SUBGRAPHS IN COMPLEX SYSTEMS

Sebastiano Stramaglia and Mario Pellicoro
Dipartimento di Fisica,
Universitá di Bari, Italy,
INFN Sezione di Bari, Italy
Email: sebastiano.stramaglia@ba.infn.it

Daniele Marinazzo and Guo-Rong Wu
Faculty of Psychology
Educational Sciences, Department of Data Analysis,
Ghent University, Henri Dunantlaan 1, B-9000 Ghent, Belgium,
Email: daniele.marinazzo@gmail.com

***Abstract*—An approach to put in evidence multiplets of variables, providing information for the future state of a subsystem, is proposed. The method employs an exact expansion of the transfer entropy; significant multiplets are associated to informational circuits present in the system, with an informational character (synergetic or redundant) which can be related to the sign of the contribution. We also present preliminary results on an fMRI data set.**

I. INTRODUCTION

Information theoretic treatment of groups of correlated degrees of freedom can reveal their functional roles as memory structures or those capable of processing information [1]. Information quantities reveal if a group of variables may be mutually redundant or synergetic [2], [3]. The application of these insights to identify functional connectivity structure is a promising line of research. Most approaches for the identification of functional relations between nodes of a complex networks rely on the statistics of motifs, subgraphs of *k* nodes that appear more abundantly than expected in randomized networks with the same number of nodes and degree of connectivity [4], [5]. An approach to identify functional subgraphs in complex networks, relying on an exact expansion of the mutual information with a group of variables, has been presented in [6].

On the other hand, understanding couplings between dynamical subsystems is a topic of general interest. Transfer entropy [7], which is related to the concept of Granger causality [8], has been proposed to distinguish effectively driving and responding elements and to detect asymmetry in the interaction of subsystems. By appropriate conditioning of transition probabilities this quantity has been shown to be superior to the standard time delayed mutual information, which fails to distinguish information that is actually exchanged from shared information due to common history and input signals. On the other hand, Granger causality formalized the notion that, if the prediction of one time series could be improved by incorporating the knowledge of past values of a second one, then the latter is said to have a *causal* influence on the former. Initially developed for econometric applications, Granger causality has gained popularity also in neuroscience (see, e.g., [9], [10], [11], [12]).

In this work we propose a formal expansion of the transfer entropy to put in evidence irreducible sets of variables which provide information for the future state of the target. Multiplets characterized by an high value, unjustifiable by chance, will be associated to informational circuits present in the system, with an informational character (synergetic or redundant) which can be associated to the sign of the contribution.

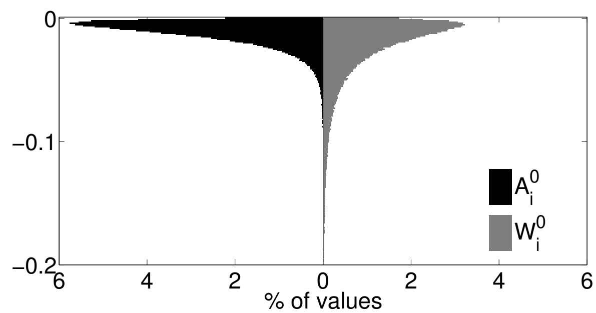

Fig. 1. Concerning fMRI data, the distribution of the first order term in the expansions, eqs. (9) and (4) are depicted.

II. Expansion of the transfer entropy

We start describing the work in [6]. Given a stochastic variable X and a family of stochastic variables $\{Y_k\}_{k=1}^{n}$, the following expansion for the mutual information has been derived there:

$$S\left(X|\{Y\}\right) - S(X) = -I\left(X;\{Y\}\right) = \sum_i \frac{\Delta S(X)}{\Delta Y_i} + \sum_{i>j} \frac{\Delta^2 S(X)}{\Delta Y_i \Delta Y_j} + \cdots + \frac{\Delta^n S(X)}{\Delta Y_i \cdots \Delta Y_n}, \tag{1}$$

where the variational operators are defined as

$$\frac{\Delta S(X)}{\Delta Y_i} = S\left(X|Y_i\right) - S(X) = -I\left(X;Y_i\right), \tag{2}$$

$$\frac{\Delta^2 S(X)}{\Delta Y_i \Delta Y_j} = -\frac{\Delta I\left(X;Y_i\right)}{\Delta Y_j} = I\left(X;Y_i\right) - I\left(X;Y_i|\,Y_j\right), \tag{3}$$

and so on.

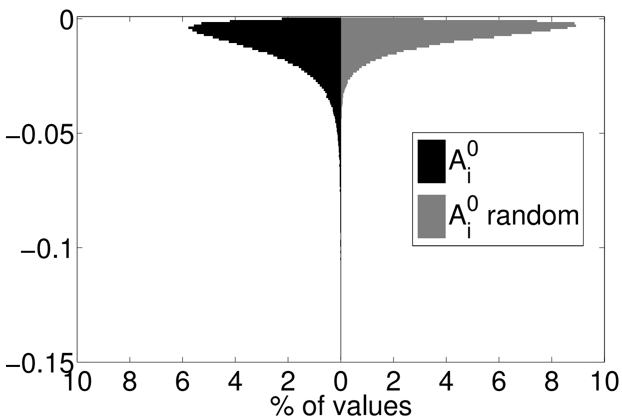

Fig. 2. Concerning fMRI data, the distribution of the first order term in the expansion of the transfer entropy, eq. (9), is compared with the results corresponding to a reshuffling of the target time series.

Now, let us consider $n+1$ time series $\{x_\alpha(t)\}_{\alpha=0,\ldots,n}$. The lagged state vectors are denoted

$$Y_\alpha(t) = \left(x_\alpha(t-m), \ldots, x_\alpha(t-1)\right),$$

m being the window length.

Firstly we may use the expansion (1) to model the statistical dependencies among the x variables at equal times. We take x_0 as the target time series, and the first terms of the expansion are

$$W_i^0 = -I\left(x_0; x_i\right) \tag{4}$$

for the first order;

$$Z_{ij}^0 = I\left(x_0; x_i\right) - I\left(x_0; x_i|x_j\right) \tag{5}$$

for the second order; and so on. Here we propose to consider also

$$S\left(x_0|\{Y_k\}_{k=1}^n\right) - S(x_0) = -I\left(x_0; \{Y_k\}_{k=1}^n\right), \tag{6}$$

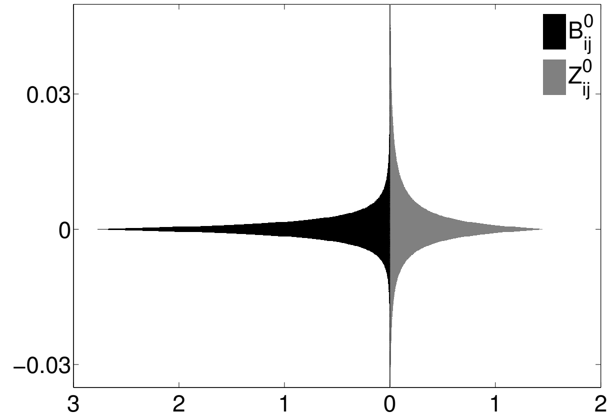

Fig. 3. Concerning fMRI data, the distribution of the second order term in the expansions, eqs. (10) and (5) are depicted.

which measures to what extent the remaining variables contribute to specifying the future state of x_0. This quantity can be expanded according to (1):

$$S\left(x_0|\{Y_k\}_{k=1}^n\right) - S(x_0) = \sum_i \frac{\Delta S(x_0)}{\Delta Y_i} + \sum_{i>j} \frac{\Delta^2 S(x_0)}{\Delta Y_i \Delta Y_j} + \cdots + \frac{\Delta^n S(x_0)}{\Delta Y_i \cdots \Delta Y_n}. \tag{7}$$

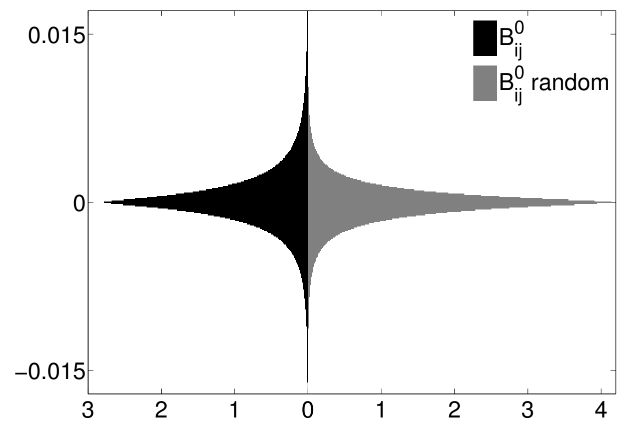

Fig. 4. Concerning fMRI data, the distribution of the second order term in the expansion of the transfer entropy, eq. (9), is compared with the results corresponding to a reshuffling of the target time series.

A drawback of the expansion above is that it does not remove shared information due to common history and input signals; therefore we propose to condition on the past of x_0, i.e. Y_0. To this aim we introduce the conditioning operator $\mathcal{C}_{Y_0}$:

$$\mathcal{C}_{Y_0} S(X) = S(X|Y_0),$$

and observe that $\mathcal{C}_{Y_0}$ and the variational operators (2) commute. It follows that we can condition the expansion

(7) term by term, thus obtaining

$$\begin{array}{l} S\left(x_0|\{Y_k\}_{k=1}^n, Y_0\right) - S(x_0|Y_0) = \\ -I\left(x_0;\{Y\}_{k=1}^n|Y_0\right) = \\ \sum_i \frac{\Delta S(x_0|Y_0)}{\Delta Y_i} + \sum_{i>j} \frac{\Delta^2 S(x_0|Y_0)}{\Delta Y_i \Delta Y_j} + \cdots + \frac{\Delta^n S(x_0|Y_0)}{\Delta Y_i \cdots \Delta Y_n}. \end{array} \quad (8)$$

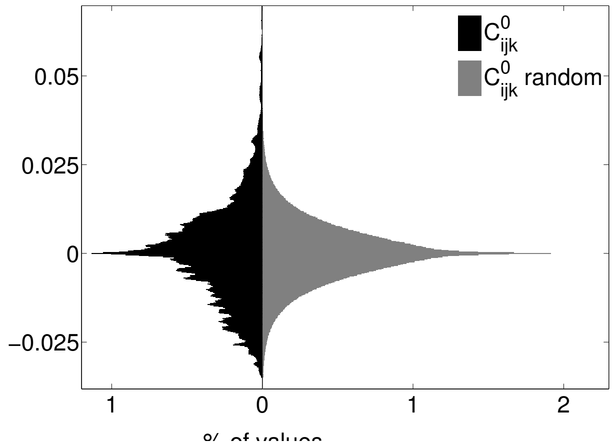

Fig. 5. Concerning fMRI data, the distribution of the third order term in the expansion of the transfer entropy, eq. (9), is compared with the results corresponding to a reshuffling of the target time series.

We note that variations at every order in (8) are symmetrical under permutations of the Y_i. Moreover statistical independence among any of the Y_i results in vanishing contribution to that order: each nonvanishing term in this expansion accounts for an irreducible set of variables providing information for the specification of the target. The first order terms in the expansion are given by:

$$A_i^0 = \frac{\Delta S(x_0|Y_0)}{\Delta Y_i} = -I\left(x_0; Y_i|Y_0\right), \quad (9)$$

and coincide with the bivariate transfer entropies $i \to 0$ (times -1). The second order terms are

$$B_{ij}^0 = I\left(x_0; Y_i|Y_0\right) - I\left(x_0; Y_i|Y_j, Y_0\right), \quad (10)$$

whilst the third order terms are

$$\begin{array}{rl} C_{ijk}^0 = & I\left(x_0; Y_i|Y_j, Y_0\right) + I\left(x_0; Y_i|Y_k, Y_0\right) \\ & -I\left(x_0; Y_i|Y_0\right) - I\left(x_0; Y_i|Y_j, Y_k, Y_0\right). \end{array} \quad (11)$$

An important property of (8) is that the sign of nonvanishing terms reveals the informational character of the corresponding set of variables: a negative sign indicates that the group of variables contribute with more information, than the sum of its subgroups, to the state of the target (synergy), while positive contributions correspond to redundancy.

Another important point that we address here is how get a reliable estimate of conditional mutual information from data. In this work we adopt the assumption of Gaussianity and we use the exact expression that holds in this case [14] and reads as follows. Given multivariate Gaussian random variables X, W and Z, the conditioned mutual information is

$$I\left(X; W|Z\right) = \ln \frac{|\Sigma(X|Z)|}{|\Sigma(X|W \oplus Z)|}, \quad (12)$$

where $|\cdot|$ denotes the determinant, and the partial covariance matrix is defined

$$\Sigma(X|Z) = \Sigma(X) - \Sigma(X,Z)\Sigma(Z)^{-1}\Sigma(X,Z)^{\top}, \quad (13)$$

in terms of the covariance matrix $\Sigma(X)$ and the cross covariance matrix $\Sigma(X,Z)$; the definition of $\Sigma(X|W \oplus Z)$ is analogous.

III. Applications: magnetic resonance

In order to test this approach on a real neuroimaging dataset we used resting state fMRI data downloaded from the website fcon_1000.projects.nitrc.org, and described in [15].

The resting-state scans were obtained for each participant using a Siemens Allegra 3.0 Tesla scanner. Each scan consisted of 197 contiguous EPI functional volumes (TR = 2000 ms; TE = 25 ms; flip angle = 90°, 39 slices, matrix = 64×64; FOV = 192 mm; acquisition voxel size = $3 \times 3 \times 3$ mm). All individuals were asked to relax and remain still with their eyes open during the scan. Processing of BOLD signal was performed using the Statistical Parametric Mapping software (SPM8, http://www.fil.ion.ucl.ac.uk/spm), including slice-timing correction, head motion correction, normalization into the Montreal Neurological Institute space, and then resampled to 3-mm isotropic voxels. The functional images were segmented into 90 regions of interest (ROIs) using the automated anatomical labeling (AAL) template reported in previous studies [16]. For each subject, the representative time series of each ROI was obtained by averaging the fMRI time series across all voxels in the ROI. Several procedures were used to remove possible spurious variances from the data through linear regression [17],[18]. These were 1) six head motion parameters obtained in the realigning step, 2) signal from a region in cerebrospinal fluid, 3) signal from a region centered in the white matter.

For each subject, we evaluated the first terms in the expansions of the conditional mutual information. We then pooled all the values of the terms in the expansions, from all subjects, and we report their distributions in the following figures. In figure (1) we compare the distributions of A_i^0, the first order terms in the expansion of the information flow (equivalent to the bivariate transfer entropy), with those of the equal time dependencies W_i^0. This figure shows that the data set is characterized by equal time statistical dependencies and by nontrivial causal connections. In figure (2) the distribution of the bivariate transfer entropies is compared with those obtained after a random reshuffling of the target time series: it shows that a relevant fraction of bivariate interactions is statistically significant. In figure (3) we report the distributions of the second order terms, both for information flow and for instantaneous correlations: negative and positive terms are present, i.e. both synergetic and redundant circuits of three variables are evidenced by the proposed approach. Some of these interactions are statistically significant, see figure (4).

In figure (5) we report the distribution of the third order terms for the information flow which correspond to the target Posterior cingulate gyrus, a major node within the default mode network (DMN) with high metabolic activity and dense structural connectivity to widespread brain regions, which suggests it has a role as a cortical hub. The region appears to be involved in internally directed thought, for example, memory recollection [19]. We compare with the corresponding distribution for shuffled target; it appears that there are significant circuits of four variables, involving Posterior cingulate gyrus, and most of them are redundant.

IV. Conclusions

In this work we have proposed to generalize a recently proposed a formal expansion of the mutual information, between a stochastic variable and a set of other variables, so as to introduce a corresponding expansion for the transfer entropy. The terms of the proposed expansion put in evidence irreducible sets of variables which provide information for the future state of the target channel. The sign of the contribution due a given multiplet is related to its informational character (synergetic or redundant). We have reported preliminary results concerning the application of the proposed approach to fMRI data, where it has put in evidence the presence of informational circuits of three and four variables. It is worth mentioning that recently a approach which has been conceived for the same task has been developed in a different frame [20], [21].

References

[1] A. Borst, F.E. Theunissen, Nat. Neurosci. **2**, 947 (1999).
[2] E. Schneiman, W. Bialek, M.J. Berry II, J. Neuroscience **23**, 11539 (2003).
[3] L. Bettencourt et al., Phys. Rev. **E 75**, 21915 (2007).
[4] R. Milo et al., Science 298, 824 (2002)
[5] E. Yeger-Lotem et al., Proc. Natl.Acad. Sci. U.S.A. 1010, 5934 (2004).
[6] L.M.A. Bettencourt, V. Gintautas, M.I. Ham, Phys. Rev. Lett. **100**, 238701 (2008).
[7] T. Schreiber, Phys. Rev. Lett. **85**, 461 (2000).
[8] C.W.J. Granger, Econometrica **37**, 424 (1969).
[9] K.J. Blinowska, R. Kus, M. Kaminski, Phys. Rev. E **70**, 50902(R) (2004)
[10] D.A. Smirnov, B.P. Bezruchko, Phys Rev. **E 79**, 46204 (2009)
[11] M. Dhamala, G. Rangarajan, M. Ding, Phys. Rev. Lett. **100**, 18701 (2008)
[12] D. Marinazzo, M. Pellicoro, S. Stramaglia, Phys. Rev. Lett. **100**, 144103 (2008)
[13] W.J. McGill, Psychometrika **19**, 97-116 (1954).
[14] L. Barnett, A.B. Barrett, and A.K. Seth, Phys Rev. Lett. **103**, 238701 (2009)
[15] Z. Shehzad, A.M.C. Kelly, P.T. Reiss, D.G. Gee, K. Gotimer, L.Q. Uddin, S.H. Lee, D.S. Margulies, A.K. Roy, B.B. Biswal, E. Petkova, F.X. Castellanos, M.P. Milham, Cerebral cortex, **19** (2009)
[16] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer, M. Joliot, Neuroimage **15**, 273 (2002)
[17] M.D. Fox, A.Z. Snyder, J.L. Vincent, M. Corbetta, D.C. Van Essen, M.E. Raichle, Proc Natl Acad Sci U S A. **102**, 9673 (2005)
[18] R. Salvador, J. Suckling, M.R. Coleman, J.D. Pickard, D. Menon, E. Bullmore, Cereb. Cortex **15**, 1332 (2005)
[19] R. Leech, R. Braga, and D. J. Sharp, The Journal of Neuroscience 32, 215-222 (2012).
[20] P.L. Williams, R.D. Beer, *Nonnegative Decomposition of Multivariate Information*, preprint arXiv:1004.2515 (2010).
[21] P.L. Williams, R.D. Beer, *Generalized Measures of Information Transfer*, preprint arXiv:1102.1507 (2011).