What lies underneath: Precise classification of brain states using time-dependent topological structure of dynamics

Fernando Soler-Toscano (✉ fsoler@us.es)

Universidad de Sevilla <https://orcid.org/0000-0003-1953-4136>

Javier Galadí

Department of Differential Equations and Numerical Analysis, University of Seville

Anira Escrichs

Universitat Pompeu Fabra <https://orcid.org/0000-0002-6482-9737>

Yonatan Sanz-Perl

Universitat Pompeu Fabra

Ane López-González

Pompeu Fabra University <https://orcid.org/0000-0001-9109-0424>

Jacobo Sitt

INSERM

Jitka Annen

University of Liège <https://orcid.org/0000-0002-7459-4345>

Olivia Gosseries

University of Liège <https://orcid.org/0000-0001-9011-7496>

Aurore Thibaut

University Hospital of Liège

Rajanikant Panda

Coma Science Group, Liège University

Francisco J. Esteban

Department of Experimental Biology, University of Jaén <https://orcid.org/0000-0002-7135-2973>

Steven Laureys

Coma Science Group <https://orcid.org/0000-0002-3096-3807>

Morten Kringelbach

Department of Psychiatry, University of Oxford

José A. Langa

Department of Differential Equations and Numerical Analysis, University of Seville

<https://orcid.org/0000-0002-8765-0764>

Gustavo Deco

Universitat Pompeu Fabra <https://orcid.org/0000-0002-8995-7583>

Research Article

Keywords: Dynamical Systems, Information Structures, Lotka-Volterra Transform, Consciousness, Disorders of Consciousness, Complexity Measures, Model Transform, Network frondosity

Posted Date: December 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1093655/v3>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

What lies underneath: Precise classification of brain states using time-dependent topological structure of dynamics

F. Soler-Toscano,^{1,*} J. A. Galadí,² A. Escrichs,³
Y. Sanz Perl,³ A. López-González,³ J.D. Sitt,⁴ J. Annen,⁵
O. Gosseries,⁵ A. Thibaut,⁵ R. Panda,⁵ F.J. Esteban,⁶
S. Laureys,⁵ M.L. Kringelbach,^{7,8,9} J. A. Langa,² G. Deco^{3,10}

¹Grupo de Lógica, Lenguaje e Información, Universidad de Sevilla, Spain.

²Departamento de Ecuaciones Diferenciales y Análisis Numérico,
Universidad de Sevilla, Spain.

³Computational Neuroscience Group, Center for Brain and Cognition,
Universitat Pompeu Fabra, Barcelona, Catalonia, Spain.

⁴INSERM, Paris, France.

⁵Coma Science Group, Liège University, Belgium.

⁶Departamento de Biología Experimental, Universidad de Jaén, Spain.

⁷Department of Psychiatry, University of Oxford, UK.

⁸Centre for Music in the Brain, Department of Clinical Medicine,
Aarhus University, Denmark.

⁹Life and Health Sciences Research Institute (ICVS),
School of Medicine, University of Minho, Portugal.

¹⁰Institució Catalana de la Recerca i Estudis Avançats (ICREA),
Universitat Pompeu Fabra, Barcelona, Spain.

*Corresponding author. E-mail: fsoler@us.es

December 14, 2021

Abstract

The self-organising global dynamics underlying brain states emerge from complex recursive nonlinear interactions between interconnected brain regions. Until now, all efforts of capturing the causal mechanistic generating principles have proven elusive, since they have been unable to describe the non-stationarity of brain dynamics, i.e. time-dependent changes. Here, we present a novel framework able to characterise brain states with high specificity, precisely by modelling the time-dependent dynamics. Through describing the topological structure of the brain at each moment in time (its

‘information structure’), we are able to classify different brain states by using the statistics across time of these exact ‘information structures’ hitherto hidden in the neuroimaging dynamics. Proving the strong potential of this framework, we were able to classify the neuroimaging data from two classes of post-comatose patients with disorders of consciousness compared with healthy controls with very high precision.

1 Introduction

Brain states such as wakefulness, sleep, and altered states of consciousness emerge through continuously evolving dynamics of self-organised whole-brain networks, which depending on the underlying condition, go through transient, “metastable”, arrangements [1]. The challenging question is to how best to describe them through disentangling the mechanisms underlying functional neuroimaging data capturing their whole-brain dynamics over time and space [2, 3, 4, 5]. Whole-brain models have been very successful in capturing many of the key features of brain dynamics including spatiotemporal aspects [2, 6], but they show stationarity of the underlying energy landscape which empirically has been shown not to be the case [7, 8]. In general, until now, it has proven very difficult to fully describe the principles generating the brain dynamics.

Here, the aim is to develop a mathematical formal framework able to characterise the dynamics of brain states with high specificity. Within the field of Dynamical Systems Theory, it has been shown that a coupled-system of differential equations has an associated Information Structure. This is given by a directed graph describing the structure of the global attractor which can be given in terms of invariant subsets (typically, stationary points or periodic orbits) and the trajectories in phase space connecting them [9]. Under some conditions, all invariant subsets of the global attractor can be ordered by their level of attraction or stability (energy levels [10]).

The Attractor Landscape (AL) analysis converts the behaviour of a dynamical system into a landscape of structures to which the system potentially tends to approach or move away. Every state of the system at a particular time is affected by the AL. This provides a number of topological measures in the structure of this attractor landscape, namely number of energy levels (NoEL), frondosity, criticality, synchronicity and cooperation. The Information Structure (IS) contains all stable points in the AL together with their relations (see Figure 1). NoEL corresponds to the number of layers of the IS. Frondosity is the ratio of nodes in the IS with respect to the maximum for its NoEL. Criticality measures how close are the parameters defining the IS to a bifurcation point that would change the global stable point. Synchronicity measures the ratio of a subject ISs having the global stable point with all components (brain networks) in the same state (active or inactive). Finally, cooperation measures look in different ways how some components of the system are influenced by the action of others.

The IS can be computed exactly when the number of dynamical variables is low. It has been shown that the information structure can be extracted by a Lotka-Volterra transformation procedure [7, 11]. This simple model matches the conditions so that the invariants can be ordered in energy levels, supports an algorithm of low computational complexity, and has well-known conditions for the existence and uniqueness of its global attractor, which can be characterized in detail.

We apply this precise mathematical framework to two empirical neuroimaging datasets

Figure 1: Measures of Information Structures. An information structure (IS) is shown on the left. It is determined by the structural connectivity matrix (fixed) and the α_i values (variable at each instant) for the 7 networks in Yeo's parcellation. The nodes of the information structure correspond to stable states of the system. Networks with a value greater than 0 are coloured. The IS can be studied through several measures. *NoEL* (number of energy levels) corresponds to the number of layers of the IS (levels 0 to 4). *Frondosity* is the ratio of nodes in the IS with respect to the maximum for its NoEL. Cooperation measures are applied on cooperative nodes, which are those (except for level 1) where a network that did not appear in previous levels is activated thanks to the activity of other networks. The *highest cooperation level* is given by the highest level at which a cooperative node appears. Cooperation values consider cooperative nodes in different ways. *Cooperation value A* counts all cooperative nodes, adding in each case the level of the node from which it proceeds. *Cooperation value B* considers only one level (the lowest) for each new network, and *cooperation value C* operates in the same way but by adding powers of 2. Other used measures are *criticality* and *synchronicity*. *Criticality* measures how close are the alpha values to a bifurcation point that modifies the globally stable node. Finally, *synchronicity* measures the ratio of IS of a subject (across time) in which all networks appear in the same state (active or inactive) in the globally stable solution.

(Liège and Paris) including healthy controls (HC) and two groups of post-comatose patients with disorders of consciousness (DOC) after severe brain injury: minimally conscious state (MCS) and unresponsive wakefulness syndrome (UWS). Patients in MCS [12] present some behaviour that may indicate awareness (i.e., visual pursuit, orientation to pain, or reproducible command following). Patients in UWS [13] show arousal (eyes opening) but unresponsive (no response to simple commands) and without signs of awareness (never presenting non-reflex voluntary movements). This allows us to characterise the instantaneous information structure of the brain at each moment in time, for each measurement. Repeating this for all time points in the data provides statistics (i.e. the mean and variability of the information structure measures) which captures a brain state accurately, characterised by the exact “information structures” hitherto hidden in the neuroimaging dynamics.

Metrics on information structures (Figure 1) characterise the brain activity of HC and differentiate it from DOC patients (Figures 2–4). Cooperation values are the most relevant of these metrics. The networks showing more cooperative behaviour are frontoparietal and default mode networks. Cooperation in these networks is altered in MCS and practically disappears in UWS (Figure 5). Conscious states are significantly distinguished using the statistics of the time-varying information structures (Table 1). Furthermore, complementing this with a machine learning approach, we were able to classify the state of each subject with a precision of 95.6% for HC/DOC and 86.6% for MCS/UWS (Table 2).

2 Results

By using the Lotka-Volterra Transform (LVT) [7], the IS has been computed for each subject at every time instant, given the seven timeseries of the Yeo’s parcellation [14] and the structural connectivity matrix. The values of the IS measures (Figure 1) can be compared between different groups using the Wilcoxon signed-rank test. Table 1 shows the p-values of the comparisons between groups for centrality (mean or median) and dispersion (standard deviation) of IS measures. Compared groups comprise 147 participants (81 from Liège and 66 from Paris) including 49 healthy controls (HC, 36 from Liège and 13 from Paris), 63 in MCS (31 from Liège and 32 from Paris) and 35 with UWS (14 from Liège and 21 from Paris). Low p-values for the Wilcoxon test ensure that the measures are detecting relevant differences in the distributions. For a single measure, a typical significance level is $p < 0.05$. This threshold may be corrected for multiple comparisons. The eight measures with high %f values in Table 1 are the most relevant features for the machine learning classifiers distinguishing between HC/DOC and MCS/UWS (see Table 2). For these 8 measures the Bonferroni correction lowers the significance threshold to $p < 0.05/8 \simeq 0.006$. Most of the p-values for these features are below it, so detecting relevant differences between groups.

Figures 2 and 3 show the distributions corresponding to NoEL, frondosity, criticality and synchronicity for the subjects in the three groups. Together with the distributions for all subjects in the same state (All), Liège and Paris participants are shown separately to highlight the similarity between groups of subjects sharing the same state of consciousness.

The interpretation of frondosity as a measure of the absence of integration would result in the integration being higher in the control group and reaching its lowest value in the unresponsive group. This coincides with other criteria for the measure of integration [6, 15]. The variability of the frondosity can be interpreted as a measure of complexity so that the greater functional complexity would correspond again to the control group and the lower to

Table 1: Wilcoxon Signed-Rank test for different IS measures. The mean (μ) and standard deviation (σ) of each measure across all IS of a subject are calculated. In the case of criticality, the median (M) is used instead of μ , as it is more stable. Synchronicity is just one value per subject, so there is no mean and standard deviation. The Wilcoxon test compares the distributions corresponding to two different groups of the measure indicated in each row. Low Wilcoxon test p-values ensure that the measures are detecting relevant differences in the distributions. Machine learning is used to search for classifiers discriminating between HC/DOC and MCS/UWS. The performance of the resulting classifiers was evaluated by using leave-one-out cross-validation (Table 2). This requires to train the classifier as many times (folds) as samples are in the dataset, leaving each time one out for validation. The classifier determines which features provide more information within the training set and uses them to classify the validation sample. The %f columns show the percentage of folds using each measure in the best found classifiers.

		HC / DOC				MCS / UWS			
		All	Liège	Paris	%f	All	Liège	Paris	%f
NoEL	μ	$< 10^{-10}$	$< 10^{-6}$	$< 10^{-3}$	100	$< 10^{-4}$	0.003	0.002	0
	σ	$< 10^{-8}$	$< 10^{-5}$	0.002	0	$< 10^{-4}$	0.004	0.004	0
Frondosity	μ	$< 10^{-13}$	$< 10^{-11}$	0.005	95	$< 10^{-6}$	$< 10^{-3}$	$< 10^{-3}$	0
	σ	$< 10^{-12}$	$< 10^{-10}$	0.011	1	$< 10^{-6}$	$< 10^{-3}$	$< 10^{-3}$	1
Criticality	M	$< 10^{-13}$	$< 10^{-10}$	$< 10^{-3}$	100	$< 10^{-5}$	$< 10^{-3}$	0.001	94
	σ	0.144	0.134	0.393	0	$< 10^{-3}$	0.003	0.010	1
Synchronicity		$< 10^{-13}$	$< 10^{-9}$	$< 10^{-4}$	96	$< 10^{-4}$	0.002	0.002	0
Coop. Level	μ	$< 10^{-11}$	$< 10^{-10}$	0.005	0	$< 10^{-6}$	$< 10^{-4}$	0.001	0
	σ	$< 10^{-10}$	$< 10^{-10}$	0.025	0	$< 10^{-6}$	$< 10^{-4}$	$< 10^{-3}$	1
Coop. Val A	μ	$< 10^{-9}$	$< 10^{-7}$	0.010	1	$< 10^{-6}$	$< 10^{-4}$	$< 10^{-3}$	100
	σ	$< 10^{-4}$	0.001	0.025	0	$< 10^{-5}$	$< 10^{-3}$	0.003	100
Coop. Val B	μ	$< 10^{-12}$	$< 10^{-10}$	0.004	100	$< 10^{-6}$	$< 10^{-4}$	$< 10^{-3}$	0
	σ	$< 10^{-10}$	$< 10^{-10}$	0.051	0	$< 10^{-6}$	$< 10^{-3}$	$< 10^{-3}$	99
Coop. Val C	μ	$< 10^{-11}$	$< 10^{-10}$	0.024	1	$< 10^{-6}$	$< 10^{-4}$	$< 10^{-3}$	0
	σ	$< 10^{-9}$	$< 10^{-8}$	0.066	94	$< 10^{-6}$	$< 10^{-3}$	$< 10^{-3}$	82

Figure 2: Distributions of NoEL, Frondosity and Criticality. Each subject contributes with one value in the distributions (the mean or standard deviation of the corresponding measure across time). Standard deviation of NoEL can be considered a measure of metastability, since it reflects the tendency of the system to change the attractors. Frondosity is related to integration: ISs with low frondosity exhibit greater cooperative interactions between nodes (see the cooperation measures on Fig. 4). Mean frondosity values very close to 1 (like those of UWS patients) denote a trivial brain activity. Criticality indicates how close is the system to a major change on the attractor shape (affecting the globally stable state). The lower the criticality, the closer the system is to a bifurcation point and the easier it is for the IS to undergo large changes. The median criticality distributions show that the IS of healthy subjects move closer to bifurcation points.

Figure 3: Distributions of Synchronicity. This measure is not applied to individual ISs. It is the ratio of ISs having the global stable point with all nodes in the same state (either 0 or greater to 0). That is, the extreme values of NoEL. Subjects with low Synchronicity have information structures with more differentiated behaviour of the nodes. UWS patients have synchronicity values very close to 1, denoting trivial brain activity.

the unresponsive group. NoEL and frondosity are complementary metrics, as NoEL measures how many layers the IS has and frondosity measures how populated are these layers. The combination of high values of both measures that occurs in UWS patients (together with a NoEL variability close to 0) implies triviality of the IS, which continually produce the same attractor in which all networks are equally present (see Fig. 3). Therefore, standard deviation of NoEL can be considered a measure of metastability, since it reflects the tendency of the system to change the attractors.

The measure of criticality indicates that the control group is the one closest to bifurcation points, while the unresponsive group is the farthest, having more stable but trivial information structures. It agrees with the idea that phenomenal consciousness is realized by a particular level of brain configuration guided by criticality and self-organisation [16, 17, 18].

Fig. 4 shows the distributions of the mean and standard deviation of both the highest cooperation level and the different cooperation values. These measures are of particular relevance for identifying the type of brain dynamics characterising conscious states, as shown in Figure 5. In the top row, the seven networks of Yeo’s parcellation are coloured according to their presence at the globally stable point of the IS. In the bottom row, they are coloured according to their presence due to cooperation. It can be seen that healthy subjects have more cooperative interactions (mean) and higher variability across time (standard deviation). In contrast, UWS patients (and to a lesser degree also MCS) have high levels of NoEL and frondosity but the brain dynamics is almost trivial, as there is barely any cooperation among the different networks. The most relevant networks in terms of cooperation are DMN and frontoparietal (bottom row of Fig. 5). This is consistent with some results pointing to their key role in conscious activity [19, 20, 21].

Using the IS measures in Table 1, classifiers have been trained using Weka. Table 2 (top) shows the confusion matrices of the classifiers together with several performance measures. The precision of the classifiers is 95.6% for HC/DOC and 86.6% for MCS/UWS. The areas under the ROC and PRC curves are in all cases greater than 0.92.

Figure 4: Distributions of cooperation measures. These measures consider in different ways the cooperative relationships between different networks (Fig. 1). It can be observed that the higher the consciousness level, the more cooperation is in the IS (mean) and with a higher variability (standard deviation).

Table 2: Performance of the classifiers. Confusion matrices describing the performance of the Weka classifiers for HC/DOC (left) and MCS/UWS (right). Classifiers are trained with the 15 measures in Table 1 and validated using leave-one-out cross-validation. This strategy trains the classifier as many times (folds) as subjects are in the dataset, leaving one of them out of the training for validation. At each fold, Weka selects the most relevant measures to train the classifier and the training is validated with the patient that was left out. Table 1 (column %f) shows the percentage of folds in which each of the 15 measures was selected for training. The resulting classifiers (JRip and REPTree) were found by Auto-Weka, an automatic mode for model selection and hyperparameter optimization. Several performance metrics are shown in the bottom table for both classifiers, for each of the classes and the weighted average. The true positive (TP) rate (also called sensitivity) is the probability that a subject belonging to the class is correctly identified. The false positive (FP) rate is the probability that a subject not belonging to the class will be misclassified. Precision and recall are complementary accuracy measures. Precision is the proportion of positive predictions that actually belong to the class. Recall is the ratio of positive predictions to total positive cases in the dataset. The F-measure is an accuracy measure that is calculated as the harmonic mean of precision and recall. The Matthews Correlation Coefficient (MCC) is a correlation (between -1 and 1) between the observed and predicted values. Finally the areas under the ROC (Receiver Operating Characteristic) curve and PRC (Precision-Recall Curve) are widely used measures of classifier performance. These areas are 1 for perfect classifications and classifiers with a value above 0.9 are considered to perform very well.

True label	HC	42	7
	DOC	0	98
		HC	DOC
		Predicted label	

True label	MCS	58	5
	UWS	8	27
		MCS	UWS
		Predicted label	

Classifier	Class	TP Rate	FP Rate	Precision	Recall	F-Measure	MCC	ROC Area	PRC Area
JRip	HC	0.857	0.000	1.000	0.857	0.923	0.894	0.929	0.905
	DOC	1.000	0.143	0.933	1.000	0.966	0.894	0.929	0.933
	Weighted Avg.	0.952	0.095	0.956	0.952	0.951	0.894	0.929	0.924
REPTree	MCS	0.921	0.229	0.879	0.921	0.899	0.707	0.938	0.953
	UWS	0.771	0.079	0.844	0.771	0.806	0.707	0.938	0.881
	Weighted Avg.	0.867	0.175	0.866	0.867	0.866	0.707	0.938	0.927

Figure 5: Presence of brain networks in the IS and cooperative interactions. The proportion in which each network appears in the global stable point of the IS (which is equal to appearing in any point of the IS) is shown above. Values range from 0.8 to 1. The highest values appear in UWS patients, followed by MCS. This is due to higher values of NoEL and frondosity. However, this does not imply complex behaviour in brain dynamics. The proportion of occurrences of each network in the IS due to cooperative interactions of other networks is shown below. The values are between 0 and 0.1. The greatest values belong to HC (the leading group in terms of cooperative measures, followed by MCS, see Fig. 4). A greater differentiation between networks is observed than when looking at the global stable point alone. The highest values in all three groups correspond to DMN followed by frontoparietal.

3 Discussion

Information structures [22, 23] have been previously used to determine the level of integrated information for different states such as wakefulness and different stages of sleep [7]. Identifying attractors in phase space and transitions between attractors may serve as useful descriptors for global brain dynamics [24], as they can be seen as a proper mathematical framework describing the space-time flow of observed dynamics. In addition, we can confront concepts with real data from human brain dynamics. The results presented in this paper are the first application of IS measures to DOC patients. Using mathematical concepts from Dynamical System Theory, our approach provides measures that discriminate subjects in different states of consciousness with an accuracy of 86.6% for MCS/UWS classification, which is comparable with other (f)MRI/EEG based methods in the literature [20, 25]. We think this mathematical construction provides information about the real underneath structure of the informational flow in the human brain dynamics. Among all measures on Table 1 we find particularly interesting the case of cooperation values. It is a notion that cannot be watched by looking only at the global stable point of the attractor, as most whole-brain models do. The relevance of cooperation in frontoparietal and default mode networks (Figure 5) can only be observed by looking underneath the globally stable solution (bottom row of the figure). The global stable point is a very relevant state in the dynamics of the system but by itself does not inform how and through which pathways it is reached. Notions like metastability, information integration, or criticality require to look at the whole information structure. LV dynamical systems is an ideal framework because, as mentioned above, it

allows these structures to be built and studied in depth.

Many informational measures of consciousness in the literature are defined for theoretical systems but difficult to apply in practice without major reductions. For example, Φ in IIT 3.0 is applicable only to discrete Markovian systems [26], and, even when proposals have been made to define the ON and OFF states of IIT 3.0 in terms of emergent properties of assemblies of neurons [27], simplifications in the theory must be assumed for practical use [28]. On the contrary, our theoretical framework can be implemented without simplifying the theory. Other measures can be estimated from real data using empirical distributions only if stationarity can be assumed. Non-stationarity is a remaining important challenge in many practical scenarios. For long data segments, it can be unrealistic to assume that all the statistics are constant throughout, while for shorter data segments, one cannot be confident that the system has explored all the states [29]. However, our measures are designed to be applied directly to non-stationary empirical data.

4 Methods

We aim to characterise different consciousness states by looking at the evolution in time of the attractor underlying the brain dynamics. Lotka-Volterra cooperative systems are used, looking at several measures on the Information Structures (Figure 6.A) underlying the system dynamics. Supplementary material (see B) contains details about the used measures and their computation. Figure 1 contains an example of the calculation for a specific Information Structure (IS). In summary, the first of them, *Number of Energy Levels* (NoEL), measures the levels in the IS. *FronDOSity* corresponds to the proportion of nodes in the IS with respect to a maximum depending on the NoEL. *Criticality* indicates the proximity of the system to a phase transition. *Synchronicity* is the ratio of ISs having either maximum or minimum NoEL value (all nodes of the system are together present or absent in the IS global stable point). The *Cooperation values* (a vector of three components) measure different aspects of the interactions between nodes of the dynamical system enabling the presence (value greater to 0) of one of them in some level of the IS thanks to the presence of some others in previous levels. Finally, the *Highest cooperation level* is the maximum level of the IS in which a cooperation (emergence of a new node thanks to some others) is produced.

Given a system like that in Figure 6.B with fixed connectivity and changing activity in the nodes, it is possible to look at the changes on the attractor governing the system behaviour by looking at the variability of the IS measures.

The methodology is depicted in Figure 7. We have applied it to data corresponding to 147 participants (81 from Liège and 66 from Paris) including 49 healthy controls (HC, 36 from Liège and 13 from Paris), 63 in minimally conscious state (MCS, 31 from Liège and 32 from Paris) and 35 in unresponsive wakefulness syndrome (UWS, 14 from Liège and 21 from Paris). These datasets have been previously described in [30, 18]. The diagnosis was obtained using CRS-R by trained clinicians, with some differences between both datasets. In case of Liège patients, the diagnosis was confirmed with Positron Emission Tomography (PET), to avoid misclassification of MCS* patients [31, 32]. Details on data acquisition and preprocessing are in Supplementary Material (see A). Brain activity is mapped into the 7 areas in the well-known Yeo parcellation atlas: (1) Visual, (2) Somatomotor, (3) Dorsal attention, (4) Ventral attention, (5) Limbic, (6) Frontoparietal, and (7) Default Mode Network [14].

To extract the attractor landscape at each instantaneous time point, we apply the Lotka-

Figure 6: Information Structures and their dynamics. **A.** Left: Lotka-Volterra 7-nodes dynamical system. Relevant parameters are those affecting just one node (α_i) and those representing cooperation, given by the weighted links (γ_{ij}) between nodes (i and j). Right: Associated to each system (for given α_i and γ_{ij} parameters) there is an Information Structure (IS), containing the attractor landscape, that is, stable points of the system dynamics and the solutions linking them. Black nodes in the stable points represent a value greater than 0 of the corresponding node of the dynamical system. White nodes stand for 0 value of the corresponding node. Different γ_{ij} and α_i values produce different ISs in both the global stable point (the one in the bottom) and the nodes in the intermediate levels. The structure of the IS can be studied through several measures (see Fig. 1) depending not only on the number of levels and nodes (NoEL and Frondosity, respectively) but also on the interaction between nodes (Synchronicity, Criticality and Cooperation measures). **B.** For a dynamical system with fixed connectivity (γ_{ij} parameters) and changing activity among the nodes (α_i) it is possible to study the evolution of the IS measures. The top graphic represents the change in time of the α_i parameters in a Lotka-Volterra 7-nodes system with fixed connectivity γ_{ij} . Associated to each instant there is an IS with the structure of the attractor underlying the dynamics of the system. The evolution of the system dynamics can be characterised by looking at the mean and standard deviation across time of the IS measures. Several notions like metastability, cooperation or information integration can be interpreted in terms of these measures.

Figure 7: Measuring the changes in the ISs underlying brain activity. The brain activity registered through fMRI is mapped into seven brain networks using Yeo’s 7-network parcellation. For each subject, given the timeseries of the activity and the structural connectivity matrix, Lotka-Volterra Transform produces the α_i values at each instant. This allows the study of the Information Structures evolution in time. Machine learning is used to train classifiers which identifies the state of each subject with a precision of 95.6% (HC/DOC) and 86.6% (MCS/UWS).

Volterra Transform (LVT) [7, 11]. Similar to whole-brain models, this consists of coupling local dynamics with anatomical brain connectivity (Figure 6). However, different from whole-brain models, the LVT is applied to each single time point to reveal the evolution in time of the α_i parameters which reproduce exactly the filtered empirical BOLD fMRI signals and determine an IS. For the subjects with data acquired with $TR = 2000$ ms (all participants from Liège and 32 from Paris: 21 MCS and 11 UWS), $h = 3.55 \times 10^{-4}$ was used in the LVT. For the other 34 Paris participants with $TR = 2400$ ms. (13 HC, 11 MCS and 10 UWS) $h = 4.26 \times 10^{-4}$ was used. The average SC matrix of all Liège HC subjects multiplied by $g = 0.27$ was used for all participants. We computed GASS, NoEL, frondosity, criticality, synchronicity and cooperation of the corresponding IS at each time instant. Figure 1 introduces and illustrates these measures.

IS measures were compared between the different groups (HC/DOC and MCS/UWS) using the Wilcoxon Signed-Rank test and then used as the input for machine learning classifiers. Class classification models were selected using Auto-WEKA, an automatic model selection and hyperparameter optimization tool implemented in WEKA [33].

Acknowledgements

This work was partially supported by FEDER Ministerio de Economía, Industria y Competitividad grant PGC2018-096540-B-I00, and Proyectos Fondo Europeo de Desarrollo Regional (FEDER) and Consejería de Economía, Conocimiento, Empresas y Universidad de la Junta de Andalucía, by Programa Operativo FEDER 2014-2020 references US-1254251 and P20-00592.

Author contributions

Design of the methodology: FST, JAG, JAL, MLK, GD. Data acquisition: JDS, JA, OG, AT, RP, SL. Data preprocessing: AE, YSP, ALG. Data analysis: FST, JAG, FJE, JAL.

Writing of the manuscript: FST, JAG, JAL, AE, MLK, GD. Revision and discussion of the manuscript: all authors. Funding acquisition: JAL.

Data availability

The fMRI datasets analyzed during the current study are not publicly available due to constraints imposed by the ethics approval. Reasonable requests can be addressed to S. Laureys (Liège data) and J.D. Sitt (Paris data). A table with the values of all IS measures (the data producing the results in Table 1 and Figures 2–4) is available at <https://github.com/fersoler/CooperativeInformationStructures>.

Code availability

A Jupyter notebook for SageMath/Python allowing the creation and visualization of Information Structures for cooperative Lotka-Volterra systems is available at <https://github.com/fersoler/CooperativeInformationStructures>. It also computes all IS measures introduced in this paper and contains an example of the calculation of mean and standard deviation for a timeseries of 295 α_i values of a 7-node system.

References

- [1] G Deco and ML Kringelbach. Great expectations: Using whole-brain computational connectomics for understanding neuropsychiatric disorders. *Neuron*, 84(5):892 – 905, 2014.
- [2] Gustavo Deco, Josephine Cruzat, Joana Cabral, Enzo Tagliazucchi, Helmut Laufs, Nikos K. Logothetis, and Morten L. Kringelbach. Awakening: Predicting external stimulation to force transitions between different brain states. *Proceedings of the National Academy of Sciences*, 116(36):18088–18097, 2019.
- [3] Damien Gervasoni, Shih-Chieh Lin, Sidarta Ribeiro, Ernesto S. Soares, Janaina Pantoja, and Miguel A. L. Nicolelis. Global forebrain dynamics predict rat behavioral states and their transitions. *Journal of Neuroscience*, 24(49):11137–11147, 2004.
- [4] G. Northoff. *Unlocking the Brain: Volume 1: Coding*. Oxford University Press, 2013.
- [5] G Tononi, O Sporns, and G M Edelman. A measure for brain complexity: relating functional segregation and integration in the nervous system. *Proceedings of the National Academy of Sciences*, 91(11):5033–5037, 1994.
- [6] A. Demertzi, E. Tagliazucchi, S. Dehaene, G. Deco, P. Barttfeld, F. Raimondo, C. Martial, D. Fernández-Espejo, B. Rohaut, H. U. Voss, N. D. Schiff, A. M. Owen, S. Laureys, L. Naccache, and J. D. Sitt. Human consciousness is supported by dynamic complex patterns of brain signal coordination. *Science Advances*, 5(2), 2019.

- [7] J.A. Galadí, S. Silva Pereira, Y. Sanz Perl, M.L. Kringelbach, I. Gayte, H. Laufs, E. Tagliazucchi, J.A. Langa, and G. Deco. Capturing the non-stationarity of whole-brain dynamics underlying human brain states. *NeuroImage*, 244:118551, 2021.
- [8] Arnaud Messé, David Rudrauf, Habib Benali, and Guillaume Marrelec. Relating structure and function in the human brain: Relative contributions of anatomy, stationary dynamics, and non-stationarities. *PLOS Computational Biology*, 10(3):1–9, 03 2014.
- [9] A Carvalho, JA Langa, and J Robinson. *Attractors for infinite-dimensional non-autonomous dynamical systems*. Applied Mathematical Sciences. Springer New York, 2012.
- [10] ER Aragao-Costa, T Caraballo, AN Carvalho, and JA Langa. Continuity of lyapunov functions and of energy level for a generalized gradient semigroup. *Topol. Methods Nonlinear Anal.*, 39(1):57–82, 2012.
- [11] JA Galadí. *Dynamical systems applied to consciousness and brain rhythms in a neural network*. PhD thesis, Department of Differential Equations and Numerical Analysis. University of Seville, April 2020.
- [12] J. T. Giacino, S. Ashwal, N. Childs, R. Cranford, B. Jennett, D. I. Katz, J. P. Kelly, J. H. Rosenberg, J. Whyte, R. D. Zafonte, and N. D. Zasler. The minimally conscious state: definition and diagnostic criteria. *Neurology*, 58(3):349–353, Feb 2002.
- [13] S. Laureys, G. G. Celesia, F. Cohadon, J. Lavrijsen, J. León-Carrión, W. G. Sannita, L. Sazbon, E. Schmutzhard, K. R. von Wild, A. Zeman, and G. Dolce. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. *BMC Med*, 8:68, Nov 2010.
- [14] B. T. Thomas Yeo, Fenna M. Krienen, Jorge Sepulcre, Mert R. Sabuncu, Danial Lashkari, Marisa Hollinshead, Joshua L. Roffman, Jordan W. Smoller, Lilla Zöllei, Jonathan R. Polimeni, Bruce Fisch, Hesheng Liu, and Randy L. Buckner. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, 106(3):1125–1165, sep 2011.
- [15] Pablo Barttfeld, Lynn Uhrig, Jacobo D. Sitt, Mariano Sigman, Béchir Jarraya, and Stanislas Dehaene. Signature of consciousness in the dynamics of resting-state brain activity. *Proceedings of the National Academy of Sciences*, 112(3):887–892, 2015.
- [16] Walter Freeman. Indirect biological measures of consciousness from field studies of brains as dynamical systems. *Neural networks*, 20:1021–31, 12 2007.
- [17] Enzo Tagliazucchi, Pablo Balenzuela, Daniel Fraiman, and Dante Chialvo. Criticality in large-scale brain fmri dynamics unveiled by a novel point process analysis. *Frontiers in Physiology*, 3:15, 2012.
- [18] Ane López-González, Rajanikant Panda, Adrián Ponce-Alvarez, Gorka Zamora-López, Anira Escrichs, Charlotte Martial, Aurore Thibaut, Olivia Gosseries, Morten L. Kringelbach, Jitka Annen, Steven Laureys, and Gustavo Deco. Loss of consciousness reduces the stability of brain hubs and the heterogeneity of brain dynamics. *Communications Biology*, 4(1), September 2021.

- [19] J Long, Q Xie, Q Ma, MA Urbin, L Liu, L Weng, X Huang, R Yu, Y Li, and R Huang. Distinct interactions between fronto-parietal and default mode networks in impaired consciousness. *Scientific reports*, 6, 2016.
- [20] Athena Demertzi, Georgios Antonopoulos, Lizette Heine, Henning U. Voss, Julia Sophia Crone, Carlo de Los Angeles, Mohamed Ali Bahri, Carol Di Perri, Audrey Vanhau-denhuysse, Vanessa Charland-Verville, Martin Kronbichler, Eugen Trinkka, Christophe Phillips, Francisco Gomez, Luaba Tshibanda, Andrea Soddu, Nicholas D. Schiff, Susan Whitfield-Gabrieli, and Steven Laureys. Intrinsic functional connectivity differentiates minimally conscious from unresponsive patients. *Brain*, 138(9):2619–2631, June 2015.
- [21] Carol Di Perri, Aurore Thibaut, Lizette Heine, Andrea Soddu, Athena Demertzi, and Steven Laureys. Measuring consciousness in coma and related states. *World Journal of Radiology*, 6(8):589, 2014.
- [22] Francisco J. Esteban, Javier A. Galadí, José A. Langa, José R. Portillo, and Fernando Soler-Toscano. Informational structures: A dynamical system approach for integrated information. *PLOS Computational Biology*, 14(9):1–33, 09 2018.
- [23] Piotr Kalita, José A. Langa, and Fernando Soler-Toscano. Informational structures and informational fields as a prototype for the description of postulates of the integrated information theory. *Entropy*, 21(5), 2019.
- [24] Alicia Juarrero. *Top-Down Causation and Autonomy in Complex Systems*, pages 83–102. Springer Berlin Heidelberg, Berlin, Heidelberg, 2009.
- [25] Johan Stender, Kristian Nygaard Mortensen, Aurore Thibaut, Sune Darkner, Steven Laureys, Albert Gjedde, and Ron Kusters. The minimal energetic requirement of sustained awareness after brain injury. *Current Biology*, 26, 05 2016.
- [26] M Oizumi, L Albantakis, and G Tononi. From the phenomenology to the mechanisms of consciousness: Integrated information theory 3.0. *PLOS Computational Biology*, 10(5):1–25, 05 2014.
- [27] JA Galadí, JJ Torres, and J Marro. Emergence and interpretation of oscillatory behaviour similar to brain waves and rhythms. *Communications in Nonlinear Science and Numerical Simulation*, 83:105093, April 2020.
- [28] Adenauer G. Casali, Olivia Gosseries, Mario Rosanova, Mélanie Boly, Simone Sarasso, Karina R. Casali, Silvia Casarotto, Marie-Aurélié Bruno, Steven Laureys, Giulio Tononi, and Marcello Massimini. A theoretically based index of consciousness independent of sensory processing and behavior. *Science Translational Medicine*, 5(198), August 2013.
- [29] Pedro A.M. Mediano, Anil K. Seth, and Adam B. Barrett. Measuring integrated information: Comparison of candidate measures in theory and simulation. *Entropy*, 21(1), 2019.
- [30] Anira Eschrichs, Yonatan Sanz-Perl, Carme Uribe, Estela Camara, Basak Türker, Nadya Pyatigorskaya, Ane López-González, Carla Pallavicini, Rajanikant Panda, Jitka Annen, Olivia Gosseries, Steven Laureys, Lionel Naccache, Jacobo Sitt, Helmut Laufs, Enzo

- Tagliazucchi, Morten L Kringelbach, and Gustavo Deco. Unifying turbulent dynamics framework distinguishes different brain states. *bioRxiv*, 3:2021.10.14.464380, oct 2021.
- [31] Aurore Thibaut, Rajanikant Panda, Jitka Annen, Leandro R. D. Sanz, Lionel Naccache, Charlotte Martial, Camille Chatelle, Charlène Aubinet, Estelle A. C. Bonin, Alice Barra, Marie-Michèle Briand, Benedetta Cecconi, Sarah Wannez, Johan Stender, Steven Laureys, and Olivia Gosseries. Preservation of brain activity in unresponsive patients identifies mcs star. *Annals of Neurology*, 90(1):89–100, 2021.
 - [32] Johan Stender, Olivia Gosseries, Marie-Aurélié Bruno, Vanessa Charland-Verville, Audrey Vanhaudenhuyse, Athena Demertzi, Camille Chatelle, Marie Thonnard, Aurore Thibaut, Lizette Heine, Andrea Soddu, Mélanie Boly, Caroline Schnakers, Albert Gjedde, and Steven Laureys. Diagnostic precision of pet imaging and functional mri in disorders of consciousness: a clinical validation study. *Lancet (London, England)*, 384:514–22, 8 2014.
 - [33] C. Thornton, F. Hutter, H. H. Hoos, and K. Leyton-Brown. Auto-WEKA: Combined selection and hyperparameter optimization of classification algorithms. In *Proc. of KDD-2013*, pages 847–855, 2013.
 - [34] Christian F. Beckmann and Stephen M. Smith. Probabilistic Independent Component Analysis for Functional Magnetic Resonance Imaging. *IEEE Transactions on Medical Imaging*, 23(2):137–152, feb 2004.
 - [35] Mark Jenkinson, Peter Bannister, Michael Brady, and Stephen Smith. Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *NeuroImage*, 17(2):825–841, oct 2002.
 - [36] Stephen M. Smith. Fast robust automated brain extraction. *Human Brain Mapping*, 17(3):143–155, nov 2002.
 - [37] Gholamreza Salimi-Khorshidi, Gwenaëlle Douaud, Christian F. Beckmann, Matthew F. Glasser, Ludovica Griffanti, and Stephen M. Smith. Automatic denoising of functional MRI data: Combining independent component analysis and hierarchical fusion of classifiers. *NeuroImage*, 90:449–468, apr 2014.
 - [38] Ludovica Griffanti, Gwenaëlle Douaud, Janine Bijsterbosch, Stefania Evangelisti, Fidel Alfaro-Almagro, Matthew F. Glasser, Eugene P. Duff, Sean Fitzgibbon, Robert Westphal, Davide Carone, Christian F. Beckmann, and Stephen M. Smith. Hand classification of fMRI ICA noise components. *NeuroImage*, 154:188–205, jul 2017.
 - [39] D Carone, R Licenik, S Suri, L Griffanti, N Filippini, and J Kennedy. Impact of automated ICA-based denoising of fMRI data in acute stroke patients. *NeuroImage. Clinical*, 16:23–31, 2017.
 - [40] M Jenkinson and S Smith. A global optimisation method for robust affine registration of brain images. *Medical image analysis*, 5(2):143–56, jun 2001.
 - [41] Jesper L R Andersson, Mark Jenkinson, and Stephen Smith. Non-linear registration aka Spatial normalisation FMRIB Technial Report TR07JA2. Technical report, FMRIB Centre, Oxford, United Kingdom, 2007.

- [42] Gaolang Gong, Pedro Rosa-Neto, Felix Carbonell, Zhang J Chen, Yong He, and Alan C Evans. Age- and gender-related differences in the cortical anatomical network. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 29(50):15684–93, dec 2009.
- [43] Qingjiu Cao, Ni Shu, Li An, Peng Wang, Li Sun, Ming-Rui Xia, Jin-Hui Wang, Gao-Lang Gong, Yu-Feng Zang, Yu-Feng Wang, and Yong He. Probabilistic diffusion tractography and graph theory analysis reveal abnormal white matter structural connectivity networks in drug-naive boys with attention deficit/hyperactivity disorder. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 33(26):10676–87, jun 2013.
- [44] Muthuraman Muthuraman, Vinzenz Fleischer, Pierre Kolber, Felix Luessi, Frauke Zipp, and Sergiu Groppa. Structural Brain Network Characteristics Can Differentiate CIS from Early RRMS. *Frontiers in Neuroscience*, 10:14, feb 2016.
- [45] Jesper L.R. Andersson and Stamatios N. Sotiropoulos. An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *NeuroImage*, 125:1063–1078, jan 2016.
- [46] Alexander Leemans and Derek K. Jones. The B -matrix must be rotated when correcting for subject motion in DTI data. *Magnetic Resonance in Medicine*, 61(6):1336–1349, jun 2009.
- [47] T.E.J. Behrens, M.W. Woolrich, M. Jenkinson, H. Johansen-Berg, R.G. Nunes, S. Clare, P.M. Matthews, J.M. Brady, and S.M. Smith. Characterization and propagation of uncertainty in diffusion-weighted MR imaging. *Magnetic Resonance in Medicine*, 50(5):1077–1088, nov 2003.
- [48] T.E.J. E J Behrens, H. Johansen Berg, S. Jbabdi, M.F.S. F S Rushworth, and M.W. W Woolrich. Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? *NeuroImage*, 34(1):144–155, jan 2007.
- [49] M.C Bortolan, A.N. Carvalho, and J.A. Langa. *Attractors under autonomous and non-autonomous perturbation*, volume 246 of *Mathematical Surveys and Monographs*. American Mathematical Society Providence RI, 2020.
- [50] Y Takeuchi and N Adachi. The existence of globally stable equilibria of ecosystems of the generalized volterra type. *Journal of Mathematical Biology*, 10(4):401–415, Dec 1980.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [WhatLiesUnderneathsupplementary.pdf](#)