



## Research Paper

## Dynamic Cross-Entropy

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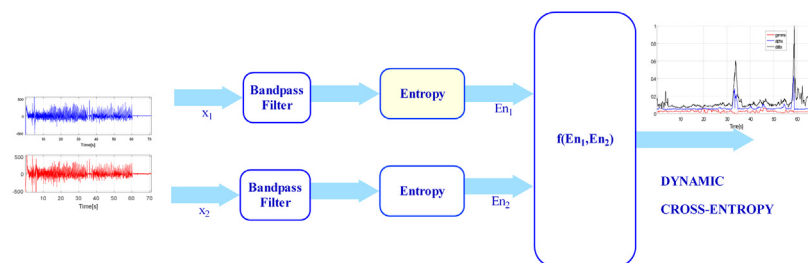


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## HIGHLIGHTS

- Dynamic Cross-Entropy (DCE) quantifies the degree of regularity of EEG signals in selected frequency bands.
- DCE analysis can be used to analyze the transition from order to chaotic behavior in complex nonlinear systems.
- The presence of bifurcations is consistent with transitions into less ordered states and chaos.
- The transition to irregular dynamics appears to follow a similar path in case of logistic equation and in the brain.

## GRAPHICAL ABSTRACT



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## ABSTRACT

**Background:** Complexity measures for time series have been used in many applications to quantify the regularity of one dimensional time series, however many dynamical systems are spatially distributed multidimensional systems.

**New Method:** We introduced Dynamic Cross-Entropy (DCE) a novel multidimensional complexity measure that quantifies the degree of regularity of EEG signals in selected frequency bands. Time series generated by discrete logistic equations with varying control parameter  $r$  are used to test DCE measures.

**Results:** Sliding window DCE analyses are able to reveal specific period doubling bifurcations that lead to chaos. A similar behavior can be observed in seizures triggered by electroconvulsive therapy (ECT). Sample entropy data show the level of signal complexity in different phases of the ictal ECT. The transition to irregular activity is preceded by the occurrence of cyclic regular behavior. A significant increase of DCE values in successive order from high frequencies in gamma to low frequencies in delta band reveals several phase transitions into less ordered states, possible chaos in the human brain.

**Comparison with Existing Method:** To our knowledge there are no reliable techniques able to reveal the transition to chaos in case of multidimensional times series. In addition, DCE based on sample entropy appears to be robust to EEG artifacts compared to DCE based on Shannon entropy.

**Conclusions:** The applied technique may offer new approaches to better understand nonlinear brain activity.

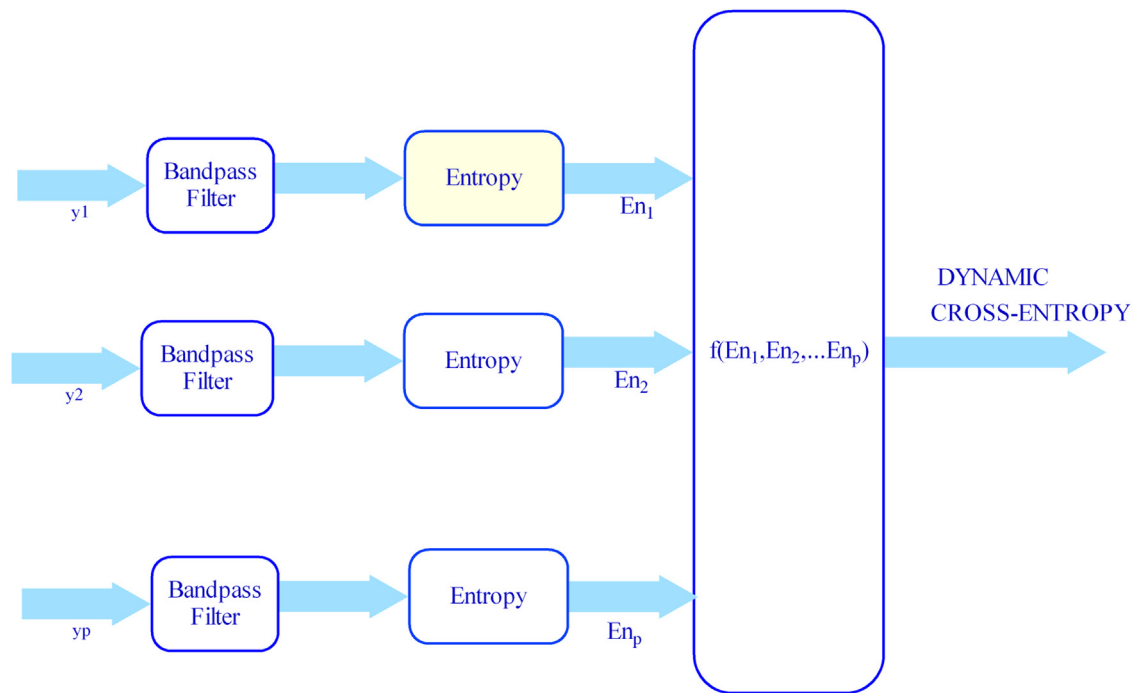
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## 1. Introduction

The brain is a biological system characterized by the interaction of many constituents that are interdependent and span several scales (i.e. molecular, cellular, brain nuclei, etc). The interplay of these constituents leads to emergence and self-organization phenomena, and therefore the brain should be regarded as a complex

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**Fig. 1.** Schematic representation of required steps to compute dynamic cross entropy.

system. As such, its functioning is governed by interplay of linear and non-linear behavior both in health and disease states. In order to better understand how the brain works, tools to appraise nonlinear dynamic and complex behavior are essential (Kaplan and Yorke, 1979; Cvitanovic, 1984; Jensen et al., 1984; Grebogi et al., 1983; Sprott, 2003; Pikovsky et al., 2003; Crutchfield, 2012; Strogatz, 2014).

In this work, we describe a novel multidimensional complexity measure, Dynamic Cross-Entropy (DCE) and its application to understanding brain dynamics represented by electroencephalographic data. The notion of entropy originates from statistical physics and refers to disorder or uncertainty. Introduced by Claude Shannon in 1948, information entropy has a consistent mathematical formulation, and is widely used in time series analysis application (Cincotta et al., 1995).

Complexity entropy measures are essential tools to understand the behavior of nonlinear systems. Approximate entropy (ApEn), sample entropy (SampEn), and permutation entropy (PE) were originally introduced by Pincus (Pincus, 1995), Richman and Moorman (Richman and Moorman, 2000), and Bandt and Pompe respectively (Bandt and Pompe, 2002) to quantify the regularity of one dimensional time series. Costa et al. have proposed the multi-scale entropy, a technique for computation of the sample entropy over a range of temporal scales (Costa et al., 2002). Recently, Wu and colleagues have introduced refined scale-dependent permutation entropy to analyze systems complexity (Wu et al., 2014).

A wide range of applications has been developed using complexity entropy techniques. Approximate entropy was used as an electroencephalographic measure to study the effect of drugs during anesthesia (Bruhn et al., 2000) or heart rate variability (Acharya et al., 2006). Sample entropy falls before clinical signs of neonatal sepsis (Lake et al., 2002) and permutation entropy analyses have predicted the absence of seizures (Li et al., 2007) and preictal states (Bruzzo et al., 2008). In addition, permutation entropy and permutation Lempel–Ziv complexity measure can be used to monitor the electroencephalographic effects during anesthesia (Li et al., 2008; Bai et al., 2015) while modified sample entropy measures proved to be closely correlated with anesthetic effect (Wang et al., 2014).

All the above techniques have been used in many applications to quantify the regularity or complexity of one dimensional time series, however many dynamical systems are spatially distributed multidimensional systems. In this paper we show that application of entropy measures can be extended to multidimensional time series.

## 2. Materials and methods

Shannon information entropy is defined in the context of a probabilistic model to measure the information contained in a message:

$$ShEn = - \sum_i p_i \log p_i \quad (1)$$

where  $ShEn$  is a measure of uncertainty associated with the probability distribution  $p_i$  (Shannon, 1951). Information entropy can be used to measure the average uncertainty of a signal source. In general terms Shannon's entropy measures our ignorance about the state of the system. The algorithm to compute Shannon's Entropy is fast, simple, and intuitive.

Sample entropy quantifies the likelihood that two sequences of data points will match with a tolerance of  $r$ . If  $(x_i)_{i=1}^L = \{x_1, x_2, \dots, x_L\}$  is a time series of length  $L$ , sample entropy is defined as:

$$SampEn = \ln(C_M(k, r, (x_i)_{i=1}^L) - \ln(C_M(k+1, r, (x_i)_{i=1}^L)) \quad (2)$$

where count matches are computed using the formula:

$$C(k, r, (x_i)_{i=1}^L) = \frac{2}{(L-k-1)(L-k)} n(i, j) : 1 \leq i \leq j < L-k+1, \max(x_{i+i} - x_{j+i}) \quad (3)$$

and  $n\{A\}$  stands for the number of elements in a given set (Keller et al., 2014). Sample entropy can be used to estimate the complexity of time series and displays similar results as the Lyapunov exponent which measures the sensitivity to initial conditions (Li et al., 2011). We have selected  $SampEn$  since it is considered to be less sensitive to changes in data length, and it has fewer problems with relative consistency (Yentes et al., 2013).  $SampEn$  provides

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