

Synergetic and redundant information flow detected by unnormalized Granger causality: application to resting state fMRI

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Abstract

Objectives: We develop a framework for the analysis of synergy and redundancy in the pattern of information flow between subsystems of a complex network. *Methods:* The presence of redundancy and/or synergy in multivariate time series data renders difficult to estimate the neat flow of information from each driver variable to a given target. We show that adopting an unnormalized definition of Granger causality one may put in evidence redundant multiplets of variables influencing the target by maximizing the total Granger causality to a given target, over all the possible partitions of the set of driving variables. Consequently we introduce a pairwise index of synergy which is zero when two independent sources additively influence the future state of the system, differently from previous definitions of synergy. *Results:* We report the application of the proposed approach to resting state fMRI data from the Human Connectome Project, showing that redundant pairs of regions arise mainly due to space contiguity and interhemispheric symmetry, whilst synergy occurs mainly between non-homologous pairs of regions in opposite hemispheres. *Conclusions:* Redundancy and synergy, in healthy resting brains, display characteristic patterns, revealed by the proposed approach. *Significance:* The pairwise synergy index, here introduced, maps the informational character of the system at hand into a weighted complex network: the same approach can be applied to other complex systems whose normal state corresponds to a balance between redundant and synergetic circuits.

1 Introduction

The inference of dynamical networks from time series data is related to the estimation of the information flow between variables [1]. Granger causality (GC) [2] has emerged as a major tool to address this issue. This approach is based on prediction: if the prediction error of the first time series is reduced by including measurements from the second one in the linear regression model, then the second time series is said to have a Granger causal influence on the first one. An important application of this notion is neuroscience, see, e.g., [3, 4, 5, 6].

Interactions in dynamical networks analysis have also been studied with state space models [7], or using Kalman filters [8] to deal with multivariate system identification. Other approaches are rooted in information theory [9, 10] and have been applied to the analysis of complex spatio-temporal systems, e.g. Earth's climate [11]. Whilst these methods are effective in the detection and quantification of directed interactions, they are not suitable to elucidate the informational character of groups of variables, i.e. whether a group of variables provides information about a given target in a synergetic, redundant, or independent way. Synergetic here means that they convey more

information in their joint responses than the sum of their individual informational contributions; redundant means that they jointly convey less than that. Redundancy and synergy are intuitive yet elusive concepts, which have been investigated in different fields, including pure information theory [12, 13, 14, 15, 16]. The role of synergy and redundancy has also been investigated in epilepsy [17] and disorders of consciousness [18]. Those studies suggest that complex systems in normal conditions tend to display a proper balance between redundant and synergetic circuits, and pathologies to disrupt it.

Coming back to Granger causality, it is worth recalling that its pairwise version consists in assessing influence between each pair of variables, independently of the rest of the system. It is well known that the pairwise analysis cannot disambiguate direct and indirect interactions among variables, neither can detect synergy. We remark that the synergetic effects that we consider here, related to the analysis of dynamical influences in multivariate time series, are similar to those encountered in sociological and psychological modeling, where *suppressors* is the name given to variables that increase the predictive validity of another variable after its inclusion into a linear regression equation [19]. Some information-based approaches addressing the issue of collective influence are [20, 14]. The most straightforward extension of pairwise Granger causality, the conditioning approach, removes indirect influences by evaluating to which extent the predictive power of the driver on the target decreases when the conditioning variable is removed. Sometimes though a full conditioning can encounter conceptual limitations, on top of the practical and computational ones: in the presence of redundant variables the application of the standard analysis leads to underestimation of influences [22]. As a convenient alternative to this suboptimal solution, a partially conditioned approach, consisting in conditioning on a small number of variables, chosen as the most informative ones for the driver node, has been proposed [21].

The purpose of the present work is to show that, taking into account the above mentioned problems encountered by the standard definition of Granger causality, an *unnormalized* Granger causality index is better suited for the analysis of systems of many variables, in presence of synergy and redundancy, to provide information for the future state of the system. The novel approach presented here provides a further description of complex systems where the informational character of multiplets of variables is highlighted. The proposed method in principle may be applied to any system characterized by complex regulatory mechanisms.

The paper is organized as follows. The next section is devoted to a brief account on Granger causality, with particular attention to the problems which arise due to redundancy and synergy. In Section III we describe our definition of *unnormalized* Granger causality, providing some examples to show that the proposed metrics disentangles independent sources of information. In Section IV we introduce the Pairwise Synergy Index, a weighted network associated to the informational character of a set of variables, which allows to use methods of complex networks to analyze the informational pattern of large data sets; we will show the application of the proposed approach to resting state fMRI data. Some conclusions will be drawn in section V.

2 Granger causality

Granger causality is a powerful and widespread data-driven approach to determine whether and how two time series exert direct dynamical influences on each other [23]. A convenient nonlinear generalization of GC has been implemented in [24], exploiting

the kernel trick, which makes computation of dot products in high-dimensional feature spaces possible using simple functions (kernels) defined on pairs of input patterns. This trick allows the formulation of nonlinear variants of any algorithm that can be cast in terms of dot products, for example Support Vector Machines [25]. Hence in [24] the idea is still to perform linear GC, but in a space defined by the nonlinear features of the data. This projection is conveniently and implicitly performed through kernel functions [26] and a statistical procedure is used to avoid overfitting.

Quantitatively, let us consider n time series $\{x_\alpha(t)\}_{\alpha=1,\dots,n}$; the lagged state vectors are denoted

$$X_\alpha(t) = (x_\alpha(t-m), \dots, x_\alpha(t-1)),$$

m being the order of the model (window length). Let $\varepsilon(x_\alpha|\mathbf{X})$ be the mean squared error prediction of x_α on the basis of all the vectors $\mathbf{X} = \{X_\beta\}_{\beta=1}^n$ (corresponding to the kernel approach described in [27]). The fully conditioned GC index $\delta_{mv}(\beta \rightarrow \alpha)$ is defined as follows: consider the problem of predicting x_α on the basis of all the variables but X_β and the problem of predicting x_α using all the variables, then the GC is the logarithm variation of the prediction error in the two conditions, i.e.

$$\delta_{mv}(\beta \rightarrow \alpha) = \log \frac{\varepsilon(x_\alpha|\mathbf{X} \setminus X_\beta)}{\varepsilon(x_\alpha|\mathbf{X})}. \quad (1)$$

In [28] it has been shown that not all the kernels are suitable to estimate GC. Two important classes of kernels which can be used to construct nonlinear GC measures are the *inhomogeneous polynomial kernel* (whose features are all the monomials in the input variables up to the p -th degree; $p = 1$ corresponds to linear Granger causality) and the *Gaussian kernel*. We also remark that the complexity of the regression model can be controlled as explained in [27], hence the causality values may be assumed to be not affected by overfitting.

The pairwise Granger causality is given by:

$$\delta_{bv}(\beta \rightarrow \alpha) = \log \frac{\varepsilon(x_\alpha|X_\alpha)}{\varepsilon(x_\alpha|X_\alpha, X_\beta)}. \quad (2)$$

The following examples show that conditioned GC tends to be reduced in presence of redundancy and increased in presence of synergy, the latter occurrence being a problem for pairwise GC, see [15, 29].

2.1 Redundancy due to a hidden source

We show here how redundancy constitutes a problem for fully conditioned GC. Let $h(t)$ be a zero mean and unit variance hidden Gaussian variable, influencing n variables $x_i(t) = h(t-1) + s\eta_i(t)$, and let $w(t) = h(t-2) + s\eta_0(t)$ be another variable which is influenced by h but with a larger delay. The $\{\eta\}$ variables are unit variance Gaussian noise and s controls the noise level. In figure (1) we depict both the linear fully connected and pairwise GC from one of the x 's to w (note that h is not used in the regression model). As n increases, the fully conditioned GC vanishes as a consequence of redundancy, whilst the GC relation is found for any n in the pairwise analysis.

2.2 Synergetic contributions

Let us consider three unit variance iid Gaussian noise terms x_1 , x_2 and x_3 . Let

$$x_4(t) = 0.1(x_1(t-1) + x_2(t-1) + \eta(t)) + \rho x_2(t-1)x_3(t-1).$$

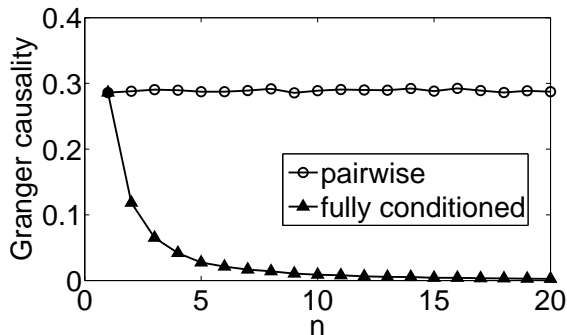


Figure 1: Fully conditioned and pairwise Granger causality are plotted versus the number of variables for the example regarding redundancy. The causality displayed is from one of variables x to the target w . Results are averaged over 100 runs of 1000 time points. In both cases the regression model is linear.

Considering the influence $3 \rightarrow 4$, the fully conditioned GC reveals that 3 is influencing 4, whilst pairwise GC fails to detect this causal relationship, see figure (2), where we use the method described in [22] with the inhomogeneous polynomial kernel of degree two; x_2 is a suppressor variable for x_3 w.r.t. the influence on x_4 . This example shows that pairwise analysis fails to detect synergetic contributions. We also remark that use of nonlinear GC is mandatory in this case to evidence the synergy between x_2 and x_3 .

3 Methods

3.1 Unnormalized Granger Causality

As the two examples at the end of last section show, the presence of relevant synergy and/or redundancy in the data influences the output of standard Granger causal analysis, thus calling for effective methods to deal with those cases.

Firstly, we remark that interaction information is a classical measure of the amount of information (redundancy or synergy) bound up in a set of three variables [30, 31]. In [32] a generalization of the interaction information, to the case of lagged interactions, has been proposed together with an expansion that allows to extend the definition to any number of variables. As the sign of the interaction information corresponds to synergy or redundancy, this interpretation implies that synergy and redundancy are taken to be mutually exclusive qualities of the interactions between variables [33]. Other approaches instead regard synergy and redundancy as separate entities, for example in [34] a *partial information decomposition* (PID) was proposed: the information that two 'source' variables Y and Z hold about a third 'target' variable X can be decomposed into four parts: (i) the unique information that only Y (out of Y and Z) holds about X ; (ii) the unique information that only Z holds about X ; (iii) the redundant information that both Y and Z hold about X ; and (iv) the synergistic information about X that only arises from knowing both Y and Z . These quantities have been evaluated analytically for Gaussian systems [35], and lead to some undesirable results, e.g., redundancy reduces to the minimum information provided by either source variable, and hence is independent of correlation between sources. As suggested in [35], this occur-

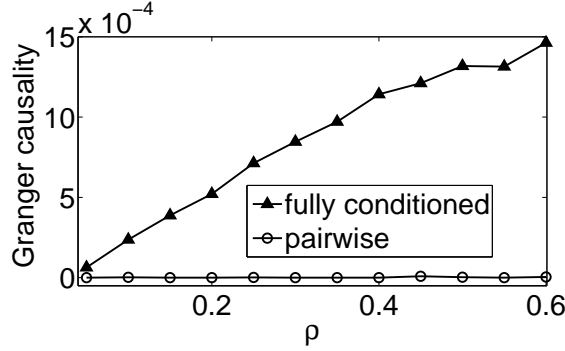


Figure 2: For the example dealing with synergy, CGC and PWGC are plotted versus the coupling ρ , for the causality $x_3 \rightarrow x_4$. Results are averaged over 100 runs of 1000 time points. The regression model here corresponds to the polynomial kernel of order two in the approach[27], i.e. the features are all the monomials in the input variables up to the second order.

rence may be related to the fact that Shannon information between continuous random variables is more precisely based on differential, and the limit to the continuum is not straightforward [36]. Therefore in the case of continuous variables we propose here to describe the informational character of a subset of variables in terms of the reduction of variance of residuals of the target due to inclusion of driver variables, along the lines described in [22]. The informational character of each multiplet will be associated to a single number, which may be seen as the difference of redundancy and synergy in every formalism where these two notions are separately defined (see the discussion in [33]).

First of all we note that the straightforward generalization of Granger causality for driving sets of variables is

$$\delta_{\mathbf{X}}(B \rightarrow \alpha) = \log \frac{\varepsilon(x_\alpha | \mathbf{X} \setminus B)}{\varepsilon(x_\alpha | \mathbf{X})}, \quad (3)$$

where B are a subset of variables, x_α is the target variable and $\mathbf{X} \setminus B$ means the set of all variables except for those X_β with $\beta \in B$. Note that we have isolated the variable X_α , i.e. the present state of the target. The subscript \mathbf{X} has been included to put in evidence the conditioning variables used to evaluate GC.

On the other hand, an unnormalized version of it, i.e.

$$\delta_{\mathbf{X}}^u(B \rightarrow \alpha) = \varepsilon(x_\alpha | \mathbf{X} \setminus B) - \varepsilon(x_\alpha | \mathbf{X}), \quad (4)$$

can be easily shown to satisfy the following interesting property: if $\{X_\beta\}_{\beta \in B}$ are statistically independent and their contributions in the model for x_α are additive, then

$$\delta_{\mathbf{X}}^u(B \rightarrow \alpha) = \sum_{\beta \in B} \delta_{\mathbf{X}}^u(\beta \rightarrow \alpha). \quad (5)$$

We remark that this property does not hold for the standard definition of Granger causality neither for entropy-rooted quantities [33], due to the presence of the logarithm.

In order to identify the informational character of a set of variables B , concerning the causal relationship $B \rightarrow \alpha$, we remind that, in general, synergy occurs if B contributes to α with more information than the sum of all its variables, whilst redundancy corresponds to situations with the same information being shared by the variables in B . We can render quantitative these notions and define the variables in B *synergetic* if $\delta_{\mathbf{X}}^u(B \rightarrow \alpha) > \sum_{\beta \in B} \delta_{\mathbf{X} \setminus B, \beta}^u(\beta \rightarrow \alpha)$, and *redundant* if $\delta_{\mathbf{X}}^u(B \rightarrow \alpha) < \sum_{\beta \in B} \delta_{\mathbf{X} \setminus B, \beta}^u(\beta \rightarrow \alpha)$. If GC is computed conditioning on the whole set of time series \mathbf{X} , the condition for synergy becomes $\delta_{\mathbf{X}}^u(B \rightarrow \alpha) < \sum_{\beta \in B} \delta_{\mathbf{X}}^u(\beta \rightarrow \alpha)$, and that for redundancy becomes $\delta_{\mathbf{X}}^u(B \rightarrow \alpha) > \sum_{\beta \in B} \delta_{\mathbf{X}}^u(\beta \rightarrow \alpha)$. All these conditions are exemplified graphically in fig.(3) for the simple case of two sources $B = \{X_1, X_2\}$. Note that the case of independent variables (and additive contributions) does not fall in the redundancy case neither in the synergetic case, due to (5), as it should be.

Two analytically tractable cases are now reported as examples. First, consider two stationary and Gaussian time series $x(t)$ and $y(t)$ with $\langle x^2(t) \rangle = \langle y^2(t) \rangle = 1$ and $\langle x(t)y(t) \rangle = \mathcal{C}$; they correspond, e.g., to the asymptotic regime of the autoregressive system

$$\begin{aligned} x_{t+1} &= ax_t + by_t + \sigma \xi_{t+1}^{(1)} \\ y_{t+1} &= bx_t + ay_t + \sigma \xi_{t+1}^{(2)}, \end{aligned} \quad (6)$$

where $\xi^{(i)}$ are i.i.d. unit variance Gaussian variables, $\mathcal{C} = 2ab/(1 - a^2 - b^2)$ and $\sigma^2 = 1 - a^2 - b^2 - 2ab\mathcal{C}$. Considering the time series $z_{t+1} = A(x_t + y_t) + \sigma' \xi_{t+1}^{(3)}$ with $\sigma' = \sqrt{1 - 2A^2(1 + \mathcal{C})}$, we obtain for $m = 1$:

$$\delta_{\mathbf{X}}^u(\{x, y\} \rightarrow z) - \delta_{\mathbf{X}}^u(x \rightarrow z) - \delta_{\mathbf{X}}^u(y \rightarrow z) = A^2(\mathcal{C} + \mathcal{C}^2). \quad (7)$$

Hence x and y are redundant (synergetic) for z if \mathcal{C} is positive (negative).

Let's then consider a nonlinear case, i.e. a target vector given by $w_{t+1} = B x_t \cdot y_t + \sigma'' \xi_{t+1}^{(4)}$ with $\sigma'' = \sqrt{1 - B^2(1 + 2\mathcal{C})^2}$, and using the polynomial kernel with $p = 2$, we have

$$\delta_{\mathbf{X}}^u(\{x, y\} \rightarrow z) - \delta_{\mathbf{X}}^u(x \rightarrow z) - \delta_{\mathbf{X}}^u(y \rightarrow z) = B^2(4\mathcal{C}^2 - 1); \quad (8)$$

x and y are synergetic (redundant) for w if $|\mathcal{C}| < 0.5$ ($|\mathcal{C}| > 0.5$).

The presence of redundant variables leads to under-estimation of their Granger causality when the standard multivariate approach is applied (as it is clear from the discussion above, this is not the case for synergetic variables). Redundant variables should then be grouped to get a reliable measure of Granger causality, and to characterize interactions in a more compact way. As it is clear from the discussion above, grouping redundant variables is connected to maximization of the un-normalized Granger causality index (4) and, in the general setting, can be made as follows. For a given target α , we call B the set of the remaining $n - 1$ variables. The partition $\{A_\ell\}$ of B , maximizing the total Granger causality

$$\Delta = \sum_{\ell} \delta_{\mathbf{X}}^u(A_\ell \rightarrow x_\alpha),$$

consists of groups of redundant variables.

As an example, we consider a redundant doublet of variables. Let $h(t)$ be a zero mean and unit variance hidden Gaussian variable, influencing two variables $x_i(t) = h(t - 1) + 0.5\eta_i(t)$, $i = 1, 2$; let $x_3 = \eta_3(t)$ and $w(t) = h(t - 2) + 0.1\eta_0(t)$ be another variable which is influenced by h but with a larger delay. The $\{\eta\}$ variables are unit variance Gaussian noise terms. In table 1 we report the value of the total Granger

Table 1: Total Granger causality in the redundant example

partition	Δ
$\{123\}$	0.88
$\{12\}\{3\}$	0.88
$\{13\}\{2\}$	0.18
$\{23\}\{1\}$	0.18
$\{1\}\{2\}\{3\}$	0.18

causality (to w) for all the partitions of the three variables x_1, x_2, x_3 . We note that in this example the correct partition, $\{12\}\{3\}$, is the maximizer of the total Granger causality; however $\{123\}$ has the same value of Δ . We note, however, that merging variables is justified only if the total Granger causality increases; therefore, in case of degeneracy, the partition that must be chosen, among the maximizers, is the one with the highest number of sets.

3.2 Pairwise synergy index

The discussion in the previous section suggests to quantitatively describe the informational character of two variables i and j , providing information for the future state of the variable x_α , by the following pairwise index:

$$\begin{aligned}\psi_\alpha(i, j) &= \delta_{\mathbf{X} \setminus j}^\mu(i \rightarrow \alpha) - \delta_{\mathbf{X}}^\mu(i \rightarrow \alpha) \\ &= \delta_{\mathbf{X}}^\mu(\{i, j\} \rightarrow \alpha) - \delta_{\mathbf{X}}^\mu(i \rightarrow \alpha) - \delta_{\mathbf{X}}^\mu(j \rightarrow \alpha),\end{aligned}$$

where \mathbf{X} is the set of conditioning variables. ψ is negative for increased unnormalized causality $i \rightarrow \alpha$ due to the inclusion of j in the conditioning variables (positive PSI corresponds to redundancy), see figure (3) for a graphical interpretation of ψ . Note that if i and j are statistically independent and they cause α additively then PSI is zero, differently from interaction information, where a common effect of two causes induces a dependency among the causes that did not formerly exist [37].

Another interpretation of ψ is given by the cumulant expansion of the prediction error of x_α :

$$\varepsilon(x_\alpha | X_\alpha) - \varepsilon(x_\alpha | \mathbf{X}) = \sum_{B \subset \mathbf{X}} S(B). \quad (9)$$

An important formula in combinatorics is the Moebius inversion formula [38], which allows to reconstruct $S(B)$ from equations (9) and (4). Calling $|n_B|$ and $|n_\Gamma|$ the number of variables in the subsets B and Γ respectively, and exploiting also the relation:

$$\sum_{\Gamma \subset B} (-1)^{|n_\Gamma|} = 0,$$

leads to the cumulant expansion:

$$S(B) = \sum_{\Gamma \subset B} (-1)^{|n_B| + |n_\Gamma|} \delta_B^\mu(\Gamma \rightarrow \alpha). \quad (10)$$

The first order cumulant is then

$$S(i) = \delta_i^\mu(i \rightarrow \alpha), \quad (11)$$

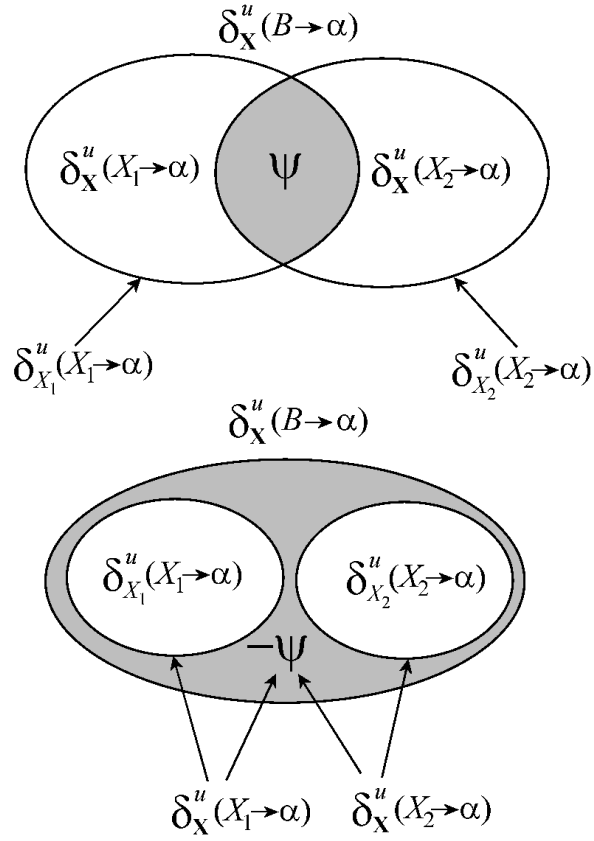


Figure 3: Venn diagrams depicting the informational character of two sources $B = \{X_1, X_2\}$ influencing a target α . Top: redundant source interaction ($\psi > 0$); bottom: synergetic source interaction ($\psi < 0$). In both cases, the overall unnormalized Granger causality from B to α is decomposed as: $\delta_X^u(B \rightarrow \alpha) = \delta_{X_1}^u(X_1 \rightarrow \alpha) + \delta_{X_2}^u(X_2 \rightarrow \alpha) + \psi = \delta_{X_1}^u(X_1 \rightarrow \alpha) + \delta_{X_2}^u(X_2 \rightarrow \alpha) - \psi$.

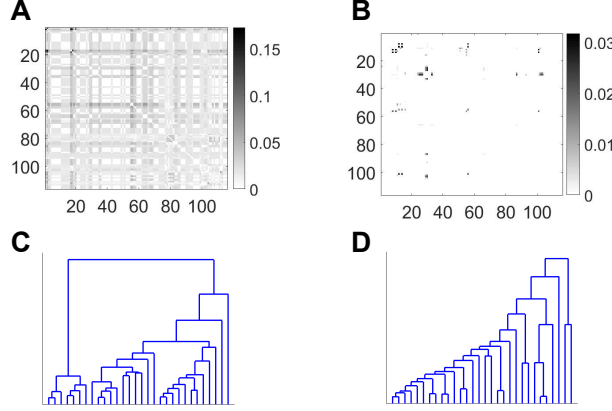


Figure 4: For the fMRI application, the matrices containing the values of redundant and synergetic duplets, and respective dendrograms, are depicted. Top left (A): Ψ_r , redundant values for each pair; Bottom left (C): dendrogram of the redundant matrix. Top right (B): Ψ_s , synergetic values for each pair; Bottom right (D): dendrogram of the synergetic matrix.

the second cumulant is

$$S(i, j) = \delta_{ij}^u(\{ij\} \rightarrow \alpha) - \delta_{ij}^u(i \rightarrow \alpha) - \delta_{ij}^u(j \rightarrow \alpha), \quad (12)$$

the third cumulant is

$$\begin{aligned} S(i, j, k) = & \delta_{ijk}^u(\{ijk\} \rightarrow \alpha) - \delta_{ijk}^u(\{ij\} \rightarrow \alpha) \\ & - \delta_{ijk}^u(\{jk\} \rightarrow \alpha) - \delta_{ijk}^u(\{ik\} \rightarrow \alpha) \\ & + \delta_{ijk}^u(i \rightarrow \alpha) + \delta_{ijk}^u(j \rightarrow \alpha) + \delta_{ijk}^u(k \rightarrow \alpha), \end{aligned} \quad (13)$$

and so on. The index ψ may then be seen as the order two cumulant of the expansion of the prediction error of the target variable; equation (10) allows also the generalization to higher order terms. Obviously ψ also depends also on the choice of the kernel, i.e. on the choice of the regression model.

In order to go a step beyond, we observe that the pairwise synergy index, as well as the cumulant expansion described above, is dependent on the target α . To get rid of this dependency, we make the assumption that the essential features of the dynamics of the system under consideration are captured using just a small number of characteristic modes, and use principal components analysis to obtain a compressed representation of the future state of the system. Calling $\{\xi_\lambda(t)\}_{\lambda=1, \dots, n_\lambda}$ the time courses of the largest n_λ principal components of the whole system, we define the pairwise synergy index:

$$\Psi(i, j) = \sum_{\lambda=1}^{n_\lambda} \psi_\lambda(i, j), \quad (14)$$

obtained summing over the first n_λ principal components taken as targets.

The matrix Ψ may be seen as a weighted network describing the informational character of pairs of variables influencing the future state of the system, zero entries meaning that the corresponding variables provide independent information for the future. The introduction of Ψ allows to describe redundancy and synergy in terms of a

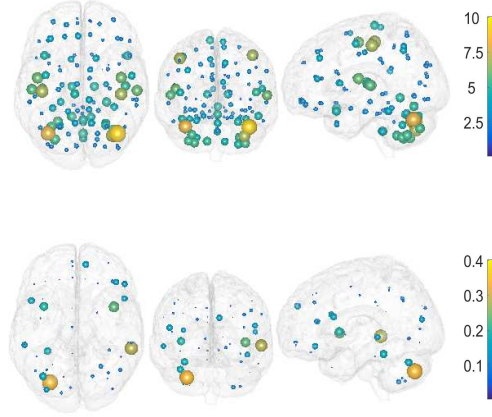


Figure 5: The strengths, sum of the redundant (top) and synergetic (bottom) contributions for each of the 116 brain regions, represented as spheres centered in the respective MNI coordinates. The size of the spheres is proportional to the depicted value.

weighted complex network. In principle this makes complex networks measures (e.g., modular decomposition) suitable to analyze these patterns in large systems.

4 Redundancy and synergy in resting state fMRI

We now turn to investigate synergetic and redundant contributions in large scale brain networks at rest. To this aim we consider resting state functional magnetic resonance imaging (fMRI) recordings from the Human Connectome Project (www.humanconnectome.org). Data are acquired with a repetition time (TR) of 0.72 seconds, slice thickness 2 mm, 72 slices, 2 mm isotropic voxels, 1200 frames. All the parameters are reported in the project documentation. In this study, the first 93 subjects in the 500 subjects release were used. Data were preprocessed as described in [39]. It is well known [40] that the hemodynamic response function (HRF) can confound the temporal precedence when lag-based methods are used to infer directed connectivity in fMRI data, characterized by a slow sampling rate. In order to address this issue in resting state data, for which the onset of the HRF is not explicit, we used the blind deconvolution approach described in [41]. The resulting deconvolved BOLD signal was then averaged according to the 116 anatomical regions of the Automated Anatomical Labeling (AAL) template [42]. Many choices of the parcellation are possible, each one with its pros and cons, here we stick to this widely used one.

The matrix Ψ , averaged over all the subjects, has been split in two: the matrix of positive values, corresponding to redundancy and defined as $\Psi_r = \theta(\Psi)$, θ being the Heaviside function, and the matrix of negative values, corresponding to synergy and defined as $\Psi_s = \theta(-\Psi)$. In figure (4) we depict the two matrices and the corresponding dendrograms. A very small number of pairs are characterized by synergy, whilst the matrix of redundant pairs is much more dense, and the corresponding dendrogram (differently from the dendrogram of synergetic pairs) shows high values of modularity: it follows that the modular decomposition of the redundancy matrix (obtained considering the positive entries of Ψ) provides correlated sets of variables acting as sources

of information for the dynamics of the system (modularity has been evaluated, varying the resolution of the dendrogram, as described in [43]).

In figure (5) we depict the strength of the two matrices, the synergy and the redundancy ones, on the brain. We see that the pattern of redundancy is highly symmetric w.r.t. the two hemispheres, whilst this is not the case for synergy, the highest source of synergy being localized in the cerebellum.

In figure (6) we show some examples of redundant and synergetic pairs of regions. In panel A we consider the cerebrum area with highest redundancy strength, and plot the corresponding absolute value of Ψ w.r.t. all the other regions, showing that homologous regions in the two hemispheres are redundant; this is confirmed in panel B where a cerebellar region is considered. We remark that the AAL partition allows to have homologous areas, thus putting in evidence synergy-redundancy differences in the brain localization. Redundancy is thus governed by contiguity in space as well as by inter-hemispheric symmetry. In panel C and D, instead, we consider the synergy between two given regions and all the others, and observe that, accordingly, synergetic pairs are not homologous, and pairs of regions with highest synergy correspond to a cerebrum region and a cerebellar one on the opposite hemisphere. Maps for all the regions are reported in the supplementary material.

5 Conclusions

In this paper we have considered the inference, from time series data, of the information flow between subsystems of a complex network, an important problem in medicine and biology. In particular we have analyzed the effects that synergy and redundancy induce on the Granger causal analysis of time series. On one side, we have shown that the presence of redundancy and synergy degrades the performance of GC methods; on the other side, we have introduced a frame for data analysis based on unnormalized Granger causality, i.e. the reduction of variance of the residuals of each target variables when candidate driver variables are included in the regression model. Maximizing the total unnormalized Granger causality leads to groups of redundant variables. We have introduced a novel pairwise index of synergy, which for each pair of variables measures how much they interact to provide better predictions of the future state of the system, assumed to be synthesized in terms of a small number of principal components. Such index can be seen as the second cumulant in the expansion of the prediction error of the target variables, to be compared with the expansion of the transfer entropy in [32] which provides the interaction information as the second cumulant. The advantages provided by the present cumulant expansion are (i) conceptual problems found in the Gaussian case [35] are avoided, and (ii) the nonlinearity of Ψ can be easily controlled by varying the kernel in the regression model. A disadvantage of unnormalized GC is the occurrence that the connection with information theory is lost, but the aim of the present approach is to identify redundant and synergetic circuits rather than quantifying the information flow in the system. Our approach can be applied to any multivariate time series data, here we have shown the efficacy of the proposed network approach to resting state fMRI data. Redundancy appears to be more bilateral than synergy, whilst the modular decomposition of the redundancy matrix leads to correlated components of the system under study. We have shown that redundancy is connected with space contiguity of regions and interhemispheric symmetry, whilst synergy occurs mainly between non-homologous pairs of regions in opposite hemispheres.

Summarizing, we have addressed a novel framework to study interdependencies

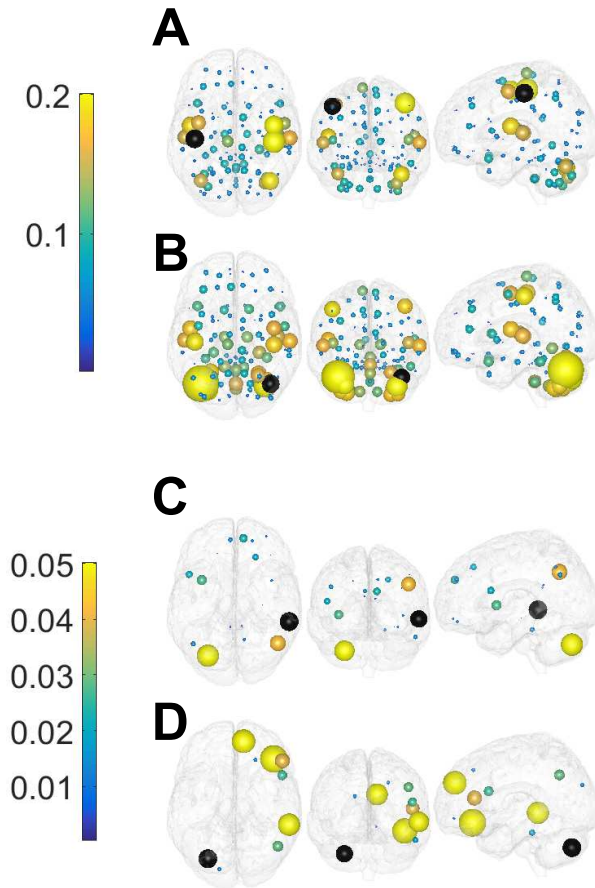


Figure 6: Regions which form redundant and synergetic duplets with representative regions, separately selected among cerebrum and cerebellar regions as those maximizing the overall informational contributions (see fig. 5). Regions are indicated by spheres centered in the MNI coordinates. The size of the spheres is proportional to the value of the duplet formed by the region and the representative one, depicted in black. A: values of the redundant duplets involving the Left Postcentral Gyrus B: values of the redundant duplets involving the Right Middle Temporal Gyrus C: values of the synergetic duplets involving the Left Postcentral Gyrus D: values of the synergetic duplets involving the Left Cerebellar Crus II. All the displayed values are significant as assessed using the closed form available for Gaussian processes. Figures for all regions are available at <https://dx.doi.org/10.6084/m9.figshare.3101947>

among subcomponents of complex systems from time series, which aim at highlighting redundant and synergetic interactions. Whilst many examples of redundant interactions have been reported in the literature, less attention has been spent so far to synergetic interactions between variables whose joint state influence the future of the system. Using the pairwise synergy matrix we have shown that redundancy and synergy display characteristic patterns in healthy brains at rest; such patterns provide information about the system which are complementary to those provided by standard multivariate analysis tools, such as correlations and multivariate Granger causality. A further step will be the assessment of alterations of these patterns in pathologies and different brain states.

References

- [1] E. Pereda, R. Quiroga, J. Bhattacharya. Nonlinear multivariate analysis of neurophysiological signals. *Progress in Neurobiology* 77: 1-37 (2005)
- [2] C.W.J. Granger. Investigating Causal Relations by Econometric Models and Cross-spectral Methods. *Econometrica* 37: 424-438 (1969)
- [3] L.A. Baccalà, K. Sameshima. Partial directed coherence: a new concept in neural structure determination. *Biological Cybernetics* 84: 463-474 (2001)
- [4] V. Nicosia, M. Valencia, M. Chavez. A. Daz-Guilera, V. Latora; Remote Synchronization Reveals Network Symmetries and Functional Modules. *Phys. Rev. Lett.* 110: 174102-174105 (2013)
- [5] G. Plomp, C. Quairiaux, C. M. Michel, L. Astolfi. The physiological plausibility of time-varying Granger-causal modeling: normalization and weighting by spectral power. *NeuroImage* 97: 206-216 (2014)
- [6] A. Porta, L. Faes, *Wiener-Granger Causality in Network Physiology With Applications to Cardiovascular Control and Neuroscience*, Proceedings of the IEEE, Volume:PP, Issue: 99, 1-28 (2015)
- [7] L. Barnett, A.K. Seth. Granger causality for state-space models. *Phys. Rev. E* 91: 040101-040104 (2015).
- [8] M. Havlicek, J. Jan, M. Brazdil, V.D. Calhoun. Dynamic Granger causality based on Kalman filter for evaluation of functional network connectivity in fMRI data. *NeuroImage* 53: 65-77 (2010)
- [9] T. Schreiber. Measuring Information Transfer. *Phys. Rev. Lett.* 85: 461-464 (2000)
- [10] M. Staniek and K. Lehnertz. Symbolic Transfer Entropy. *Phys. Rev. Lett.* 100: 158101-158104 (2008)
- [11] J. Runge et al. Identifying causal gateways and mediators in complex spatio-temporal systems. *Nature Communications* 6: Article number 8502 (2015)
- [12] V. Griffith and C. Koch, Quantifying synergistic mutual information, in *Guided Self-Organization: Inception*, Vol. 9, ed. M. Prokopenko (Berlin: Springer), 159-190 (2014)

- [13] M. Harder, C. Salge and D. Polani. Bivariate measure of redundant information. *Phys. Rev. E* **87**: Article number 012130 (2013)
- [14] J.T. Lizier, B. Flecker, P.L. Williams Artificial Life (ALIFE), 2013 IEEE Symposium on , pp.43,51, doi: 10.1109/ALIFE.2013.6602430 (2013)
- [15] P. Wollstadt, U. Meyer, M. Wibral, A Graph Algorithmic Approach to Separate Direct from Indirect Neural Interactions, arXiv:1504.00156 [cs.IT].
- [16] L. Faes, D. Kugiumtzis, A. Montalto, G. Nollo, D. Marinazzo. Estimating the decomposition of predictive information in multivariate systems. *Phys. Rev. E* **91**: Article number 032904 (2015)
- [17] A. Erramuzpe, G. Ortega, J. Pastor, R. de Sola, D. Marinazzo, S. Stramaglia, J. Cortes. Identification of redundant and synergetic circuits in triplets of electrophysiological data. *Journal of Neural Engineering* **12**: Article number 066007 (2015)
- [18] D. Marinazzo, O. Gosseries, M. Boly, D. Ledoux, M. Rosanova, M. Massimini, Q. Noirhomme, S. Laureys. Directed Information Transfer in scalp electroencephalographic recordings: insights on disorders of consciousness. *Clinical EEG and Neuroscience* **45**: 33-39 (2014)

- [19] A.J. Conger. A Revised Definition for Suppressor Variables: a Guide To Their Identification and Interpretation. *Educational and Psychological Measurement* 34(1): 35-46 (1974)
- [20] D. Chicharro, A. Ledberg. Framework to study dynamic dependencies in networks of interacting processes. *Phys. Rev. E* 86: Article number 041901 (2012)
- [21] D. Marinazzo, M. Pellicoro, and S. Stramaglia. Causal Information Approach to Partial Conditioning in Multivariate Data Sets. *Computational and Mathematical Methods in Medicine*, Volume 2012: Article ID 303601 (2012)
- [22] L. Angelini, M. de Tommaso, D. Marinazzo, L. Nitti, M. Pellicoro, and S. Stramaglia. Redundant variables and Granger causality. *Phys. Rev. E* 81: Article number 037201 (2010)
- [23] K. Hlavackova-Schindler, M. Palus, M. Vejmelka, J. Bhattacharya. Causality detection based on information-theoretic approaches in time series analysis. *Physics Reports* 441: 1-46 (2007)
- [24] D. Marinazzo, M. Pellicoro and S. Stramaglia. Kernel-Granger causality and the analysis of dynamical networks. *Phys. Rev. E* 77: Article number 056215 (2008)
- [25] V. Vapnik. *The Nature of Statistical Learning Theory*. Springer, N.Y., 1995.

- [26] J. Shawe-Taylor and N. Cristianini, *Kernel Methods For Pattern Analysis*. (Cambridge University Press, London, 2004)
- [27] D. Marinazzo, M. Pellicoro, S. Stramaglia. Kernel Method for Nonlinear Granger Causality. *Phys. Rev. Lett.* 100: Article number 144103 (2008)
- [28] N. Ancona and S. Stramaglia. An invariance property of predictors in kernel-induced hypothesis spaces. *Neural Comput.* 18: 749-759 (2006)
- [29] S. Stramaglia, J.M. Cortes and D. Marinazzo. Synergy and redundancy in the Granger causal analysis of dynamical networks. *New J. Phys.* 16: Article number 105003 (2014)
- [30] W.J. McGill. Multivariate information transmission. *Psychometrika* 19, 97-116 (1954).
- [31] E. Schneidman, W. Bialek, M.J. Berry. Synergy, redundancy, and independence in population codes. *Journal of Neuroscience* 23: 11539-11553 (2003)
- [32] S. Stramaglia, G. Wu, M. Pellicoro, D. Marinazzo. Expanding the transfer entropy to identify information circuits in complex systems. *Phys. Rev. E* 86: Article number 066211 (2012)

- [33] N. Timme, W. Alford, B. Flecker, JM Beggs. Synergy, redundancy, and multivariate information measures: an experimentalists perspective. *J. Comput. Neurosci.* 36(2):119-140 (2014)
- [34] P. L. Williams and R. D. Beer, Nonnegative Decomposition of Multivariate Information, preprint (14 pages) arXiv:1004.2515 [cs.IT], 2010, unpublished.
- [35] A.B. Barrett. Exploration of synergistic and redundant information sharing in static and dynamical Gaussian systems. *Phys. Rev. E* 91: Article number 052802 (2015)
- [36] N. Cufaro Petroni. Entropy and Its Discontents: A Note on Definitions. *Entropy* 16(7): 4044-4059 (2014)
- [37] J. Pearl, Probabilistic Reasoning in Intelligent Systems: Networks of Plausible Inference, Morgan Kaufmann, San Mateo, CA (1988)
- [38] R. McEliece, C. Ash, Introduction to Discrete Mathematics, 1st ed. New York: Random House, 1989.
- [39] M.F. Glasser, S.N. Sotiropoulos, J.A. Wilson, T.S. Coalson, B. Fischl, J.L. Andersson, J. Xu, S. Jbabdi, M. Webster, J.R. Polimeni, D.C. Van Essen, M. Jenkinson; WU-Minn HCP Consortium. The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* 80: 105-24 (2013)

- [40] A.K. Seth, P. Chorley, L.C. Barnett. Granger causality analysis of fMRI BOLD signals is invariant to hemodynamic convolution but not downsampling. *NeuroImage* 65:540-55 (2013)
- [41] G. Wu, W. Liao, S. Stramaglia, J. Ding, H. Chen, D. Marinazzo. A blind deconvolution approach to recover effective connectivity brain networks from resting state fMRI data. *Medical Image Analysis* 17(3):365-74 (2013)
- [42] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer and M. Joliot. Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain. *NeuroImage* 15 (1): 273-289 (2002)
- [43] M. Newman. Modularity and community structure in networks. *PNAS* 103 (23): 8577-8582 (2006).