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INTRODUCTION

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 MEdidias de Sincronización (which roughly translates to English as "Tools for the Assessment of Synchronization").

CONNECTIVITY MEASURES

CM	PS	GS	GC	IT
COR	PLV	S index	GC	MI
xCOR	PLI	H index	DTF	TE
COH	WPLI	N index	PDC	Embed Dim
Max lags	RHO	M index	Order	Embed Delay
	CenterFreqs	L index		Theiler
	Bandwidth	Embed Dim		N neighbours
		Embed Delay		
		Theiler		
		N neighbours		

1. CLASSICAL MEASURES

1. **Pearson's correlation coefficient (COR)**
2. **Cross-correlation function (XCOR)**
3. **Coherence (COH)**

[CM PARAMETERS]

- **Max lags (t)** (for XCOR): [1, Nsamples-1]. DEF: Nsamples/5

2. PHASE SYNCHRONIZATION INDEXES

1. **Phase Locking Value (PLV)** (Lachaux et al. 1999)
2. **Phase-Lag Index (PLI)** (Stam et al. 2007)
3. **Weighted Phase-Lag Index (WPLI)** (Vinck et al. 2011)
4. **ρ index (RHO)** (Tass et al. 1998)

[PS PARAMETERS]

- **Central band frequencies:** [0,fs/2] Hz. DEF: fs/4 Hz
- **Bandwidth:** [4,fs/2] Hz. DEF: 4 Hz

3. GENERALIZED SYNCHRONIZATION INDEXES

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

[GS PARAMETERS]

- **Embedding dimension (d):** [2,10]. DEF: Cao's method.
- **Embedding delay (t):** [1, the first minimum of the mutual information function]. DEF: signal autocorrelation time.
- **Theiler correction:** [t/2,t]. DEF: t (delay time)
- **Number of nearest neighbors:** [d,2d]. DEF: 4

4. GRANGER CAUSALITY MEASURES

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

[GC PARAMETERS]

- **AR order** (for GC): [3,Nsamples-1]. DEF: 10
- **MAR order** (for PDC and DTF): [3,Nsamples-1]. DEF: 3

5. INFORMATION THEORETIC MEASURES

1. **Mutual Information (MI)**
2. **Transfer Entropy (TE)** (Schreiber 2000)

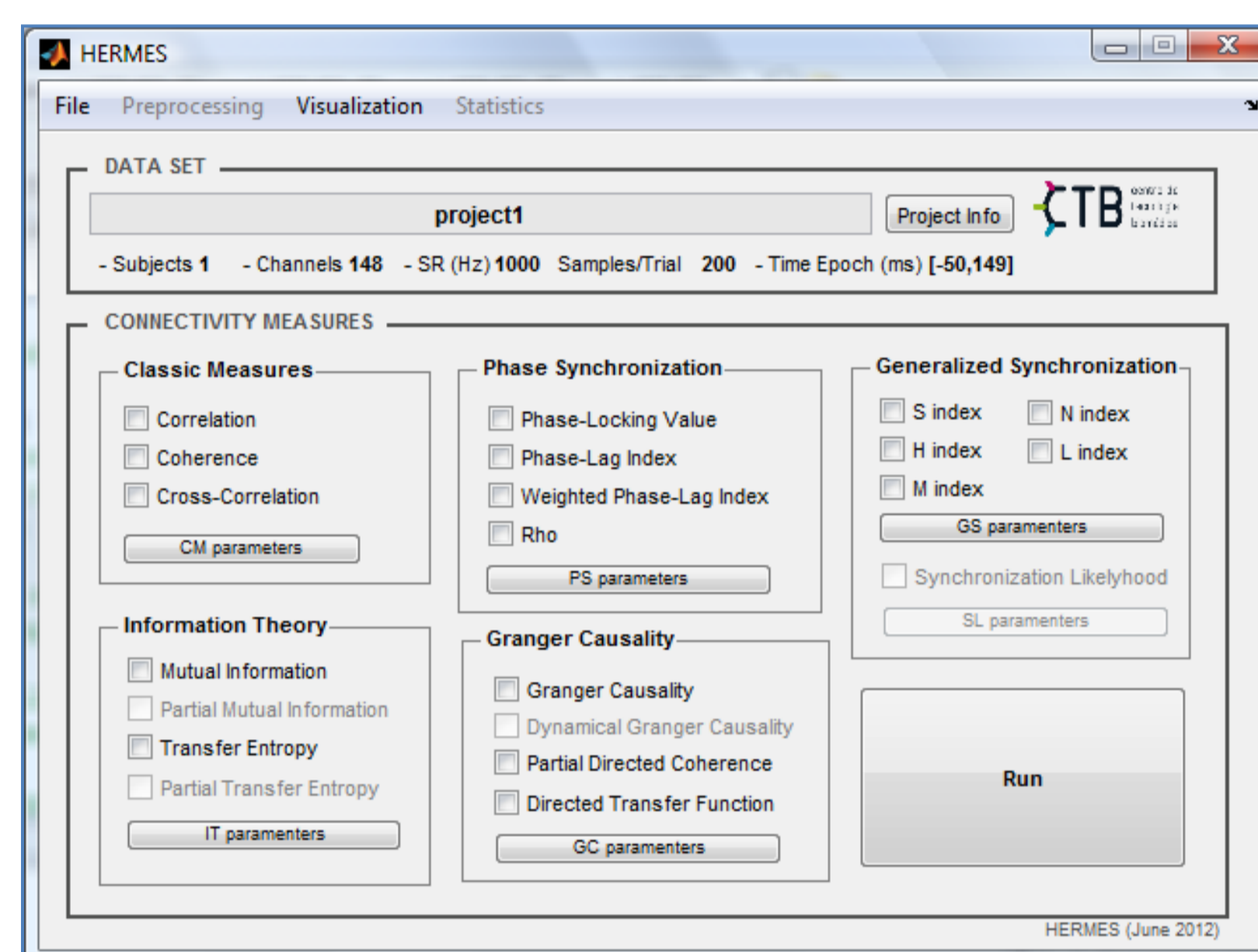
[IT PARAMETERS]

- The same as for GS

Index	Non linear	Causality	Normal ized	Only direct links
COR	x	x	x	x
xCOR	x	x	✓	x
COH	x	x	✓	x
PLV	✓	x	✓	x
PLI	✓	x	✓	✓
wPLI	✓	x	✓	✓
RHO	✓	x	✓	x
S index	✓	x	✓	x
H index	✓	x	x	x
N index	✓	x	✓	x
M index	✓	x	✓	x
L index	✓	x	✓	x
SL	✓	x	✓	x
GC	x	✓	x	x
PDC	x	✓	✓	✓
DTF	x	✓	✓	x
MI	✓	x	x	x
TE	✓	✓	x	x
PMI	✓	✓	x	✓
PTE	✓	✓	x	✓

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.

[WINDOWING PARAMETERS]

- **Length of the sliding window (ms):** [t₁₀,t_{end}]. DEF: t_{end} ms (no windowing)
- **Overlapping (%):** [0,100] %. DEF: 0 % (no overlapping)
- **Windows 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
- 4D Neuroimaging MAGNES 2500 WH 148 MEG system
- Elekta Neuroscan 306 MEG system

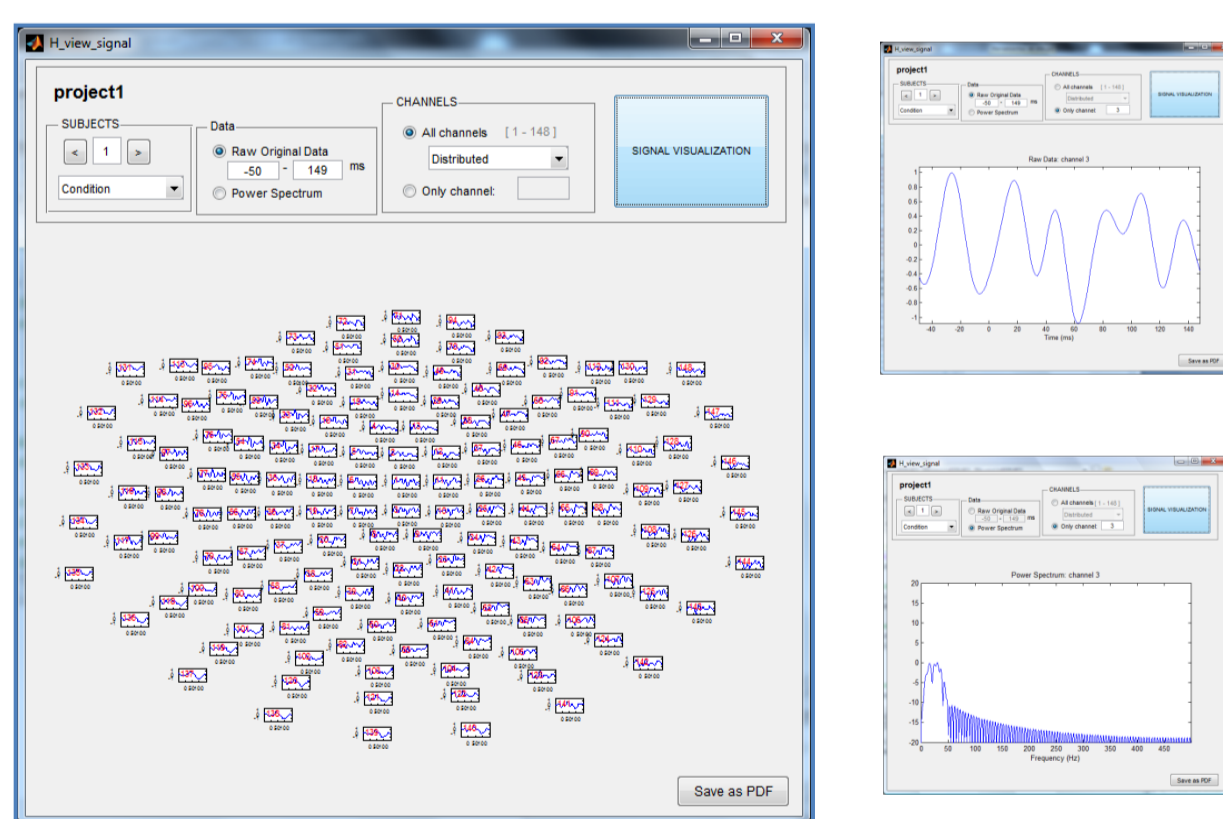
A project can be exported, stored as a file (with the extension **.her**) and imported in other run of HERMES.

PROJECT	INDEX
version	INDEX1
name	name
filename	type
date	date
description	dimensions
baseline	config
channels	data
samples	pval
time	
fs	
source	
orig	
sensors	labels
	Coord2D
	Coord3D
subjects	Name
	group
	trials

DATA REPRESENTATION

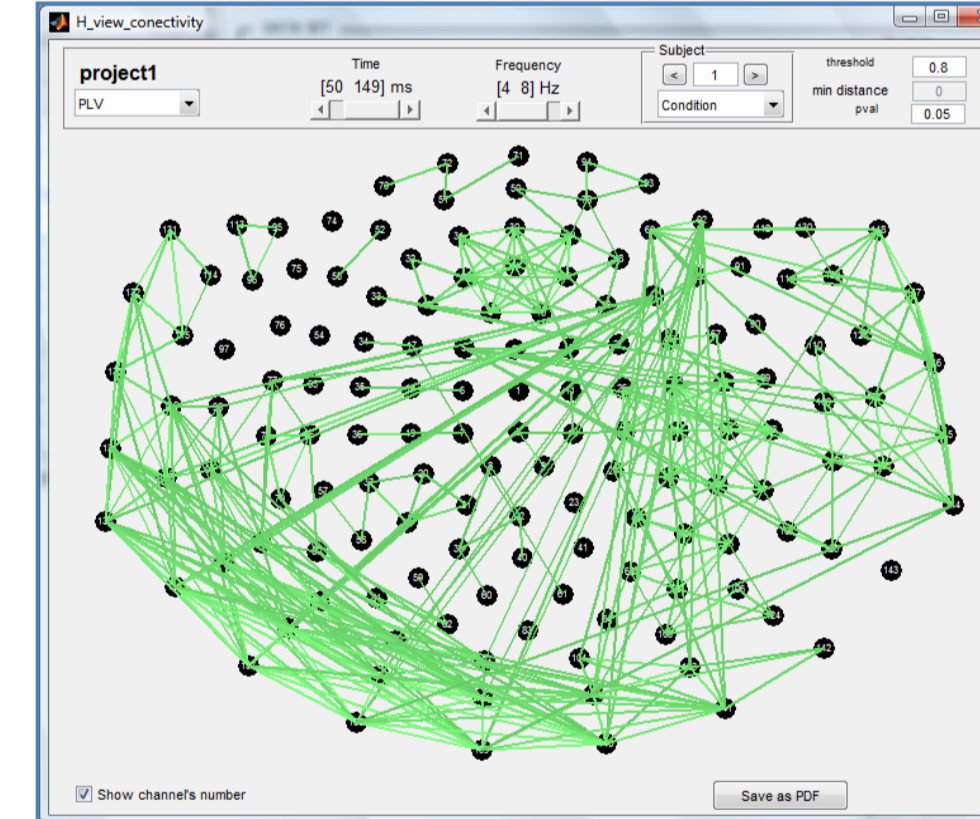
Signal Visualization

Signal and spectrum

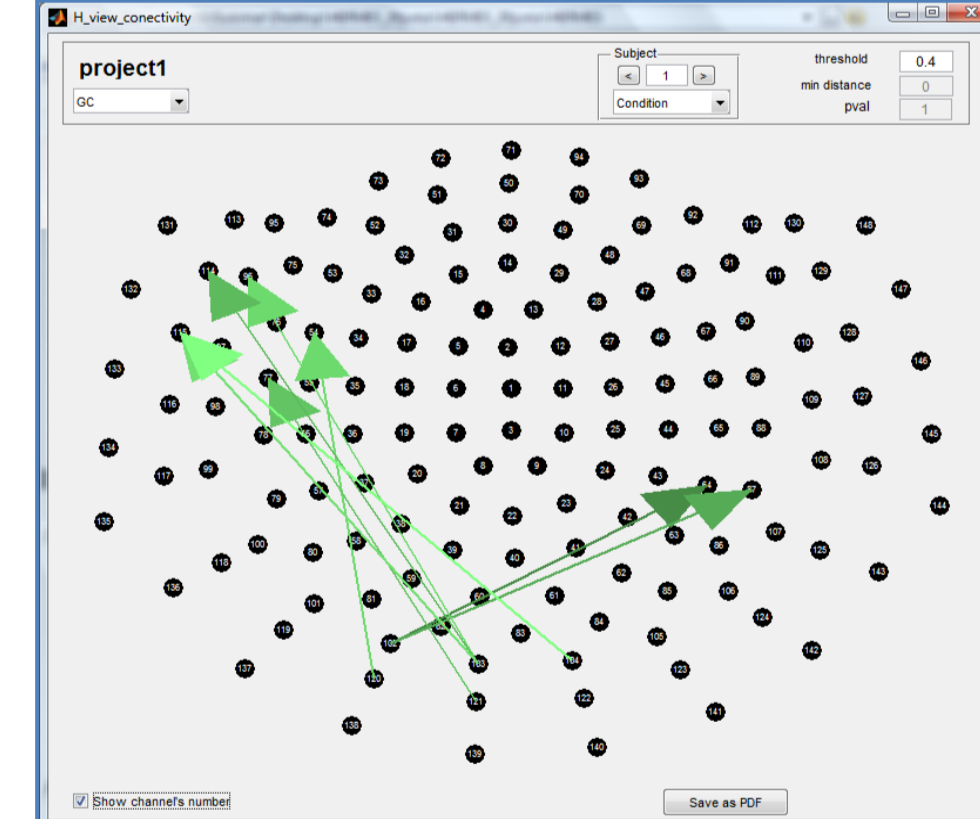


Connectivity Visualization

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

[SURROGATE PARAMETERS]

- Number of surrogates: to have a p-value P for the confidence of your test, you will need at least 1/P surrogates. DEF: 100, for a minimum p-value of 0.01.

STATISTICS BETWEEN CONDITIONS AND GROUPS

HERMES allows the possibility of computing statistics between different groups and conditions. One of the statistical methods used for multiple hypothesis testing is false discovery rate (FDR), which corrects for multiple comparisons. In a list of rejected hypotheses, FDR controls the expected proportion of incorrectly rejected null hypotheses (type I errors). It is a less conservative procedure for comparison than the Bonferroni correction, with greater power than familywise error rate (FWER) control, at a cost of increasing the likelihood of obtaining type I errors. In practical terms, the FDR is the expected proportion of false positives among all significant hypotheses.