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Reply to comment

Chimeras at the interface of physics and life sciences Reply to comments on "Chimera states in neuronal networks: A review"

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We would like to thank all the experts for their insightful and very interesting comments that have been submitted in response to our review "Chimera states in neuronal networks: A review" [1]. We are delighted with the large number of comments that have been written, and even more so with the overwhelmingly positive opinions that these comments communicate to the wider audience [2–8]. Although methods of statistical physics have long proven their value in relevantly addressing challenges at the interface of chimeras and life sciences, such interdisciplinary research often still struggles for funding and recognition at many academic levels.

In this reply, we would like to highlight the coming of age of the very fruitful synergy between physics and life sciences, and in particular between chimeras and neuronal dynamics.

Several outstanding challenges are pointed by Guo et al. through their comment [2]. One of them is the effect of neuronal plasticity. In this review article, we have not considered the effect of the neuronal plasticity and excitability on the emergence of chimeric features on the neuronal network. By incorporating these two neuronal factors on the appearance of the collective behavior may lead to attractive dynamic phenomena. Similar kind of chimera research in neuronal systems is also suggested by Parastesh et al. [4]. Most of the existing studies on chimera pattern [9–12] is restricted to simplified neuronal models, we completely agree with this reviewer's opinion. But including neuronal plasticity and excitability features [13] will essentially increase the complexity of the study of collective behavior

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of interacting neurons. However, theoretical development and experimental studies while combining these intrinsic biological factors will uncover a very interesting research domain.

The second issue is about the mechanism of formation of chimera patterns in the neuronal systems. Reviewers mention that the existing chimera research on neuronal dynamics is mostly surrounded in its spiking region [14] whereas the most neuronal systems are well known for different spiking and bursting patterns. In this regard, it would be interesting to investigate the spike chimeric patterns in a different spatiotemporal scale other than spiking region. Mainly, firing and resting patterns coexist in the entire neuronal time evolution [15]. So, the existence of multi-timescale in the neuronal systems may be one of the main ingredients for the emergence of chimera patterns in the neuronal network. In addition, the effect of irregular firing, neuronal avalanches and stochastic neuronal oscillations on the investigation of this collective property of neurons will be a challenging issue.

Another important point proposed by the reviewers is that of the experimental studies of the chimera states in the electrophysical recorded data. Although few experimental evidence has supported the existence chimera states in various perspectives of science besides computational study [16,17], but the investigation on symmetry-breaking self-organized neuronal activity is still missing.

Frolov et al. [3] raise an issue about the lack of experimental evidence of the chimera features in the neurobiological systems and suggest the several possible experimental investigations on chimera states in this context. Among the real world systems, interneuronal communication in the human brain forms one of the most complex one. So, understanding the connectivity patterns among the neurons and their functional property is a big challenging issue. Regarding this, some recent results may assist to understand various self-organized collective features of the neuronal systems. Such as a neurophysiological technique based on optogenetic neural simulation and closed-loop control [18] has been developed to study neuronal activity in the neural systems. Using this approach, one can theoretically investigate the collective behavior of the interacting neurons in the entire neuronal populations. Such mechanism uncovers a way to revive or suppress the endemic coherent patterns of neurons based on the governing properties of the functional brain neural network. So, this method can be extremely important to make a proper prescription for controlling chimera-like states in the neuronal network. The experimental investigation corresponding to this theoretical finding may have an important application in the area of neuronal disease therapy.

Another possible experimental study is proposed by Frolov et al. [3] about the detection of the chimera features in the normal human brain activity. It is already established that the concept of multi and metastability are closely related to the functional property of the neuronal groups in the brain cortex [19,20]. Also, recent experimental evidence revealed the appearance of the multistability feature in the cognitive brain function in visual cortex. So, procreation and coexistence of various self-organized complex patterns may have a strong resemblance with chimera like characteristics in the cortical network and theoretical and experimental investigation may explore several captivating phenomena.

Through the last point of their comment, the authors suggest about the experimental realization of chimera states in network of networks. [21]. The chimera state is interesting mainly since it is a symmetry breaking state appearing in symmetry preserving systems. Here the symmetry means symmetry in the connectivity patterns and also in their local dynamical properties. In this case, most of the network of network organizations are basically asymmetric as each network has its own connectivity pattern and may differ with the other network and also intra and inter-network coupling mechanisms may be different. So, such asymmetrically coupled systems may usually lead to the symmetry breaking states (chimera). In our point of view, the study of asymmetrically interacting network of networks may not lead to an emergence of surprising phenomena, but one can investigate theoretically and experimentally, concerning the mechanism of formation of the coherent and incoherent states or their coexistence.

An excellent point is raised by Parastesh et al. [4] regarding the study of chimera states under the influence of time-varying interaction [22,23]. It is well known that time-varying interacting patterns are inherent features of the interneuronal communications [24]. Depending on the coupling mechanism and several neuronal processes, neuronal activities are not static in time, rather their behavior is time variant in space and time. So, investigating various complex patterns together with chimera states in neuronal networks under the effect of this time-varying characteristic would be interesting. In this regard, one important subject is that of neuronal plasticity which controls the excitability behavior of the neurons. So, incorporating the effect of neuronal plasticity on chimera studies in the time-varying neuronal networks may lead to the emergence of intriguing neuronal behavior and the outcomes may be fruitful to understand the collective properties of neurons.

Also, they mentioned the other possible chimera research on the neuronal hypernetworks [22,23]. When different types of network architectures coexist in a single network, then such network formation is called hypernetwork. In this network organization, different classes of networks are associated with different interaction patterns. Interneuronal communications mainly happen through two synaptic interactions [25], one is electrical coupling via gap junction channel and other one is chemical synapse. Apart from these synaptic communications, there is a non-synaptic communication, known as ephaptic coupling [12]. The simultaneous existence of these two synaptic interactions has been observed in most of the nervous systems [25], and such types of synaptic and non-synaptic communications arrangement constitute the neuronal hypernetwork. So, the study of various collective behavior and particularly chimera states in neuronal hypernetwork have great importance to understand the neurons' structural and functional properties. In this context, one can investigate the existence of chimera states in a systematic way, by incorporating all these neuronal interactions, associated with different network architectures [14,26–28]. A similar kind of investigation on chimera states in the network of network is also pointed by Florov et al. [3].

Another important point is emphasized by the reviewer is the study of non-stationary chimera patterns in the neuronal networks. Previously, by taking local gradient chemical synaptic interaction and ephaptic coupling, the emergence of imperfect traveling and alternating types of non-stationary chimera patterns were respectively studied in refs. [9,12]. As brain functions have temporal features, so the study of temporal patterns of chimera under the influence of time-varying effect on neuronal hypernetwork would lead to a fruitful investigation.

The comment by Kozma [5] brings new insights on associating different scientific disciplines evoking analogous phenomena to the reviewed "chimera-like" coexisting patterns. This correspondence would, of course, deliver a profound and extensive perception on several practically crucial issues in science, technology, and societal systems. For instance, Kelso's principle of complementarity [29] can contribute to a broad and better understanding of chimera states through the explanation of the coexistence of contrasting properties as a result of spontaneous symmetry breaking. Chimera dynamics may also have resemblances in intelligent systems, as recent developments in neuroimaging demonstrate certain parity between global dominance of coherence and fragmentation of incoherent localized components across the hemisphere [30]. On the other hand, Rabinovich et al. [31] studied two related cognitive processes of sequential working memory and attention sharing and consequently analyzed a typical intermittent dynamics (named as heteroclinic chimera) involving ordered switching between few cognitive modes interrupted by intervals with chaotic switching among some other modes in a functional global network comprising of inhibitory heterogeneous connections. As far as such concurrence of diverse dynamical regimes is concerned, Freeman and Kozma et al. [32,33] have also reported spatial and temporal synchronization and desynchronization of electrocorticogram (ECoG) recordings.

Dana et al. [6] put forward a few important notions regarding the research of chimera-like states right from the very beginning. Firstly, they address the fact that even before the observation of Kuramoto et al. [34] of coexistence of coherence and incoherence, researchers had claimed concurrence of order and disorder in a single ensemble. For example, Domínguez et al. [35] reported the partially ordered states apart from the fully ordered and turbulent regimes in globally coupled Josephson junction series arrays. Next, Dana et al. call up the issue of stability of chimera states in terms of long time persistency in coupled oscillators, particularly in small sized networks. But as far as one is trading with neuronal ensembles having large number of neurons, then it is not going to be troubling enough. However, the possibility in alteration of chimera patterns under variation in the systems' parameters could be significant indeed. Finally, one would agree with the remarks that such ideal non-local, local or global network connectivity in neuronal ensembles may not be realistic and of course, the actual organization of brain is far complex. That's why we have tried to incorporate a few findings for modular [14] and multilayer [27,36] architectures as well. In our review, we had already raised this issue as a possible impactful future research direction to analyze such coexisting exotic chimera-like patterns in neuronal networks on the top of much more complex architectures that may have more comparability with the brain structures. At the same time, we would like to additionally point out that the aim of this review is basically to bring up the primary outcomes related to this fascinating dynamical phenomenon of chimeras encircling the existing studies in neuronal ensembles only.

Omelchenko et al. in their commentary [7] remark on the exquisite importance of the study of fascinating partially synchronized complex patterns in neuronal networks. They particularly emphasize on the correlation between chimeras and functional brain disorders like epileptic seizures. In this context, Andrzejak et al. [37] have successfully analogized the collapse of chimera patterns into a globally synchronous dynamics to the epileptic seizures in humans as depicted through the spatiotemporal correlation profiles realized from intracranial electroencephalographic recordings (EEG) of seizures in epilepsy patients. Considering a model of 51 nonlocally coupled identical phase oscillators, the authors demonstrated the emergence of chimera state in terms of coexisting high-coherence and low-coherence groups, along with hypo-coherence events triggering its collapse towards a fully synchronized state. This process has then been linked to epileptic seizures on the basis of intracranial EEG recordings. Further, Rothkegel et al. [38] examined chimera dynamics in an ensemble of integrate-and-fire-like oscillators with refractory periods and time delays, interacting through δ-pulses on small world network. Recurrent synchronizations embedded in extended periods of asynchronous process with variable duration were observed, analogous to typical observations in case of epileptic seizures. Omelchenko et al. also mention about some of the recent advancement in the chimera study in networks with temporal synaptic connections. For instance, the investigation of chimera-like patterns along with multicluster states in networks of adaptively coupled Kuramoto phase oscillators by Kasatkin et al. [39] is clearly notable. Moreover, a new dynamical regime named "itinerant chimera" [40] characterized by spontaneous temporal switching of coherent and incoherent domains by the oscillators yeilding traveling core of chimera across the network, has also been reported in globally coupled phase oscillators' network with phase dependent coupling weights.

On the basis of our concern about the impacts of initial conditions for setting on chimera patterns, Dudkowski and the co-authors [8] come up with a very engaging prospect of chimera patterns and the hidden attractors [41]. Quite interestingly, contrary to the self-excited attractors, the basin of attraction of hidden attractors does not intersect with any open neighborhood of an unstable fixed point (if exists at all) and are generally located far away from such points. Thus, the localization of these attractors becomes non-trivial as there does not exist transient processes approaching them from the neighborhoods of unstable fixed points. This essentially makes the study of such peculiar chimera phenomenon in systems exhibiting hidden attractors very challenging. Along this line, the authors have considered a non-locally coupled network of bi-stable van der Pol-Duffing oscillators. With appropriate choice of system parameters, each isolated dynamical unit having exactly two coexisting attractors, namely a self-excited chaotic one and a hidden period-7 attractor have been dealt with there. On the top of such a setup, the authors have examined diverse chimera patterns with the oscillators resting on existing as well as newly generated chaotic, quasiperiodic and periodic attractors, while varying the interaction strength in the ref. [41]. At this point, we must admit that the research of chimeras on hidden attractors is still unexplored and more importantly it can be perceived that such study in neuronal networks can be extremely fascinating.

To summarize, above discussions and the enthusiastic opinions of all the contributors regarding our review on chimera state in neuronal systems, direct to a proper prescription for exhaustive understanding of the symmetry-breaking features in neuronal networks. Especially, they concerned about experimental verification of the chimeric states in the neurobiological systems and the outcome of this research is expected to assist in learning different types of neuronal synchronization patterns which are related to various cognitive functional processes [42] and different neuronal disorders. It is very well known that the neuronal interaction patterns and their inter-neuronal processes form one of the most complex systems [13,43] in the living world and also there are several limitations for theoretical studies as well as experimental investigations. But dynamical neuronal network science is a young research domain and rapidly growing field and hopefully in the near future, development of new methods through network approach will relax these limitations and will lead to more integrated research on neuronal networks. Finally, we have proposed some of the possible fruitful extensions regarding the future chimera research in neuronal ensembles while incorporating the commenters' opinions. Although in this short reply, it was extremely difficult for us to address all the issues put forward in the commentaries, we have tried our best to explain most of the suggestions and to incorporate a few notable references that we missed to discuss in our review. And we hope that this information can provide useful guidance to open a new research direction in symmetry breaking phenomena in neuronal systems, and that it could be linked up with other interdisciplinary research domains as well.

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