



## Coordination of respiratory muscles assessed by means of nonlinear forecasting of demodulated myographic signals

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### ABSTRACT

Pulmonary diseases such as obstructive sleep apnea syndrome (OSAS) affect function of respiratory muscles. Individuals with OSAS suffer intermittent collapse of the upper airways during sleep due to unbalanced forces generated by the contraction of the diaphragm and upper airway dilator muscles.

Respiratory rhythm and pattern generation can be described via nonlinear or coupled oscillators; therefore, the resulting activation of different respiratory muscles may be related to complex nonlinear interactions. The aims of this work were: to evaluate locally linear models for fitting and prediction of demodulated myographic signals from respiratory muscles; and to analyze quantitatively the influence of a pulmonary disease on this nonlinear forecasting related to low and moderate levels of respiratory effort.

Electromyographic and mechanomyographic signals from three respiratory muscles (genioglossus, sternomastoid and diaphragm) were recorded in OSAS patients and controls while awake during an increased respiratory effort.

Variables related to auto and cross prediction between muscles were calculated from the  $r^2$  coefficient and the estimation of residuals, as functions of prediction horizon. In general, prediction improved linearly with higher levels of effort.

A better prediction between muscle activities was obtained in OSAS patients when using genioglossus as the predictor signal. The prediction was significant for more than two respiratory cycles in OSAS patients compared to only a half cycle in controls. It could be concluded that nonlinear forecasting applied to genioglossus coupling with other muscles provides a promising assessment to monitor pulmonary diseases.

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### 1. Introduction

Pulmonary diseases such as chronic obstructive pulmonary disease (Mañanas et al., 2000) or obstructive sleep apnea syndrome (OSAS) (Alonso et al., 2007; Ryan and Bradley, 2005) affect respiratory muscle functioning. Whereas diaphragm is the main respiratory muscle, other accessory muscles such as the sternomastoid are active at higher levels of ventilatory effort associated with exercise or with pulmonary diseases (Hudson et al., 2007; Mañanas et al., 2000; Ratnovsky et al., 2003). The genioglossus muscle plays a special role in apnea generation, as it is considered the main muscle responsible for upper airways occlusion (Svanborg, 2005).

Individuals with OSAS experience intermittent collapse of the upper airways during sleep due to unbalanced forces generated by the contraction of the diaphragm and upper airway dilator muscles.

In OSAS, weak coordination of genioglossus and diaphragm is expected, and therefore also between genioglossus and sternomastoid because sternomastoid and diaphragm are activated in parallel in cases where both are active (Mañanas et al., 2000; Ratnovsky et al., 2003). In healthy subjects, on one hand, coordination of genioglossus and diaphragm might be stronger; however, on the other hand, coordination is less critical so it may be weaker. Thus, it is difficult to predict whether muscle coordination would be stronger or weaker in OSAS patients with respect to healthy subjects, but differences between both groups can be expected, particularly, in situations of increased respiratory effort. Some differences in levels of activity and coordination were found in previous studies (Alonso et al., 2007; Mañanas et al., 2003) but more studies are necessary to fully understand the patterns of respiratory muscle activities and their interactions.

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Muscle function can be assessed from electromyographic (EMG) and mechanomyographic (MMG) signals (Merletti and Parker, 2004), which are related to electrical and mechanical muscle activity, respectively. Surface electromyography is widely used in the analysis of skeletal and also respiratory muscles whereas mechanomyographic signals are less common but they provide additional information on muscle activity to that obtained through electromyography (Esposito et al., 2009; Torres et al., 2010). Among the main advantages of these techniques it is noticeable that these measures are not invasive and allow a high temporal resolution that is very necessary to obtain information about the coupling between muscles within a respiratory cycle and between respiratory cycles. This requirement is not met by other advanced techniques such as fMRI and computerized tomography which are very useful to assess muscle mass and length changes during contraction (Legrand et al., 2003). Compared to intramuscular recordings, information recorded by surface electromyography is less focused and it may be affected by interfering signals such as cardiac activity and cross-talk from nearby muscles. In this study, these effects were minimized respectively using adaptive and singular value decomposition based filtering (Mañanas et al., 2001a), and recording signals from relatively distant muscles whose respiratory function was clearly different.

Overall activity of respiratory muscles during breathing can be evaluated by demodulated myographic signals (Bruce, 1984; Zhang and Bruce, 1998). Myographic signals are complex signals that can carry a considerable amount of information about muscular function. In some cases, only the global activity of the motoneuron pool is to be considered and thus, the total electrical activity reflecting the action of a muscle is measured. In these cases, it is common to process the EMG signal to obtain a waveform that tracks its envelope, performing the so called amplitude demodulation (see Fig. 1). The resulting demodulated signal is taken as a continuous indication of the entire electrical activity of a muscle.

Global muscular pattern during normal and increased respiratory effort can be measured by temporal interactions between muscles. Some of these interactions have already been assessed by means of different approaches: cross-spectrum between EMG (Mañanas et al., 2001a) signals and EMG–MMG signals, in order to evaluate mechanical–electrical coupling (Mañanas et al., 2001a; Orizio, 1993), magnitude squared coherence (Bruce and Ackerson, 1986); cross-correlation (Mañanas et al., 2001a) and cross mutual information function (Alonso et al., 2007). These techniques provide interesting information about couplings between different muscles, but only cross mutual information function evaluates nonlinear

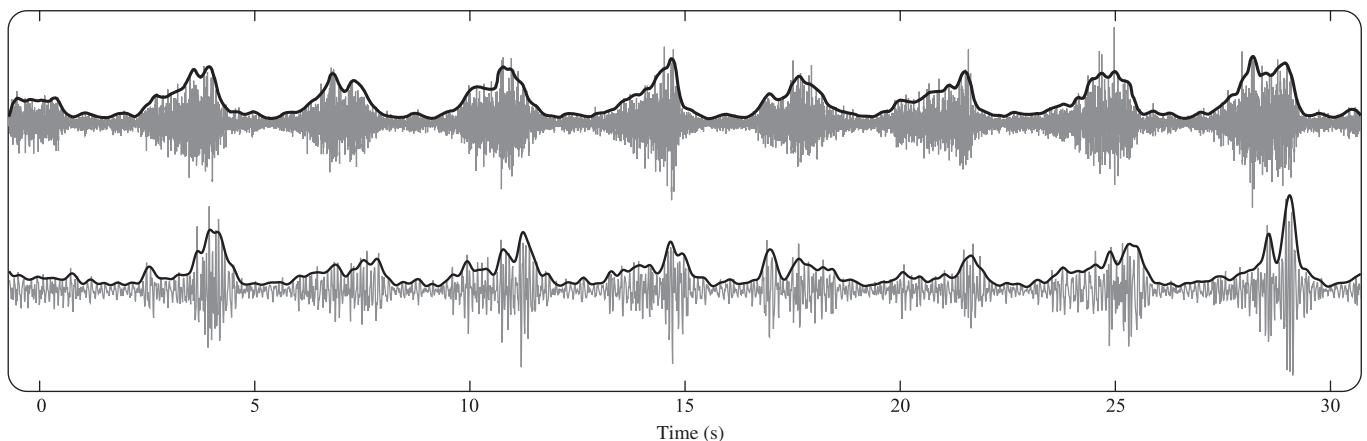
interactions. In general, nonlinear dynamics and complexity have usually been assessed with regard to one single time scale (correlation dimension, Lyapunov exponents and Kolmogorov entropy, among others), disregarding complex physiology organized in different time scales. This is an essential limitation with regard to complex multimatched control loops acting on different time horizons within the respiratory mechanisms. This drawback has been overcome by information transfer functions that take into account different time scales; see, for example (Alonso et al., 2007).

Correlations between data, either linear or nonlinear, can be expressed in terms of predictability. The most common and best-studied sources of predictability are linear correlations in time. Regarding linear dynamics, determinism and linear correlations are synonymous. This is not the case for nonlinear dynamical systems and therefore the construction of a deterministic model for prediction cannot rely on autocorrelations.

Nonlinear determinism means that equal states have the same future, and also that similar states will develop similarly, at least over short times. In other words, if points spread more or less along time are related with intrinsic underlying properties and provide similar information for future data, short-term forecasts exploiting a deterministic evolution law can be reasonable (Kaplan and Glass, 1995; Kantz and Schreiber, 1997). In contrast to relationships obtained by autocorrelation functions, those imposed by nonlinear deterministic dynamics are only found by using nonlinear statistics. These usually called nonlinear correlations have to be detected employing new techniques, such as nonlinear prediction. If this prediction is calculated as a function of a prediction horizon, this approach can provide information about biological processes at different time scales.

Assuming that data are associated with an underlying dynamical system with a deterministic structure, a nonlinear prediction algorithm based upon a simple prediction layout can be used, given that the current state of the system is known and the future state is to be predicted. For this purpose, a certain number of past and already visited states is searched in order to select the closest state to the current one with respect to some distance measure. If the number of past states is large enough, that is, if the system has been observed for a long time, a good estimate is obtained. Direct application of this prediction algorithm is not strictly valid with real data but this prediction approach can be considered by taking into account only a few concerns (Kantz and Schreiber, 1997), for example applying an estimator on a certain number of nearest neighbors.

In (Caminal et al., 2004) nonlinear prediction methods were applied to find a set of indices that characterized the variability



**Fig. 1.** Examples of surface EMG (upper traces) and MMG signals (lower traces) of the sternomastoid. Gray traces represent filtered myographic signals and black lines correspond to their demodulated counterparts.

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