DEPARTMENT OF INFORMATION ENGINEERING
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Cross-frequency coupling: an application of modulation theory to electrophysiology

G. Cisotto, M. Scattolin and L. Badia

INTRODUCTION

Cross-frequency coupling (CFC) generally labels the interactions between two signals at different frequencies. In electrophysiology, empirical evidences revealed the presence of coupling between low-(δ or θ) and high-(β or γ) frequency oscillations, which provided a novel perspective for characterizing and understanding executive functions.

Several methods have been employed to quantify this phenomenon in different kinds of electrophysiological signals. Unfortunately, several parameters had to be determined (e.g. the frequency/bandwidth of the two components interacting in the CFC) and their selection is often data-driven.

This contribution aims at translating the well-known theoretical framework about signal modulation from its original field of communication engineering to the study of CFC. Thanks to this approach, it is possible to limit the range of the most important parameters in order to ensure a proper coupling.
Thus, this work provides a platform to (i) simulate an expected strength of CFC, (ii) test the effectiveness of any other method of quantification of CFC and (iii) optimally decode the neural code, i.e., the components of an electrophysiological signal with CFC, underlying specific executive functions.

This contribution will support the study of executive functions (especially working memory, attention, decision-making and perception) where CFC has been found to reflect their periodic nature and inter-networks communications have been suggested to exploit CFC mechanisms to communicate among different areas during perception and cognition.

CROSS-FREQUENCY COUPLING MODEL

A widely accepted model for CFC was given in [2] and it was used for this work.

Three components can be identified:
Low-Frequency Oscillations (LFO), typically in the δ or θ band;
High-Frequency Oscillations (HFO), typically in the γ band;
Pink noise, the physiological noise into the brain.

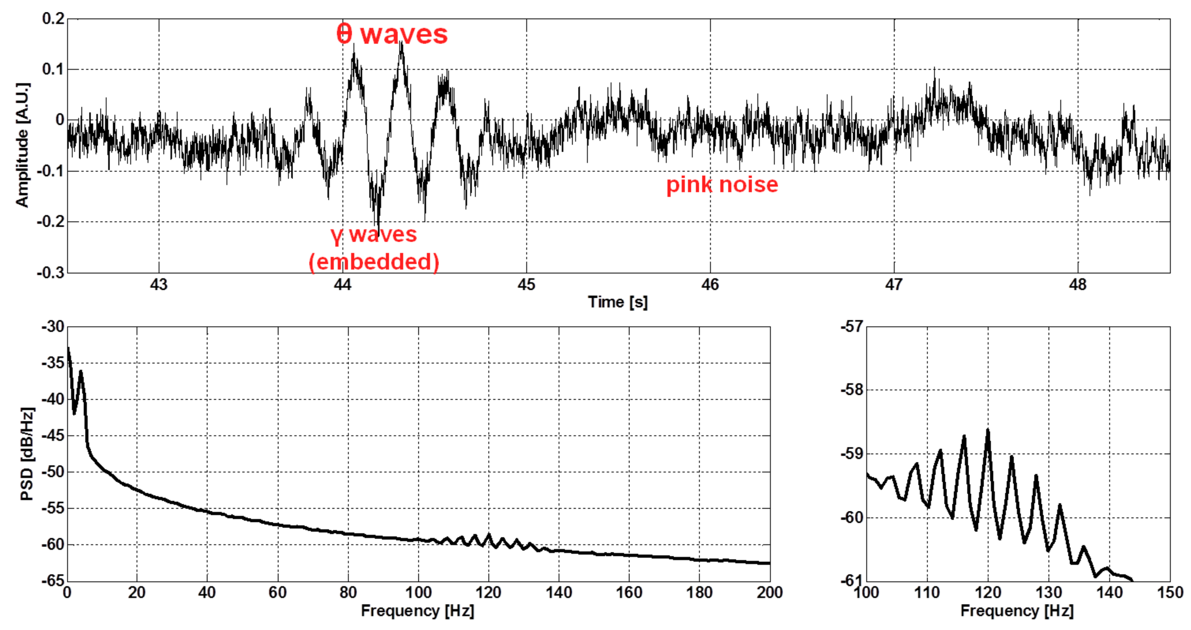

Figure 1. An example of synthetic CFC. (SNR = -3 dB, f_L =4 Hz, f_H = 120 Hz, 8 γ cycles/trough, 6 θ cycles/event).

DEMODULATION

The demodulation is operated at the received of a transmission system and deals with the identification and extraction of the useful component(s) of the received signal, after it has been modulated (at the transmitter) and modified by attenuations and/or distortions (by the transmission channel).

1) STANDARD ALGORITHM (SA):
- Define the HFO band (a-priori).
- Select the *has* value and LFO band:
  - Compute the mean vector length (MVL) or other measure .
  - By trial-and-error procedure, to find the (*has*, LFO) combination giving the highest MVL value.

  Note: one *has* value and one (only) frequency bin (about 1 Hz wide) are selected.
- Filter the electrophysiological data in LFO band and in HFO band, separately.
- Apply the Hilbert transform to get the phase from the LFO component and the amplitude from the HFO component.
- Compute the MVL as measure of CFC.

2) MODIFIED ALGORITHM (MA):
- Select the *has* value and LFO band:
  - Compute the mean vector length (MVL) or other measure .
  - Consider maximum (*max*) and minimum (*min*) MVL values and the *threshold* = *max* – 0.2(*max-min*).
  - Define the LFO band as the frequency band where MVL assumes values between *max-threshold* and *max.*
- Filter the electrophysiological data in the LFO band.
- AM-demodulate the LFO component.
- Find all CFC periods in the demodulated signal.
- Compute the average power spectrum.
- Find its maximum and the correspondent frequency F_{max} ,
- Define HFO band as the frequency band ($F_{max} – 4\ F_L$, $F_{max} + 4\ F_L$), with F_L the LFO center of band.
- Apply the Hilbert transform to get the phase from the LFO component and the amplitude from the HFO component.
- Compute the MVL as measure of CFC.

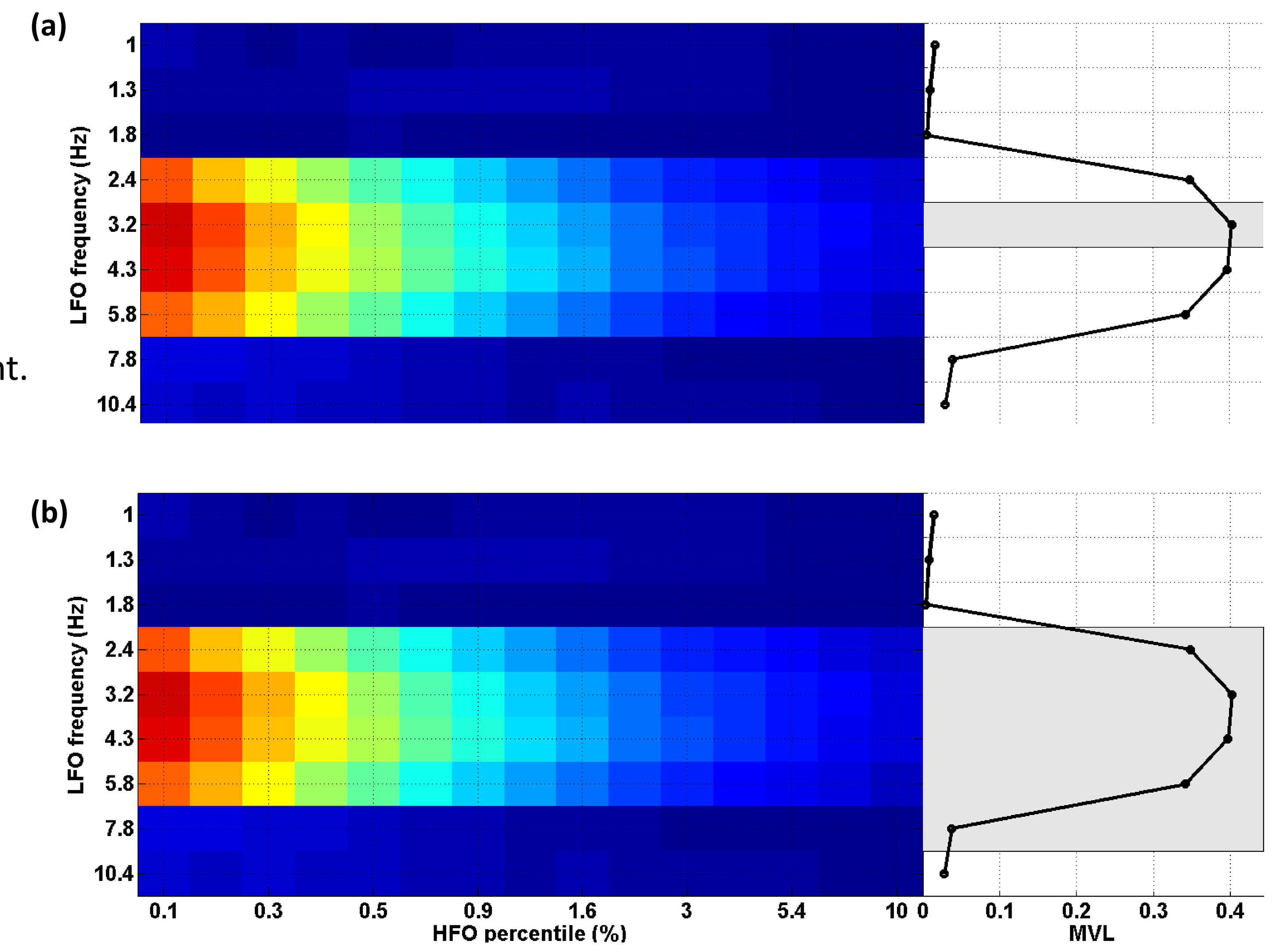

Figure 2. Selection of *has* value and LFO band in the (a) SA and the (b) MA.

RESULTS

The results show the effectiveness of the demodulation provided by the modified algorithm, compared with that of the standard algorithm.

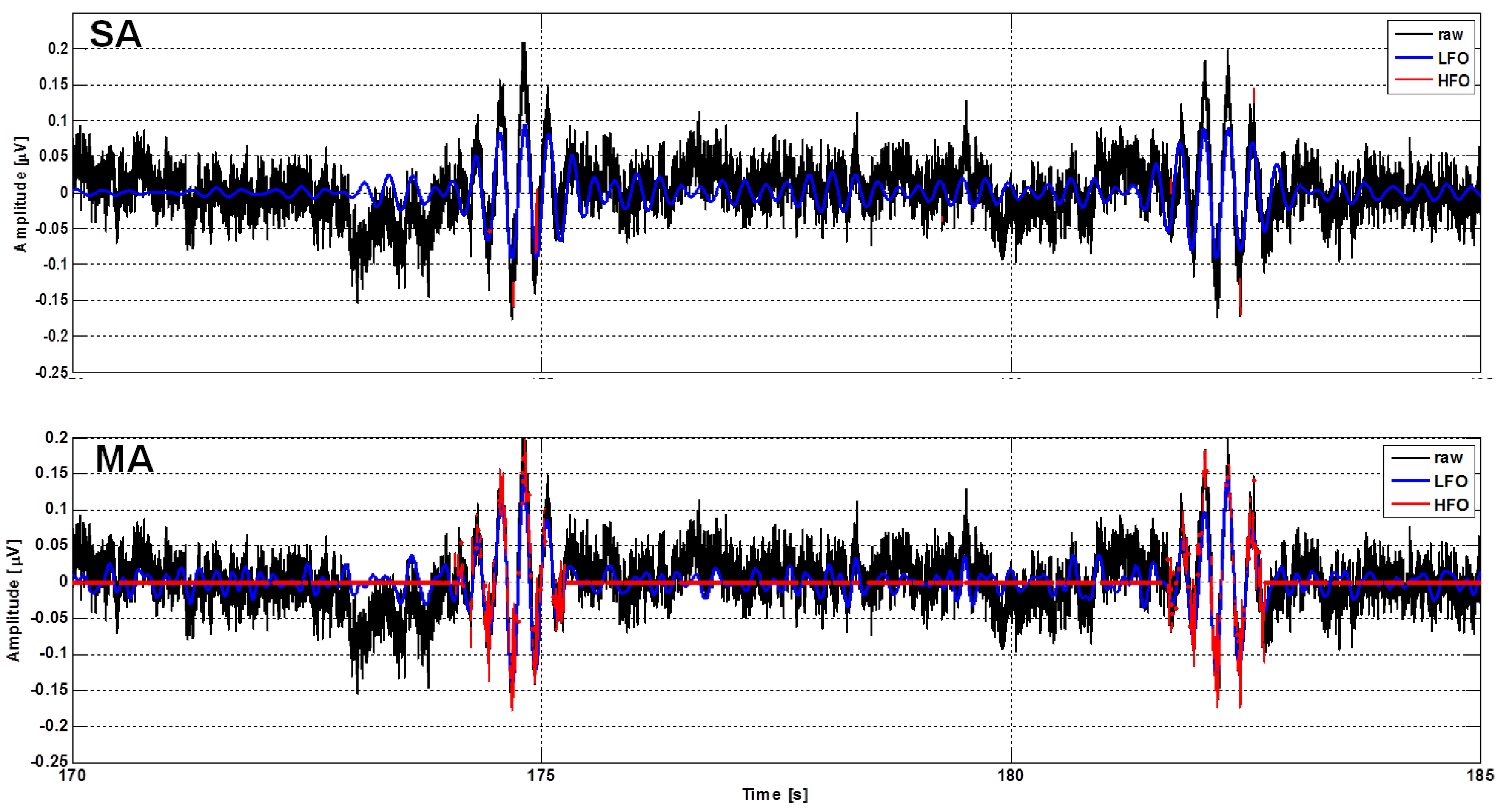

Figure 3. Example of demodulation with the standard algorithm (SA) and the modified algorithm (MA).

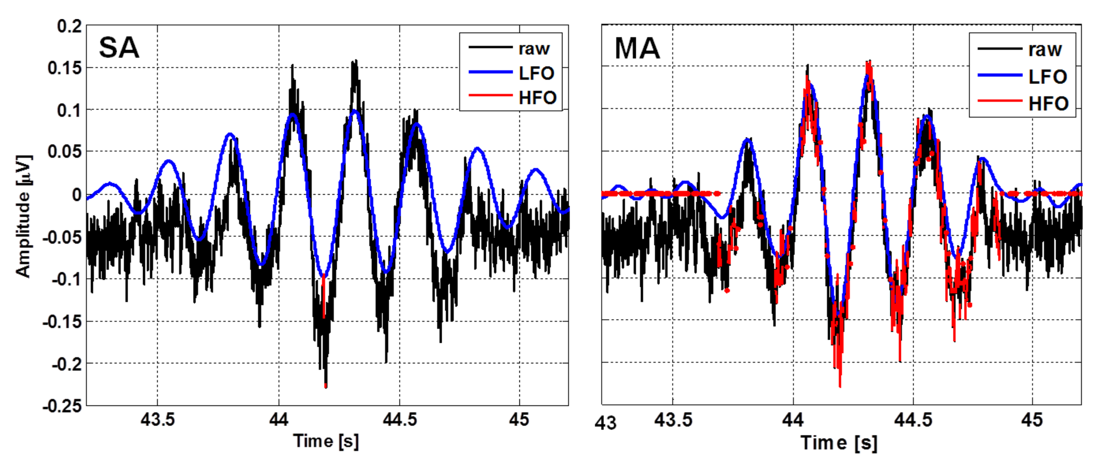

Figure 4. A detail from Figure 3.

Performance Measures

Correct identifications (CID): Root-mean square error between the raw signal and the identified LFO component.

Mis-detections (MD):Number of HFO events identified by the algorithm over the total number of HFO embedded events in the whole signal.

Performance comparison between standard and modified algorithms:

	SA	MA
CID	3.02 (1.26)	1.99 (1.23)
MD	29.2%	66%

DISCUSSION

Results showed that MA outperforms the SA , taking advantage from the well-known modulation theory (40 years-long history). The main benefits of this new CFC identification method are:
- the correct selection of the LFO band, that preserves the full information related to LFO.
- an adaptive selection of the HFO band that does not need for any a-priori knowledge but is data-driven.

Two performance measures (the correct identifications and the mis-detections) are provided to quantitatively assess the effectiveness of the new CFC identification algorithm.

FUTURE DEVELOPMENTS

Application of the modified algorithm to real local field potentials (LFPs) signals.
Inclusion of phase precession in the model and update of the demodulation algorithm.
Extension of the model and the demodulation algorithm to other kinds of CFC mechanisms, e.g., phase-phase and amplitude-amplitude.

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Email contacts: giulia.cisotto@dei.unipd.it melissa.scattolin@studenti.unipd.it leonardo.badia@dei.unipd.it