**Editorial**

# Editorial on the special issue on brain physiology meets complex systems

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## 1 Introduction

Our brain is a state within a state that not only controls the functioning of organs, but also determines the future of mankind. Great discoveries in science, the emergence of new civilizations, art, love, and everything that we realize and feel is a great work of different nerve centers. The structure of the brain is similar to the galaxy, where many planets form a complex system. That is why for many centuries the physiology of the brain was presented as a black square of Malevich, meaning that we know very little about how our brain works. It is well known that all diseases are from the brain [1, 2]. However, it remains a particular challenge to understand how human diseases and disorders develop from internal neural level irregularities. The complex systems science and brain dynamics have advanced significantly, giving rise to high expectations of tying separate neurological phenomena into the new system of knowledge about the brain physiology and pathophysiology [3, 4].

This *European Physical Journal Special Topics Special Issue* is a collection of papers highlighting new approaches for the study of brain functions, including the use of complex and interdisciplinary methods, modeling, imaging, and monitoring technologies for neuronal architecture, cerebral vessels, and the meningeal lymphatic system, new approaches to studying the sleeping brain, and drainage of its tissues.

## 2 Computational models of neural–glial networks

There is a recently emerged understanding that the brain's activity cannot be considered in isolation from physiological processes, which occurs in the extracellular space. At the same time, the respective transport processes are sufficiently complex and their modelling encounters several controversial issues. This situation induces a need for developing a physical phantom model with a structure resembling the brain's parenchyma tissue, but having controlled properties. Vanina et al. [5] reports the synthesis and study of properties of a novel phantom medium, based on collagen hydrogel with additions aimed at coordinating the phantom's composition and structure with that of the brain, as demonstrated by chemical analysis, electron microscopy, and computed tomography in the regime of clinical brain scanning. In addition, the quantification of the fluorescent marker spread was carried out. It demonstrated that the types of transport in the developed medium correspond to the specific features detected earlier in the rat's brain.

Due to the high nonlinearity of oscillators resembling neuronal activity, even their small coupled systems can exhibit a wide variety of nontrivial dynamical regimes. Dogonasheva et al. [6] demonstrate two main objectives: (i) to explore dynamical regimes and transition between them for the system of two synaptically coupled FitzHugh–Nagumo oscillators mimicking the pyramidal and basket cells, and (ii) to propose a method and a workflow for the analysis of transitions between these regimes via the continuous wavelet analysis aimed

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at overcoming limitations of the conventional bifurcation analysis in the case of dynamical transitions and metastability. It is demonstrated that the usage of the Morlet wavelet as the analyzing function can be considered as a generalization of Andronov's decomposition over limit cycles and, supplied with a special smoothing procedure, allows for building bifurcation diagrams highlighting the specificity of changes in the spike trains and their spectral composition, including period doubling, chaos, etc. in the dependence on slowly varying parameters of the synaptic coupling.

In another modeling study, Postnov et al. [7] contribute to the understanding of how spatiotemporal activity patterns are formed during spreading depolarization. Isolated wave segments are a type of spatiotemporal activity that has been repeatedly reported in experimental studies of spreading depolarization on the cerebral cortex and retina of laboratory animals. However, it has been theoretically shown that such a pattern cannot be stable in a continuous excitable medium. The authors argue that for the correct description of this behavior in the nervous tissue of the brain, it is necessary to use a model of a continuous-discrete type. Such a model shows that isolated wave segments can exhibit the properties of a space–time attractor by cyclically changing its shape and approaching it from different initial conditions. Moreover, they show that the behavior they found persists also under conditions of a heterogeneous propagation medium.

Authors believe that the obtained results will be useful, in particular, for the analysis of similar phenomena in case of spreading cortical depression, or activity patterns, in migraines.

Kachenko's [8] review highlights a series of recent theoretical advancements related to the spiking neural networks, which are rapidly reaching an accuracy similar to more traditional neural networks with stable equilibrium states and more closely mimic natural neural networks. The article describes a new model of neural environment, which uses waveform to store information. Another highlighted topic is development of analytical methods for the nonlinear and nonlocal oscillations in a time-delay model of a neuronal population.

Barabash et al. [9] proposed a new mean-field model of neuron–glial interactions, which reproduces bursting activity. The novelty of our research is the extension of a classical Tsodyks–Markram model that allows taking into account the effects of glial cells to understand the mechanisms for the generation of the bursting activity in neuronal populations.

Mukdasai et al. [10] presented the computing numerical procedures on the basis of the fractional mathematical susceptible/infected/quarantine (SIQ) system of the lockdown impacts using the coronavirus. The fractional-order investigations have been used to provide precise solutions of the SIQ dynamical system. The investigations based on the integer and nonlinear based on the mathematical SIQ dynamical system, together with the effects of lockdown, have also been presented.

## 3 Analysis of sleeping brain function

There are many researches, investigating pathophysiological links between obstructive sleep apnea (OSA) and cognitive decline or Alzheimer's disease (AD), but the results in childhood are very contradictory. Given the important role of slow-wave activity (SWA) during sleep and sleep spindles (SSs) in mediating pathways of impaired cognitive function by β-amyloid (Aβ), Berdina et al. [11] investigated whether SSs and SWA during the sleep are associated with plasma Aβ42 levels in adolescents with different weight and OSA status. It has been proven that changes in the characteristics of the SWA and SSs in adolescents are associated with plasma Aβ42 levels, while the nature and strength of the relationship depends on the presence or absence of OSA and weight status. The most significant multidirectional correlations were obtained in patients with a combination of OSA and obesity, as well as a pronounced deficiency of SWA. The results of the study confirm the hypothesis about the role of SWA in the processes of drainage of brain tissues from metabolites formed during the activity of neurons, and may indicate an early dysfunction of Aβ42 metabolism, both as a result of a decrease in the depth of sleep and exposure to hypoxia as a trigger for increased secretion of this protein. At the same time, a change in the permeability of the blood–brain barrier as a result of hypoxia and metabolic stress, as well as a violation of Aβ42 clearance in metabolically active tissues in the periphery, can cause the elevation of Aβ42 in the blood. So, SWA, SSs, and plasma Aβ42 could be considered potential new biomarkers of early neuronal dysfunction at a young age, which is the subject of our further research.

Yakunina et al. [12] studied the transitions between different stages of sleep to suggest objective markers of interactions between underlying on–off switching mechanisms. The authors consider the transitions between stages of the sleep cycle as a sequence of episodes of the "struggle" between three permanently competing mechanisms.

The concepts from the studies of complex systems can be also applied to the study of the mechanisms regulating the substates of awake state. The dominated methodology for such a study differs from the methodology for the study of sleep substates (i.e., sleep stages). Unlike sleep substates, the sleepiness substate of the awake state has not yet been clearly separated from other awake or sleep substates by applying objective polysomnographic criteria. On the other hand, sleepiness, unlike sleep substates, can be consciously perceived by anybody, and, therefore, it can be assessed with a questionnaire. However, research of the subjective concept of sleepiness produced many controversial questions, including such questions as whether the physiological component of subjective feeling of sleepiness can be precisely defined in scientific terms, and whether the reliable physiological markers of subjective sleepiness can be identified. Dorokhov et al. [13] revealed the physiologic underpinnings of subjectively

assessed sleepiness in the study of afternoon napping attempts of university students. They concluded that, given that these students demonstrated the signs of elevated sleep pressure during such napping attempts and that they are chronically sleep deprived during weekdays (when they are attending classes), their self-reports on excessive daytime sleepiness can be trusted.

## 4 Methods for nonlinear signal analysis

Epilepsy is a chronic neurological disorder characterized by abnormal electrical activity in the brain, i.e., epileptic seizures. The electroencephalographic (EEG) examination is the main diagnostic test for evaluating epilepsy. EEG epileptic activity might originate from a certain brain area (such as the hippocampus in temporal lobe epilepsy) or from a distributed neuronal network (such as hypersynchronous spike-wave discharges in idiopathic generalized epilepsy). Generalized seizures are characterized by abnormally high synchronization between EEG channels. Less attention has been paid to periods between generalized EEG seizures (or interictal periods), which are suggested to be "healthy". To define seizure-related changes in EEG synchronization "healthy" periods, we examined long-term EEG records in a well validated rat model of absence epilepsy, in which spike-wave discharges appear spontaneously. Sitnikova [14] evaluated EEG synchronization profiles during slow-wave sleep and wake/rapid eye movement (REM) sleep. Synchronization was measured with multiscale calculation of wavelet bicoherence in the most representative nonoverlapping frequency bands (1–4–5–9–12–14–20 Hz). Another important feature of generalized epilepsy is a developmental profile, i.e., progression or regression with age. In human patients, typical absence seizures (generalized type) are common in childhood and adolescent ages. Our subjects also showed a clear developmental profile of spike-wave discharges. At the age of 5 months, they displayed only immature spike-wave epileptic discharges (preclinical stage). At the age of 9 months matured spike-wave seizures (clinical stage). The control group comprised nonepileptic subjects that showed almost no seizures at both ages. Bilateral fronto-frontal synchronization in subjects with epilepsy during both "healthy" periods (slow-wave sleep and wake/REM sleep) was lower than in nonepileptic subjects. Only on the preclinical stage, unilateral fronto-occipital synchronization in epileptic rats was lower than in nonepileptic ones (only during slow-wave sleep in alpha (10–14 Hz) and 5–9 Hz). A reduction in unilateral fronto-occipital synchronization may be a sign of early epileptogenesis in genetically predisposed subjects.

Simonyan et al. [15] provided a modification of spectral analysis on the basis of continuous wavelet transformation. The proposed estimation of the oscillatory components existing on a two-dimensional time–frequency plane, calculated on the basis of the wavelet transformation on a one-dimensional signal, makes the expansion of the possibilities possible to evaluate the properties of signals. This technique is suggested for biomedical signals, but can also be adapted to solve radiophysical problems, for example, in developing complex algorithms for encrypting/decrypting signals of a wide spectrum.

An important part of this special issue is devoted to signal processing techniques, since the complex organization of the brain requires advanced tools for analyzing experimentally recorded signals that reflect the current state of the body and its changes caused by variations in environmental conditions. The given collection includes papers on extended/modified versions of fairly versatile data analysis tools and their various applications. Thus, Koronovskii et al. [16] consider an extension of detrended cross-correlation analysis, proposed for inter-related signals in complex systems with time-varying behavior. They showed how such an approach improves the quantification of changes in brain electrical activity caused by sleep deprivation. The work by Pavlov [17] introduces a multiresolution cross-correlation analysis that combines wavelet-based decomposition of time series with cross-correlation analysis of the detail decomposition coefficients. The latter makes it possible to more clearly interpret the results in terms of the mechanisms responsible for the occurring phenomena. The work by Ishbulatov et al. [18] explores how spectral analysis parameters affect the accuracy of computing indices for the heart rate variability. The study considers mathematical models of heart rate variability in normal conditions and on the example of patients with arterial hypertension. Borovkova et al. [19] analyzed a number of biomarkers of the psychophysiological state of healthy individuals at rest and during performance of stressful cognitive tasks. They show that nonlinear phase coherence and integrated power in a certain frequency range are the most sensitive biomarkers. Guyo et al. [20] explore the possibility of separation between different types of complex dynamics using transients and consider how transient duration affects the reliability of system state quantification. In addition to simulated data sets, EEG transients induced by artificial sleep are discussed. An approach involving two different techniques, namely multifractal formalism and multiresolution wavelet analysis, is proposed by Pavlova et al. [21]. Within this approach, the transition from measured physiological time series to sets of wavelet coefficients at distinct levels of resolution is provided, followed by the performance of the wavelet-based multifractal formalism to these sets. The application of this approach to EEG signals during mental tasks is described. Another combined method, described by Pavlov and Pavlova [22] deals with the coarse-graining procedure, which is considered together with the detrended fluctuation analysis. This paper illustrates improved diagnostics of transitions between system's states in models and experiments with laser speckle contrast analysis.

Ferdinando et al. [23] proposed a method for separating patients with Alzheimer's disease from a control group at rest. They showed that the spectral entropy

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of brain signals recorded with functional near-infrared spectroscopy is a useful biomarker for Alzheimer's disease.

Ren et al. [24] described a discrete memristor model and a two-dimensional hyperchaotic map on the basis of discrete memristor systems for time series prediction that can improve the performance of the reservoir computing. The performance of the model was tested on the Santa Fe dataset B data prediction task. The results suggest that the hyperchaotic map based on the discrete memristor can effectively optimize the performance of reservoir computing. The proposed model also requires no selection of hyperparameters, and is overall easier to use.

Karpov [25] discovered a new approach to automated analysis of the electroencephalogram signals aimed at classification of patients with epilepsy and localization of the brain area where the seizures originate. The algorithm uses machine-learning techniques, which performance depends on selection of the appropriate features of the EEG features. The authors have shown that an algorithm, based on expert domain knowledge of the data, outperforms the algorithms relying on the data-based features, such as principal components.

Kurkin et al. [26] investigated the age-related changes in the brain networks organization in children and adolescents with autism spectrum disorder. The authors have shown that connection strengths in the brain areas related to the emotional state and consciousness is lower in the children with autism when compared with neurotypical children; also, children with autism have lower network global clustering in the delta and theta bands. The authors also revealed hyperactivation of the alpha band patterns in children on the autism spectrum and below ages of 6–7 years, and hypoactivation at older ages. The obtained results could explain difficulties, which children with autism experience with controlling emotions.

Pei and Wong [27] trained the obtained series by reservoir computing and get the predicated result of its future. After taking its exponent function, the predicated data for original precipitation data are obtained. Authors demonstrated that reservoir computing, combined with other processes, can potentially bring about the accurate precipitation forecast.

The search for functional biomarkers for automatic detection of the early stages of various diseases is among the daunting tasks of interdisciplinary data analysis. It should be noted that nearly all currently existing systems for automatic detection of biomarker processes, in fact, are images of rather slow processes, such as, for example, well-known algorithms and algorithms used in medicine for detecting precursors of the development of benign and malignant skin lesions, and systems for supporting medical decisions when performing X-ray and magnetic resonance tomography, etc. Hence, the interest of researchers in the search for simple informative biomarkers that are resistant to noise and do not require complex medical and computer equipment has

not subsided. The processing of sleep data is a particular challenge due to the characteristics of night recordings, such as a large amount of data (often a recording lasts more than 6 h) and the presence of several types of physiological signals (EEG, ECG, and respiratory sensor readings, etc., are recorded simultaneously). For this reason, we use one of the simplest, universal and, at the same time, the most efficient methods of nonlinear dynamics, viz., the construction of recurrent surfaces and their further numerical analysis.

Selskii et al. [28] propose a solution to the problem of recurrent estimation of long duration signals via analyzing them in a double window, both independently moving over the signal record and fixed at various sleep stages. It was shown that the recurrence parameters of the two nocturnal sleep recordings, both for patients with severe obstructive sleep apnea syndrome and for healthy participants, do not show statistical differences. At the same time, comparison of the recurrent characteristics of the stages of nocturnal sleep in the two groups demonstrate statistical differences that are promising for further analysis. During the deepest stages of non-REM (NREM) sleep (N3 and N4), the recurrence rates of healthy participants are reduced and significantly homogeneous against the background of heterogeneous results of the group of patients with obstructive sleep apnea. The opposite situation is observed for stage N2, at which the dynamics of recurrence rates in patients with obstructive sleep apnea becomes monotonous, repeating from participant to participant. The maximum differences for apparently healthy participants and patients with obstructive sleep apnea were observed during the REM sleep stage, when the average recurrence rates from slip stage value increased significantly in the presence of respiratory disorders.

## 5 Outlook

The issue collected articles highlighting modern multidisciplinary approaches to the study of the brain as a complex system, including the studies of sleeping brain function, computational models of neural–glial networks, and methods for nonlinear signal analysis. These approaches are unique tools in understanding the complex functions of the sleeping and waking brain, allowing significant progress in the development of breakthrough technologies for predicting the risk of developing brain diseases, such as epilepsy, Alzheimer's disease, strokes, etc.

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