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eCOALIA: Neocortical Neural Mass Model for simulating electroencephalographic signals

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5 Abstract

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This paper introduces eCOALIA, a Python-based environment for simulat-6 ing intracranial local field potentials and scalp electroencephalography (EEG) 7 signals with neural mass models. The source activity is modeled by a novel 8 neural mass model respecting the layered structure of the neocortex. The 9 whole-brain model is composed of coupled neural masses, each representing a 10 brain region at the mesoscale and connected through the human connectome 11 matrix. The forward solution on the electrode contracts is computed using 12 biophysical modeling. eCOALIA allows parameter evolution during a simu-13 lation time course and visualizes the local field potential at the level of cor-14 tex and EEG electrodes. Advantaged with the neurophysiological modeling, 15 eCOALIA advances the *in silico* modeling of physiological and pathological 16 brain activity. 17

Keywords: neural mass modeling, whole-brain modeling, forward solution,
EEG, Python

20 Metadata

²¹ 1. Motivation and significance

Electroencephalography (EEG) recordings are invaluable tools in clinical and research settings, offering insights into the complexities of brain function. From clinical diagnosis of neurological conditions to monitoring brain activity during surgeries, EEG plays a crucial role in healthcare. Beyond medical applications, EEG is utilized in cognitive research to study attention, memory, and language while also serving as a cornerstone in the development of brain-computer interfaces and neurofeedback therapy. With its ability to

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Nr.	Code metadata description	Please fill in this column
C1	Current code version	V1
C2	Permanent link to code/repository	https://github.com/ymmx2/
C3	Permanent link to Reproducible	
00	Capsule	
C4	Legal Code License	GNU GENERAL PUBLIC LI-
		CENSE Version 3, 29 June 2007
C5	Code versioning system used	git
C6	Software code languages, tools, and	python3.10 or 3.11
	services used	
C7	Compilation requirements, operat-	PyQt6>=6.6.1, Numpy>=1.23.5,
	ing environments & dependencies	Scipy>= $1.10.1$, matplotlib>= $3.8.3$,
		$vtk \ge 9.2.6$
C8	Link to developer documenta-	https://github.com/ymmx2/
	tion/manual	eCOALIA/blob/main/README.md
C9	Support email for questions	maxime.yochum@univ-rennes.fr

Table 1: Code metadata

²⁹ map brain function and detect abnormalities, EEG stands at the forefront ³⁰ of understanding the human brain and advancing medical treatments. How-³¹ ever, deciphering the neurophysiological factors leading to electroencephalo-³² graphic observations remains limited in humans due to the unavailability of ³³ simultaneous multiscale (from single cells to populations of cells) recordings. ³⁴ Computational modeling can fill this gap. ³⁵ Whole brain modeling has now become a standard method for in cilies and ³⁶ and ³⁷ and ³⁷

Whole-brain modeling has now become a standard method for *in silico* ex-35 ploration of the healthy and pathological brain dynamics [1], and interpreta-36 tion of the electrophysiological recordings. Whole-brain modeling tools have 37 made predictions between the electrophysiological recordings and simulations 38 based on the relation between excitation/inhibition [2], noise level, variations 39 on whole-brain connectivity matrices [3], or give insights on functional ac-40 tivity and controllability [4, 5, 6, 7]. However, they are limited in detailing 41 neurophysiological factors leading to a typical type of transient activity. 42 The most common whole-brain modeling and multimodel imaging platform 43

⁴³ The most common whole-brain modeling and mutualided imaging platform
⁴⁴ is The Virtual Brain (TVB) [8, 9]. More recently, a Python package was
⁴⁵ released for whole-brain modeling for simulating BOLD (blood-oxygen-level⁴⁶ dependent) signals [10]. These tools face two main issues. First, they assume
⁴⁷ that measured signals are either a direct reflection of the firing rate or mem⁴⁸ brane perturbations, while the layered structure of the neocortex imposes
⁴⁹ a more complex picture for the generation of electrophysiological signals.

⁵⁰ Second, they focus on simulating oscillatory activity without accounting for ⁵¹ the physiology of transient signals, such as interictal epileptic discharges or

⁵² event-related potentials. eCOALIA addresses these issues with a neurophys-

⁵³ iologically plausible approach.

The groundbreaking nature of eCOALIA comes from the fact that it fol-54 lows the layered structure of the neocortex and includes different inhibitory 55 and excitatory neuronal populations. In addition to simulating cortical os-56 cillations, the model simulates signal morphology of transient events (in-57 terictal epileptic discharges and event-related potentials) observed at the 58 level of EEG electrodes [11]. The implementation of the neocortical layered 59 structure allows distinguishing the layer-wise impact of the intra- and inter-60 regional (cortico-cortical and subcortico-cortical) interactions on the signal 61 morphology. Therefore, eCOALIA can help to uncover the population-level 62 physiological mechanism leading to observed events. This generic model can 63 be developed further for patient-specific modeling and source localization of 64 EEG signals [12], for generating a large amount of data for training artificial 65 intelligence algorithms, and for optimization of brain stimulation technolo-66 gies. 67

68 2. Software description

69 2.1. Model description

eCOALIA is based on a generic model of a neocortical region [11, 12], which 70 accounts for excitatory and inhibitory neuronal subpopulations found in the 71 neocortex. Each brain region is represented by the NMM given in (1) which 72 is connected to other brain regions according to the structural network of the 73 human brain; which combines axonal connections and propagation delays be-74 tween regions. These connectivity matrices were generated using the Human 75 Connectome Project database [13] with Diffusion Tensor Imaging and Trac-76 tography techniques. In particular, the connectivity matrices were created 77 using data from 487 adult subjects. Fractional anisotropy values were ex-78 tracted from each subject and then averaged. These connectivity matrices 79 represent the strength of the connections between neural masses. The delay 80 matrix, which represents the time it takes for signals to travel between re-81 gions, was calculated using a distance matrix multiplied by an average signal 82 propagation velocity of 7.5 m/s [14]. 83

The generic NMM accounts for the firing rate, synaptic kinetics and connectivity between the subpopulations. The post-synaptic potential (PSP) emitted by a single neuronal subpopulation i in a particular brain region K

reads: 87

$$\ddot{y}_{K,i} = \frac{W_{K,i}}{\tau_{w_{K,i}}} \left(S \left(\sum_{K,j} C_{\{K,j\} \to \{K,i\}} y_{K,j} + \sum_{M,j} C_{\{M,j\} \to \{K,i\}} y_{M,j} \right) \right)$$
(1)

$$- \frac{2}{\tau_{w_{K,i}}} \dot{y}_{K,i} - \frac{1}{\tau_{w_{K,i}}^2} y_{K,i} + \frac{W_{K,i}}{\tau_{w_{K,i}}},$$

where $W_{K,i}, \tau_{w_{K,i}}$ are PSP amplitude and time constant, $C_{\{K,j\}\to\{K,i\}}$ is the 88 coupling coefficient calibrating the afferent PSP from a subpopulation $\{K, j\}$ 89 within the region K and $C_{\{M,j\}\to\{K,i\}}$ from a subpopulation $\{M,j\}$ within the 90 region M. The sigmoidal transfer function S(.) relates the membrane pertur-91 bations of the subpopulation $\{K, i\}$ due to incoming signals to its firing rate. 92 The NMM reprenting a neocortical column integrates two excitatory subpop-93 ulations (P (P) and P' (P1)), and four types of inhibitory interneurons (i.e., 94 neuroglia form cells (NGFC), vasoactive intestinal peptide (VIP), parvalbu-95 min (PV) and somatostatin (SST) positive interneurons), represented by six 96 subpopulations (PV (I1), PV' (I1b), SST (I2), VIP (I3), NGFC (I4) and 97 NGFC' (I4)). The NMM representing the thalamus integrates one excita-98 tory subpopulations (thalamic nucleus cells (TC)) and two types (slow and 99 fast) of inhibitory neuronal subpopulations (reticular neurons (RT1, RT2)). 100 All the subpopulations within the region K can receive inputs from the exci-101 tatory subpopulation of the region M (subpopulation P for the neocortical 102 regions and subpopulation TC for the thalamus). The model is schematized 103 in Figure 1 and the model equations are given in Supplementary Material. 104 The model equations are integrated using the Euler–Maruyama integration 105 scheme [15] which is suitable when model incorporates statistical phenomenon.

2.2. Forward problem 107

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The source activity (model output) is computed from the synaptic inputs 108 targeting the layer V excitatory neurons. The macroscale EEG signal is 109 computed using the current dipole approximation [16, 17]: 110

$$\phi(r) = \frac{1}{4\sigma\pi} \frac{\sum_{n=1}^{M} I_n^{axial}(t) \overline{d}_n^{\gamma} \cos(\theta)}{|r - r_{source}|^2},\tag{2}$$

where $I_n^{axial}(t) = \eta y(t)$ is an axial current along the vector $\overrightarrow{d_n}$ at r_{source} and 111 $\cos(\theta)$ is the angle between $\overrightarrow{d_n}$ and and the distance vector from the source 112 and the electrode E. The parameter σ is the conductivity of the extracellular 113 milieu and $\eta = 10^{-3}S$ is a conversion factor relating the PSP to postsynaptic 114 current [18]. 115



Figure 1: Single NMM with the labels of the subpopulations and connectivity coefficients as coded in eCOALIA.

The simulated source activity defines a time series, S of $N_R \times T$ matrix, 116 N_R being the number of brain regions and T the size of the time vector 117 of the simulated activity. eCOALIA uses the Colin head model [19] and 118 Desikan Atlas [20] with $N_R = 66$ neocortical regions, which are available on 119 Brainstorm [21]. A lead field matrix A ($66 \times N_E$), generated from 3-layer 120 Boundary Element Method (BEM) model [22, 23], was used to compute the 121 projection of the source activity onto the N_E number of EEG contacts. The 122 $X (N_E \times T)$ matrix of simulated EEG signals is obtained by X = AS. 123

124 2.3. Software architecture

The software was designed to be used via a Python script that instanti-125 ate a Cortex model which represents the brain with its interacting regions 126 each modeled by a NMM. The user can load a simulation file or can modify 127 the cortex model directly. It is possible to integrate parameter variations 128 along the simulation as well as stimulation signals that account for electrical 129 stimulation therapies (deep brain stimulation or transcranial electrical stim-130 ulation). Some visualization tool can be used to display the source LFP and 131 EEG time series and their spectrograms. A 3D view allows also to display 132 the LFP onto a 3D mesh of the cortex. Parameter evolution and stimulation 133

can be displayed as well. The use of scripts gives the flexibility for employing
user-specific routines and fine tuning of the simulation.

The provided documentation for the software package offers comprehensive explanations and illustrative examples for using classes and functions. This includes instantiating of a model, tuning parameters, conducting simulations, and visualizing results.

The software package includes two scripts for performing single node ($N_{NMM} = 1$) and whole brain ($N_{NMM} = 67 - 1$ thalamic and 66 neocortical regions) simulations, and one script for creating a network from scratch:

• Single node simulation: a Python script is available on the repository 143 to simulate a single node simulation starting from a previously saved 144 simulation file. The node's parameters can be changed and an external 145 stimulation can be applied. Displayed results of the source signal can 146 be firing rates of the subpopulations, PSPs, LFP, or the mean mem-147 brane potential of the layer V excitatory neurons using the EEG_view 148 module. Additionally, the time courses of parameter evolution and 149 stimulation signals are displayed in separate windows. The number of 150 NMMs and their parameters, parameter evolution, and the parameters 151 of the stimulation signal are saved in a user-named txt file, which can 152 be loaded for a new simulation. 153

- Whole-brain simulation: a Python script is available on the repository 154 to simulate 67 nodes starting from a previously saved simulation file 155 including parameter sets and evolutions, coupling matrices, and stimu-156 lation. After loading the saved simulation files, the script can be modi-157 fied to include parameter variations and stimulation signals on desired 158 nodes. Simulated network activity is projected to scalp electrodes. In 159 this projection the first node represented the thalamus was excluded. 160 since it is not considered in the lead field matrix. 161
- After solving the system of differential equations, six different displays appear: time courses and spectrogram of LFP signals, parameter evolution, stimulation, and the time courses of EEG signal, as well as a spatial projection of the source (LFP) signals onto the cortex 3D mesh.
- As it is for the single node simulation, the whole-brain simulation can be saved in a txt file, which can be loaded for a new simulation later on.
- Network from scratch: a network of NMMs can be created and saved for further simulations by defining the number of NMMs, the connectivity and delay matrices, their parameter values and evaluations, and

stimulation signals. Similar to single node simulation, results of the numerical integration, parameter evaluation, and stimulation signals can
be displayed. While eCOALIA uses by default the Colin head model,
the Desikan atlas, and lead field matrices for 66 cortical regions, the
user can replace them with other head models, brain atlases, and lead
field matrices.

178 2.4. Software functionalities

¹⁷⁹ In this section we introduce briefly the functionalities of eCOALIA. Imple-¹⁸⁰ mentation details are given in the developer documentation (see Table 1).

181 2.4.1. Parameter exploration

The parameter evolution module enables the analysis of the model's dynamics in response to parameter variations. Users have the flexibility to define a series of temporal points corresponding to specific parameter values in a numpy list and choose the interpolation technique to infer parameter values throughout the specified time span.

187 2.4.2. Stimulation

In order to mimic the impact of a certain type of brain stimulation (e.g. 188 transcranial electrical stimulation), eCOALIA includes a stimulation module. 189 The stimulation module enables applying an external stimulation to a single 190 NMM or concurrently to multiple ones. A stimulation signal perturbs the 191 membrane of the subpopulations of the NMMs if it is applied before the 192 sigmoid functions or the synapses if it is applied after the sigmoid functions. 193 The impact of the stimulation signal is scaled to differentiate the stimulation 194 impact on the subpopulation. The stimulation signal can take a diverse 195 range of forms (including sinusoidal, square, sawtooth, triangular, ramp, 196 chirp, or mono/biphasic pulses). Each form has different parameters, such as 197 amplitude, frequency, start time, and end time, that can be adjusted (Table 198 2) Furthermore, different types of stimulation signals can be combined if 199 applied on the same NMM to investigate potential synergistic effects. 200

201 2.4.3. Selection of the scalp EEG

The scalp EEG signal is computed by solving the forward problem, which cor-202 responds to the projection of the source activity of size $N_R = 66$ onto the N_E 203 number of scalp EEG contacts (Section 2.2). Since the real EEG caps that are 204 available to clinicians and researchers have different numbers of contacts, the 205 eCOALIA user may want to develop pipelines including direct comparison be-206 tween the simulation results and real recordings. For this, eCOALIA provides 207 8 different lead field matrices that correspond to artificial EEG caps contain-208 ing different number of electrodes $(N_E = \{21, 32, 65, 110, 131, 200, 256, 257\}).$ 209

Type of the stimulation	Required parameters
For all types	Starting time, end time
Constant	Amplitude
Sinus, Square, Sawtooth, Triangle	Amplitude, frequency, phase
Ramp	Starting amplitude, end amplitude
Sinus Ramp	Starting amplitude, end amplitude,
	frequency, phase
Square Pulse Biphasic	Amplitude, frequency, phase, pulse width
Chirp	Amplitude, starting frequency,
	end frequency, phase
Chirp Pulse	Amplitude, starting frequency,
	end frequency, phase, pulse width
Chirp Pulse Biphasic	Amplitude, starting frequency,
	end frequency, phase, pulse width
Square Pulse Rand	Amplitude, frequency, phase, pulse width
Square Pulse Biphasic Rand	Amplitude, frequency, phase, pulse width

Table 2: Stimulation forms and required parameters

210 2.4.4. Displaying source signal on neocortex

The Source View window projects the source activity on the cortex model and 211 displays the EEG contacts with their names around the cortex model. The 212 source activity is highlighted with a color code computed from the energy 213 in the frequency domain (delta, theta, alpha, beta, and gamma bands) or 214 amplitude domain (maximum, mean, and root mean square (RMS)). Time 215 evaluation of the source activity within a sliding window defined by the user 216 can be visualized by pressing the play button. This evaluation is performed 217 within a sliding window defined by the user, with the default being 1 second. 218 The Source View window contains sliding bars that allow the user to adjust 219 transparency and brightness. Additionally, the user can select from a variety 220 of color maps. 221

222 3. Illustrative examples

²²³ Usage of the software package is illustrated with two examples of whole-²²⁴ brain simulation. The simulation files of these examples are available on ²²⁵ the GITHUB repository. The parameter sets are given in Supplementary ²²⁶ Material.

Figure 2 demonstrates a whole-brain simulation of a typical epileptic discharge recorded during interictal periods (outside of seizures). In this example, epileptic activity is associated with the right-precentral (r-PREC) region,



Figure 2: Whole-brain simulation of epileptic discharges. Left: Source activity given by local field potential. The right-precentral (r-PREC) region undergoes spike-and-wave discharges. Middle: Project of the source activity on the head model. The green region undergoes spike-and-wave discharges. Right: EEG signals measured by the scalp electrodes shown on the left panel. Corresponding simulation files is available on the code repository (Table 1) src/SaveFiles/67NMM_spikewave_2.txt.

as shown on LFP and Source View windows. The source signal is projected
on 32 scalp-EEG channels as represented by markers positioned around the
cortex. We can appreciate the large amplitude signals on the contacts closer
to the r-PREC region, namely Cz, F4, FC6, FC2 C4, and CP2, as it can be
verified.

The second example is a whole-brain simulation of a resting state and eyes-235 closed alpha band activity under healthy conditions (Fig 3). In this example, 236 parameters of the left and right occipital lobes are changed in t = [2,7]237 seconds to mimic the transition from resting state to eyes-closed alpha-band 238 activity. The parameter evolution is visualized in the Parameter Evolution 239 window. Notice that in this example we used an alpha-band filter and the 240 coolwarm color code while demonstrating the alpha-band activity on the 241 head model. The source signal is projected on 32-EEG channels. 242

²⁴³ 4. Impact

Whole-brain modeling plays a key role in the discovery and analysis of electrophysiological signals [8, 9, 22, 10]. Despite this importance, modeling the



Figure 3: Whole-brain simulation of alpha-band oscillations. Left: Source activity given by local field potential. The left occipital lobe (l-LOCC) and the right occipital lobe (r-LOCC) undergo alpha-band oscillations in t = [2, 7] seconds. Top middle: Project of the source activity on the head model with the occipital lobes in light blue. Bottom middle: The corresponding parameter evolution yielding these alpha-band activities. The legend indicates the indexes of the NMMs of which parameters were varied. In this example, the parameters $A, C_{I2b,P}, C_{I2,I3}$, and B_a of the 11th and 44th NMMs were modified. Right: EEG signals measured by the scalp electrodes shown on the left panel. Corresponding simulation files is available on the code repository (Table 1) src/SaveFiles/67NMM_resting_alpha_4.txt.

²⁴⁶ morphology of electrophysiological signals has been less of a concern of the²⁴⁷ whole-brain modeling tools.

To address this challenge, we present eCOALIA, a Python-based modular 248 software. eCOALIA integrates a neurophysiologically plausible model of a 249 neocortical column that interacts via human connectome at the macroscale. 250 Parameter variation functionality allows the user to explore the parameter 251 space of eCOALIA. Stimulation signals can be used to test how electrical 252 stimulation can interact with cortical activity. 2-dimensional time and 3-253 dimensional spatial representations of simulated activity simplify the inter-254 pretation of simulations. Projection on EEG electrodes with different num-255 bers of contacts can facilitate the comparison between the simulations and 256 available recorded signals. The modular structure of the software facilitates 257 further implementations and explorations. 258

Quantifying the similarity between simulated and real EEG signals is chal-259 lenging due to asynchronous event timing, limiting the accuracy of classical 260 methods like cross-correlation. Although, the current version of the soft-261 ware lacks direct tools for comparing real and simulated EEG signals, visual 262 inspection can still be useful. Additionally, the built-in spectrogram tool 263 allows frequency-based comparisons, helping assess whether both signals ex-264 hibit similar rhythms and patterns. Further analytical methods, such as 265 coherence analysis or phase locking value, could improve this comparison 266 which would be implemented in future. 267

Different than the earlier version of the software [22], which simulates healthy brain activity [14], eCOALIA can simulate both healthy and pathological brain dynamics [12]. Therefore, it enables studying the impact of perturbations caused by pathological activity on healthy ones, which is an asset for brain research. By providing an *in silico* ground truth, eCOALIA can be used to develop inverse solution methods for estimating cortical-level sources [14, 24] or as a data-generator for training machine learning algorithms [25].

275 5. Conclusions

We introduced the eCOALIA software for neurophysiologically plausible modeling of whole-brain dynamics. Thanks to the biophysical solution of the forward problem, eCOALIA can simulate EEG signals by respecting the observed morphology of pathophysiological events. eCOALIA advances the realism of simulated EEG signals, interpretation of recordings, and patientspecific whole-brain modeling.

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286 Declaration of competing interest

²⁸⁷ Authors have no competing interest.

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