Human Movement Science

Dynamic Networks of Physiologic Interactions of Brain Waves and Rhythms in Muscle Activity

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Corresponding Author:	Plamen Ch. Ivanov, Professor Boston University UNITED STATES
First Author:	Rossella Rizzo, Dr.
Order of Authors:	Rossella Rizzo, Dr.
	Sergi Garcia-Retortillo
	Plamen Ch. Ivanov, Professor
Abstract:	The brain plays a central role in facilitating vital body functions and in regulating physiological and organ systems, including the skeleto-muscular and locomotor system. While neural control is essential to synchronize and coordinate activation of various muscle groups and muscle fibers within muscle groups in relation to body movements and distinct physiologic states, the dynamic networks of brain-muscle interactions have not been explored and the complex regulatory mechanism of brain-muscle control remains unknown. Here we present a first study of network interactions between brain waves at different cortical locations and peripheral muscle activity across key physiologic states – wake, sleep and distinct sleep stages. Utilizing a novel approach based on the Network Physiology framework and the concept of time delay stability, we find that for each physiologic state the network of cortico-muscular interactions is characterized by a specific hierarchical organization of network topology and network links strength, where particular brain waves are main mediators of interaction and control of muscular activity. Further, we uncover that with transition from one physiological state to another, the brain-muscle interaction network undergoes marked reorganization in the profile of network links strength, indicating a direct association between network structure and physiological state and function. The pronounced stratification in brain-muscle network characteristics across sleep stages is consistent for chin and leg muscle groups and persists across subjects, indicating a remarkable universality and a previously unrecognized basic physiologic mechanism that regulates muscle activity even during rest and in the absence targeted direct movement. Our findings demonstrate previously unrecognized coordination between brain waves and activation of different muscle fiber types within muscle groups, laws of brain-muscle cross-communication and principles of network integration and control. These investigations demonstrate the potential of network-based biomarkers for classification of distinct physiological states and conditions, for the diagnosis and prognosis of neurodegenerative, movement and sleep disorders, and for developing efficient treatment strategies.
Suggested Reviewers:	Ruedi Stoop, Prof. Professor, Institute of Neuroinformatics and Physics, UZH/ETHZ Zürich ruedi.stoop@gmail.com Experience in: - biological computing - statistical physics - time series - physiological signals
	Sebastiano Stramaglia, Prof. Professor, Università di Bari Sebastiano.Stramaglia@ba.infn.it

	Experience in: complex systems data analysis network neuroscience network physiology signal processing

Highlights

- Network Physiology approach to brain-muscle interactions reveals complex networks.
- Time delay stability measure identifies coupling of brain waves with muscle rhythms.
- Hierarchical organization in brain-muscle networks with distinct profiles of links strength.
- Distinct profiles for network links strength during wake, sleep and sleep stages.
- Brain-muscle network universality for different muscle groups and subjects.

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Abstract

The brain plays a central role in facilitating vital body functions and in regulating physiological and organ systems, including the skeleto-muscular and locomotor system. While neural control is essential to synchronize and coordinate activation of various muscle groups and muscle fibers within muscle groups in relation to body movements and distinct physiologic states, the dynamic networks of brain-muscle interactions have not been explored and the complex regulatory mechanism of brain-muscle control remains unknown. Here we present a first study of network interactions between brain waves at different cortical locations and peripheral muscle activity across key physiologic states – wake, sleep and distinct sleep stages. Utilizing a novel approach based on the Network Physiology framework and the concept of time delay stability, we find that for each physiologic state the network of cortico-muscular interactions is characterized by a specific hierarchical organization of network topology and network links strength, where particular brain waves are main mediators of interaction and control of muscular activity. Further, we uncover that with transition from one physiological state to another, the brain-muscle interaction network undergoes marked reorganization in the profile of network links strength, indicating a direct association between network structure and physiological state and function. The pronounced stratification in brain-muscle network characteristics across sleep stages is consistent for chin and leg muscle groups and persists across subjects, indicating a remarkable universality and a previously unrecognized basic physiologic mechanism that regulates muscle activity even during rest and in the absence targeted direct movement. Our findings demonstrate previously unrecognized coordination between brain waves and activation of different muscle fiber types within muscle groups, laws of brain-muscle cross-communication and principles of network integration and control. These investigations demonstrate the potential of network-based biomarkers for classification of distinct physiological states and conditions, for the diagnosis and prognosis of neurodegenerative, movement and sleep disorders, and for developing efficient treatment strategies.

Keywords: Network physiology, Dynamic networks, Time delay stability, Bursts, Brain waves, Muscle activity, Wake, Sleep

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1. Introduction

The human body comprises diverse organ systems, which continuously interact to synchronize and coordinate their dynamics and to generate various physiological functions. Mapping the network of interactions among physiological systems is thus of primary importance to fully understand basic physiological states and functions, to rigorously define and discriminate between healthy and pathological conditions. A new field, Network Physiology (Ivanov, 2021; Ivanov, Liu & Bartsch, 2016), has been established to address the fundamental question of how physiological states and functions emerge at the organism level through integrated networks of interactions among diverse systems and subsystems across spatiotemporal scales (Bashan et al., 2012; Bartsch et al., 2015; Ivanov & Bartsch, 2014). In this context, the brain-muscle communication network, which is essential for locomotor control of posture and movements during distinct physiologic states, remains not understood. Traditional approaches to cortico-muscular coordination focus on associations between movement tasks or exercises and the activation of particular brain waves at specific cortical areas (Ciria et al., 2019; Rendeiro & Rhodes, 2018; Yokoyama et al., 2016). However, neural control of the muscular system is continuously present even at rest. Recent studies have shown that network interactions among brain waves are characterized by distinct coupling profiles and network plasticity that are essential to generate physiological states and functions (Lin et al., 2020; Bartsch & Ivanov, 2022; Liu et al., 2015a,b). We hypothesize that network interactions between brain waves and rhythms embedded in muscle activity may also reflect changes in physiologic regulation as a function of physiological states. We investigate the coupling between physiologically relevant brain waves at distinct cortical locations with peripheral EMGactivity in different frequency bands across four major, well defined physiological states — Wake, REM, Light Sleep (LS),Deep Sleep (DS). We aim to map the default brain-muscle interaction network corresponding to low level of physical activity in the absence of directed and targeting movements during sleep and quiet restful wake. Importantly, we find that cortico-muscular interaction profiles of network links strength and related network topology uniquely identify each physiological state and hierarchically reorganize with transition fromone state to another – wake to sleep and across sleep stages.

2. Methods

2.1. Data

We analyze cortical EEG and surface leg and chin muscle EMG signals from 36 healthy young subjects (ages 20-40, M = 29 years old), synchronously and continuously recorded during nocturnal sleep (ave. record duration 7.8h) from EU SIESTA databases (Klosh et al., 2001). Data were divided in 30 s epochs and scored as Wake, REM, LS and DS (Klosh et al., 2001). Analyzed data include EEG from six scalp locations (Fp1, Fp2, C3, C4, O1, O2)and the EMG of left leg muscle (anterior tibialis) and chin muscle (mentalis). Data were visually inspected to remove noisy segments, usually located at the beginning and the end ofthe recordings. Power-line interferences were removed usinga 50 Hz notch filter, and signals were bandpass filtered in the range [0.5 98.5] Hz. The spectral power of seven frequency bands of the EEG and EMG signals was parallelly extractedin moving windows of 2s with a 1s overlap: δ [0.5–3.5] Hz, θ [4–7.5] Hz, α [8–

11.5] Hz, σ [12–15.5] Hz, β [16–19.5] Hz, γ_1 [20–33.5] Hz and γ_2 [34–98.5] Hz. Thus, all time series have the same time resolution of 1s before the analysis.

2.2. Time Delay Stability

We use the Time Delay Stability (TDS) method (Bashan et al., 2012) to quantify periods of synchronous activity in two systems, where bursts in one system are followed with constant time delay by bursts in the other system, as a measure of degree of coupling. TDS quantifies the stability of the time delay with which bursts in the output dynamics of a given system are consistently followed by corresponding bursts in the signal output of another system. Longer periods of TDS between the output signals of two systems reflect more stable interaction and stronger coupling. Strong coupling (high TDS) between two systems corresponds to a strong link in the interaction network between brain waves and muscle activity rhythms. Network links strength is defined as %TDS, i.e., the fraction of segments with TDS (constant time delay) in the entire recording. To test the statistical significance and physiological relevance of the network interactions identified by the TDS method, we perform a surrogate test: for each link in a given sleep stage, 200 surrogates are generated considering signals from two randomly chosen subjects, and a surrogate average link strength (%TDS) is obtained. The procedure is repeated for each network link to obtain a distribution of surrogate link strengths for each sleep stage. For each distribution the mean μ_{surr} and standard deviation σ_{surr} are estimated. Thus, the significance threshold at 95% confidence level for the network links strength is defined as $\mu_{surr} + 2\sigma_{surr}$ corresponding to %TDS = 2.3%, and is represented by horizontal green lines in all figure panels showing bar plots of average links strength.

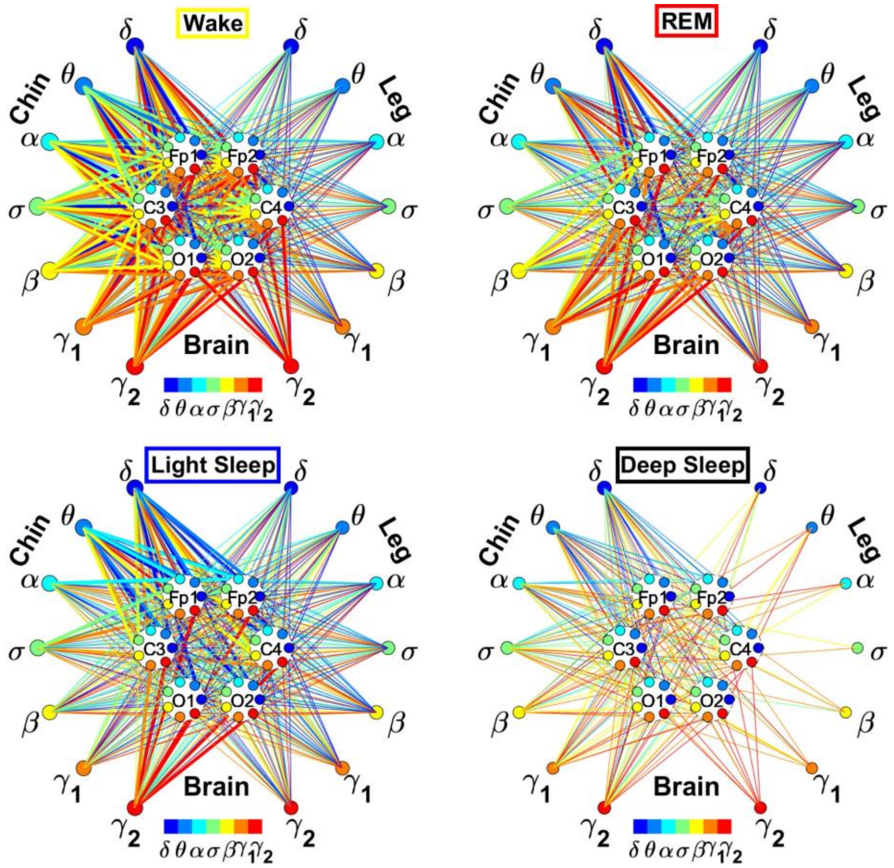

Figure 1

2.3. Averaging procedure for estimating links strength in physiological networks

For each physiologic state, we calculate a group-average %TDS representing the coupling of each leg/chin EMG frequency band with the brain waves (cortical rhythms) embedded in each EEG channel across all subjects. To avoid coupling artifacts related to noisy data inthe calculation of the group-average TDS for each network link, we remove outlier subjects for which the strength of the link is outside +/-2 standard deviation of the group-average TDS, and we recalculate the new updated group-average link strength.

In the cortico-muscular network (Fig. 1), group-average TDS link strength is represented by the link thickness. To obtain information on the average link strength representing the interaction of a brain wave from a given brain area withall EMG rhythms (integrated EMG activity), we calculate the average coupling strength (%TDS) of a given brain wave froma given EEG channel with all EMG bands of the leg (or chin) muscle (Fig. 2). Similarly, to obtain information on the relative contribution in the brain-muscle communication network of each muscle activity rhythm (EMG frequency band) with the integrated EEG activity, we consider the average coupling strength of a given EMG frequency band with all brain waves at a given EEG channel location (Fig. 3). We refer to these two types of coarse-grained networks as ’brain waves to integrated muscle activity’ and ’muscle rhythms to integrated brain activity’ interaction networks.

3. Results

3.1. Brain-muscle network and its dynamical reorganization across physiologic states

We identify and characterize the brain-muscle interactions network across four major physiologic states: Wake, REM, LS and DS. We consider brain activity from six major cortical areas — Fp1, Fp2, C3, C4,O1, and O2 —, leg muscle tone, and chin muscle tone, simultaneously recorded overnight-sleep using EEG and EMG. We then quantify couplings and network interactions by means of the TDS method [1]. The cortico-muscular network in Fig. 1 reorganizes across physiologic states. Specifically, the networkis denser and exhibits stronger links during Wake, and sparser during LS and DS. Brain-chin network links are generally stronger than brain-leg links, in particular during Wake and REM. Particular cortical rhythms and EMG frequency bands emerge as main mediators of the brain-muscle interaction. During Wake and REM the strongest links correspond to interactions mediated by the high frequency cortical rhythms, in particular γ_2 (red links). We observe that the network markedly reorganizes with transition to LS, and strong links related to slower cortical rhythms appear in the network (dark and light blue links), in particular between the chin and the frontal region of the brain. Finally, the link number and strength abruptly decline during DS (Fig. 1).

3.2. Coarse-grained interaction networks of cortical rhythms with integrated leg muscle tone

To identify the role of different brain rhythms in muscle control across cortical locations, we coarse-grain the TDS links strength across EMG rhythms (Sect. II), and represent in coarse-grained networks and corresponding bar charts (Fig. 2). The brain-leg interaction network significantly changes with transition across sleep, with strong interactions during Wake, intermediate during REM and LS, and weak during DS (One-Way ANOVA rank test for each brain location shows a statistically significant difference between sleep stages; $p < .001$). No significant differences in network links strength are found between theleft and right hemisphere for each sleep stage (MW test, $p > .67$), nor among different brain areas within a brain hemisphere for a given sleep stage (One-Way ANOVA rank test; $p > .44$). The frequency profile of network links remains stable for all brain areas in a given sleep stage, and reorganizes with transitions across sleep stages. During Wake, brain-to-leg interaction is characterized by strongest links for the high-frequency bands γ_1 and γ_2 and a gradual decreasein links strength for the lower-frequency bands, followed by a slight kink up in link strength for the δ band (One-Way ANOVA rank test and multiple pairwise comparison performed for Fp1 show $p < .005$). Differences between links involving different cortical rhythms gradually decrease in REM, LS and DS, although remaining significant. Similar patterns inthe network structure and frequency profile reorganization are observed for brain-chin interactions.

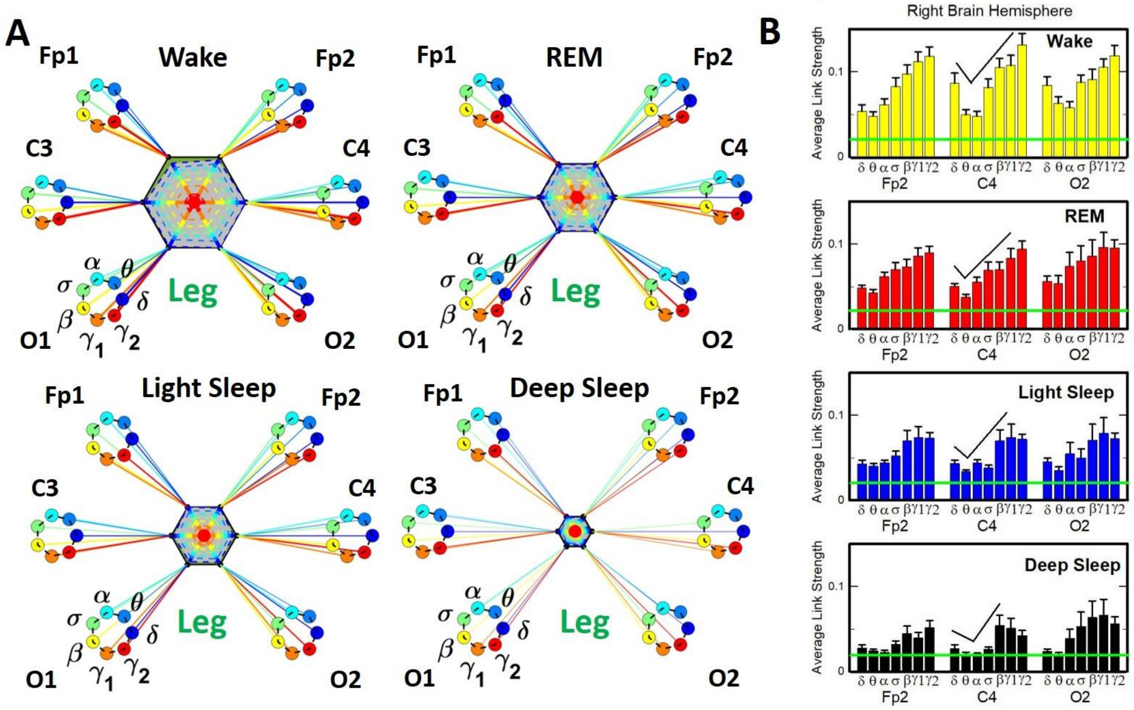

Figure 2

3.3. Coarse-grained interaction networks of integrated brain activity at cortical locations and leg EMG frequency bands

We next consider the average coupling strength of a given EMG frequency band with all brain waves derived from an EEG channel (Fig. 3). The leg-brain network reorganizes across states, with uniform distribution of links over cortical areas, and a symmetry between left and right hemispheres. In contrast to brain-to-leg network, we do not observe dominant links in the interactions of leg EMG bands with integrated cortical areas for all sleep stages (One-way ANOVA $p > .21$). Links are stronger during Wake, with decreasing strength for REM, LS and DS. Chin-to-brain networks exhibit similar stratification and reorganization across sleep stages.

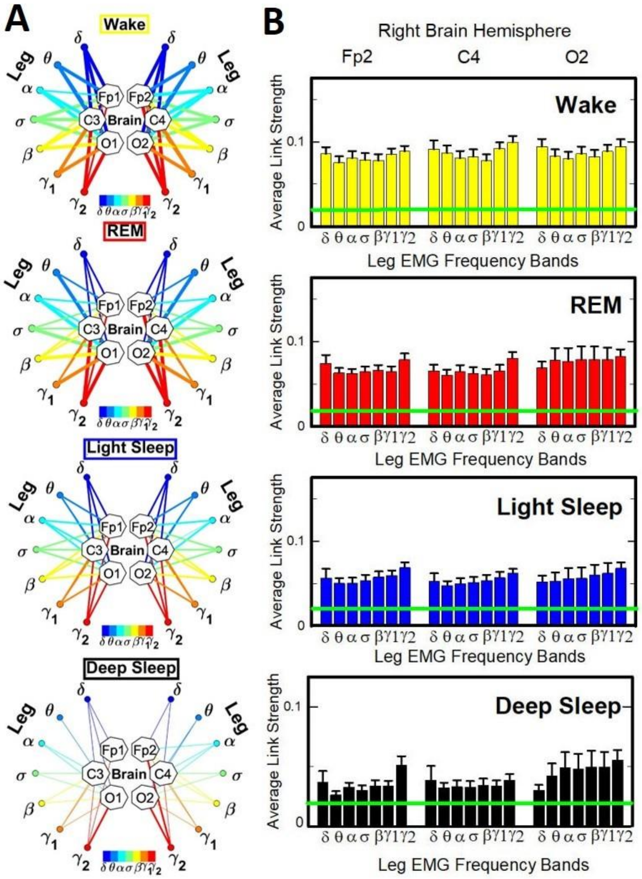

Figure 3

4. Discussion

We systematically study brain-muscles interaction networks and their associations with physiologic states. We find that neuromuscular control is mediated through complex network interactions between brain waves and rhythms in muscle activity, with hierarchical organization of network links strength as hallmark of physiologic state. The reported results are robust and consistent across subjects indicating universal laws in brain-muscle network communication. Furthermore, we uncover preferred pathways in network communication between brain waves and rhythms in the skeletal muscles activity that uniquely identify sleep stages through a previously unrecognized hierarchical network organization. The reported findings open new perspectives on the regulatory mechanisms of brain dynamics and neuromuscular activity in the absence of directed and targeted movement during quiet wake and sleep. They show that in addition to neural synchrony within the motor system (Wijk, Beek, & Daffertshofer), synergy among muscle groups (Bach, Daffertshofer, & Dominici; Kerkman et al., 2020) and activation of brain waves across cortical areas during active movement (Ciria et al., 2019), there is a previously unrecognized physiologic mechanism regulating network interactions between brain waves and rhythms in muscle activity. These investigations raise new questions of how cortical waves and spectral rhythms in muscle activity representing different types of muscle fibers (Garcia-Retortillo et al., 2020; Garcia-Retortillo, Rizzo & Ivanov, 2021) synchronize and integrate as a network during exercise and breakdown with fatigue (Balagué et al., 2020). Further, our study shows that different brain waves play role as the main mediators of brain-muscle network interactions compared to the brain-heart regulatory network (Lin et al., 2016), which demonstrates that markedly different dynamic networks with distinct structure and dynamics mediate autonomic regulation and brain control of different organ systems (Ivanov et al., 2017). The reported empirical observations of hierarchical reorganization in brain-muscle networks with transitions across states, where distinct profiles of network links strength represent each physiologic state, indicate the potential utility of the Network Physiology framework and derived network-based novel biomarkers with implications for neurodegenerative, locomotor and sleep disorders (Moorman, Lake & Ivanov, 2016).

5. Funding Sources

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Figure captions

*Figure 1***.** Dynamic networks of cortico-muscular interactions across physiological states. Network maps represent physiological interactions during wake, REM, LS and DS. Brain areas are represented by two Frontal, two Central and two Occipital EEG channels, where nodes with different color in each brain area represent distinct brain waves. Peripheral nodes indicate EMG frequency bands of leg and chin muscle tone shown in the same color as the brain waves. Network links show the coupling strength of each cortical rhythm across cortical areas with each EMG frequency band as quantified by the TDS measure. Links strength is marked by line width: thin lines for $3\% < \%TDS < 12\%$; thick lines for $\%TDS > 12\%$. TDS = Time Delay Stability.

Figure 2. Dynamic network interactions between cortical rhythms and integrated leg-muscle activity across physiological states. (A) Radar-chart representation of group-averaged TDS coupling strength of the interactions between each brain rhythm at a given cortical location and the leg muscle tone, after averaging over all leg EMG frequency bands. Brain areas are represented by six EEG channels, where network nodes with different colors mark different cortical waves. A centered hexagon represents the integrated leg muscle tone. Links strength is indicated by line thickness; links color corresponds to the color of brain rhythms involved. Networks include only links with strength above the significance threshold $\%TDS = 2.3\%$. The length of each colored segment along each radius in the radar-charts represents the TDS coupling strength between each cortical rhythm at each EEG location and the leg muscle tone averaged over all EMG bands. Segments in the radar-charts are shown with same color as the

corresponding brain rhythms. (B) Characteristic profiles of network links strength for cortical rhythms interactions with integrated leg-muscle tone for right brain hemisphere. Link strengths are grouped by brain areas, and are ordered from low- to high-frequency cortical rhythms. Error bars represent the standard error; horizontal green lines are the significance threshold.

Figure 3. Dynamic networks of leg EMG frequency bands and integrated brain activity at cortical areas for different physiological states. (A) Links in network maps represent group-averaged TDS coupling strength between each frequency band of leg muscle tone and a given cortical area, after averaging network links to all brain waves at the cortical area. Cortical areas are represented by EEG channel locations, while peripheral network nodes with different colors represent leg EMG frequency bands. Line thickness indicates link strength (weak links with 3% < TDS < 5%, intermediate links with 5% < TDS < 7.5% and strong links with TDS >7.5%); links color corresponds to the color of the leg EMG frequency bands. (B) Characteristic profiles of network links strength representing interactions between integrated brain activity at distinct cortical areas in the right brain hemisphere and individual leg EMG frequency bands. Links are grouped by cortical areas, and are ordered from low- to high-frequency leg EMG bands. Error bars represent standard error for all subjects; horizontal green lines mark the physiologically relevant significance threshold $\%TDS = 2.3\%$.

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Rossella Rizzo[1], Sergi Garcia-Retortillo[1] & Plamen Ch. Ivanov[1]

[1]Keck Laboratory for Network Physiology, Department of Physics, Boston University, Boston, MA 02215, USA.

Rossella Rizzo
Rossella.rizzo@unical.it

Sergi Garcia-Retortillo
sgarciaretortillo@gmail.com

Plamen Ch. Ivanov (Corresponding Author)
plamen@buphy.bu.edu
590 Commonwealth Avenue, 2nd Floor, SCI-210, Boston, MA 02215, USA.