Characterizing Time-Evolving Functional Networks

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Abstract

Understanding spatially-extended, complex dynamical systems is a vital task in the natural sciences. From the climate over eco-socio-cultural systems to the human brain, time-evolving complex systems abound. These systems can exhibit various dynamical phenomena, some of which are only partially understood and can drastically and disastrously affect all areas of life – from climate change over a loss of resilience of ecosystems to other extreme events like epileptic seizures. Typically exceeding our ability to comprehend in total due to the their sheer complexity, a powerful tool to understand these systems is the functional network ansatz. With this ansatz, a system is reduced to a network of interacting elementary units. Here, network vertices are associated with sampled units and network edges represent interactions between the units. In case interactions can not be assessed directly, one resorts to characterizing properties of interactions from recordings of the units' dynamics employing multivariate time series analysis techniques in a time-resolved manner. Then, the time-evolving functional networks can be investigated in lieu of the original complex dynamical system and assessed with network characteristics from graph theory on different scales – from the global scale encompassing the whole network to the local scale of single network constituents (vertices and edges). Relationships between the various time-evolving characteristics and the dynamics of the underlying system – both its emergent global dynamics as well as the dynamics of its elementary units –, however, are not yet fully understood. With this thesis, we set out to improve our understanding of such relationships. We critically assess the functional network ansatz and its assumptions and identify confounding variables in order to evaluate the approach's suitability for field data analysis. To this end, we investigate paradigmatic model systems with well-known constraints as well as a complex natural system, the human brain. We provide novel insights into the rich interplay between structural organization, dynamics and functional relationships in these systems. Of note, local but not global network characteristics, that describe structural organization, robustly indicated the emergent global system dynamics, including the generation of extreme events. Regarding the latter, we developed a non-perturbative, data-driven approach to evaluate a system's stability against endogenous and exogenous perturbations by aggregating edge characteristics, thereby providing a proxy for the system's resilience. Notwithstanding these advancements, the problem of bridging various spatial and temporal scales in a time-evolving functional networks remains. Nevertheless, an improved understanding of complex systems and their dynamics can be achieved with the functional network approach, whose full potential is yet to be exhausted.

Contents

In the following, the journal articles summarized in this cumulative thesis are listed as well as how their authors contributed to them:

- **Chapter II: T. Rings, T. Bröhl and K. Lehnertz. Network structure from a characterization of interactions in complex systems. *Sci. Rep.* 12, 11742 (2022). DOI:** `https://doi.org/10.1038/s41598-022-14397-2`
  - Thorsten Rings performed the research regarding global network characteristics and local network characteristics.
  - Timo Bröhl performed the research regarding local network characteristics.
  - Klaus Lehnertz supervised the research.
  - All authors conceived the research project and wrote the manuscript.
- **Chapter III: T. Rings and K. Lehnertz. Distinguishing between direct and indirect directional couplings in large oscillator networks: Partial or non-partial phase analyses? *Chaos* 26, 093106 (2016). DOI:** `https://doi.org/10.1063/1.4962295`
  - Thorsten Rings performed the research.
  - Klaus Lehnertz supervised the research.
  - Both authors conceived the research project and wrote the manuscript.
- **Chapter IV: T. Rings, G. Ansmann and K. Lehnertz. How important are hubs for the generation of extreme events in networks of excitable units? *Eur. Phys. J. Spec. Top.* 226, 1963–1970 (2017). DOI:** `https://doi.org/10.1140/epjst/e2017-70021-3`
  - Thorsten Rings performed the research.
  - Gerrit Ansmann provided guidance in simulating dynamical systems.
  - Klaus Lehnertz supervised the research.
  - All authors conceived the research project and wrote the manuscript.
- **Chapter V: T. Rings, R. von Wrede and K. Lehnertz. Precursors of seizures due to specific spatial-temporal modifications of evolving large-scale epileptic brain networks. *Sci. Rep.* 9, 10623 (2019). DOI:** `https://doi.org/10.1038/s41598-019-47092-w`
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- **Chapter VI: T. Rings, M. Mazarei, A. Akhshi, C. Geier. M. Reza Rahimi Tabar and K. Lehnertz. Traceability and dynamical resistance of precursor of extreme events. *Sci. Rep.* 9, 1744 (2019). DOI:** `https://doi.org/10.1038/s41598-018-38372-y`
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  - Klaus Lehnertz and M. Reza Rahimi Tabar supervised the research.
  - All authors conceived the research project and wrote the manuscript.

I Introduction

"*Chaos was the law of nature; order was the dream of man.*"
— Henry Adams

A. Motivation

Spatially-extended, complex dynamical systems account for large parts of nature and can exhibit various phenomena like synchronization and de-synchronization [PRK01], chimera states [Sch16], wave propagation [Mer92], phase transitions [Sch20], or extreme events [CGUF15]. In current times of climate change [Wor21], political turmoil [HT17], a pandemic [SMP+22], and mass extinction [RRMV22], understanding such systems is crucially important – especially when the systems undergo extensive changes over time. Yet, the sheer complexity of many systems can make this task highly difficult [Pro88, vK99, Wil02, AO04, HSA06, HDL17, Fie21] and simplifying a system under investigation becomes necessary.

Assuming that the system under investigation can be decomposed into delimitable elementary units, one ansatz is to describe the system as a *network* of vertices – representing the units – and edges – representing couplings and/or interactions between units. The system's collective dynamics is then thought to emerge from the interplay as well as the coupling structure of the units' dynamics, and analysis of the system's internal structure and organization can be performed on the network instead with so-called *network characteristics* from graph theory [New18]. These characteristics describe various topological and spectral properties of networks and of their key constituents (vertices resp. edges). This ansatz has proven highly successful in providing deeper insights into structure of and relationships within systems in diverse areas of science including physics, quantum information theory, earth and climate sciences, sociology, quantitative finance, biology, and the neurosciences [BLM+06, ADGK+08, BS09, DZMK09a, AE11, Bar11, BGL11, New12, BFPS+13, LAB+14, HSP15, GBB16, GV17, BFDD19]. However, the relationships between collective and individual dynamics of elementary units, coupling structure and internal organization, as well as the system's function (in the sense of purpose, impact, capability to act, and operating principles of the system) are still only partially understood.

If a network is derived from traceable, physical couplings between units of a system, it is called a *structural network* and such networks are often interpreted as an accurate representation of a system's internal structure. However, access to a system's couplings is often restricted or impossible without critically damaging the system through disassembly, (strong) perturbation of a system's units, or the introduction of a tracer agent. Examples of structural networks include representations of man-made systems such as road systems [BBG+18] and computer networks [KKR+99] or of natural systems simple and transparent (or dispensable) enough to allow investigation such as, e.g., a muscle and nerve cell network of a P. pacificus nematode [BRRS13].

When deriving a structural network is impractical, dangerous, or outright impossible with current technology and methodology, *functional networks* represent an often used alternative. Instead of the aforementioned tracing of couplings, functional networks are based on characterizing interactions between elementary units derived from (ideally passive) observations of the units' dynamics in the form of time series data. Furthermore, and depending on the actual research question, functional networks might also present a more accurate picture of the internal organization of the systems: e.g., in a traffic system, even though two cities are connected by a highway (a structural connection), commuter do not necessarily drive along that road unless workplace and home align with the two cities (a functional connection). Deriving a functional network form traffic (starting and end points of individual car drives, etc.) might provide more accurate information about congestion and a need for street maintenance than the corresponding road map (i.e., the structural network) alone. The ansatz of functional networks has been successfully applied in the study of diverse systems in nature such as (functional) brain networks [BS09], climate networks [DZMK09b, ZGAH15], protein-protein interactions [UGC+00], gene interactions [TAWM09], plant-pollinator interactions [HNL+09, OBD+11], food-webs [DBB+19], or communication and social networks [OSH+07, PBV07].

Of special interest, a system might evolve with time due to, e.g., changing control parameters or some hidden rule or function. For example, the use of a transportation network is highly dependent on typical working hours (including deviations on irregular holidays and holiday seasons, etc.), most biological systems are dependent on the alternation of day and night, and stock markets follow events such as the slow development and consolidation of globalization as well as the rapid onset of global financial crises [STZM11]. So called *evolving networks* [HS12, BdKP14] extend the concept of networks to represent such behavior and allow for the investigation of the system's time evolution. For this purpose, a common method is to derive – with a moving window ansatz – a sequence of functional *snapshot networks* as a representation of the evolving network[1]. Then, tracking changes between the snapshot networks along the sequence informs on phenomena exhibited by the system.

Problematic in a technical sense, comparing networks – and, consequently, identifying significant and meaningful changes between successive snapshot networks – currently remains an unsolved issue. While tailored metrics do exist (see, e.g., [BBK06, AMPL08, MHVD09, Mém11, DDSA16, MWH20]), they often place strong constraints on the investigated networks (equal number of vertices or equal edge density, etc.) or their interpretation is unclear. Alternatively, comparing quantifiable network characteristics necessitates appropriate normalization of characteristics for various circumstances. Furthermore, characteristics can be very specific, so that interpretations regarding the networks (and, by extension, the underlying system) require unintuitively summarizing multiple characteristics in unison. Even then, statements often can only be made relative to compared snapshot networks (e.g., *an evolving network exhibit a higher clustering coefficient at one time than at another time*).

In this thesis, we aim to further our understanding of the interplay between coupling structure, dynamics, and functional relationships within complex dynamical systems that undergo changes with time. We trace these changes by characterizing time-evolving functional networks derived from time series data of the systems' dynamics. The resulting temporal sequences of characteristics are then compared to the phenomena encountered in the collective dynamics of the system – e.g., synchronization, extreme events, or changes of resilience. We address fundamental challenges of characterizing time-evolving functional networks in nature and of their interpretation at the example of paradigmatic model systems – oscillator networks with complex coupling topologies – and one of the most complex systems in nature – the human brain.

B. Central Concepts

In the following, we present central concepts essential for the time-evolving functional networks approach.

1. *Networks*

Mathematically, a network is equivalent to a graph: a set $\mathcal{V}$ of discrete objects together with a set $\mathcal{E}$ of relations between the discrete objects. The objects are typically called *vertices* (or *nodes*) and the relations are called *edges* (or *links*). An edge connects two vertices. The terms network and graph are largely interchangeable and the choice of the term is

[1] Structural networks can and do evolve with time as well – indeed, changes in functional networks are thought to represent changes in structural networks.

context driven [BP14] with network being the term mostly employed for systems in nature and graph for abstract concepts. For simplicity, in this thesis we typically employ the term network.

Historically, the negative solution to the *Seven Bridges of Königsberg* problem by Leonard Euler [Eul41] published in 1741 is considered the first use of network theory in a mathematical proof (see Fig. I.1). Euler proved the impossibility of crossing each of the seven bridges exactly once while traversing Königsberg (now Kaliningrad, Russia) from an arbitrary starting point. To be more precise: Euler proved it to be possible to pass each edge in a network exactly once only for networks with exactly zero or two vertices with an odd number of edges connected to them.

The unfortunate destruction of two of the seven bridges during World War I modified the network such that this condition is now fulfilled and one can now traverse each of the *five* bridges of Kaliningrad exactly once. This anecdote also emphasizes an often neglected aspect of networks: it is possible for a network to change with time and modify its characteristics.

Generally, a network can be *binary* (an edge either exists between two vertices or not) or *weighted* (an edge carries an additional information – a weight). A weight can be any property relevant to the described network: from simple (e.g., the physical length of a street between two places) to abstract (e.g., the probability of a virus to spread between two populations of animals or people) to complex (e.g., the estimated strength of an interaction between coupled dynamical elementary units). Furthermore, we distinguish between *directed networks* and *undirected networks*. In directed networks, an edge starts at one vertex and terminates at another – two edges connecting the same vertices but with opposing direction are called a *bidirectional edge*. In undirected networks, all edges are bidirectional. A network, in which one can reach every vertex via edges starting at any other vertex is called *connected*. We explicitly do not consider unconnected networks in this thesis – i.e., networks that are separated into disconnected sub-networks. Furthermore, we also exclude so-called *multi-edges* – two vertices connected by more than one edge (cf. the network representing Königsberg before World War I in Fig. I.1).

A binary network of $\mathrm{N} = |\mathcal{V}|$ vertices can be represented by an *adjacency matrix* $\mathcal{A} \in \{0,1\}^{\mathrm{N}\times\mathrm{N}}$, where $\mathcal{A}_{ij} = 1$ if vertex i and j are connected by an edge or $\mathcal{A}_{i,j} = 0$ otherwise[2]. A weighted network on the other hand can be described by a *weight matrix* $\mathcal{W} \in \mathbb{R}_+^{\mathrm{N}\times\mathrm{N}}$, where each element $\mathcal{W}_{ij}$ equals the weight of the edge between vertices i and j. In this case, the absence of an edge is represented by $\mathcal{W}_{ij} = 0$. To exclude so-called self-loops, we set $\mathcal{A}_{ii} := 0$ respectively $\mathcal{W}_{ii} := 0 \; \forall \, i \in \mathcal{V}$. For undirected networks, $\mathcal{A}$ respectively $\mathcal{W}$ are symmetric[3].

The *topology* of a network describes the manner in which all vertices and edges in the network are arranged and comprises a number of properties important for the study of networks. These *topological properties* include the size – number of vertices N as well as of edges E –, the *paths*, and the (local) *coupling structure* among others. Here, paths are routes through a network described by sets $\mathcal{P}_{ij}$ of edges which have to be traversed while traveling from one network constituent (vertex or edge) i to another j. The coupling structure, however, illustrates which vertices are connected to which other vertices by edges and what commonalities are shared between connected vertices[4]. In weighted networks, the weights of edges and their distribution can also be considered part of the topological properties. For convenience, it is possible to

[2] While not a common moniker, it would be more accurate to call $\mathcal{A}$ the *vertex adjacency matrix*. This indicates the point of view which is used to describe the network: it is vertices that are connected by edges. Note, that the inverse point of view – edges are connected by vertices – is equivalent.

[3] Equivalently, a binary network of $\mathrm{E} = |\mathcal{E}|$ edges can also be described by an *edge adjacency matrix* $\mathcal{A}^{(\mathrm{e})} \in \{0,1\}^{\mathrm{E}\times\mathrm{E}}$ while a weighted network can be represented by a *weighted edge adjacency matrix* $\mathcal{W}^{(\mathrm{e})} \in \mathbb{R}_+^{\mathrm{E}\times\mathrm{E}}$. The entries $\mathcal{A}_{lm}^{(\mathrm{e})}$ of the edge adjacency matrix are either 1 if two edges l and m share a vertex or 0 otherwise, and the entries $\mathcal{W}_{lm}^{(\mathrm{e})}$ of the weighted edge adjacency matrix are assigned the average of the weights of edges l and m. Again, $\mathcal{A}_{ll}^{(\mathrm{e})} := 0$ respectively $\mathcal{W}_{ll}^{(\mathrm{e})} := 0, \; \forall \, l \in \mathcal{E}$.

[4] Or, conversely, what commonalities are shared between edges connected to the same vertices.

FIG. I.1. Depiction of the Seven Bridges of Königsberg problem. Left: map of Königsberg in Leonard Euler's time; adapted from [Mer50]. It is impossible to cross every bridge (marked by green and turquoise lines) exactly once while traversing Königsberg. Two of the seven bridges were destroyed (turquoise lines) during World War I and it now possible to cross every existing bridge exactly once. Upper right: representation of Königsberg's bridges and riversides as a network. Black lines represent the bridges (edges) and black circles represent the land (vertices) divided by the Pregolya River. Numbers inside the circle represent the number of edges connected to the respective vertices. Lower right: Same as upper right but without the two edges representing the bridges destroyed during World War I.

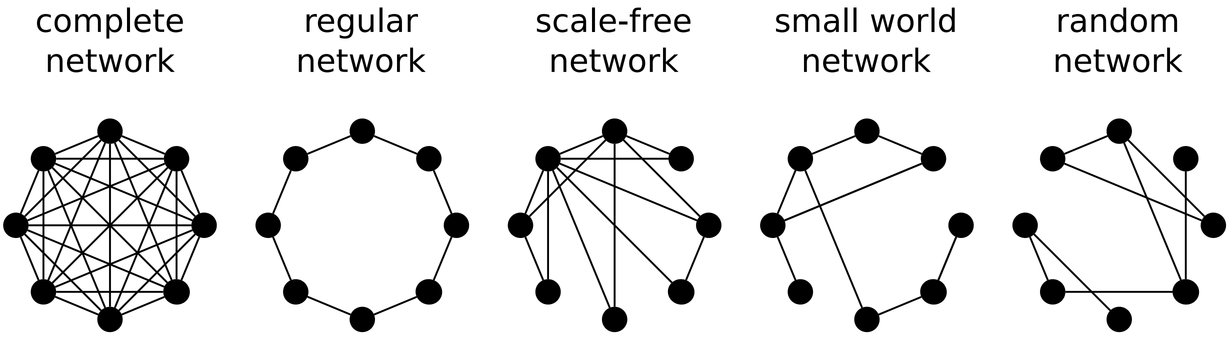

FIG. I.2. Schematics of five archetypal network topologies. Black dots depict vertices and black lines depict edges. The examples have N = 8 vertices and varying number of edges[a]. From left to right: a complete network, a regular network in the form of a ring with each vertex being connected to its two nearest neighbors, a scale-free network generated by preferential attachment [AB02], a small world network based on a ring with two rewired edges (equivalent to a rewiring probability of $p_r = 0.25$) [WS98], and a random network topology where each pair of vertices is connected with a probability of $p_e = 0.3$ [ER59].

[a] Arguably, properties of the described archetypal networks typically hold for $N \to \infty$. However, the networks still represent reasonable approximations for finite N of the anyhow idealized archetypes.

define distinct types of topologies, and five archetypal types of topologies (see Fig. I.2) are:

- **complete network**: every vertex is connected to every other vertex in the network.
- **regular network**: vertices are connected in some regular pattern including rings, grids, and stars. Regular network topologies are common in man-made systems (e.g., a typical bus in computer architecture [NL18] or the infamous checkerboard pattern of streets and junctions in the Untied States of America [Boe21] or of the city center of Mannheim, Germany).
- **scale-free network**: for this type of network, the distribution of the number of edges connected to each vertex follows a

power law. This *s*cale-free property indicates *self-similarity* over different spatial scales and often allows for a description of the network by a *core* (or *hub*) of vertices with a large number of connected edges and a *periphery* of vertices with lower numbers of connected edges. Postulated to be the result of a network generation mechanism based on *preferential attachment* [AB02], many systems in nature are thought to have a scale-free topology.

- **small world network**: a regular structure (e.g., a ring or a lattice) of vertices and edges is disrupted by edges connecting (seemingly) random vertices. Small world networks can be easily generated with, e.g., the Watts–Strogatz model [WS98]: starting from a regular network, each edge is rewired with some small probability p_r by exchanging one of the vertices connected by the edge with another randomly chosen vertex. Small world networks are often interpreted as the connecting link between an arbitrary regular network topology and a random network topology where the mixing of the two can be controlled by the rewiring probability. It has been reported (and doubted) that many systems in nature have small-world network topology [BS09, BHL10, PZMB16].
- **random network**: every vertex is connected to any other vertex with some probability p_e [ER59]. Random network topologies share a connection with random matrix theory [Meh04] and are often employed as a null model when studying order (or lack thereof) in networks.

These types of topologies, while not necessary exhaustive, are typically used as references for networks found in nature. Problematically, comparisons with such references are sensitive to the methods used to estimate networks from data as well as measurement and statistical errors [BHL10, HHP12, PZMB16].

Furthermore – and important for this thesis –, the concept of networks can also be used for representing a system with high numbers of degrees of freedom, for which (at least in some abstract sense) elementary units can be determined. In this case, an elementary unit is represented by a vertex and functional connections resp. interactions are depicted as edges[5].

2. Networked dynamical systems

Before we discuss how to derive networks from time series data, we briefly consider dynamical systems coupled according to network topologies. Based on the assumption that couplings act additive on the time evolution of an elementary unit i of a system, the network decomposition of dynamical systems reads

$$\dot{\mathbf{x}}_i = \mathbf{f}_i(\mathbf{x}_i) + \mathbf{h}\left(\epsilon, \mathcal{M}; \mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_{\mathrm{N}}\right), \quad (\mathrm{I.1})$$

where $\mathbf{x}_i$ represent the unit's state variables. Boldfaced symbols indicate vector-valued dynamical variables resp. functions or (in the case of $\mathcal{M}$) matrices. The function $\mathbf{f}_i$ represents the i-th unit's *self-dynamics*[6] including all of its control parameters.

The function $\mathbf{h}(\epsilon, \mathcal{M}; \mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_{\mathrm{N}})$ represents the *dynamical coupling structure*, which describes the form and effect of the couplings between the various units. It includes a (global) *coupling strength* ϵ, the system's coupling topology in the form of entries of the adjacency matrix ($\mathcal{M} = \mathcal{A}$) or weight matrix[7] ($\mathcal{M} = \mathcal{W}$), and the *coupling function* $\mathbf{g}(\mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_{\mathrm{N}})$. The latter is typical separated into (yet not necessarily restricted to) *diffusive* – or alternatively termed *attractive* – *coupling* and *repulsive coupling*, which either turn the coupled units' dynamical variables closer together or further apart with time, respectively. Interestingly, both types can induce various forms of synchronization between the dynamics of the elementary

[5] For simplicity, we will use the same index i (as well as j) for vertices and elementary units, since we assume a one-to-one relationship between vertices and units: each of the system's units is represented by exactly one vertex. In this context, N is also the number of elementary units of a system.

[6] E.g., the right-hand-side of a first order differential equation corresponding to the equation of motion of a physical oscillator.

[7] A weight matrix effectively individualizes the coupling strength of couplings between all (or a selected number of) pairs of interacting elementary units of the system.

units [PRK01]. Other forms of coupling (e.g., multiplicative couplings or couplings influencing control parameters of the self-dynamics) are intentionally excluded in this decomposition and from the deliberations in this thesis.

3. *Deriving networks from time series data*

There are an almost infinite number of possible approaches to derive networks from natural systems – e.g., labeling all junctions of an arbitrary city map as vertices and then adding edges for every street between two junctions [Boe21] or defining different species in a food web as vertices and add predator-prey relationships as edges [DBB+19]. However, in this thesis, we concentrate on networks derived from time series data. For this purpose, vertices are associated with parts of a system that were sampled by sensors (when investigating natural systems) or by dynamical variables of elementary units described by equations of motion (when simulating model systems). Edges are associated with properties of interactions between elementary units that can be estimated from time series of recordings from sensors or from time series of dynamical variables. Networks constructed by this means are functional networks and can differ drastically from the underlying structural network (sometimes also called *coupling topology*) of actually existing connections between elementary units (see Chapter II). On the most fundamental level, estimators for properties of interactions assume that an interaction between two elementary units change the time evolution of the trajectory of the units' dynamical variables in state space. Properties of interactions are:

- **the strength of interaction**: a numerical value that describes the level of interdependence between two elementary units[8]. Estimating the strength of interaction requires a quantification of the impact of the dynamics of interacting elementary units on each other – typically by concentrating on different aspects of the dynamics (e.g., amplitude distribution, phase positions, information content, etc.). Most estimators for the strength of interaction are designed to be limited to the interval $[0, 1]$. With respect to the aspect (or aspects) utilized by the employed estimator, values close to 0 indicate independence of the elementary units, and values close to 1 indicate the strongest discernible coupling[9]. This property is often used as a weight of a bidirectional edge between the two subsystems and we predominantly concentrate on networks based on the strength of interactions in this thesis.
- **the direction of interaction**: a numerical value indicating which of the two interacting elementary units is driving the other. Many estimators for the direction of interaction are based on assumptions about cause and effect between elementary units and on (not necessarily universal) models for the temporal evolution of their dynamics. While the value of an estimator for the direction of interaction can indicate the confidence of the estimate, in most cases only the sign of the value indicates the direction. Small values of the estimator can indicate both independence of the two elementary units or a strong bidirectional interaction [LD15]. The direction of interaction is sometimes used to derive directed networks, where weights of directed edges between two vertices (i, j; edge $i \to j$) indicate to what degree the elementary unit associated with the vertex i can be assumed to drive the one associated with the vertex j. Problematically, this version of networks does not inform on the strength of interactions between elementary units without addi-

[8] Strength of interaction can be interpreted as an estimation of the coupling strength ϵ (cf. Section I B 2) and ideally changes monotonically with changes in ϵ.

[9] Given that very high coupling strengths ϵ can produce overshoot-like effects which might seemingly decouple elementary units (cf. Eq. I.1 for $\mathbf{h} \gg \mathbf{f}_i$), the "strongest discernible coupling" might not be associated with $\epsilon \to \infty$ but with some finite value of ϵ.

tional strength-of-interaction-based estimates, yet there are currently no commonly accepted methods to combine strength and direction of interactions.

- **the functional form of interaction**: a function dependent on dynamical variables (or derivatives thereof) describing how two elementary units react to each other. Estimating the functional form of an interaction requires a number of (implicit and often restrictive) assumptions about the elementary units [SDMS12, TLI19]. To our knowledge, no networks were derived from estimates of the functional form of interactions so far and doing so would require a highly abstract, possibly symbolic assignment of edges (and edge weights).

The different properties of interactions can be estimated with various analysis techniques derived from statistics, nonlinear dynamics, synchronization theory, statistical physics, and information theory, among others. These techniques are based on (statistical) correlation [RN88], Kramers–Moyal theory [RGHLT19, ARZL21], predicitability [Gra69, Eic05], information flow [Sch00, Liu04], phase synchronization [MLDE00, RP01, SDMS12], or generalized synchronization [AGLE99, QQAG00, ACLM11, ASR12], to name but a few. Since each technique relies on certain characteristic aspects of the dynamics – capturing different aspects of an interaction – and exhibit various sensitivities [KMA+07], the use of the respective techniques for an investigation of interaction properties depends on the specific problem.

In this work, we predominately[10] focus on weighted networks derived with the phase-synchronization-based estimator *mean phase coherence* [MLDE00], which assesses the strength of interaction [KMA+07]. For the systems investigated in this thesis (weakly chaotic oscillators and oscillatory brain dynamics), phase-based approaches have proven successful in the past and are robust under a range of influencing factors including noise [MLDE00, PKL14].

For systems with time-evolving coupling structures and coupling strengths or changing sensitivity of elementary units to interactions (possibly due to changing control parameters or some hidden rule or function), the generation of a single, all encompassing network is impractical or even conceptually misleading. Instead, evolving networks allow for a better description of such systems. By using a moving window approach, one can generate a sequence (basically a time series) of snapshot networks, where in each window the interaction property of interest is calculated for each pair of elementary units. The length of non-overlapping windows, then, can be chosen according to a balance between the number of data points necessary for good (statistical) accuracy of the estimator of the interaction property and approximate stationarity of the system.

4. *Characterizing networks*

Networks can be characterized with a large number of characteristics, that reflect their specific topological and spectral properties. These characteristics describe either single network constituents (vertices and edges) on a *local network scale* or the network as a whole on a *global network scale*[11]. The largest class of local network characteristics are so called *centralities* based on concepts that reflect a multitude of different roles a vertex or an edge can

[10] In Chapter II, we utilize two other estimators for the strength of interaction: maximum-lag cross correlation [KMA+07] and mutual information [TRW+98, KSG04, KMA+07]. For a brief discussion of these two techniques, see the corresponding Methods Section **??**. Note, that for the specific investigation presented in Chapter II (cf. Section I C 1, Rössler oscillators), results attained for maximum-lag cross correlation are largely comparable to those for mean phase coherence.
Furthermore, in Chapter III, we utilize two phase-based estimators for the direcetion of interaction – namely the *evolution map approach* [RP01] and its partialized extension, the *partialized triplet approach* [KPR14].

[11] Additionally, on a *mesoscopic network scale*, characteristics can describe groups of constituents sorted according to specific rules (often based on local characteristics). Often the grouping itself is considered the characteristic (e.g., in some social network, a vertex representing a person belongs to one or multiple cliques of "friend"-vertices that can be identified with the correct method).

occupy in a network. We concentrate on vertex centralities[12] and present four widely used centralities showcasing different approaches to *importance* of vertices.

The arguably simplest (and most straightforward) local network characteristics is the *degree* k of a vertex. Predating first definitions of centralities – Leonard Euler already used this characteristic for his solution to the Seven Bridges of Königsberg problem in 1736 (cf. Figure I.1) –, the degree is the number of edges connected to a vertex i: $k(i) := \sum_{j=1}^{\mathrm{N}} \mathcal{A}_{ij}$. The equivalent of the degree in a weighted network is the *strength centrality* [BBPSV04, OAS10]: $\mathcal{C}^{\mathrm{S}}(i) := \sum_{j=1}^{\mathrm{N}} \mathcal{W}_{ij}$. Both characteristics describe to what extent a given vertex can affect (and is affected by) other vertices in the network.

The *eigenvector centrality* $\mathcal{C}^{\mathrm{E}}$ of a vertex i [Bon87] is defined as the i-th entry of the eigenvector $\vec{v}$ corresponding and normalized to the dominant eigenvalue $\lambda_{\max}$ of a matrix $\mathcal{M}$, where $\mathcal{M} = \mathcal{A}$ for binary networks or $\mathcal{M} = \mathcal{W}$ for weighted networks. A vertex assessed as central with eigenvector centrality is connected to other central vertices.

Closeness centrality $\mathcal{C}^{\mathrm{C}}$ utilizes the average distance of a vertex to all other vertices in a network [Fre79]. Here, distance is defined as the *length* d of the *shortest path* between two network constituents. In binary networks this length is the shortest number of edges needed to be traversed to travel from vertex i to vertex j. In weighted networks, this length is defined as the minimum sum of the inverse weights of edges along each possible path [Fre79]. A vertex with a large closeness centrality has short shortest paths connecting the vertex to all other constituents of its type. Therefore, it is an ideal starting point to reach other vertices and is considered important for spreading processes in the network.

Betweenness centrality $\mathcal{C}^{\mathrm{B}}$ of a specific vertex i assesses the amount of shortest paths between all vertices traversing the vertex [New01, BBPSV04, WHV08, OAS10]. The amount is then normalized to the number of all possible shortest paths between vertices. A vertex with a large betweenness centrality acts as a bottleneck or bridge between the other vertices.

Strength and eigenvector centrality are often grouped as degree/weight-based (resp. strength-of-interaction-based) local network characteristics, while closeness and betweenness centrality are grouped as based on the organization of shortest paths in a network. Additionally, the rank order of the values of a local network characteristics is used to define importance of network constituents [LMM+17]: the vertex associated with the largest value of a local network characteristics is typically deemed the most important in the network with respect to the concept behind the characteristics.

Four of the most commonly utilized global network characteristics are *global clustering coefficient* C [WS98], *average shortest path length* L [New01], *assortativity* A [New02b], and *synchronizability* S [BP02b]. The first three characteristics – C, L, and A – can be grouped as sensitive to topological properties of networks, while synchronizability evaluates spectral properties that are linked to stability and robustness of dynamics of coupled elementary units arranged on the corresponding network.

The global clustering coefficient C assesses the degree to which vertices in a network tend to cluster together and characterizes the functional segregation of a network. In a binary network, C assesses the relative amount of all vertices adjacent to any specific vertex that are also connected with each other [WS98]. In a weighted network, the geometric average of weights of edges between such mutually connected triplets of vertices can be considered [OSKK05]. A large global clustering coefficient indicates a highly interconnected network (at the extreme, a network with complete network topology), while a small global clustering coefficient indicates sparsely connected networks (e.g., a network with random network topology and only a small number of

[12] In Chapter II, we also evaluate various edge centralities. However, we do not utilize the related concepts when interpreting changes in evolving functional networks related to dynamical phenomena and treat edge centralities as a sideshow in this thesis. For more information on edge centralities, we refer to the corresponding Methods Section ?? and references therein.

edges).

The average shortest path L assesses a network's functional integration and is the average of the length of all shortest paths between any pair of vertices in the network. Typically associated with information flow in a network, a small value of L indicates fast transport of information and a small degree of separation between all vertices in the network [New01].

The assortativity A of a network describes the preference of vertices with similar characteristics to be connected by an edge [New02b, BL13]. A typical choice of the characteristics in question is the degree of the vertices. Interestingly, the dynamics of coupled elementary units arranged on an assortative network are reported to be harder to synchronize than ones on a less assortative or even disassortative network [MZK06, dBGS07].

The synchronizability S of a network describes the stability of (and the possibility to exhibit) a synchronized state of the networked dynamics [BP02b, ABJ06, vMSK+11], where each unit is synchronized with each other unit. Derived from the ratio of the largest and smallest non-vanishing eigenvalue of the *Laplacian matrix* $\mathcal{L}$ of a network, a large value of S indicates an unstable synchronized state (elements of the Laplacian matrix are defined as $\mathcal{L}_{ij} = \sum_i \mathcal{A}_{ij}\delta_{ij} - \mathcal{A}_{ij}$ for binary networks resp. $\mathcal{L}_{ij} = \sum_i \mathcal{W}_{ij}\delta_{ij} - \mathcal{W}_{ij}$ for weighted networks). Interestingly, a large synchronizability can indicate – depending on the dynamics of the elementary units – that the system in question can not exhibit a synchronized state independent of the coupling strength between the units.

In evolving networks, the network characteristics can change with time. Network constituents may lose or gain placement in one centrality ranking and may stay at their placement in another. Networks as a whole can become more or less segregated, while their assortativity monotonically decreases with time. Interpreting these changes can be difficult, as there is no established way for comparing networks as a whole [ABC99, vWSD10, TITP19]. Tracking network characteristics over a sequence of snapshot networks, network characteristics can be calculated for each snapshot resulting in time series of characteristics that then can be analyzed further.

5. *Interpreting time-evolving network characteristics*

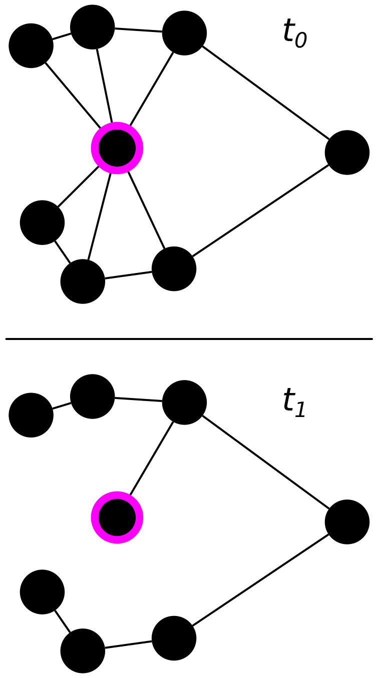

FIG. I.3. Example of a network alteration. Vertices are depicted as black dots, edges as black lines. Top: network before at time t_0. The magenta-framed vertex is a bottleneck in the network and exhibits the highest betweenness centrality in the network at that point in time. The average shortest path in the network is short thanks to the magenta-framed vertex acting as a bridge between different groups of vertices. Bottom: network after at time t_1 after an alteration. The magenta-framed vertex looses five edges and is no longer the most central vertex according to betweenness centrality. Shortest paths are rerouted via a remote vertex, and the average shortest path length of the network increased.

To gain a comprehensive picture of possible modifications a network undergoes with time, it is often necessary to interpret changes in a combination of different local and global network characteristics. For example, if we only know, that the average shortest path length of a network gets longer with time, we can conclude, that information flow in the network decreases in efficiency. If we include knowledge about a simultaneous change in the rank order of betweenness centrality, where the most "betweenness-central" vertex becomes significantly less central, we can make a more refined interpretation: a bottleneck-like vertex got closed off and the rerouting of a number of shortest paths through some other vertex or vertices produce shortest paths of higher lengths (see figure I.3).

An important factor when interpreting the changes an evolving networks undergoes is statistical validation of results [N+12]. Without appropriate models, the significance of a change in the various properties of a network can often only be evaluated with bootstrapping methods and Monte-Carlo simulations – i.e., with *surrogate techniques*. Such techniques can be applied on various levels of the chain of analysis under formulation of appropriate null hypotheses [Efr04].

Briefly, an ensemble of surrogate data is created by simulating realizations of an appropriate null model with Monte Carlo methods. In these realizations, all important statistical and dynamical aspects of the original data are preserved – but not the property which is tested for. The null hypothesis can then be rejected – with reasonable confidence depending on the number of statistically independent constrained realizations – if some discriminating statistics for the original data is outside the range of values determined for the surrogate ensemble.

On the level of time series analysis, surrogates can help affirm confidence in the existence of, e.g., non-linearity or interactions. Non-linearity – or, more correctly, the absence of non-linearity, – can be tested with so-called *iterative amplitude adjusted Fourier transform surrogates* [SS96, SS00]. By randomizing aspects of the dynamics that include all effects of a possible non-linearity[13], we can create surrogates that resemble the original time series with high precision but without its possible non-linearity. Then, if the value of an indicator for non-linearity exceeds or falls below the values for the surrogates, we can reject the null hypothesis of an absence of non-linearity.

Partially extending from these monovariate techniques and by randomizing the aspect of a recorded dynamics on which the estimator for the property of interaction is based, we can generate constrained realizations of the multivariate time series [Sch98, SS00, AKS+03, Pal07, LIP+18, RCR+20]. If an estimation for a property of interaction is then outside the range of estimations for the surrogates, we then can reject the null hypothesis that a possible interaction is not related to the aspect of the dynamics.

As a special consideration, an aspect of a time series can be a temporally close, upcoming event (e.g., an extreme event). So-called seizure time surrogates[14] [AMK+03] can be used to test the null hypothesis of the non-existence of an event-permissive (or even facilitating) state. Under the assumption that such a state exists in some interval prior to the event and that the state can be discriminated by some statistics from the time intervals where we assume the system to behave "normal", a straightforward way to generate a suitable surrogate is to randomize the points in time of the events while keeping the distribution of inter-event intervals. This changes what time intervals are considered prior to an event resp. what intervals are during normal behavior. For the original data, a statistically significant difference between the discriminatory statistics from the two types of intervals can then be considered a first indicator for the existence of precursors. However, if this difference is equal or greater for the surrogates than for the original data, the null hypothesis – i.e., the non-existence of a event-permissive state – can not be rejected. In that case, the event might be an abrupt phenomenon without precursors.

On the level of networks, surrogates can be based on, e.g., preservation of degree or strength distributions of networks [AL11, AL12, KDGBT12, ZGC12, RA13, FLPA15,

[13] By combining Parseval's theorem and the Wiener–Khinchin theorem, one can conclude that all effects which can not be explained by linear dynamics are expressed in the time series' Fourier phases. Consequently, randomizing the phase position of the Fourier transformation resp. of the inverse Fourier transformation while fixing the amplitude distribution and the distribution of Fourier coefficients destroys non-linearity in time series.

[14] The name refers to the original purpose of this surrogate concept: the identification of a seizure-permissive state in data from epileptic human brains. Revealing such a state can be considered an important step for seizure prediction [KLR+18].

SMG15, SL17] while randomizing the existence resp. the weights of edges. A change in network characteristics can than be considered significant, if the change puts the characteristic outside the range derived for the surrogate networks, which were generated from the network before the change.

C. Overview of this thesis

Having addressed central concepts, we continue with outlining the different systems and phenomena investigated in this thesis with the approach of time-evolving functional networks. We also introduce new methods important to our investigation.

1. *Investigated systems and phenomena*

In this work, investigated systems can be largely separated in two groups: *simulated systems* for evaluation and testing of methods and a *natural system* that we aim to gain a better understanding of.

a *Simulated systems*

We employ networks of coupled *Rössler oscillators* and of coupled *FitzHugh-Nagumo oscillators* to simulate complex dynamics for preliminary studies regarding the derivation of networks from time series data and regarding the relationship of (local or global) network properties with different dynamical phenomena such as synchronization and extreme events. The two types of oscillators support rich dynamics and act as excitable media when diffusively coupled while still being comparably simple.

Rössler oscillators

The Rössler oscillator was initially designed to exhibit similar dynamics to the Lorentz oscillator [Lor63], while being easier to analyze [R7̈6]. Anecdotally, the oscillator was inspired by the movement of a taffy puller and was not explicitly designed to represent physical systems. Instead, the Rössler oscillator is often used to illustrate chaotic dynamics which here arises from a weak non-linearity.

The i-th Rössler oscillator in some set of N uncoupled oscillators is described by the following 3-dimensional differential equation:

$$\begin{aligned} \dot{x}_i &= -\omega_i y_i - z_i \\ \dot{y}_i &= \omega_i x_i - a y_i \\ \dot{z}_i &= b + z_i(x_i - c). \end{aligned} \tag{I.2}$$

The parameters a, b, and c control the dynamics of the system. Depending on their setting, the system can exhibit convergence to a fixed point or to a limit circle as well as chaotic dynamics. Furthermore, we introduce an eigenfrequency ω_i[15] to the original equation [R7̈6], which we use to diversify oscillators – a common method to hamper synchronization in networks of coupled oscillators [BLM+06]. Fig. I.4 shows exemplary time series of the dynamical variables of a single Rössler oscillator as well as a portrait of its state space.

Coupled Rössler oscillators can exhibit various phenomena like complete (phase or otherwise) synchronization, chimera states [DSBI+20, KJ21] or oscillator resp. amplitude death [KVK13]. For networks of coupled Rössler oscillators, Eq. I.2 can be extended to

$$\begin{aligned} \dot{x}_i &= -\omega_i y_i - z_i + \widetilde{h}(x_i; x_1, \ldots, x_\mathrm{N}) \\ \dot{y}_i &= \omega_i x_i - a y_i \\ \dot{z}_i &= b + z_i(x_i - c). \end{aligned} \tag{I.3}$$

where $\widetilde{h}(x_i; x_1, \ldots, x_\mathrm{N})$ is the coupling term. For diffusive coupling as used in this thesis,

$$\widetilde{h}(x_i; x_1, \ldots, x_\mathrm{N}) = \frac{\epsilon}{k} \sum_{j=1}^{\mathrm{N}} \mathcal{A}_{ij}(x_j - x_i) \tag{I.4}$$

with coupling strength ϵ and degree k. All information about the network's topology is encoded in the entries $\mathcal{A}_{ij}$ of the adjacency matrix. Time series of the dynamical variables of a network of coupled Rössler oscillators are

[15] The eigenfrequency is not the actual frequency of the weakly non-linear oscillator, but nonetheless directly influences the oscillator's speed of revolution around its center.

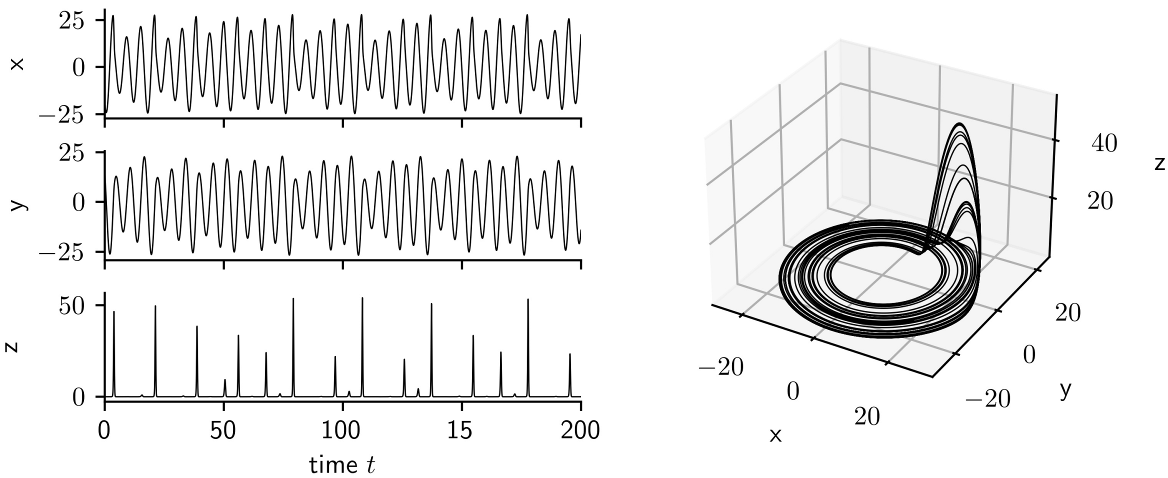

FIG. I.4. Exemplary time series of dynamical variables x (top), y (middle), and z (bottom) of a Rössler oscillator (left; cf. Eq. I.2) and a 3-dimensional depiction of its corresponding state space (right). Parameter were set to $a = 0.1$, $b = 0.1$, $c = 18$, $\omega = 1$, and initial conditions for x, y, and z were randomly chosen from the interval $[0, 1]$ resulting in chaotic dynamics of the oscillator. We here dropped indices i for readability. To generate the time series, Eq. I.2 was integrated with the Dormand–Prince method [DP80] and with a step size of 0.01 for 200 time units after initial transients of 200 time units were discarded.

depicted in Fig. I.5.

Analogously to Arnold tongues [PRK01] in the case of two coupled oscillators, synchronization in networks of coupled Rössler oscillators is affected by the diversity of the oscillators – the variety in eigenfrequencies ω_i – and by the coupling strength ϵ. However the relationship between the set of $\{\omega_i, \epsilon\}$ and the system's global dynamics is typically less straight forward compared to Arnold tongues in the two-oscillator case. While phase synchronization[16] usually increases with an increase of coupling strength and a decrease of inhomogeneity of the eigefrequencies (e.g., a decrease of the range or variance of the distribution of eigenfrequencies), this behavior is not necessarily monotonic (see Chapter II). Interestingly, changes in the coupling topology can affect the global dynamics of the networked dynamical system akin to changes in coupling strength [ALF16]. An increase in the rewiring probability of a small-world coupling topology (increasing the randomness of which vertices and associated oscillators are coupled), e.g., can affect the dynamics similar to an increase in coupling strength.

[16] The global phase synchronization of a network of oscillators is quantifiable with, e.g., the Kuramoto order parameter [Kur84] or as an average over phase-based strength of interaction estimates of time series from pairs of oscillators.

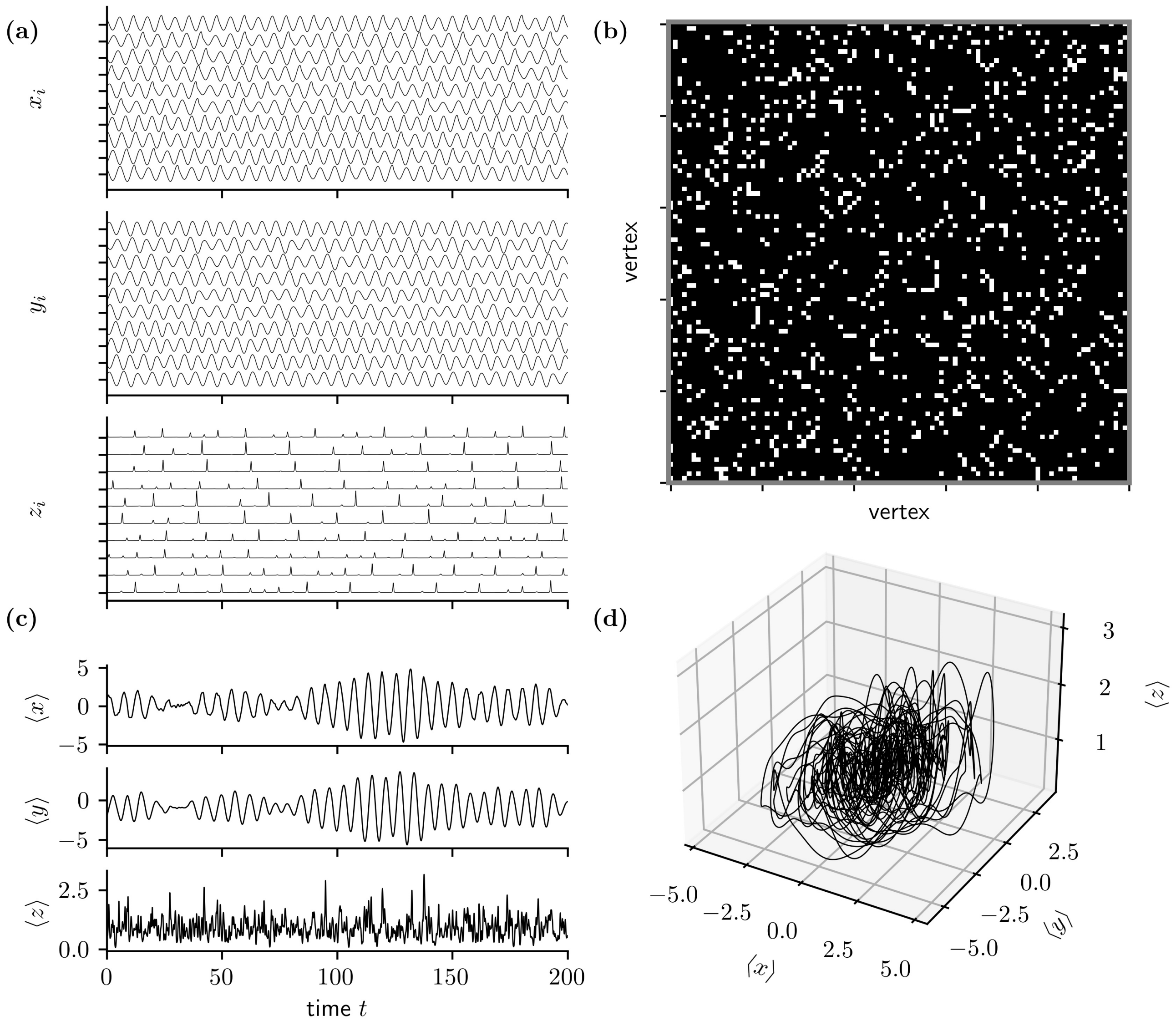

FIG. I.5. Exemplary dynamics of a network of 100 coupled Rössler oscillators. (a) 10 randomly selected time series of dynamical variables x_i (top), y_i (middle), and z_i (bottom) of the oscillators. For visibility, time series are plotted with an offset. (b) Symmetric adjacency matrix representing the bidirectional couplings between the Rössler oscillators. White (black) colored pixel indicate an existing (an absent) coupling between two oscillators. The network has with random coupling topology and two oscillators are coupled with a probability of $p = 0.1$. (c) Time series of the averaged dynamical variables $\langle x \rangle$ (top), $\langle y \rangle$ (middle), and $\langle z \rangle$ (bottom). (d) 3-dimensional projection of $\langle x \rangle$, $\langle y \rangle$, and $\langle y \rangle$. While $\langle x \rangle$ and $\langle y \rangle$ evolve in an oscillatory pattern, $\langle z \rangle$ evolves seemingly erratically. Control parameters of the Rössler oscillators were set to $a = 0.1$, $b = 0.1$, and $c = 18$. Eigenfrequencies ω_i were drawn from a normal distribution $\mathcal{N}(1, 0.05)$ and initial conditions for all x_i, y_i, and z_i were randomly chosen from the interval $[0, 1]$. To generate the time series, Eq. I.2 was integrated with the Dormand–Prince method [DP80] and with a step size of 0.01 for 200 time units after initial transients of 200 time units were discarded.

FitzHugh-Nagumo oscillators

The FitzHugh-Nagumo oscillators was initially designed as a simplification of the Hodgkin-Huxley model for the initiation and propagation of action potentials in squid giant axons [Fit61] but variations of this oscillator found diverse use in model studies in a large number of fields like cardiology [Rap22], social sciences [PV22], or material sciences resp. simulated electronics [BG22] to name but a few. We use a modified version of this weakly non-linear oscillator:

$$\begin{aligned} \dot{x}_i &= x_i(\iota - x_i)(x_i - 1) - y_i \\ \dot{y}_i &= \nu_i x_i + \gamma y_i. \end{aligned} \tag{I.5}$$

x_i is known as the excitatory variable of the i-

th oscillator, while y_i is the inhibitory variable and ι, ν_i, and γ are control parameters. In lieu of an eigenfrequency, we diversify FitzHugh–Nagaumo oscillators via the control parameter ν_i that regulates how strongly the inhibitory variable reacts to the excitatory one. Lower values of ν_i facilitate excitation and short refractory periods. Figure I.6 shows exemplary time series of the dynamical variables of a FitzHugh–Nagumo oscillaor and a state space representation of the system.

When coupled, FitzHugh–Nagumo oscillators can be considered an excitable medium and, as such, are sometimes used to simulate phenomena like wave propagation and excitation on complex coupling topologies [AKLF13, ALF16, Ans16]. For networks of coupled FitzHugh–Nagumo oscillators, Eq. I.5 can be extended to

$$\begin{aligned} \dot{x}_i &= x_i(\iota - x_i)(x_i - 1) - y_i + \widetilde{h}(x_i; x_1, \ldots, x_\mathrm{N}) \\ \dot{y}_i &= \nu_i x_i + \gamma y_i. \end{aligned} \tag{I.6}$$

Here, $\widetilde{h}$ again represents diffusive coupling (cf. equation I.4).

In such systems, excitation is marked by a high-amplitude oscillation[17] of an oscillator induced by a weak input via a coupling. Figure I.7 shows exemplary time series of the dynamical variables of 100 FitzHugh–Nagumo oscillators coupled onto a random coupling topology. Interestingly – and for the correct range of control parameter settings – the diffusive couplings between the oscillators dampen the amplitude most of the time (cf. Figs. I.6 and I.7) with oscillations whose amplitudes compare to the case of an uncoupled oscillator at seemingly random times. These rare, recurring high-amplitude oscillations coincidentally executed by all (or almost all) oscillators can be considered extreme events [AKLF13]. While individual oscillators frequently exhibit such high-amplitude oscillations in a form of *proto-events*, the dynamics only evolve into a full extreme event if a sufficient number of oscillator are excited during a proto-event at the same time. In this case, the rest of the oscillators are recruited to join in generating the extreme event. In Chapter IV, we discuss which and why oscillators are prone proto-events with respect to control parameter settings and local aspects of coupling topologies.

[17] A high-amplitude oscillation is distinguished from other (low-amplitude) oscillation by a maximum value of the dynamical variable x_i during an oscillation that exceeds the maximum values during other oscillations many times over.

b Natural system

Next, we introduce the natural system, we aim to gain a better understanding of.

Perhaps the most complex system in nature known to men, the human brain is a conglomerate of about 86.1×10^{10} neurons and about as many other cells (glia, epithelial and endothelial cells as well as pericytes) [ACG+09]. Depending on type and anatomical location, each neuron is connected to other neurons by between 1 and approximately 200000 synapses (effectively, receivers for incoming electrical activity). Axons (parts of neurons that act as organic cabling between cells) vary in length between approximately 10^{-6} m and 1 m and their total length is estimated to exceed the average distance between Earth and Moon.

From the point of view of spatial organization, networks in the brain are highly interconnected and neither random nor entirely regular, span multiple spatial scales, from individual cells and synapses via cortical columns to (sub)cortical areas. Besides this structural complexity, the brain also supports a enormous number of cognitive and behavioral functions [HY00, EFS01, SS01, VLRM01, MDOD04, BM10, FA11, BAK12, Fre12, RFV12, SDE12]. Typically, these functions are shared among all humans even though differences in morphology and in connection structure are prevalent. Additionally, in the case of brain pathologies, normal and abnormal functions and structures can coexist [SG05, US06, SNV14].

Historically, our knowledge of brain functions originates from observations of subjects with disrupted functions like, e.g., loss of motor control after an injury of the motor cortex or loss of sight due to a damaged visual cortex [Lur62]. A treatise on trauma dated

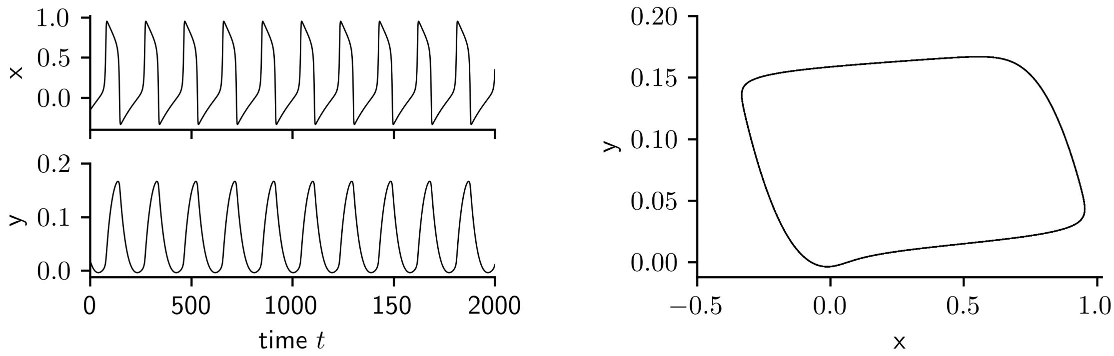

FIG. I.6. Exemplary time series of dynamical variables x (top) and y (bottom) of a FitzHugh–Nagumo oscillator (left) and a 2-dimensional depiction of its corresponding state space (right). Parameter were exemplarily set to $\iota = -0.027$, $\nu = 0.006$, and $\gamma = 0.02$, and initial conditions for x and y were randomly chosen from the interval $[0, 1]$. We dropped indices i for readability. To generate the time series, Eq. I.5 was integrated with the Dormand–Prince method [DP80] and with a step size of 0.1 for 2000 time units after initial transients of 2000 time units were discarded.

to circa 1600 BCE[18] [All05], the so-called Edwin Smith Papyrus, already describes paralysis due to brain injury as well as a connection between the position of a cranial injury and the affected side of the body [ZV61, SB07]. In more recent history, head injuries during the Russo-Japanese War, World War I, and World War II expanded our understanding of brain (dis-)function drastically (e.g., the functional partitioning of visual processes in the occipital cortex [Lan09]) at the cost of a colossal loss of lives.

Fortunately, nowadays, the development of non-invasive (or, at least, weakly invasive) techniques to assess brain dynamics allows for the study of brain function and dynamics in healthy subjects[19]. While there is a small number of theses techniques (e.g., functional magnetic resonance tomography [HSM04], magnetoencephalography [HHI+93], or positron emission tomography [BMTV05]), we concentrate on *electroencephalography* (EEG) in this work as it is the only techniques capable of long term (days to weeks) continuous recordings [Lop93, WDHK+19, VDHG+21].

Electroencephalography measures the aggregated electrical activity[20] of the surfaces layer of the brain as electrical potential differences between sensors placed along the scalp of a subject [TT09, FQ12, SC13]. The placement of sensors is internationally standardized in the so-called 10–20 system (see Fig. I.8). Problematically, EEG is a measurement of electrical potentials without a well defined ground due to safety concerns. While the choice of reference is matter of ongoing debate with various schemes providing different advantages and disadvantages [FRBM88, NSW+97, HNT01, GVN+05, Sch05, YWO+05, ZDS06, GL17b], an EEG sensor can be chosen as reference (unless otherwise noted, the interhemispheric sensor Cz was chosen in this work as to not amplify signals from one hemisphere). Furthermore, movement of facial muscles can significantly interfere with EEG recordings and can produce severe artifacts especially in recordings from pre-frontal brain regions[21].

The first human EEG was recorded by Hans Berger in 1924 [Haa03]. The German psychi-

[18] Terminology and grammar indicate this papyrus to be a copy of an even older text, possibly from the *Old Kingdom* (circa 3000–2500 BCE) [Bre30].

[19] Research into the human brain falls under human experimentation and is as such subject to supervision by research ethics committees and to accordance to the declaration of Helsinki [Wor13]. Use of data from research subjects requires informed consent.

[20] Notably, it is unclear how exactly an EEG signal arises from the electrophysiologic activity of brain tissue [NL05], as it is an inverse problem. Furthermore, important electromagnetic characteristics (e.g., permittivity and permeability) of biological matter are currently impossible to measure, subject specific, and/or generally unknown in vivo [GGC96, FVDMDMH99, AMB+10, LE19].

[21] Sensors sampling these regions are placed atop the forehead and voltage differences are consequentially strongly affected by the electrical activity of the occipitofrontalis muscle.

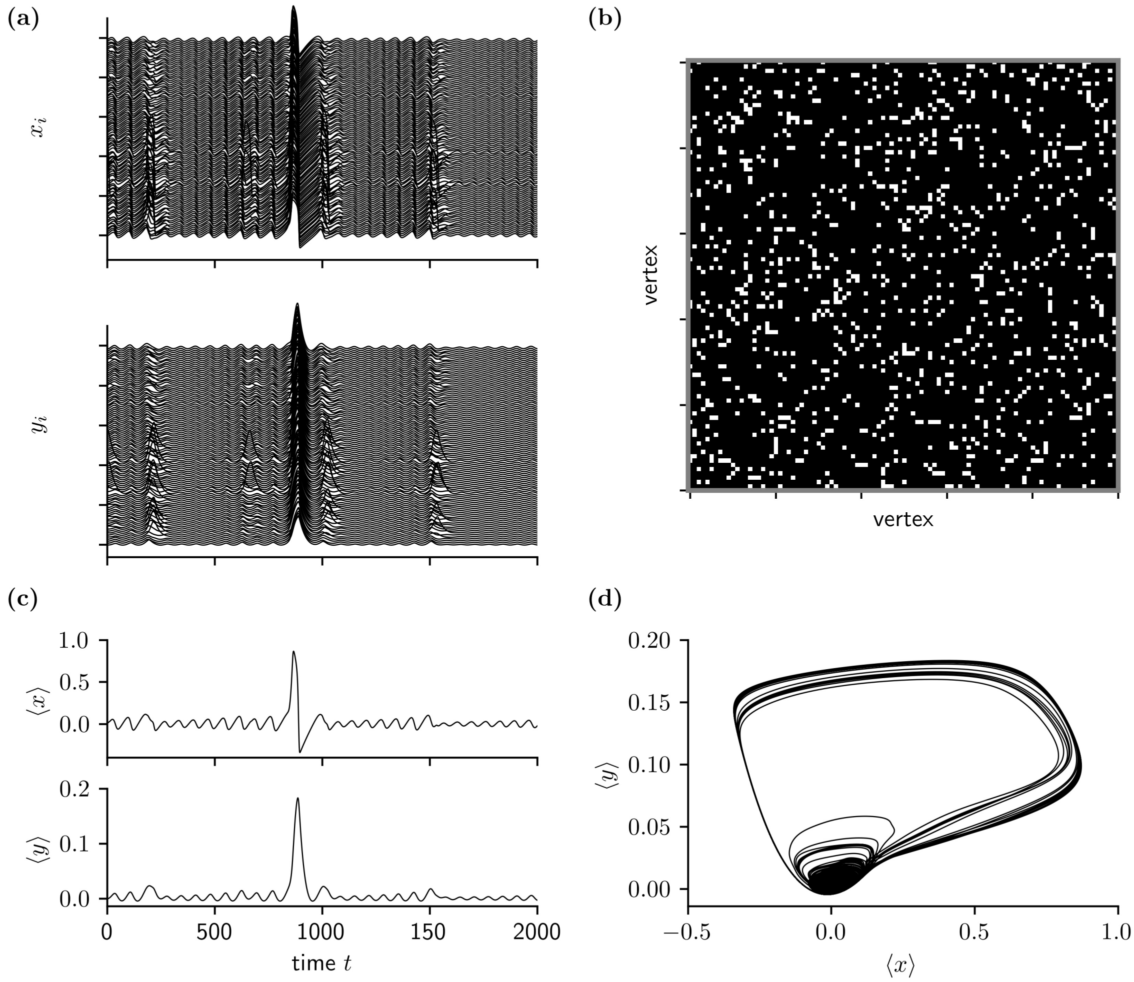

FIG. I.7. Exemplary dynamics of a network of 100 coupled FitzHugh–Nagumo oscillators. (a) Cutouts of time series of dynamical variables x_i (top) and y_i (bottom) of FitzHugh–Nagumo oscillators. For visibility, time series are plotted with an offset and each consecutive pair of ticks along the y-axis frames 20 time series. (b) Symmetric adjacency matrix representing the bidirectional couplings between the FitzHugh–Nagumo oscillators. White (black) colored pixel indicate an existing (an absent) coupling between two oscillators. The network has random coupling topology and two oscillators are coupled with a probability of $p = 0.1$. (c) Cutouts of time series of the averaged dynamical variables $\langle x \rangle$ (top) and $\langle y \rangle$ (bottom). (d) 2-dimensional projection of $\langle x \rangle$ and $\langle y \rangle$ as an approximation of the system's state space derived from the whole length of the time series. Parameter were set to $\iota = -0.027$, $\nu_i = 0.006 + i \cdot 0.00008$, and $\gamma = 0.02$, and initial conditions for x_i and y_i were randomly chosen from the interval $[0, 1]$. To generate the time series, Eq. I.5 was integrated with the Dormand–Prince method [DP80] and with a step size of 0.1 for 20000 time units after initial transients of 2000 time units were discarded. The cutouts of length of 2000 time units are selected to show a rare and recurring high-amplitude event at $t \approx 800$, that is interpreted as an extreme event and of which 17 occurred over the whole observation period.

atrist was also the first to describe the alpha rhythm[22] and thereby had a formative influence on the popular (and sometimes contested) interpretation of EEG signals as signs of *brain waves.*

Besides basic research, EEG is used for medical diagnosis of neurological diseases such as stroke, epilepsy, dementia or brain tumors [LFB$^+$16]. EEG is also auxiliary used to assess the depth of anesthesia during surgery [Pic12, AKRA13].

Intracranial EEG (iEEG) is a decidedly invasive technique to more directly measure electrophysiological brain activity. By implanting sensors within the skull, iEEG cir-

[22] Oscillatory EEG signals in the range of 8–12 Hz, that can predominantly be recorded from the occipital lobe during wakeful relaxation with closed eyes. Amplitudes of alpha waves are reduced when eyes are open or during sleep [MP20].

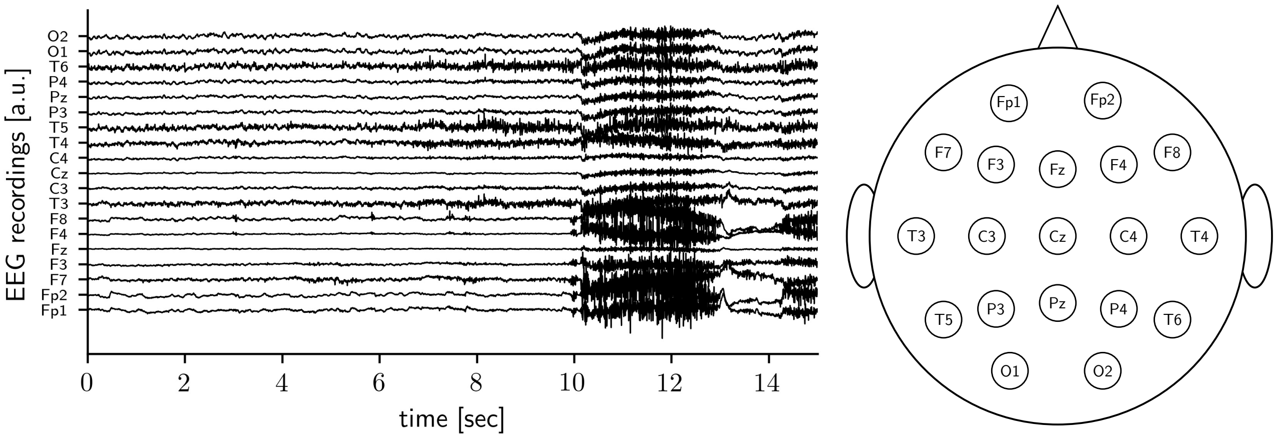

FIG. I.8. Exemplary time series of EEG recordings (left) of a subject suffering from epilepsy and schematic of the location of sensors of the international 10–20 system (right). Time series from different sensors were plotted with an offset for visibility and are 15 sec cutouts from longer recordings acquired during the medical evaluation of the subject's epilepsy. An epileptic seizure begins approximately at the 10 sec mark and continues beyond the length of the cutout.

cumvents some of the problems encountered with scalp sensors (muscle artifacts, skin effect, etc.) increasing signal-to-noise ratios by a factor of ≈ 100 [BKM$^+$09] at the cost of introducing foreign matter to a system as sensitive and essential as the human brain. Typically, the iEEG sensors are either placed directly on top of the cerebral cortex with so-called strip and grid electrodes[23] or within subjacent brain regions with depth electrodes[24]. Due to the inherent risks of intracranially implanting sensors, iEEG is typically only used as a diagnostic tool for, e.g., pre-surgical evaluation for epilepsy surgery [RL01]. Accordingly, number and anatomical location of intracranial sensors are solely adapted to the individual subject's needs and are highly non-uniform.

2. *New methods*

Next, we briefly introduce new and unconventional methods for investigating aspects of time-evolving functional networks.

a Identifying dynamical regimes

To classify the dynamics of spatially-extended, complex systems, we do not identify dynamics via measuring information content [Sha48], spectral energy densities [Boa92], attractor geometry [KS03], or other commonly employed pattern identifying schemes. Instead, we utilize the dynamical coupling structure (cf. Sec. I B 2 and function $\mathbf{h}\left(\epsilon, \mathcal{M}; \mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_{\mathrm{N}}\right)$ in Eq. I.1), which we probe in a time-resolved manner with an estimator for the strength of interactions between each pair of time series data. Following Münnix et al. [MSS$^+$12], we then check for recurrences of this structure in time. We identify recurring patterns of the dynamical coupling structure as dynamical regimes of the system. Contrariwise, we consider the self-dynamics of the elementary units themselves to be stationary and interactions (and their underlying couplings) to change with time.

Technically, this can be achieved by identifying recurrences of snapshot networks in a sequence of functional networks either with a recurrence plot and an appropriate recurrence threshold [EOR87] or by clustering the weight matrices representing the snapshot networks with a cluster algorithm (e.g., k-means algorithm [Mac67]). Problematically, the number of recurrent patterns – i.e., the number of dynamical regimes in the system – is typically

[23] Frames with 4, 8, 8×4, or 8×8 sensors with an inter-sensor distance of 10 mm.
[24] Typically, poles with 8 or 10 cylindrical sensors with an inter-sensor distance of 4 mm.

a priori unknown and might not be uncovered even by a thorough preliminary investigation. In such cases, a hierarchical clustering algorithm might at least provide a range of numbers of dynamical regimes, for which the classification method procures comparable results. Finally, each dynamical regime can be described by an average weight matrix (i.e., the centroid of its cluster representation).

Dynamical regimes derived from time series of stock returns have been shown to relate to emerging financial crises [MSS$^+$12] and those derived from iEEG time series to emerging epileptic seizures and to other brain activities like sleep (Chapter VI). Generally, the existence of identifiable dynamical regimes in the dynamics of a system indicates a recurrence of the dynamical coupling structures and internal strengths of interaction – i.e., elementary units of the system react to each other in various but recurring ways.

b Estimating dynamical resistance as a proxy for resilience

Resilience is a notoriously ill-defined catch-all term for all properties of a system that allows the system to maintain its current functions and operations under any endogenous or exogenous stress. Probably most broadly defined as "the capacity of a system to absorb disturbance and reorganize while undergoing change so as to still retain essentially the same function, structure, identity, and feedbacks" [WHCK04] (see also [Hol73]), methods to characterize resilience of a system utilize various approaches from bifurcation theory [Sey09], stability and perturbation theory [Lya92, Nay11], statistical physics [Tab19], non-linear time series analysis [KS03, LLM15], ecology [Wis84, SF21], or economics [QR65, Tay15] among others. However, methods are usually dependent on intimate knowledge of the system's equations of motion or of its responses to perturbation.

If the system's equations of motion are unknown and perturbation experiments are either impractical, dangerous, or unethical (e.g., a power network at risk of a blackout or a human brain at risk of death), the number of available methods drastically declines.

To the best of the author's knowledge, there are currently two methods available to evaluate resilience of a system from time series data that are either based on changes in the variance of time series due to *critical slowing down* [DSvN$^+$08, SBB$^+$09] or on changes in the dynamical coupling structure as exploited by *dynamical resistance* (Chapter VI).

Conceptionally, critical slowing down is a property of a saddle-node bifurcation (see, e.g. [Cra91, Wis84, SBB$^+$09, BH13, DCvS15, MS16, DJ10, HWS$^+$21]). Briefly, in the case of such a bifurcation, a potential wall separating two equilibrium states (one preferred, one adverse) decreases with the change of some control parameter, which in turn weakens the restoring force affecting a system in the preferred state under some weak perturbation. As a consequence, the rate of recovery of the preferred state decreases. Before the critical transition between the preferred and the adverse state, then, the variance of the related state variable increases, which is interpreted as a loss of resilience[25] [Kub66]. However, for many real world systems, this ansatz has proven to be too simplistic. Careful analyses of some real world systems for which loss of resilience is postulated has indicated no or even opposite phenomena to critical slowing down (i.e., critical speeding up) [WRL19, RCR17]. Especially, resilience in multi-stable systems with various states representing normal functioning with innocuous transitions can not be described by critical slowing down alone.

For dynamical resistance, we return to Eq. I.1 and reinterpret the equation from a different point of view:

$$\dot{\mathbf{x}}_i = \mathbf{f}_i(\mathbf{x}_i) + \mathbf{h}\left(\epsilon, \mathcal{M}; \mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_\mathrm{N}\right).$$

Instead of reading the dynamical coupling structure $\mathbf{h}\left(\epsilon, \mathcal{M}; \mathbf{x}_i; \mathbf{x}_1, \ldots, \mathbf{x}_\mathrm{N}\right)$ as the inter-

[25] Other markers for a loss of resilience concomitant with critical slowing down are an increase in the integrated power spectrum of the state variable resp. a larger zero-crossing time of the state variable's autocorrelation function. However, changes in the variance of a variable are related to changes in the variable's Fourier spectrum by Parseval's theorem and the spectrum, then, are related to the variable's autocorrelation function by the Wiener-Khinchin theorem. Accordingly, the three typically proposed markers of critical slowing down are highly correlated.

action between the system's elementary units, we now interpret $\mathbf{h}$ as a perturbation acting upon the self-dynamics $\mathbf{f}_i(\mathbf{x}_i)$ of the units. However, at the same time, we neglect the self-dynamics and concentrated on differences in the relative strength of perturbation over time as a proxy for the system's resilience. In practice, we sort the dynamics from some time span of intermediate length to different dynamical regimes as described above. The Euclidean distances between regimes' average weight matrices, then, is proportional to the strength of perturbation, which the system can absorb by switching between regimes representing the system's normal (preferred) states. A large distance indicates a high capability of the system to absorb disturbance and reorganize, i.e., a large resilience.

D. Structure of this thesis

In Chapter II, we investigate if and to what extend the structural organization of a coupling topology – here connecting Rössler oscillators – can be revealed from strength-of-interaction estimates from time series of the system's dynamics.

Subsequently, in Chapter III, we explore the relative merit of partialization techniques to weaken the effect of indirect couplings resp. transitivity. We do this at the example of a pairwise and a partialized phase-based estimator for the direction of interaction in systems of directionally coupled Rössler oscillators and in the human brain.

Chapter IV, then, illustrates how topological properties of vertices can affect the dynamics of the corresponding elementary units and of the system as a whole. Specifically, we show the influence of the degrees of vertices on the generation and spreading of extreme events in a system of coupled FitzHugh–Nagumo oscillators.

In following Chapter V, we provide evidence that changes in local network characteristics of evolving networks are entwined with changes in the collective dynamics of the underlying system – in this case the human brain. We identify precursor states of epileptic seizures as an elementary step to understand and eventually predict the genesis of these harmful events.

Finally, in Chapter VI, we introduce a novel measure for the evaluation of resilience of complex extended dynamical systems – dynamical resistance – and provide evidence for the utility of the measures again at the example of the human brain.

This thesis is closed with a short summery of the conducted research, an outlook, and concluding remarks.

II Synopsis of "Network structure from a characterization of interactions in complex systems: possibilities and limitations"

Thorsten Rings, Timo Bröhl, and Klaus Lehnertz

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The functional network approach – reducing a spatially-extended, complex system to vertices (representing the system's elementary units) and edges (interactions between units) via the data-driven estimation of properties of interactions – has been recognized as a useful tool in the investigation of various systems in nature. This approach has been successfully employed in, e.g., the study of the human brain [BS09], climate systems [DZMK09a, ZGAH15], protein-protein interactions [UGC+00], gene interactions [TAWM09], plant-pollinator interactions [HNL+09, OBD+11], food-webs [DBB+19], or communication and social networks [OSH+07, PBV07].

Often, a functional network is assumed to be a proxy of the underlying coupling structure of a system when this coupling structure (or structural network) can not be sufficiently accessed, e.g., without damaging the system or due the system's scale. Then, the functional network – instead of the structural one – is investigated with methods from graph theory designed to reveal information about aspects of the system's internal organization by means of characterizing the network's topological and spectral properties or key constituents. However, revealing the structural network – the system's coupling topology – from a functional network is an inverse problem and might not have a unique solution. A large number of previous studies investigated the limits of identifying a structural network's edges from a corresponding functional network [MZL17, Tim07, LP11, ST11, WLGY11, PDG12, CLL13, LP14, TC14, CLL15, Pik16, WLG16, CNHT17a, Lai17, NCT17, Pei18, Pik18, STŽ+18, LLTŽ19, PCL+19, Pei19, AdCEG20, FRCM20, CP+21, RMBM+14, TSEBM15, BMRAB16, LMK16, LKT17, MHM+17, CMT18, HD19, LMM+19, GMCR20, FOTMP21] and reported a good – but not perfect – performance. However, since failure to correctly identify even a single edge can drastically alter the appearance of a structural network (topologically, the difference between, e.g., a line and a ring of coupled units is just one edge), it is still an unsolved issue if and to what extend properties of functional networks match those of the corresponding structural networks.

In the present article, consequently, the authors investigate the extend of this match of properties – an unusual approach to the intricate task of comparing networks (for other methods see, e.g., [BBK06, AMPL08, MHVD09, Mém11, DDSA16, MWH20]) – on two different scales: the global scale encompassing the whole network and the local scale of single network constituents (vertices as well as edges). For this purpose, Thorsten Rings simulated – as ground truth –the dynamics of complex networks of bidirectionally coupled Rössler oscillators [R7̈6, RL12]. These oscillators are a weakly nonlinear and, as a simplified model of the Lorenz attractor, are used to model a large variety of systems including lasers and electrical circuits, to name just a few. In addition, Thorsten Rings coupled the aforementioned oscillators onto an empirical network, namely the fully identified neuron network of the nematode P. pacificus [BRRS13]. For these networks, he generated time series of the dynamics of the oscillators and derived functional networks employing different time series analysis techniques (an amplitude-based one and a more general one based on entropy). For a number of factors that modify the oscillators' dynamics, he investigated the degree of concurrence between global properties as well as local vertex properties of structural and functional networks. Timo Broehl did the same for local edge properties [BL19].

Surprisingly, the authors of the present article observe that especially key constituents of functional networks coincide with ground truth. Both, concurrence between the rank order of constituents from structural and functional networks as well as the concurrence between their most central constituents (largest centrality values) clearly exceed chance levels – at least for weak to intermediate coupling strengths; too weak or too strong coupling strengths lead to either independently oscillating or indistinguishable dynamics, which do not allow for conclusions to be drawn about the structural makeup of the system. Global network characteristics of functional networks on the other hand clearly deviate from ground truth independent of factors impacting the dynamics.

The authors conjecture that an extension of the employed pairwise ansatz to characterize properties of interactions (e.g., based on partialization methods [Dah00, BS01, EDS03, CRFD04, SWE+06, PKKD13, KPR14, PKL14, MHD16]; see next chapter) together with Monte-Carlo-based techniques to minimize faulty concurrences [AL11, AL12, KDGBT12, ZGC12, RA13, FLPA15, SMG15, SL17] could help to enhance the detection of correspondences between structural and functional networks. Finally, the authors imagine that characterizing properties of networks on a mesoscopic scale [Alo07, KGH+10, GSH12, FZB15, EA16, FH16, BL19] and the tracing of time-dependent changes of networks [HS12, DDSRC+13, BBC+14] will add to understanding the relationship between structure, function, and dynamics of complex systems.

III Synopsis of "Distinguishing between direct and indirect directional couplings in large oscillator networks: Partial or non-partial phase analyses?"

Thorsten Rings and Klaus Lehnertz

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Transitivity is a problematic effect often encountered in the study of spatially-extended, complex dynamical systems [AHD18]. It describes the indirect influence an elementary unit of a system can have on another unit, which is not coupled to it. This influence is thought to be mediated by another, unobserved unit assumed to be coupled to both the first and the second one. When utilizing time series analysis techniques– e.g., to derive functional networks from recordings of system dynamics –, such indirect influences can lead to an overestimation of various properties of interaction, which in turn can lead to misinterpretations regarding the internal organization of the investigated system. Especially sensitive to this effect is the notoriously intricate estimation of the direction of an interaction.

Various methods to handle transitivity based on partialization analysis have been proposed in the past [Dah00, BS01, EDS03, CRFD04, SWD+06, SWE+06, FP07, SB09, VKM09, NRT+10, ZRT+11, RHPK12, SWPM12, BDBTS13, Kug13a, Kug13b, LPD+13, PKKD13, REI+13, ESTS15, FKN+15, MMT+15, Run15] with the central idea of conditioning the estimators for properties of interactions between two units on a third, possibly interaction-mediating unit. More recent to the publication of the present article, Kralemann et al. [KPR14] proposed a novel phase-based time series analysis technique to estimate direction of interaction – called partial triplet approach (PTA) – as an extension to a previously introduced estimator [RP01] – called evolution map approach (EMA) – by incorporating the partializaiton method. While the PTA already showed promising results [KPR14, STMS15] in small networks of phase oscillators, it remains unclear to what degree this approach also qualifies for a data-driven analysis of larger networks with hundreds of vertices or more.

To investigate suitability of the partialized approach in large networks, Thorsten Rings simulated – as ground truth – the dynamics of complex networks of bidirectionally coupled Rössler oscillators [R7̈6, RL12]. For these networks, he generated time series of the dynamics of the oscillators, and from these time series, he derived weighted, directed networks with both the EMA and the PTA. He, then, investigated the relative merit of the PTA over the EMA for several factors that modify the oscillators' dynamics – especially, network size as well as additive and multiplicative noise contaminations. To also assess the two approaches' suitability in an empirical example, he furthermore derived directed, weighted functional network from a multichannel, multiday intracranial electroencephalographic recording of human electrical brain activity,

For the simulated systems, Thorsten Rings compared the derived functional networks with the ground truth of existing or non-existing directional couplings with a threshold approach. For the empirical system, he evaluated the two approaches with directionality indices and identified the amount of congruent indications of the same direction from both approaches. The latter evaluation was based on the assumption that a complex system like the human brain should – at least to some degree – exhibit indirect interactions. If the PTA indeed improves the EMA when handling indirect interactions, the findings achieved with the PTA should provide an improved characterization of the system's directed couplings by deviating from the findings achieved with the EMA – otherwise, there is no relative advantage of the partialized approach over the pairwise one when investigating the directions of interactions in the human brain.

The authors observe that coupling strength as well as network size influence to what degree directed couplings can be identified from the weighted and directed functional networks. Too weak coupling strengths lead to independently oscillating dynamics for which direction is basically randomly assigned, while too strong coupling strength lead to basically indistinguishable dynamics. Since estimators of direction of interaction, however, exploit differences in the time evolution of elementary units, both cases results in no reliable indication of direction. A larger network size, on the other hand, drastically impairs the ability to identify directed couplings and only in small networks (number of vertices $\leq$ 10), the PTA performs better than the EMA by a small margin. For larger systems, the pairwise approach even overtakes the performance of the PTA. However, both approaches diminish in performance due to an increased number of couplings per elementary unit. For the PTA, this effect is more severe, since the uncertainty about which third unit the estimator should be conditioned on increases with the number of units. Interestingly, both types of noise affects both estimators' performance roughly the same way and, for the sensitive intermediate range of coupling strengths, the estimators are resistant against noise contaminations up to noise-to-signal ratios of 0.1.

For the empirical system human brain, the EMA and the PTA predominantly indicate the same directions in spite of the high physiological variability that is to be expected when observing brain activity over longer periods. This indicates an inability of the PTA to consistently handle the expected transitivity in this system.

The authors conclude that partialization methods do not improve the performance of time series analysis techniques to estimate properties of interactions in larger (number of elementary units $>$ 10) systems and point to similar findings with other techniques extended with partialization methods [MFL+08, JK11, ZFLH14, REI+13, Kug13a, HKKN11, RMBM+14]. The authors also note that while the inverse relationship between estimator performance and number of elementary units can, in principle, be balanced by increasing the length of the time series [SB09, RMBM+14], this often invites other adverse effects due to, e.g., non-stationarity. Finally, the authors project that methods [PR13, SWF+14, ZMD15, TB16] exploiting the sparseness of couplings of many real world systems might prove helpful for distinguishing direct and indirect couplings in the future.

IV Synopsis of "How important are hubs for the generation of extreme events in networks of excitable units?"

Thorsten Rings, Gerrit Ansmann, and Klaus Lehnertz

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Extreme events are well-known phenomena in various natural and man-made systems, whose exact mechanisms are often beyond current understanding. Defined as a rare, recurrent, but drastic deviation of a system's dynamics from its otherwise typical behavior [CGUF15], extreme events commonly have strong and harmful consequences for the systems in which they occur and can be a strain on human security and interests. Examples include earthquakes, tsunamis, extreme weather events, wars, market crashes, large-scale blackouts in power-supply networks, and epileptic seizures in the human brain (see, e.g., [Hob94, BKS02, Sor03, AJK06, GYH+11, WMGT+13]). Capturing early warning signs of – or even controlling – these events in many scenarios is a currently unsolved problem whose solution might strongly depend on an improved understanding of the generation mechanisms of extreme events.

A growing interest into whether and how the coupling structure of a spatially-extended, complex system influences the emergence of extreme events in such a system (see, e.g., [KSA11, RL11, KSA12, AKLF13, KSS13, BBB+14, CHL14, LGB+14, Xia14, HMSK15, ALF16]) motivated the authors of the current article to extend this line of inquiry and to investigate the influence of local network properties on the generation of extreme events. For this purpose, Thorsten Rings simulated networked dynamics of coupled FitzHugh–Nagumo oscillators [AKLF13, KAFL14, ALF16], thereby mimicking excitable media with diffusion-like transport processes between adjacent oscillators. Here, excitation is characterized by a high amplitude oscillation which is followed by a refractory period that suppresses the excitation. The oscillators' control parameters were chosen such that the collective dynamics exhibited rare, recurring high-amplitude oscillations, i.e., extreme events. Oscillators had a refractory period of different duration and were coupled onto a scale-free network [AB02]. This topology is characterized by a small number of strongly interconnected vertices (the core) surrounded by low-degree vertices (the network's periphery). The core mostly consists of hubs, i.e., vertices with high degree, here representing oscillators with many couplings. The scale-free topology is also thought to be commonly encountered in nature and is often associated with phenomena such as growth, structural resilience, and extreme events [AB02, Cal07, Bar09, KSA11, ZL13, LKLK15].

For various numbers of elementary units and with the guidance of Gerrit Ansmann, Thorsten Rings generated time series of the oscillators' dynamics and identified their associated vertex degrees. As a next step, he singled out the extreme events in the time evolution of the (explicitly stationary) oscillator dynamics and, with high temporal resolution, traced the excitation of the single oscillators during such events.

In a joint effort, the authors observe that both the control parameters and the vertex degree of an elementary unit provide information about the role the unit plays in generating extreme events. The authors also observe that especially the units associated with low-degree vertices are responsible for the initiation of the extreme events. This result is notably surprising considering that scale-free networks are renowned for the small amount of strongly interconnected, high-degree vertices (the hubs, which are typically deemed important for associated dynamics). The latter, according to the authors observations, only act as facilitators of the spreading of excitation that results in an extreme event. They are, however, never involved in the initial generation of the events.

The authors conclude that warning signs of upcoming extreme events might be more likely to be encountered in a wide-scale observation of a system's less strongly interconnected elementary units. This is in stark contrast to the often-employed approach of observing only the dynamics of the hubs to gather information about the system's collective dynamics. Control of a system, then, might include a minimal perturbation [KSS13, CHL14] of peripheral units or a pinning of states of such peripheral units.

V Synopsis of "Precursors of seizures due to specific spatial-temporal modifications of evolving large-scale epileptic brain networks"

Thorsten Rings, Randi von Wrede, and Klaus Lehnertz

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Epilepsy is one of the most common neurological disorders affecting approximately 65 million people worldwide. It is intractable with anti-epileptic drugs in roughly one third of people suffering from epilepsy [KSB11] and has a highly negative impact on the quality of live of the affected people. A severe factor of the burden of epilepsy is the apparent unpredictability of epileptic seizures – sudden surges of abnormal and excessive electrical activity in the brain that can affect motor and cognitive functions. Consequently, the field of seizure prediction aims to predict the onset of seizures ahead of time to improve quality of life for people suffering from epilepsy – e.g., by enabling them to take countermeasures before an upcoming seizure – and to improve treatment options with methods that anticipate an upcoming seizure to deliver on-time treatments. In addition to the immediate value of identifying precursors of seizures, understanding the underlying mechanism that allows the seizure to occur, or at least identifying changes in the dynamics of elementary units – i.e., brain regions – associated with that mechanism, have value on their own and might lead to new treatment options for epilepsy [LDP+16].

From a physics point of view, epileptic seizures fulfill the criteria for extreme events: they are a rare and recurrent deviation of the system's dynamics from its average behavior. The brain region whose dynamics shows the first such strong deviation is typically deemed the seizure onset zone (SOZ), which was long thought to be an initiator of a seizure. However, a number of previous studies on the predictability of seizures with an identifiable SOZ reported time evolution of interactions between brain regions distant to the SOZ to carry relevant, predictive information [LDP+16, MKR+05, DVE+05, KVS+05, LSN+05, BMJB09, KFL+10, FSS+11, BSM+12, PDG13, LD15]. These results led to the concept of an epileptic brain network [BZM+98, Spe02, Ric10, KC12, Lau12, LAB+14] responsible for the generation of seizures.

Employing this concept, the authors of the present article conceived a research project to investigate possible precursors of epileptic seizures in the time evolution of local network characteristics – vertex centralities – of time-evolving functional brain networks. Randi von Wrede provided guidance in clinical research, while Klaus Lehnertz supervised the research. Employing a moving window approach, Thorsten Rings derived the functional networks from multichannel, multiday intracranial electroencephalographic recordings of human electrical brain activity from a large number of people suffering from epilepsy. In each time window, he estimated the strength of interaction between the dynamics of each pair of brain regions to derive weighted functional networks and calculated their local characteristics (strength centrality and betweenness centrality) for each vertex (i.e., the sampled brain region). Next, Thorsten Rings separated data from the resulting sequences of the local characteristics for each vertex into two distributions: data from a 4 h period preceding seizure activity during which precursors are assumed to occur (pre-ictal time span), and data from time spans temporally distant from seizure activity during which brain activity is assumed unrelated to seizure activity (inter-ictal time span).

Using advanced statistical techniques (non-parametric tests and Monte-Carlo methods), the authors of the present article observe that prior to the majority of seizures the pre-ictal local network characteristics of some few vertices clearly deviate from the inter-ictal ones. These vertices are exclusively associated with brain regions outside of the clinically defined seizure onset zone. The authors also observe that precursor-carrying vertices are typically connected by edges whose weight alterations also carry predictive information as already reported on earlier [LDP+16]. Together, the findings indicate a redistribution of edge weights, which reveals a backbone-like structure in the investigated functional brain networks. This structure, which consists of only a few vertices and associated edges, appears resistant against pre-ictal changes of the network as these changes modify the rest of the network and shift associated shortest paths toward a few backbone-associated brain regions distant from the SOZ. There these paths form bottlenecks.

Based on their findings and together with previous research [MAEL07, KLR+18, GLMG16], the authors of the present article propose a model for the generation of seizures in epileptic brain networks, which interprets the observed pre-ictal changes of functional brain networks as possible components of a mechanism of seizure generation. Changes of the functional brain networks appear to begin hours before the seizure but not at vertices associated with the seizure onset zone, with effects on electrical brain activity near the SOZ becoming more pronounced as the seizure onset approaches. The proposed model puts into perspective the role of SOZ in seizure generation in an epileptic brain network – the SOZ appears like a weak spot that breaks first when the rest of the brain is putting it under increasing strain. The authors subsequently hypothesise that control techniques that aim at the spatial and temporal emergence of seizure precursors [HCHB08, NAK+18] combined with novel approaches to track changes in resilience of evolving epileptic networks (see next chapter) represent promising avenues for further research.

VI Synopsis of "Traceability and dynamical resistance of precursor of extreme events"

Thorsten Rings, Mahmood Mazarei, Amin Akhshi, Christian Geier, M. Reza Rahimi Tabar, and Klaus Lehnertz

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Extreme events are rare, (apparently) unpredictable strong deviations from the average behavior of complex systems. They can critically determine the evolution and character of a vulnerable man-made or natural system [BKS02, Sor03, AJK06, FBS+12, Hel13, Buz17] and can have disastrous consequences for such systems. Well-known examples include heat waves, floods, earthquakes, epileptic seizures in the human brain [Leh06], meltdown of nuclear power plants [CFA+11], and large-scale blackouts in power supply networks [AAN04, BPP+10].

Together with progress in the identification of precursors of extreme events [MSS+09, SBB+09, SCL+12, BH13, KZG15, KVADR+15, LCAC15, JREM17, LHCZ17, KLR+18] (see also chapter V), a current research focus is the development of strategies for adaption, mitigating, and avoidance of such events. For such strategies to be effective, however, knowledge about possible time-dependent alterations of stability and resilience of a system is indispensable. However, the continuous, data-driven monitoring of such system properties remains a problem for which there currently are no satisfactory solutions.

Motivated by this issue, the authors proposed a novel, data-driven approach allowing to measure the so-called dynamical resistance – a proxy for resilience. Thorsten Rings, Reza Rahimi Tabar, and Klaus Lehnertz developed the underlying theoretical concepts with support of Mahmood Mazarei and Amin Akshi. Thorsten Rings with support of Christian Geier implemented the approach and carried out all investigations.

For dynamical resistance, interactions are assumed to be endogenous perturbations upon the dynamics of a system's elementary units. Thus, the authors concentrated on differences in the relative strength of perturbations over time as a proxy for the system's resilience thereby neglecting the units' self-dynamics. A system's current state, then, is defined by its current strength-of-interaction-based, weighted functional network (i.e., its snapshot network), and the time-evolution of the system's state is encoded in its sequence of snapshot networks (i.e., the system's time-evolving functional network). Hence, system states are identified employing a hierarchical clustering scheme, which sorts the snapshot networks to one of several so-called dynamical regimes – the number of dynamical regimes is assumed to be system dependent. Finally, dynamical resistance is defined as the smallest Euclidean distances between the matrix representations of the different dynamical regimes and acts as a worst-case estimate of the system's resilience.

To illustrate the approach, Thorsten Rings investigated whether resilience of the human epileptic brain changes prior to epileptic seizures. Intuitively, one would expect a weakening of resilience in order to facilitate the generation of a seizure. Employing a moving window approach, he derived sequences of functional networks from multichannel, multiday intracranial electroencephalographic recording of electric brain activity from a large number of people suffering from epilepsy. In each time window, he estimated the strength of interaction between each pair of brain regions to derive weighted functional networks. From the sequences of functional brain networks, he derived sequences of dynamical resistance for each subject.

The authors observe an influence of day and night (possibly related to the circadian rhythm) on dynamical resistance with it being higher during the night, as expected. Using advanced statistical techniques (non-parametric tests and Monte-Carlo methods), the authors also identify changes in dynamical resistance prior to seizures, that might serve as seizure precursors. These changes, however, appear counterintuitive at first glance. Prior to the majority of investigated seizures, the authors observe dynamical resistance to increase.

The authors explain this finding as a possible consequence of the investigated types of epilepsy – subjects suffered from seizures that could not be controlled sufficiently with anti-epileptic drugs – and they speculate that the relative (in-)effectiveness of treatments might be related to this increase. They further hypothesize that control schemes for epileptic seizures or other extreme events may benefit from estimations of a system's resilience and stability to determine how and when to apply control to a system. The authors also note limits of the proposed approach – e.g., a comparably high demand on the number of data points or the typically a-priori-unknown number of dynamical regimes. Finally, the authors point out that the only other technique that is thought to estimate resilience in a data-driven way, namely the time-resolved analysis of variance exploiting the concept of critical slowing down [DSvN+08, SBB+09], is only suitable for low-dimensional systems with simple critical transitions.

VII Summary, Outlook, and Concluding Remarks

Various spatially-extended, complex dynamical systems in nature exhibit phenomena that drastically affect and shape our world. Examples include synchronization in diverse systems from clocks over cardiac pacemaker cells to applauding audiences [PRK01], extreme events like epileptic seizures in the human brain [LGRS17] or extreme weather conditions in the climate system [AJK06], and spreading of diseases in social systems [New02b]. Understanding these systems and their phenomena, however, is often an arduous task due to the systems' eponymous complexity [Pro88, vK99, Wil02, AO04, HSA06, HDL17, Fie21]. In particular, the rich interplay between a system's structural organization, its functional relationships, and the individual as well as collective dynamics of its elementary units is only partially understood – especially if these aspects change with time.

In this thesis, we assessed the time-evolving functional network approach devised to facilitate the understanding of such complex systems, and we evaluated the approach's suitability for field data analysis. To this end, we explored changes of time-evolving network characteristics accompanying various dynamical phenomena of interest exhibited by system dynamics including transitivity [AHD18], extreme events [CGUF15], and changes in resilience [SCF+01]. Specifically, we investigated paradigmatic model systems with well-known constraints such as coupling strengths, coupling topologies, number of elementary units, and several noise contaminations. Furthermore, we investigated a natural complex system which exhibits rich dynamics and supports a large variety of functions and dysfunctions: the human epileptic brain. We provided novel insights into the aforementioned interplay between a system's structural organization, its functional relationships, and the individual as well as collective dynamics of its elementary units. We furthermore developed a non-perturbative, data-driven approach to evaluate a system's stability against endogenous and exogenous perturbation based on pooled characteristics of edges (i.e., strengths of interactions between elementary units).

In the following we recite key results of this thesis.

Interpreting a functional network is mostly based on the assumption that properties of interactions reflect the coupling structure of the system from which the network is derived. However, retrieving the coupling structure from observations of the dynamics of units can be regarded an inverse problem. Consequently, as a preliminary investigation, we checked if and to what extent at least the organization of a coupling structure can be revealed from properties of interactions estimated from time series of the system's dynamics.

Advantageously, especially local network characteristics (rank orders of centralities and most central constituents) of functional networks indeed reflected those of the underlying coupling structures to a large extent. On the other hand, most global network characteristics of functional networks differed substantially from ground truth.

Nevertheless, global network characteristics have been successfully employed to describe and characterize climate [TR04, DZMK09a, ZFLH14], geo-physical [PSH15, AS06, HSP15, CIK+19], and economical systems [HH18] among others. These characteristics have also been extensively employed in the neurosciences (see, e.g., [BS09, BFPS+13, LGRS17]), and they are capable of tracking changes in the organization of interactions within a system induced by perturbations [RVWB+21, HRB+22, vWRS+21, vWBR+22]. These characteristics resp. their changes, however, can currently not be directly mapped to the underlying coupling structures of the systems.

Explaining some of the difference between functional networks and coupling structures, transitivity is one of the prominent difficulties encountered when estimating properties of interactions. Often, it is problematic to distinguish a direct interaction between a system's elementary units (unit i is coupled with unit j) from an indirect one (unit i is not coupled with unit j, however, both are coupled to a third unit k, which mediates interactions). This typically leads to an overestimation of properties of interactions between units, and the concept of partialization is often considered an answer to this issue. By effectively conditioning an estimator for a property of interaction between two units on a possible third, mediating unit, partialized estimators are considered to be more robust against transitivity.

However, at the example of estimators for the direction of interaction – the evolution map approach [RP01] and its partialized extension [KPR14] – used to identify the direction of couplings in directed networks of coupled oscillators, we observed that the partialized approach only outperforms the non-partialized one for small systems (number of elementary units $\mathrm{N} \leq 10$). In larger systems (here, 20 or 100 units), this small improvement vanishes. Furthermore, in an exemplary natural system (dynamics of the brain of a subject suffering from epilepsy), estimates of the direction of interaction between units (here, sampled brain regions) did not differ substantially when using either the partialized or the non-partialized estimator.

Similar findings have been reported with other partialized estimators (e.g., partial correlation [MFL$^+$08, JK11, ZFLH14], renormalized partial directed coherence [REI$^+$13], partial transfer entropy, and conditional Granger causality index [Kug13a]). We hypothesize that the predominant difficulty with partialization is the question on which third unit in a larger system estimations should be conditioned. When a system is composed of many elementary units, a potential third unit is much harder to correctly identify compared to the case of a system of only few units. Consequently, in large systems, it is more probable to condition an estimator on an uninvolved unit, impairing the characterization of properties of interactions instead of improving it.

Next, we showed that local network characteristics are indeed related to the role of elementary units in the emergence of global system dynamics in networks with complex coupling topologies. Specifically, we investigated the generation and spreading of extreme events – rare and recurrent abnormally large amplitude values – in scale-free networks of coupled FitzHugh–Nagumo oscillators.

In these systems, we were able to show that extreme events originate from vertices with low vertex degree[26]. High-degree vertices (in various contexts also called hubs), on the other hand, act as a facilitator for the spreading of an extreme event, while their large number of diffusive couplings dampen their ability to initiate an event themselves. The larger the vertex degree, the stronger the trend of the associated unit's dynamics to an effectively averaged (and typically non-extreme) dynamics of the units coupled to it. In this sense, low-degree vertices have more leeway to deviate and, possibly, to exhibit extreme motion. Then, if enough low-degree vertices do exhibit such an extreme motion, the high-degree vertices follow and spread the extreme event to the remaining vertices.

Similar indications of the importance of low-degree vertices have been reported for dynamical robustness with respect to node removal [TMA12], noise [BGP$^+$13], or signal generation and transmission in recurrent networks [JMT14] as well as for dynamical impact on long-term time evolution [QAS13]. More recently, Ray et al. [RBM$^+$22] observed similar findings for extreme events in oscillator networks with repulsive couplings. Ironically, these observations indicates that controlling vertices with low vertex degree – which are often deemed *less important* [LMM$^+$17] – might be more suitable for the prevention of extreme events than controlling hubs.

Contrasting these findings from static networks, in brain networks derived from iEEG time series of subjects suffering from epilepsy,

[26] More precisely: the event originates from the elementary units associated with the low-degree vertices, but linguistics details become tedious in this context. We hope that the one-to-one association of vertices and elementary units is clear at this point.

we observed that the networks underwent significant reorganization of their coupling structure prior to epileptic seizures. Specifically, the organization of shortest paths in the epileptic brain networks underwent significant restructuring in pre-seizure periods when compared to the remaining seizure-free time periods.

Brain regions usually deemed unaffected by focal epileptic processes [RL01, LNN+06] appear more akin to bottlenecks during pre-seizure periods, bridging remote brain areas. On average, the interactions between brain regions that make up the shortest paths increase in strength, while the remaining edges vary only little between pre-seizure and seizure-free periods. These observations were validated and refined by Fruengel et al. [FBRL20] with additional vertex centrality concepts. In total, we hypothesize, that the emergence of a backbone-like sub-structure in the brain networks leads to the generation of epileptic seizures in a not yet understood fashion.

Current research into the role of edges with so-called edge centralities [Gra73, GN02, CRS+10, BL19, BL20, BL22] might further improve our understanding of seizure generation and pre-seizure dynamics in the foreseeable future. Otherwise and while the approach to characterize – in a time resolved manner – the role of network constituents to improve our understanding of dynamical phenomena is flexible and well-suited for multivariate field data analysis, studies utilizing this approach are comparably rare. Diverse examples, however, include the exploration of phenomena like grooming of ants in response to pathogens [AUF+21], the development of interdisciplinary research by reference to citation networks [LS08], and solar activity during stages of the solar cycle [MF22].

Building onto the discriminatory properties of time-evolving networks for dynamics (pre-seizure periods vs. the remaining seizure-free periods) and recurrence patterns in functional networks [MSS+12], we then described dynamical regimes (effectively states of global system dynamics) by representations of the associated snapshot networks. We hypothesized and found some evidence that abstract properties of the dynamical regimes are indicative of the resilience of systems as defined by Holling [Hol73], and we derived the so-called dynamical resistance.

Dynamical resistance could successfully trace the change in brain dynamics due to sleep – an increased resilience of the system at night. Unexpectedly, however, we observed an increase of dynamical resistance prior to seizures in approximately 2/3 of the investigated seizures, which might be a consequence of the brain's ability to defy control based on its inherent plasticity and adaptiveness [Sch02, HCHB08].

In general, the relationship between brain dynamics as recorded by EEG or iEEG and the brain's resilience appear to be more complex than a simple pitchfork-like bifurcation as assumed by the ansatz of critical slowing down [DSvN+08, SBB+09] – a point of view which was validated by other recent studies [DJ10, DHW15, MS16, RCR17, JF19, WRL19]. More recently, Fischer et al. [FRRRTL22] affirmed our hypothesis by providing a versatile test bed for resilience and assaying dynamical resistance, which hopefully will facilitate the data-driven analysis of resilience in diverse areas of science.

While we hope that the advances documented in this thesis prove valuable, they are by no means exhaustive. Further improvements of our understanding of complex systems and their dynamics via the ansatz of time-evolving functional networks might be achieved with further research into the following open topics.

For a large number of complex systems, interacting elementary units operate on different temporal and spatial scales. Temporal scales of, e.g., the human organism easily span from microseconds (e.g., neuron activity) over hours (e.g, digestion) to years (e.g., growth circles) with numerous scales in between [Hil91]. Already characteristics of EEG signals and of EEG-derived time-evolving functional networks on their own exhibit various ultra-, circa-, and infradian rhythms [LRB21]. Other examples include changes in the climate system spanning various time scales from hours to millennia [Cla85, Ben02], transport networks where decade-spanning infrastructure projects amalgamate with traveler's short-term needs [Roc17], or even the way our mesoscopic world arises from interacting microscopic system [Suc19]. Bridging such scales, however, is a currently unsolved problem of great importance not only in network science but in physics in general [Cal11, Suc19, LBR20]. Attempts to solve this issue are currently centered around coarse-grained modeling – especially in molecular chemistry [PSK08, Noi13, ILU+14, KGK+16] – or (non-generalizable) temporal normalization[27], which circumvent the need to actually understand the processes involved in connecting various scales.

As a direct extension of the research presented in this thesis, evaluating the importance of edges resp. interaction with so-called edge centralities may further improve our understanding of changes in networks. Recent interest in the development and use of these measures [DMFFR12, PR12, QLZ+17, WTL18, BL19, BL22, vRB+22] already provided novel insights in studies of various man-made and natural systems including commuter networks, social networks, and brain networks among others. Given that the functional network ansatz assumes system dynamics to emerge from interacting elementary units and that edges represent these interactions, we conjecture that edge centralities will significantly improve our understanding of the relationship between interactions and local resp. global dynamics of complex systems.

Next, information regarding an arbitrary system is not necessarily limited to the global scale of the network as a whole and the local scale of single network constituents. Arguably, investigating mesoscopic network scales of groups of constituents has the potential to generate transparency in the research of currently opaque phenomena. We conjecture that by identifying and describing groups of constituents utilizing concepts such as network decompositions based on local network characteristics [KGH+10, BL19] as well as by characterizing the structure of inter-group couplings [LAS08], further insights into the complex interplay of structure, function, and dynamics of complex systems can be gained. Especially, tracking changes in the composition of these groups might prove enlightening.

From a descriptive perspective – and abreast of macroscopic aspects –, so-called *networks of networks* provide the means to more intuitively describe complex systems composed of large, interconnected components which can exhibit different functions and modes of operation [DS14]. With this approach, these components are described as (sub-)networks that are connected with each other with some inter-network coupling topology[28]. Various terminologies describing networks of networks already exist (e.g., multiplex or multi-layer networks) and are used to describe organizational structures in nature (see, e.g., [DS14, BNL14, BBC+14, AM19]). Examples for which the description of complex systems as a networks of networks already proved useful include describing the human organism as a whole [IB14], global trade [MD15], seismic activity [LDR18], and the spreading of epidemics [DHS12]. However, how alterations of networks of networks affect (local or global) system dynamics is even less understood than for classical networks[29]. Particularly, recent discoveries regarding an asymmetric impact of within sub-network and between sub-network couplings on the dynamics of coupled oscillators [RGSA+18] hint at mechanisms underlying the emergence of several yet-to-be-understood dynamics.

Another topical extension of the network ansatz is called *hyper graphs* [Ber84]. By allowing single edges to connect more than two

[27] So-called fast-slow systems represent a mathematical framework for this class of modeling; see, e.g., [Kue15] for an overview

[28] In a transport network, sub-networks could describe train tracks, streets, and air-lanes with airports and train stations connecting the sub-networks.

[29] Multiplex networks, e.g., interpret time as a direction in a network – a vertex from one point in time is connected by an edge with the same vertex at a different point in time. This can easily obfuscate what a network characteristic actually characterizes.

vertices, hyper graphs are designed to capture couplings with structures of higher dimensional simplices (dimension > 2), that are otherwise excluded from the network ansatz. Besides conceptual deliberations, current methodological and technical improvements allow for the estimation of properties of *higher-order interactions*[30] (see, e.g., [BAB+21] for an overview). In principle, this then also allows for deriving time-evolving functional hyper graphs from time series data. However, advantages of hyper graphs over classical networks have yet to be shown in practice. Also, it is currently unclear how to model and simulate higher-order interactions consistently[31].

On the topic of simulations, studies regarding the impact of non-uniform (local) coupling strengths on the dynamics of elementary units are curiously underrepresented in current research aside from the odd investigation of so-called Bellerophon states[32] [BHB+16]. Considering that most functional network representations of natural systems derived with strength-of-interaction estimates show highly non-uniform strengths, this direction of research might prove important in the intermediate future.

Finally, fundamental assumptions of the description of complex dynamical systems with the network ansatz might be inaccurate or incomplete. Unlike the fundamentally additive network decomposition, it is possible that the dynamical coupling structure is multiplicatively connected to a unit's self-dynamics or that the coupling topology itself is dependent on the units' state variables. While such situations have little impact on deriving functional networks from observations of systems in nature[33], our interpretation of results from the network ansatz would be significantly affected. First simulations of systems with systems with state-dependent coupling topologies have already displayed rich dynamics [Sca10, YFX+21, FRRRTL22] and might bring observations of complex systems and current models closer together in the future.

To summarize, the approach of time-evolving functional networks is a powerful tool for improving our understanding of complex dynamical systems. In this thesis, we explored advantages and disadvantages of the approach, and we provided novel insights into the rich interplay between structural organization, dynamics and functional relationships in complex systems. Overall, we rate the approach suitable for field data analysis. However, the approach's full potential is yet to be exhausted, and additional refinement of the approach as well as exploration of the above-mentioned topics can be expected to further advance our understanding of the natural world.

[30] Higher-order interactions are mutual interactions between three or more elementary units of a system that can not be separated into several pairwise interactions and which are explicitly not transitive.

[31] While it appears that any combination of three or more dynamical variables in a coupling term can be interpreted as an higher-order interaction, the argued scientific hypothesis demands that their impact on the dynamics can not be modeled by groups of pairwise interactions. This can only achieved by non-linear coupling terms, which typically increases a model's complexity excessively.

[32] Bellerophon states describes systems, whose non-transient dynamics exhibit partial phase synchrony, where (seemingly quantized) groups of oscillators exhibit coherent phases on average over time. However, single oscillators repeatedly break from the coherent groups to perform oscillations of higher (or lower) frequency until they return to the coherent group for a intermediate time span.

[33] We are currently unable to reliable separate eigendynamics and dynamical coupling structure anyway. However, advances in, e.g., Kramers–Moyal analysis of multidimensional systems might change that in the future [RGHLT19, ARZL21].

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Auxiliaries

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Besides the necessary hardware and a large amount of self-programmed software written in Python 2 and Python 3 with Jupyter notebook, I employed the software packages pandas, matplotlib, numpy, scikit-learn, and scipy for numerical simulations and data analysis. I furthermore used the software Inkscape for image processing.

I hereby declare that I have written this thesis independently and without the use of other than the stated aids. All passages taken verbatim or in spirit from published and unpublished works are marked as such. This thesis has not yet been submitted in the same or similar form or in excerpts within the framework of another examination. I assure that the submitted electronic version corresponds completely to the submitted printed version.

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