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Artificial neural network predicts inter-areal functional connectivity

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ABSTRACT

In the present paper, we introduce an extended machine-learning-based approach to detect inter-areal functional connectivity based on an artificial neural network (ANN). Using the concept of generalized synchronization, we show that the proposed approach is relevant to infer functional dependencies between remote brain areas of interest from multivariate EEG recordings. We verify the ANN-based method to capture the reconfiguration of functional connectivity during motor execution. The proposed model showed good ability to approximate functional relations between the electrical activity of parietal and frontal areas and motor cortex at different stages of motor execution, providing an adequate pattern of functional connectivity network.

Keywords: Multilayer perceptron, artificial neural network, generalized synchronization, functional connectivity, EEG, motor execution

1. INTRODUCTION

A brain neural system is a complex network that can be represented as a large-scale graph with brain areas as nodes and functional dependencies between them as links.[1] Traditionally, brain activity is assessed via neuroimaging techniques such as fMRI or magneto-/electroencephalography (M/EEG) data and functional connectivity inference is based on the concept of synchronization of brain rhythms between different areas of the brain.[2–8]

In the present paper, we propose method for estimation of functional dependencies between the states of different brain areas detecting the establishment of generalized synchronization (GS). GS refers to the presence of functional relationship between two coupled system, i.e., drive system $x(t)$ and response system $y(t)$:[9,10]

$$y(t) = F(x(t)). \tag{1}$$

The interaction between drive and response systems may be very complicated, and various of methods were introduced to detect GS, such as the auxiliary system approach for the systems with unidirectional coupling,[11–13] mutual false nearest neighbours,[9,14] Lyapunov exponent,[10,15] recurrence plots,[16,17] etc. However, the number of studies of functional relationships detection between remote brain areas is rather limited. Detection of GS in neurophysiological data is indeed a challenging task due to it's high noise level and nonstationarity.

In present paper, we apply the concept of GS to detect functional relationships associated with motor-related activity between remote brain areas. In our previous study, we introduced model-free approach based on artificial neural network to detect GS on ECoG data set of WAG/Rij rats with genetic predisposition to absence epilepsy.[18] Recently, the machine learning approach attracted the researchers' attention for detection of GS in coupled chaotic system. In this context, the most promising results were achieved via echo state networks (ESN). ESN is an implementation of recurrent neural network with randomly generated and very sparsely connected hidden layer.[19] ESN demonstrated good ability to predict chaotic dynamics[20] and evolution of chaotic systems[21–23] among others.

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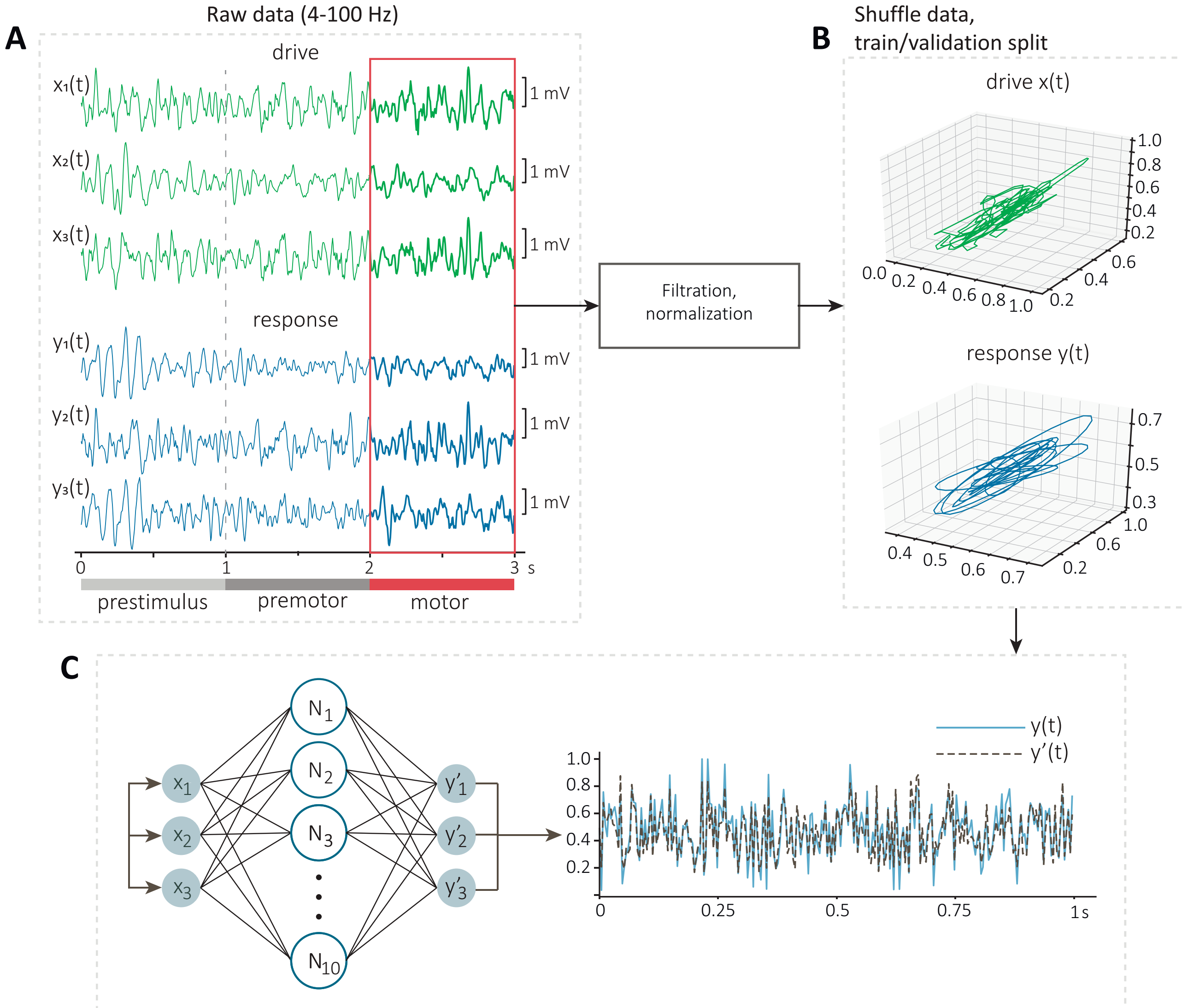

Figure 1. **A**: An example of raw EEG data filtered in the range from 4 to 100 Hz. Here, $x(t)$ (drive) and $y(t)$ (response) represents the multivariate subsets of EEG data recorded from different regions of scalp. **B** The 3D trajectory of 3-dimensional subsets $x(t)$ and $y(t)$ after normalization and filtration of initial raw data. **C** A simplified scheme of feed-forward multilayer perceptron with one hidden layer (left) and the result of functional dependence estimation, where $y(t)$ is a response state and $y'(t)$ is a state predicted by FF-MLP model based on the drive state.

We propose an approach based on feed-forward multilayer perceptron (FF-MLP), which is less computationally costly and is able to train from short EEG time-series.[24,25] In our previous work,[18] FF-MLP demonstrated good ability to approximate functional dependence between coupled chaotic model systems based on Rössler oscillators, showing the agreement with the well-known concepts. Considering neurophysiological data, proposed method successfully predicted the formation of functional relations between cortical layers and thalamic nuclei after the onset of an epileptic discharge in ECoG data of WAG/Rij rats. Here, we apply FNN-MLP to assess functional dependence in motor-related EEG data recorded from remote brain areas. We show that our method is able to predict functional connectivity of brain network on different stages of motor execution.

2. METHODS

2.1 Experimental dataset

Motor-related EEG data was recorded during experimental sessions with 10 healthy volunteers (26.1 ± 5.2 years, 3 females). During the experimental session, participants were seated in a comfortable chair with their hands lying on the table in front of them to exclude any non-task-related muscle contractions (see in detail in Ref.[26]). In the beginning of the experimental session, the 5 min of the eyes-open resting state activity was recorded. Then, all participants were performing motor tasks according to the instruction: clench hand into a fist on the first audio command (a short signal for the left hand and a long signal for the right, 350 and 750 ms, respectively), and relax it after the second audio command. Each participant performed a total of 30 movements with each hand. Each motor task lasted 4-5 s, and after the movement was completed, the 6-8 seconds long pause was given before the next motor task.

EEG data were recorded via EEG amplifier Encephalan-EEGR-19/26 (Medicom MTD, Russia) with a sampling rate 250 Hz. We used 31 Ag/AgCl electrodes according to the "10-10" international system.[27] Acquired EEG signals were filtered using the 50 Hz Notch filter to avoid the power-line interference. Additionally, we applied the 5^{th}-order Butterworth filter in the range 4–100 Hz to remove low-frequency artifacts.

For the FF-MLP model we sliced each EEG dataset into epochs, each epoch containing 3 seconds of recording corresponding to the prestimulus period (1 s before audio command), premovement period (1 s after audio command) and 1 s of motor-related activity (see Fig. 1).

2.2 Feed-forward neural network

2.2.1 Training and validation datasets

Fig. 1AB show the process used to generate training and validation data for FF-MLP model from raw motor-related EEG data. First, we selected 5 subgroups of EEG sensors corresponding to the brain areas of interest: parietal area (P, sensors P4, Pz, P3), frontal area (F, sensors F4, Fz, F3), left hemisphere of motor cortex (MC_l, sensors Fc3, C3, Cp3), right hemisphere of motor cortex (MC_r, sensors Fc4, C4, Cp4) and midline of motor cortex (MC_z, sensors Fcz, Cz, Cpz). Thus, each pair of the subsets can be represented as follows:

$$\begin{aligned} \mathbf{x}(t) &= (x_1(t), x_2(t), x_3(t))^T, \\ \mathbf{y}(t) &= (y_1(t), y_2(t), y_3(t))^T. \end{aligned} \tag{2}$$

According to the proposed approach, we use our model to predict the state of brain area $\mathbf{y}(t)$ using the state of the other brain area $\mathbf{x}(t)$. Each subset represents can be treated as a 3D trajectory, with corresponding time-series representing the state variables (see Fig. 1B). Before proceeding with the FF-MLP training, the data were filtered in the frequency bands of interest, normalized in the range [0,1], shuffled and split in half on training and validation sets.

2.2.2 MLP model configuration

The multilayer perceptron (MLP) is a class of feed-forward artificial neural networks that is well-known as universal approximator, being able to establish functional relationships, if any, between the input and output data.[28] Therefore, FF-MLP model is of particular interest in the current task, since the functional connection between remote brain areas implies the presence of functional dependence between them. Considering our multivariate sets $\mathbf{x}(t)$ and $\mathbf{y}(t)$, our model establishes the relation between them and makes a prediction $\mathbf{y}'(t)$ of $\mathbf{y}(t)$ based on $\mathbf{x}(t)$. The successful approximation indicates the presence of functional connection between brain areas corresponding to the $\mathbf{x}(t)$ and $\mathbf{y}(t)$ trajectories. An example of FF-MLP with one hidden layer is shown in Fig. 1C (left).

Our model consisted of 3 input and 3 output *linear* units corresponding to the dimensionality of the multivariate datasets, and two hidden layers with 10 *softmax* units each. The training process was performed using the Adam optimizer (learning rate = 0.001) for 1000 epochs. The degree of functional dependence between response and predicted sets we estimated via the R^2-score measure:

$$R^2 = 1 - \frac{\sum_{d=1}^{D}\sum_{i=1}^{N}(y_d(t_i) - y'_d(t_i))^2}{\sum_{d=1}^{D}\sum_{i=1}^{N}(y_d(t_i) - \bar{y}_d)^2} \tag{3}$$

with the number of dimensions $D = 3$, and $y'_d(t)$, $y_d(t)$, $\bar{y}_d(t)$ are the d^{th} components of predicted and original time series and the mean value of the latter, respectively.

3. RESULTS

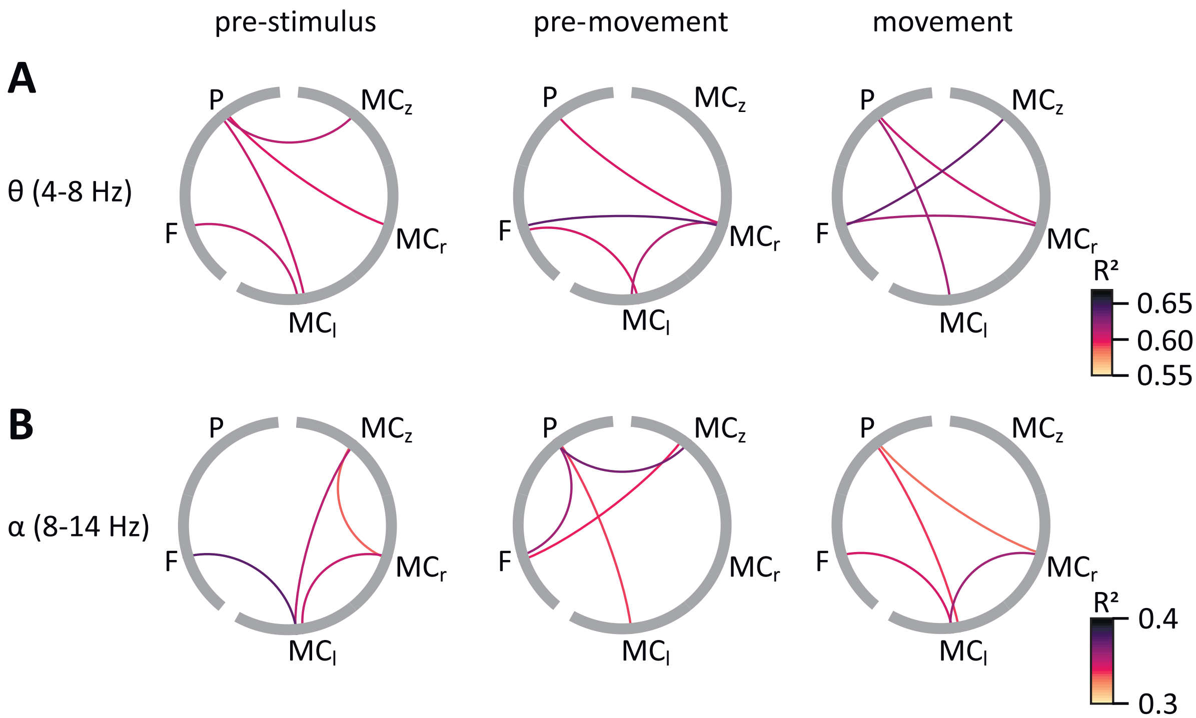

Figure 2. Functional connectivity of human brain during three stages of motor execution, obtained via FF-MLP for **A** θ and **B** α EEG rhythms. The links between brain areas are color-coded with the coupling strength based on the R^2 score.

Fig 1C shows an example of the response trajectory prediction via proposed FF-MLP model. We used an unfiltered single trial motor-related EEG. One can see that the model demonstrated a good ability to predict response trajectory based on the drive one, with $R^2 = 0.74$, which indicates an established functional dependence between $\mathbf{x}(t)$ and $\mathbf{y}(t)$.

We proceed with the analysis of functional connectivity between the remote brain areas in θ- (4-8 Hz) and α- (8-14 Hz) EEG rhythms, which are known to be associated with the processes of motor initiation and execution in healthy participants. The results are shown in Fig. 2.

The highest degree of functional dependence was obtained in the θ-band (see Fig.2A). During the prestimulus period, the strongest connections were established between motor and parietal cortices ($MC_l - P$, $MC_z - P$, $MC_r - P$), and between motor and frontal cortices ($MC_l - F$). Shortly after the audio stimulus, the network structure changes by terminating the link with midline motor area MC_z. Increased coupling in the motor cortex may be associated with working memory activated during the motor initiation.[26,29] The motor execution is associates with increased coupling between F and (MC_z,MC_r) and P and (MC_r,MC_l).

Considering the α-band connectivity (see Fig. 2B), most of the connections are concentrated in the motor cortex, which agrees with the known studies of the brain functional connectivity during motor execution assessed with more conventional methods.[30] One can notice, that most functional links are concentrated in MC_l area, which reflects contralaterality of motor activation in healthy participants. Besides, activation of parietal group of sensors during motor execution has been previously reported in[31] and linked to somatosensory-motor association.

4. CONCLUSION

We proposed an ANN-based approach to infere functional dependencies between remote brain areas during motor execution. Using the concept of generalized synchronization, we used multivariate subsets of EEG data as drive and response time series to train the FF-MLP model and obtain predictions of response set based on the state of drive set. Proposed model showed good ability to approximate functional relations between remote brain areas, with sufficient value of R^2 score in slow θ-band. Despite moderate level of R^2 score in α-band, FF-MLP model was able to provide an adequate estimation of functional connectivity during the motor execution.

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REFERENCES

[1] Hutchison, R. M., Womelsdorf, T., Allen, E. A., Bandettini, P. A., Calhoun, V. D., Corbetta, M., Della Penna, S., Duyn, J. H., Glover, G. H., Gonzalez-Castillo, J., et al., "Dynamic functional connectivity: promise, issues, and interpretations," *Neuroimage* **80**, 360–378 (2013).

[2] Pisarchik, A. N., Maksimenko, V. A., Andreev, A. V., Frolov, N. S., Makarov, V. V., Zhuravlev, M. O., Runnova, A. E., and Hramov, A. E., "Coherent resonance in the distributed cortical network during sensory information processing," *Scientific Reports* **9**(1), 1–9 (2019).

[3] Cai, R.-l., Shen, G.-m., Wang, H., and Guan, Y.-y., "Brain functional connectivity network studies of acupuncture: a systematic review on resting-state fmri," *Journal of Integrative Medicine* **16**(1), 26–33 (2018).

[4] Maksimenko, V. A., Runnova, A. E., Frolov, N. S., Makarov, V. V., Nedaivozov, V., Koronovskii, A. A., Pisarchik, A., and Hramov, A. E., "Multiscale neural connectivity during human sensory processing in the brain," *Physical Review E* **97**(5), 052405 (2018).

[5] Farràs-Permanyer, L., Guàrdia-Olmos, J., and Peró-Cebollero, M., "Mild cognitive impairment and fmri studies of brain functional connectivity: the state of the art," *Frontiers in psychology* **6**, 1095 (2015).

[6] Stam, C. J., Nolte, G., and Daffertshofer, A., "Phase lag index: assessment of functional connectivity from multi channel eeg and meg with diminished bias from common sources," *Human brain mapping* **28**(11), 1178–1193 (2007).

[7] Chang, C., Liu, Z., Chen, M. C., Liu, X., and Duyn, J. H., "Eeg correlates of time-varying bold functional connectivity," *Neuroimage* **72**, 227–236 (2013).

[8] Srinivasan, R., Winter, W. R., Ding, J., and Nunez, P. L., "Eeg and meg coherence: measures of functional connectivity at distinct spatial scales of neocortical dynamics," *Journal of neuroscience methods* **166**(1), 41–52 (2007).

[9] Rulkov, N. F., Sushchik, M. M., Tsimring, L. S., and Abarbanel, H. D., "Generalized synchronization of chaos in directionally coupled chaotic systems," *Physical Review E* **51**(2), 980 (1995).

[10] Moskalenko, O. I., Koronovskii, A. A., Hramov, A. E., and Boccaletti, S., "Generalized synchronization in mutually coupled oscillators and complex networks," *Physical Review E* **86**(3), 036216 (2012).

[11] Abarbanel, H. D., Rulkov, N. F., and Sushchik, M. M., "Generalized synchronization of chaos: The auxiliary system approach," *Physical Review E* **53**(5), 4528 (1996).

[12] Rakshit, S. and Ghosh, D., "Generalized synchronization on the onset of auxiliary system approach," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **30**(11), 111102 (2020).

[13] Ma, W., Li, C., and Deng, J., "Synchronization in tempered fractional complex networks via auxiliary system approach," *Complexity* **2019** (2019).

[14] Koronovskii, A. A., Moskalenko, O. I., and Hramov, A. E., "Nearest neighbors, phase tubes, and generalized synchronization," *Physical Review E* **84**(3), 037201 (2011).

[15] Koronovskii, A. A., Moskalenko, O. I., Shurygina, S. A., and Hramov, A. E., "Generalized synchronization in discrete maps. new point of view on weak and strong synchronization," *Chaos, Solitons & Fractals* **46**, 12–18 (2013).

[16] Senthilkumar, D., Lakshmanan, M., and Kurths, J., "Transition from phase to generalized synchronization in time-delay systems," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **18**(2), 023118 (2008).

[17] Pitsik, E., Frolov, N., Hauke Kraemer, K., Grubov, V., Maksimenko, V., Kurths, J., and Hramov, A., "Motor execution reduces eeg signals complexity: Recurrence quantification analysis study," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **30**(2), 023111 (2020).

[18] Frolov, N., Maksimenko, V., Lüttjohann, A., Koronovskii, A., and Hramov, A., "Feed-forward artificial neural network provides data-driven inference of functional connectivity," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **29**(9), 091101 (2019).

[19] Gallicchio, C., Micheli, A., and Pedrelli, L., "Design of deep echo state networks," *Neural Networks* **108**, 33–47 (2018).

[20] Lukoševičius, M. and Jaeger, H., "Reservoir computing approaches to recurrent neural network training," *Computer Science Review* **3**(3), 127–149 (2009).

[21] Pathak, J., Wikner, A., Fussell, R., Chandra, S., Hunt, B. R., Girvan, M., and Ott, E., "Hybrid forecasting of chaotic processes: Using machine learning in conjunction with a knowledge-based model," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **28**(4), 041101 (2018).

[22] Lorenz, E. N., "Deterministic nonperiodic flow," *Journal of the atmospheric sciences* **20**(2), 130–141 (1963).

[23] Doan, N. A. K., Polifke, W., and Magri, L., "Physics-informed echo state networks," *Journal of Computational Science* **47**, 101237 (2020).

[24] Hramov, A. E., Maksimenko, V. A., Pchelintseva, S. V., Runnova, A. E., Grubov, V. V., Musatov, V. Y., Zhuravlev, M. O., Koronovskii, A. A., and Pisarchik, A. N., "Classifying the perceptual interpretations of a bistable image using eeg and artificial neural networks," *Frontiers in neuroscience* **11**, 674 (2017).

[25] Hramov, A. E., Maksimenko, V., Koronovskii, A., Runnova, A. E., Zhuravlev, M., Pisarchik, A. N., and Kurths, J., "Percept-related eeg classification using machine learning approach and features of functional brain connectivity," *Chaos: An Interdisciplinary Journal of Nonlinear Science* **29**(9), 093110 (2019).

[26] Frolov, N. S., Pitsik, E. N., Maksimenko, V. A., Grubov, V. V., Kiselev, A. R., Wang, Z., and Hramov, A. E., "Age-related slowing down in the motor initiation in elderly adults," *Plos one* **15**(9), e0233942 (2020).

[27] Nuwer, M. R., Comi, G., Emerson, R., Fuglsang-Frederiksen, A., Guérit, J.-M., Hinrichs, H., Ikeda, A., Luccas, F. J. C., and Rappelsburger, P., "Ifcn standards for digital recording of clinical eeg," *Electroencephalography and clinical Neurophysiology* **106**(3), 259–261 (1998).

[28] Cybenko, G., "Approximation by superpositions of a sigmoidal function," *Mathematics of control, signals and systems* **2**(4), 303–314 (1989).

[29] Gruzelier, J., "A theory of alpha/theta neurofeedback, creative performance enhancement, long distance functional connectivity and psychological integration," *Cognitive processing* **10**(1), 101–109 (2009).

[30] Xu, L., Zhang, H., Hui, M., Long, Z., Jin, Z., Liu, Y., and Yao, L., "Motor execution and motor imagery: a comparison of functional connectivity patterns based on graph theory," *Neuroscience* **261**, 184–194 (2014).

[31] Hanakawa, T., Immisch, I., Toma, K., Dimyan, M. A., Van Gelderen, P., and Hallett, M., "Functional properties of brain areas associated with motor execution and imagery," *Journal of neurophysiology* **89**(2), 989–1002 (2003).