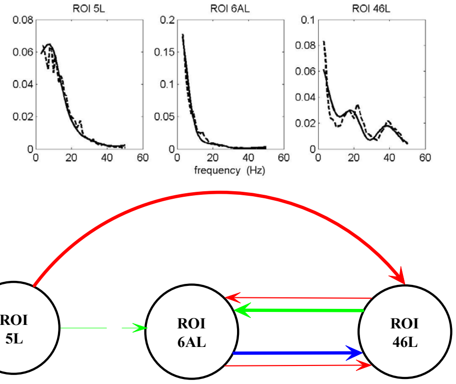

Fig. 5. Fitting of 3 real power spectral densities with the connectivity model. Estimated parameters are the excitation/inhibition ratio of the 3 populations of each ROI and the connectivity weights. Continuous lines represent experimental PSDs, while dashed lines the model ones.

IV. CONCLUSION

The study of brain connectivity represents a fundamental aspect of neurophysiology today. In fact, an integrate understanding of human brain function requires not only knowledge of the different areas involved in a given task, but also of their reciprocal connections and functional links. The present work aspires at analyzing the possible use of an update neural mass model, for the study of brain connectivity. The study was developed in different phases, which represent necessary steps toward a deeper understanding of the potential benefits and limitations of the proposed model.

The first simple step was to realize a model able to simulate the main characteristics of cortical EEG power density in the range 3-50 Hz, by simply acting on its input and on excitation/inhibition ratio of synapses. This was a necessary requisite to use the model as an instrument to generate reliable signals and/or to infer connectivity from data. The subsequent step was to test how connectivity may modify EEG power density. Although in the present work we displayed just a few exemplary simulations, see Fig.4, (but many others can be performed) these clearly show that connectivity induces evident changes in spectral content. The previous two steps confirmed that the model can be used as a simulation tool, able to produce reliable signals with different patterns of EEG power spectral density, and to mimic the effect of different imposed patterns of connectivity.

The last, an more ambitious step of our work, was to check whether the present model, trained with a minimization algorithm, can “discover” a simple pattern of connectivity, starting from real data, under a few basic hypotheses.

Results obtained with the minimization algorithm are encouraging. The algorithm found a simple pattern of connectivity, which explains EEG power spectral density carefully, and seemed quite repetitive in a second subject. Moreover, several connections (including all self-connections) assume a negligible strength.

Finally, we wish to stress that, in this work, we did not aspire to find “true” connectivity from data (indeed, the connectivity concept is strongly model dependent) but to show how the proposed model, trained with real signals, can discover “one possible” solution which describes data quite well. Multiple equivalent solutions may exist, and the algorithm discovers just one of them. This is a clear limitation of all minimization algorithms for non-linear problems, i.e., the solution is not unique, and alternative solutions may be found depending on the initial guess.

In conclusion, the present work was focused on the possibility to use neural mass models to analyzing data on brain function, in the same direction as that previously investigated by other groups [10]-[13]. The emphasis of our paper is on the possibility to use these models to infer information on connectivity, either using the model as a simulator, to generate signals and/or to gain a deeper insight into the possible effect of connectivity on measured data, or as a part of an algorithm, to derive connectivity from data. Although the last step is still at a preliminary stage, the present work represents a first promising attempt in that direction.

REFERENCES

[1] F. Wendling, F. Bartolomei, J. J. Bellanger, and P. Chauvel, "Epileptic fast activity can be explained by a model of impaired GABAergic dendritic inhibition," *Eur. J. Neurosci.*, vol. 15, no. 9, pp. 1499-1508, May2002.

[2] H. R. Wilson and J. D. Cowan, "Excitatory and inhibitory interactions in localized populations of model neurons," *Biophys. J.*, vol. 12, no. 1, pp. 1-24, Jan.1972.

[3] T. B. Schillen and P. Konig, "Binding by temporal structure in multiple feature domains of an oscillatory neuronal network," *Biol. Cybern.*, vol. 70, no. 5, pp. 397-405, 1994.

[4] B. H. Jansen and V. G. Rit, "Electroencephalogram and visual evoked potential generation in a mathematical model of coupled cortical columns," *Biol. Cybern.*, vol. 73, no. 4, pp. 357-366, Sept.1995.

[5] W. J. Freeman, "Simulation of chaotic EEG patterns with a dynamic model of the olfactory system," *Biol. Cybern.*, vol. 56, no. 2-3, pp. 139-150, 1987.

[6] F. Wendling, J. J. Bellanger, F. Bartolomei, and P. Chauvel, "Relevance of nonlinear lumped-parameter models in the analysis of depth-EEG epileptic signals," *Biol. Cybern.*, vol. 83, no. 4, pp. 367-378, Oct.2000.

[7] O. David and K. J. Friston, "A neural mass model for MEG/EEG: coupling and neuronal dynamics," *Neuroimage.*, vol. 20, no. 3, pp. 1743-1755, Nov.2003.

[8] M. A. Tagamets and B. Horwitz, "A model of working memory: bridging the gap between electrophysiology and human brain imaging," *Neural Netw.*, vol. 13, no. 8-9, pp. 941-952, Oct.2000.

[9] F. Babiloni, F. Cincotti, C. Babiloni, F. Carducci, D. Mattia, L. Astolfi, A. Basilisco, P. M. Rossini, L. Ding, Y. Ni, J. Cheng, K. Christine, J. Sweeney, and B. He, "Estimation of the cortical functional connectivity with the multimodal integration of high-resolution EEG and fMRI data by directed transfer function," *Neuroimage.*, vol. 24, no. 1, pp. 118-131, Jan.2005.

[10] B. Horwitz, M. A. Tagamets, and A. R. McIntosh, "Neural modeling, functional brain imaging, and cognition," *Trends Cogn Sci.*, vol. 3, no. 3, pp. 91-98, Mar.1999.

[11] B. Horwitz, "The elusive concept of brain connectivity," *Neuroimage.*, vol. 19, no. 2 Pt 1, pp. 466-470, June2003.

[12] D. L. Rowe, P. A. Robinson, and C. J. Rennie, "Estimation of neurophysiological parameters from the waking EEG using a biophysical model of brain dynamics," *J. Theor. Biol.*, vol. 231, no. 3, pp. 413-433, Dec.2004.

[13] O. David, L. Harrison, and K. J. Friston, "Modelling event-related responses in the brain," *Neuroimage.*, vol. 25, no. 3, pp. 756-770, Apr.2005.