

# Experimental electronic modeling of focal and progressive brain lesion processes using a network of single-transistor chaotic oscillators

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Understanding how neurodegenerative diseases disrupt brain dynamics requires models capable of capturing the interplay between network structure and functional activity. This study presents a hardware emulation of progressive disconnection, implemented using a physical network of transistor-based chaotic electronic oscillators inspired by a biological neuronal culture. We evaluate several node disruption scenarios under different coupling strengths. These included single-node disruption and progressive damage sequences from core to periphery and periphery to core. The changes in network and node-level dynamics are assessed through the evaluation of synchronization, entropy, spectral content, and graph-theoretic properties. These analyses show that the network's response to progressive alteration depends strongly on its topology and the coupling strength. The single-node disruption scenario revealed a high level of network resilience. Changes in average phase synchronization and topology remained modest in this scenario, consistent with functional imaging and lesion studies showing early compensatory mechanisms in healthy and mildly impaired brains. While the periphery-to-core scenario causes gradual and delayed deterioration, the core-to-periphery scenario leads to a sharp breakdown in synchronization, as well as structural and functional graph-based metrics. These profiles of degradation are comparable to those observed in neurodegenerative diseases and, in particular, Alzheimer's disease, characterized by marked damage to central regions. Remarkably, it is found that modularity reaches a peak and then decreases just before the network collapses, a pattern that may be considered a meaningful marker of network degradation. Spectral analyses reveal a progressive shift toward low frequencies and fragmentation of the oscillatory dynamics, characterized by a decrease in high-frequency power and emergence of local frequency peaks. This study provides insights into how topology-dependent degeneration shapes brain rhythms and functional connectivity. It demonstrates that physical oscillator networks are suitable for emulating the progressive breakdown of neural circuits. The obtained insights could form the basis for hypothetical biomarkers.

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## I. INTRODUCTION

### A. Complex networks and resilience to attacks

Complex networks are ubiquitous, emerging across diverse domains [1,2]. Among the most studied examples are social networks [3–5], information networks [6], technological networks [7,8], and biological networks [9,10]. However, such networks are vulnerable to attacks and perturbations that may critically impair their functionality and stability [11,12]. Network resilience is therefore a fundamental concept that allows understanding how complex networks respond to change. Although its definition varies across disciplines, it mainly refers to their ability to withstand and recover from disruptions. Attacks on networks can take several forms, namely, targeted attacks, where specific nodes or links are deliberately disabled [13], random attacks, where nodes or links are removed unpredictably [13,14], and locally clustered attacks, in which entire groups of neighboring nodes (regional clusters or communities) are simultaneously removed [15].

Since the connectivity structure of a network is a key determinant of its resilience, different topologies confer distinct vulnerabilities as well as protective mechanisms. To understand and model the structure and dynamics of complex networks, a wide range of generative models has been proposed. Among the classical models are the Erdős-Rényi (ER) random graph [16], the Watts-Strogatz (WS) small-world network [17], and the Barabási-Albert scale-free network [18]. These models are distinguished by their topological features. The WS model, in particular, combines high clustering with short characteristic path length, a hallmark property also observed in brain networks [19]. On the other hand, scale-free networks, characterized by highly heterogeneous degree distributions following a power law (a minority of highly connected nodes referred to as hubs against a backdrop of many sparsely connected nodes), are prevalent in

diverse real-world systems, including power grids [20], airline transportation networks [21], and in some functional networks of the brain [22,23]. It has been shown that random networks are relatively homogeneous, such that failures are evenly distributed [20], whereas small-world networks combine local robustness with efficient global communication [17,24]. By contrast, scale-free networks exhibit overall strong resilience to random failures, owing to the abundance of low-degree nodes, but extreme fragility when hubs are selectively targeted [25]. Consequently, extensive graph-theoretic research has focused on identifying the most central nodes, whose removal would severely compromise global connectivity and functionality [26–28].

Although classical metrics such as degree and betweenness centrality are useful benchmarks, they often fail to predict the potential influence of a node on system dynamics. In fact, the functional effects of a disruption depend as much on the structure as on the dynamic interactions between network elements [29,30]. It has been shown in the experimental work in Ref. [31] that altering a node can paradoxically improve overall synchronization, highlighting the need to move toward physical networks to better capture the effects of damage. Besides, the analyses of network resilience are crucial for understanding how structural alterations in brain networks translate into cognitive decline, fostering growing interest in network neuroscience, with efforts directed toward quantifying and predicting the loss of resilience in these networks. A major goal is to identify early pathological biomarkers and therapeutic targets to counteract progressive disconnection [32,33].

### B. Lesion patterns in brain networks and disease

The brain is often conceptualized as a complex network of structurally and functionally interconnected regions

(commonly referred to as the connectome) whose collective dynamics support cognition, perception, memory, and behavior [34,35]. Features such as small-world topology, modular arrangement, and rich-club organization facilitate both local specialization and long-range integration, promoting rapid, efficient communication while minimizing wiring and metabolic costs [19,23,36–40]. This structural organization, together with the nonlinear dynamics that play out across its constituent nodes, underpins functional connectivity, defined as the statistical interdependence of activity between brain regions. In other words, this interdependence, at least partially, reflects the synchrony of neuronal activity and the brain's capacity to reconfigure itself and form dynamic coalitions of interacting areas. Although resilience in the brain is attributed to its organization, the same features also introduce vulnerabilities. For instance, selective damage to hubs or connector nodes disproportionately disrupts communication efficiency and functional integration, denoting a hallmark of many neurodegenerative conditions [41–44]. Lesions in the brain are therefore suitable for being conceptualized as network attacks, whether random, targeted, or localized. Evidence from functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), postmortem staging, and animal models has consistently demonstrated that the core areas of the connectome are preferentially targeted in most cases of progressive, particularly degenerative, brain disorders. In other words, disruptions preferentially originate in hub regions and propagate outward, reflecting long-standing imbalances in connectivity between core and peripheral systems [45–49]. The peripheral regions of the brain are organized into specialized subnetworks that support localized sensorimotor and other unimodal functions, such as the primary visual cortex for vision, the somatosensory cortex for tactile perception, and the auditory cortex for sound processing. These regions are structurally situated at the edge of the cortical hierarchy and functionally dedicated to processing specific modalities of sensory input.

A typical example of neurodegenerative conditions where hubs are preferentially targeted is Alzheimer's disease (AD). Positron emission tomography, resting-state functional magnetic resonance imaging (rs-fMRI), and DTI studies conjointly show that the accumulation of amyloid- $\beta$  and hyperphosphorylated tau peptides affect synaptic transmission, impairing pathways between distant, interconnected regions [43,47,50–57]. Although pathological changes often originate in subcortical structures, they rapidly affect hub regions responsible for function. This vulnerability is explained by the high metabolic activity of these regions, which renders them more susceptible to metabolic stress and amyloid accumulation [38,47,55,58–60]. Numerous studies have identified the hub regions preferentially affected during AD progression, including the posterior cingulate cortex, medial and lateral prefrontal cortices, lateral temporal cortex, and lateral parietal cortex. Besides, the entorhinal cortex and hippocampus have consistently been identified as the earliest sites of amyloid- $\beta$  deposition, leading to localized atrophy and explaining the early impairments of memory and spatial navigation [38,39,52,55,61–65].

For example, Fig. 1 shows that the distribution of functional hubs found in healthy controls closely matches the

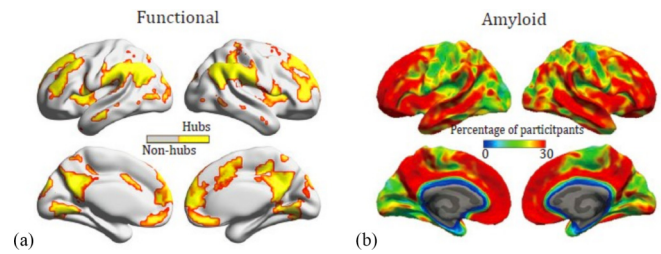


FIG. 1. Spatial correspondence between functional hub distribution and amyloid- $\beta$  deposition in AD. (a) Functional hub and nonhub regions derived from rs-fMRI. (b) Regional prevalence of amyloid- $\beta$  deposition across participants, illustrating the preferential vulnerability of high-centrality hubs. Adapted from Ref. [66] with permission from the authors.

spatial pattern of amyloid- $\beta$  accumulation. It shows that regions such as the posterior cingulate, lateral parietal, and medial prefrontal cortices exhibit high centrality and elevated amyloid burden. Moreover, the regional prevalence of amyloid- $\beta$  deposition across participants in these regions underscores the preferential vulnerability of integrative hub regions to amyloid- $\beta$  deposition [66]. This spatial convergence between network centrality and amyloid- $\beta$  deposition supports the view that AD selectively disrupts the functional core of the brain.

By contrast, other neurodegenerative diseases, such as Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS), originate in relatively peripheral or subcortical parts of the network and progressively invade the cortical hubs. As shown in Ref. [45], typical idiopathic PD is initially confined to the brainstem and peripheral nervous structures and only involves cortical hubs later in the course of disease progression, after which global network topology becomes severely disrupted. The same study reported that ALS initially targets lower motor neurons in the spinal cord or brainstem alongside upper motor neurons in the primary motor cortex, but in later stages also extends to higher-order areas, including core networks such as the default mode network (DMN). Compared to AD, these diseases hallmark an opposite sequence of cumulative network damage, which starts from the periphery rather than the core. Moreover, certain sudden-onset brain injuries, such as focal ischemia or localized traumatic lesions, affect neural networks in a largely random manner. Such damage is analogous to randomly removing nodes in a complex network, a perturbation that the brain can partially resist thanks to its plasticity [25]. However, when neuronal loss exceeds a critical threshold, functional integrity inevitably deteriorates. This phenomenon is related to the concepts of cognitive reserve and network redundancy, which are far from being fully understood [15]. Besides, focal lesions such as ischemic strokes affect specific brain regions and are analogous to the removal of connected nodes in a network. Their impact depends critically on location: damage to a hub can disrupt the entire network, whereas peripheral lesions often remain localized in their influence. Simulations confirm that lesions in central areas such as the medial prefrontal cortex or the temporoparietal junction severely disrupt connectivity between brain regions, whereas those in primary sensory or

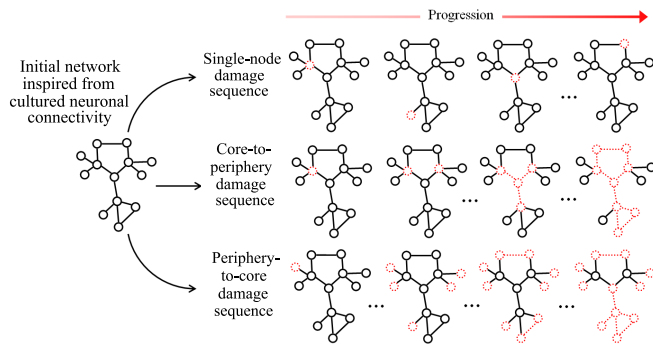


FIG. 2. Schematic representation of the three damage sequences implemented in the experimental network model. From top to bottom are single-node damage, modeling localized lesions; core-to-periphery damage, modeling targeted hub disruption as in AD; and periphery-to-core damage, modeling progression of neurodegenerative diseases such as PD and ALS.

motor areas have more limited global effects, as the network can compensate, even though their clinical significance may be substantial. A similar pattern is observed clinically where a small stroke in the thalamus or posterior cingulate cortex can induce cognitive deficits far beyond the lesion's size, whereas a larger lesion in peripheral regions might have surprisingly domain-specific effects [67].

Taken together, these examples illustrate that the brain is potentially subject to all three archetypal lesioning sequences. The diversity of these pathological mechanisms highlights that the functional outcome of damage cannot be explained by lesion size alone but critically depends on the topological embedding of the affected regions within the broader network. These paradigms inspire the three disruption strategies considered in this work (see Fig. 2).

### C. Physical experiment and purpose of the work

A variety of computational approaches have enabled advances in understanding brain function and dysfunction through the analysis of dynamics and synchronization in networks of coupled systems [68]. Biological models of neuronal dynamics have been extensively developed to study brain dynamics, ranging from microscopic spiking neuron models [69–71] to mesoscopic neural mass and mean-field descriptions [72–75]. In parallel, abstract dynamic systems such as the Kuramoto model and the Ising model have been used to study synchronization transitions in oscillator networks [76–78]. More recently, connectome-based frameworks integrating anatomical connectivity from diffusion magnetic resonance imaging or tract tracing have enabled whole-brain simulations, where local dynamics are modeled using the aforementioned approaches [79–82]. This framework has proven useful for examining disorders associated with the disease under real-world conditions. Notable examples include projects such as The Virtual Brain [83–85]. Biological modeling approaches complement computational frameworks by introducing an additional layer of realism through the use of living tissues. These include *in vivo* animal models, *ex vivo* brain slices, *in vitro* cultures of neuronal cells, and brain-derived organoids. These models

allow the direct investigation of activity patterns, plasticity, and proteinopathies under experimental manipulation, offering insight into cellular and molecular mechanisms [86–88]. In addition, graph-theoretic methods have yielded insights into topology-driven phenomena such as synchronization transitions, clustering, and resilience [19,23,30,89]. Despite these advances, computational approaches on the one hand remain limited by underlying simplifying assumptions and often require significant computational resources for large-scale simulations. On the other hand, biological models face challenges in terms of reproducibility, limited experimental control, and ethics.

By contrast, physical systems are particularly well suited to emulate the complex, heterogeneous, and noisy nature of brain function due to their inherent susceptibility to imperfections such as parameter mismatches, nonidealities, and noise; these are features that are challenging to capture numerically but essential for encapsulating the complex and imperfect nature of biological systems. Furthermore, such physical systems evolve naturally over time and, unlike biological recordings, provide a well-defined ground truth together with extensive possibilities for experimental manipulation. Since the seminal work of Pecora and Carroll [90] on synchronization in a pair of electronic chaotic oscillators, experimental research on synchronization has expanded across multiple domains, including mechanics, optics, and electronics, thereby allowing a better understanding of real-world systems. Experiments across these fields have successfully demonstrated synchronization and revealed emergent patterns, including community formation and remote interdependencies [81,91–98].

Despite significant advances in optics and early breakthroughs in laser synchronization [99], most experimental setups remain limited to two-node configurations. Only a few studies explore small networks with regular topologies, such as rings and lattices [100,101], while others rely on continuous media or virtual-node architectures with time-delayed feedback [102]. Moreover, although delay-line system strategies enable large-scale dynamics, they lack true parallelism and flexible topologies [103–105]. Similar constraints affect mechanical and chemical systems, which are typically limited to small networks, such as coupled pendulums, metronomes, or reaction-diffusion media [106–109]. Although these implementations are powerful, since they offer precise control over parameters and fast sampling, they nevertheless lack effective node scalability, structural flexibility, and consequently the ability to model irregular, asymmetric, and biologically plausible connectivity patterns, as observed in neural systems. In contrast, while less energy efficient, electronic implementations have reached relatively larger scales. Although most circuits remain confined to regular network topologies, such as chains or rings, they offer scalability, flexibility, and parallelization, making them suitable for biologically plausible emulations. Notably, some studies have demonstrated that such regular arrangements of electronic networks can successfully reproduce core neurodynamical phenomena, including synchronization transitions, chimera states, and modular community formation under controlled perturbations [110]. Similarly, it has also been demonstrated that a network of coupled transistor-based chaotic oscillators, designed as a

“toy” model of the DMN, successfully replicates the preferential generation of low-dimensional chaotic dynamics in hub regions [96].

As said, the number of experimental studies investigating synchronization phenomena in physical systems remains very limited compared to computational studies and is generally restricted to simple configurations. Recently, large-scale experimental platforms have started to bridge this gap. For example, the experimental platform FUSHIGHI-1, proposed in Ref. [111], implements a large-scale analog emulator of a low-resolution human brain connectome with 360 nodes, realized as a low-power array of complementary metal-oxide semiconductor (CMOS)-based chaotic oscillators. Another recent platform dubbed QOHELET-1, based on a mesoscopic representation of a neuronal culture, reproduced noteworthy emergent features of biological neural networks in a 59-node configuration of single-transistor chaotic oscillators [112].

Building upon the analog electronic circuit board designed from the connectivity scheme of the neuronal culture model introduced in Ref. [112], this study experimentally emulates the hallmark patterns of network disruption that characterize primarily neurodegenerative diseases across different etiologies. To this end, systematic structural alterations are introduced by selectively damaging connections of targeted nodes. Three disruption schemes are considered: (1) damaging a single randomly chosen node at each step with no propagation to evaluate the effect of a focal lesion on the network integrity; (2) progressively damaging nodes starting from the most connected and spreading toward the least connected (core to periphery); and (3) progressively damaging nodes starting from least connected and spreading toward the most connected ones (periphery to core). As reviewed above, the disruption schemes (2) and (3) represent, in a generic sense, two notable trajectories commonly reported in neurodegenerative diseases such as AD, Frontotemporal dementia (FTD), and ALS. Voltage signals were recorded across a range of coupling strengths, and dynamical analyses, including phase synchronization and graph-based metrics, were then performed to quantify how these structural alterations reshape network synchrony and dynamic complexity.

The remainder of this paper is organized as follows. Section II briefly describes the network topology and the associated experimental setup. The node disruption protocol is provided along with the data acquisition settings. Section III details the disruption modeling. In Sec. IV, the data analysis methods are presented. Section V illustrates the results obtained as the damage progresses over a systematic sweep of the voltage controlling the coupling strength. Section VI discusses the relevance, implications, and outlook for disease modeling.

## II. CONCEPTUAL OUTLOOK, NETWORK, AND EXPERIMENTAL SETUP

### A. Conceptual outlook and network topological features

A conceptual overview of the present study is shown in Fig. 3. The dashed box indicates the preliminary steps carried out in Ref. [113], where spontaneous spiking activity from self-organized *in vitro* neuronal cultures was recorded

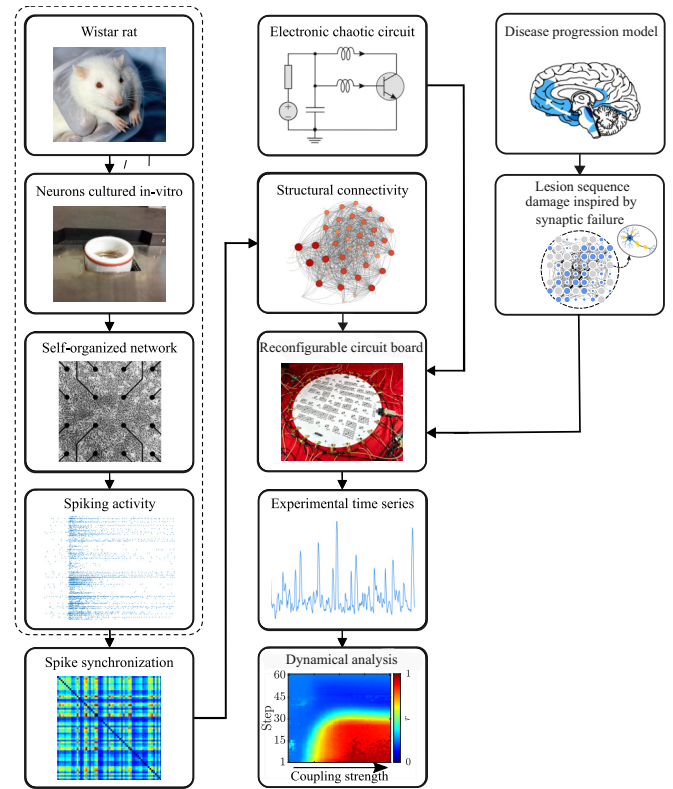


FIG. 3. Conceptual outlook of the study, illustrating the steps from the *in vitro* neuronal culture through the progressive damage procedures implemented on the electronic oscillator network. Dashed box denotes the steps undertaken in Ref. [113]. The subsequent steps until the construction of the board were undertaken and described in Ref. [112]. Reprinted and adapted from Ref. [112] with permission from Elsevier.

using multielectrode arrays. The activity from a representative culture was subsequently transformed into a structural connectivity matrix, which served as the blueprint for the physical network realization introduced in Ref. [112]. The remaining steps represent the specific contribution of the present work, which involves, on the one hand, the introduction of progressive damage of the connections of nodes on the physical board inspired by synaptic failures to emulate neurodegenerative processes, and, on the other hand, the dynamical analysis of the network under damage based on time series recorded from each node, thereby capturing the interplay between structural damage and functional reorganization.

As mentioned previously, the network topology plays a crucial role in shaping synchronization patterns, and, as such, connectome-based or biologically derived networks are more realistic and well suited for studying brain function and, consequently, neurodegenerative disorders compared to regular topologies and abstract models. Here, the structural connectivity of the network was obtained from a mesoscopic representation of a real biological culture of dissociated neurons, which led to an undirected graph consisting of 59 nodes and 1352 links.

As reported in Ref. [112], this network exhibits hallmark features of small-world organization, with an average clustering coefficient of 0.73, an average shortest path length of 1.75,

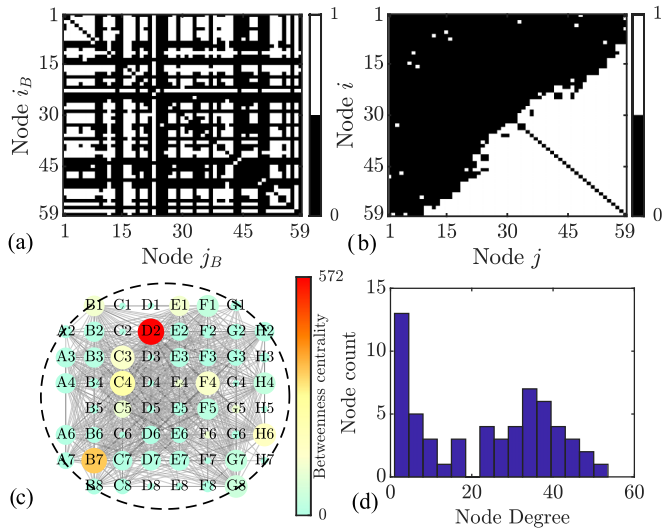


FIG. 4. Structural connectivity. (a) Adjacency matrix, with nodes ordered according to the initial order of multielectrode array channels, (b) adjacency matrix with nodes sorted from lowest to highest degree, allowing a better view of the distribution, and (c) graph representation of the network with nodes labeled and laid out as in the realized circuit board. Node diameter represents the structural degree, whereas color encodes their betweenness centrality, and (d) degree distribution.

a link density of 0.395, and a coefficient of variation of 0.7. It shows a small-worldness coefficient of  $S = 1.71 \pm 0.07$  ( $p < 0.001$ ) computed as  $S = (C/C_{\text{rand}})/(L/L_{\text{rand}})$  [89], with  $C$  and  $L$ , respectively, the average clustering coefficient and average shortest path length of the culture-derived network, and  $C_{\text{rand}}$  ( $0.40 \pm 0.10$ ,  $p < 0.001$ ) and  $L_{\text{rand}}$  ( $1.60 \pm 0.10$ ,  $p < 0.001$ ) the corresponding values computed from an ensemble of 100 ER random networks [114] with matched size and density, and with average degree of  $22.9 \pm 3.7$  (coefficient of variation of 0.16). The culture-derived network under consideration features a notable small-world organization alongside degree heterogeneity.

Considering 100 generated WS small-world networks [17] of identical size and density, these networks exhibited high clustering ( $0.68 \pm 0.01$ ) but substantially shorter path lengths ( $0.75 \pm 0.02$ ) and extremely low heterogeneity (average degree of  $22 \pm 0.74$ , coefficient of variation of 0.03) compared to the network under consideration. While the WS model is classically associated with a small-world organization, it fails to reproduce the heterogeneous degree distribution and intermediate path length that characterize the culture-derived network.

Figure 4(a) shows a representation of the adjacency matrix, while Fig. 4(b) visualizes the adjacency matrix with the nodes sorted in ascending degree order to allow a better visualization of the distribution. Figure 4(c) illustrates the network with the nodes arranged following the physical layout of the experimental circuit board, in an  $8 \times 8$  grid-based coordinate system with five excluded, as the network contains only 59 nodes corresponding to the active electrodes used to record the initial neuronal culture [112]. This configuration was henceforth chosen to maintain the spatial organization of the neuronal

culture. Nodes are labeled based on the  $8 \times 8$  grid-based coordinate system using an alphanumeric designation where columns are indexed by letters (A–H) and rows by numbers (1–8). Labels (A1, A5, A8, H1, H8), corresponding to the unused coordinates, were removed. As observed, the network contains a prominent number of nodes with a high number of connections (hubs). Notably, in Fig. 4(c) where nodes are colored according to their betweenness centrality, nodes B1, B7, C3, C4, C5, D2, E1, E4, F4, F6, G5, and H6 (degree 37, 49, 45, 48, 29, 51, 36, 6, 45, 3, 6, and 43, respectively) possess relatively high betweenness centrality, more marked for the node D2 (degree 51), possessing the highest. These nodes may therefore act as bridges, being critical for information flow and resources. However, the disruption of nodes can reshape the network structure, resulting in a shift in the nodes with high betweenness centrality. Figure 4(d) shows the degree distribution of the network, further illustrating its structural heterogeneity. It shows a bimodal distribution consisting of a large group of peripheral nodes having low connectivity and a smaller set of nodes that are highly connected. This configuration is evidently different from standard models, such as ER or WS, which exhibit Poisson-like and peaked distributions with limited variance, respectively. The degree distribution observed from the designed network indicates a level of complexity that cannot be characterized using simple descriptors such as mean and standard deviation. This analysis of the network topology suggests the existence of a core-periphery organization, where a densely interconnected core of high-degree (hub) nodes coexists with a sparsely connected periphery of low-degree nodes. Such a structure underpins the emergence of functionally distinct dynamical regimes across the network, reflecting differences in synchronization propensity and dynamical roles between core and peripheral regions.

## B. Experimental setup

The dynamics of the network is driven by a simple autonomous chaotic oscillator (Minati-Frasca circuit [115,116]) comprising a bipolar junction transistor, two inductors ( $L_1$  and  $L_2$ ), one capacitor ( $C_1$ ), a resistor ( $R$ ), and a dc voltage supply ( $V_s$ ). The inductors connect the base and collector of the transistor to a junction point, which in turn routes current through  $C_1$  to ground and through  $R$  from the voltage source. The corresponding circuit diagram is shown in Fig. 5(a).

In this circuit, chaotic oscillations arise from the mutual interaction between two subcircuits: a relaxation-type oscillator, driven primarily by the inductor  $L_2$ , resistor  $R$ , and transistor nonlinearity, and a damped resonator composed of  $L_1$  and  $C_1$ . The relaxation unit emits pulses that periodically reset the resonant subcircuit, whose decaying oscillations feed back into the dynamics of the relaxation process. This bidirectional interplay, particularly under conditions where neither subcircuit dominates, produces persistent chaotic behavior. When appropriately tuned, especially when  $L_2$  far exceeds  $L_1$ , the system reveals a period-doubling route to chaos as the resistor  $R$  or the dc voltage supply ( $V_s$ ) is varied. The resulting dynamics is rich and varied, ranging from limit cycles to oscillations generating funnel-like attractors as spiking activity [116].

The pairwise coupling between oscillators in the network is realized by a voltage-controlled coupling circuitry, operating

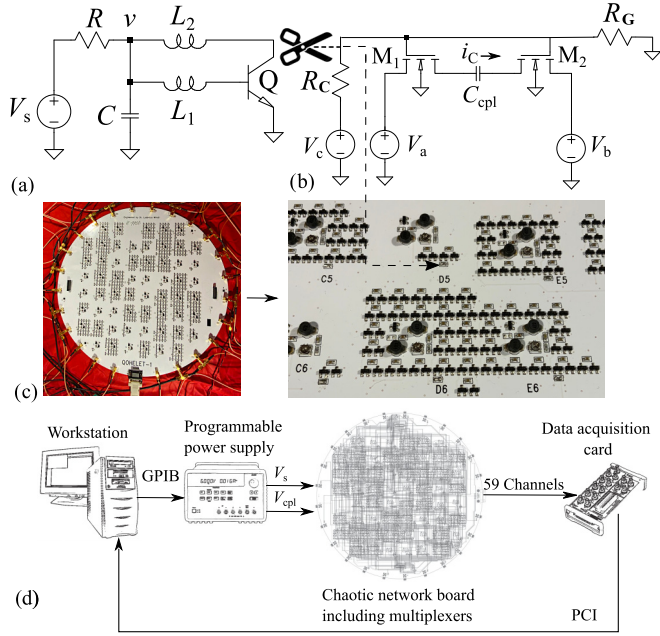


FIG. 5. Constituent elements of the network and experimental setup. (a) Chaotic oscillator circuit instantiated to realize each node in the network, (b) coupling circuit approximating a voltage-dependent resistor between the coupled oscillator outputs  $V_a$  and  $V_b$ , and (c) photograph of a prototype board with external interconnection wiring. The enlarged view on the right illustrates how damage is implemented, as indicated in panel (b) by the scissors. (d) Network board integrated into the overall experimental setup. Figure adapted from Ref. [112] with permission from Elsevier.

as a tunable resistive link between two voltage nodes, denoted  $V_a$  and  $V_b$ , as illustrated in Fig. 5(b). The coupling circuit comprises two  $n$ -type metal-oxide semiconductor transistors (NX7002AKA, Nexperia BV), labeled  $M_1$  and  $M_2$ , arranged in reverse series configuration: the source terminals of  $M_1$  and  $M_2$  are, respectively, connected to  $V_a$  and  $V_b$ , while their drain terminals are connected through a coupling capacitor  $C_{cpl}$ . This design suppresses unwanted current flow through the body diodes of the metal-oxide-semiconductor field-effect transistors (MOSFETs). Moreover, this symmetric topology enables bidirectional conduction, allowing regulated flow of current  $i_c$  across the coupling capacitor  $C_{cpl}$ , which allows decoupling the dc biases of the oscillators while facilitating interaction exclusively through dynamic components of  $i_c$ . The coupling strength is tuned through an external gate voltage  $V_c$ , which alters the effective conductance  $G$  of the transistors [112,117].

Figure 5(c) shows the photo of a representative prototype, including the external interconnection wiring, and Fig. 5(d) shows the overall experimental setup. The hardware realization of the network is based on a custom four-layer printed circuit board that enables systematic separation of signal pathways, ground references, and distribution lines. In order to minimize resistance and reduce interference, the nodes were arranged in a regular matrix with long-range interconnections that is routed orthogonally on separate layers. The global voltages, which are necessary for the biasing of the oscillator and for the modulation of the coupling parameter, were provided

via a programmable power supply. This is interfaced through a general-purpose interface bus. The outputs of the nodes were routed to a high-speed peripheral component interconnect acquisition card, thereby enabling automated high-resolution measurement.

Each oscillator was tuned to an operating point that enhances sensitivity to interactions across the network, that is, near the transition zone between periodic and chaotic regimes. The nominal values of the component were chosen as follows: inductors  $L_1 = 4.7$  mH and  $L_2 = 10$  mH, and a capacitor  $C = 22$  nF. The resistor  $R$  and voltage source  $V_s$ , key control parameters of the chaotic oscillator, were fixed to  $470\ \Omega$  and  $3$  V, respectively, to ensure the desired operating regime. The coupling capacitor was set to  $C_{cpl} = 1\ \mu\text{F}$ , and the external gate voltage  $V_c$ , modulating the coupling strength, was varied from  $2$  to  $3$  V in steps of  $1/59$  V. In the following sections, the coupling strength is directly represented by the control voltage  $V_c$ . The detailed specifications on the experimental board are available in Ref. [112].

### III. EXPERIMENTAL MODELING OF NETWORK DEGENERATION

In neurodegenerative diseases, brain regions do not stop functioning all at once. The pathology accumulates gradually, and the brain regions transition through stages of partial dysfunction, maintaining a certain level of activity while exhibiting increasing impairment [118]. In other words, these regions remain connected and responsive, yet operate with reduced efficiency and altered dynamics. The disruption strategy adopted in this study conceptually emulates such synaptic weakening, while its electronic realization ensures a controlled and progressive reduction of connectivity.

In the hardware implementation, each structural link of the network is realized as a bidirectional MOSFET-based coupling stage acting as a voltage-controlled resistor [Fig. 5(b)]. The conductance of this stage is dynamically modulated by the gate bias voltage  $V_c$  and increases monotonically with the bias voltage, following a sigmoidal-like nonlinearity as reported in Refs. [112,117]. At this level, the coupling stages do not represent specific synaptic mechanisms, but provide a controllable physical interaction through which collective network dynamics can emerge. The gate terminals of all MOSFETs corresponding to the links of a given node are routed through a multiplexed control channel, allowing centralized disruption of that node's connectivity. Selective damage was therefore implemented by isolating the corresponding gate line, forcing the MOSFET into a high-resistance (open circuit) state.

Additionally, on the board, each node was constructed along with a proportion of its designated MOSFET-based coupling stages, realizing connections built into it locally, and the remaining were distributed among its neighbors across the board (see Fig. 6). This choice was motivated primarily by routing constraints. As a result, when a node is targeted, all its MOSFET-based coupling stages are damaged. In this way, the targeted node remains electrically active and partially connected, but its effective participation in network communication is compromised. Because each disconnection also deprives the corresponding neighbors, the effect is both

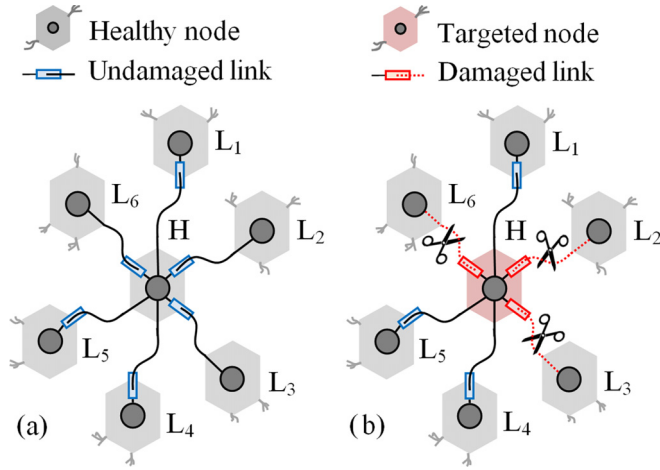


FIG. 6. Illustration of the disruption procedure in a simplified star subgraph. (a) A hub node (center) connected to six peripheral leaves, with three coupling units integrated within the hub (blue rectangles) and the remaining realized in the leaves. (b) The hub node is targeted for disruption, its internal couplings are disabled (red rectangles and dashed red lines), while the hub remains electrically active (undamaged link).

local and distributed, consistent with the cascading nature of connectivity loss in the brain. This approach used to establish connections in the proposed model provides a biologically meaningful framework for emulating partial dysfunction by preventing the instantaneous isolation of a node and thereby promoting a gradual degradation of connectivity as seen in disease progression. Indeed, it should be noted that neurons possess axonal outputs (outgoing synapses) and dendritic inputs (incoming synapses), and dysfunction often first manifests as impaired transmission rather than a sudden loss of all connectivity (inputs can still be received).

As mentioned earlier, the damage sequences are anatomically inspired, although highly abstracted. They evolve either from hubs to peripheral nodes or from peripheral nodes to hubs. This supports the modeling of different disease-specific propagation patterns, such as core-to-periphery failure in AD or periphery-to-core progression observed in ALS and PD. At each step, one node is targeted according to the predefined scenarios. Consequently, as disruption progresses, nodes that were previously targeted indirectly begin to lose additional connections in the subsequent steps during the targeting of their neighboring nodes. This leads to a gradual reduction in overall connectivity. The case of the single-node disruption serves as a baseline for normal operation and allows for tracking of cascading effects across the network.

The experimental sequence started with a baseline condition in which all nodes were fully connected ( $V_c$  applied to every MOSFET gate). Disruptions were then applied step by step from this initial state according to the selected scenario. After each step, a time delay of a few seconds was allowed to avoid transient regimes, and the time series corresponding to the voltage  $v$  at each step from all 59 nodes were simultaneously recorded through the data acquisition card at a sampling rate of 250 kS/s over a range of coupling strengths. This process was automated to be iteratively repeated following

the sequence in each scenario. The recorded data were subsequently analyzed to trace how emergent collective behaviors, such as synchronization, entropy, frequency, and graph-based metrics, respond to alterations of the structural connectivity.

Figure 6 illustrates the disruption procedure in a simplified star configuration. In this example, a hub is connected to six leaves. The hub node is designed with three coupling units (small blue rectangles), while the remaining connections are realized within the leaves [Fig. 6(a)]. When the hub is targeted, all its internal coupling units are disabled (red rectangles and dashed lines), as shown in Fig. 6(b).

## IV. DATA ANALYSIS

### A. Synchronization, entropy, and correlation coefficient

Let us consider  $\mathbf{X} = [X_1, \dots, X_N]$ , collecting all signals recorded at each node of the network, quantifying the states visited over time by the underlying dynamical system, with  $N$  being the total number of nodes. To characterize the impact of progressive node disruptions on network dynamics, multiple metrics, including phase synchronization, permutation entropy, and cross-correlation coefficient, were employed. Phase synchronization captures the consistency of the phases of pairs of nodes over time. Permutation entropy quantifies the dynamic complexity of the network. Finally, the cross-correlation coefficient assesses the effect of the network's topology on its dynamics.

For each node pair  $\{X_i, X_j\}$ , phase synchronization was assessed by computing the discrete-time analytic signals

$$\varphi_i(t) = X_i^{(0)}(t) + j\tilde{X}_i^{(0)}(t) = A_i(t)e^{j\Phi_i(t)} \quad (1)$$

and  $\varphi_j(t)$ , where  $j = \sqrt{-1}$ , with  $X_i^{(0)}(t) = X_i(t) - \langle X_i \rangle_t$  ( $\langle \cdot \rangle_t$  the temporal average) the mean-centered signal of node  $i$  and  $\tilde{X}_i^{(0)}(t) = \frac{1}{\pi} \text{P.V.} \int_{-\infty}^{\infty} \frac{X_i^{(0)}(\tau)}{t-\tau} d\tau$  is the Hilbert transform of  $X_i^{(0)}(t)$ . P.V. denotes the Cauchy principal value of the integral [119]. The instantaneous relative phase for the pair  $\{X_i, X_j\}$  is computed as

$$\Delta\varphi_{ij}(t) = \arg[\varphi_i(t)\bar{\varphi}_j(t)] \quad (2)$$

and finally, the phase synchronization value is given by

$$r_{ij} = |\langle e^{j\Delta\varphi_{ij}(t)} \rangle_t|. \quad (3)$$

From Eq. (3), the average synchronization of node  $i$  with all other nodes in the network,  $r_i$ , and the global synchronization  $r$ , are, respectively, computed as

$$r_i = \frac{1}{N-1} \sum_{j=1, j \neq i}^N r_{ij} \quad (4)$$

and

$$r = \frac{1}{N(N-1)} \sum_{i=1}^N \sum_{j=1, j \neq i}^N r_{ij}. \quad (5)$$

Permutation entropy used here to quantify the complexity of network dynamics captures the temporal irregularity of a signal based on the distribution of ordinal patterns within the time series [120,121]. For a time series  $X = x_1, x_2, \dots, x_M$ ,

the permutation entropy is defined as

$$H(n) = -\frac{\sum_{i=1}^{n!} p_i \log p_i}{\log n!}, \quad (6)$$

where  $p_i$  represent the relative frequencies of the ordinal patterns derived from the time series and  $n$  is the order of the permutation entropy, which determines the length of the ordinal patterns. Given the burstlike nature of the node's local dynamics, time-series local maxima are used in the computational process to reduce redundant information and enhance sensitivity to eventlike dynamics. In this context, low entropy values reflect regular and predictable activity, while high values indicate more complex and irregular dynamics.

The relationship between network topology and dynamics is assessed by correlating the node degree distribution with node-level permutation entropy values, thereby enabling assessment of the relationship between node connectivity and dynamical complexity. Similarly, the correlation between node degree and average synchronization is computed to evaluate how connectivity influences the ability of nodes to maintain coherent activity across the network. These relationships were quantified using Spearman's rank correlation coefficient  $\rho$ , measuring the association between the node degree vector  $\mathbf{k} = [k_1, k_2, \dots, k_N]$  and the two nodewise metrics, i.e., the permutation entropy vector  $\mathbf{H} = [H_1, H_2, \dots, H_N]$  and the average synchronization vector  $\mathbf{r} = [r_1, r_2, \dots, r_N]$ . Notably, the Spearman's correlation is computed by replacing the raw values with their ranks and then calculating the Pearson correlation [122] between the ranked variables. This allows capturing linear or nonlinear monotonic relationships between variables. Values of  $\rho$  range from  $-1$  to  $+1$ , with  $0$  meaning no correlation,  $+1$  positively correlated, and  $-1$  negatively correlated.

### B. Graph-based metrics from structural and functional connectivity

To investigate how network organization evolves under the progressive effect of damage, four fundamental graph-based measures were evaluated, namely, the clustering coefficient, the characteristic path length, the modularity, and the efficiency. These measures were computed for both the structural connectivity and functional connectivity graphs. The former was derived directly from the neuronal culture connectivity and represented as binary, undirected adjacency matrices, and the latter was derived from pairwise synchronization matrices after applying a threshold to suppress spurious or noisy links, with the resulting networks represented as weighted graphs. The thresholding procedure was based on a percolation approach. This consists of initially setting a high threshold and then gradually decreasing it till the largest connected component spans all the nodes. This dual analysis allows understanding how structural and functional architecture (pairwise synchronization matrices) respond to disruption. The four indicators provide complementary information on local segregation, global integration, modular structure, and communication efficiency.

Let  $\mathcal{N}$  be the set of nodes and recall that  $N$  the number of nodes. For functional networks,  $r_{ij}$  denotes the weight of the functional connection between nodes  $i$  and  $j$  ( $0 \leq r_{ij} \leq 1$ ),

while in structural networks,  $a_{ij}$  indicates the presence ( $a_{ij} = 1$ ) or absence ( $a_{ij} = 0$ ) of a structural connection, with  $a_{ii} = 0$  (no self-connection). Analogously,  $r_{ii}$  is manually set to zero in functional graphs, removing the trivial information that  $r_{ij}$  is always equal to 1 when  $i = j$ . The sum of all weight in the functional graph is  $l^w = \sum_{i,j \in \mathcal{N}} r_{ij}$ , while the number of links  $l$  in the structural graph was computed using the same formula but with  $r_{ij} = a_{ij}$  and counting each undirected link twice, as  $a_{ij}$  and  $a_{ji}$ .

The weighted clustering coefficient  $C^w$  was used to evaluate local segregation in the functional network by measuring how neighboring nodes are interconnected and was computed as the ratio of existing triplets (triangular connections) to the total possible triplets. Notably, the average weight of connections in each triplet was considered such that for a vertex  $i$  [89],

$$C^w = \frac{1}{N} \sum_{i \in \mathcal{N}} \frac{2t_i^w}{k_i^w(k_i^w - 1)}, \quad (7)$$

where  $k_i^w = \sum_{j \in \mathcal{N}} r_{ij}$  is the weighted degree of node  $i$  and  $t_i^w = \frac{1}{2} \sum_{j,h \in \mathcal{N}} (r_{ij} r_{ih} r_{jh})^{1/3}$  the geometric mean of weighted triangles around  $i$ . For the clustering coefficient  $C$  in the structural graphs, the same formula applies with  $r_{ij} = a_{ij}$ .

The functional characteristic path length  $L^w$  was computed to assess the network functional integration by measuring the average shortest path between all pairs of nodes [89],

$$L^w = \frac{1}{N} \sum_{i \in \mathcal{N}} \frac{\sum_{j \in \mathcal{N}, j \neq i} d_{ij}^w}{N - 1}, \quad (8)$$

where  $d_{ij}^w = \sum_{(p,q) \in g_{i \leftrightarrow j}} f(r_{pq})$  is the shortest weighted path length between  $i$  and  $j$ ,  $g_{i \leftrightarrow j}$  denotes the geodesic between  $i$  and  $j$ , and  $f(r_{pq}) = 1/r_{pq}$  is the weight-to-length mapping adopted so that stronger synchronization corresponds to shorter effective distance. For characteristic path length  $L$  in the structural graphs, the same formula applies, with  $f(a_{pq}) = 1$  if  $a_{pq} = 1$ , and  $\infty$  otherwise, so that path length counts the number of hops (a single step or transition from one node to another adjacent node in path).

Furthermore, functional modularity  $Q^w$  was computed to evaluate the extent to which the network can be decomposed into distinct communities. The computation method was particularly based on Louvain's algorithm, consisting of greedy optimization to maximize modularity of network partition [123],

$$Q^w = \frac{1}{l^w} \sum_{i,j \in \mathcal{N}} \left[ r_{ij} - \frac{k_i^w k_j^w}{l^w} \right] \delta_{m_i, m_j}, \quad (9)$$

where  $m_i$  is the community membership and  $\delta_{m_i, m_j}$  the Kronecker's delta. For structural graphs, modularity  $Q$  was computed with the same formula, with  $r_{ij} = a_{ij}$ .

Finally, the efficiency was computed to quantify how the network transmits information (in the structural graph) and to measure the level of integration (in the functional graph) at both global and local levels. Global efficiency from the functional graph  $E^w$  was computed as the average inverse

shortest path length across all nodes [89]:

$$E^w = \frac{1}{N} \sum_{i \in \mathcal{N}} \frac{\sum_{j \in \mathcal{N}, j \neq i} (d_{ij}^w)^{-1}}{N-1}, \quad (10)$$

and local efficiency  $E_{\text{loc}}^w$  was computed analogously at the neighborhood level [89]:

$$E_{\text{loc}}^w = \frac{1}{2} \sum_{i \in \mathcal{N}} \frac{1}{k_i(k_i - 1)} \sum_{j, h \in \mathcal{N}, j \neq i} (r_{ij} r_{ih} [d_{jh}^w(N_i)]^{-1})^{1/3}. \quad (11)$$

The same formula applies in the structural graph for the global efficiency  $E$  and the local efficiency  $E_{\text{loc}}$ . Again, in this case, path length counts the number of hops.

These graph-theoretic measures have been extensively used to characterize both structural and functional brain networks. In particular, the emergence of small-world properties (high clustering combined with short path length) has been documented in structural connectomes as well as in functional networks derived from electroencephalography (EEG), magnetoencephalography (MEG), and fMRI data, where it is interpreted as reflecting an optimal balance between local segregation and global integration [19,23]. All the aforementioned graph-based metrics were conducted in this study using the Brain Connectivity Toolbox [89].

In the following section, nodes are sorted according to their connectivity, from the lowest degree node to the highest one, as illustrated in Fig. 4(b). For the single-node disruption scenario, although the disruption sequence targeted one arbitrarily chosen node at each step, the results are reordered so that they reflect a progression from disruptions of the lowest-degree node to the highest-degree node. This reordering facilitates direct comparison with the core-to-periphery and periphery-to-core disruption sequences.

## V. RESULTS

### A. Synchronization and complexity shifts in the network

Figure 7 depicts the interplay between coupling strength ( $V_c$ ) and network topology. It provides an overview of how the progressive alteration of network connectivity impacts global synchronization and dynamic complexity. It is essential to note that steps 1–60 represent the progression of disruption events. For the core-to-periphery and the periphery-to-core damage sequences, the number of disrupted nodes at a given step is equal to the step index minus one, with step 1 corresponding to the initial situation, where the network is undamaged. However, this description does not apply to single-node disruption, where exactly one node was disrupted per step regardless of its degree, but in such a way that by the final step each node in the network had been damaged.

#### 1. Baseline focal disruption: synchronization and complexity signatures

The left panel shows results for the single-node disruption condition, where a randomly selected node is damaged at each step. As observed in Fig. 7(a), global phase synchronization gradually increases with coupling strength. Furthermore, the

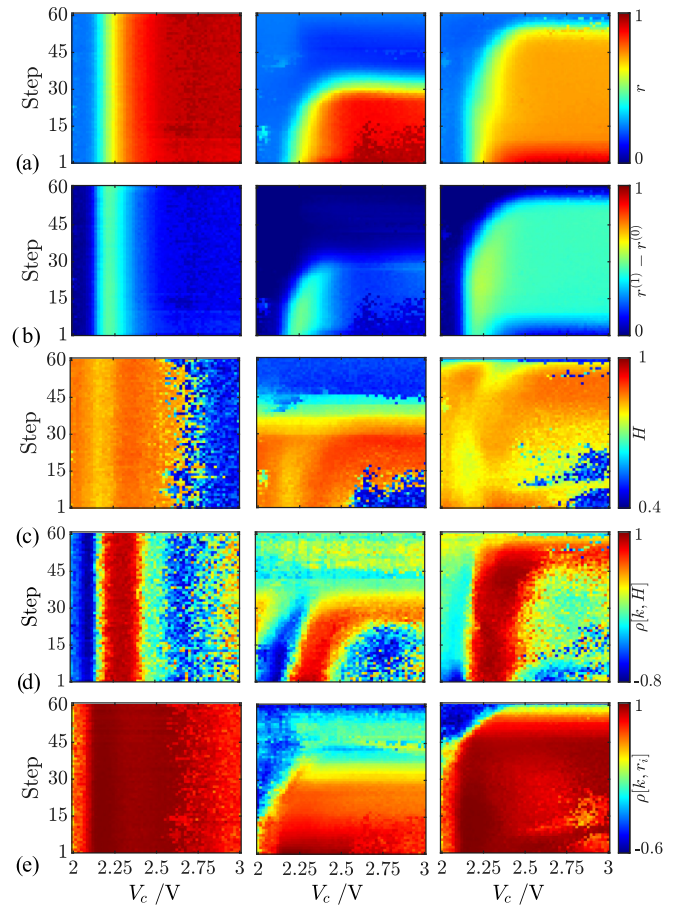


FIG. 7. Global network metrics as a function of coupling strength and disruption progression. (a) Average phase synchronization, (b) difference in average phase synchronization between connected [ $r^{(1)}$ ] and unconnected [ $r^{(0)}$ ] nodes, highlighting topological effects on synchronization, (c) permutation entropy, (d) correlation between node degree and their permutation entropy, and (e) correlation between node degree and their average phase synchronization. From left to right: single-node, core-to-periphery, and periphery-to-core disruption scenarios.

impact on global synchronization remains weak even with the high-degree nodes (hubs) being disrupted. This translates the inherent resilience of the network, which contains a substantial proportion ( $\approx 60\%$ ) of such nodes. In fact, the distributed nature of these hubs prevents any single one from critically compromising global coordination when disrupted. Figure 7(a) further highlights that the disruption of nodes having only a single neighbor [see Fig. 4(b)] leads to a slight reduction in the global synchronization, as observed between steps 2 and 10 (step 1 representing the undisturbed state, as previously mentioned).

Figure 7(b) shows the global synchronization difference between structurally connected and nonconnected nodes. It provides insight into the influence of network topology on synchronization dynamics. The latter is computed as

$$\Delta r = r^{(1)} - r^{(0)} = \frac{1}{N_c} \sum_{i,j \in \mathcal{C}} r_{ij} - \frac{1}{N_u} \sum_{i,j \notin \mathcal{C}} r_{ij}, \quad (12)$$

where  $r^{(1)}$  is the global synchronization of connected nodes,  $r^{(0)}$  is the global synchronization between unconnected nodes,  $\mathcal{C}$  is the set of connected node pairs,  $N_c$  is the number of connected node pairs, and  $N_u$  is the number of unconnected node pairs. Three regimes are observed to emerge. The first one being a weak coupling regime given by the range of coupling voltage  $V_c \in [2.0, 2.15]$  V, where the synchronization difference remains almost zero. It indicates that the network's dynamics cannot be significantly influenced by either the structural connectivity or the coupling strength. Thus, this regime reflects a completely desynchronized state dominated by chaoslike fluctuations. The second regime is an intermediate one with  $V_c \in [2.15, 2.3]$  V, where the synchronization difference increases and peaks at approximately  $V_c = 2.2241$  V. This peak marks the onset of topologically driven synchronization, where structurally connected nodes increasingly align their dynamics more strongly than unconnected pairs. Finally, the third one is a strong coupling regime  $V_c > 2.3$  V, where the synchronization difference decreases and returns close to zero. In fact, the system is observed to tend toward a fully synchronized state here. This can be justified by the fact that the coupling strength dominates and enforces global coherence across the network, regardless of the topological structure.

Figure 7(c) shows the entropy of the network dynamics that captures the system's overall complexity. Two distinct regimes emerge. A region of weak or intermediate coupling strength, corresponding to low synchronization, where the entropy remains high. This indicates rich, disordered dynamics characteristic of strong chaotic behavior among nodes. The second one is a strong coupling regime, which is characterized by low entropy due to the emergence of more predictable behavior, which in turn facilitates synchronization. Remarkably, a localized decrease in entropy is observed within the intermediate coupling range  $V_c \in [2.15, 2.3]$  V, the same regime identified earlier where synchronization is strongly influenced by topology. This highlights that the interplay between node dynamics and network topology shapes the onset of different levels of synchronization in nodes with diverse topological characteristics within this transition window. Moreover, for  $V_c > 2.5$  V, the sustained decline in entropy reflects a progressive loss of dynamical complexity of nodes, contributing to the full synchronization observed in this regime.

Figure 7(d) provides insights into how network topology influences the dynamical complexity of individual nodes, revealing a complex relationship between node degree and entropy. Notably, throughout the analysis it was found that while some hub and low-degree nodes tended to exhibit high entropy, others exhibited lower entropy. More specifically, in the regions of low entropy, typically corresponding to moderate or strong synchronization, a propensity for positive correlations is observed, indicating that hub nodes exert a dominant influence in the resulting collective dynamics. Interestingly, the transition region in the intermediate coupling regime, where the synchronization is topologically driven, shows a substantially higher correlation ( $\rho \approx 0.9$ ). For higher entropy regions, a propensity for negative correlation is observed, revealing that hubs no longer exert dominant control, and dynamic complexity is more evenly distributed across the

network. Notice that in certain cases this negative correlation is even pronounced, reaching  $\rho \approx -0.8$ , revealing an inverse situation where the peripheral nodes have more complex dynamics.

Figure 7(e) corroborates these findings. It shows a strong positive correlation between node degree and synchronization at intermediate coupling strengths. This effect is pronounced particularly in the transition region, where node topological features govern the synchronization. Moreover, this correlation remains stable across damage steps. Because strong couplings enhance network synchronization while reducing entropy, it can be inferred that the synchronization of certain peripheral nodes increases due to the reduced complexity of the node dynamics, hence the lower correlation observed. Conversely, at lower values of coupling, even the hub nodes struggle to synchronize due to their higher intrinsic complexity, which is also reflected by the entropy. Thus, it leads to weakening of their influence on global dynamics.

## 2. Progressive network degradation: topology-driven transitions and resilience

In the middle panel of Fig. 7, nodes are progressively damaged in a targeted manner, starting from the most connected. As previously noted, this targeted progression of damage generically reflects the vulnerability patterns observed in neurodegenerative diseases such as AD [32,45,47,55,66,81]. During the initial phase, ranging from the intact state to the disruption of a few hub nodes, the global synchronization profile remains comparable to the single-node damage case for the entire range of the coupling strength [Fig. 7(a)]. However, as high-degree nodes are successively disrupted, the intermediate synchronization regime observed at moderate coupling progressively shifts to higher coupling strengths following a trajectory reminiscent of a square-root function. This reflects a nonlinear reorganization of functional connectivity in response to structural damage. Such a pattern highlights the compensatory role of coupling strength in maintaining synchronization as damage accumulates, until the ultimate step at which the most critical node is disrupted. Specifically, after approximately 35 nodes (mainly those with degrees above the network mean degree) are disrupted, complete desynchronization occurs, regardless of the coupling strength. This collapse emphasizes the central role of high-degree nodes as essential integrators that sustain global functional connectivity and facilitate the transmission of information across the network [55]. Notably, a subtle increase in synchronization is observed in weak coupling regimes following the disruption of around ten nodes, further highlighting the functional reorganization of the network.

The synchronization difference between connected and unconnected nodes [Fig. 7(b)] reflects the topology-driven effects already visible in the global phase synchronization patterns. As the coupling strength increases, the difference gradually intensifies and reaches its maximum around  $V_c = 2.43$  V. Figure 7(c) shows that for strong couplings, the entropy of the network remains low throughout the early phases of disruption progression as long as a high level of synchronization is maintained (until the perturbation of about 15 nodes). In contrast, for lower levels of synchronization

as well as for completely desynchronized states, the entropy values are seen to be relatively high. In particular, they are observed before the disruption of the majority of hubs. As more hubs are disrupted, entropy steadily declines, indicating a progressive loss of dynamic complexity in the network, which becomes incapable of sustaining diverse activity patterns. Furthermore, the correlation between node degree and entropy [Fig. 7(d)] reveals a propensity for weak positive correlation in the very low entropy regions observed in the strong coupling regime and negative correlation in regions with higher entropy, as observed in the single-node damage scenario. Especially, a high positive correlation (lower than in the single-node case) is observed around and along the curve marked by a moderate synchronization level in the parameter space, belonging to the transition region from low to high coupling regime and from moderate or sustainable damage to complete breakdown of the network, which delineates the regime of high synchronization and complete desynchronization. This indicates that hubs in this region, even when structurally compromised, likely retain more irregular dynamical activity than peripheral nodes until the network collapses. After the collapse, this correlation first drops to zero regardless of the coupling strength, after which it slightly increases before decreasing again to zero when all nodes become isolated. As shown in Fig. 7(e), the most connected nodes have a higher propensity for synchronization when the coupling is moderate, even if the network suffers some damage. Conversely, this correlation weakens when the coupling is too weak (the nodes interact little) or too strong (all the nodes synchronize uniformly). However, as disruption progresses, the correlation between degree and node average synchronization diminishes and eventually becomes null or even negative, particularly once most hub nodes are disrupted. While this reversal in the sign of the correlation occurs more rapidly in the weak coupling regime, high positive correlation is observed until the damage of approximately 15 nodes, emphasizing the central role of hubs in maintaining topological influence on synchronization.

The right panel shows the results of the periphery-to-core damage sequence. This scenario of node disruption mirrors the impairment observed in diseases such as PD or ALS, in which the pathology originates in peripheral or subcortical regions before affecting the integrative cortical hubs [45]. In this case, contrasting with the targeted disruption of hubs, which induces early and disproportionate disruption of global dynamics, the observed delayed collapse highlights that while low-degree nodes contribute to the global coordination, their influence is less distributed, thereby preventing the cascading breakdown observed in the core-to-periphery scenario. This further supports the crucial role of hubs as integrative structures that maintain coherence and synchronize distributed activity across the network. Additionally, before the onset of critical disruption at which the network collapses, the overall synchronization remains lower than in the core-to-periphery damage sequences and declines more gradually as more nodes are disrupted [Fig. 7(a)]. This paradoxical observation suggests that some nodes, although peripheral and not critical for the network coordination, contribute to the network's synchronization in a way that is not immediately compensated for by the remaining nodes.

Figure 7(b) shows that the synchronization difference between connected and unconnected node pairs remains high within both the intermediate coupling regime and the strongly synchronized regime under high coupling. This implies that both coupling strength and network topology continue to coregulate synchronization in the network. As in previous cases, Fig. 7(c) shows low entropy values in regimes of high synchronization and after full network collapse, supporting the observation that synchronization becomes more difficult to achieve, the network being almost completely disconnected in this case.

In Fig. 7(d), which shows the correlation between node degree and entropy, similar observations to those made in the previous scenarios can be noted. In particular, a high positive correlation is still observed around and along the boundary curve in the parameter space, marked by a moderate synchronization level, as observed in the previous cases. Finally, in Fig. 7(e), strong positive correlations between node degree and node average synchronization are observed at intermediate coupling strengths. However, this correlation continuously decreases as the progressive disruption of high-degree nodes occurs, similar to the core-to-periphery damage sequences. High correlations are also observed in regions of strong coupling prior to the critical step that causes network collapse. This is consistent with the finding that, in many networks, strong coupling promotes synchronization, with the efficacy being determined by the underlying structural organization of the network [119].

### 3. Summary

All these analyses reveal a consistent observation; that is, the interplay between topology and coupling strength jointly shapes the resilience and complexity of synchronization within the network. Peripheral damage, whether in single-node or periphery-to-core disruption, highlights that even weakly connected nodes contribute to the network's overall synchronization, as one might expect, since their disruption rapidly isolates them and makes synchronization more difficult to achieve. In contrast, the core-to-periphery scenario initially compromises the densely interconnected core; however, the redundancy of high-degree nodes' connections keeps the network connected and sustains synchronization until a large fraction of the nodes are disrupted. This explains why synchronization remains stronger in core-to-periphery damage sequences than in periphery to core before the network collapses. Overall, high-degree nodes act as critical integrators sustaining global information flow, and their disruption triggers abrupt desynchronization. It is found that coupling strength preserves synchronization, acting as a key modulator of resilience. Entropy analysis further reveals a complex interplay: While coupling strength shapes node dynamics, network topology further modulates these patterns as observed during core-to-periphery and periphery-to-core damage sequences, where the disruption of high-degree nodes leads to the emergence of high entropy in strong coupling regimes (low in the single-node scenario). Notably, once extensive high-degree nodes are disrupted, causing the network to collapse, the entropy drops regardless of the coupling strength. Moreover, high-degree nodes consistently exhibit stronger

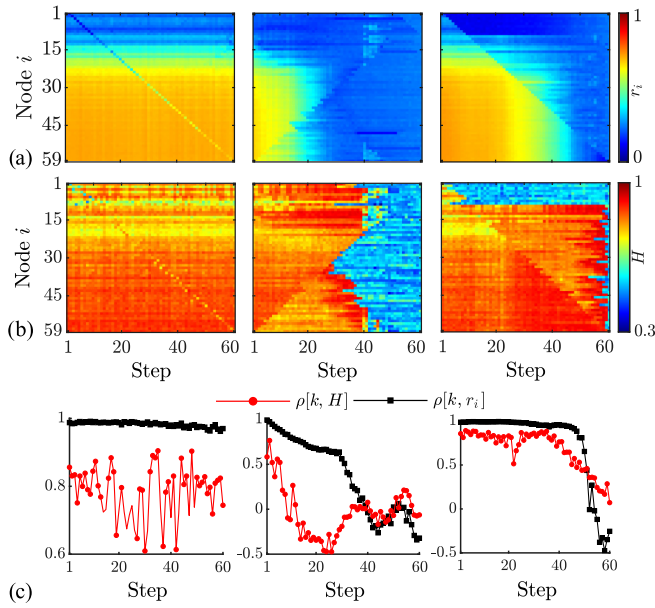


FIG. 8. Nodewise metrics in terms of the disruption progression at  $V_c = 2.2241$  V. (a) Average phase synchronization, (b) permutation entropy, and (c) average phase synchronization and entropy's corresponding correlation coefficients with degree. From left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences.

synchronization and elevated entropy in the intermediate coupling regime, and, in particular, in the region of moderate synchronization, underscoring their dual role as drivers of coherent yet dynamically rich collective behavior.

### B. Node-level contribution to network synchronization and dynamic complexity

The analyses presented in Fig. 7 focused on global network metrics, offering an overview of synchronization and dynamical complexity as functions of disruption progression and coupling strength. To gain deeper insights into the contribution of individual nodes to the network resilience and failure, a finer node-level analysis was performed. Two specific coupling strengths were examined, i.e.,  $V_c = 2.2241$  V and  $V_c = 2.7586$  V. In the former, synchronization is strongly governed by node topological properties, while the latter represents a strong coupling regime.

#### 1. Intermediate coupling regime: topology-driven synchronization and entropy dependencies

Figure 8 presents the results for the intermediate coupling case ( $V_c = 2.2241$  V). As observed in the left panel [Fig. 8(a)], for the single-node disruption scenario, the average synchronization of each node is preserved throughout the steps. Also, the least connected nodes show weak synchronization even in the absence of damage. In the core-to-periphery and the periphery-to-core damage sequences (middle and right panels), the synchronization levels of the most connected nodes (those forming the functional core) progressively decline as damage accumulates. Specifically, the targeted node shows a marked drop in synchronization while

the remaining nodes experience a more moderate decline. This reflects the combined effects of local degradation and global propagation resulting from structural damage. This pattern is clearly visible in the heatmaps, where the effect of separation observed in the diagonal or antidiagonal due to the decrease in synchronization intensity is representative of node disruption. Indeed, when a node is disrupted, it becomes less synchronized with respect to the other nodes. In the single-node case, the antidiagonal highlights the localized effects of the loss of synchronization of the disrupted nodes with the rest of the network. In contrast, in the other two scenarios, these effects propagate with the progress of disruption since the nodes remain disrupted. The diagonal or antidiagonal accounts for the direction of the disruption sequence (core to periphery or periphery to core). The emergence and expansion of low-synchronization regions across the heatmap illustrate the role of structural deterioration in driving the spatial redistribution of synchrony.

Furthermore, the low-synchronization level observed in weakly connected nodes, even when they are not disrupted, emphasizes the central role of hubs in maintaining network synchronization, as predicted in Fig. 7. Generally, synchronization increases with node degree across all disruption scenarios. However, with the progressive disruption of the hubs, the compensatory capacity of the network eventually declines. Nonetheless, even with the residual synchronization persisting for a limited number of disruptions, the system ultimately collapses as topological redundancy is exhausted.

The patterns of entropy in individual nodes reveal intricate dependencies on node degree and disruption scenario. Under the single-node disruption scenario, most nodes retain high entropy regardless of whether they are damaged or not, and only subtle reductions are observed in some nodes. Notably, when a node with only a single connection (degree = 1) is damaged, a striking localized effect occurs: either the entropy of the targeted degree-1 node decreases or the one of another degree-1 node, eventually not directly connected to the targeted one, as highlighted by the dark blue points in the left panel of Fig. 8(b). This indicates the presence of nontrivial long-range dependencies in the network dynamics.

While in the core-to-periphery damage sequences (middle panel), the entropy of nodes remains high and only starts decreasing after the network has collapsed; the periphery-to-core scenario (right panel) exhibits a combined effect of the single-node and core-to-periphery scenarios. As low-degree nodes (especially degree-1 nodes) are progressively disrupted, they undergo a drop in entropy almost in a similar way as observed in the single-node scenario; i.e., the disruption of some of these nodes triggers the drop in entropy in others not yet being disrupted (node 9 clearly exemplifies this situation, showing an early drop of entropy). However, unlike in the single-node scenario, these drops persist through subsequent steps because previously damaged nodes remain or even worsen. Entropy declines more gradually, similar to the core-to-periphery damage sequences. However, even after the complete loss of synchronization, entropy remains high for several steps before decreasing substantially. This lag suggests a delayed degradation of dynamic complexity. Figure 8(c) provides the correlation between node degree and phase synchronization and entropy. The previous observations

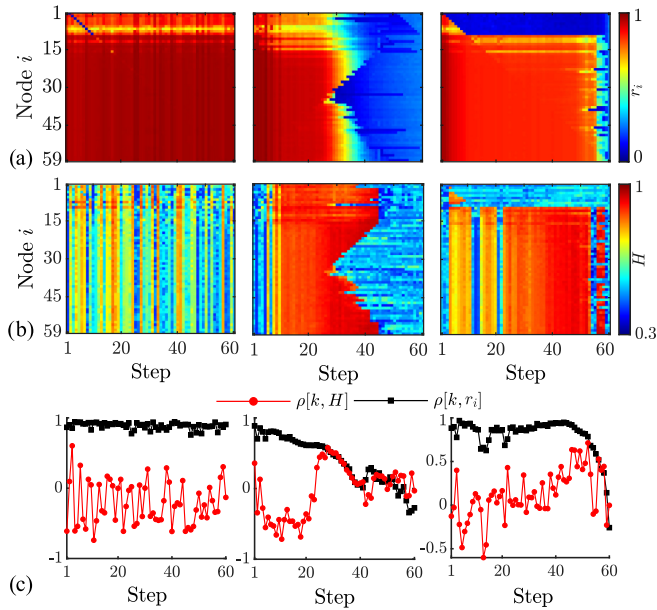


FIG. 9. Nodewise metrics in terms of the disruption progression at  $V_c = 2.7586$  V. (a) Average phase synchronization, (b) permutation entropy, and (c) average phase synchronization and entropy's corresponding correlation coefficients with degree. From left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences.

reveal that although low-degree nodes contribute minimally to network-wide information processing, they play a disproportionate role in maintaining local dynamical diversity.

## 2. Strong coupling: abrupt collapse and entropy variability

At a slightly higher coupling strength,  $V_c = 2.7586$  V, the average synchronization of each node in the network increases due to high connectivity (strong coupling), as illustrated in Fig. 9. In the single-node disruption scenario (left panel), all nodes maintain a high level of synchronization, regardless of which node is damaged.

For the core-to-periphery and periphery-to-core damage sequences (middle and right panels, respectively), the network demonstrates higher resilience, preserving synchronization even as increasingly high-degree nodes are disrupted. However, this higher resilience conferred by high connectivity has drawbacks: a sudden collapse in synchronization and dynamic complexity occurs once the critical disruption threshold is exceeded. The sharp decline in entropy accompanying the synchronization loss in this case indicates a simultaneous loss of functional integration and dynamic complexity, in contrast to the previous case at lower coupling strengths, where degradation in dynamic complexity was delayed. Furthermore, the diagonal and antidiagonal features of the synchronization patterns can still be observed, and their effect appears to be more pronounced for the nine degree-1 nodes. Additionally, significant fluctuations in node entropy are observed for all three scenarios, depending on whether the disrupted node is a high- or low-degree node. The observed entropy fluctuation reflects an increased instability in the network's functional

reorganization. Figure 9(c) provides the correlation between node degree and phase synchronization and entropy.

The correlation coefficients in Figs. 8(c) and 9(c) reveal a clear interplay between node degree, entropy, and phase synchronization, which was challenging to discern in the parameter sweep of Fig. 7. Moreover, the entropy fluctuations observed in Fig. 9(b) are reflected in the variability of the correlation between node degree and both phase synchronization and entropy shown in Fig. 9(c). This contrasts with the smoother trends observed at the lower coupling strength in Fig. 8(c). Furthermore, in contrast to Fig. 8(c), the high propensity for a negative correlation between node degree and entropy observed for strong coupling in Fig. 9(c) reveals that hub nodes morphed their role as regards the complexity of the dynamics, almost swapping with peripheral nodes.

## 3. Pairwise synchronization and modular reorganization

Pairwise synchronization across the nodes provides insights into the role of disruptions to structural connectivity in reshaping functional interactions. Indeed, it allows for the identification of localized effects along with the dynamic reorganization of functional modules. Moreover, these pairwise synchronization matrices constitute the foundation for subsequent graph-theoretical analyses. Figures 10 and 11 show the pairwise synchronization matrices across nodes for  $V_c = 2.2241$  V and  $V_c = 2.7586$  V, respectively. In both figures, the first column corresponds to the single-node disruption scenario, while the second and third columns depict the core-to-periphery and periphery-to-core damage sequences, respectively.

In all scenarios studied, it is consistently observed that network topology strongly influences synchronization patterns. High-degree nodes tend to synchronize more strongly with each other to form a tightly integrated core, while weakly connected nodes display a low pairwise synchronization index. However, such a functional organization is largely preserved under the single-node disruption scenario since the damage is localized. Consequently, the influence is quite limited on the broader network synchronization pattern.

In the second column, synchronization between all node pairs gradually decreases as disruptions progress, reflecting the gradual disintegration of global connectivity. As disruptions continue, the highest synchronized group of nodes, mainly composed of hubs, begins to fragment (starting from step 15) and forms localized clusters in which synchronization is maintained. The observed fragmentation occurs due to the deactivation (loss of synchrony) of intermediate-degree nodes (considered as hubs with degree slightly greater than the network mean degree), specifically spanning nodes 35–48 (D6, E2, E3, C7, H2, H3, A6, D7, E7, A4, B2, B3, E1, B1, respectively). The resulting clusters extend between nodes 25–35 (F2, C8, G2, B6, B8, E6, A7, G3, C5, F3, D6, respectively) and 48–59 (B1, F5, F1, G7, H4, G8, H6, C3, F4, C4, B7, D2, respectively), which preserve moderate synchronization both internally and with each other, meaning that they remain functionally connected. At this stage, approximately 24 nodes are effectively disrupted, including nodes 35–48 [Fig. 8 (middle panel)]. However, our simulations revealed that the breakdown of the subnetwork composed of

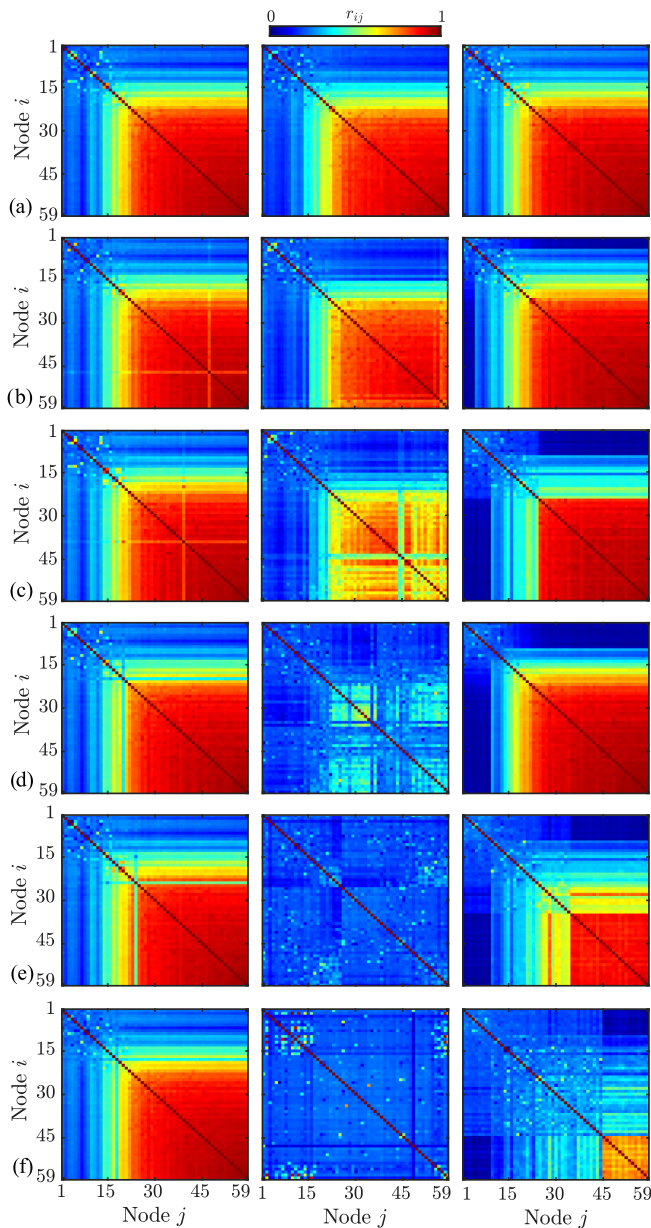


FIG. 10. Pairwise synchronization matrices at  $V_c = 2.2241$  V. Panels (a)–(f) correspond to disruption steps 1, 5, 15, 25, 35, and 45, respectively. In each panel, from left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences.

intermediate-degree nodes does not occur abruptly following the disruption of all its constituent nodes but instead, unfolds progressively with the sequential damage to individual nodes (data not shown). Finally, as additional nodes are damaged beyond this threshold leading to fragmentation, intracluster and intercluster synchronization progressively deteriorates, ultimately culminating in the collapse of global network coordination.

As shown in the right column, a distinct pattern emerges in the periphery-to-core scenario. With the low-degree nodes being gradually disrupted, the level of pairwise synchronization between them and the rest of the network gradually decreases, while the remaining nodes maintain a large and cohesive

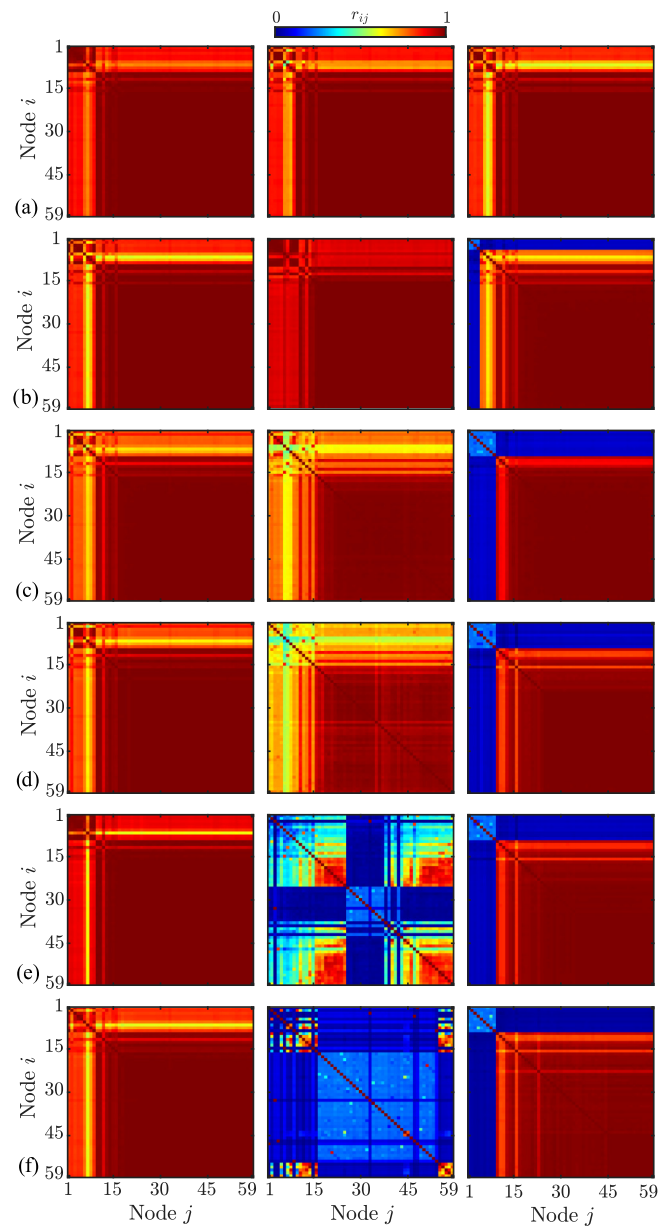


FIG. 11. Pairwise synchronization matrices at  $V_c = 2.7586$  V. Panels (a)–(f) correspond to disruption steps 1, 5, 15, 25, 35, and 45, respectively. In each panel, from left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences.

synchronized cluster. Unlike the core-to-periphery scenario, this cluster size shrinks as more nodes are disrupted and does not fragment into smaller communities until very late-stage damage (data not shown). This observation underscores an important difference in the network's responses to the different disruption scenarios. It reveals that cluster formation is not solely a consequence of node loss, but rather of the strategic disruption of structural bottlenecks (central nodes), whose disruption in a specific condition catalyzes a structural partitioning and a profound functional reorganization of the network. In this case, nodes 25–45 (F2, C8, G2, B6, B8, E6, A7, G3, C5, F3, D6, D6, E2, E3, C7, H2, H3, A6, D7, E7, A4, B2, respectively) retain a relatively higher level of

synchronization throughout the disruption progression compared with the core-to-periphery scenario. Nevertheless, as the disruption progresses, the loss of available structural pathways leads to a steady degradation of network synchrony, ultimately leading to a complete breakdown of network synchrony.

The same analysis was performed for the higher coupling strength, and the results are presented in Fig. 11. While a qualitatively similar pattern of synchronization is seen to emerge, several key differences can be observed. First, synchronization remains higher for the three scenarios, including among peripheral nodes. However, as disruptions accumulate, degradation becomes more abrupt, and the network ultimately loses long-term integrity (data not shown).

Under the core-to-periphery scenario, the region spanning nodes 28–43 (B6, B8, E6, A7, G3, C5, F3, D6, D6, E2, E3, C7, H2, H3, A6, D7, E7, respectively) becomes functionally disconnected from the rest of the network. However, the emerging clusters preserve relatively high synchronization levels both internally and with each other, even among weakly connected nodes. Further disruptions lead to the emergence of smaller clusters consisting of peripheral and highly connected nodes. While a high synchronization persists both within and between these clusters, the remaining nodes are found to be entirely desynchronized. Notably, pairwise synchronization levels between some weakly connected nodes are observed to increase at intermediate stages. This can be observed in Figs. 11(a) and 11(b), which illustrates the transition from the state of no damage to the state where four hub nodes have been disrupted.

In contrast, the periphery-to-core scenario generally reveals more resilience of the network, although the network remains vulnerable to local damage, as evidenced by the abrupt drop in synchronization between the least connected nodes (especially degree-1 nodes) and the rest of the network.

#### 4. Summary

Summing up, the node-level analyses provided substantial information. Disrupting degree-1 nodes causes entropy to drop in distant nodes, uncovering hidden long-range dependencies. Therefore, peripheral nodes are found to be determinant in maintaining local dynamic diversity. Moreover, a delayed degradation of dynamic diversity, persisting after the network collapses, is clearly observed at intermediate coupling. This is not observed for strong coupling, where the collapse of the network almost simultaneously suppresses the nodes' diversity. Furthermore, apart from the sudden drop of entropy observed in the case of strong coupling, the effect of damage on nodes' synchronization is clearly reflected in their entropy. Pairwise synchronizations finally highlighted the early emergence of functional modules (cluster synchronization) through the core-to-periphery scenario, revealing that the emergence of such clusters results from a strategic disruption of nodes with high degree/betweenness centrality.

### C. Spectral analysis and time series

#### 1. Global spectral shifts toward low frequency

The spectral analysis of the network under progressive damage reveals marked alterations in spectral content, as

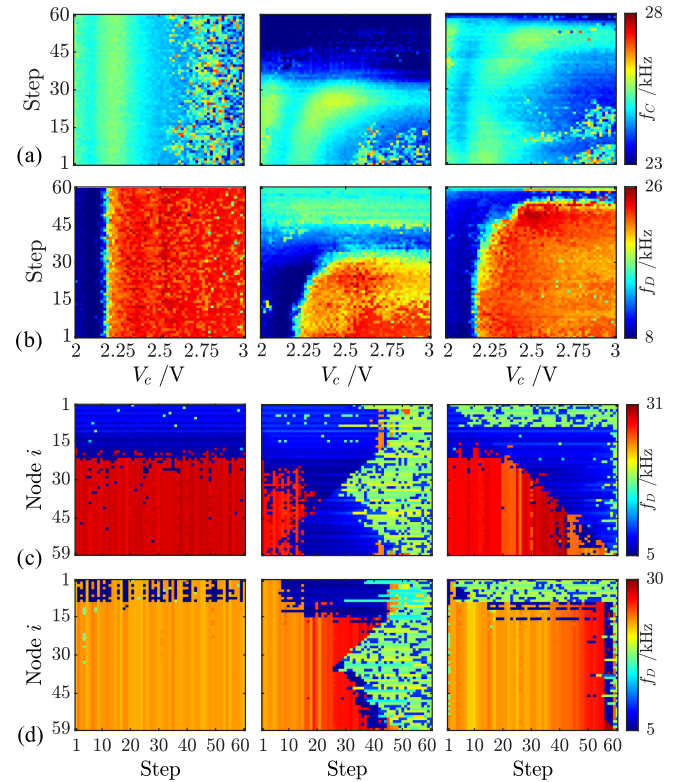


FIG. 12. Global and local spectral metrics based on centroid and dominant frequencies. (a) Average of the centroid frequencies across all nodes as a function of coupling strength and the progression of the disruption. The centroid frequency was computed from the spectra after removing frequency components above 60 kHz, which were considered meaningless due to their extremely low contribution to the power spectrum. (b) Average dominant frequency across all nodes as a function of coupling strength and the progression of the disruption. (c), (d) Nodewise variation of the dominant frequency as a function of the progression of the disruption for  $V_c = 2.2241$  V and  $V_c = 2.27581$  V, respectively. From left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences, respectively.

shown in Fig. 12. Both the centroid and dominant frequencies (averaged across all nodes) were evaluated as functions of coupling strength and the progression of disruption.

As shown in Fig. 12(a), the centroid frequency is sensitive to coupling strength and decreases progressively with damage in the core-to-periphery and the periphery-to-core scenarios. This decrease in the centroid frequency appears earlier for the core-to-periphery scenario, reflecting the sharper dynamic breakdown. In contrast, the single-node disruption scenario shows a relatively stable centroid frequency across steps.

The corresponding distributions of dominant frequencies [Fig. 12(b)] further emphasize the shift in spectral content toward the lower frequency bands. Additionally, these patterns closely mirror the synchronization trends observed in Fig. 7(a). In the single-node and periphery-to-core scenarios, high-frequency components are preserved longer during the disruption progression. In contrast, in the core-to-periphery scenario, the dominant frequency drops rapidly. Such a drop in frequency becomes particularly pronounced at the critical step

where the network collapses, thus reflecting its fragmentation into sparsely connected modules. However, regardless of the coupling strength, a slight rebound of the dominant frequency is observed beyond this transition. This suggests a spectral homogenization linked to the structural disintegration. Indeed, the nodes decouple and oscillate independently. For very low coupling strengths in the core-to-periphery scenario, a small increase in dominant frequency is observed around the disruption of approximately ten nodes. This local peak corresponds to a transient increase in synchronization, as noted previously in Fig. 7(a).

## 2. Node-level spectral differentiation

Figures 12(c) and 12(d) show the evolution of the dominant frequency at the node level for  $V_c = 2.2241$  V and  $V_c = 2.7586$  V, respectively. The trends observed in the synchronization patterns of Figs. 8(a) and 9(a) are also reflected here in the nodes' dominant frequencies as the disruption progresses. Hub nodes are seen to possess a substantially higher dominant frequency compared to peripheral nodes. The dominant frequency is therefore highly representative of the dynamical role of the nodes in the network. However, as coupling increases, the frequency of these peripheral nodes also increases, revealing frequency convergence due to synchronization. Additionally, as disruptions progress the dominant frequency at each node decreases in accordance with the trends in Fig. 12(b), further indicating that the overall slowing down of dynamics accompanies functional degradation.

Figure 13 shows the spectrograms (averaged over the spectral content of the nodes) of the top 10% highest-degree nodes (hubs) and bottom 10% lowest-degree nodes (peripheral) corresponding to the two chosen representative coupling strengths:  $V_c = 2.2241$  V and  $V_c = 2.7586$  V. It provides additional insights that complement and reinforce the entropy findings reported earlier.

Across all disruption scenarios for  $V_c = 2.2241$  V [Fig. 13(a)], hubs and peripheral nodes generally exhibit a broad spectral content in the initial steps, despite notable differences in spectral power. This power is more concentrated in three specific frequency bands in the peripheral nodes, but more distributed for hubs. This profile is almost maintained for the single-node scenario throughout the disruption progression. However, while for the periphery-to-core scenario these peripheral nodes lose their complexity early, they keep elevated complexity longer as disruption progresses in the core-to-periphery scenario. These observations emphasize once more that peripheral nodes contribute more significantly to maintaining dynamic complexity than their limited connectivity might suggest, which is also consistent with the observations made on the evolution of entropy in Fig. 8(b). Notice that the 10% least connected nodes considered are composed essentially of degree-1 nodes, explaining the loss of the spectral content richness from step 10.

At higher coupling strength  $V_c = 2.7586$  V [Fig. 13(b)], the differences in spectral content between hubs and peripheral nodes diminish in the single-node and core-to-periphery scenarios, revealing the convergence in dynamical behavior driven by stronger coupling (synchronization effect). This effect is not directly observed here in the periphery-to-core

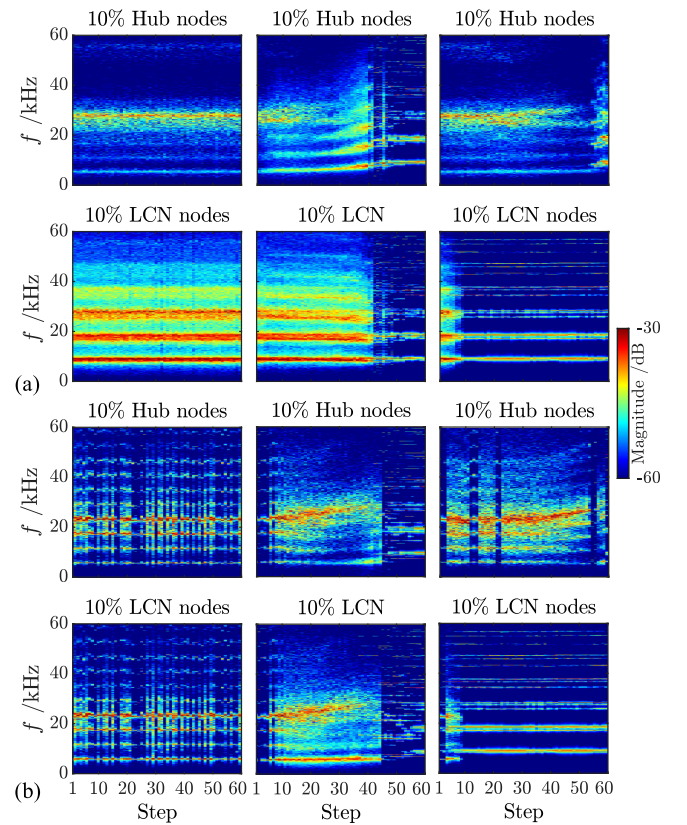


FIG. 13. Average amplitude spectrum from nodes in the top 10% most connected (hubs) and bottom 10% peripheral or least connected nodes (LCN) across the progression of the disruption for (a)  $V_c = 2.2241$  V and (b)  $V_c = 2.7586$  V. From left to right: single-node disruption, core-to-periphery, and periphery-to-core damage sequences, respectively.

scenario since degree-1 nodes are quite isolated after their disruption. Again, the rich spectral content is largely preserved under single-node disruption. However, in the core-to-periphery scenario, the spectral richness deteriorates as soon as a substantial number of hubs are disrupted, thus reflecting the network's functional collapse. Notice that in this strong coupling regime, even the disruption of a single node can lead to marked spectral depletion. This counterintuitive effect observed in single-node disruption as well as in the early and late phases of both the core-to-periphery and periphery-to-core scenarios highlights the increased vulnerability of the network at high coupling strengths, despite synchronization remaining robust. Remarkably, the spectrograms of both core-to-periphery and periphery-to-core scenarios also reveal partial network reorganization, as evidenced by the transient preservation of broad spectral content despite damage. The observed depletion in local spectral content aligns closely with the entropy trends, as shown in Fig. 9(b).

## 3. Temporal signatures of degradation: increase in amplitude and loss of variability

Figure 14 illustrates the time series of selected representative nodes at  $V_c = 2.2241$  V, taken at disruption step 5 (early), step 25 (intermediate), and step 45 (more advanced).

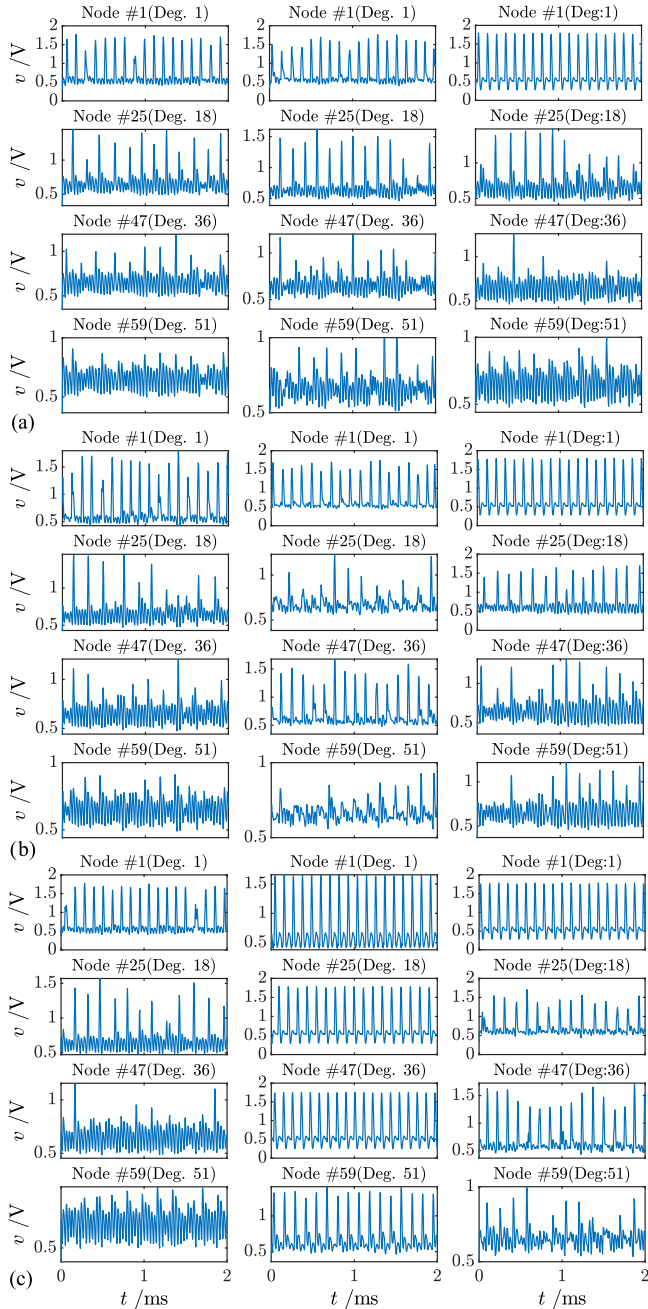


FIG. 14. Time series of some representative nodes for  $V_c = 2.2241$  V. Left to right: single-node, core-to-periphery, and periphery-to-core scenarios, respectively. Panels (a)–(c) are steps 5, 25, 45, respectively.  $v$ , the output voltage across nodes.

The mentioned time series reveal the spiking activity across the network and also highlight the contrasting degradation patterns that are observed across the three damage scenarios. Globally, there is a propensity for low-degree nodes and especially degree-1 node to produce more recurrent and large spikes compared to high-degree nodes. This trend remains consistent across all scenarios and is particularly evident in the single-node disruption case.

During the early disruption stage [Fig. 14(a)], all three scenarios preserve prominent oscillatory spiking with clear

amplitude variability (except the isolated degree-1 node in the periphery-to-core scenario), although signs of dampening begin to appear in the core-to-periphery scenario. At the intermediate stage [step 25, Fig. 14(b)] the core-to-periphery scenario displays markedly reduced waveform amplitude in higher-degree nodes, indicating a loss of power. By step 45 [Fig. 14(c)], all the chosen nodes exhibit periodic spiking dynamics except the most connected node (node 59), which still retains a certain level of variability. The observed periodic spiking activity is indicative of decoupled dynamics and network collapse. In contrast, in the periphery-to-core scenario, nodes retain spiking oscillations with amplitude variance throughout the progression of the disruption, but with a marked decrease in the baseline oscillations. In particular, the selected degree-1 node in this condition effectively maintains its dynamics, exhibiting shorter interspike intervals (more regular spiking) as damage progresses.

#### 4. Summary

In short, spectral signatures provide a clear and complementary fingerprint of neurodegenerative processes that goes beyond synchronization and entropy, namely, the shift of the spectral content toward low-frequency domains. The dominant and centroid frequencies consistently highlight this trend. In particular, the core-to-periphery scenario produces the earliest and most pronounced downward shift in frequencies, accompanied by a rapid loss of spectral richness. In contrast, single-node and periphery-to-core scenarios preserve high-frequency components and spectral richness longer. Unlike intermediate coupling, small structural damage induces pronounced spectral depletion for strong coupling, consistent with entropy analysis. Moreover, node-level spectrograms and time series reveal complex dynamics. Both high-degree and low-degree nodes show richer spectral power before the collapse of the network, except the degree-1 nodes that become isolated in the early stage of the disruption in the periphery-to-core scenario. As a result, low-degree nodes contribute disproportionately to dynamical complexity and show heightened excitability, evidenced by shorter interspike intervals and larger spikes.

#### D. Graph-based metrics from structural and functional connectivity

To characterize the evolution of functional connectivity organization, we computed graph-theoretical measures from the pairwise synchronization matrices obtained at each step of the disruption procedure. As mentioned previously, the percolation threshold was applied to the synchronization matrices to retain weak yet reliable interactions while excluding spurious correlations. This approach allows the capture of the progressive degradation of the network. All subsequent analyses were performed on weighted, thresholded adjacency matrices for functional networks. Additionally, equivalent graph-theoretical measures were also computed directly from the structural adjacency matrices after removing the damaged links, as detailed in the following paragraph.

Figure 15 shows the evolution of four key topological metrics as a function of the coupling strength  $V_c$ , under the three

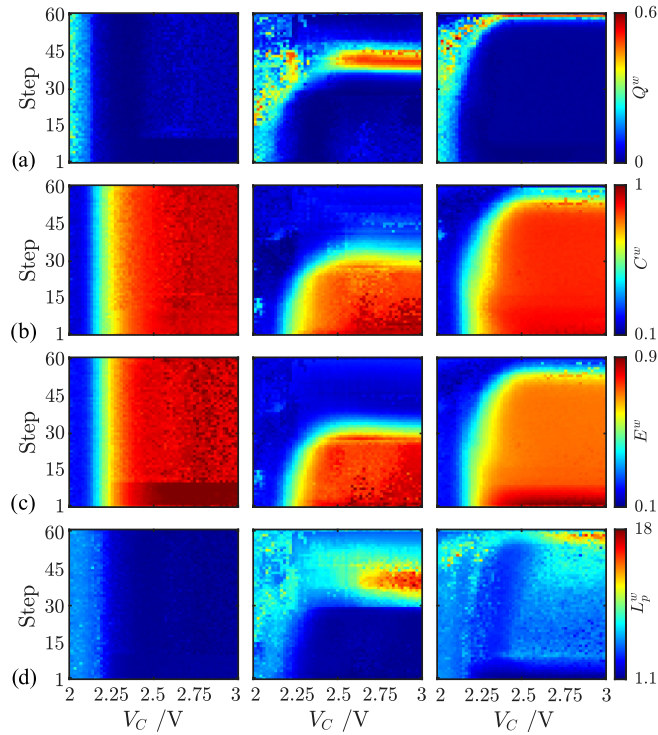


FIG. 15. Graph-based metrics from functional connectivity, derived from thresholded pairwise phase synchronization matrices. Panels (a)–(d) show modularity, clustering coefficient, efficiency, and characteristic path length, respectively. From left to right: the single-node disruption, core-to-periphery, and periphery-to-core scenarios, respectively.

disruption scenarios. These metrics are modularity, clustering coefficient, efficiency, and characteristic path length.

### 1. Functional graph-based metrics

Modularity [Fig. 15(a)] quantifies the degree of community structure in the functional network. At weak coupling strengths, modularity remains relatively high across all scenarios since limited node interactions preserve localized modules. As coupling increases, modularity typically decreases due to the emergence of global synchronization, which blurs community boundaries.

In the single-node disruption scenario, modularity remains relatively insensitive to stepwise changes, especially at intermediate coupling, where it remains particularly low due to the network's flexibility and compensatory capacity. At higher coupling strengths, the network becomes more rigid. The effect at local level of damaging nodes with a relatively high degree slightly increases modular partitioning. However, this effect is absent when low-degree nodes (especially degree-1 nodes) are disrupted.

In the core-to-periphery and periphery-to-core scenarios, modularity steadily increases during early and intermediate stages of disruption, peaking once a substantial number of hub nodes have been disrupted. This indicates fragmentation into weakly synchronized modules. As the damage progresses in the core-to-periphery scenario, modularity declines sharply, reflecting the collapse of modular organization. Consistent

with Fig. 7(a), stronger coupling slows down fragmentation in the early stages. However, beyond a critical level of damage, the coupling effect becomes negligible, and fragmentation occurs more abruptly due to the network's rigidity. However, in the periphery-to-core scenario, it resulted in a more modest increase in modularity since they mainly contribute to local clusters. These findings further highlight the role of hubs in preserving modular integration and confirm that increased modularity can serve as an early indicator of functional collapse.

Figure 15(b) shows the clustering coefficient (averaged across all nodes), which quantifies the degree of local interconnectedness among nodes. Across all disruption scenarios, it shows patterns largely consistent with the synchronization trends in Fig. 7(a), indicating stronger local aggregation among nodes as coupling strength increases. It remains relatively stable under single-node disruption scenario. However, in the core-to-periphery scenario, clustering drops markedly as a large proportion of hubs are disrupted, especially at higher coupling, since hubs are involved in several local node triplets and their disruption breaks numerous local connections. In contrast, in the periphery-to-core scenario, clustering declines more gradually with noticeable reductions only after the hubs are disrupted.

The network global efficiency shown in Fig. 15(c), which here measures the level of integration or coordination between different nodes, increased with coupling strength, reflecting stronger synchrony and enhanced functional integration. The observed trends are, like the clustering coefficient, very similar to the synchronization patterns in Fig. 7(a). In the single-node disruption scenario, efficiency remained stable across damage steps and was particularly high for intermediate and strong coupling strengths. Disruption to degree-1 nodes had little impact since they contribute minimally to long-range connectivity. In contrast, the core-to-periphery scenario led to a progressive and then accelerated decline in efficiency, especially beyond the critical number of disrupted nodes. Since hubs facilitate short paths across the network, their disruption weakens long-range connectivity and disrupts global information flow. In the periphery-to-core scenario, efficiency was largely preserved until a critical number of hubs were affected later in the damage progression, confirming again the central role of hubs in sustaining global communication in the network.

Figure 15(d) finally shows the characteristic path length, the evolution of which can be related to that of efficiency. It decreases with stronger coupling, reflecting enhanced integration (increase in efficiency), and increases with the progression of disruption. In the single-node disruption scenario, the characteristic path length remains constant throughout the disruption progression. In contrast, in the core-to-periphery and periphery-to-core scenarios, the characteristic path length substantially increases with progressive damage, especially under strong coupling, peaking at the transition step where the disruption of central integrators destroys intermodule bridges and severely hampers communication. This inverse relationship with efficiency underscores their complementary roles in capturing global integration and its vulnerability to targeted hub disruption. It should be noted that the evolution of the characteristic path length, which follows a trajectory similar

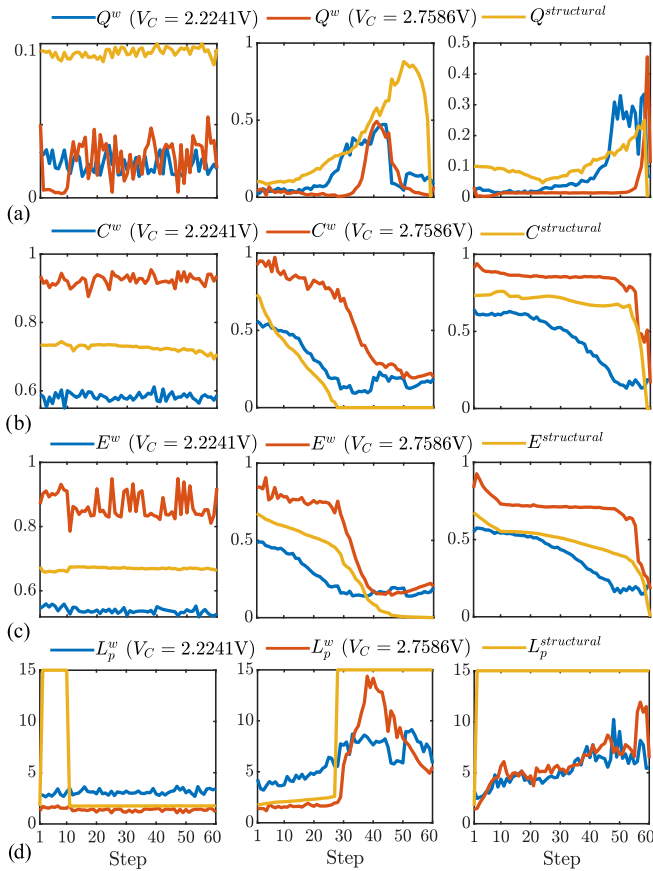


FIG. 16. Graph-based topological indices vs graph-based metrics from functional connectivity at  $V_c = 2.2241$  V and  $V_c = 2.7586$  V. Panels (a)–(d) show modularity, clustering coefficient, efficiency, and characteristic path length, respectively. From left to right: single-node disruption, core-to-periphery, and periphery-to-core scenarios, respectively.

to that of modularity (reaching a maximum before decreasing just as the network begins to collapse) in the periphery-to-core and core-to-periphery scenarios, reflects the homogenization of dynamics within the network.

## 2. Correspondence between structural and functional graph-based metrics

The previous graph metrics (Fig. 15) derived from pairwise synchronization matrices always give information about the network dynamics. However, topological indices of the network under damage can reveal insights into the interplay between topology and synchronization dynamics. Figure 16 illustrates the evolution of graph-theoretic indices derived from both structural connectivity and phase synchronization matrices, across the three disruption scenarios. Functional metrics are considered for two coupling strengths,  $V_c = 2.2241$  V and  $V_c = 2.7586$  V.

In the single-node disruption scenario, both structural and functional metrics fluctuate around a constant value. These fluctuations are more pronounced for functional graph measures, particularly at stronger coupling. For the core-to-periphery scenario, modularity increases monotonically for the structural connectivity, peaking around step 50. Afterward,

it decreases, revealing steady fragmentation of network communities. The functional modularity of the network begins to increase later in the course of the damage progression, then rises rapidly, reaching its maximum at step 40. After that, it declines sharply, approaching zero around step 50. In the periphery-to-core scenario, the structural connectivity exhibits two distinct phases: during the early stages, modularity decreases, and then increases again after the disruption of approximately 25 nodes. In contrast, the functional modularity remains relatively low and stable, and begins to rise later in the progression. Structural and functional measures of clustering coefficient and efficiency show a close correspondence. They remain almost constant with some fluctuation (more pronounced for strong coupling) in functional measures for the single-node disruption scenario, and decrease together, maintaining similar profiles for core-to-periphery and periphery-to-core scenarios. A steep decline is especially observed in the core-to-periphery scenario, where these metrics approach zero in midstage damage. Functional characteristic path length remains nearly constant and low for the single-node disruption scenario and increases progressively with damage in core-to-periphery and periphery-to-core scenarios. The structural characteristic path length follows similar trends but diverges, becoming infinite when degree-1 nodes are disrupted or when the network becomes disconnected. For clarity of representation, infinite values were capped at 15.

Visualizing the evolution of networks under damage provides insight into the interplay between the network's structural integrity and its functional organization. These representations provide a spatiotemporal view of how the structural degradation of the network translates into functional disintegration. Figure 17 shows the progression of structural connectivity (left panel) and the corresponding thresholded synchronization graphs (right panel). The nodes are color coded based on whether they are targeted in the structural graph (gray for the targeted nodes) and on their average pairwise synchronization in the functional graph. In the single-node disruption scenario, structural connectivity remains largely preserved, resulting in uniformly connected graphs with minimal disconnection. Correspondingly, functional graphs retain high synchronization values across most nodes with an emerging localized decrease in synchronization. In the core-to-periphery scenario, structural degradation rapidly affects core connectivity, and the topological backbone becomes fragmented as early as panels (c) and (d). This is clearly reflected in the functional graphs, where the high-synchrony cores visible in the early stages [panels (a) and (b)] progressively lose their cohesion and eventually give rise to isolated and desynchronized node clusters [panels (e)–(g)]. In contrast, in the periphery-to-core scenario, structural connectivity degrades slowly and retains a cohesive backbone longer in the disruption progression. As seen in the synchronization graphs, nodes involved in early damage exhibit decreased average synchronization; however, the core remains highly active and cohesive even into later stages [panels (e) and (f)]. The homogenization of the dynamics in the network at a very late stage of damage, translated by a densely connected functional graph while the structural one is completely disconnected, can also be noticed.

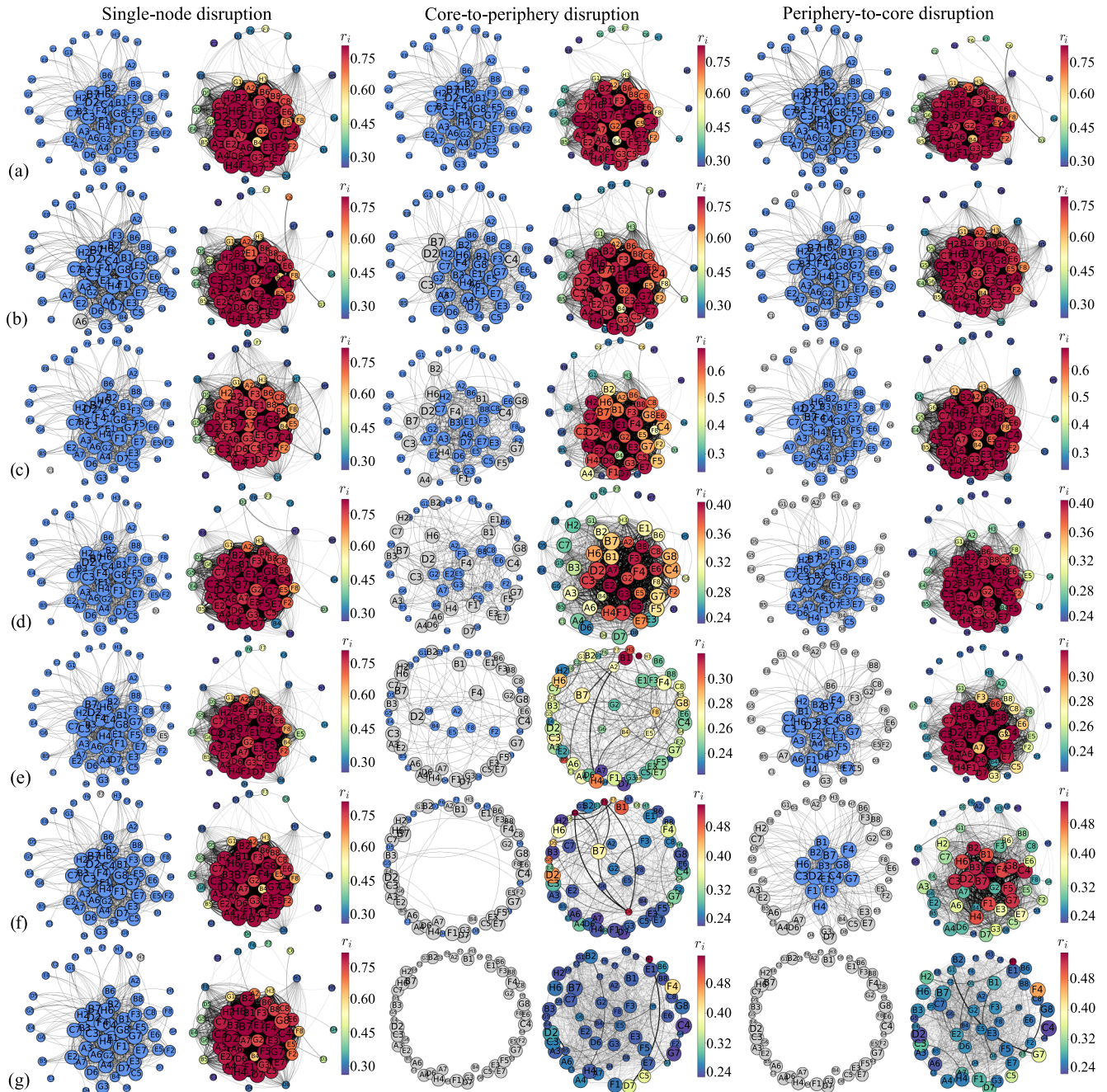


FIG. 17. Visual representation of the structural connectivity matrices and the thresholded functional connectivity matrices derived from the pairwise phase synchronization. This representation allows high-degree nodes to be attracted to the center and low-degree nodes to be repelled at the periphery, for better visualization. First, third, and fifth columns: graph of the network structural connectivity. In both structural and functional connectivity graphs, node size represents the degree centrality. For structural connectivity, color blue encodes the undamaged nodes and color gray the damaged nodes. In the case of functional connectivity, color encodes the average phase synchronization of the nodes. Edge widths are proportional to the pairwise synchronization index. Rows represent from top to bottom, the damage progression, specifically (a) no damage, (b) step 5, (c) step 15, (d) step 25, (e) step 35, (f) step 45, and (g) step 59.

### 3. Summary

Overall, these graph-theoretical analyses demonstrate that modularity increases until it peaks, then decreases just before the network collapses. This observation suggests that modularity may be a key marker of network degradation. Although structural and functional metrics show similar trends,

functional collapse precedes structural degradation. It is especially observed under the targeted attacks on high-degree nodes, which underscores the predictive value of functional connectivity analysis. Furthermore, graph visualization offers a spatial correspondence between structural and functional node centrality for the three damage scenarios. Nodes with

high degree centrality in structural networks also emerge as high-degree nodes in the functional network located near its core. Notably, along the core-to-periphery scenario, this correlation deteriorates sharply, as the targeted disruption of high-degree nodes causes a shift in functional hubs organization within the same spatial regions. Conversely, under the periphery-to-core scenario, the structural-functional alignment of high-degree nodes is maintained for a longer period, indicating that the organization of functional hubs remains resilient as long as the structural core is preserved.

## VI. DISCUSSION

Building on prior work in Ref. [112], the present study adopted an experimental approach to emulate targeted and progressive alteration of a complex network of coupled single-transistor chaotic oscillators whose connectivity scheme was designed from an *in vitro* neuronal culture. Three distinct and systematic damage sequences were applied to the circuit to roughly mimic different pathologies observed in neurodegenerative conditions. The single-node scenario was representative of localized or focal lesions, serving as a baseline for the analyses; the core-to-periphery scenario mimicked the spread of neurodegenerative diseases such as AD, which first affect densely connected regions before disseminating to other areas, and the periphery-to-core scenario emulated the propagation of diseases such as PD and ALS, which mostly originate in specialized modules with reduced connectivity and subsequently extend toward core regions.

The systematic simulations carried out in this work indicated that network topology and coupling strength fundamentally determine the network's ability to maintain synchronization and resilience against localized and progressive damage. Generally, the increase in coupling strength ensures a high level of synchronization across different scenarios. Damaging peripheral nodes resulted in a gradual decline in synchronization, indicating a high resilience to isolated damage. This is consistent with fMRI and DTI studies on patients with early PD and ALS, which demonstrate intact core network organization before the emergence of cognitive symptoms in the very late stages, as a result of cumulative loss involving hubs [124–126]. Damaging hubs did not directly result in the abrupt failure of the network; rather, it was tolerated for multiple successive steps until a critical amount of cumulated damage was reached. The network was able to maintain global synchronization through redundancy while remaining efficient through functional reorganization. This phenomenon may be paralleled by what is observed in mild cognitive impairment in patients with AD, demonstrating how the brain initially uses compensatory mechanisms to deal with the cognitive decline. However, this is followed by a sudden collapse of brain function in later stages of the disease, particularly when key hubs are damaged [49,55,127]. More specifically, only specific resting-state networks such as DMN are selectively disrupted in individuals at risk for AD, which correlates with memory loss.

The coupling strength was identified as a key modulator of resilience and dynamic diversity across the experiments. Intermediate couplings were demonstrated to engender complexity through a delicate balance between global and local

behaviors. Initially, strong couplings resulted in the preservation of coherent behavior in the network across damaging steps. However, this ultimately resulted in dangerous rigidity, which limited functional diversity and exposed the network to abrupt collapse. This interplay is consistent with computational and empirical findings, suggesting that hyperconnectivity, as frequently observed in early disease stages, can be both compensatory and ultimately maladaptive [32,47,55,66,81,128–131]. This coupling strength can be likened to the effective strength of interneuronal communication. The latter integrates synaptic efficacy, transmission reliability, and modulatory gain. Indeed, coupling between neurons is intrinsically heterogeneous and probabilistic, ranging from weak synapses prone to failure to highly reliable or strengthened connections under specific physiological or pathological conditions [132–134]. It should also be noted that modulating the coupling strength in the experimental network induced gradual changes, moving from largely independent chaotic dynamics to coherent activity, via partially synchronized regimes. This spectrum of behaviors qualitatively reflects the coupling-dependent dynamics observed in the brain and is therefore consistent with theoretical and empirical results showing that sufficient effective connectivity is essential for the emergence of large-scale neural synchronization [78,135]. Within this framework, progressive reductions in coupling can be viewed as an abstraction of synaptic weakening, metabolic impairment, or neuromodulatory dysregulation associated with neurodegenerative processes, whereas excessively strong coupling reflects hypersynchronous states that reduce dynamical flexibility [32,47,55,66,128–131,136,137].

Entropy analysis complemented these findings by highlighting a nuanced relationship between network damage, coupling strength, and complexity. A decrease in average entropy was noticed after critical damage steps involving the majority of hubs, suggesting a global decrease of complexity in network dynamics [55,138]. This underscores the role of high-degree nodes as vital integrators that sustain global information flow and oscillations complexity. The disruption of these nodes instigates the progressive loss of these vital functions, a phenomenon consistent with the progression of many neurodegenerative diseases. This may be transposed to neurological observations, which characterize healthy brains as exhibiting high complexity and consider loss of complexity as an indicator of AD onset. A low level of entropy was also observed for strong couplings and a high level of synchronization, revealing the loss of signal diversity across the network. The nonmonotonic variation of entropy across progressive damaging steps suggests the sensitivity of network dynamics to topological changes, especially under strong couplings. Spectral analyses provided an orthogonal perspective on the network's functional state, especially under the core-to-periphery scenario. As damages accumulate, the network oscillations exhibited a progressive shift toward lower frequency bands and a loss of high-frequency components. This phenomenon, often referred to as the “slowing” directly parallels a hallmark signature of some neurodegenerative diseases, where EEG and MEG recordings consistently show a reduction in higher-frequency activity and a corresponding increase in lower-frequency power. This corresponds to a dominance

of slower brain waves, specifically delta (0.5–4 Hz) and theta (4–8 Hz). While these wave types are normally associated with deep sleep and relaxation, their presence during wakefulness is considered a potential indicator of various cognitive or neurological conditions [138–140].

The loss of high-frequency components, in conjunction with the decrease in entropy measures, provides further evidence that slowing and complexity loss in oscillatory modes represent core mechanisms of network decline, especially in a core-to-periphery scenario.

Targeted damaging of high-degree nodes does not always lead to a random loss of network cohesion; instead, the system can fragment into distinct clusters. This principle applies across a wide range of complex systems, from power grids, ecosystems, to the human brain. For instance, the Internet would partition into regional networks if its core routers were to fail, and a power grid could break into self-sufficient islands if a major transmission junction were lost. In social networks, removing key connectors can lead to the formation of isolated “echo chambers.” Similarly, a functional shift toward a more segregated network and modular structures due to the degradation of long-range connections is observed in the AD condition [141,142].

Modularity was then found to be a meaningful indicator of the critical step at which the network collapses, supporting the idea that the increase of modularity may be a red flag before global functional failure [143,144]. This was supported by graph-based analyses, which reveal that modularity increases as the network accumulates damage and peaks before critical steps that cause the network to collapse. Empirical evidence across multiple domains supports such a nonmonotonic pattern of modularity under progressive disruption. In ecological networks, Sheykhal *et al.* [145] observed that the loss in the successive species initially increased modular segregation before its global collapse. Similarly, Shi *et al.* [146] reported a sharp rise in modularity during the 2010 Flash Crash, which was then followed by a decline during recovery. In brain networks, Gratton *et al.* [147] showed that lesions in connector hubs transiently enhanced modular segregation prior to a loss of global integration. These results indicate that modularity often peaks at an intermediate stage of structural degradation, which marks a transition between partial segregation and full collapse.

Furthermore, the trends observed from clustering coefficient and efficiency showed that the loss of hubs undermines local and global communication, thus underscoring the vulnerability of hub-dominated architectures. The loss of alignment between structural and functional hubs as observed under the core-to-periphery scenario emerged as an indicator of network fragility, signaling that the system is in a less optimal and compensatory state that is not sustainable in the long term. In addition, functional network failure often precedes structural breakdown. This suggests that analyzing functional connectivity can provide an early warning of impending structural decline.

This work presents a nonconventional framework integrating a biologically informed structural connectivity with a physically realized network of simple oscillators for analyzing the network response to different damage scenarios with perspectives in neurosciences and engineering. The proposed

approach deviates from traditional methods, such as neural mass models, network diffusion equations [43,148,149], or spread dynamics [150,151], that generally maintain a high level of mathematical abstraction without direct physical embodiment. Moreover, these models are contingent upon numerical environments, which impose inherent limitations, including substantial demands on computational resources, considerable simulation time, high energy consumption, and the risk of numerically induced inaccuracies stemming from the discretization and approximation of the governing differential equations. Even though these established models are biologically grounded and commonly used to simulate brain dynamics across both healthy and various pathological conditions, simpler and more experimental approaches can still reliably capture universal aspects of network dynamics and even reproduce some specific features observed in brain networks under diverse conditions.

In this context, the presence of intrinsic mismatches, component tolerances, and electronic noise, often regarded as imperfections, constitutes important sources of variability that enrich the collective dynamics and give rise to diverse dynamic and synchronization patterns. However, it is essential to emphasize that these factors only introduce variability at the level of individual trajectories and do not qualitatively alter the behaviors observed at the network level. To assess their impact at the network scale, we repeated the full progressive lesion experiment in an independent trial, and almost identical qualitative trends were observed, notably the differential impact of targeted damage on central nodes compared to peripheral damage on network synchronization and measures. Prior experiments on the same network have even demonstrated this aspect [112]. Only one realization was therefore presented in the results for the sake of simplicity.

A preliminary example of such a physical approach was presented in an earlier work, where a network designed as a “toy” model of the DMN was constructed using coupled transistor-based chaotic oscillators [96]. Although that network featured a simple topology and no lesions, it demonstrated how real-world imperfections can generate complex and biologically relevant synchronization patterns, motivating the present framework. Indeed, the proposed framework is physical in nature and consequently not subject to the aforementioned numerical constraints. Furthermore, its analog and parallel processing capabilities allow real-time observation of dynamical changes in response to the progressive topological damage. It is a unique tool for experimentally exploring compensatory mechanisms and the interplay between network topology, synchronization, and dynamics. Although currently focused on neurodegenerative diseases, the presented framework applies to diverse network perturbations. To further support reproducibility of the current work and facilitate independent verification, the complete board design and all recorded time-series data are openly available.

While the current implementation operates at a mesoscopic scale, several of the observed dynamical patterns, in particular, transitions from coherent to incoherent dynamics as damage accumulates, shifts in dynamical complexity, and “slowing” effects are consistent with behaviors reported in computational and empirical studies of complex networks across scales stages [78,80,152,153]. This suggests that the

qualitative trends reported here are not specific to network size. However, the location of critical transitions and the detailed synchronization patterns are expected to depend on network size, density, coupling strength, and topology. For example, more homogeneous networks may exhibit a more gradual loss of synchrony due to redundant pathways, whereas a larger network with similar properties to the network under study will have more densely connected hubs and may display greater initial resilience followed by a more abrupt collapse under targeted attack [25].

A major limitation of the proposed framework resides in the inability of the used platform to achieve a node-to-node correspondence between anatomical brain regions and board-level oscillator nodes, which is fundamental to emulate a more realistic spread of different neurodegenerative diseases across brain networks. This refers to the sequential staging, describing how specific misfolded proteins aggregate into pathogenic assemblies exhibiting prionlike properties [154]. This mechanism is now recognized, at least partially, in major neurodegenerative diseases, including AD (amyloid and tau), PD ( $\alpha$ -synuclein), FTD, and ALS (TDP-43) [155]. However, this issue could be addressed in future work by considering an experimental platform derived from the human connectome.

Finally, the present framework should be viewed as a potentially complementary approach to existing computational and biological models of brain dynamics that occupies an intermediate niche between *in silico* modeling and biological experimentation, offering a synthetic yet experimentally accessible test bed for probing principles relevant to network dysfunction in neurodegenerative diseases.

Looking beyond the topologically driven damage sequences adopted in the present study, future works aim to integrate pathology-informed damage rules to better track the disease course. The adoption of high-density CMOS technology could enable large-scale connectome simulations, allowing the model to emulate full brain disease trajectory-

ries like Braak staging with a node-to-node correspondence while maintaining ultralow power consumption. In the near future, such platforms could advance our understanding of neurodegenerative diseases by integrating crucial pathological phenomena, such as cell and synapse loss, with existing staging methods [156]. Adopting a network analysis-rooted grading approach, based on a physical system, would allow for a more nuanced disease description, combining the topographical spread (staging) with a qualitative assessment of the disease's characteristics (grading), similar to the integrated staging and grading system standard in oncology. More importantly, these physical platforms represent a promising advance in the field of experimental network science, enabling connectivity-based interventions such as noninvasive brain stimulation to be optimized in a physical system.

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## DATA AVAILABILITY

The data that support the findings of this article are openly available [157].

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- [1] S. H. Strogatz, Exploring complex networks, *Nature (London)* **410**, 268 (2001).
  - [2] M. E. Newman, The structure and function of complex networks, *SIAM Rev.* **45**, 167 (2003).
  - [3] P. Mariolis, Interlocking directorates and control of corporations: The theory of bank control, *Soc. Sci. Q.* **56**, 425 (1975).
  - [4] A. Rapoport and W. J. Horvath, A study of a large sociogram, *Behav. Sci.* **6**, 279 (1961).
  - [5] J. Scott, Social network analysis: Developments, advances, and prospects, *Soc. Network Anal. Min.* **1**, 21 (2011).
  - [6] B. A. Huberman, *The Laws of the Web: Patterns in the Ecology of Information* (MIT Press, Cambridge, MA, 2001).
  - [7] D. J. Watts, *Small Worlds: The Dynamics of Networks Between Order and Randomness* (Princeton University Press, Princeton, NJ, 1999).
  - [8] L. Zhou and Z. Chen, Measuring the performance of airport resilience to severe weather events, *Transp. Res. Part D: Transp. Environ.* **83**, 102362 (2020).
  - [9] O. Sporns, Network analysis, complexity, and brain function, *Complexity* **8**, 56 (2002).
  - [10] I. Farkas, H. Jeong, T. Vicsek, A.-L. Barabási, and Z. Oltvai, The topology of the transcription regulatory network in the yeast, *Saccharomyces cerevisiae*, *Physica A* **318**, 601 (2003).
  - [11] B.-L. Dou, X.-G. Wang, and S.-Y. Zhang, Robustness of networks against cascading failures, *Physica A* **389**, 2310 (2010).
  - [12] L. Xu and Y. Kajikawa, An integrated framework for resilience research: A systematic review based on citation network analysis, *Sustainability Sci.* **13**, 235 (2018).
  - [13] P. Holme, B. J. Kim, C. N. Yoon, and S. K. Han, Attack vulnerability of complex networks, *Phys. Rev. E* **65**, 056109 (2002).
  - [14] A. De Montis, A. Ganciu, M. Cabras, A. Bardi, V. Peddion, S. Caschili, P. Massa, C. Cocco, and M. Mulas, Resilient ecological networks: A comparative approach, *Land Use Policy* **89**, 104207 (2019).
  - [15] S. Shao, X. Huang, H. E. Stanley, and S. Havlin, Percolation of localized attack on complex networks, *New J. Phys.* **17**, 023049 (2015).
  - [16] P. Erdős, Graph theory and probability, *Can. J. Math.* **11**, 34 (1959).

- [17] D. J. Watts and S. H. Strogatz, Collective dynamics of “small-world” networks, *Nature (London)* **393**, 440 (1998).
- [18] R. Albert and A.-L. Barabási, Statistical mechanics of complex networks, *Rev. Mod. Phys.* **74**, 47 (2002).
- [19] D. S. Bassett and E. D. Bullmore, Small-world brain networks, *Neuroscientist* **12**, 512 (2006).
- [20] S. V. Buldyrev, R. Parshani, G. Paul, H. E. Stanley, and S. Havlin, Catastrophic cascade of failures in interdependent networks, *Nature (London)* **464**, 1025 (2010).
- [21] R. Guimera, S. Mossa, A. Turtshi, and L. A. N. Amaral, The worldwide air transportation network: Anomalous centrality, community structure, and cities’ global roles, *Proc. Natl. Acad. Sci. USA* **102**, 7794 (2005).
- [22] M. P. van den Heuvel, C. J. Stam, M. Boersma, and H. E. H. Pol, Small-world and scale-free organization of voxel-based resting-state functional connectivity in the human brain, *NeuroImage* **43**, 528 (2008).
- [23] E. Bullmore and O. Sporns, Complex brain networks: Graph theoretical analysis of structural and functional systems, *Nat. Rev. Neurosci.* **10**, 186 (2009).
- [24] M. D. Humphries and K. Gurney, Network “small-worldness”: A quantitative method for determining canonical network equivalence, *PLoS One* **3**, e0002051 (2008).
- [25] R. Albert, H. Jeong, and A.-L. Barabási, Error and attack tolerance of complex networks, *Nature (London)* **406**, 378 (2000).
- [26] M. Pirani, A. Mitra, and S. Sundaram, A survey of graph-theoretic approaches for analyzing the resilience of networked control systems, *arXiv:2205.12498*.
- [27] L. Cavallaro, S. Costantini, P. De Meo, A. Liotta, and G. Stilo, Network connectivity under a probabilistic node failure model, *IEEE Trans. Network Sci. Eng.* **9**, 2463 (2022).
- [28] L. Cavallaro, P. De Meo, G. Fiumara, and A. Liotta, On the sensitivity of centrality metrics, *PLoS One* **19**, e0299255 (2024).
- [29] T. Nishikawa and A. E. Motter, Synchronization is optimal in nondiagonalizable networks, *Phys. Rev. E* **73**, 065106(R) (2006).
- [30] S. Boccaletti, V. Latora, Y. Moreno, M. Chavez, and D.-U. Hwang, Complex networks: Structure and dynamics, *Phys. Rep.* **424**, 175 (2006).
- [31] J. D. Hart, Y. Zhang, R. Roy, and A. E. Motter, Topological control of synchronization patterns: Trading symmetry for stability, *Phys. Rev. Lett.* **122**, 058301 (2019).
- [32] C. J. Stam, Modern network science of neurological disorders, *Nat. Rev. Neurosci.* **15**, 683 (2014).
- [33] D. S. Bassett and O. Sporns, Network neuroscience, *Nat. Neurosci.* **20**, 353 (2017).
- [34] D. Papo and J. M. Buldú, Does the brain behave like a (complex) network? I. Dynamics, *Phys. Life Rev.* **48**, 47 (2024).
- [35] H. Geng, P. Xu, A. Aleman, S. Qin, and Y.-J. Luo, Dynamic organization of large-scale functional brain networks supports interactions between emotion and executive control, *Neurosci. Bull.* **40**, 981 (2024).
- [36] S. B. Laughlin and T. J. Sejnowski, Communication in neuronal networks, *Science* **301**, 1870 (2003).
- [37] O. Sporns, D. R. Chialvo, M. Kaiser, and C. C. Hilgetag, Organization, development and function of complex brain networks, *Trends Cognit. Sci.* **8**, 418 (2004).
- [38] M. P. Van Den Heuvel and O. Sporns, Rich-club organization of the human connectome, *J. Neurosci.* **31**, 15775 (2011).
- [39] M. P. Van den Heuvel and O. Sporns, Network hubs in the human brain, *Trends Cognit. Sci.* **17**, 683 (2013).
- [40] A. Fornito, A. Zalesky, and E. Bullmore, *Fundamentals of Brain Network Analysis* (Academic Press, San Diego, CA, 2016).
- [41] C. J. Stam, W. De Haan, A. B. F. J. Daffertshofer, B. F. Jones, I. Manshanden, A.-M. van Cappellen van Walsum, T. Montez, J. P. A. Verbunt, J. C. De Munck, B. W. Van Dijk, *et al.*, Graph theoretical analysis of magnetoencephalographic functional connectivity in Alzheimer’s disease, *Brain* **132**, 213 (2009).
- [42] B. M. Tijms, A. M. Wink, W. De Haan, W. M. van der Flier, C. J. Stam, P. Scheltens, and F. Barkhof, Alzheimer’s disease: Connecting findings from graph theoretical studies of brain networks, *Neurobiol. Aging* **34**, 2023 (2013).
- [43] A. Raj, A. Kuceyeski, and M. Weiner, A network diffusion model of disease progression in dementia, *Neuron* **73**, 1204 (2012).
- [44] A. Fornito, A. Zalesky, and M. Breakspear, The connectomics of brain disorders, *Nat. Rev. Neurosci.* **16**, 159 (2015).
- [45] F. Agosta, M. Weiler, and M. Filippi, Propagation of pathology through brain networks in neurodegenerative diseases: From molecules to clinical phenotypes, *CNS Neurosci. Ther.* **21**, 754 (2015).
- [46] P. McColgan, K. K. Seunarine, A. Razi, J. H. Cole, S. Gregory, A. Durr, R. A. C. Roos, J. C. Stout, B. Landwehrmeyer, R. I. Scallan, *et al.*, Selective vulnerability of rich club brain regions is an organizational principle of structural connectivity loss in huntington’s disease, *Brain* **138**, 3327 (2015).
- [47] L. Pini, M. Pievani, M. Bocchetta, D. Altomare, P. Bosco, E. Cavedo, S. Galluzzi, M. Marizzoni, and G. B. Frisoni, Brain atrophy in Alzheimer’s disease and aging, *Ageing Res. Rev.* **30**, 25 (2016).
- [48] J. W. Vogel, N. Coriveau-Lecavalier, N. Franzmeier, J. B. Pereira, J. A. Brown, A. Maass, H. Botha, W. W. Seeley, D. S. Bassett, D. T. Jones, *et al.*, Connectome-based modelling of neurodegenerative diseases: Towards precision medicine and mechanistic insight, *Nat. Rev. Neurosci.* **24**, 620 (2023).
- [49] C. J. Stam, Hub overload and failure as a final common pathway in neurological brain network disorders, *Network Neurosci.* **8**, 1 (2024).
- [50] E. Englund, A. Brun, and C. Alling, White matter changes in dementia of Alzheimer’s type: Biochemical and neuropathological correlates, *Brain* **111**, 1425 (1988).
- [51] N. Villain, B. Desgranges, F. Viader, V. De La Sayette, F. Mézenge, B. Landeau, J.-C. Baron, F. Eustache, and G. Chételat, Relationships between hippocampal atrophy, white matter disruption, and gray matter hypometabolism in Alzheimer’s disease, *J. Neurosci.* **28**, 6174 (2008).
- [52] R. L. Buckner, J. Sepulcre, T. Talukdar, F. M. Krienen, H. Liu, T. Hedden, J. R. Andrews-Hanna, R. A. Sperling, and K. A. Johnson, Cortical hubs revealed by intrinsic functional connectivity: Mapping, assessment of stability, and relation to Alzheimer’s disease, *J. Neurosci.* **29**, 1860 (2009).
- [53] B. Kuczynski, E. Targan, C. Madison, M. Weiner, Y. Zhang, B. Reed, H. C. Chui, and W. Jagust, White matter integrity

- and cortical metabolic associations in aging and dementia, *Alzheimer's Dementia* **6**, 54 (2010).
- [54] J. Zhou, E. D. Gennatas, J. H. Kramer, B. L. Miller, and W. W. Seeley, Predicting regional neurodegeneration from the healthy brain functional connectome, *Neuron* **73**, 1216 (2012).
- [55] N. A. Crossley, A. Mechelli, J. Scott, F. Carletti, P. T. Fox, P. McGuire, and E. T. Bullmore, The hubs of the human connectome are generally implicated in the anatomy of brain disorders, *Brain* **137**, 2382 (2014).
- [56] S. Villeneuve, G. D. Rabinovici, B. I. Cohn-Sheehy, C. Madison, N. Ayakta, P. M. Ghosh, R. La Joie, S. K. Arthur-Bentil, J. W. Vogel, S. M. Marks, *et al.*, Existing pittsburgh compound-b positron emission tomography thresholds are too high: Statistical and pathological evaluation, *Brain* **138**, 2020 (2015).
- [57] S. Palmqvist, M. Schöll, O. Strandberg, N. Mattsson, E. Stomrud, H. Zetterberg, K. Blennow, S. Landau, W. Jagust, and O. Hansson, Earliest accumulation of  $\beta$ -amyloid occurs within the default-mode network and concurrently affects brain connectivity, *Nat. Commun.* **8**, 1214 (2017).
- [58] M. P. Van Den Heuvel, R. S. Kahn, J. Goñi, and O. Sporns, High-cost, high-capacity backbone for global brain communication, *Proc. Natl. Acad. Sci. USA* **109**, 11372 (2012).
- [59] D. Tomasi, G.-J. Wang, and N. D. Volkow, Energetic cost of brain functional connectivity, *Proc. Natl. Acad. Sci. USA* **110**, 13642 (2013).
- [60] N. A. Crossley, A. Mechelli, P. E. Vértes, T. T. Winton-Brown, A. X. Patel, C. E. Ginestet, P. McGuire, and E. T. Bullmore, Cognitive relevance of the community structure of the human brain functional coactivation network, *Proc. Natl. Acad. Sci. USA* **110**, 11583 (2013).
- [61] P. M. Thompson, M. S. Mega, R. P. Woods, C. I. Zoumalan, C. J. Lindshield, R. E. Blanton, J. Moussai, C. J. Holmes, J. L. Cummings, and A. W. Toga, Cortical change in Alzheimer's disease detected with a disease-specific population-based brain atlas, *Cereb. Cortex* **11**, 1 (2001).
- [62] P. M. Thompson, K. M. Hayashi, G. De Zubicaray, A. L. Janke, S. E. Rose, J. Semple, D. Herman, M. S. Hong, S. S. Dittmer, D. M. Doddrell, *et al.*, Dynamics of gray matter loss in Alzheimer's disease, *J. Neurosci.* **23**, 994 (2003).
- [63] P. Hagmann, L. Cammoun, X. Gigandet, R. Meuli, C. J. Honey, V. J. Wedeen, and O. Sporns, Mapping the structural core of human cerebral cortex, *PLoS Biol.* **6**, e159 (2008).
- [64] P. Vitali, R. Migliaccio, F. Agosta, H. J. Rosen, and M. D. Geschwind, Neuroimaging in dementia, in *Seminars in Neurology* (Thieme Medical Publishers, New York, NY, 2008), Vol. 28, pp. 467–483.
- [65] M. P. Van den Heuvel and O. Sporns, An anatomical substrate for integration among functional networks in human cortex, *J. Neurosci.* **33**, 14489 (2013).
- [66] S. Jin, J. Wang, and Y. He, The brain network hub degeneration in Alzheimer's disease, *Biophys. Rep.* **10**, 213 (2024).
- [67] J. Alstott, M. Breakspear, P. Hagmann, L. Cammoun, and O. Sporns, Modeling the impact of lesions in the human brain, *PLoS Comput. Biol.* **5**, e1000408 (2009).
- [68] A. Arenas, A. Díaz-Guilera, J. Kurths, Y. Moreno, and C. Zhou, Synchronization in complex networks, *Phys. Rep.* **469**, 93 (2008).
- [69] R. FitzHugh, Impulses and physiological states in theoretical models of nerve membrane, *Biophys. J.* **1**, 445 (1961).
- [70] J. L. Hindmarsh and R. M. Rose, A model of neuronal bursting using three coupled first order differential equations, *Proc. R. Soc. London Ser. B* **221**, 87 (1984).
- [71] E. M. Izhikevich, Simple model of spiking neurons, *IEEE Trans. Neural Networks* **14**, 1569 (2003).
- [72] H. R. Wilson and J. D. Cowan, Excitatory and inhibitory interactions in localized populations of model neurons, *Biophys. J.* **12**, 1 (1972).
- [73] M. Koenigsberg and L. M. Freeman, Multinuclide evaluation of hepatic mass lesions, *CRC Crit. Rev. Clin. Radiol. Nucl. Med.* **6**, 113 (1975).
- [74] B. H. Jansen and V. G. Rit, Electroencephalogram and visual evoked potential generation in a mathematical model of coupled cortical columns, *Biol. Cybern.* **73**, 357 (1995).
- [75] F. Wendling, F. Bartolomei, J. J. Bellanger, and P. Chauvel, Epileptic fast activity can be explained by a model of impaired gabaergic dendritic inhibition, *Eur. J. Neurosci.* **15**, 1499 (2002).
- [76] Y. Kuramoto, Self-entrainment of a population of coupled non-linear oscillators, in *International Symposium on Mathematical Problems in Theoretical Physics: January 23–29, 1975, Kyoto University, Kyoto, Japan* (Springer, Berlin, Heidelberg, 1975), pp. 420–422.
- [77] D. Golomb, D. Hansel, B. Shraiman, and H. Sompolinsky, Clustering in globally coupled phase oscillators, *Phys. Rev. A* **45**, 3516 (1992).
- [78] M. Breakspear, S. Heitmann, and A. Daffertshofer, Generative models of cortical oscillations: Neurobiological implications of the kuramoto model, *Front. Hum. Neurosci.* **4**, 190 (2010).
- [79] R. Schmidt, K. J. LaFleur, M. A. de Reus, L. H. van den Berg, and M. P. van den Heuvel, Kuramoto model simulation of neural hubs and dynamic synchrony in the human cerebral connectome, *BMC Neurosci.* **16**, 54 (2015).
- [80] G. Deco, V. K. Jirsa, and A. R. McIntosh, Emerging concepts for the dynamical organization of resting-state activity in the brain, *Nat. Rev. Neurosci.* **12**, 43 (2011).
- [81] L. Minati, G. Varotto, L. D'Incerti, F. Panzica, and D. Chan, From brain topography to brain topology: Relevance of graph theory to functional neuroscience, *Neuroreport* **24**, 536 (2013).
- [82] V. M. Saenger, J. Kahan, T. Foltynie, K. Friston, T. Z. Aziz, A. L. Green, T. J. van Hartevelt, J. Cabral, A. B. A. Stevner, H. M. Fernandes, *et al.*, Uncovering the underlying mechanisms and whole-brain dynamics of deep brain stimulation for parkinson's disease, *Sci. Rep.* **7**, 9882 (2017).
- [83] P. Ritter, M. Schirner, A. R. McIntosh, and V. K. Jirsa, The virtual brain integrates computational modeling and multimodal neuroimaging, *Brain Connect.* **3**, 121 (2013).
- [84] T. Proix, F. Bartolomei, M. Guye, and V. K. Jirsa, Individual brain structure and modelling predict seizure propagation, *Brain* **140**, 641 (2017).
- [85] Y. Sanz Perl, H. Bocaccio, C. Pallavicini, I. Pérez-Ipiña, S. Laureys, H. Laufs, M. Kringelbach, G. Deco, and E. Tagliazucchi, Nonequilibrium brain dynamics as a signature of consciousness, *Phys. Rev. E* **104**, 014411 (2021).
- [86] C. Lesuisse and L. J. Martin, Long-term culture of mouse cortical neurons as a model for neuronal development, aging, and death, *J. Neurobiol.* **51**, 9 (2002).
- [87] G. Quadrato, J. Brown, and P. Arlotta, The promises and challenges of human brain organoids as models of neuropsychiatric disease, *Nat. Med.* **22**, 1220 (2016).

- [88] J. Kim, B. K. Koo, and J. A. Knoblich, Human organoids: Model systems for human biology and medicine, *Nat. Rev. Mol. Cell Biol.* **21**, 571 (2020).
- [89] M. Rubinov and O. Sporns, Complex network measures of brain connectivity: Uses and interpretations, *NeuroImage* **52**, 1059 (2010).
- [90] L. M. Pecora and T. L. Carroll, Synchronization in chaotic systems, *Phys. Rev. Lett.* **64**, 821 (1990).
- [91] S. H. Strogatz and I. Stewart, Coupled oscillators and biological synchronization, *Sci. Am.* **269**, 102 (1993).
- [92] T. L. Carroll and L. M. Pecora, *Synchronizing chaotic circuits, Nonlinear Dynamics in Circuits* (World Scientific, Singapore, 1995), pp. 215–248.
- [93] J. L. P. Velazquez, Brain research: A perspective from the coupled oscillators field, *NeuroQuantology* **4**, 55 (2006).
- [94] L. Minati, Experimental synchronization of chaos in a large ring of mutually coupled single-transistor oscillators: Phase, amplitude, and clustering effects, *Chaos* **24**, 043108 (2014).
- [95] L. Minati, Remote synchronization of amplitudes across an experimental ring of non-linear oscillators, *Chaos* **25**, 123107 (2015).
- [96] L. Minati, P. Chiesa, D. Tabarelli, L. D’Incerti, and J. Jovicich, Synchronization, non-linear dynamics and low-frequency fluctuations: Analogy between spontaneous brain activity and networked single-transistor chaotic oscillators, *Chaos* **25**, 033107 (2015).
- [97] B. Cao, Y.-F. Wang, L. Wang, Y.-Z. Yu, and X.-G. Wang, Cluster synchronization in complex network of coupled chaotic circuits: An experimental study, *Front. Phys.* **13**, 130505 (2018).
- [98] L. Minati, H. Ito, A. Perinelli, L. Ricci, L. Faes, N. Yoshimura, Y. Koike, and M. Frasca, Connectivity influences on non-linear dynamics in weakly-synchronized networks: Insights from rössler systems, electronic chaotic oscillators, model and biological neurons, *IEEE Access* **7**, 174793 (2019).
- [99] R. Meucci, F. Salvadori, M. V. Ivanchenko, K. A. Naimee, C. Zhou, F. T. Arecchi, S. Boccaletti, and J. Kurths, Synchronization of spontaneous bursting in a CO<sub>2</sub> laser, *Phys. Rev. E* **74**, 066207 (2006).
- [100] A. M. Hagerstrom, T. E. Murphy, R. Roy, P. Hövel, I. Omelchenko, and E. Schöll, Experimental observation of chimeras in coupled-map lattices, *Nat. Phys.* **8**, 658 (2012).
- [101] J. D. Hart, K. Bansal, T. E. Murphy, and R. Roy, Experimental observation of chimera and cluster states in a minimal globally coupled network, *Chaos* **26**, 094801 (2016).
- [102] V. Fernandez-Gonzalez, S. Echeverría-Alar, J. Vergara, P. I. Hidalgo, and M. G. Clerc, Topological transition between disordered patterns through heating rate-induced defect emergence, *Chaos, Solitons & Fractals* **180**, 114508 (2024).
- [103] M. Nixon, M. Friedman, E. Ronen, A. A. Friesem, N. Davidson, and I. Kanter, Synchronized cluster formation in coupled laser networks, *Phys. Rev. Lett.* **106**, 223901 (2011).
- [104] M. Nixon, M. Friedman, E. Ronen, A. A. Friesem, N. Davidson, and I. Kanter, Controlling synchronization in large laser networks, *Phys. Rev. Lett.* **108**, 214101 (2012).
- [105] J. D. Hart, L. Larger, T. E. Murphy, and R. Roy, Delayed dynamical systems: Networks, chimeras and reservoir computing, *Philos. Trans. R. Soc. A* **377**, 20180123 (2019).
- [106] T. Kapitaniak, P. Kuzma, J. Wojewoda, K. Czołczynski, and Y. Maistrenko, Imperfect chimera states for coupled pendula, *Sci. Rep.* **4**, 6379 (2014).
- [107] D. Dudkowski, K. Czołczyński, and T. Kapitaniak, Traveling chimera states for coupled pendula, *Nonlinear Dyn.* **95**, 1859 (2019).
- [108] I. Z. Kiss, Y. Zhai, and J. L. Hudson, Emerging coherence in a population of chemical oscillators, *Science* **296**, 1676 (2002).
- [109] D. Mersing, S. A. Tyler, B. Ponboonjaroenchai, M. R. Tinsley, and K. Showalter, Novel modes of synchronization in star networks of coupled chemical oscillators, *Chaos* **31**, 093127 (2021).
- [110] L. V. Gambuzza, A. Buscarino, S. Chessa, L. Fortuna, R. Meucci, and M. Frasca, Experimental investigation of chimera states with quiescent and synchronous domains in coupled electronic oscillators, *Phys. Rev. E* **90**, 032905 (2014).
- [111] P. D. K. Kuate, H. Ito, J. T. Fossi, M. Zhao, T. F. Fozin, H. B. Fotsin, P. A. Valdes-Sosa, S. Boccaletti, and L. Minati, From connectome to silicon: A biologically-inspired complex network of CMOS chaotic oscillators for analog brain emulation, *Nonlinear Dyn.* **113**, 20227 (2025).
- [112] L. Minati, L. Sparacino, J. V. N. Tegnitsap, M. Zhao, F. Fang, G. Mijatovic, Y. Antonacci, P. A. Valdes-Sosa, H. Ito, M. Frasca, *et al.*, Spontaneous dynamical differentiation in an experimental network of single-transistor chaotic oscillators modeling a biological neuronal culture, *Chaos, Solitons & Fractals* **200**, 117111 (2025).
- [113] D. A. Wagenaar, J. Pine, and S. M. Potter, An extremely rich repertoire of bursting patterns during the development of cortical cultures, *BMC Neurosci.* **7**, 11 (2006).
- [114] P. Erdős and A. Rényi, On random graphs i, *Publ. Math. Debr.* **6**, 290 (1959).
- [115] J. C. Sprott and W. J.-C. Thio, *Elegant Circuits: Simple Chaotic Oscillators* (World Scientific, Singapore, 2022).
- [116] L. Minati, G. Innocenti, G. Mijatovic, H. Ito, and M. Frasca, Mechanisms of chaos generation in an atypical single-transistor oscillator, *Chaos, Solitons & Fractals* **157**, 111878 (2022).
- [117] L. Minati, L. Sparacino, L. Faes, H. Ito, C. Li, P. A. Valdes-Sosa, M. Frasca, and S. Boccaletti, Chaotic dynamics and synchronization under tripartite couplings: Analyses and experiments using single-transistor oscillators as metaphors of neural dynamics, *Chaos, Solitons & Fractals* **189**, 115567 (2024).
- [118] M. R. Brier, J. B. Thomas, and B. M. Ances, Network dysfunction in Alzheimer’s disease: Refining the disconnection hypothesis, *Brain Connect.* **4**, 299 (2014).
- [119] S. Boccaletti, J. Kurths, G. Osipov, D. L. Valladares, and C. S. Zhou, The synchronization of chaotic systems, *Phys. Rep.* **366**, 1 (2002).
- [120] C. Bandt and B. Pompe, Permutation entropy: A natural complexity measure for time series, *Phys. Rev. Lett.* **88**, 174102 (2002).
- [121] V. A. Unakafova and K. Keller, Efficiently measuring complexity on the basis of real-world data, *Entropy* **15**, 4392 (2013).
- [122] K. Pearson, Contributions to the mathematical theory of evolution, *Philos. Trans. R. Soc. London A* **185**, 71 (1894).
- [123] E. A. Leicht and M. E. J. Newman, Community structure in directed networks, *Phys. Rev. Lett.* **100**, 118703 (2008).

- [124] H. Braak, K. Del Tredici, U. Rüb, R. A. De Vos, E. N. J. Steur, and E. Braak, Staging of brain pathology related to sporadic parkinson's disease, *Neurobiol. Aging* **24**, 197 (2003).
- [125] F. Agosta, P. Valsasina, M. Absinta, N. Riva, S. Sala, A. Prella, M. Copetti, M. Comola, G. Comi, and M. Filippi, Sensorimotor functional connectivity changes in amyotrophic lateral sclerosis, *Cereb. Cortex* **21**, 2291 (2011).
- [126] N. Shu, Y. Duan, M. Xia, M. M. Schoonheim, J. Huang, Z. Ren, Z. Sun, J. Ye, H. Dong, F.-D. Shi, *et al.*, Disrupted topological organization of structural and functional brain connectomes in clinically isolated syndrome and multiple sclerosis, *Sci. Rep.* **6**, 29383 (2016).
- [127] W. W. Seeley, R. K. Crawford, J. Zhou, B. L. Miller, and M. D. Greicius, Neurodegenerative diseases target large-scale human brain networks, *Neuron* **62**, 42 (2009).
- [128] K. Abuhassan, D. Coyle, A. Belatreche, and L. Maguire, Compensating for synaptic loss in Alzheimer's disease, *J. Comput. Neurosci.* **36**, 19 (2014).
- [129] R. Cabeza, M. Albert, S. Belleville, F. I. Craik, A. Duarte, C. L. Grady, U. Lindenberger, L. Nyberg, D. C. Park, P. A. Reuter-Lorenz, *et al.*, Maintenance, reserve and compensation: The cognitive neuroscience of healthy ageing, *Nat. Rev. Neurosci.* **19**, 701 (2018).
- [130] I. Aganj, A. Frau-Pascual, J. E. Iglesias, A. Yendiki, J. C. Augustinack, D. H. Salat, and B. Fischl, Compensatory brain connection discovery in Alzheimer's disease, in *2020 IEEE 17th International Symposium on Biomedical Imaging (ISBI)* (IEEE, Piscataway, NJ, 2020), pp. 283–287.
- [131] P. Ranasinghe and M. S. Mapa, Functional connectivity and cognitive decline: A review of rs-fMRI, EEG, MEG, and graph theory approaches in aging and dementia, *Explor. Med.* **5**, 797 (2024).
- [132] M. Volgushev, I. Kudryashov, M. Chistiakova, M. Mukovski, J. Niesmann, and U. T. Eysel, Probability of transmitter release at neocortical synapses at different temperatures, *J. Neurophysiol.* **92**, 212 (2004).
- [133] H. Wen, M. J. McGinley, G. Mandel, and P. Brehm, Nonequivalent release sites govern synaptic depression, *Proc. Natl. Acad. Sci. USA* **113**, E378 (2016).
- [134] C. D. Dürst, J. S. Wiegert, C. Schulze, N. Helassa, K. Török, and T. G. Oertner, Vesicular release probability sets the strength of individual schaffer collateral synapses, *Nat. Commun.* **13**, 6126 (2022).
- [135] G. Deco, V. Jirsa, A. R. McIntosh, O. Sporns, and R. Kötter, Key role of coupling, delay, and noise in resting brain fluctuations, *Proc. Natl. Acad. Sci. USA* **106**, 10302 (2009).
- [136] A. Malkov, I. Popova, A. Ivanov, S.-S. Jang, S. Y. Yoon, A. Osypov, Y. Huang, Y. Zilberter, and M. Zilberter, A $\beta$  initiates brain hypometabolism, network dysfunction and behavioral abnormalities via NOX2-induced oxidative stress in mice, *Commun. Biol.* **4**, 1054 (2021).
- [137] Y. Yu, D. E. Sanabria, J. Wang, C. M. Hendrix, J. Zhang, S. D. Nebeck, A. M. Amundson, Z. B. Busby, D. L. Bauer, M. D. Johnson, *et al.*, Parkinsonism alters beta burst dynamics across the basal ganglia–motor cortical network, *J. Neurosci.* **41**, 2274 (2021).
- [138] C. Babiloni, R. Lizio, N. Marzano, P. Capotosto, A. Soricelli, A. I. Triggiani, S. Cordone, L. Gesualdo, and C. Del Percio, Brain neural synchronization and functional coupling in Alzheimer's disease as revealed by resting state EEG rhythms, *Int. J. Psychophysiol.* **103**, 88 (2016).
- [139] J. Jeong, Eeg dynamics in patients with Alzheimer's disease, *Clin. Neurophysiol.* **115**, 1490 (2004).
- [140] Z. Jafari, B. E. Kolb, and M. H. Mohajerani, Neural oscillations and brain stimulation in Alzheimer's disease, *Prog. Neurobiol.* **194**, 101878 (2020).
- [141] L. Wang, Y. Zang, Y. He, M. Liang, X. Zhang, L. Tian, T. Wu, T. Jiang, and K. Li, Changes in hippocampal connectivity in the early stages of Alzheimer's disease: Evidence from resting state fmri, *NeuroImage* **31**, 496 (2006).
- [142] G. Allen, H. Barnard, R. McColl, A. L. Hester, J. A. Fields, M. F. Weiner, W. K. Ringe, A. M. Lipton, M. Brooker, E. McDonald, C. D. Rubin, and C. M. Cullum, Reduced hippocampal functional connectivity in Alzheimer disease, *Arch. Neurol.* **64**, 1482 (2007).
- [143] A. F. Al Musawi, S. Roy, and P. Ghosh, Examining indicators of complex network vulnerability across diverse attack scenarios, *Sci. Rep.* **13**, 18208 (2023).
- [144] K. E. Joyce, S. Hayasaka, and P. J. Laurienti, The human functional brain network demonstrates structural and dynamical resilience to targeted attack, *PLoS Comput. Biol.* **9**, e1002885 (2013).
- [145] S. Sheykhal, J. Fernández-Gracia, A. Traveset, and V. M. Eguíluz, Extinction-induced community reorganization in bipartite networks, *Appl. Network Sci.* **4**, 23 (2019).
- [146] F. Shi, J. P. Broussard, and G. G. Booth, The complex nature of financial market microstructure: The case of a stock market crash, *J. Econ. Interact. Coord.* **20**, 1 (2025).
- [147] C. Gratton, E. M. Nomura, F. Pérez, and M. D'Esposito, Focal brain lesions to critical locations cause widespread disruption of the modular organization of the brain, *J. Cognit. Neurosci.* **24**, 1275 (2012).
- [148] A. Raj, E. LoCastro, A. Kuceyeski, D. Tosun, N. Relkin, and M. Weiner, Network diffusion model of progression predicts longitudinal patterns of atrophy and metabolism in Alzheimer's disease, *Cell Rep.* **10**, 359 (2015).
- [149] F. Agosta, S. Basaia, E. G. Spinelli, F. Facente, L. Lumaca, A. Ghirelli, E. Canu, V. Castelnovo, E. Sibilla, C. Tripodi, *et al.*, Modelling pathological spread through the structural connectome in the frontotemporal dementia clinical spectrum, *Brain* **148**, 1994 (2025).
- [150] Y. Iturria-Medina, R. C. Sotero, P. J. Toussaint, and A. C. Evans, Epidemic spreading model to characterize misfolded proteins propagation in aging and associated neurodegenerative disorders, *PLoS Comput. Biol.* **10**, e1003956 (2014).
- [151] J. Weickenmeier, M. Jucker, A. Goriely, and E. Kuhl, A physics-based model explains the prion-like features of neurodegeneration in Alzheimer's disease, parkinson's disease, and amyotrophic lateral sclerosis, *J. Mech. Phys. Solids* **124**, 264 (2019).
- [152] M. Scheffer, J. Bascompte, W. A. Brock, V. Brovkin, S. R. Carpenter, V. Dakos, H. Held, E. H. Van Nes, M. Rietkerk, and G. Sugihara, Early-warning signals for critical transitions, *Nature (London)* **461**, 53 (2009).
- [153] C. Meisel, E. Olbrich, O. Shriki, and P. Achermann, Fading signatures of critical brain dynamics during sustained wakefulness in humans, *J. Neurosci.* **33**, 17363 (2013).

- [154] M. Jucker and L. C. Walker, Self-propagation of pathogenic protein aggregates in neurodegenerative diseases, *Nature (London)* **501**, 45 (2013).
- [155] Z. Jaunmuktane and S. Brandner, Invited review: The role of prion-like mechanisms in neurodegenerative diseases, *Neuropathol. Appl. Neurobiol.* **46**, 522 (2020).
- [156] K. Del Tredici and H. Braak, To stage, or not to stage, *Curr. Opin. Neurobiol.* **61**, 10 (2020).
- [157] Publicly available experimental time series datasets, <https://doi.org/10.5281/zenodo.17411410>.