



## Computational Neuroscience

## Performance comparison between gPDC and PCMI for measuring directionality of neural information flow



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## HIGHLIGHTS

- Neural mass model was used to compare performance between gPDC and PCMI algorithms.
- PCMI index is more close to a theoretical value in bidirectional mode than gPDCs.
- gPDC is more sensitive to the alteration of coupling strength than that of PCMI.
- PCMI performance is better than gPDC for measuring levels of neural connectivity.
- gPDC is more likely to distinguish the differences of coupling than that of PCMI.

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## ABSTRACT

**Background:** General partial directed coherence (gPDC) and permutation conditional mutual information (PCMI) have been widely used to analyze neural activities. These two algorithms are representative of linear and nonlinear methods, respectively. However, there is little known about the difference between their performances in measurements of neural information flow (NIF).

**New method:** Comparison of these two approaches was effectively performed based on the neural mass model (NMM) and real local field potentials.

**Results:** The results showed that the sensitivity of PCMI was more robust than that of gPDC. The coupling strengths calculated by PCMI were closer to theoretical values in the bidirectional mode of NMM. Furthermore, there was a small Coefficient of Variance (C.V.) for the PCMI results. The gPDC was more sensitive to alterations in the directionality index or the coupling strength of NMM; the gPDC method was more likely to detect a difference between two distinct types of coupling strengths compared to that of PCMI, and gPDC performed well in the identification of the coupling strength in the unidirectional mode.

**Comparison to existing method(s):** A comparison between gPDC and PCMI was performed and the advantages of the approaches are discussed.

**Conclusions:** The performance of the PCMI is better than that of gPDC in measuring the characteristics of connectivity between neural populations. However, gPDC is recommended to distinguish the differences in connectivity between two states in the same pathway or to detect the coupling strength of the unidirectional mode, such as the hippocampal CA3–CA1 pathway.

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## 1. Introduction

A number of neuroscience studies have focused on how the brain understands the world. However, an important issue remains how widely distributed brain areas communicate with each other, even though the anatomical structure of the brain has been clearly

identified. It is hard to demonstrate how information flows along anatomical brain pathways when animals perceive their environments, learn about their world and behave in a particular way. Similarly, it is almost impossible to understand how information transfers from one region to another in our brain when we think, because the brain anatomical structure is a static structure (Smith et al., 2006). Accordingly, a dynamic indicator is required – so-called neural information flow (NIF) – rather than a static one, to represent the coupling of neurons or coupling of neural assemblies in a neural network (Smith et al., 2006). Consequently,

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mathematical or dynamic approaches, by which the directionality of neural information flow (NIF) can be determined, are necessary.

Recently, several algorithms have been developed to determine the directionality of NIF. In general, these can be divided into two types; nonlinear and linear approaches. Generalized partial directed coherence (gPDC) is a representative of linear algorithms, which has been widely applied to the analysis of neural signals in many cases: MRI signals in the normal rat sensorimotor system (Shim et al., 2013), the local field potential of rats in a vascular dementia rat model (Xu et al., 2012), the EEG of patients with Parkinson's disease (Tropini et al., 2009) and to functional connectivity between cortices (Taxidis et al., 2010). The algorithm of gPDC was developed in accordance with the definition of Granger causality, and its index was evaluated by using multivariate autoregressive models. Alternatively, conditional mutual information (CMI), which is a typical nonlinear method often employed to detect the strength of coupling (Jin et al., 2011; Zhang et al., 2011), was developed based on information theory. As an improved algorithm of CMI, permutation conditional mutual information (PCMI) was proposed to perform causal connectivity measures between neuronal populations (Li and Ouyang, 2010). It has been reported that PCMI is superior to both CMI and Granger causality approaches for identifying the coupling direction between neural populations (Li and Ouyang, 2010). However, little is known about the limitations and differences between gPDC and PCMI algorithms.

It is well known that the neural mass model (NMM) has been widely used to simulate neural activities (David et al., 2004; Zavaglia et al., 2008). The NMM is a so-called macroscopic model, whose variables represent the average behavior of neural populations (David and Friston, 2003). In the present study, the NMM model was employed to generate simulation data. The model was applied to several aspects of imitating the activity of neuronal populations, e.g., olfactory responses (Freeman, 1987), focal attention (Suffczynski et al., 2001) and to evoke activity (Trong et al., 2012), and epilepsy (Goodfellow et al., 2012). The signal validated by the neural mass model could directly be applied to analyze real data obtained from animals or humans for physiological interpretation (Zavaglia et al., 2006). Accordingly, the NMM model was employed to compare the performance between these two approaches. In addition, two different modes of the connection were carefully considered: unidirectional and bidirectional modes.

The present study aimed to evaluate differences in the relative efficacy and characteristics between these two algorithms, to measure better the directionality of NIF. This was performed by generating data for local field potentials from two connective channels, between which the coupling strength and direction could be varied by alternating parameters of the NMM model. This allowed us to assess the performance of different interactions using oscillatory signals. In this study, the NMM and the two algorithms were introduced, and the NMM was used to generate simulated data. The sensitivities of these two algorithms were evaluated and compared, to detect the connectivity in different modes. Finally, the real experimental data for animals was obtained and the analysis was performed.

## 2. Materials and methods

### 2.1. Mathematical model

The NMM is a macroscopic model based on several simplifying assumptions. However, it can still simulate general features of macroscopic brain signals (David and Friston, 2003). One main assumption is the so-called mean field approximation, which expresses neural activities via lumped state variables. These variables represent the behavior of millions of interacting neurons. To

date, the simulating signals validated by the neural mass model have been directly applied to the analysis of real data obtained from either animals or humans for physiological interpretation (Zavaglia et al., 2006).

Generally, there are two operations in the NMM (David et al., 2004). The first is a sigmoid function to transfer the electrical signals to the mean firing rate. The second is a group of conversion functions with two conditions, including excitatory and inhibitory functions. Using the conversion functions, the mean postsynaptic response can be assessed by a linear convolution of the incoming spike rate. The sigmoid and conversion functions are as follows:

$$S(v) = \frac{2e_0}{1 + \exp(r(v_0 - v))} \quad (\text{for sigmoid function})$$

$$H_e(t) = u(t) \frac{H_e}{\tau_e} t \exp\left(\frac{-t}{\tau_e}\right) \quad (\text{for excitatory conversion function})$$

$$H_i(t) = u(t) \frac{H_i}{\tau_i} t \exp\left(\frac{-t}{\tau_i}\right) \quad (\text{for inhibitory conversion function})$$

In the present study, the parameters were defined to be the same as in the model used in a previous study (David et al., 2004).

The NMM model is presented (Fig. 1A) and shows that Channels 1 and 2 represent the two regions of the brain. A time delay is symbolized by  $\delta$ , which represents the transmission time between neuronal populations. The coupling strength between two channels is defined by  $K_{12}(K_{21})$ , which represents the connectivity of two cortical regions. Here,  $P_i$ ,  $i = 1, 2$  are stochastic variables that indicate information from the rest of the brain (Sen Bhattacharya et al., 2011).  $\langle p_1 \rangle = \langle p_2 \rangle = 220$ ,  $\text{std}(p_1) = \text{std}(p_2) = 22$ . The structure of Channel 1(2) is shown in Fig. 1B, in which  $H_{e,i}^j$ ,  $j = 1, 2$  measure the two different frequencies, whereas the relative parameters and the details of the model can be seen in David et al. (2004).

### 2.2. Acquisition of simulated data

An experiment was performed to detect the sensitivity of the two approaches. To evaluate this, both  $K_{12}$  and  $K_{21}$  were varied from 0 to 50 with a step of 2. For simplicity, we only focused on the sensitivity of  $K_{12}$  for the following reasons. Firstly, the function of  $K_{12}$  and  $K_{21}$  was symmetrical as shown in Fig. 1; accordingly, there was only one direction in which the investigation could be performed. Secondly, in each simulation experiment, the value of  $K_{21}$  was fixed, while  $K_{12}$  was varied from 0 to 50. Therefore, we only focused on the sensitivity of  $K_{12}$ . In addition, the indices of these approaches would be more accurate together with an increase in  $K_{12}$ . In other words, the coupling sensitivity of  $K_{12}$  would be better with an increase in the  $K_{12}$  value. More details concerning the coupling sensitivity are shown below.

The performance of two approaches with the changes in coupling strength was further compared. Two modes were employed to distinguish the characteristics of the approaches and to compare the performance between gPDC and PCMI algorithms. Firstly, a unidirectional mode was used, in which the coupling strength  $K_{21}$  was set to zero and the value of  $K_{12}$  ranged from 0 to 100 in steps of 5. Secondly, to simulate a bidirectional mode, the coupling  $K_{21}$  was set to 50, while the value of  $K_{12}$  was varied from 0 to 100 in steps of 5. Moreover, 20 measurements were obtained for each value of  $K_{12}$ . The differential equations were solved numerically using a fourth-fifty order Runge–Kutta algorithm. Initial conditions were set to zero in all simulations with an integration step size of 1 ms (sampling frequency: 1000 Hz). To avoid transient signals at the beginning of the simulation, the first 5000 points were discarded.

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