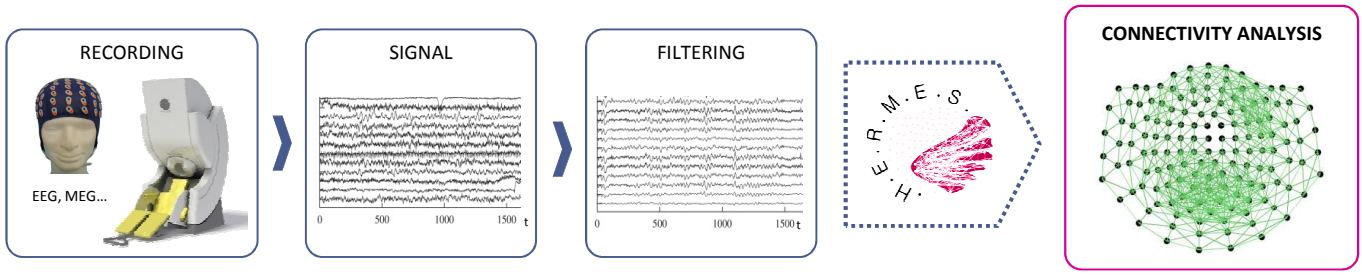
HERMES:
towards an integrated toolbox to characterize functional and effective brain connectivity

Guiomar Niso[1,*], Ricardo Bruña[1], Ernesto Pereda[2], Ricardo Gutiérrez[1], Ricardo Bajo[1], Fernando Maestú[1], Francisco del-Pozo[1]

1 Center for Biomedical Technology, Technical University of Madrid, Spain
2 Electrical Engineering and Bioengineering Group, Dept. of Basic Physics, University of La Laguna, Tenerife, Spain

* Corresponding author: **guiomar.niso@ctb.upm.es**



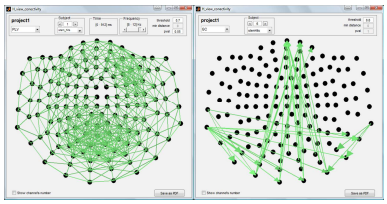
The analysis of the **interdependence between time series** has become an important field of research, mainly as a result of advances in the characterization of dynamical systems from the signals they produce, and the introduction of concepts such as Generalized (GS) and Phase synchronization (PS). This increase in the number of approaches to tackle the existence of the so-called functional (FC) and effective (EC) connectivity (Friston 1994) between two (or among many) neural networks, along with their mathematical complexity, makes it desirable to arrange them into a **unified toolbox**, thereby allowing neuroscientists, neurophysiologists and researchers from related fields to easily access and make use of them.

In this same line, we hereby present a new Matlab® toolbox: HERMES, which includes several commonly used indexes for the assessment of both FC and EC, along with some useful preprocessing tools.

HERMES is the Spanish abbreviation for ***HERramientas de MEdidas de Sincronización*** (which roughly translates to English as "*Tools for the Assessment of Synchronization*").

CONNECTIVITY

Functional and Effective connectivity



Classical Measures

1. **COR**: Pearson's correlation coefficient
2. **XCOR**: Cross-correlation function
3. **COH**: Coherence
4. **PSI**: Phase Slope Index (Nolte et al. 2008)

Phase Synchronization

1. **PLV** : Phase Locking Value (Lachaux et al. 1999)
2. **PLI**: Phase-Lag Index (Stam et al.2007)
3. **WPLI**: Weighted Phase-Lag Index (Vinck et al. 2011)
4. **RHO**: ρ index (Tass et al. 1998)
5. **DPI**: Directionality Phase Index (EMA/IPA) (Rosenblum et al. 2002; Rosenblum & Pikovsky 2001)

Generalized Syncronization

1. **S** Index (Arnhold 1999)
2. **H** Index (Arnhold 1999)
3. **N** Index (Quian Quiroga et al. 2002)
4. **M** Index (Quian Quiroga et al. 2002)
5. **L** Index (Chicharro & Andrzejak 2009)
6. **SL**: Synchronization Likelihood (Stam & van Dijk 2002)

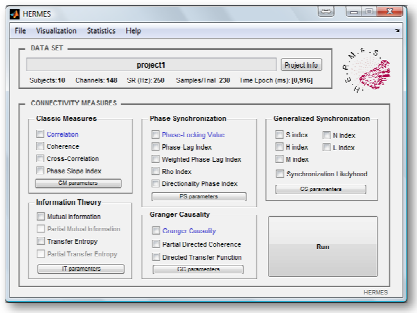
Granger Causality Measures

1. **GC**: Clasical Linear Granger Causality (Granger 1969)
2. **PDC**: Partial Directed Coherence (Sameshima & Baccalá 1999)
3. **DTF**: Direct Transfer Function (Kamiński & Blinowska 1991)

Information Theoretic Measures

1. **MI**: Mutual Information
2. **PMI**: Partial Mutual Information
3. **TE**: Transfer Entropy (Schreiber 2000)
4. **PTE**: Partial Transfer Entropy

HERMES

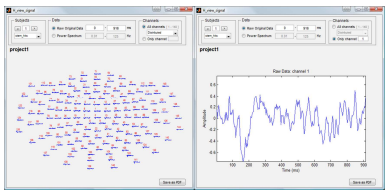


http://hermes.ctb.upm.es

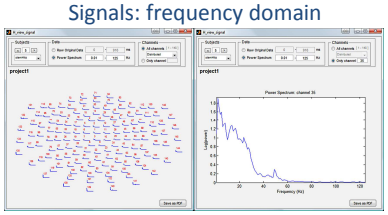
(Niso et al. 2013)

SIGNALS

Signals: time domain

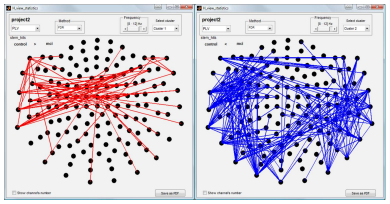


Signals: frequency domain



STATISTICS

Statistics between groups/conditions



Statistical Significance of the Indexes

Sometimes indexes may present values, which are not reflecting the existence of statistical or causal relationship between the time series, but are the result of some feature of the individual signals. To test whether an index is actually measuring interdependence, multivariate surrogate data can be constructed compatible with the null hypothesis that the signals are independent.

- **Surrogate Data for Nonlinear Synchronization Indexes**
- **Surrogate Data for Amplitude and Phase**

Statistical Test for Multiple Comparisons

HERMES allows the possibility of computing statistics between different groups and conditions, correcting for multiple comparisons.

1. **False discovery rate (FDR)**

   Basic statistical tests can be selected between parametric (t-test) and non-parametric (Wilcoxon) tests, and the type of FDR can be set to 1 or 2.

   FDR controls the expected proportion of incorrectly rejected null hypotheses (Benjamini & Yekutieli 2001; Genovese et al. 2002).

2. **Nonparametric Cluster-Based Permutation Test (CBPT)**

   If a statistical effect found in the comparison between groups or experimental conditions is to be considered significant, it should be 'larger' than the effects found when the measurements are randomly assigned to groups or conditions.

   'Largeness' refers to a combination of the statistical strength of the effect and its spatial largeness (and also, in the case, its time duration and its frequency content, if the functional connectivity measure selected is sensitive to those dimensions). (Maris & Oostenveld 2007; Nichols & Holmes 2002)

Financial support of the Spanish Ministry through grants TEC2012-38453-CO4-01 and -03, Ministry of Education of the Community of Madrid through R&D program NEUROTEC-CM (S2010/BMD-2460). Guiomar Niso: FPU grant AP2008-02383.