Direction of Coupling from Phases of Interacting Oscillators: A Permutation Information Approach

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We introduce a directionality index for a time series based on a comparison of neighboring values. It can distinguish unidirectional from bidirectional coupling, as well as reveal and quantify asymmetry in bidirectional coupling. It is tested on a numerical model of coupled van der Pol oscillators, and applied to cardiorespiratory data from healthy subjects. There is no need for preprocessing and fine-tuning the parameters, which makes the method very simple, computationally fast and robust.

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Natural systems are typically highly complex, and so also are the signals derived from them. This is especially true of the cardiovascular system and brain, and an enormous amount of effort has been made in recent years to develop time series analysis for diagnostic applications, i.e., to find ways to determine the physiological state by analysis of the corresponding complex signals. Measures of complexity have been developed that distinguish between regular, chaotic, and random behaviors [1], and can try to predict a heart attack or epileptic seizure [2,3]. Synchronization and related phenomena in coupled complex systems [4] have been found to occur, not only in physical, but also in many biological systems, e.g., the cardiorespiratory interaction [5–8] and neural signals [9–13]. It is often important to detect, not only the existence of synchronization, but also the predominant *direction* of the coupling between the systems. The coupling direction [14] has been extracted from the amplitudes of the system observables by evaluation of their mutual predictability [9,10], or from mutual nearest neighbors in reconstructed state spaces [15], or by use of information-theoretic approaches [12,13,16].

Most of these methods involve the quantification of certain aspects of nearest neighbors in phase space and, as a result, are computationally expensive. Typically, the time series is partitioned into m sections. The method in use is then applied within each section; m can then be increased in order to seek limiting behavior. The appropriate partitions can be hard to find. To circumvent this difficulty, Bandt and Pompe (BP) [1] suggest that the symbol sequence should come naturally from the time series, without further model assumptions, and that one should therefore take partitions as given by comparisons of neighboring values of the series (see below).

In this Letter, we apply the BP approach to the directionality index obtained from information theory [17], thereby deriving the system dynamics and directionality of the interacting systems. We test the scheme on a pair of coupled van der Pol (VDP) oscillators and then apply it to cardiorespiratory time series from healthy subjects.

We first define the *permutation entropy* (PE). Consider a time series $\{X(t)\}$: n consecutively numbered real data can be sorted in an increasing order. In this way, we have $n!$ permutations π of order n which are considered here as possible order types of n different numbers. So these n points are mapped to one out of $n!$ permutations. It is clear that each point in the embedding space, indexed by i, can be mapped to one of the $n!$ permutations. When each such permutation is considered as a symbol, then the reconstructed trajectory is represented by a symbol sequence. The number of distinct symbols can be at most $n!$. Let the probability distribution for the symbols be $\pi_1, \pi_2, \ldots, \pi_k$, where $k \leq n!$. Then the PE for the time series is defined [1] as the Shannon entropy for the k symbols $H(n) = -\sum_{i=1}^{k} \pi_i \ln \pi_i$. The PE shows the same behavior for different values of n [1]; it is also evident that use of the PE is extremely fast since it uses easy comparison between neighboring values, rather than partitioning the amplitude into different sections (which must be optimized by trial and error). BP have shown that the PE is an appropriate complexity measure for chaotic time series, in particular, in the presence of dynamical and observational noise. Unlike other complexity parameters, it is not significantly affected by weak noise.

We now introduce the information-theoretic tools. The conditional mutual information (CMI) [12] of two random variables X_1, X_2, given the variable X_3, is $I(X_1; X_2|X_3) = H(X_1|X_3) + H(X_2|X_3) - H(X_1, X_2|X_3)$. The entropies $H(X_1|X_3)$, $H(X_2|X_3)$, $H(X_1, X_2|X_3)$ are taken in the PE sense. Consider two time series $\{X_1(t)\}$ and $\{X_2(t)\}$ representing the observables of two possibly coupled systems. Dependence structures between the two processes, as revealed by their time series, can be studied using the simple mutual information $I(\pi_{x_2}; \pi_{x_{1\tau}})$, where points $x_2(t)$ and $x_1(t+\tau)$ are mapped to π_{x_2} and $\pi_{x_{1\tau}}$. $I(\pi_{x_2}; \pi_{x_{1\tau}})$ measures the average amount of information contained in the process $\{X_2\}$ about the process $\{X_1\}$ in its future τ time units ahead. Predictability measures that can also carry information about the τ future of the process contained within the process itself, i.e., if $I(x_1; x_2) > 0$ so that the processes $\{X_1\}$ and $\{X_2\}$ are not independent.

For inferring causal relationships, i.e., the directionality of coupling between the processes $\{X_1\}$ and $\{X_2\}$, we need to estimate the net information about the τ future of the process $\{X_1\}$ contained within the process $\{X_2\}$. To do so, we increment vectors of n points (in what follows we use $n = 3$) of $\{X_1\}$ as $x_1(t_i) - x_1(t_{i+\tau})$, $x_1(t_{i+1}) - x_1(t_{i+\tau+1}), \ldots, x_1(t_{i+n}) - x_1(t_{i+\tau+n})$ $(\tau \geq n)$, and then map these vector to $\pi_{\Delta x_1}$ ($\pi_{\Delta x_2}$ related to increments in $\{X_2\}$). We then introduce a directionality index (DI) defined in analogy with those of Rosenblum *et al.* [18,19] and Paluš and Stefanovska [17]

$$D_{12} = \frac{I_{12} - I_{21}}{I_{12} + I_{21}}, \tag{1}$$

where the measure I_{12} of how system 1 drives system 2 is equal to the conditional mutual information $I(\pi_1; \pi_{\Delta x_2} | \pi_2)$ for a chosen time lag τ. Assuming that $I_{ij} \neq I_{ji} \neq 0$, D_{12} is positive if the driving from system 1 to system 2 prevails, and negative for the opposite case.

Nonlinear oscillators have been a subject of particular interest in recent years [8,20,21] on account of their importance for modeling phenomena and processes in, e.g., physics, chemistry, biology, and engineering. Among them, the self-sustained classical VDP oscillator often serves as a paradigm for smoothly oscillating limit cycle or relaxation oscillations. So, before applying our new method to determine directionality in a cardiorespiratory signal, we test it by investigating directionality in a pair of coupled VDP oscillators.

$$\begin{aligned} \ddot{x}_1 - \mu(1 - x_1^2)\dot{x}_1 + \omega_1 x_1 + \epsilon_1 x_2 &= \eta_1(t), \\ \ddot{x}_2 - \mu(1 - x_2^2)\dot{x}_2 + \omega_2 x_2 + \epsilon_2 x_1 &= \eta_2(t). \end{aligned} \tag{2}$$

We set $\omega_{1,2} = 1 \pm 0.05$, and consider mutually independent Gaussian noises of zero mean and covariance $\eta_i(t)\eta_j(t') = \sigma^2\delta(t - t')\delta_{i,j}$ with standard deviation $\sigma_j = 0.3$ for $j = 1, 2$. We have used two coupled VDP oscillators and fixed all the parameters except the coupling from oscillator 1 to 2, ϵ_2, and *vice versa* ϵ_1. Thus any change detected by our directionality method can be related to changes made in the actual couplings between the two systems: the sign and magnitude of the calculated directionality index should reflect the coupling asymmetry implemented. We generate time series of $x_{1,2}(t)$ for different fixed values of the coupling parameters ϵ_1 and ϵ_2. In analogy with the analysis techniques for cardiorespiratory data, we extract instantaneous frequencies of the two oscillators by using the marked events method [22]. The I_{ij} were averaged over a short range of lags (5–10 s) to decrease fluctuations of the estimates. To test the significance of our results, we used surrogate data [17,23]; here, realizations in which the data were randomly shuffled in 100 different ways, were used. Estimating the CMIs and DIs for the surrogate data sets, we assessed the fluctuations of these quantities for data where there could be neither coupling nor directionality. We illustrate the range within which 95% of the surrogate I_{ij} fall by the dashed lines in Fig. 1, labeled as I^*_{ij}. Only those CMIs and corresponding DIs that lie in the 5% of the right-hand tail of probability density function (pdf) of realizations of surrogate data are inferred as significant. The dependence of D_{12} on ϵ_1 when ϵ_2 is fixed at 0.1, is shown in Figs. 1(c) and 1(d). It is clear that the bigger ϵ_1, the larger and more negative D_{12} becomes (when $\epsilon_1 = \epsilon_2$ the accuracy is decreased). To test for symmetry, we fixed the coupling parameter $\epsilon_1 = 0.1$

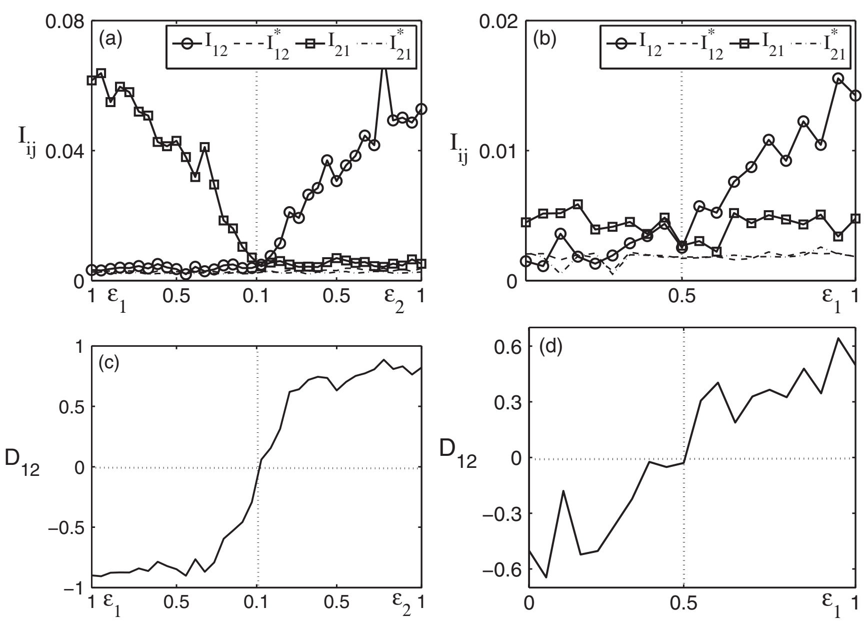

FIG. 1. Directionality results for the noisy VDP oscillators (2), computed from a time series of length 1500 s: (a) The CMIs I_{ij} (see panel) for $\epsilon_2 = 0.1$, as a function of ϵ_1 (left), and for $\epsilon_1 = 0.1$ as a function of ϵ_2 (right); (b) I_{ij} for $\epsilon_2 = 0.5$, as a function of ϵ_1; (c) and (d), the directionality indices D_{12} corresponding to (a) and (b), respectively. The I^*_{ij} represent surrogate data (see text). The positivity of D_{12} implies that the driving from system 1 to system 2 prevails, and vice versa.

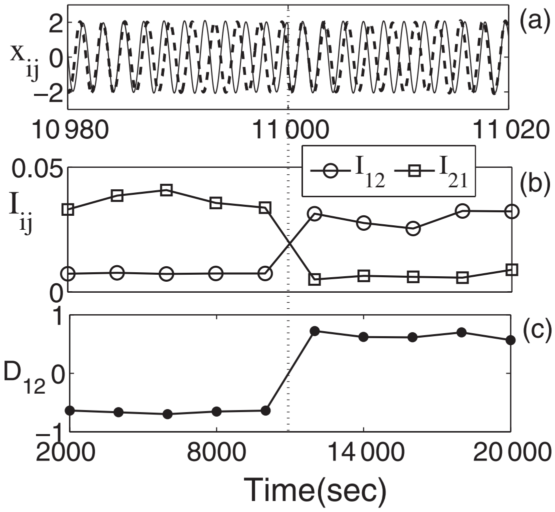

FIG. 2. Detection of a change in directionality for the noisy VDP oscillators, illustrating the sensitivity of the PI approach. At $t = 11\,000$ s (vertical dotted line), the coupling coefficients are inverted from $\epsilon_1 = 0.5$, $\epsilon_2 = 0.1$ to $\epsilon_1 = 0.1$, $\epsilon_2 = 0.5$: (a) the corresponding signals; (b) the CMIs (see panel) as a function of time; and (c) the corresponding evolution of D_{12}. The changes in the CMIs and in D_{12} at $t = 11\,000$ s are strikingly evident.

and generated time series of $x_{1,2}(t)$ for different values of the coupling parameter ϵ_2, as shown in Fig. 1(a). For additional validation, we have also derived the same quantity for other regimes: by fixing $\epsilon_2 = 0.5$ and changing ϵ_1. In this case too the directionality D_{12} varied in the manner expected. Figure 2 illustrates the sensitivity of this approach in detecting changes in directionality with time. Initially, $\epsilon_1 = 0.5$ and $\epsilon_2 = 0.1$; then, at $t = 11\,000$, the values of ϵ_1, ϵ_2 were reversed. This event is clearly detected by the corresponding changes in I_{12}, I_{21}, and D_{12}. The figure also provides a useful indication of the variation in time of the DI and CMIs using 2000 s windows.

Given that the ratio of cardiac and respiratory frequencies can in practice be rather large, we have also studied systems (2) with such frequency ratios as $\omega_1{:}\omega_2 = 4{:}1$. The results are shown in Fig. 3. The DI D_{12} detects the correct coupling directionality for the majority of the coupling parameter values. Again we have investigated two cases, first fixing $\epsilon_2 = 0.1$ and taking different values of ϵ_1, and secondly vice versa. The DI successfully reveals the correct relationships. Comparison of the left and right-hand parts of 3(a) illustrates an important feature of coupled oscillators with different frequencies: that the influence of the lower frequency oscillator on the higher one is in general stronger than in the opposite case.

Cardiorespiratory data was obtained from a group of 20 healthy subjects (age 66 ± 6, median 64, 9 F and 11 M). The data were all recorded noninvasively for 30 min with the subjects in repose [24] using, respectively, a 3-lead ECG system and piezoresistive sensor attached to a belt around the thorax. A sampling rate of 400 Hz was used. None of the subjects was on medication or had any history of cardiovascular disease.

The instantaneous frequencies of the cardiac and respiratory oscillations were extracted using the marked events method [22]. The CMIs I_{21} and I_{12}, and the DI D_{12}, were then calculated as shown for a typical example in Fig. 4 with confidence level of 95% of 1000 realizations of the surrogate data. Here, 1 represents the cardiac and 2 represents the respiratory system. It was found that I_{12} was bigger than I_{21} for 18 subjects, showing that respiration drives the heart more than vice versa, an outcome that is consistent with the results of methods developed for detecting the coupling directionality of interacting phases [17,19], and with direct physiological observations. Note that D_{12} was found to be negative for all subjects, but our surrogate data test reveals (with a 95% level of confidence) that its value is statistically significant in only 18 out of 20 cases. This simply means that for the remaining 2 subjects, no statistically meaningful result can be derived with this level of confidence. If we reduce the required level of confidence to, e.g., 75%, the I_{21} indices for these two subjects also lie in the significant area. This actually has a physical explanation, which is due to intersubject differences. Certainly, all the subjects are different because of complex behavior of the human body and also because of the different conditions of different subjects. Therefore, for some of the subject we can recognize the pattern of directionality with 100% accuracy, but for others, the accuracy is smaller. Nevertheless, the method can still recognize the directionality pattern for all of the subjects, conditional on acceptance of a lower level of significance. In fact, comparison with surrogates saves us from making an unreliable inference of the directionality, at the same time, one de-

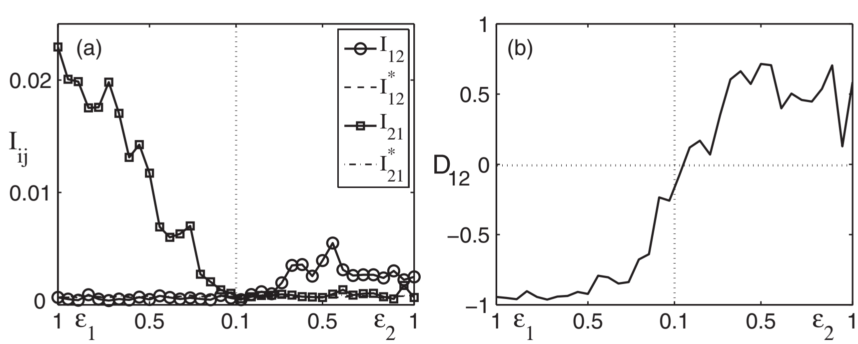

FIG. 3. Directionality results for the pair of noisy VDP oscillators (2) for the case where $\omega_1 : \omega_2 = 4{:}1$, computed from a time series of length 1500 seconds: (a) the CMIs I_{ij} (see panel) for $\epsilon_2 = 0.1$, as a function of ϵ_1 (left), and for $\epsilon_1 = 0.1$ as a function of ϵ_2 (right); (b) the corresponding directionality index D_{12} showing the correct behavior.

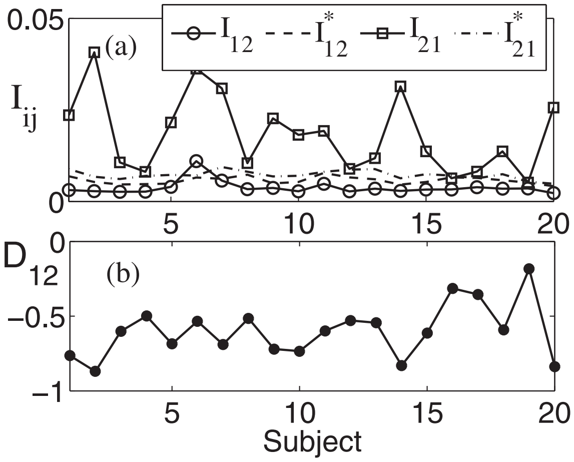

FIG. 4. Results of applying the PI method to cardiorespiratory data measured from 20 healthy subjects: (a) The CMIs I_{ij} (see panel); and (b) the directionality index D_{12}. The index 1 is related to the heart and 2 to respiration. The observed negativity of D_{12} in (b) implies that respiration is driving cardiac activity. The dashed lines in (a) are surrogate data (see text).

termines the accuracy of the results. The necessity of establishing the significance level is obvious, as even relatively large positive values of I_{12} do not necessarily reflect the presence of a driver response.

In summary, our PI method enables the quantification of the directionality of coupling between interacting oscillators and the detection of dynamical changes in complex time series, which are needed not only in relation to the cardiovascular system but also in the study of superachiasmatic nucleus neurons [20], brain waves, and the heart [8], and the modeling of calcium oscillations in living cells [21]. By analyzing two coupled VDP oscillators as well as a number of cardiorespiratory data, we have shown that the PI can indeed be effectively used to detect driver-response relationships between the systems studied. Compared to earlier approaches [17,23], the PI method is faster, since making and optimizing partitions needs time, whereas here the partitions come out naturally without any model assumptions. Moreover, noise has less influence here as we do not use values related to amplitudes: we just compare consecutive points. Even for relatively large noise intensity, we expect local effects to be relatively small whereas, for partitions computed from the whole signal, the errors induced by noise are much bigger. The most attractive features of the PI method, namely, its conceptual simplicity and computational efficiency, make it an excellent candidate for a fast and useful screener and detector of unusual patterns in complex coupled time series.

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