

Quantify Physiologic Interactions Using Network Analysis

Thuy T. Pham(✉) and Eryk Dutkiewicz

Faculty of Engineering and IT, University of Technology Sydney, Sydney, NSW 2006, Australia
thuy.pham@uts.edu.au

Abstract. To better understand the neural interactions amongst human organ systems, this work provides a framework of data analysis to quantify forms of neural signalling. We explore network interactions among the human brain and motor controlling. The main objective of this work is to provoke unique challenges in the emerging Network Physiology field. The proposed method applies network analysis techniques including power coherence for connectivity discovering and correlation measurement for profiling relationships. We used a well-designed dataset of 50 subjects over 14 different scenarios for each individual. We found network models for these interactions and observed informative network behaviours. The information can be used to study impaired communications that can lead to dysfunction of organs or the entire system such as sepsis.

Keywords: Physiology network · Data analysis · Brain · Network interactions

1 Introduction

The human body consists of diverse physiological organ systems of which each has its own structural and functional complexity, causing transient and nonlinear output information from each system [1]. Furthermore, complex signalling between these organ systems and sub-systems has been found among distinct physiologic states, e.g., wake and sleep; light and deep sleep; dreams; consciousness and unconsciousness (i.e., a person fails to respond normally to painful stimuli, light, or sound) [2,3]. Therefore, at the system level, the human organism can be considered as an integrated network with its own regulatory mechanism among physiological organ systems. Each organ system, referred to as a node continuously interacts with each other to maintain their functions. Recent works [4,5] showed that impaired communications can lead to dysfunction of organs or the entire system such as sepsis. However, the mechanisms of interactions over space and time scales are not well-understood and in need of a suitable analysing tool or theory-based framework [6].

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S. Misra et al. (Eds.): ICCSA 2019, LNCS 11619, pp. 142–151, 2019.
https://doi.org/10.1007/978-3-030-24289-3_12

The main challenge to study these interactions is the network complexity [3]. Each node of the network represents an individual physiological system and thus has different characteristics and outputs against others, therefore it is hard to identify and quantify their signalling. For example, each organ can be characterized by unsteady, periodic and non-linear output signals [7]. Furthermore, physiological organ systems operate in a wide range of time scales (*ms* to hours) and can be chaotic oscillators [8]. In contrast to traditional complex network theory, edges (i.e., links) in this field are non-deterministic, i.e., they do not constitute static connection graphs. In fact, changes in physiologic state can lead to collective network behaviours [3].

As a result, approaches in this area often span from statistical physics, applied mathematics to biomedical signals processing, human physiology and clinical medicine [3]. Recently, interdisciplinary methods have been found to address the aforementioned challenges. Biomedical engineers, data scientists, physiologists and medical specialists have worked as a team to shape a new field of Network Physiology [6]. Latest achievement examples are discoveries of differences in nonlinear heart dynamics during rest and exercise [9], a network-analysis tool to localize the epileptogenic zone [10], synchronous behaviour in network model based on human cortico-cortical connections [11], network structure of the human musculoskeletal system shapes neural interactions on multiple time scales [12].

Earlier nonlinear methods were used to tackle the complexity in non-linearity including phase synchronization, coherence in heart and brain [13], mutual information [14], and the Granger causal analysis [15]. Lately, the time delay stability [16] has been a new concept to identify physiologic interactions across distinct physiologic states (e.g., brain-organ communications as a signature of neuroautonomic control [16]). Specifically, if the time delay between systems is more consistent, the interaction is more stable and longer periods of the delay stability indicate stronger coupling [16]. These methods quantified the strength and directionality of links in the network.

From a data science perspective, information calculating has been applied to find the network of interaction. For example, entropy was measured between the brain and the heart [14]. Time-variant coherence analysis was introduced to study the control network of the cardiovascular and cardiorespiratory systems in patients with epilepsy [13]. Temporal interactions were investigated with bursts of activity in neural networks [17] to show whether bursting arise from inherent nodes or as a result of network interaction. Coherence measurement over time scale were found in latest works [10–12].

Above approaches have not been targeted to data mining for a diverse recording system at a large scale. More appropriate techniques should be deeply based on advances in complex network theory. Several pioneers proposed in near similar fields such as human symptoms-disease network [18]. The typical approach often involves weighted correlation analysis for module detection, variable selection, topological information extraction. Nevertheless, these methods adopted *temporal network* forms (i.e., modelling as graphs of vertices coupled by edges) [19]. Though the *static* network topologies were developed to time-dependent

models [19], the complex activities of individual nodes and the time-variant links were missed [6]. Hence, merging of those techniques could help alleviate aforementioned unique challenges in the network physiology.

We propose network analysis techniques such as power coherence to model the connectivity of network and correlation measures for profiling relationships. The main contribution of this work: propose a new framework of using network analysis techniques for physiology interactions within a human body.

2 Methods

From graph theory perspective, we consider each data channel (i.e., one of 64 recording location on the scalp) as a node of a network. The relationship between two electrophysiological signals recorded at two nodes is the *link* (or edge) of two nodes. The strength of the relationship is called *weight* of the link. In this work, to compute the weight, we first computed pairwise spectral coherence C_{xy} between the two data windows of nodes x and y. C_{xy} is calculated by the Fourier transform (the Welch method [20] Eq. 1) between two EEG channels across time windows (size of 2.5s sliding each second) in the frequency range of 30–90 Hz (so-called *gamma* band).

$$C_{xy}(\omega) = \frac{P_{xy}(\omega)}{\sqrt{P_{xx}(\omega).P_{yy}(\omega)}} \tag{1}$$

where ω is frequency, $P_{xx}(\omega)$ is the power spectrum of signal x, $P_{yy}(\omega)$ is the power spectrum of signal y, and $P_{xy}(\omega)$ is the cross-power spectrum for signals x and y. When $P_{xx}(\omega) = 0$ or $P_{yy}(\omega) = 0$, then also $P_{xy}(\omega) = 0$ and we assume that $C_{xy}(\omega)$ is zero. The power and cross spectra are estimated by the Fourier transform. In the continuous domain, let $\mathfrak{F}_x(\omega)$ and $\overline{\mathfrak{F}_x(\omega)}$, denote the Fourier transform and its conjugate of signal x, respectively, i.e. $\mathfrak{F}_x(\omega) = \int_{-\infty}^{+\infty} x(t).e^{-j\omega t}dt$.

Then, the neural interactions are represented by a three-dimension matrix of which one dimension is for time windows and the others are for a connectivity matrix, C. The centrality of a node at a time point is measured by the strength and number of connections a node makes with others. In this work, the centrality is computed from the singular vector decomposition of C. The leading eigenvector is extracted to represent for each node (further details of *eigenvector centrality* was analysed in the earlier works [10]).

To analyse properties of the constructed network, we propose to depict the strength of relationship between two nodes across time windows (i.e., the entire experiment task) using the Pearson correlation coefficient definition [21]. Because we are looking for the strength of relationships, the direction of the coefficients is ignored (i.e., coefficients $=|r|$ and is from $0 \rightarrow 1$). When $|r|$ is closer to 1, the more closely two nodes are related. In order to investigate leading interactions, we applied a threshold p ($0 < p < 1$) to filter out minor links (i.e., links with small weights, thus, represent weak relationships). Specifically, we preserved a

proportion p of the links with largest weights; all other links including self-node connections were assigned with weight of 0. We can vary this p to better visualise the network models. The proposed method was implemented using MATLAB scripts R2018b (The MathWorks Inc., Natick, MA, 2000).

3 Datasets

We used a well-designed dataset of 50 subjects across 14 different scenarios for each individual. This data set is a portion of a larger collection [22] originally contributed to PhysioBank [23] by Gerwin Schalk and his colleagues using their BCI2000 system [24] (www.bci2000.org) at Wadsworth Center, New York State Department of Health, Albany, NY. W.A.

The dataset consists of 700 electroencephalogram (EEG) recordings. This measurement technique depicts electrical activity of the brain as wave patterns. Electrodes (i.e., small metal discs with thin wires) were placed on the scalp, and then send signals to a computer for further processes. The system was used in this dataset is a 64-channel type (Fig. 1) that covers the scalp from frontal left /right, central left/right, to occipital left/ right. The electrode map is as per the

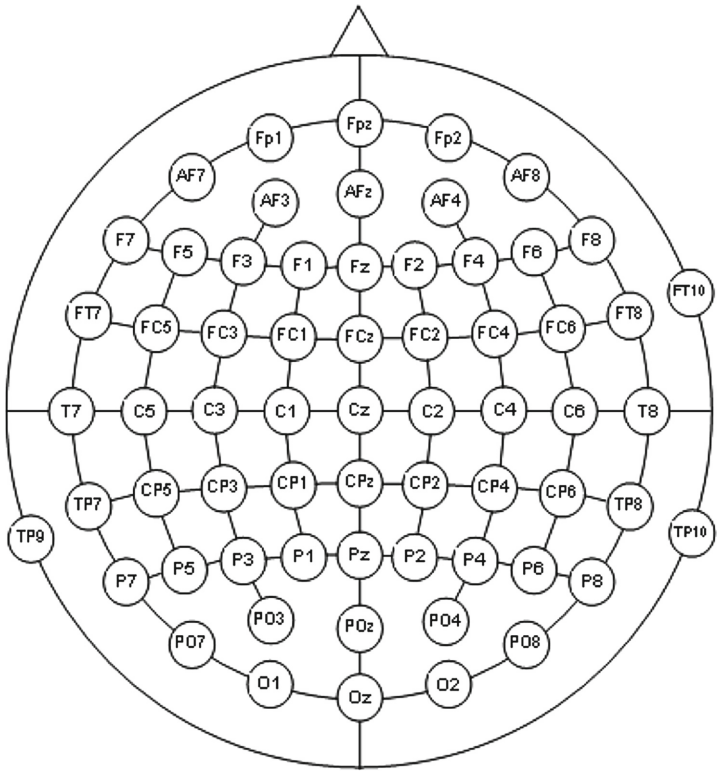


Fig. 1. The electrode map of 64 channels from BCI2000 [22].

international 10-10 system (excluding electrodes Nz, F9, F10, FT9, FT10, A1, A2, TP9, TP10, P9, and P10). The numbers below each electrode name indicate the order in which they appear in the records.

There are 14 experimental runs for each individual as in Table 1. Each recording measures for one or two minutes. Sampling rate was set at 160 samples per second. Raw EEG data were filtered by a Butterworth notch filter of order 4 (built-in MATLAB function) for the range of 59.5–60.5 Hz. We eliminated correlated noise across channels by taking an average signal from all recordings of the same subject and subtract this from each channel. We also discarded channels which were labelled as *artefacts contaminated*. Each network is calculated for each subject then we investigate neural interactions by looking at the average network for each scenario (i.e., averaging weights of the same link during a same task description across 50 subjects).

4 Results

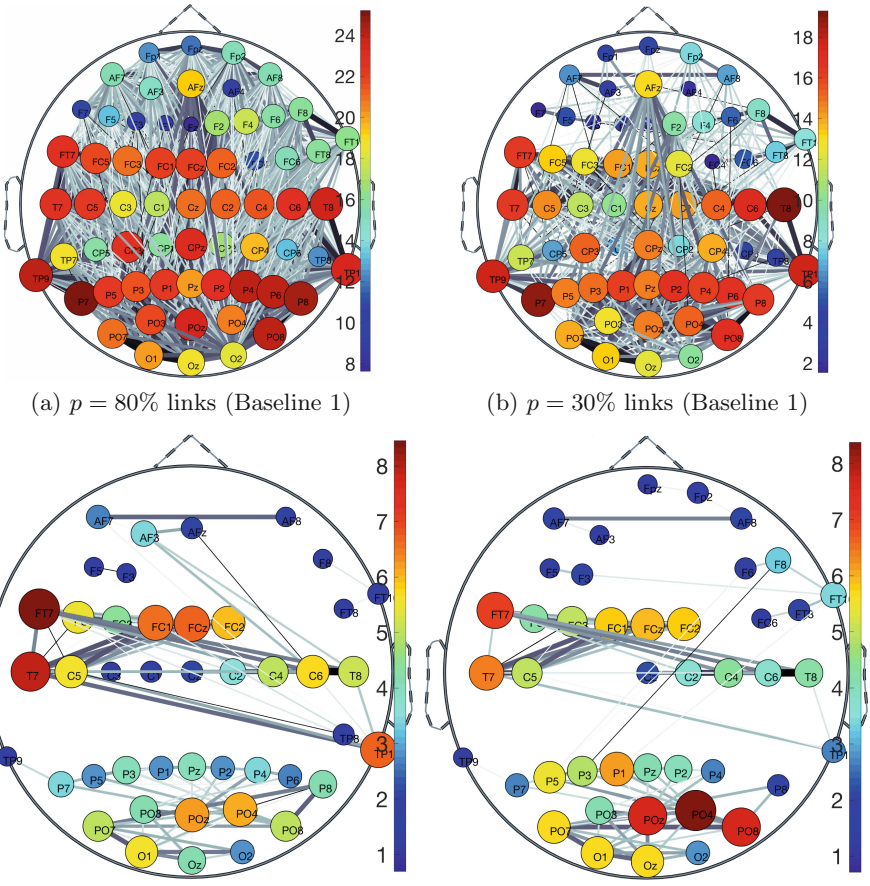
We varied parameter p from only $1 \rightarrow 100\%$ for the proportion of links with largest weights to be preserved. Figure 2 (a, b, c) illustrates examples of different p in the same Baseline 1 task (i.e., when the subject only open eyes Table 1).

Table 1. Specifications of experimental tasks for each individual [22].

Task Name	Length (seconds)	Repeats	Task Description
Baseline 1	60	1	Eyes open
Baseline 2	60	1	Eyes closed
Task 1	120	3	A target appears on either the left or the right side of the screen. The subject opens and closes the corresponding fist until the target disappears. Then the subject relaxes
Task 2	120	3	A target appears on either the left or the right side of the screen. The subject imagines opening and closing the corresponding fist until the target disappears. Then the subject relaxes
Task 3	120	3	A target appears on either the top or the bottom of the screen. The subject opens and closes either both fists (if the target is on top) or both feet (if the target is on the bottom) until the target disappears. Then the subject relaxes
Task 4	120	3	A target appears on either the top or the bottom of the screen. The subject imagines opening and closing either both fists (if the target is on top) or both feet (if the target is on the bottom) until the target disappears. Then the subject relaxes

We found that at level of 30% preserved links the network constructed still has a high level of complication for analysis by visualisation method. In the scope of this work, we suggest to further analyse the model with 5% preserved links.

According to the top 5% of all possible relationships, we can clearly observe major interactions by the colour and size of each node which are upon the number of connections associated with the node. The links are also illustrated in a similar way in the grayscale. For example, Fig. 2(c, d) compares two networks between baselines (i.e., open and close eyes). In the *open eyes* action, the main active areas are at electrodes FT7, T7, then TP1, FC1, FCz. In the *close eyes* action, most active electrodes shifted to electrode POz, PO4, PO8 (Fig. 2c, d).



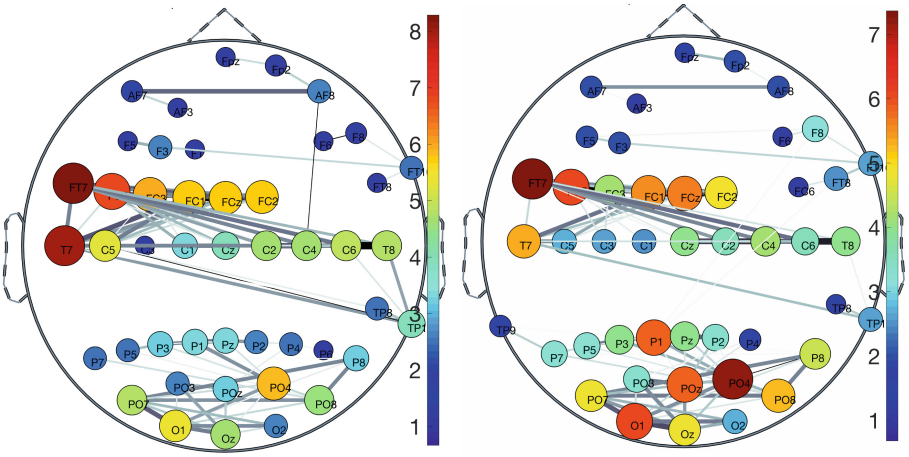
(a) $p = 80\%$ links (Baseline 1)

(b) $p = 30\%$ links (Baseline 1)

(c) $p = 5\%$, open eyes (Baseline 1)

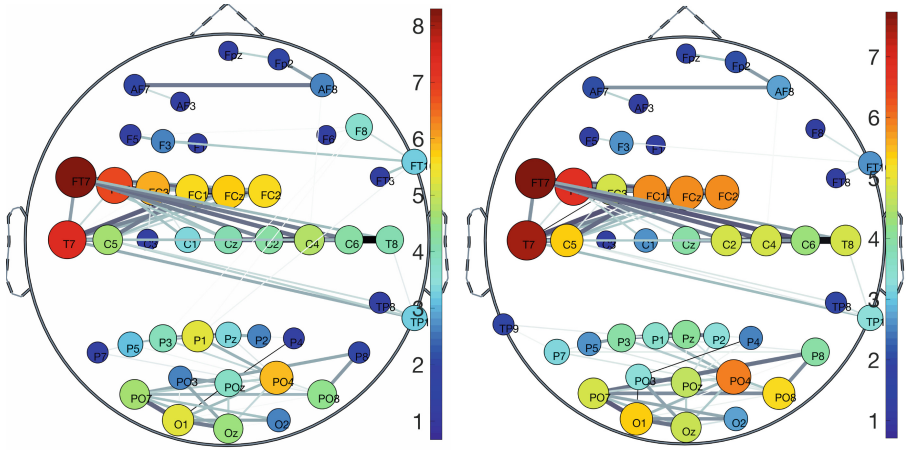
(d) $p = 5\%$, close eyes (Baseline 2)

Fig. 2. Varying the proportion parameter p for preserved links with largest weights. (a, b, c) are for different p in the same Baseline 1 (Table 1). (c, d) are between open and close eyes when $p = 5\%$. Colour and size of each node are up to the number of connections. Links are weighted in the grayscale.



(a) Open and close left/right fist (Task 1) (b) Imagine Task 1 (Task 2)

Fig. 3. Comparisons of networks across tasks. (a, b) are for Task 1 and its *imagine* version (Table 1). Colour and size of a node are up to the number of connections. Links are weighted in the grayscale.



(a) Open and close both fists/feet (Task 3) (b) Imagine Task 3 (Task 4)

Fig. 4. Comparisons of networks across tasks. (a, b) are for Task 3 and the *imagine* (Table 1). Colour and size of a node are up to the number of connections. Links are weighted in the grayscale.

Regarding to four other tasks, they can be grouped into two scenarios of controlling movements (open and close) of one or both hands/feet. In both scenarios, each subject was asked to do and imagine doing the action. Figures 3 and 4 shows four networks construct through these four tasks. We noted that state of the network only changed slightly between acting on one to both hands

(Figs. 3a and 4a). However, the changes of network appeared clearly between doing the action and imagine doing so (Fig. 3a, b). Specifically, more connections appeared in the back area of the scalp (e.g., electrode PO4, POz, and O1) than in the task of *in action*.

5 Conclusion

In this work, we attempt to analyse physiologic networks. We propose a framework to construct relationships between nodes using power spectral coherence and singular decomposition. Then we use correlation measurements to represent major interactions through largest link weights and node attributes. We demonstrated the method with a real dataset of 64 EEG channels across different experimental tasks such as open and close one hand or both hands or imagine doing each of these actions.

We found changes in network properties between these different tasks. At level of more than 5% preserved links, the network is highly complicated to analyse by visualisation method. Major interactions are depicted by the number of connections associated with the node. During *open eye* tasks, electrodes of FT7, T7, then TP1, FC1, FCz are main active areas. During *close eye* tasks, the participating area shifted to electrode POz, PO4, PO8.

In other tasks (i.e., two scenarios of controlling movements (open and close) of one or both hands/feet), state of the network only changed slightly between acting on one to both hands. However, more connections appeared in the back area of the scalp (e.g., electrode PO4, POz, and O1) when imagining the task than doing so in action.

6 Discussion

These informative network behaviours can be used to study impaired communications that can lead to dysfunction of organs or the entire system such as sepsis. For example, in the next steps of this works, we will intensively investigate changes in network topologies and other characteristics to find associations of neural interactions between different controlling scheme of the brain and other body parts. This may require new data collections and more specific experimental designs of trials. Nevertheless, the framework of this work will continue to be applied to the aforementioned extension or even a new clinical application such as network analysis for freezing of gait monitoring in patients with Parkinson's disease [25,26]. The underlying mechanism of the freezing is not well-understood while sensory information channels have been successfully demonstrated in our earlier works [25–27]. Therefore, this network-based framework would open a new way to investigate freezing of gait occurrences.

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