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 connectivity (EC) (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 MEASURES

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Pearson’s correlation coefficient (COR)</td>
<td>$r_{xy}$</td>
<td>Measure of linear dependence of two variables</td>
</tr>
<tr>
<td>Cross-correlation function (XCOR)</td>
<td>$C_{xy}(t)$</td>
<td>Correlation of two signals at time lag $t$</td>
</tr>
<tr>
<td>Coherence (CDH)</td>
<td>$</td>
<td>\gamma_{xy}(\omega)</td>
</tr>
</tbody>
</table>

#### 1. CLASSICAL MEASURES
- Pearson’s correlation coefficient (COR)
- Cross-correlation function (XCOR)
- Coherence (CDH)

#### 2. PHASE SYNCHRONIZATION INDEXES
- Phase Locking Value (PLV) (Baccalà & Sameshima, 2000)
- Phase-Lag Index (PLI) (Stark et al., 2007)
- Weighted Phase-Lag Index (WPLI) (Baccalà & Sameshima, 2000)
- p-Index (Baccalà & Sameshima, 2000)

#### 3. GENERALIZED SYNCHRONIZATION INDEXES
- S Index (Arnold, 1998)
- H Index (Arnold, 1998)
- N Index (Juan-Guirao et al., 2002)
- M Index (Juan-Guirao et al., 2002)
- R Index (Frijters and Andrade, 2003)

#### 4. GRANGER CAUSALITY MEASURES
- Classical linear Granger Causality (GC) (Granger, 1969)
- Partial Directed Coherence (PDC) (Baccalà & Sameshima, 2000)
- Direct Transfer Function (DTF) (Kaminski and Babiloni, 1999)

#### 5. INFORMATION THEORETIC MEASURES
- Mutual Information (MI) | $I(X;Y)$ | Measures the amount of information shared by two variables |
- Transfer Entropy (TE) (Schreiber, 2000)

### HERMES INTERFACE

The simplest and most straightforward way of using HERMES is through its graphical user interface.

### WINDOWING DATA
To have some degree of dynamical information, HERMES gives the opportunity of windowing the data.

- **Length of the sliding window (ms)**: $[T_1,T_2]$, DEF: $T_1 = T_2 = 4$ ms
- **Overlapping (%)** [0, 100], DEF: 0 % (no overlapping)
- **Window alignment** (for trials): “With the epoch” or “With the stimulus”

### PROJECT CREATION
A project can be created, containing a single data matrix or data obtained from different subjects and/or under different conditions.

HERMES can load FieldTrip structures and matrices stored in MAT files. Some systems of coordinates are included:
- 10-20 international EEG system with 10-10 and 10-5 extensions
- 40 Neuroimaging MAGNIES 2500 WH 148 MEG system
- Elekta Neuroscan 306 MEG system

A project can be exported, stored as a file (with the extension .her) and imported in other run of HERMES.

### DATA REPRESENTATION
- **Signal Visualization**
  - Signal and spectrum
- **Connectivity Visualization**
  - Functional connectivity
  - Effective connectivity

### 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 phase synchronization indexes
- Surrogate data for amplitude and phase

### STATISTICS BETWEEN CONDITIONS AND GROUPS
HERMES allows the possibility of computing statistics between different groups and conditions, correcting for multiple comparisons. Two methods are included:
- False discovery rate (FDR), which controls the expected proportion of incorrectly rejected null hypotheses (type I errors).
- Nonparametric cluster-based permutation test (CBPT) (Maris & Oostenveld, 2007; Nathan & Oostenveld, 2010), which evaluates a combination of the statistical strength of the effect and its spatial lageness (and also, in the case, its time duration and its frequency content, if the functional connectivity measure selected is sensitive to those dimensions).