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Information Theory for Network Physiology

Multivariate and Multiscale Methods to Dissect the Information Content of Brain, Cardiovascular and Muscular Networks

Luca Faes

IRCS-HTA Laboratory, Bruno Kessler Foundation, Trento, Italy

BIOtech, University of Trento, Italy

NETWORK PHYSIOLOGY: A NEW FIELD IN SYSTEM MEDICINE AND BIOLOGY

"The human organism is an integrated network where complex physiologic systems, each with its own regulatory mechanisms, continuously interact, and where failure of one system can trigger a breakdown of the entire network"

[A. Bashan et al., Nature Communications 2012]

*A new field, **Network Physiology**, is needed to probe the interactions among diverse physiologic systems*

Different organ systems dynamically interact to accomplish vital functions

- **Traditional, "reductionist" approach**

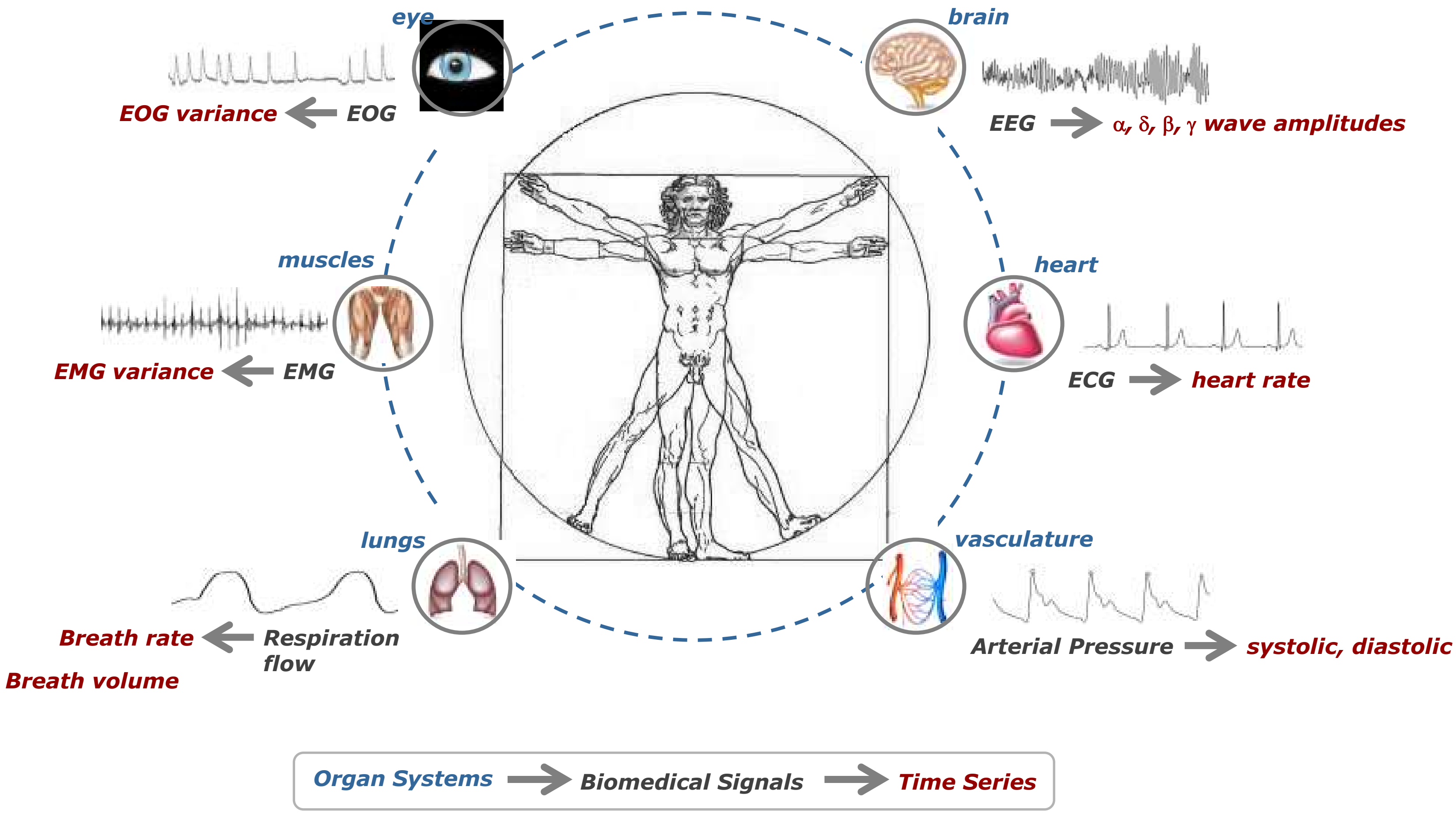
  To study the function of single organ in isolation

- **New approach, fostered by Network Physiology**

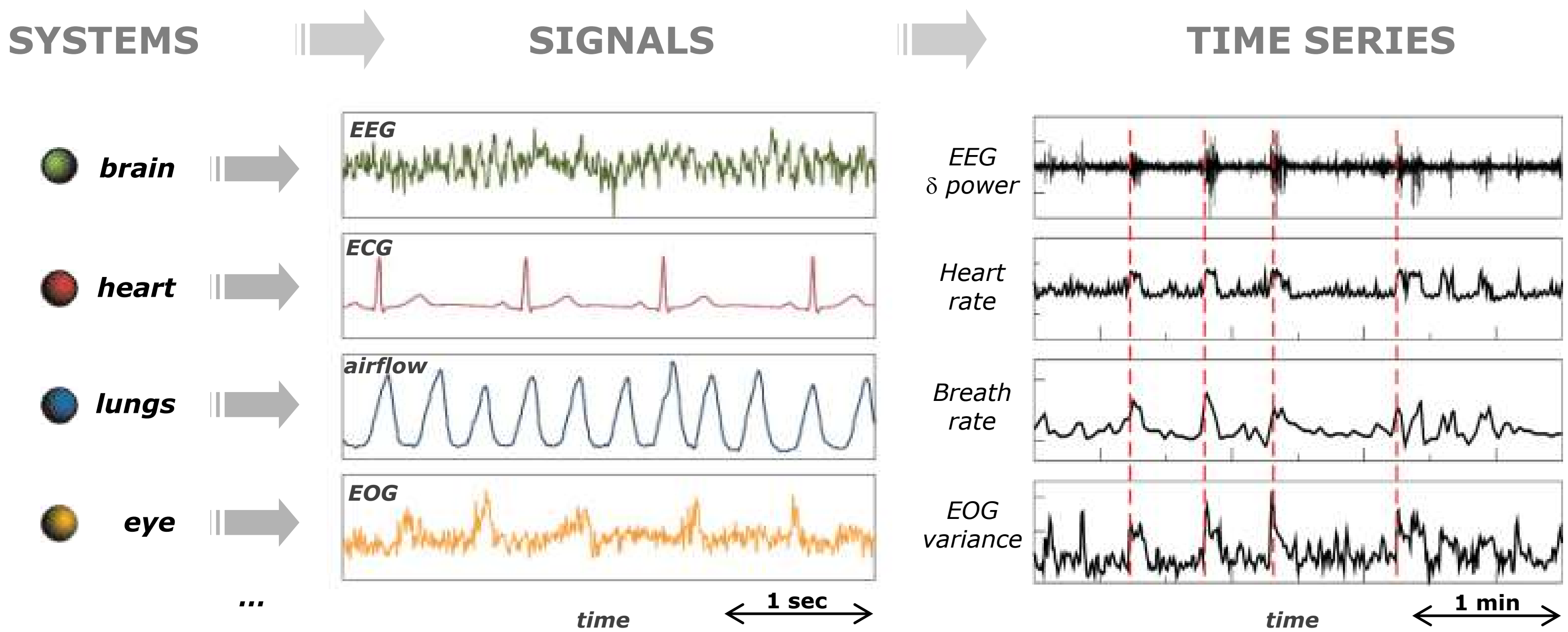
  To look simultaneously at multiple organs

  Each organ system is seen as a node of a complex network of physiological interactions

How to extract valuable information from physiological signals?



Network Physiology has high potential but is still in large part unexplored



ISSUES:

- ✓ ***Multiple network nodes*** → ✓ **Multivariate measures**
- ✓ ***Multiple time scales*** → ✓ **Multi-scale measures**
- ✓ ***non-linear dynamics*** → ✓ **Nonlinear measures**

- **Challenging problems for physicists, engineers and physiologists**

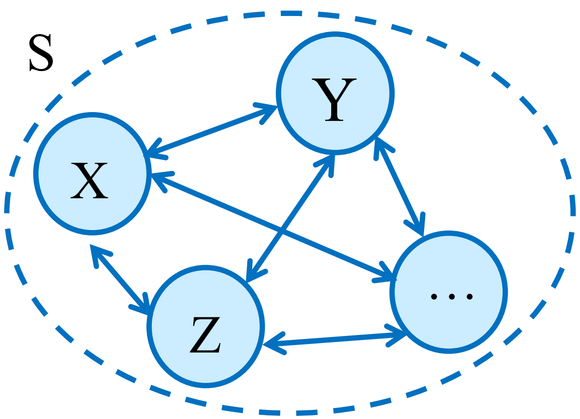
- **We face these issues with the unifying framework of INFORMATION DYNAMICS**

INFORMATION DYNAMICS: THEORY

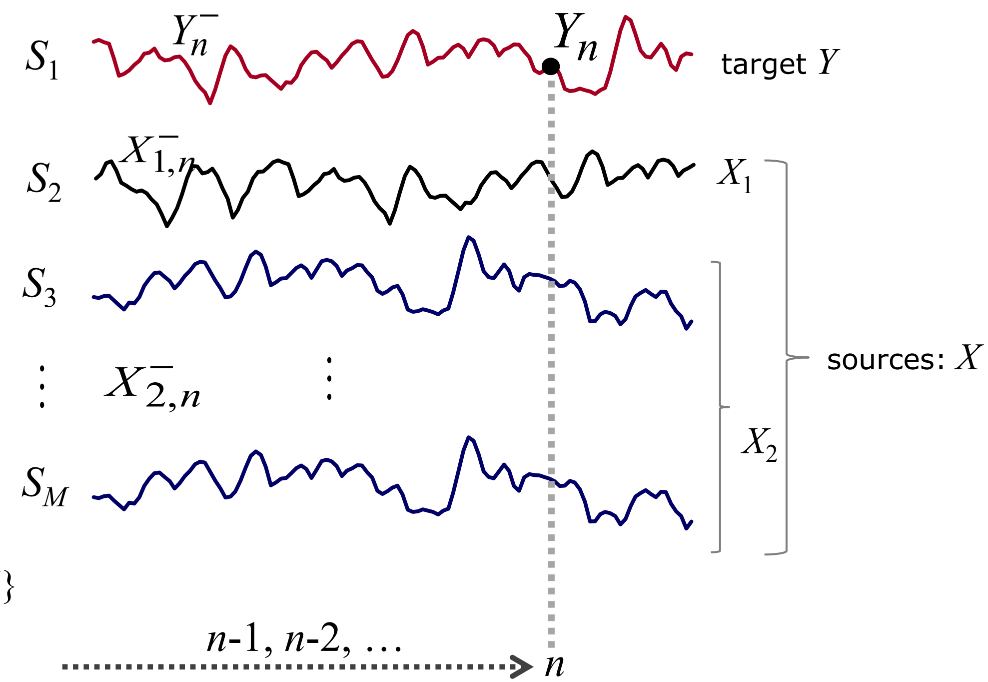
- **Information-theoretic analysis of dynamical systems**
- **Information Measures**
- **Information Decomposition**
  - ***Information Storage***
  - ***Information Transfer***
  - ***Information Modification***

Physiological Networks ⟷ Networks of Dynamical systems

- Dynamic System $S=\{S_1,\dots,S_M\}$



- Dynamic Process S



- With reference to a target system Y :

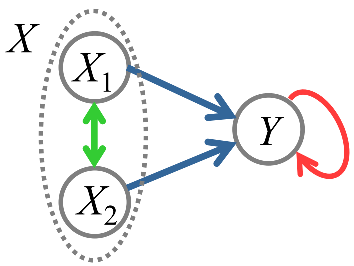
$X=\{X_1,\dots,X_{M-1}\}$ ⇒ $S=\{X_1,\dots,X_{M-1}, Y\} = \{X,Y\}$

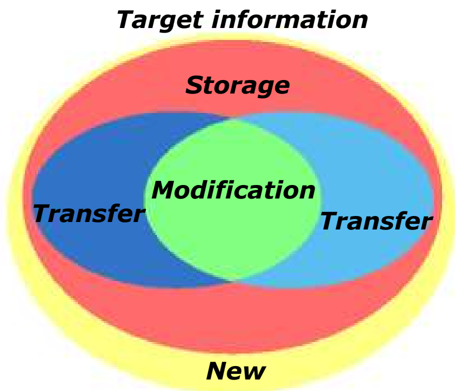
- **Investigation of Statistical dependencies:**
  - ✓ **SELF effects:** $Y_n^- \rightarrow Y_n$ ⇒ **Information storage**
  - ✓ **CAUSAL effects:** $X_n^- \rightarrow Y_n$ ⇒ **Information transfer**
  - ✓ **INTERACTION effects:** $(X_{1,n}^- \leftrightarrow X_{2,n}^-) \rightarrow Y_n$ ⇒ **Information modification**

THE FRAMEWORK OF INFORMATION DYNAMICS

- **Decomposition of the "information" contained in the target process**

$S=\{X,Y\}=\{X_1,X_2,Y\}$





$$H_Y = S_Y + T_{X_1 \to Y} + T_{X_2 \to Y} + I_{X_1 X_2 \to Y} + N_Y$$

Information

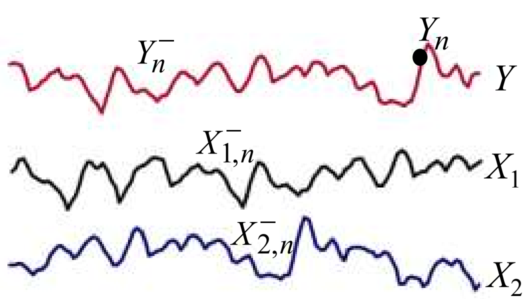
Information Storage *activity*

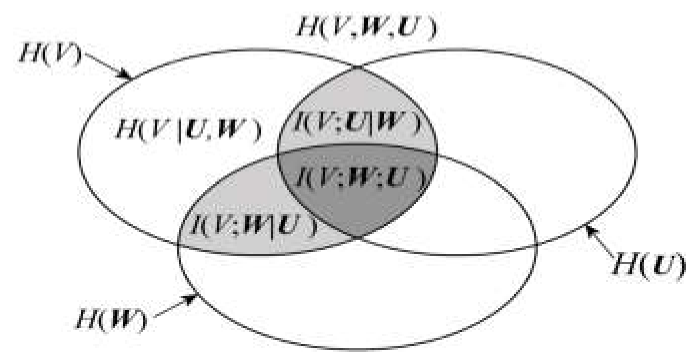
Information Transfer *connectivity*

Information Modification *interaction*

New Information *non-predictable dynamics*

- **Computation: basic information theoretic measures**





ENTROPY:

$H(V) = -\mathrm{E}[\log p(v)]$

CONDITIONAL ENTROPY:

$H(V|U) = H(V,U) - H(U)$

MUTUAL INFORMATION:

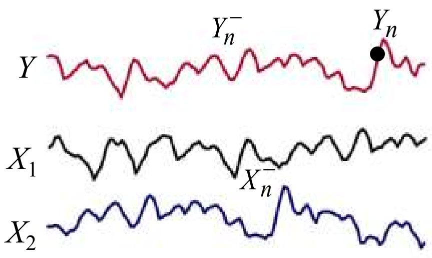
$I(V;U) = H(V) - H(V|U)$

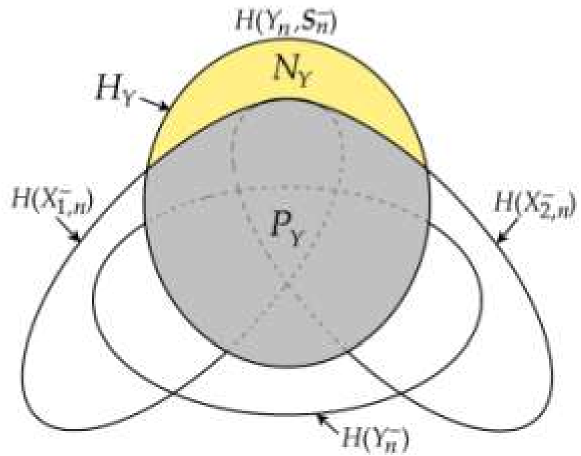
$I(V;U|W) = H(V|W) - H(V|U,W)$

INTERACTION INFORMATION:

$I(V;U;W) = I(V;U) + I(V;W) - I(V;U,W)$

TARGET INFORMATION DECOMPOSITION





$$H(Y_n) = I(Y_n; \mathbf{X}_n^-, Y_n^-) + H(Y_n \mid \mathbf{X}_n^-, Y_n^-)$$

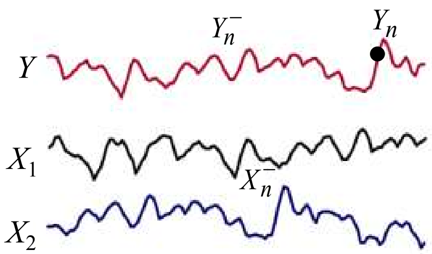
H_Y	P_Y	N_Y
Information	**Predictive Information**	**New created Information**

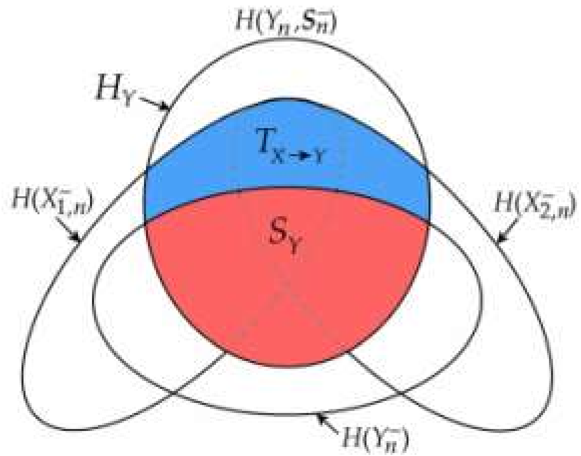
- **Present Information** about Y : $H_Y = H(Y_n)$
  Information contained in the present of the process Y
  → ***Uncertainty about the present state of the target***

- **Predictive Information** about Y : $P_Y = I(Y_n; Y_n^-, X_n^-)$
  Information contained in the past of $S=(X,Y)$ that can be used to predict the present of the target Y
  → ***Predictability of the target given the past network states***

- **New information** about Y : $N_Y = H(Y_n \mid Y_n^-, X_n^-)$
  Information contained in the present of Y that cannot be predicted from the past of $S=(X,Y)$
  → ***Information generated in the target by the state transition***

PREDICTIVE INFORMATION DECOMPOSITION





$$I(Y_n;\mathbf{X}_n^-,Y_n^-)=I(Y_n;Y_n^-)+I(Y_n;\mathbf{X}_n^-\,|\,Y_n^-)$$

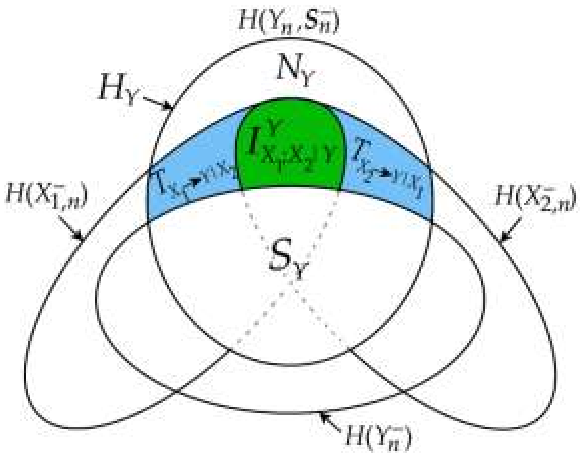
P_Y	S_Y	$T_{X\to Y}$
Predictive Information	**Information Storage**	**Information Transfer**

- **Predictive Information** about Y : $P_Y=I(Y_n;Y_n^-,X_n^-)$
  Information contained in the past of S=(X,Y) that can be used to predict the present of the target Y
  → ***Predictability of the target given the network past states***

- **Information Storage** in Y : $S_Y=I(Y_n;Y_n^-)$
  Information contained in the past of Y that can be used to predict its present
  → ***Predictability of the target from its own past states***

- **Information transfer** from X to Y : $T_{X\to Y}=I(Y_n;X_n^-\,|\,Y_n^-)$
  Information contained in the past of X that can be used to predict the present of Y above and beyond the information contained in the past of Y
  → ***Causal interactions from all sources to the target***

INFORMATION TRANSFER DECOMPOSITION



$$I(Y_n;\mathbf{X}_n^- \mid Y_n^-) = I(Y_n;X_{1,n}^- \mid Y_n^-, X_{2,n}^-) + I(Y_n;X_{2,n}^- \mid Y_n^-, X_{1,n}^-) + I(Y_n;X_{1,n}^-;X_{2,n}^- \mid Y_n^-)$$

$T_{X\to Y}$ — **Information Transfer**

$T_{X_1\to Y|X_2}$, $T_{X_2\to Y|X_1}$ — **Conditional information transfer**

$I^Y_{X_1;X_2|Y}$ — **Interaction Information Transfer**

- **Information transfer** from X to Y : $T_{X\to Y} = I(Y_n;X_n^- \mid Y_n^-)$

  Information contained in the past of X that can be used to predict the present of Y above and beyond the information contained in the past of Y

  → ***Causal interactions from all sources to the target***

- **Conditional information transfer**: $T_{X_1\to Y|X_2} = I(Y_n;X_{1,n}^- \mid Y_n^-, X_{2,n}^-)$

  Information contained in the past of X_1 that can be used to predict the present of Y above and beyond the information contained in the past of Y and X_2

  → ***Causal interactions from one source to the target***

- **Interaction information transfer**: $I^Y_{X_1;X_2|Y} = I(Y_n;X_{1,n}^-;X_{2,n}^- \mid Y_n^-)$

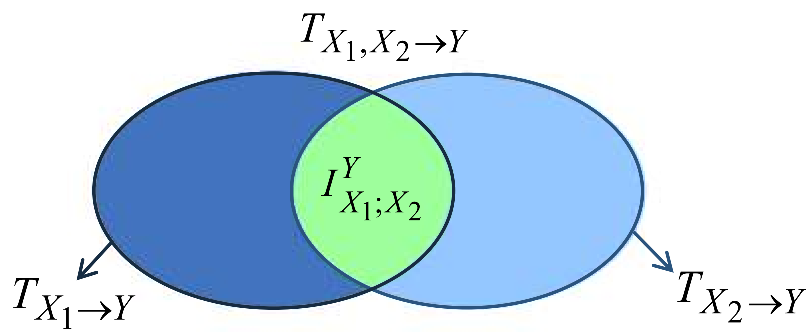
  Information contained in the past of X_1 and X_2 that can be used to predict the present of Y when X_1 and X_2 are taken individually but not when they are taken together

  → ***Redundant or synergistic interactions contributing to transfer***

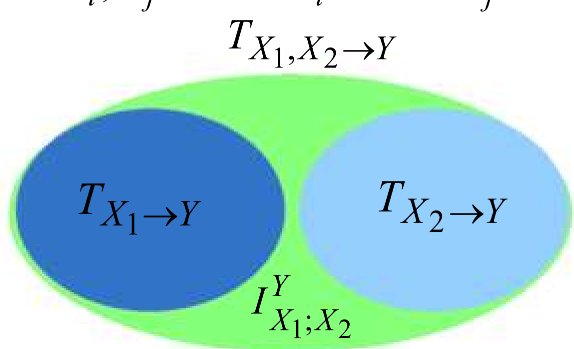
INFORMATION MODIFICATION: REDUNDANCY AND SYNERGY

- **Interpretation of Information Modification:** $I^{Y}_{X_1;X_2} = T_{X_1 \to Y} + T_{X_2 \to Y} - T_{X_1,X_2 \to Y}$

REDUNDANCY: $T_{X_1,X_2 \to Y} < T_{X_1 \to Y} + T_{X_2 \to Y} \;\rightarrow\; I^{Y}_{X_1;X_2} > 0$

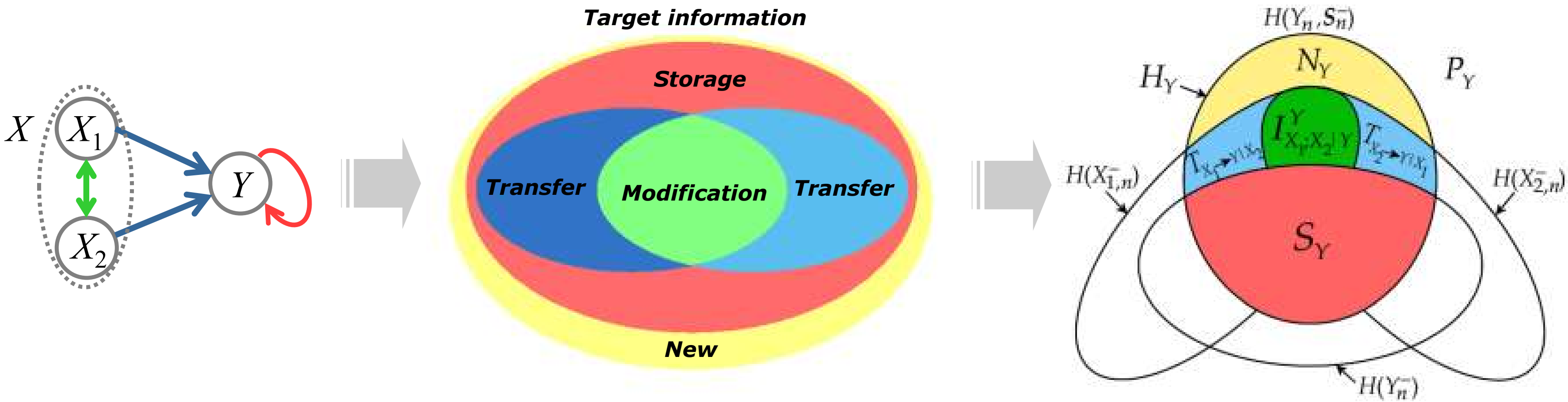


SYNERGY: $T_{X_i,X_j \to Y} > T_{X_i \to Y} + T_{X_j \to Y} \;\rightarrow\; I^{Y}_{X_i;X_j} < 0$



Interaction information can be negative: synergy!

THE FRAMEWORK OF INFORMATION DYNAMICS



$$H_Y = N_Y + P_Y = N_Y + S_Y + T_{X \to Y} = N_Y + S_Y + T_{X_1 \to Y|X_2} + T_{X_2 \to Y|X_1} + I^{Y}_{X_1;X_2|Y}$$

Information

Predictive

Information Storage
predictable activity

Conditional Transfer
direct causal connectivity

Interaction Transfer

New Information
unpredictable dynamics

Information Transfer
causal connectivity

Information Modification
interaction between systems

L Faes, A Porta, G Nollo, *'Information decomposition in bivariate systems: theory and application to cardiorespiratory dynamics'*, ***Entropy, special issue on "Entropy and Cardiac Physics", 2015***, 17:277-303.

L Faes, A Porta, G Nollo, M Javorka, 'Information decomposition in multivariate systems: definitions, implementation and application to cardiovascular networks', ***Entropy, special issue on Multivariate Entropy Measures and their applications***, 2017, 19(1), 5

INFORMATION DYNAMICS: ESTIMATION

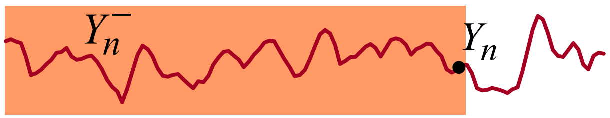
- Linear model-based estimator
- Nonlinear model-free estimators →
  - *Binning*
  - *Kernel*
  - *Nearest neighbor*
- Challenges of model-free estimation

PRACTICAL COMPUTATION OF INFORMATION DYNAMICS

- All measures of Information dynamics are expressed in terms of measures of **(conditional) entropy**, **(conditional) mutual information**, or **interaction information**

- **Estimation of entropy for variables with different dimension**

- **Example: Information Storage**



target Y

$$S_Y = I(Y_n; Y_n^-) = H(Y_n) - H(Y_n \mid Y_n^-) = H(Y_n) - H(Y_n, Y_n^-) + H(Y_n^-)$$

Approximation of the past history

$$Y_n^- = [Y_{n-1} Y_{n-2} \cdots] \quad \Rightarrow \quad Y_n^- \cong Y_n^L = [Y_{n-1} Y_{n-2} \cdots Y_{n-L}]$$

Computation

Discrete variables

$$H(Y_n) = -\sum_{y_n \in \Omega_Y} p(y_n) \log p(y_n) \qquad H(Y_n^-) \cong H(Y_n^L) = -\sum_{y_{n-1}} \cdots \sum_{y_{n-L}} p(y_n^L) \log p(y_n^L)$$

Continuous variables

$$H(Y_n) = -\int_{D_Y} p(y_n) \log p(y_n) dy_n \qquad H(Y_n^-) \cong H(Y_n^L) = -\int_{D_Y} \cdots \int_{D_Y} \cdots p(y_n^L) \log p(y_n^L) dy_{n-1} \ldots dy_{n-L}$$

PARAMETRIC ESTIMATION: LINEAR METHOD

- Exact Computation under the **assumption of Gaussianity**

✓ **Entropy of Y_n :** $H_Y = H(Y_n) = \frac{1}{2}\ln 2\pi e \cdot \sigma(Y_n)$

✓ **Conditional Entropy of Y_n given** $Y_n^- \cong Y_n^L$ **:** $H(Y_n | Y_n^-) \cong H(Y_n | Y_n^L) = \frac{1}{2}\ln 2\pi e \cdot \sigma(Y_n | Y_n^L)$

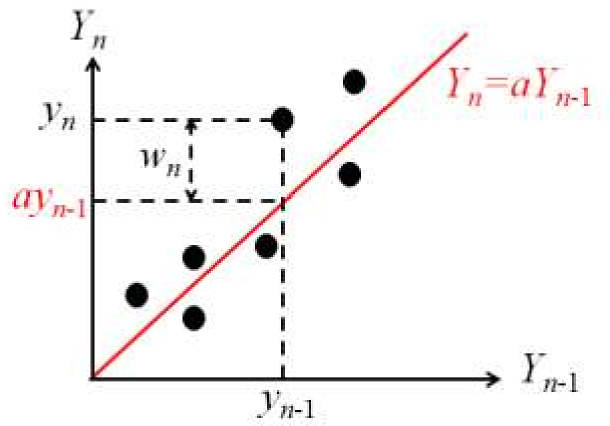
linear regression of** Y_n on $Y_{n-1}, \ldots, Y_{n-L}$ **: $Y_n = a_1 Y_{n-1} + \cdots a_L Y_{n-L} + W_n$

$\sigma(Y_n | Y_n^L) = \sigma_W^2$ **[Barnett et al, Phys Rev Lett 2009]**

✓ **Information Storage of** Y **:** $S_Y = I(Y_n; Y_n^-) \cong H(Y_n) - H(Y_n | Y_n^L) = \frac{1}{2}\ln\frac{\sigma_Y^2}{\sigma_W^2}$

- Example: L=1

$$Y_n^L \cong Y_n^1 = Y_{n-1}$$



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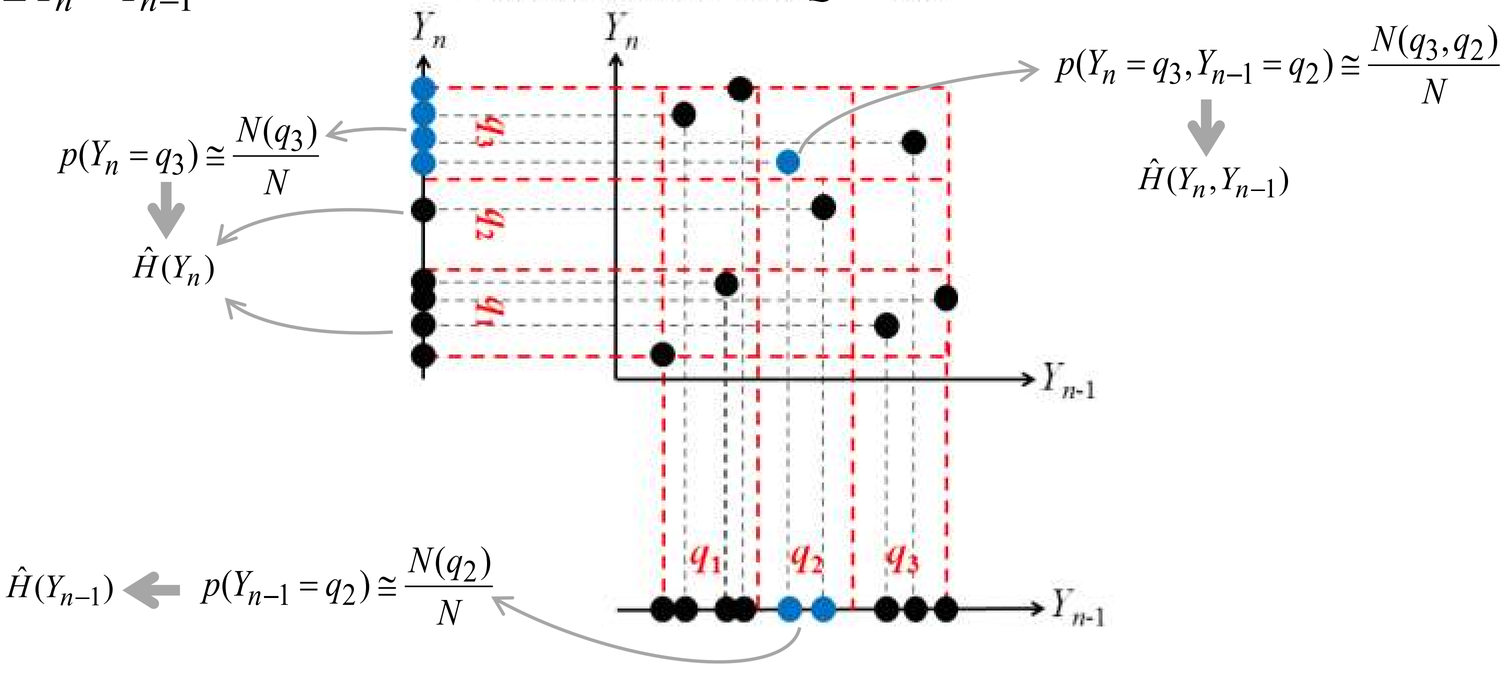
NONPARAMETRIC ESTIMATION: BINNING METHOD

- Discretization of continuous random variables using quantization levels
  - ✓ **Target Information of** Y **:** $H_Y = H(Y_n)$
  - ✓ **Information Storage of** Y **:** $S_Y = I(Y_n;Y_n^-) \cong I(Y_n;Y_n^L) = \hat{H}(Y_n) - \hat{H}(Y_n,Y_n^L) + \hat{H}(Y_n^L)$
    - ✓ Example: L=1

$Y_n^L \cong Y_n^1 = Y_{n-1}$

Uniform partition with Q=3 bins



L Faes, A Porta, 'Conditional entropy-based evaluation of information dynamics in physiological systems', in ***Directed Information Measures in Neuroscience***, R Vicente, M Wibral, J Lizier (eds), Springer-Verlag; 2014, pp. 61-86

NONPARAMETRIC ESTIMATION: KERNEL METHOD

- Entropy computation using kernel functions to weight distances between points
  - Probability of d-dimensional variable X: $\hat{p}(x_n) = \frac{1}{N}\sum_{i=1}^{N} K(\|x_n - x_i\|)$
  - ***Entropy:*** $H(X) = -\mathrm{E}[\log p(x)] \cong -\log\langle \hat{p}(x)\rangle$

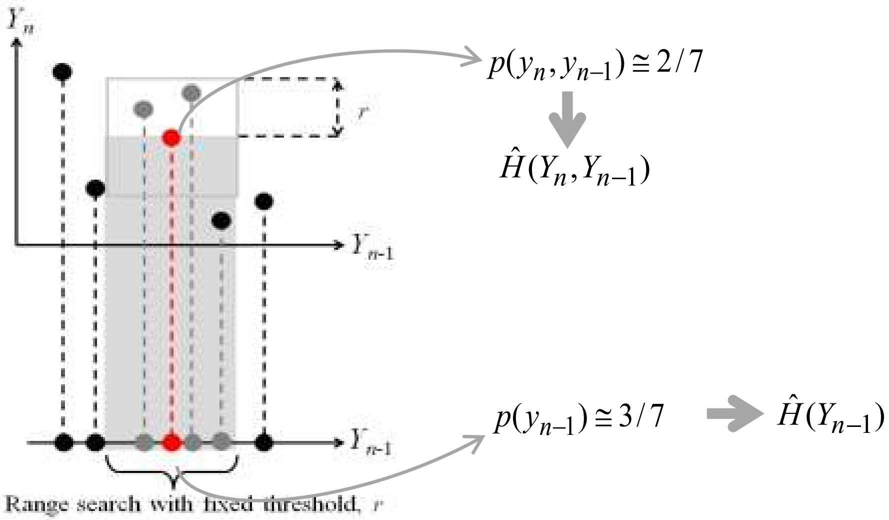
Heaviside kernel function: $K = \Theta(\|z_n - z_i\|) = \begin{cases} 1 \ , & \|z_n - z_i\| \le r \\ 0 \ , & \|z_n - z_i\| > r \end{cases}$

✓ **Target Information of** Y **:** $H_Y = H(Y_n) = -\log\langle p(y_n)\rangle$

✓ **Information Storage of** Y **:** $S_Y = I(Y_n;Y_n^-) \cong I(Y_n;Y_n^L) = \hat{H}(Y_n) - \hat{H}(Y_n,Y_n^L) + \hat{H}(Y_n^L)$ ➜ $S_Y = \log\left\langle \frac{p(y_n, y_n^L)}{p(y_n)p(y_n^L)} \right\rangle$

- Example: L=1

$Y_n^L \cong Y_n^1 = Y_{n-1}$



W Xiong, **L Faes**, P Ch Ivanov, 'Entropy measures, entropy estimators and their performance in quantifying complex dynamics: effects of artifacts, nonstationarity and long-range correlations', Phys. Rev. E, in press, 2017.

NONPARAMETRIC ESTIMATION: NEAREST NEIGHBOR METHOD

- Entropy computation from the statistics of distances between neighboring points in a multidimensional space

$$H(X) = -\mathrm{E}[\log p(x)] \cong -\psi(k) + \psi(N) + d\langle \log \varepsilon_n \rangle$$

ψ : *Digamma function* $\psi(x) = \frac{d \log \Gamma(x)}{dx}$

ε : *2·distance from x_n to its k-th neighbor*

N : *number of outcomes of X*

- Strategy for bias compensation in the estimation of entropies for variables of different dimension

$$\hat{H}(Y_n, Y_n^L) = -\psi(k) + \psi(N) + (L+1)\langle \log \varepsilon_n \rangle$$ → **Neighbor Search**

distance from (y_n, y_n^L) to its k-th neighbor in the outcomes of (Y_n, Y_n^L)

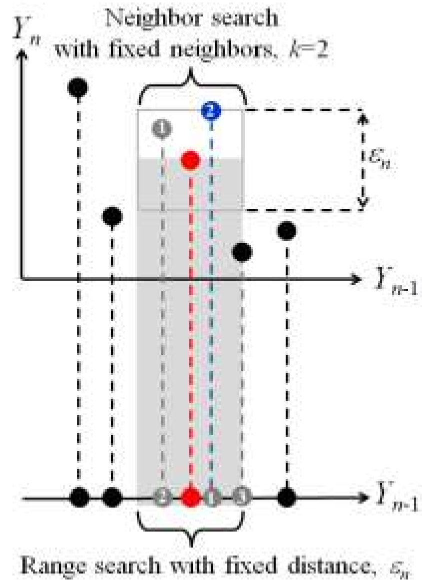
$$\hat{H}(Y_n) = -\langle \psi(N_{Y_n}) \rangle + \psi(N) + \langle \log \varepsilon_n \rangle$$ → **Range Search**

$$\hat{H}(Y_n^L) = -\langle \psi(N_{Y_n^L}) \rangle + \psi(N) + L\langle \log \varepsilon_n \rangle$$ → **Range Search**

number of outcomes of Y_n^L with distance to y_n^L strictly lower than $\varepsilon_n/2$

$$S_Y = \hat{H}(Y_n) - \hat{H}(Y_n, Y_n^L) + \hat{H}(Y_n^L) = \psi(N) + \psi(k) - \langle \psi(N_{Y_n^L}) + \psi(N_{Y_n}) \rangle$$

Example: L=1 $Y_n^L \cong Y_n^1 = Y_{n-1}$



L Faes, D Kugiumtzis, A Montalto, G Nollo, D Marinazzo, 'Estimating the decomposition of predictive information in multivariate systems', Phys. Rev. E 2015; 91:032904.

ESTIMATION: SIMULATION EXAMPLE

- **Test on stochastic process with short-term dynamics and long-range correlations**

- **Fractionally-integrated autoregressive process:** $A(L)(1-L)^d Y_n = U_n$

Autoregressive polynomial: *sets stochastic oscillation with amplitude ρ and frequency f*

$$A(L) = 1 - 2\rho \cos 2\pi f L - \rho^2 L^2$$

Fractional differencing: *sets long-range correlations depending on the differencing parameter d*

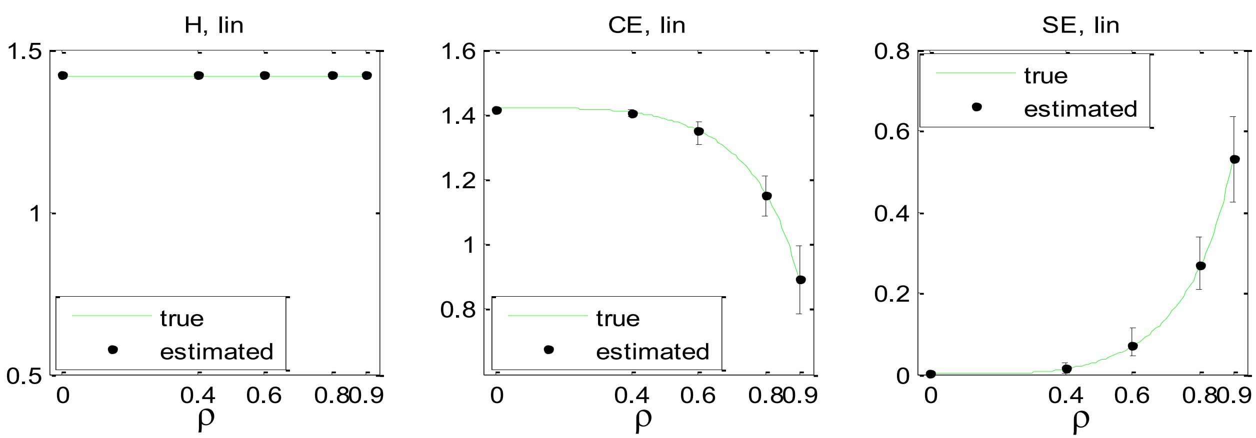
$$(1-L)^d = \sum_{k=0}^{\infty} \frac{\Gamma(k-d) L^k}{\Gamma(-d)\Gamma(k+1)}$$

- **Estimation of Entropy, Conditional Entropy and Information Storage**

$$S_Y = I(Y_n; Y_n^-) = H(Y_n) - H(Y_n \mid Y_n^-)$$

L=2 ➔ $Y_n^- \cong Y_n^L = [Y_{n-1} Y_{n-2}]$

- **Estimation: theoretical profiles** and **estimates, linear method**



W Xiong, **L Faes**, P Ch Ivanov, 'Entropy measures, entropy estimators and their performance in quantifying complex dynamics: effects of artifacts, nonstationarity and long-range correlations', Phys. Rev. E, in press, 2017.

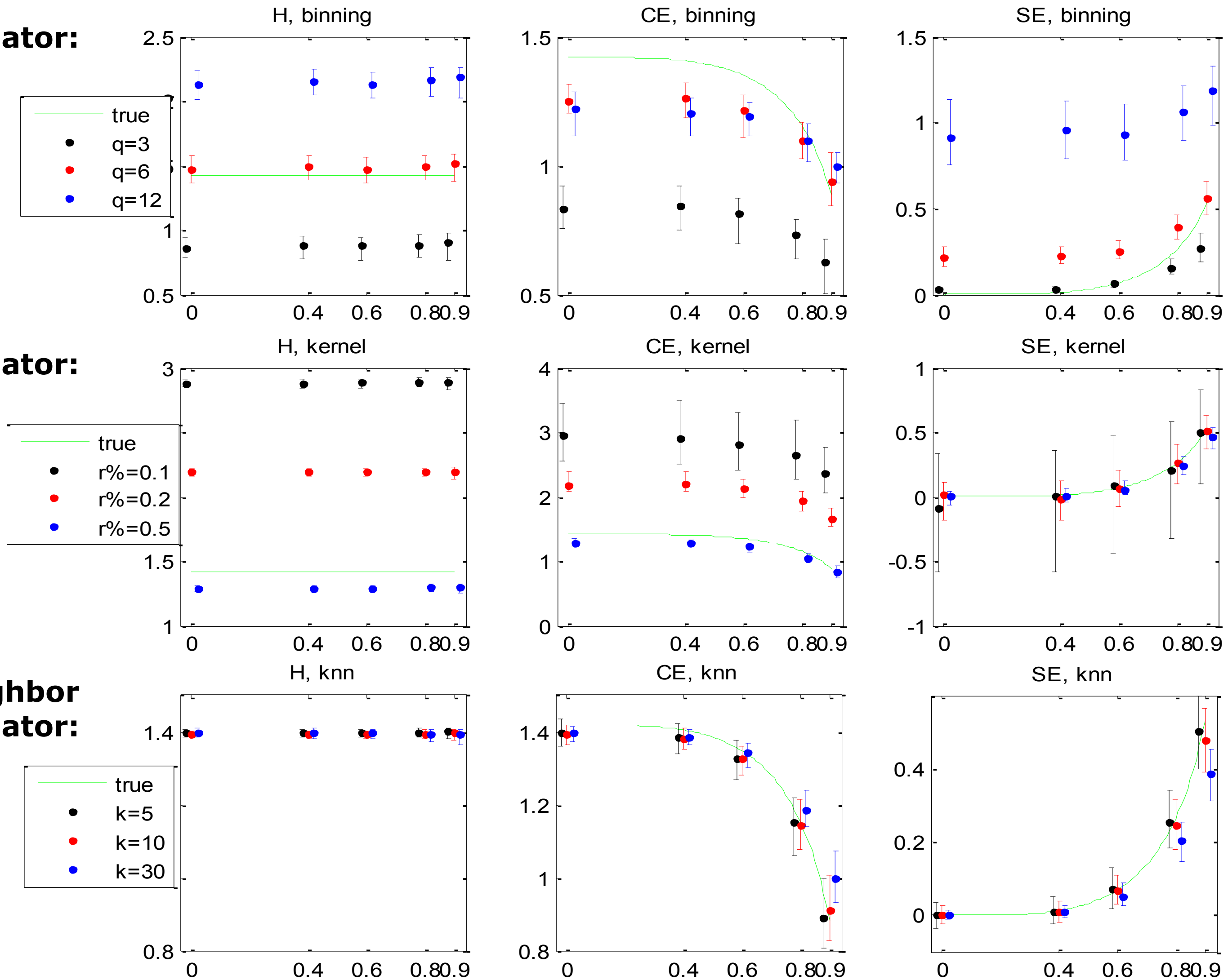
ESTIMATION: SIMULATION EXAMPLE

- **Estimation: theoretical profiles** and **estimates**, **non-parametric model-free methods**

Binning estimator:

Kernel estimator:

Nearest neighbor estimator:



MODEL-FREE ESTIMATION: APPROXIMATION OF THE SYSTEM PAST

- **Uniform embedding (UE):** $X_n^- \approx [X_{n-m_X} \dots X_{n-L_X m_X}]$ $Y_n^- \approx [Y_{n-m_Y} \dots Y_{n-L_Y m_Y}]$

  UE introduces irrelevant and redundant components → ***Curse of dimensionality***

- **Non-uniform embedding (NUE):** The embedding vector is formed progressively, including at each step the lagged variable better describing the target process

  - ***Sequential procedure:***

    (a) k=0: Initialization

    Set of initial candidate components (e.g., $\Omega = \{X_{n-1},\dots,X_{n-L}, Y_{n-1},\dots,Y_{n-L}\}$)

    Initial embedding vector: $V_n^{(0)} = [\cdot]$

    (b) $k \geq 1$: Selection – maximum relevance, minimum redundancy

    Select the component $W_n \in \Omega$ that maximizes $I(Y_n, W_n | V_n^{(k-1)})$ → $V_n^{(k)} = [\hat{W}_n, V_n^{(k-1)}]$

    (c) Termination – randomization test

    Generate N surrogates of $\hat{W}_n$ by sample shuffling: $\hat{W}_n^{(S_1)},\dots,\hat{W}_n^{(S_N)}$; Threshold for $I(Y_n, \hat{W}_n | V_n^{(k-1)})$: I_{th}

    Stop if $I(Y_n, \hat{W}_n | V_n^{(k-1)}) < I_{th}$; final set of components: $V_n = V_n^{(k-1)}$

    (d) After termination – embedding vector $V_n = [V_n^X, V_n^Y]$ → $X_n^- \approx V_n^X$ $Y_n^- \approx V_n^Y$

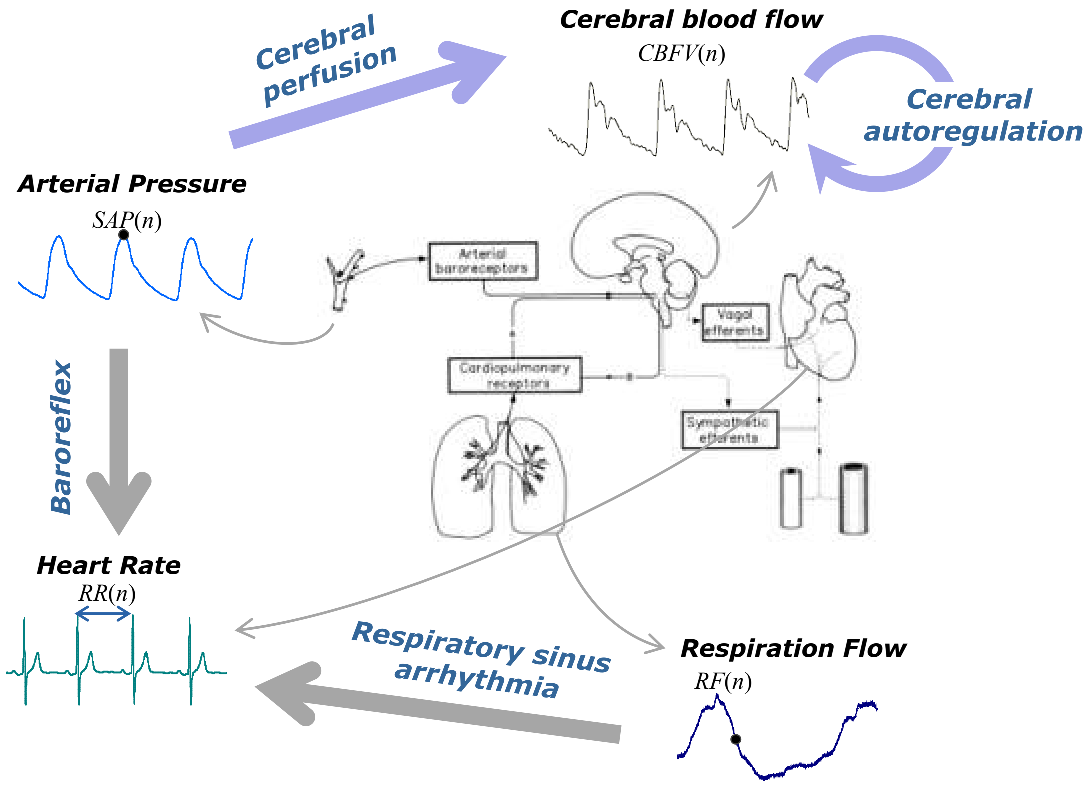
L Faes, G Nollo, A Porta: 'Information-based detection of nonlinear Granger causality in multivariate processes via a nonuniform embedding technique', ***Physical Review E***; 2011; 83(5 Pt 1):051112.

INFORMATION DYNAMICS: APPLICATIONS TO NETWORK PHYSIOLOGY

- Short-term Cardiovascular, Cardiorespiratory, Cerebrovascular control
- Brain-heart and brain-brain interactions during sleep
- Brain networks (EEG, fMRI) and muscular networks (EMG)

PRACTICAL APPLICATIONS OF INFORMATION DYNAMICS

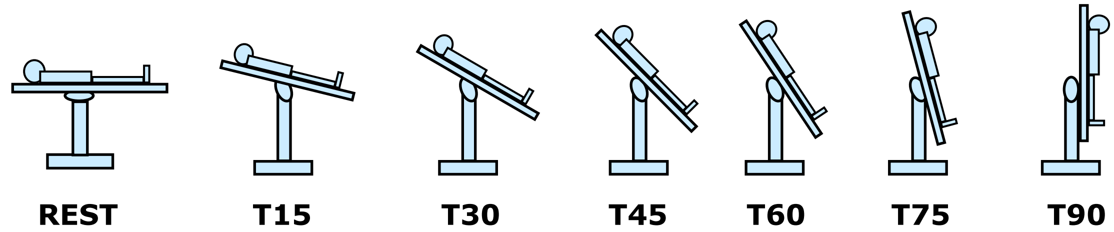
Network of cardiovascular, cardiorespiratory and cerebrovascular short-term physiological interactions



Applications: CARDIAC CONTROL

Graded Head-up tilt protocol

17 young healthy subjects



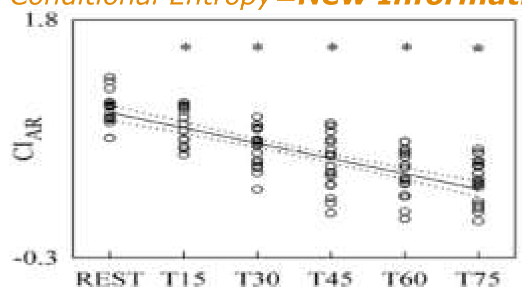
- **The dynamical complexity of short-term heart period variability decreases progressively with tilt-table angle**

- ***Linear estimator***
- ***Univariate analysis***

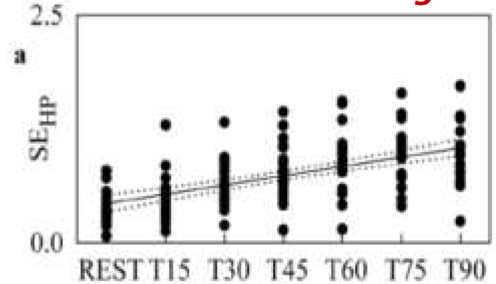
  New Information N_Y

  Information Storage S_Y

Conditional Entropy=***New Information***

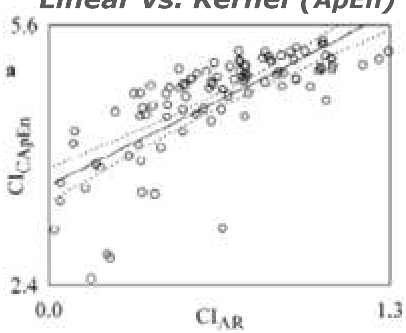


Information Storage

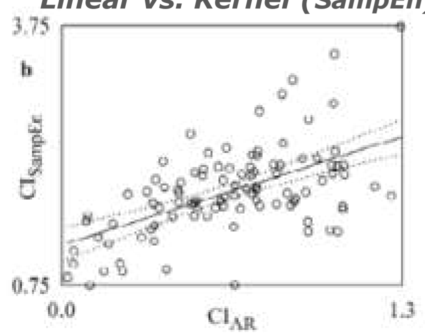


- **Complexity assessed by linear model-based estimators significantly correlates with model-free estimates**

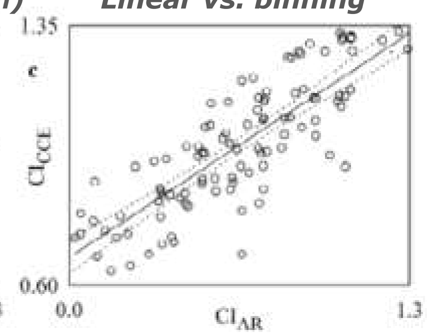
Linear vs. Kernel (ApEn)



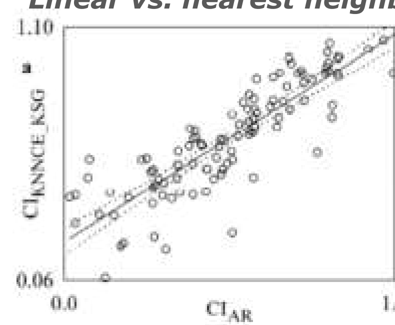
Linear vs. Kernel (SampEn)



Linear vs. binning



Linear vs. nearest neighbors



A Porta, B De Maria, V Bari, A Marchi, **L Faes**, 'Are nonlinear model-free approaches for the assessment of the entropy-based complexity of the cardiac control superior to a linear model-based one?', ***IEEE Trans. Biomed. Eng.***, in press, 2017

Applications: CARDIOVASCULAR and CARDIORESPIRATORY INTERACTIONS

- ***Protocol: 61 young healthy subjects during head-up tilt and mental stress tasks***

- ***Measured time series:***
  - Heart period (H)
  - Systolic arterial pressure (S)
  - Respiration (R)

  300 points in each condition

- ***Linear estimator***

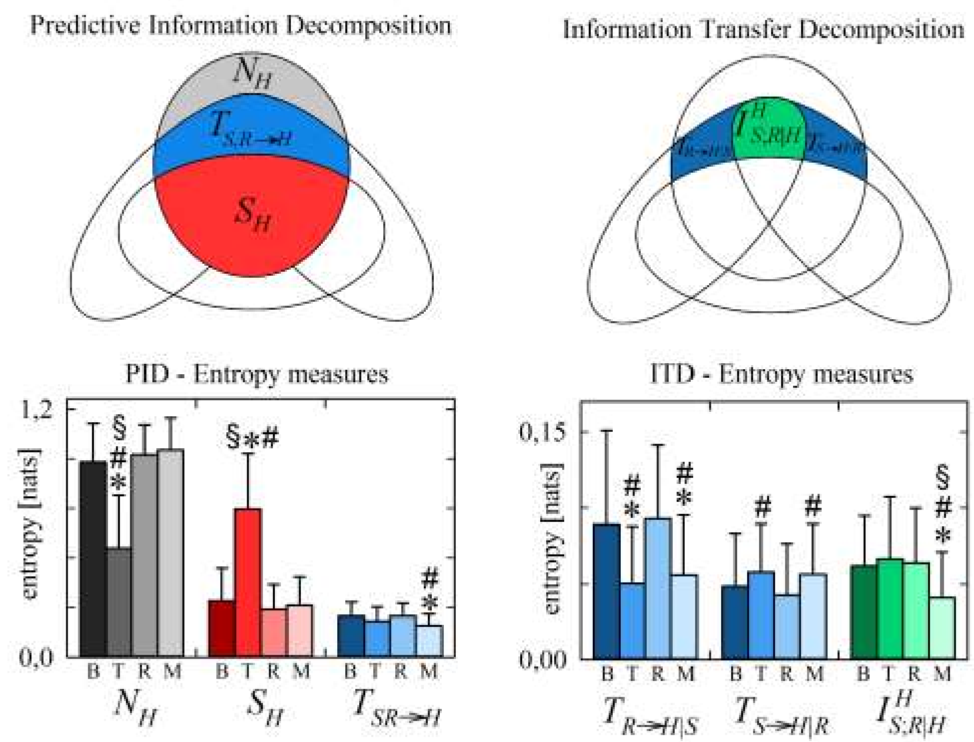
- ***Network analysis***

  full information decomposition:

  $$H_Y = N_Y + S_Y + T_{X\to Y}$$

  $$T_{X\to Y} = T_{X_1\to Y|X_2} + T_{X_2\to Y|X_1} + I^Y_{X_1;X_2|Y}$$

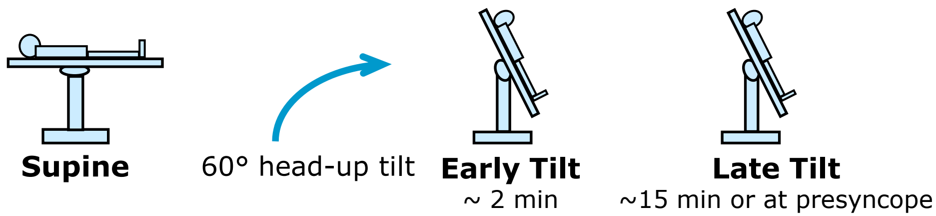
  target: Y=H



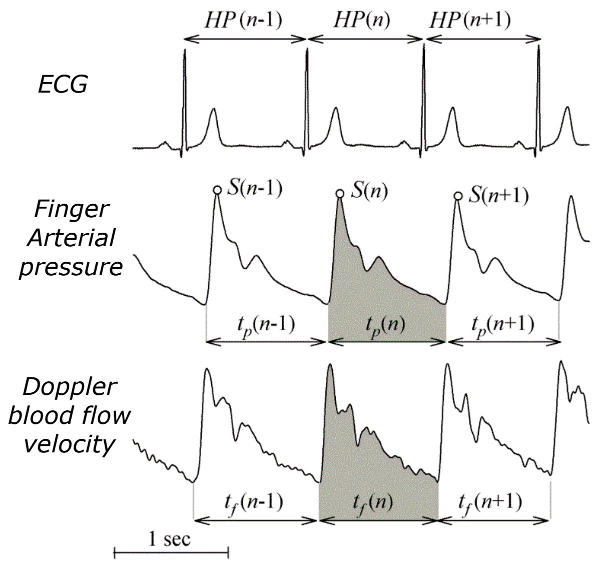
L Faes, A Porta, G Nollo, M Javorka, 'Information decomposition in multivariate systems: definitions, implementation and application to cardiovascular networks', ***Entropy, special issue on Multivariate Entropy Measures and their applications***, 2017, 19(1), 5

Applications: CARDIOVASCULAR AND CEREBROVASCULAR INTERACTIONS

- ***Protocol: 10 subjects with postural-related syncope***



- ***Signals and time series***



- *Binning estimator with NUE*
- *Bivariate analysis,* ***target HP or FV***

Entropy decomposition:

$$H_Y = S_Y + T_{X \to Y} + N_Y$$

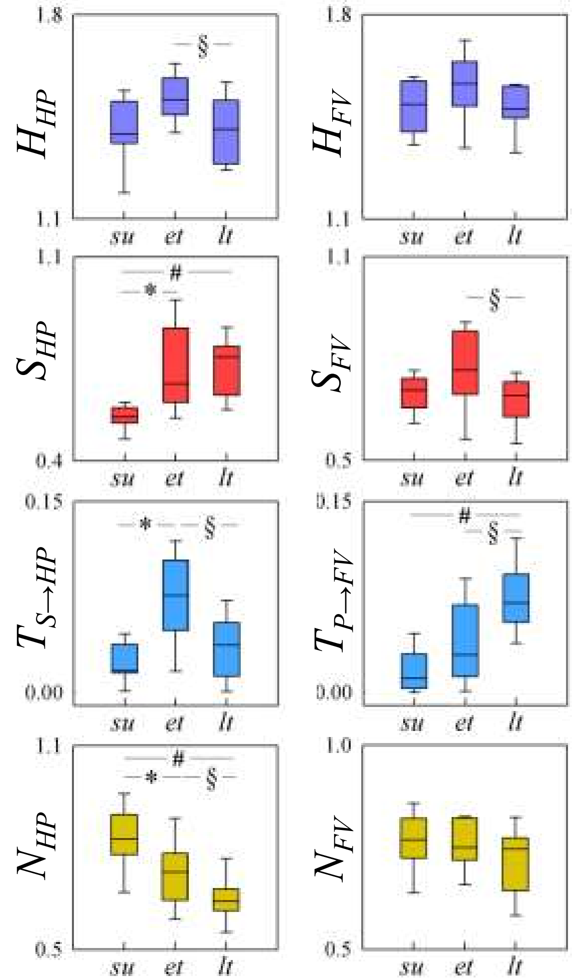
Information

Information Storage

Information Transfer

New Information

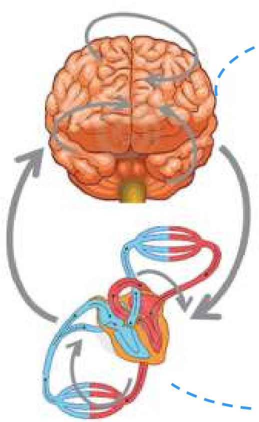
- ***Results***



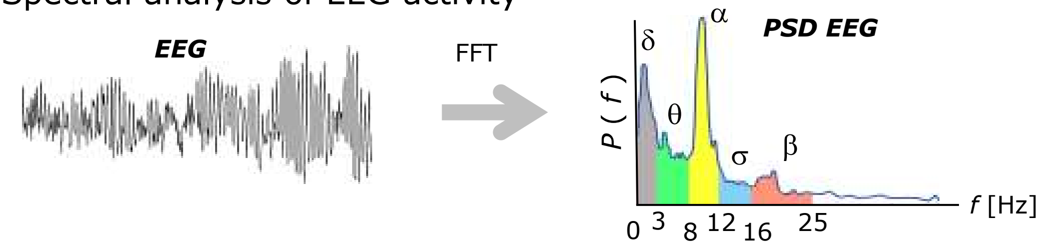
L **Faes**, A Porta, G Rossato, A Adami, D Tonon, A Corica, G Nollo: 'Investigating the mechanisms of cardiovascular and cerebrovascular regulation in orthostatic syncope through an information decomposition strategy', *Autonomic Neuroscience* 2013; 178:76-82.

PRACTICAL APPLICATIONS OF INFORMATION DYNAMICS

Network of brain-heart and brain-brain physiological interactions during sleep



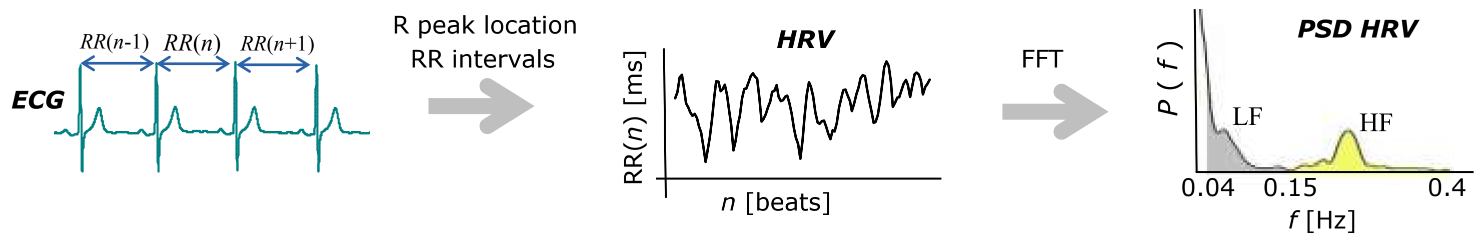
- Spectral analysis of EEG activity

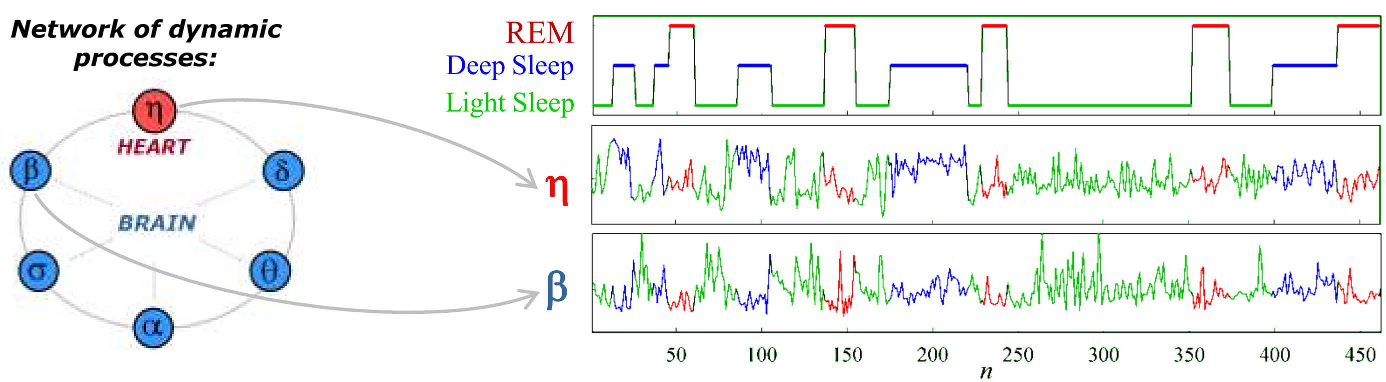


Brain wave amplitudes:

$$P_\delta , P_\theta , P_\alpha, P_\sigma, P_\beta$$

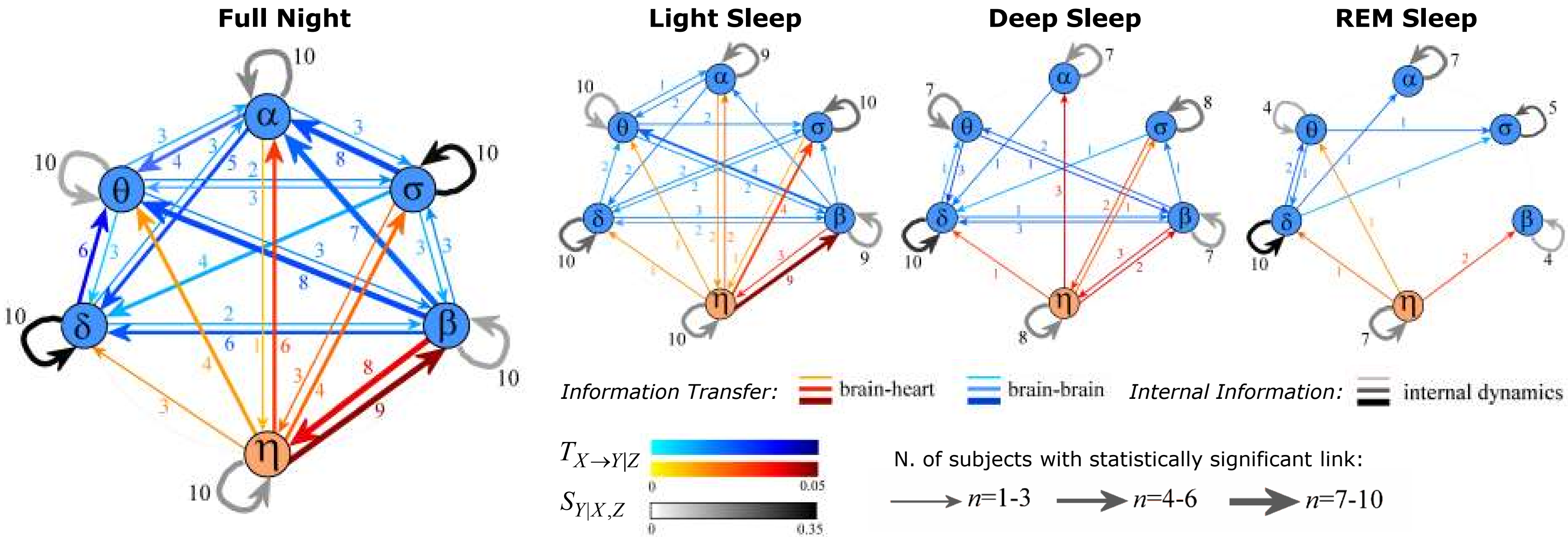
- Spectral analysis of heart rate variability (HRV)





Applications: BRAIN-BRAIN AND BRAIN-HEART INTERACTIONS

- ***Protocol: full night polysomnography in 10 healthy subjects***
- ***Linear estimator***
- ***Network analysis*** *Conditional information transfer + internal information*
  Statistical significance assessed by F-test



Structured brain-heart and brain-brain network, with the EEG β wave acting as network hub

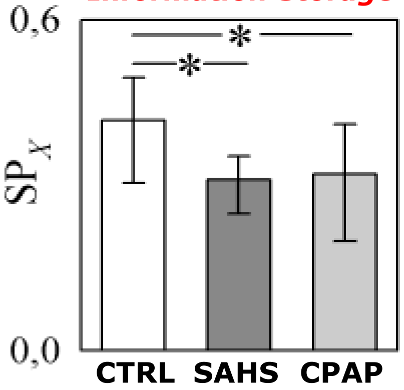
The interaction network is sustained by the sleep stage transitions

L Faes, G Nollo, F Jurysta, D Marinazzo, 'Information dynamics of brain-heart physiological networks during sleep', *New Journal of Physics* 2014; 16:105005.

Applications: BRAIN-HEART INTERACTIONS IN SLEEP APNEAS

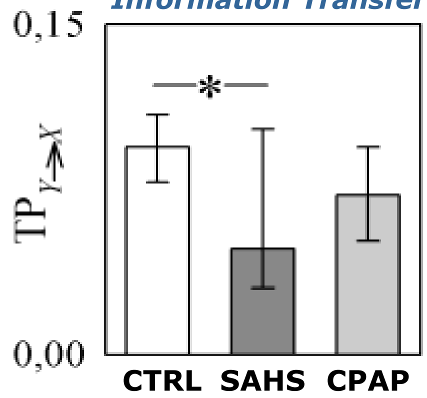
- ✓ 8 sleep apnoea-hypopnoea patients **SAHS**
- ✓ same patients after continuous positive airway pressure therapy **CPAP**
- ✓ 14 healthy controls **CTRL**

Cardiac Information Storage



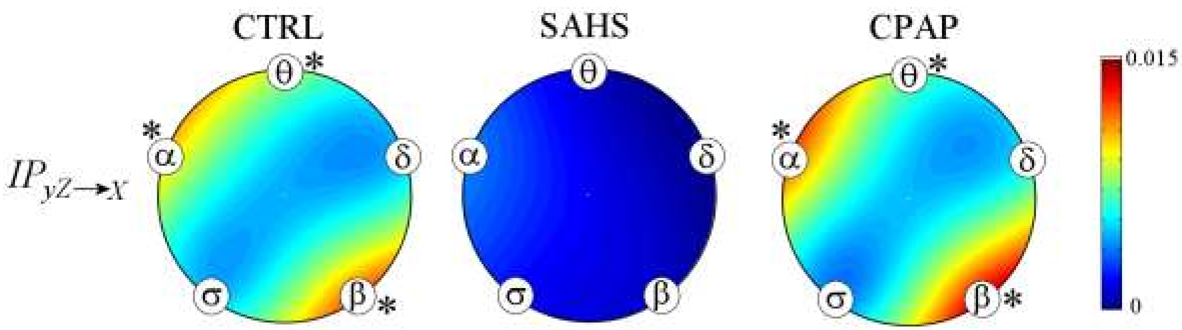
Cardiac dynamics are more complex during sleep apneas, with no recovery after treatment

brain → heart Information Transfer



brain → heart causal interactions are impaired by sleep apneas, and partially restored by CPAP therapy

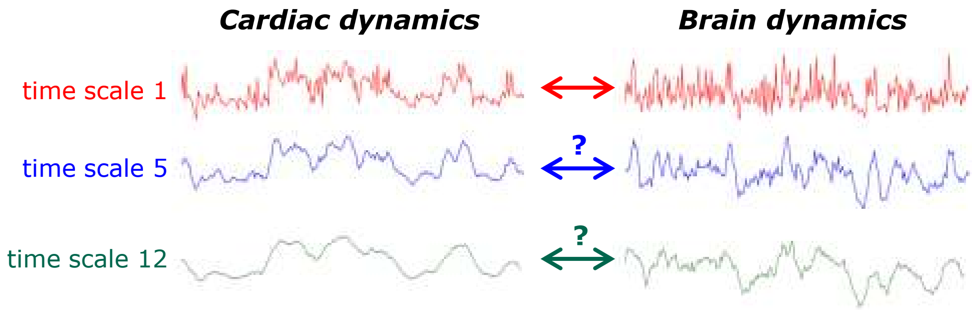
brain → heart Information Modification



Redundancy is a feature of undisturbed sleep, lost in SAHS and recovered by treatment

L Faes, D Marinazzo, S Stramaglia, F Jurysta, A Porta, G Nollo, 'Predictability decomposition detects the impairment of brain-heart dynamical networks during sleep disorders and their recovery with treatment', ***Phil. Trans. R. Soc. A*** 2016; 374:20150177.

Applications: MULTISCALE BRAIN-HEART INTERACTIONS

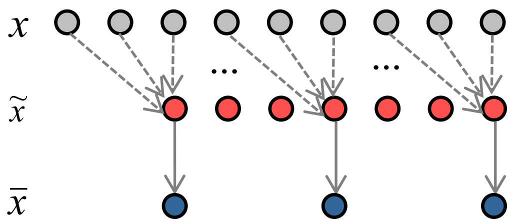


- ***Multiscale methods to study individual dynamics are well established*** [M Costa et al, Phys. Rev. Lett. 89, 2002]
- ***Multiscale computation of information transfer is non-trivial***

- **Exact computation of Information Dynamics for multivariate Gaussian processes**
  - ***Procedure for rescaling a (vector) time series***

$$Y_n = \{x_n, y_n\} \quad n = 1,\dots,N$$

$$\bar{x}_n = \frac{1}{\tau}\sum_{l=0}^{\tau-1} x_{n\tau-l} \;,\quad \bar{y}_n = \frac{1}{\tau}\sum_{l=0}^{\tau-1} y_{n\tau-l}$$



1) AVERAGING $\tilde{x}_n = \frac{1}{\tau}\sum_{l=0}^{\tau-1} x_{n-l} \;,\; n = \tau,\dots,N$

2) DOWNSAMPLING $\bar{y}_n = \tilde{y}_{n\tau} \;,\; n = 1,\dots,N/\tau$

  - ***Multiscale representation of vector Autoregressive processes using state-space models***

Observed time series: $VAR(\mathbf{A},\boldsymbol{\Sigma})$

$$Y_n = \sum_{k=1}^{p} \mathbf{A}_k Y_{n-k} + \mathbf{U}_n$$

AVERAGING (τ) →

Averaged time series: $VARMA(\mathbf{A},\mathbf{B},\boldsymbol{\Sigma}) \longleftrightarrow SS(\tilde{\mathbf{A}},\tilde{\mathbf{C}},\tilde{\mathbf{K}},\tilde{\mathbf{V}})$

$$\tilde{Y}_n = \sum_{k=1}^{p} \mathbf{A}_k Y_{n-k} + \sum_{l=0}^{\tau-1} \mathbf{B}_l \mathbf{U}_{n-l}$$

$$\tilde{Z}_{n+1} = \tilde{\mathbf{A}}\tilde{Z}_n + \tilde{\mathbf{K}}\tilde{E}_n$$
$$\tilde{Y}_n = \tilde{\mathbf{C}}\tilde{Z}_n + \tilde{E}_n$$

DOWNSAMPLING (τ) →

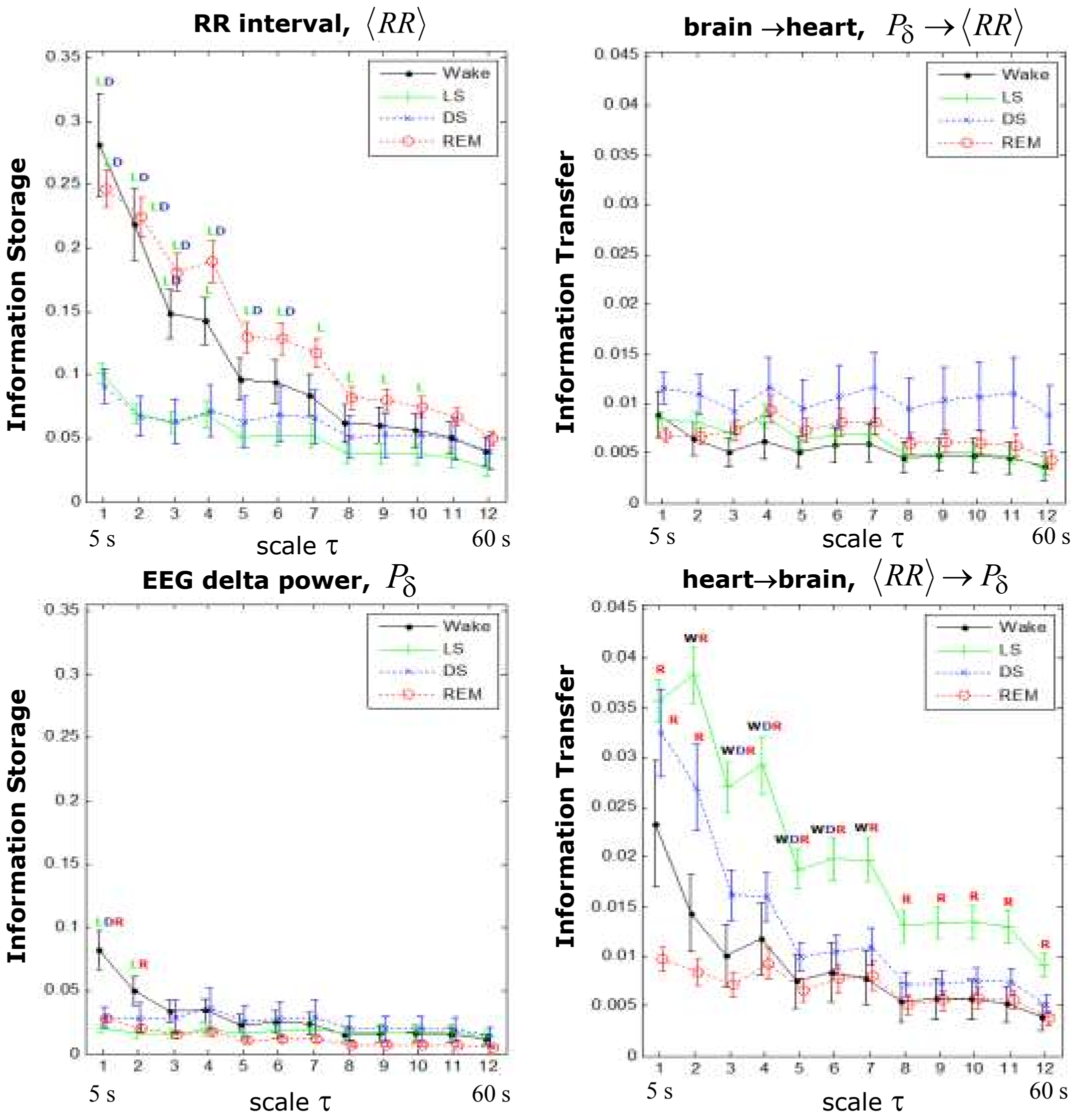
Rescaled time series: $SS(\bar{\mathbf{A}},\bar{\mathbf{C}},\bar{\mathbf{K}},\bar{\mathbf{V}})$

$$\bar{Z}_{n+1} = \bar{\mathbf{A}}\bar{Z}_n + \bar{\mathbf{K}}\bar{E}_n$$
$$\bar{Y}_n = \bar{\mathbf{C}}\bar{Z}_n + \bar{E}_n$$

Information dynamics after rescaling can be obtained from the original VAR parameters and the scale factor τ

L **Faes**, S Stramaglia, G Nollo, D Marinazzo 'Multiscale Granger causality', *Phys Rev E*; under revision, 2017.

Applications: MULTISCALE BRAIN-HEART INTERACTIONS



Wake, REM sleep :

- ***High Storage of cardiac dynamics***
- ***Low Storage of brain dynamics***
- ***Generally low transfer***

Light sleep , Deep sleep :

- ***High transfer heart → brain***
- ***Low transfer brain → heart***
- ***Generally low storage***

L Faes, D Marinazzo, S Stramaglia, A Montalto, G Nollo, 'Multiscale information-theoretic analysis of coupled processes: theory and application to brain-heart interactions', ***Brain Modes 2017***; Bruxelles, Belgium, Dec 1-3 2016.

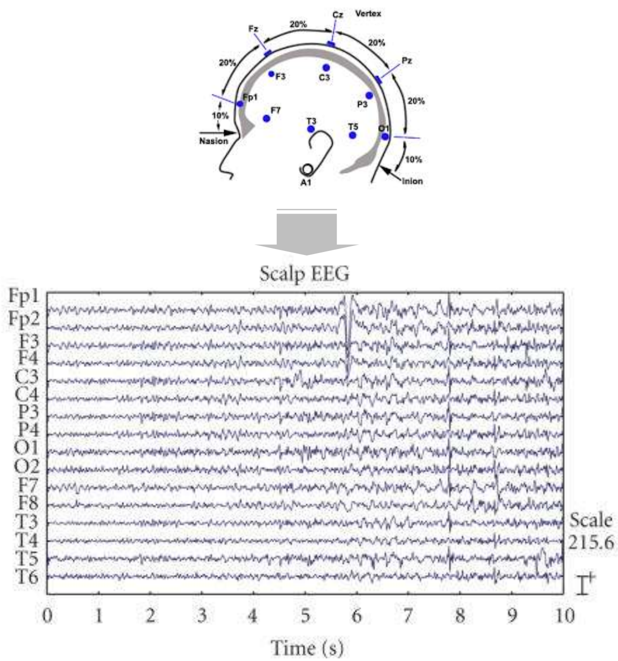
PRACTICAL APPLICATIONS OF INFORMATION DYNAMICS

Physiological networks: EEG brain networks and muscular networks

- **Study of networks formed by multichannel acquisitions of the same biomedical signal**

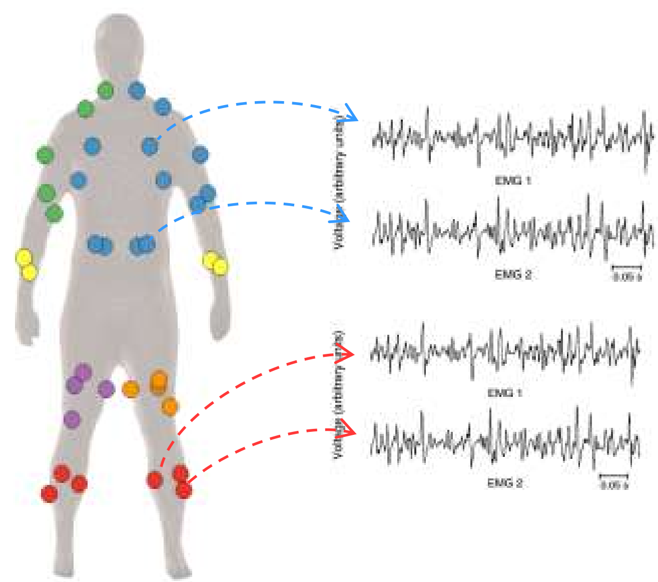
Brain Networks

Scalp multichannel EEG



Muscular Networks

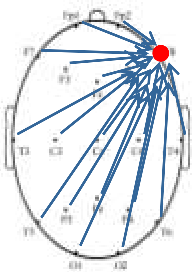
Whole-body multichannel EMG



Information Dynamics of Scalp EEG Networks

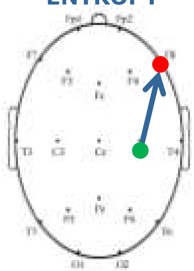
- *Protocol: scalp EEG in 21 healthy subjects during eyes open and eyes closed*
- *Nearest neighbor estimate of information transfer and conditional information transfer between all sensors*

TRANSFER ENTROPY



Y :target
X :sources

PARTIAL TRANSFER ENTROPY



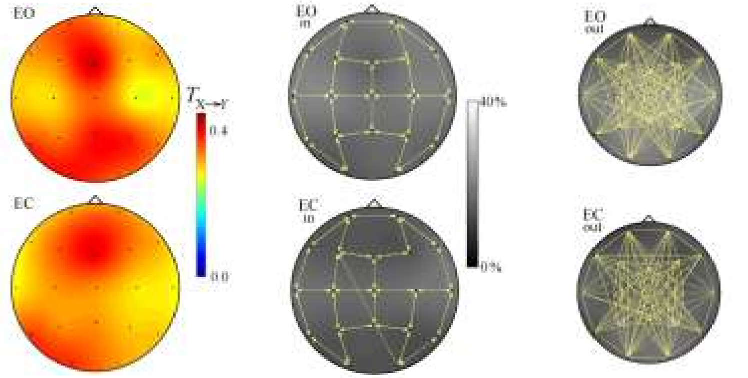
Y :target
X :source
Z :other

Classical measures

TRANSFER ENTROPY | **CONDITIONAL TRANSFER ENTROPY** | **INSTANTANEOUS EFFECTS**

EYES OPEN

EYES CLOSED



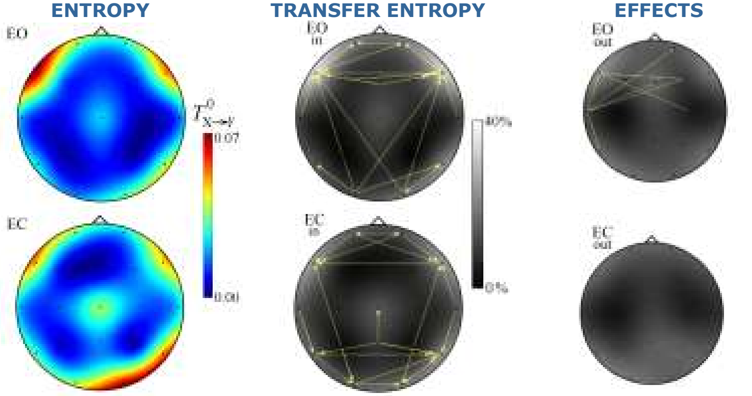
- ***Uniform Information transfer***
- ***Dense connectivity between adjacent sensors***
- ***Instantaneous dependencies between all sensors***
- ***Patterns unchanged between conditions***

Compensated measures

TRANSFER ENTROPY | **CONDITIONAL TRANSFER ENTROPY** | **INSTANTANEOUS EFFECTS**

EYES OPEN

EYES CLOSED



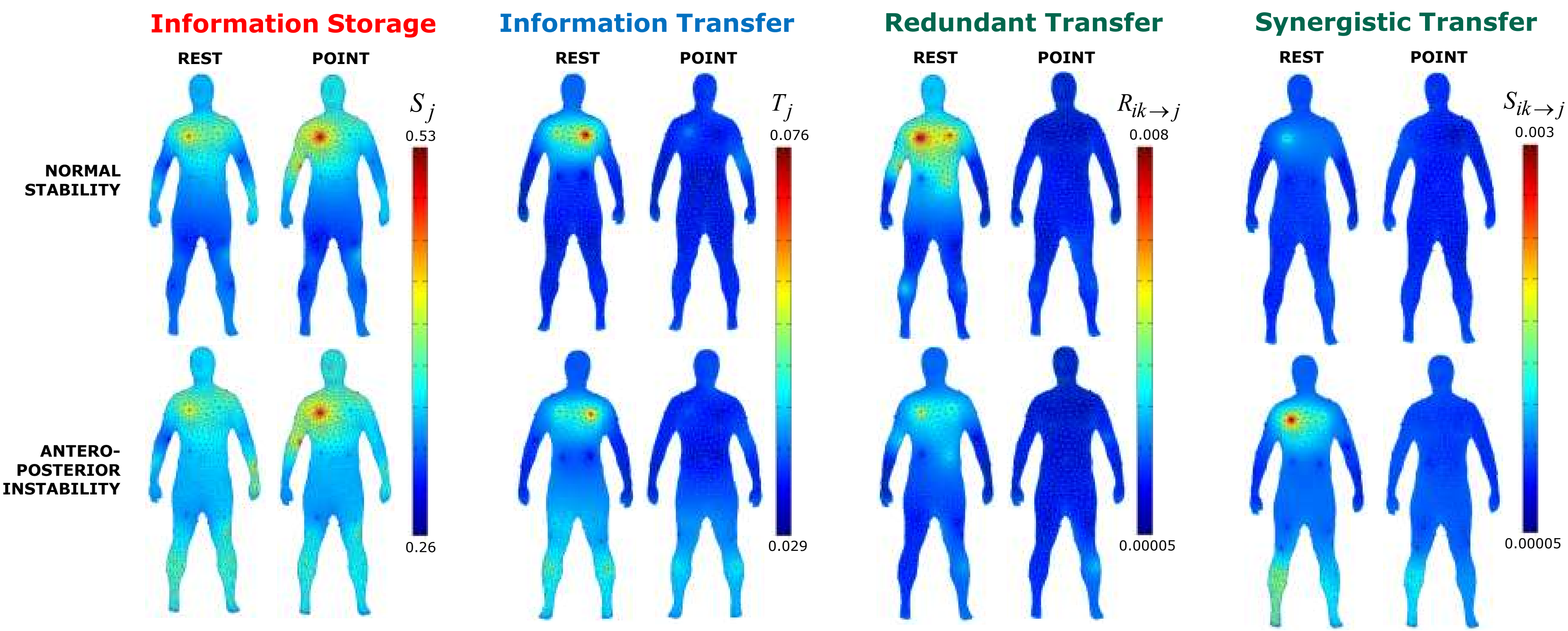
- ***Abolishment of instantaneous correlations***
- ***Emergence of patterns of causal connectivity***

Local sinks of information flow:
- **anterior during EO**
- **anterior + occipital during EC**

L Faes, D Marinazzo, G Nollo, A Porta 'An information-theoretic framework to map the spatio-temporal dynamics of the scalp electroencephalogram', *IEEE Trans. Biomed. Eng., special issue on Brain Connectivity*, 2016; 63(12):2488-2496

Information Dynamics of Muscle Networks

- *Protocol: multichannel EMG in 14 healthy subjects*
- *Conditions: standing and pointing to a target during normal altered stability*



↑ Storage in chest at rest

↑ Storage with pointing

↑ Storage in leg muscles during instability

↑ Transfer to chest at rest

↓ transfer with pointing

↑ transfer to leg muscles during instability

↑ Redundancy to chest at rest

↓ Redundancy with pointing

↓ Synergy at rest

↑ Synergy to chest and leg during instability

L Faes, D Marinazzo, TJ Boonstra, J Kerkman, 'An exploration of information storage, transfer and modification in whole-body human muscular networks', *in preparation*, 2017.

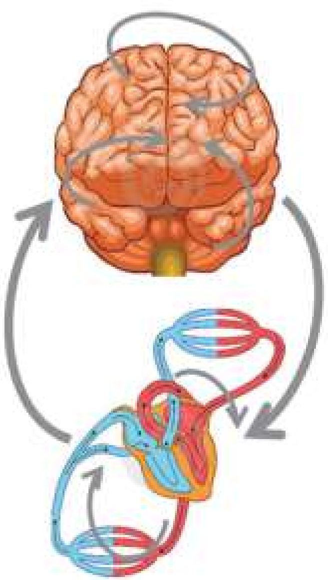
Network Physiology and Information Dynamics

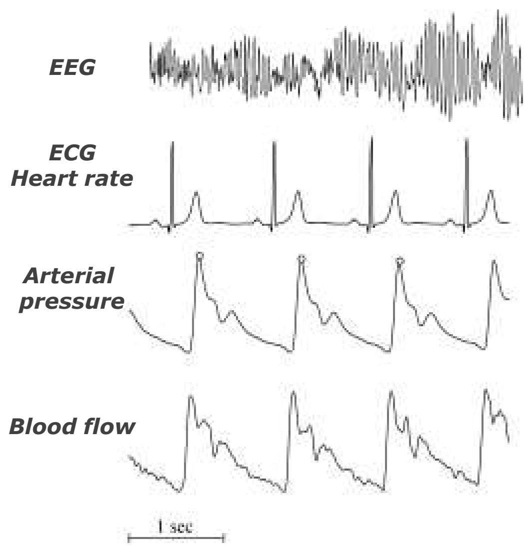
"The human organism is an integrated network where complex physiologic systems, each with its own regulatory mechanisms, continuously interact, and where failure of one system can trigger a breakdown of the entire network"

[A. Bashan et al., Nature Communications 2012]

*A new field, **Network Physiology**, is needed to probe the interactions among diverse physiologic systems*

SYSTEMS → **SIGNALS** → **INFORMATION DYNAMICS**

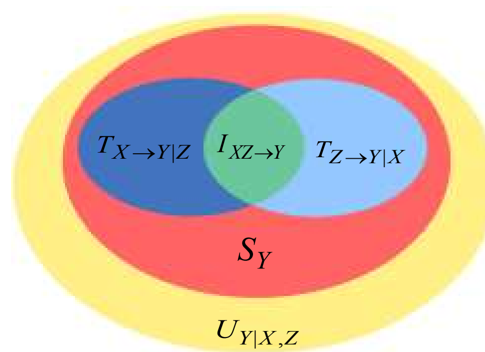




Information Storage

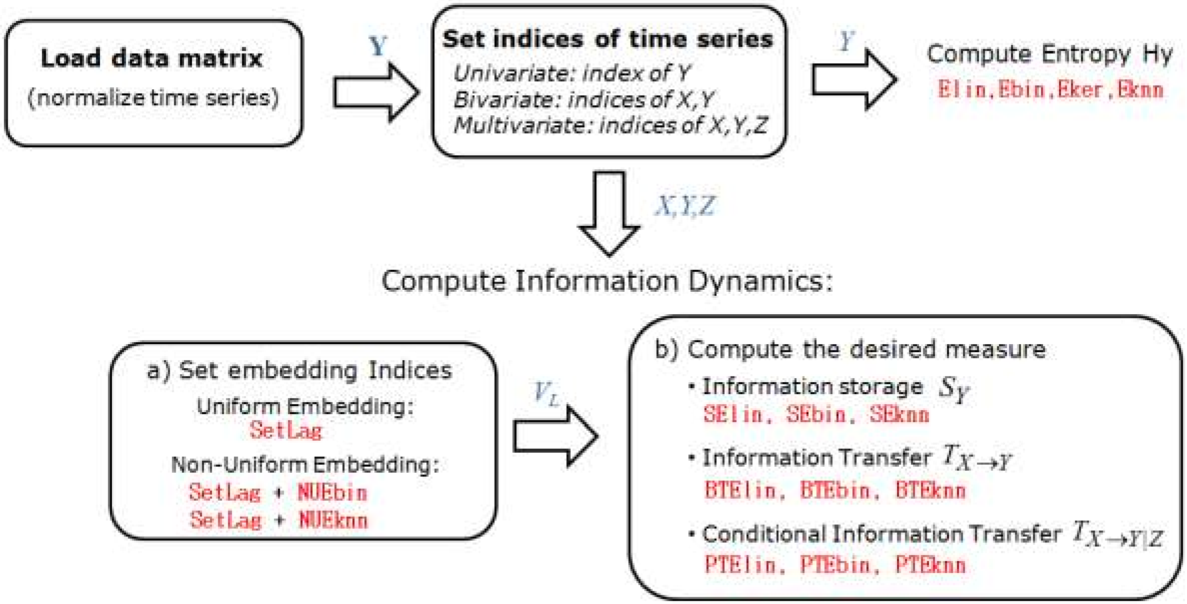
Information Transfer

Information Modification



ITS Toolbox:

A Matlab toolbox for the practical computation of Information Dynamics



http://www.lucafaes.net/its.html

faes.luca@gmail.com