Total connectivity: a marker of dynamical functional connectivity applied to consciousness

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Abstract

In the last years functional connectivity (FC) has become one of the most popular tools to explore and characterize information contained in fMRI time series. The classical hypothesis on FC consists of considering it as constant (or *static*) over the whole fMRI time series. However, it has been emphasized recently that FC should be treated as a dynamical quantity, for example by using sliding windows of the fMRI time courses in order to compute a *dynamical* FC [1].

We propose a comprehensive marker of FC based on an auto-regressive (AR) model of fMRI time series capturing its *static* and *dynamic* properties. We call it **total connectivity** and we illustrate the benefits of our approach on data of patients undergoing four different states of consciousness.

Highlights

The correlation between two time series depends on their phase-logging. In fMRI time series such spurious delays can arise from a different hemodynamic response function [2] leading to a significant decrease in the *static* correlation ρ:

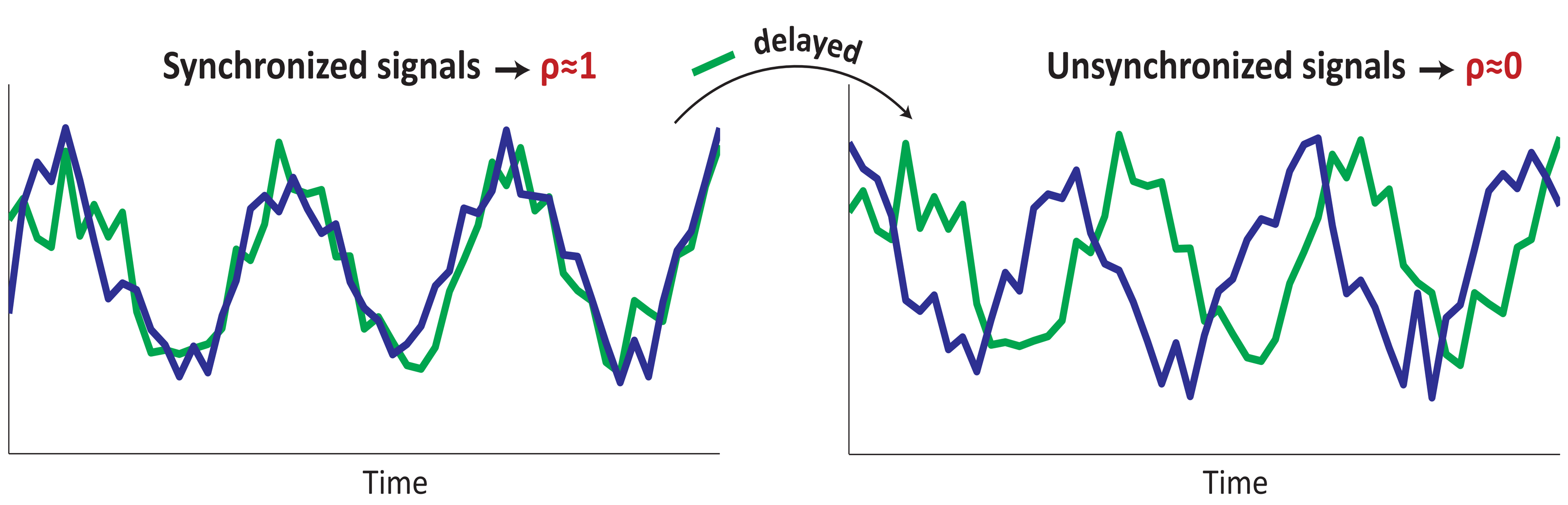


Figure 1: *(Left)* Two highly correlated signals. *(Right)* If one of the signals is delayed (for example due to a different hemodynamic response function in the case of fMRI time series), correlation drops down.

Questions:

① How can we measure FC in order to avoid the caveat presented in Figure 1 ?

② What is the corresponding underlying model ?

③ What is the interpretation of the markers of FC proposed here ?

➔ We show that FC can be comprehensively characterized by an ensemble of three markers: $\boldsymbol{\sigma_s}$,$\boldsymbol{\sigma_d}$,and **δ**, taking into account the *static* and *dynamic* contributions of connectivity. We define this set as the **total connectivity (TC)** and show its application on fMRI data coming from patients undergoing four different states of consciousness:

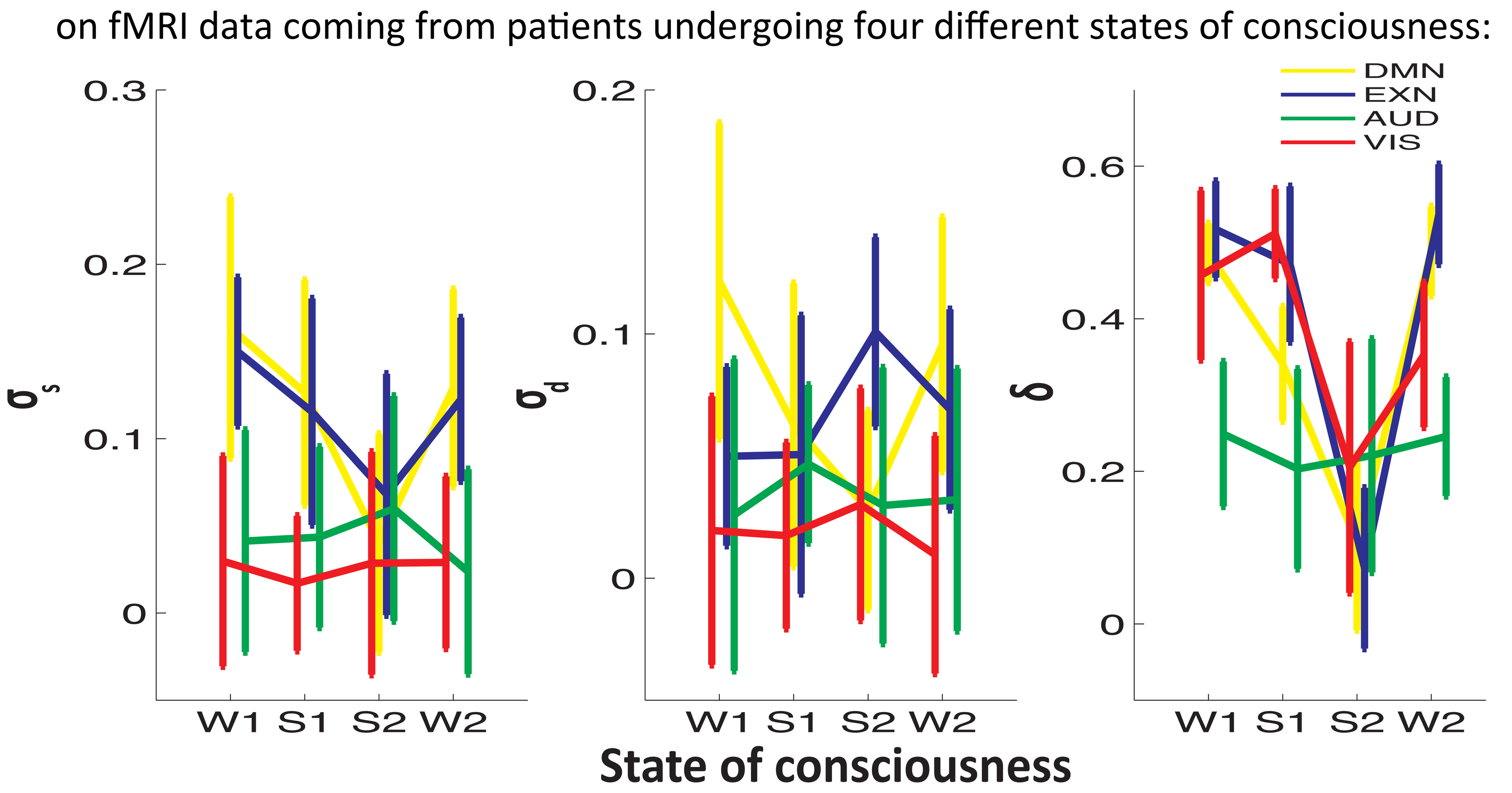


Figure 2: Average and StD values of the three markers of TC in four different states of consciousness and in four networks.

Methods and Answers

fMRI data

Data was collected from 19 healthy volunteers. The subjects underwent four states of consciousness: wakefulness (W1), mild sedation (S1), deep sedation (S2) and subsequent recovery of consciousness (W2). The preprocessing includes 0.007-0.1Hz bandpass filtering and global signal regression. Representative seeds of four resting state networks (Default Mode, Executive Control, Visual and Auditory networks) were then selected [3].

Auto-regressive (AR) models

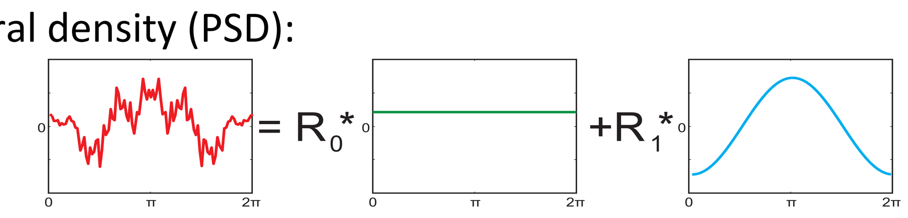
AR models assume that each time sample can be expressed from *p* previous samples:

$$X(t) = \sum_{i=1}^{p} A_i X(t-i) + \varepsilon(t)$$

where X(t) is a vector of size (1×n) encoding the n variables at time t, A_i is a (n×n) matrix encoding the contribution of X(t−i) to X(t), p is the order of the AR(p) model, ε(t)~N(0,Σ) is gaussian white noise.

Following [4] we identify the AR(1) model corresponding to the fMRI time series which results in an estimated power spectral density (PSD):

$$\Phi = \sum_{k=[0,1]} R_k \exp(jk\theta) \rightarrow \quad = R_0^* \quad + R_1^*$$



where R_k are the estimated covariance lags. R_0 encodes the classical *static* connectivity (no lag) whereas R_1 captures the *dynamical* properties of connectivity.

Total connectivity

In order to exploit the information contained in R_0 and R_1, we define three markers of connectivity within each network:

- σ_s is the average classical static connectivity in the network, computed as the mean of the off-diagonal terms of R_0.
- σ_d is the average dynamic connectivity which measures how each region is dynamically connected to each other, and is computed as the mean of the off-diagonal terms of R_1.
- δ is a measure of the dynamics driving a time course based on the influence that each of the n regions has on itself, or internal memory. It is computed as the mean of the diagonal terms of R_1.

Answers to the questions

① σ_s, σ_d, and δ are complementary measures of connectivity forming what we define as **total connectivity (TC)**. **Figure 3** shows that TC does not disappear if a signal is delayed.

② AR models are basic dynamical models allowing to capture static and dynamical contributions of connectivity. Time series are considered as the realization of *one random process* instead of a collection of realizations of *random variables*.

③ - σ_s can be considered as the static contribution of connectivity. In Figure 2 we observe a decrease of this marker during S2 for consciousness-related networks (DMN, EXN).
- σ_d can be considered as the dynamic contribution of connectivity. Figure 2 shows an increase of this marker during S2, meaning that connectivity does not disappear but is 'shifted' during this state.
- δ measures temporal consistency, or coherence of time series and can be used to disentangle noise from 'structured' signals.

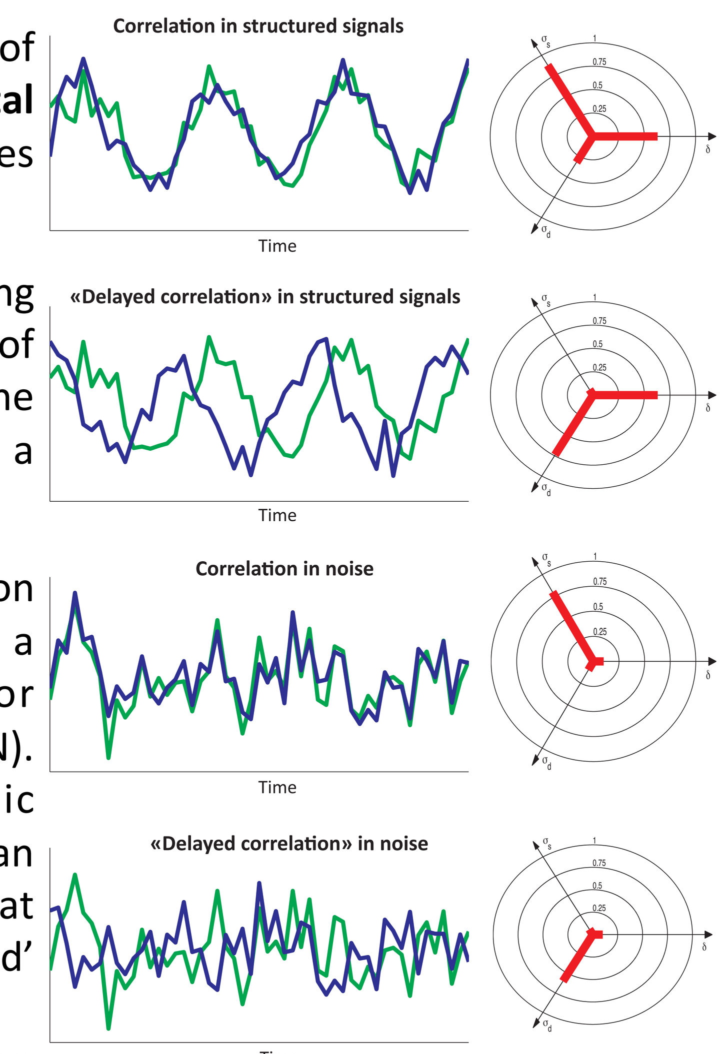


Figure 3: Total connectivity in four different and representative cases.

Take-home Messages

Using an auto-regressive model of fMRI time series, we show that **total connectivity** provides a comprehensive description of static and dynamic properties of FC:

➔ The classical static connectivity is a partial measure of connectivity,

➔ Having a decrease in static connectivity σ_s could be compensated by an increase in dynamic connectivity σ_d (as in the EXN, see **Figure 2**) meaning that connectivity does not disappear but is 'shifted', or 'delayed'.

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