Measuring Information Dynamics in Complex Physiological Networks

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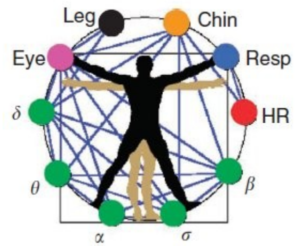
OUTLINE

- **INTRODUCTION – Network Physiology**
- **INFORMATION THEORY**
- **INFORMATION DYNAMICS – Univariate System Analysis**
  - System Information – Information Storage – Unexplained information
- **INFORMATION DYNAMICS – Multivariate System Analysis**
  - Predictive Information →
    - Information Storage
    - Information Transfer
    - Internal Information
- **ESTIMATION APPROACHES**
  - Linear model-based
  - Nonlinear model-free
- **APPLICATIONS**
  - Cardiorespiratory interactions
  - Cardiovascular and cerebrovascular regulation in syncope
  - Brain-heart and brain-brain networks during sleep

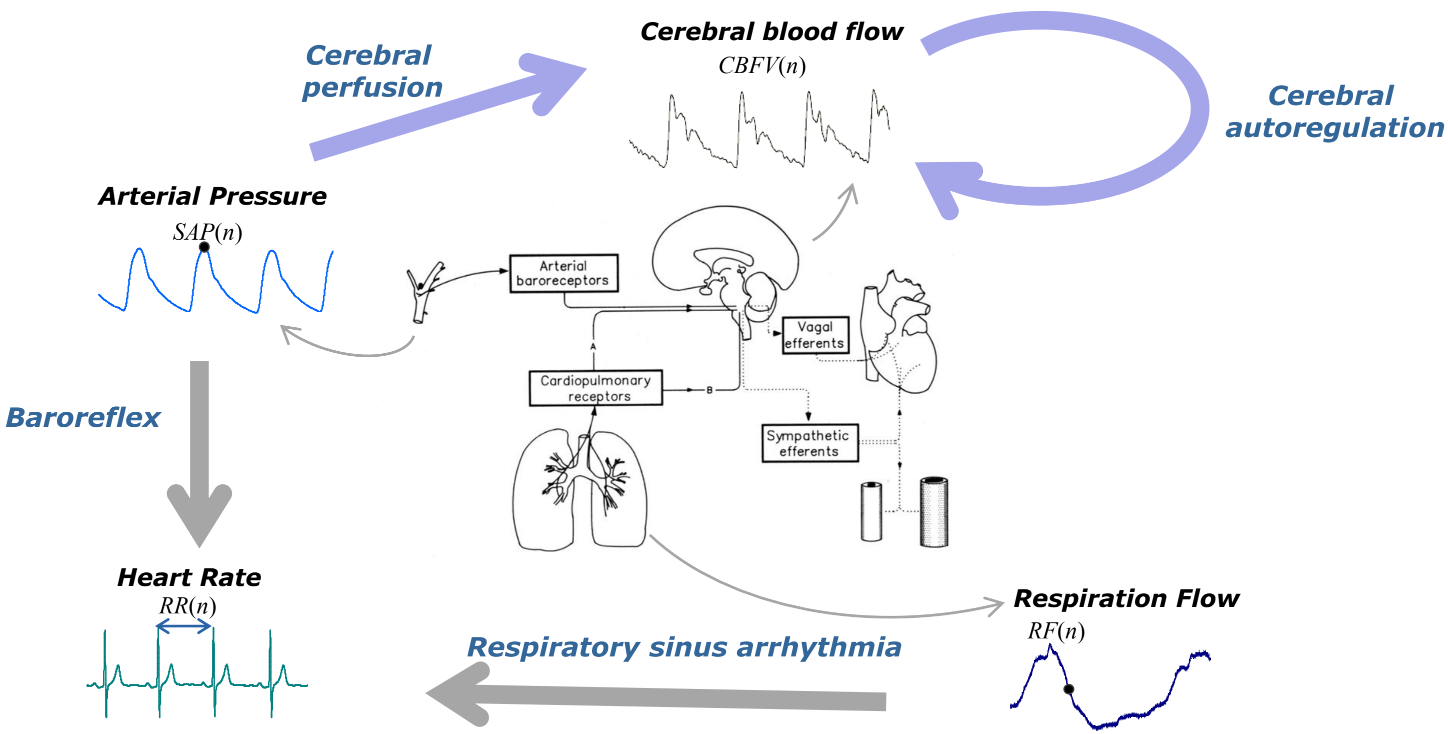
OUTLINE

- **NETWORK PHYSIOLOGY:** [Bashan A et al., Nature Comm 2012]



Organ systems exhibit a degree of activity and interactivity depending on the physiological state

- **EXAMPLE: Cardiovascular, cardiorespiratory and cerebrovascular physiology**

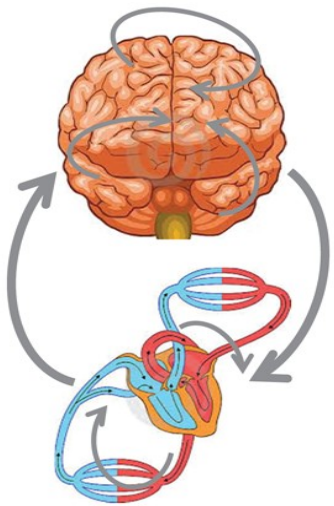


INTRODUCTION

Physiological Networks ⟷ **Networks of Dynamical systems**

Physiological (dynamical) Systems

- *BRAIN*
- *CARDIAC*
- *VASCULAR*
- *RESPIRATORY*
- *. . .*



Physiological Variables

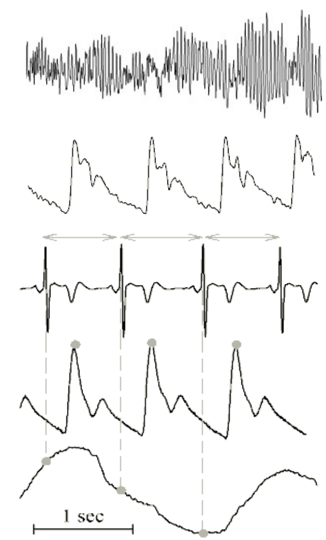
EEG
Brain wave activity

Transcranial Doppler
Cerebral blood flow

ECG
Heart rate

Arterial pressure
Systolic, Mean

Respiration
Respiratory flow



Multivariate time series analysis approaches are needed to describe complex physiological networks

- **Framework for physiological network analysis, based on information theory applied to multivariate time series**

ENTROPY OF A RANDOM VARIABLE

- Discrete random variable X with alphabet $\Omega=\{x_1, \ldots, x_Q\}$

ENTROPY: $$H(X) = -\sum_{x\in\Omega} p(x)\log p(x)$$

Measures the information contained in X as the average uncertainty about its outcomes

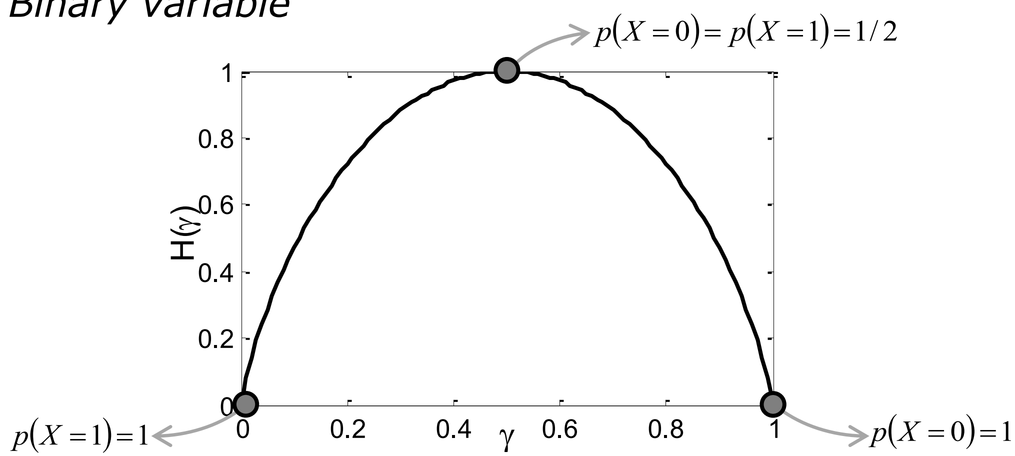
- Units of measure: log_2 ➡ [bits] $ln=log_e$ ➡ [nats]

- Bounds: $0 \le H(X) \le \log Q$ ➡
  $H(X)=0 \Leftrightarrow X$ is deterministic
  $H(X)=\log Q \Leftrightarrow X$ is uniformly distributed over Ω

- ***Example***: *Entropy of a Binary variable*

$\Omega=\{0,1\}$

$p(X=0)=\gamma \quad p(X=1)=1-\gamma$



ENTROPIES FOR TWO RANDOM VARIABLES

- JOINT ENTROPY:

$$H(X,Y) = -\sum_{x,y\in\Omega} p(x,y)\log p(x,y)$$

Information contained in X and Y considered as a vector variable (X,Y)

- CONDITIONAL ENTROPY:

$$H(X|Y) = -\sum_{x,y\in\Omega} p(x,y)\log p(x|y) \quad \longleftarrow \quad p(x|y) = \frac{p(x,y)}{p(y)}$$

Residual information contained in X when Y is known

Uncertainty which remains about X when Y is known

- MUTUAL INFORMATION (MI):

$$I(X;Y) = \sum_{x,y\in\Omega} p(x,y)\log\frac{p(x,y)}{p(x)p(y)} = \sum_{x,y\in\Omega} p(x,y)\log\frac{p(x|y)}{p(x)}$$

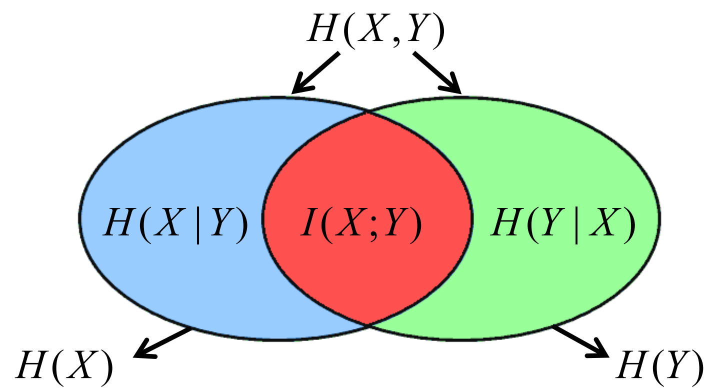
Amount of information about X provided by Y

Reduction in uncertainty about X when Y is known

ENTROPIES FOR TWO RANDOM VARIABLES

- Relations:

$$
\begin{aligned}
I(X;Y) &= H(X)+H(Y)-H(X,Y) \\
&= H(X)-H(X|Y) \\
&= H(Y)-H(Y|X)
\end{aligned}
$$



- Properties:
  - ✓ *Non-negativity:* $I(X,Y)\geq 0,\ H(X,Y)\geq 0,\ H(X|Y)\geq 0,\ H(Y|X)\geq 0$
  - ✓ *Conditioning does not increase entropy:* $H(X|Y)\leq H(X)$
  - ✓ *Symmetry of MI:* $I(X;Y)=I(Y;X)$
  - ✓ *Independent variables:* $X\perp Y \Leftrightarrow I(X,Y)=0$ $\quad H(X)=H(X|Y)\quad H(Y)=H(Y|X)$
    $p(x|y)=p(x)$
  - ✓ *Fully dependent variables:* $X=f(Y) \Leftrightarrow I(X,Y)=H(X)=H(Y)$
    $p(x|y)=1$
    $H(X|Y)=H(Y|X)=0 \quad I(X;Y)$

CONDITIONAL MUTUAL INFORMATION

- Conditional MI between X and Y given Z :

$$I(X;Y|Z)=\sum_{x,y,z\in\Omega}p(x,y,z)\log\frac{p(x,y|z)}{p(x|z)p(y|z)}=\sum_{x,y,z\in\Omega}p(x,y,z)\log\frac{p(x|y,z)}{p(x|z)}$$

Residual mutual information between X and Y when Z is known

$$I(X;Y|Z)=H(X|Z)-H(X|Y,Z)=H(Y|Z)-H(Y|X,Z)$$

- Properties: ✓ *Non-negativity:* $I(X;Y|Z)\geq 0$
  ✓ *Symmetry:* $I(X;Y|Z)=I(Y;X|Z)$

- Test for conditional independence

Conditional independence: $X\perp Y|Z$ $\quad p(x,y|z)=p(x|z)p(y|z)\Rightarrow p(x|y,z)=p(x|z)$

Conditional independence entails null conditional MI: $X\perp Y|Z \Leftrightarrow I(X;Y|Z)=0$

✓ *To probe dependence between X and Y :* $I(X;Y)>0$

✓ *To probe direct dependence between X and Y given Z :* $I(X;Y|Z)>0$

CONDITIONAL INDEPENDENCE AND GRANGER CAUSALITY

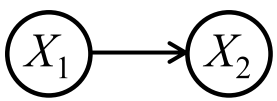
- Principle of Granger causality
  - ✓ *The cause **precedes in time** its effect*
  - ✓ *The cause contains **unique information** about the future values of its effect*

disentangle symmetry of MI

***Conditional** MI*

- Two time-ordered variables $\{X_1, X_2\}$

  X_1 *is Granger-causal to* X_2 *if and only if:* $X_1 \not\perp X_2 \;\Leftrightarrow\; I(X_1;X_2) > 0$

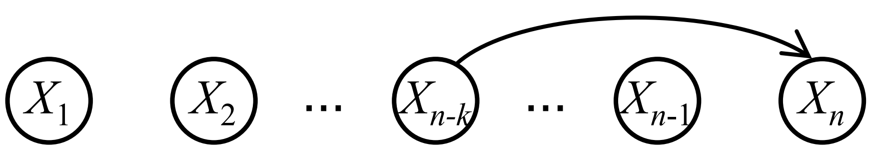


$X_1 \xrightarrow{G} X_2$

- N time-ordered variables $\{X_1, X_2, \cdots, X_{n-1}\}$

  $X_{n\text{-}k}$ *is Granger-causal to* X_n *if and only if:*

$$X_n \not\perp X_{n-k} \mid V \setminus X_{n-k} \quad \Leftrightarrow \quad I(X_n; X_{n-k} \mid V \setminus X_{n-k}) > 0$$



$X_{n-k} \xrightarrow{G} X_n$

INFORMATION DECOMPOSITION

Assume a target Y *and a driver* $X=(X_1, X_2)$

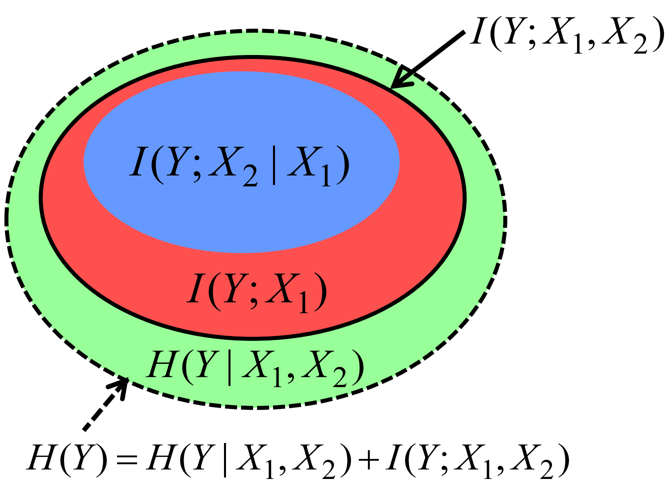
- *Mutual information:*

$$I(Y;X_1,X_2)=H(Y)-H(Y|X_1,X_2)$$

- *Chain rule for mutual information:*

$$I(Y;X,Z)=I(Y;Z)+I(Y;X|Z)$$

- *Entropy decomposition for the target* Y *in the presence of two drivers* X_1 *and* X_2



INFORMATION DYNAMICS FOR UNIVARIATE SYSTEMS

DYNAMIC SYSTEMS AND DYNAMIC PROCESSES

- Dynamic System X (example: cardiac system)

- Dynamic Process $X=(X_1, X_2, \ldots, X_n, \ldots, X_N)$ (example: heart rate)

  The Process X describes the states visited by the system X over time

- The process X is ***stationary*** if $p(X_n=x)=p(X_k=x) \quad \forall\ n,k\ ,\forall x \in \Omega$

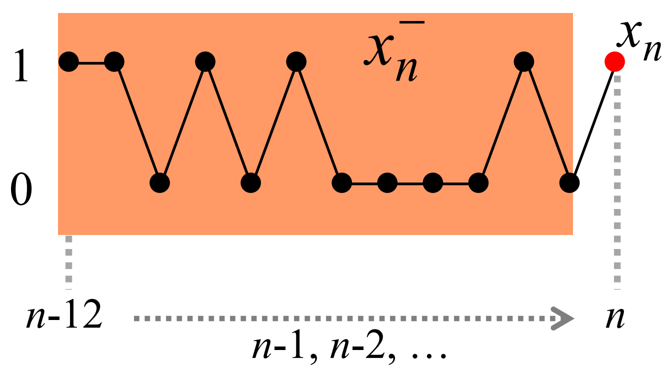
  For stationary processes, probabilities can be computed pooling data over time rather than over realizations

- Present of X : X_n
  univariate (scalar) random variable

- Past of X : $X_n^-=(X_{n-1}, X_{n-2}, \ldots)$
  Multivariate (vector) random variable

- A **realization** of the process is a time series $x=(x_1, x_2, \ldots, x_n, \ldots, x_N)$

- *Example: binary process* $\Omega=\{0,1\}$



$x_n=1$

$x_n^-=(\ldots,1,1,0,1,0,1,0,0,0,0,1,0)$

MARKOV PROCESSES

- $X = (X_1, X_2, \dots, X_n, \dots, X_N)$ is a Markov process if $p(x_n \mid x_n^-) = p(x_n \mid x_{n-1}) \quad \forall\ x_n, x_n^-$

  Transition probabilities (fully define the process)

  A Markov process is "memory-less"

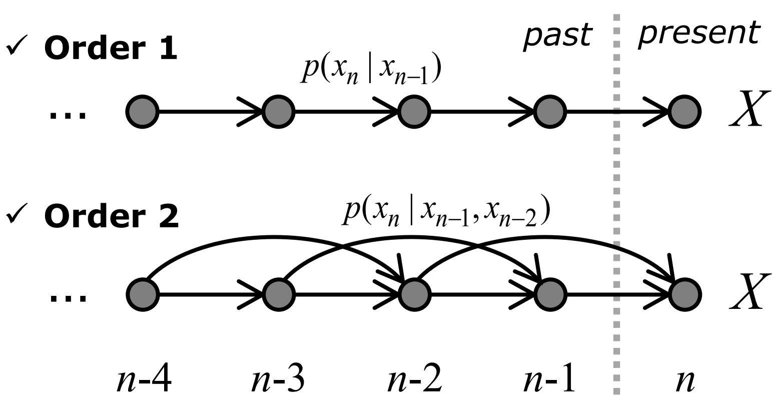
- Markov process of order m : $p(x_n \mid x_n^-) = p(x_n \mid x_{n-1}, x_{n-2}, \dots, x_{n-m}) \quad \forall\ x_n, x_n^-$

  The memory extends over the past m states

- If the process is *stationary*, $p(x_n \mid x_{n-1})$ does not depend on n

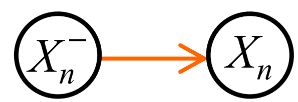
- Graphical representation of stationary Markov processes

Time series graph



$X_{n-k} \xrightarrow{G} X_n \Leftrightarrow X_n \not\perp X_{n-k} \mid X_n^- \setminus X_{n-k}$

Granger causality graph



Internal dynamics:

$X_n^- \xrightarrow{G} X_n \Leftrightarrow X_n \not\perp X_n^-$

$I(X_n; X_n^-) > 0$

INFORMATION STORAGE

- Information generated by X (system information) :

$$H_X = H(X_n) = -\sum_{x\in\Omega} p\left(X_n = x\right)\log p\left(X_n = x\right) = -\sum_{x_n\in\Omega} p(x_n)\log p(x_n)$$

Uncertainty about the present state of the system X

Information contained in the present of the process X

- Unexplained information in X :

$$U_X = H(X_n \mid X_n^-) = -\sum_{x_n, x_n^- \in\Omega} p(x_n, x_n^-)\log p(x_n \mid x_n^-)$$

Uncertainty remaining about the present state of the system X when the past states are known

Information contained in the present of the process X that cannot be predicted from its past

- Information stored in the system X : **SELF ENTROPY**

$$S_X = I(X_n; X_n^-) = \sum_{x_n, x_n^- \in\Omega} p(x_n, x_n^-)\log\frac{p(x_n \mid x_n^-)}{p(x_n)}$$

Uncertainty about the present state of the system X that is resolved by the knowledge of the past states

Information contained in the past of the process X that can be used to predict its present

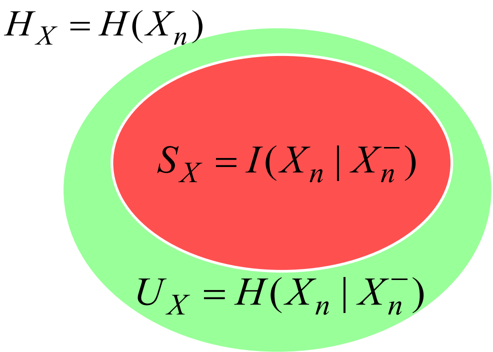
$$H_X = H(X_n) = I(X_n; X_n^-) + H(X_n \mid X_n^-) = S_X + U_X$$

INFORMATION STORAGE

- Graphical representation (Venn diagram)

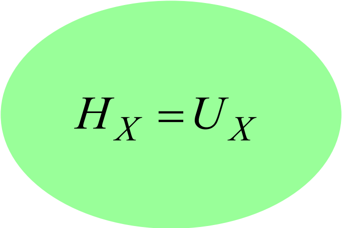
$$S_X = H(X_n) - H(X_n \mid X_n^-) = I(X_n; X_n^-)$$

$$H_X = S_X + U_X$$



✓ *Unpredictable process:*

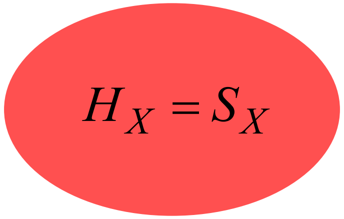
$$X_n \perp X_n^- \quad \Leftrightarrow S_X = 0$$



The whole information generated by the process remains unexplained

✓ *Fully predictable process:*

$$X_n = f(X_n^-) \Leftrightarrow S_X = H_X$$



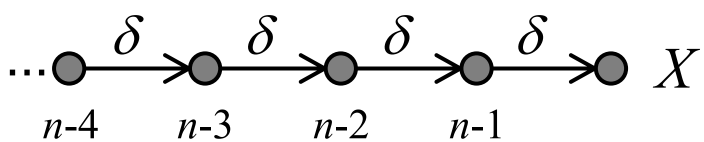
The whole information generated by the process is stored in it

INFORMATION STORAGE

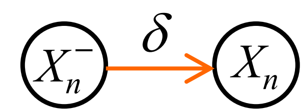
- ***Example***: *Self Entropy of a stationary binary Markov process of order 1*

Time series graph

$$p(x_n = x_{n-1}) = \frac{1-\delta}{2}$$



Granger causality graph



$$S_X = \sum_{x_n, x_n^- \in \Omega} p(x_n, x_n^-) \log \frac{p(x_n \mid x_n^-)}{p(x_n)}$$

- Transition probabilities: $p(x_n \mid x_n^-) = p(x_n \mid x_{n-1})$ ⇒

$$\begin{array}{cc} & X_{n\text{-}1} \\ & \begin{array}{cc} 0 & 1 \end{array} \\ X_n \begin{array}{c} 0 \\ 1 \end{array} & \begin{bmatrix} \frac{1-\delta}{2} & \frac{1+\delta}{2} \\ \frac{1+\delta}{2} & \frac{1-\delta}{2} \end{bmatrix} \end{array}$$

- Marginal probability: $p(x_n) \overset{\text{marginalization}}{=} \sum_{x_{n-1}} p(x_n \mid x_{n-1}) p(x_{n-1}) \overset{\text{stationarity}}{=} p(x_{n-1})$ ⇒ $p(X_n = 0) = p(X_n = 1) = \frac{1}{2}$

- To find joint probabilities, approximate to lag L:

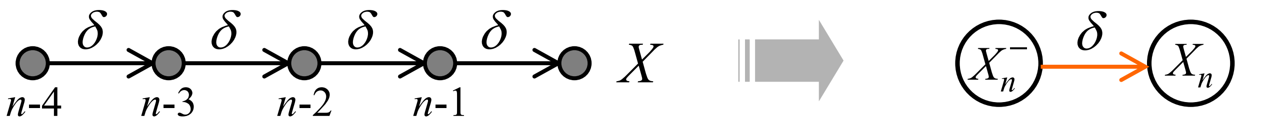
$$p(x_n, x_n^-) \cong p(x_n, x_{n-1}, \ldots, x_{n-L}) = p(x_n \mid x_{n-1}) \cdots p(x_{n-L+1} \mid x_{n-L}) p(x_{n-L})$$

Example: L=3, sequence $(0,1,0,0)$ ⇒ $p(X_n = 0, X_{n-1} = 1, X_{n-2} = 0, X_{n-3} = 0) = \underbrace{\frac{1+\delta}{2}}_{p(X_n = 0 \mid X_{n-1} = 1)} \cdot \frac{1+\delta}{2} \cdot \frac{1-\delta}{2} \cdot \underbrace{\frac{1}{2}}_{p(X_{n-3} = 0)}$

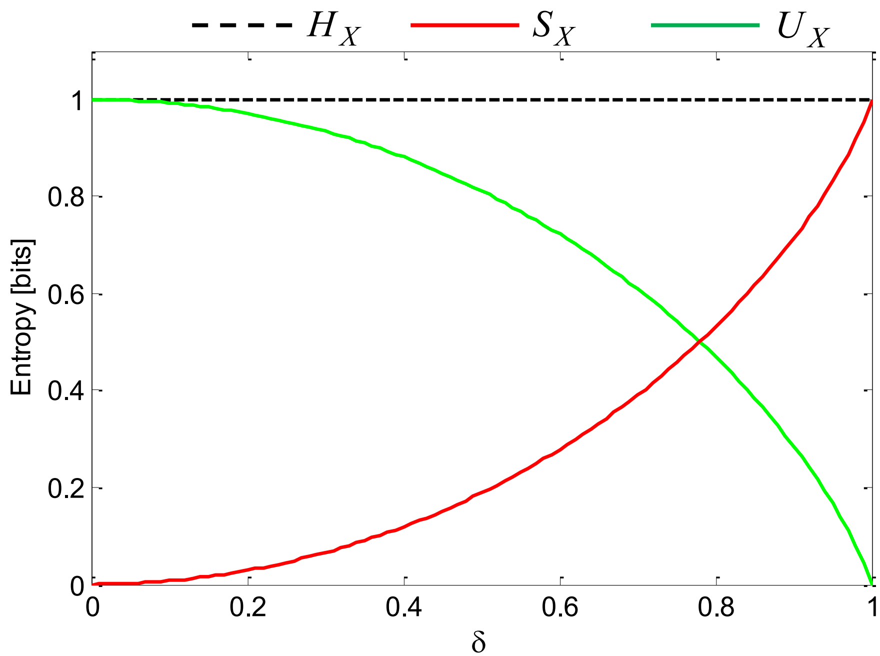
INFORMATION STORAGE

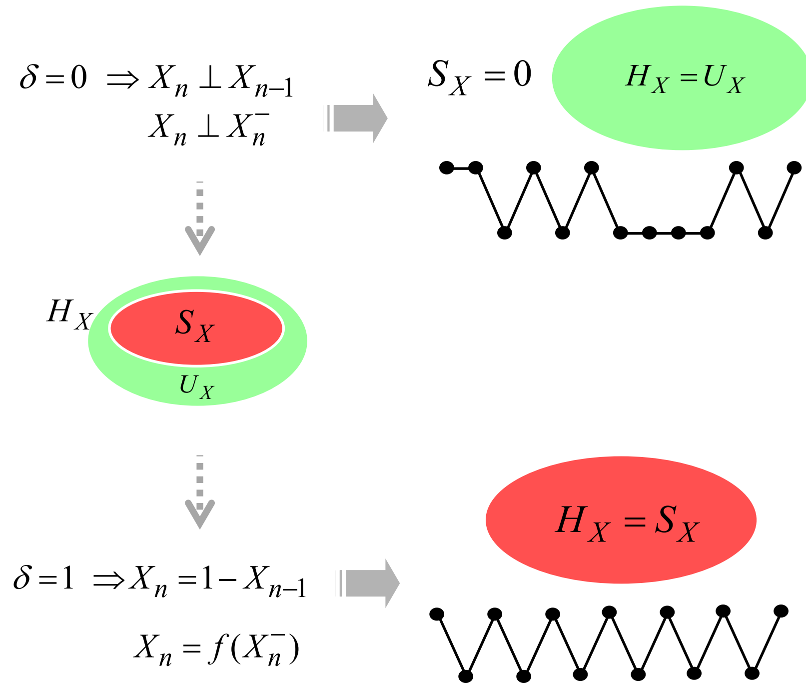
- ***Example**: Self Entropy of a Binary Markov process*

Time series graph | Granger causality graph



- Information dynamics: $H_X = S_X + U_X$





- The information storage assesses causal interactions in the univariate system:

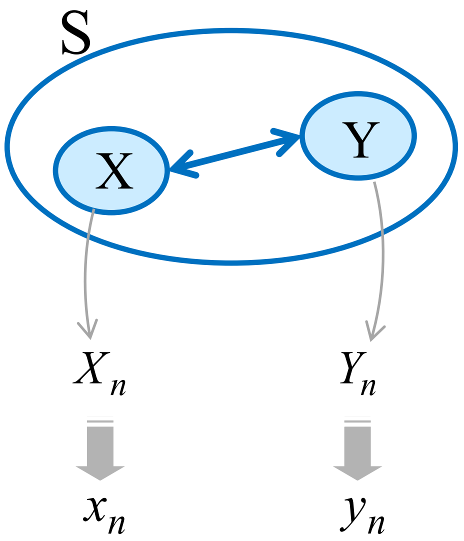
$$X_n^- \xrightarrow{G} X_n \quad \Leftrightarrow \quad S_X > 0$$

INFORMATION DYNAMICS FOR MULTIVARIATE SYSTEMS

BIVARIATE DYNAMIC SYSTEM

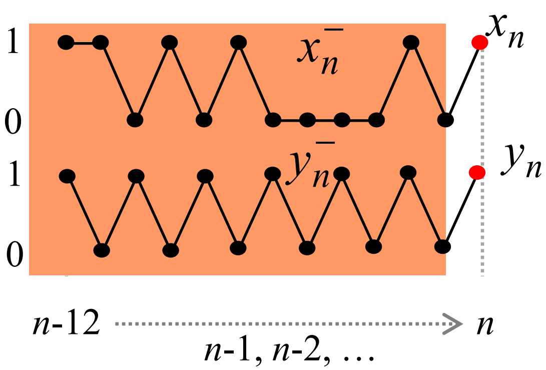
- Dynamic System $\mathrm{S}=\{\mathrm{X},\mathrm{Y}\}$
- Dynamic Process $S=(X,Y)$

  $X=(X_1, X_2, \ldots, X_n, \ldots, X_N)$, $Y=(Y_1, Y_2, \ldots, Y_n, \ldots, Y_N)$
- Present of S : $S_n=(X_n, Y_n)$
- Past of S : $S_n^-=(X_n^-, Y_n^-)$



- A **realization** of the process is given by the time series

  $x=(x_1, x_2, \ldots, x_n, \ldots, x_N)$, $y=(y_1, y_2, \ldots, y_n, \ldots, y_N)$
- *Example - binary bivariate process:*

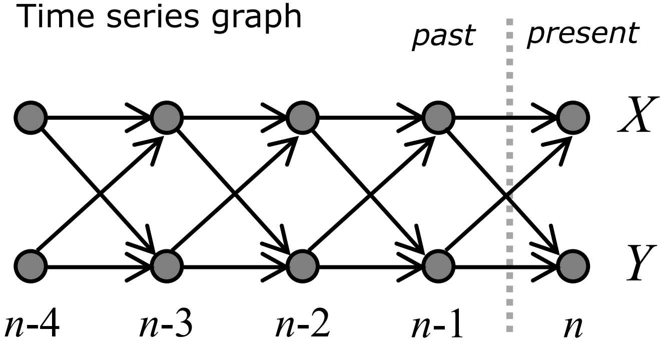


BIVARIATE MARKOV PROCESSES

- $S=(X,Y)$ is a bivariate Markov process of order m if:

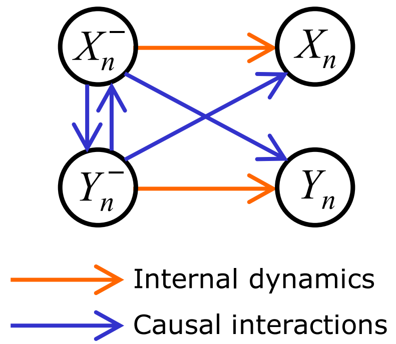
$$p(s_n \mid s_n^-) = p(s_n \mid s_{n-1}, s_{n-2}, \dots, s_{n-m}) \quad \forall\, s_n, s_n^- \qquad s_n = (x_n, y_n) \;\;,\;\; s_n^- = (x_n^-, y_n^-)$$

- ***Example***: *Stationary bivariate Markov process of order 1*
  - Transition probabilities: $p(s_n \mid s_{n-1}) = p(x_n, y_n \mid x_{n-1}, y_{n-1})$
  - Time series graph



$$X_{n-k} \xrightarrow{G} Y_n \iff Y_n \not\perp X_{n-k} \mid S_n^- \setminus X_{n-k}$$

- Granger causality graph



The Granger causality graph depicts Granger-causal relations:

Causal interactions from X to Y: $X_n^- \xrightarrow{G} Y_n \iff Y_n \not\perp X_n^- \mid Y_n^- \iff I(Y_n; X_n^- \mid Y_n^-) > 0$

Internal dynamics of Y: $Y_n^- \xrightarrow{G} Y_n \iff Y_n \not\perp Y_n^- \mid X_n^- \iff I(Y_n; Y_n^- \mid X_n^-) > 0$

PREDICTIVE INFORMATION

- Given the system S=(X,Y), set a target sub-system (e.g., Y)

- Information generated by Y (system information):

$$H_Y = H(Y_n) = -\sum_{y_n \in \Omega} p(y_n) \log p(y_n)$$

Information contained in the present of the process Y

- Unexplained information about the present of Y given the past of S

$$U_{Y|X} = H(Y_n \mid X_n^-, Y_n^-) = -\sum_{y_n, x_n^-, y_n^- \in \Omega} p(y_n, x_n^-, y_n^-) \log p(y_n \mid x_n^-, y_n^-)$$

Information contained in the present of Y that cannot be predicted from the past of $S=(X,Y)$

- Predictive Information about Y : **PREDICTION ENTROPY**

$$P_Y = I(Y_n; X_n^-, Y_n^-) = \sum_{y_n, x_n^-, y_n^- \in \Omega} p(y_n, x_n^-, y_n^-) \log \frac{p(y_n \mid x_n^-, y_n^-)}{p(y_n)}$$

Information contained in the past of $S=(X,Y)$ that can be used to predict the present of the target Y

$$H_Y = H(Y_n) = I(Y_n; X_n^-, Y_n^-) + H(X_n \mid X_n^-, Y_n^-) = S_Y + U_{Y|X}$$

PREDICTIVE INFORMATION DECOMPOSITION

- Expansion of the predictive information

$$P_Y = I(Y_n; X_n^-, Y_n^-) = I(Y_n; Y_n^-) + I(Y_n; X_n^- | Y_n^-)$$

Information Storage: *SELF ENTROPY* S_Y

Information Transfer: *TRANSFER ENTROPY* $T_{X \to Y}$

- Information stored in the system Y : **SELF ENTROPY (SE)**

$$S_Y = \sum_{y_n, y_n^- \in \Omega} p(y_n, y_n^-) \log \frac{p(y_n | y_n^-)}{p(y_n)} = H(Y_n) - H(Y_n | Y_n^-)$$

Information contained in the past of Y that can be used to predict its present

- Information transferred from X to Y : **TRANSFER ENTROPY (TE)**

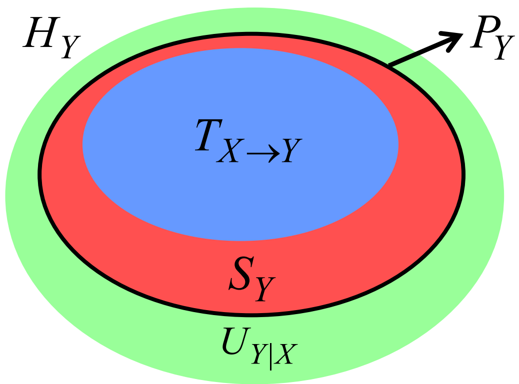
$$T_{X \to Y} = \sum_{y_n, x_n^-, y_n^- \in \Omega} p(y_n, x_n^-, y_n^-) \log \frac{p(y_n | x_n^-, y_n^-)}{p(y_n | y_n^-)} = H(Y_n | Y_n^-) - H(Y_n | X_n^-, Y_n^-)$$

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

INFORMATION DYNAMICS

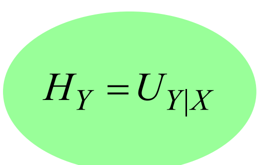
- Graphical representation (Venn diagram)

$$H_Y = P_Y + U_{Y|X} \qquad P_Y = S_Y + T_{X \to Y}$$



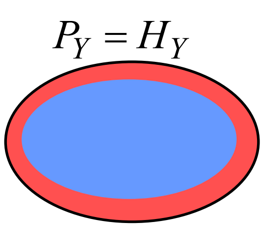
✓ *Unpredictable process:*

$$Y_n \perp X_n^-, Y_n^- \quad \Leftrightarrow P_Y = 0$$



The whole information generated by the process remains unexplained

✓ *Fully predictable process:*

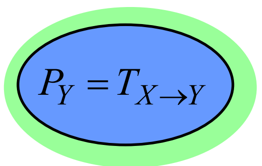


$$Y_n = f(X_n^-, Y_n^-) \Leftrightarrow U_{Y|X} = 0$$

The whole information generated by the process can be predicted from the system past

✓ *Full information transfer:*

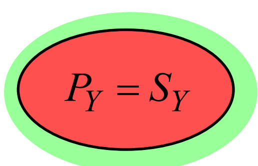
$$Y_n \perp Y_n^- \quad \Leftrightarrow S_Y = 0$$



The whole predictive information about the target is transferred from the driver

✓ *Full information storage:*

$$Y_n \perp X_n^- \mid Y_n^- \quad \Leftrightarrow T_{X \to Y} = 0$$



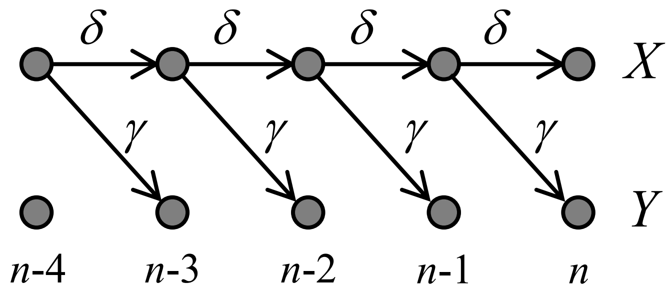
The whole predictive information about the target is stored in it

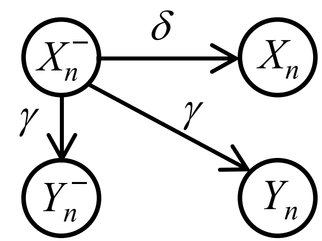
INFORMATION DYNAMICS

- ***Example****: Information dynamics for a stationary binary bivariate Markov process*

$$p(x_n = x_{n-1}) = \frac{1-\delta}{2}$$

$$p(y_n = x_{n-1}) = \frac{1+\gamma}{2}$$





- Transition probabilities: $p(s_n \mid s_{n-1}) = p(x_n, y_n \mid x_{n-1}, y_{n-1}) = p(x_n \mid x_{n-1})\, p(y_n \mid x_{n-1})$

$$\begin{array}{cc} & S_{n-1}=(X_{n-1},Y_{n-1}) \\ & \begin{array}{cccc} (0,0) & (0,1) & (1,0) & (1,1) \end{array} \\ S_n=(X_n,Y_n) \begin{array}{c} (0,0) \\ (0,1) \\ (1,0) \\ (1,1) \end{array} & \begin{bmatrix} a & a & b & b \\ c & c & d & d \\ d & d & c & c \\ b & b & a & a \end{bmatrix} \end{array}$$

$$a = \frac{1-\delta}{2}\frac{1+\gamma}{2} \qquad b = \frac{1+\delta}{2}\frac{1-\gamma}{2}$$

$$c = \frac{1-\delta}{2}\frac{1-\gamma}{2} \qquad d = \frac{1+\delta}{2}\frac{1+\gamma}{2}$$

- Marginal probabilities: $p(s_n) \underset{\text{marginalization}}{=} \sum_{x_{n-1}} p(s_n \mid s_{n-1})\, p(s_{n-1}) \underset{\text{stationarity}}{=} p(s_{n-1})$ *System of linear equations*

- To find joint probabilities, approximate to lag L:

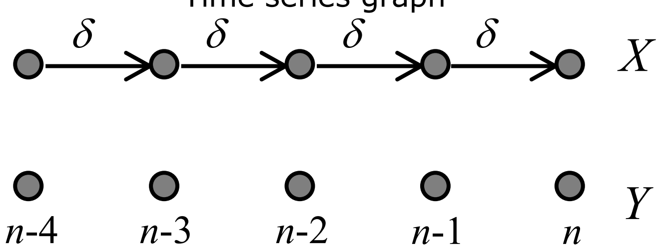
$$p(s_n, s_n^-) \cong p(s_n, s_{n-1}, \dots, s_{n-L}) = p(s_n \mid s_{n-1}) \cdots p(s_{n-L+1} \mid s_{n-L})\, p(s_{n-L})$$

$$= p(x_n, y_n, x_{n-1}, y_{n-1}, \dots, x_{n-L}, y_{n-L})$$

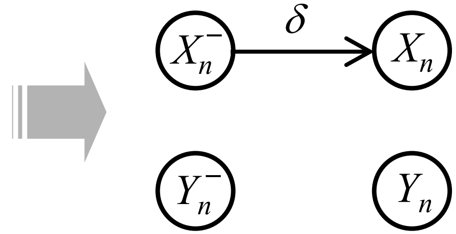
INFORMATION DYNAMICS

- ***Example:*** $\gamma = 0$

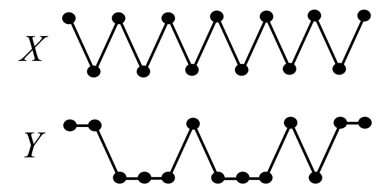
Time series graph



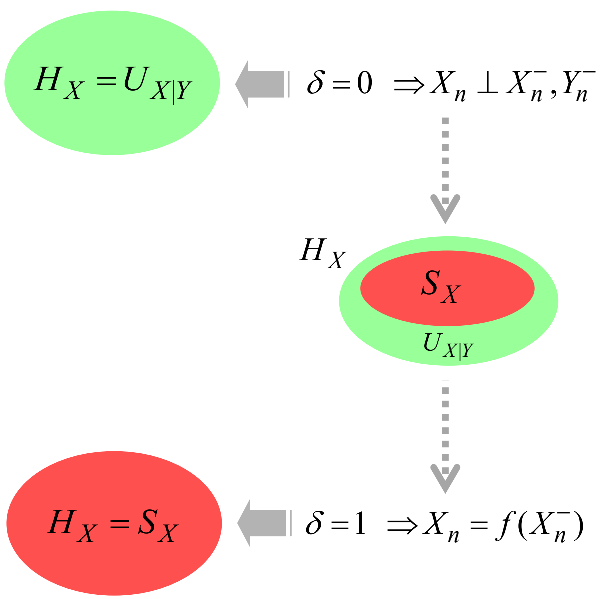
Granger causality graph

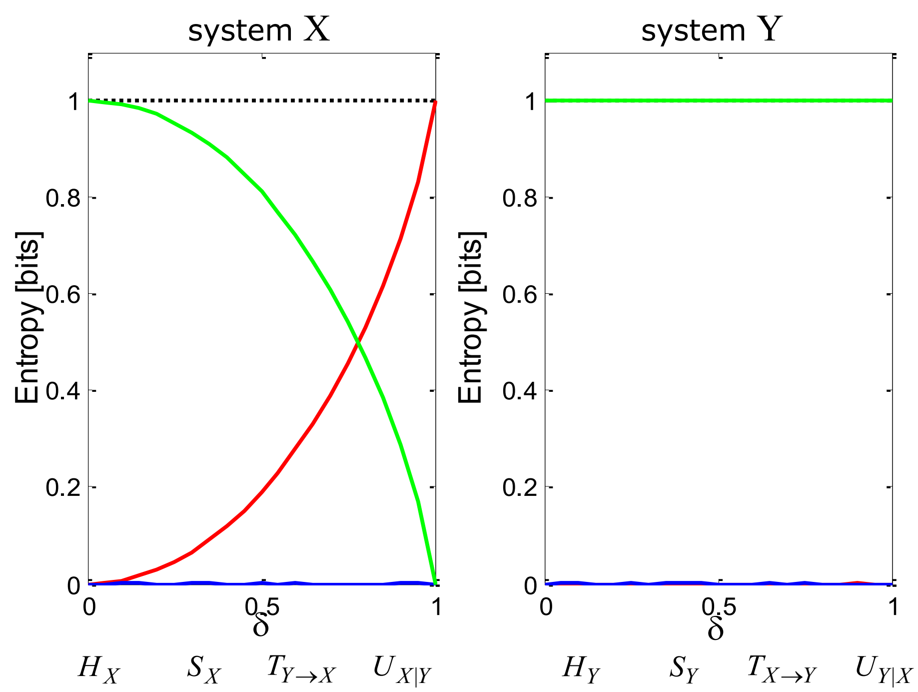


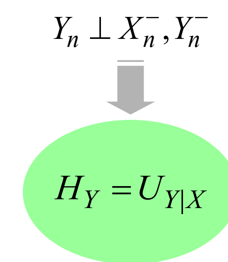
Example: $\delta = 1, \gamma = 0$



- Information dynamics: $H_X = S_X + T_{Y\to X} + U_{X|Y} \quad , \quad H_Y = S_Y + T_{X\to Y} + U_{Y|X}$



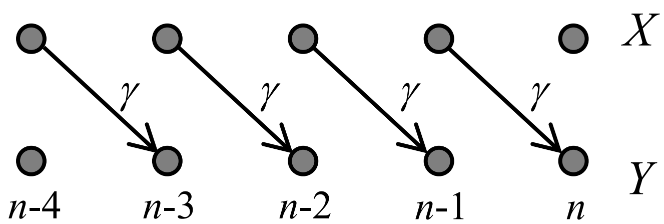




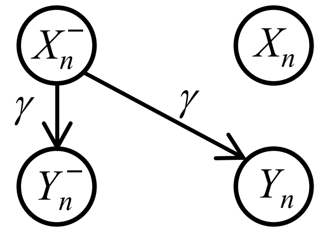
INFORMATION DYNAMICS

- ***Example***: $\delta = 0$

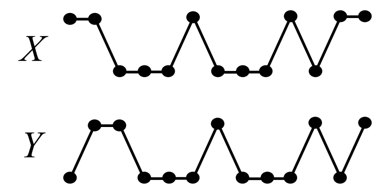
Time series graph



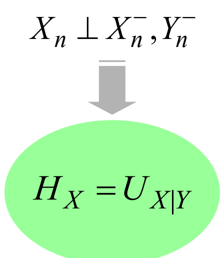
Granger causality graph



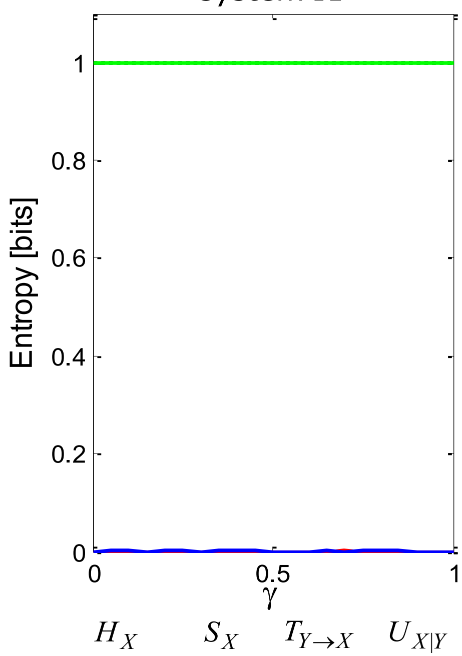
Example: $\delta = 0, \gamma = 1$



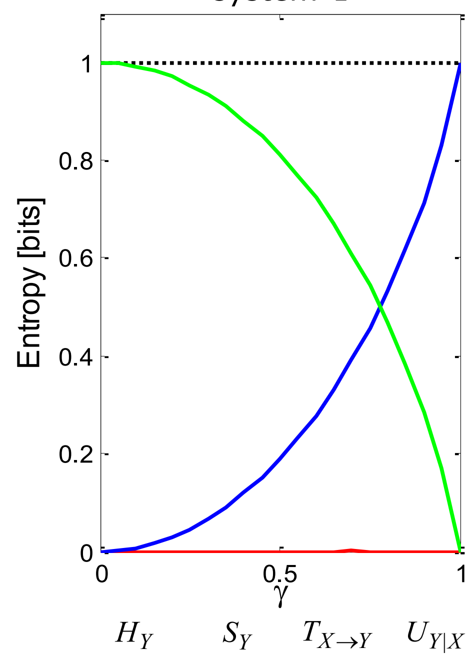
- Information dynamics: $H_X = S_X + T_{Y \to X} + U_{X|Y}$, $H_Y = S_Y + T_{X \to Y} + U_{Y|X}$

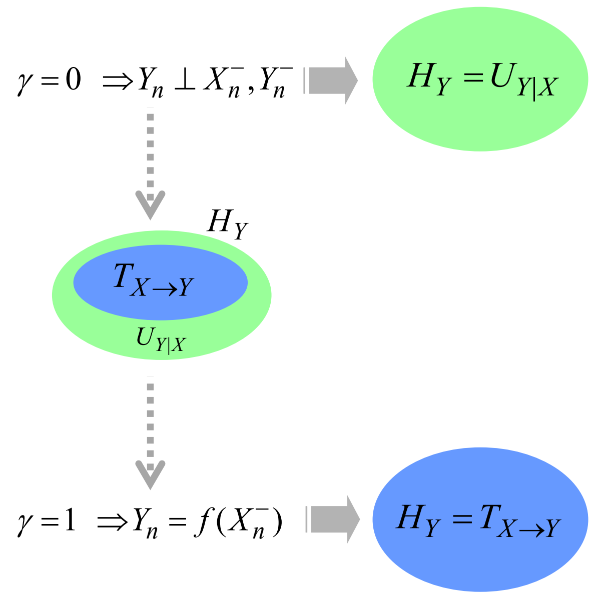


system X



system Y

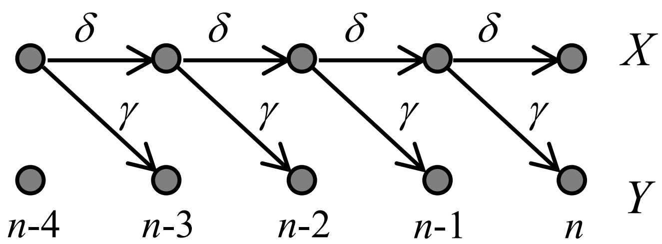


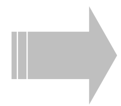


INFORMATION DYNAMICS

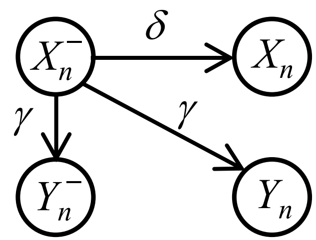
- ***Example:*** variable δ and γ

Time series graph

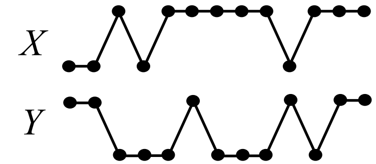




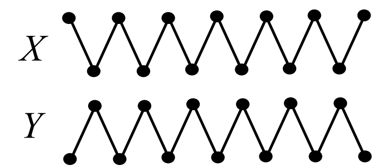
Granger causality graph



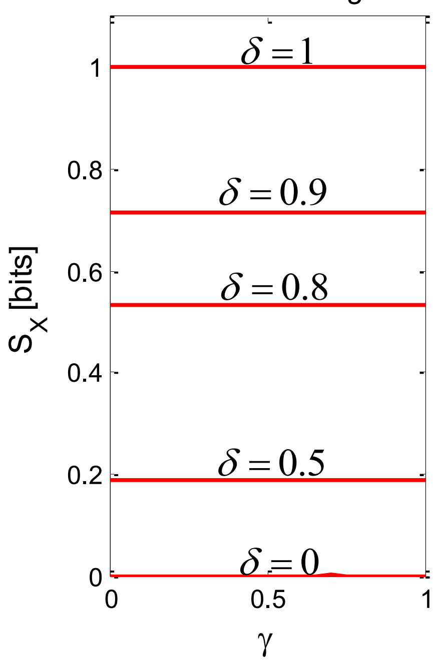
Example: $\delta = \gamma = 0$

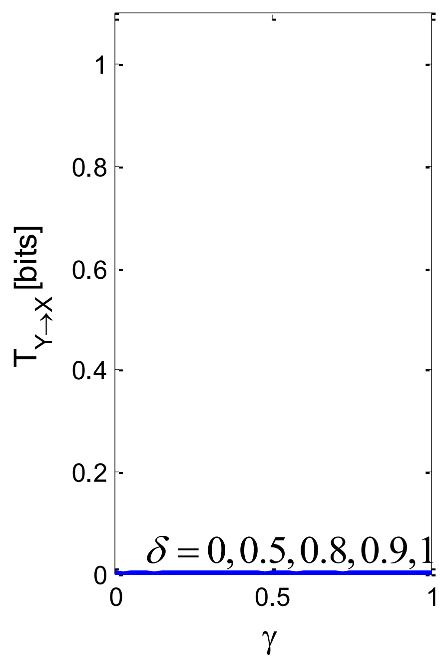


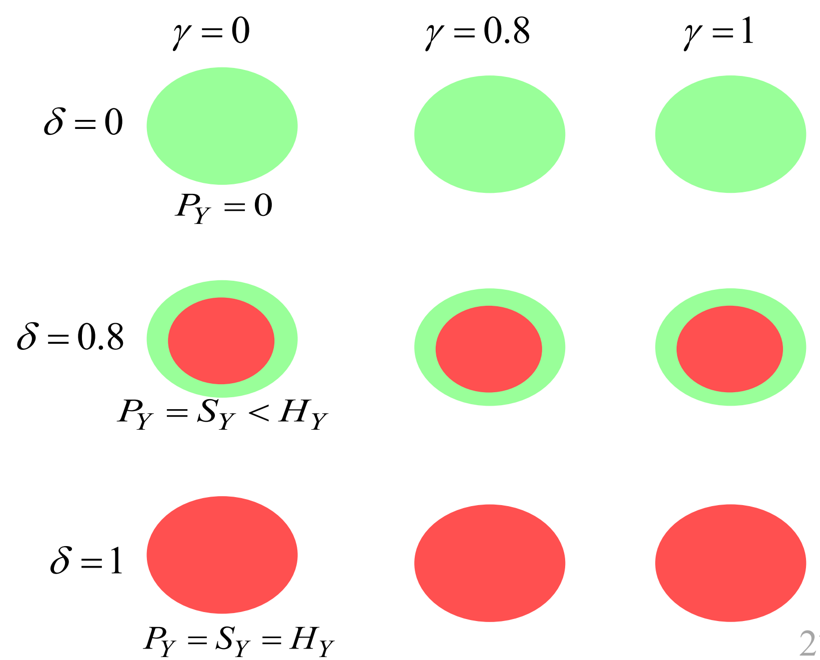
Example: $\delta = \gamma = 1$



- Information dynamics – system X : $H_X = P_X + U_{X|Y} = S_X + T_{Y\rightarrow X} + U_{X|Y}$



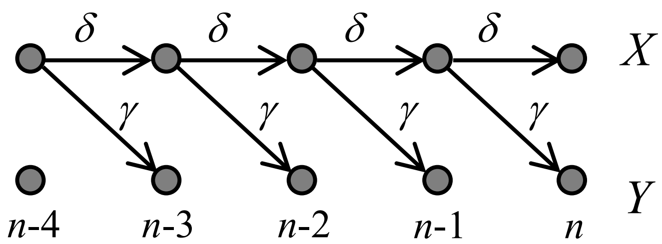




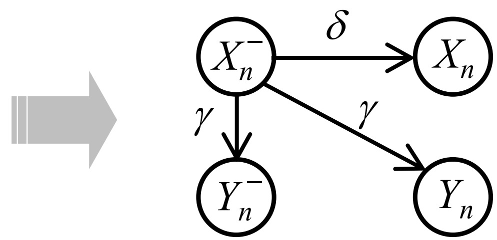
INFORMATION DYNAMICS

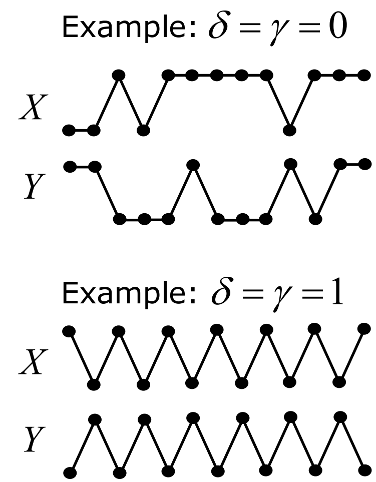
- ***Example:*** variable δ and γ

Time series graph

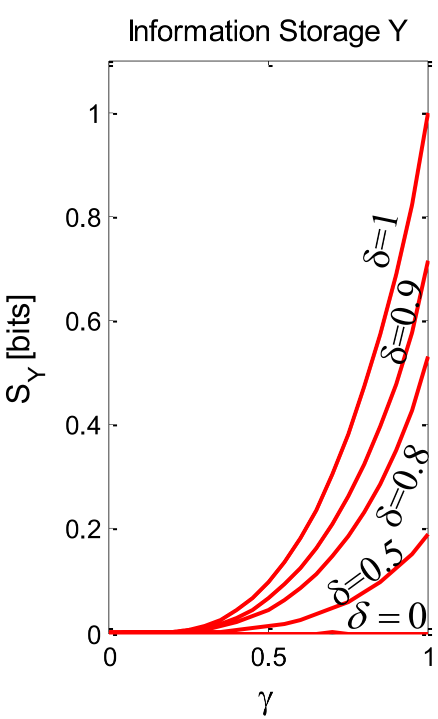


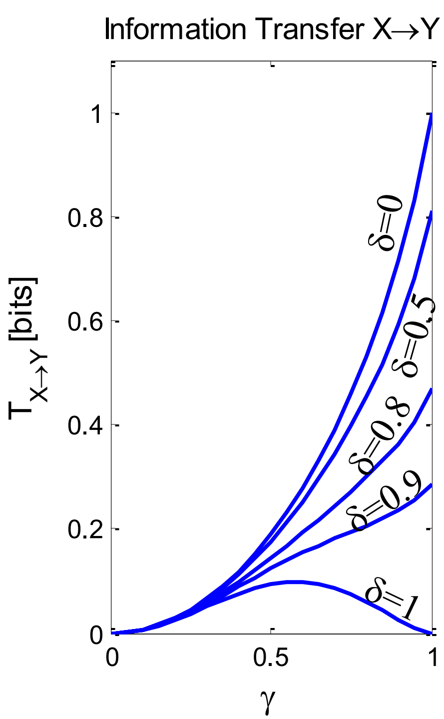
Granger causality graph

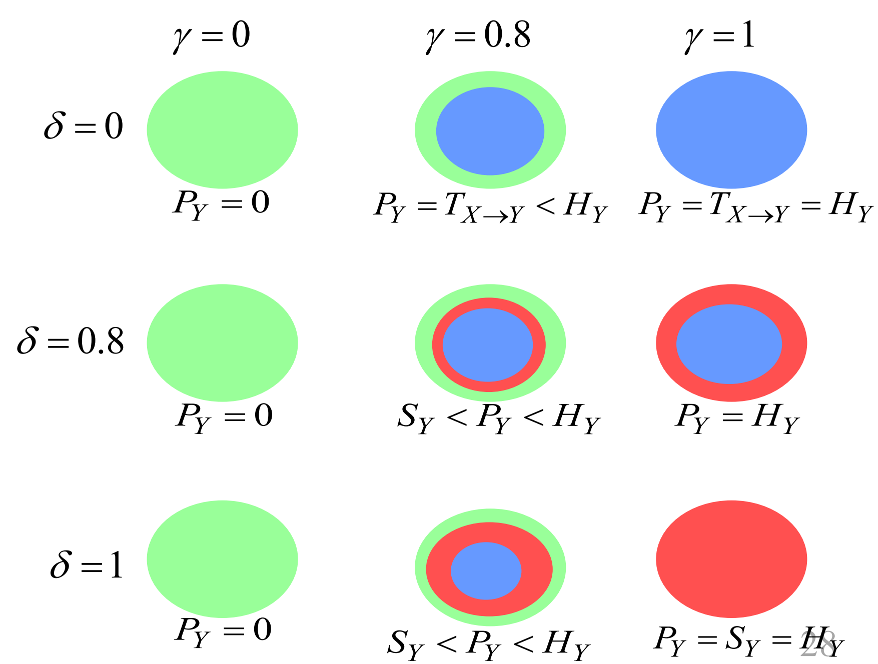




- Information dynamics – system Y : $H_Y = P_Y + U_{Y|X} = S_Y + T_{X\to Y} + U_{Y|X}$

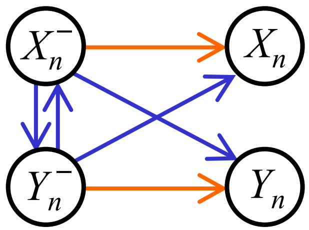




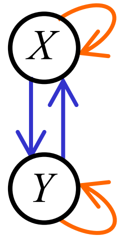


INFORMATION DYNAMICS: CAUSAL INTERPRETATION

Granger causality graph



Process graph:



Internal dynamics: $X_n^- \xrightarrow{G} X_n$, $Y_n^- \xrightarrow{G} Y_n$

Causal interactions: $X_n^- \xrightarrow{G} Y_n$, $Y_n^- \xrightarrow{G} X_n$

- The information transfer assesses causal interactions from driver to target
  - ✓ TE = 0 whenever causal connections are absent
  - ✓ TE increases with the strength of the causal interactions
  - ✓ TE may vary also with the internal dynamics of the driver process
  - ✓ The monotonic behavior of TE with the coupling strength may be lost when the system approaches the deterministic regime (TE=0 if the target is deterministic!)

- The information storage assesses the whole information contained by the past of the target which may be useful for predicting its present
  - ✓ SE = 0 if *both* internal dynamics and causal connections are absent
    SE > 0 reflects *both* internal dynamics and causal interactions
  - ✓ SE is not suitable to assess internal dynamics

- While information transfer reflects causal interactions, information storage does not reflect internal dynamics

INTERNAL INFORMATION

- Alternative expansion of the predictive information

$$P_Y = I(Y_n; X_n^-, Y_n^-) = I(Y_n; X_n^-) + I(Y_n; Y_n^- \mid X_n^-)$$

Cross-Information: *CROSS ENTROPY* $C_{X \to Y}$

Internal Information: *Conditional SELF ENTROPY* $S_{Y|X}$

- Information stored in the system Y : **Conditional SELF ENTROPY (cSE)**

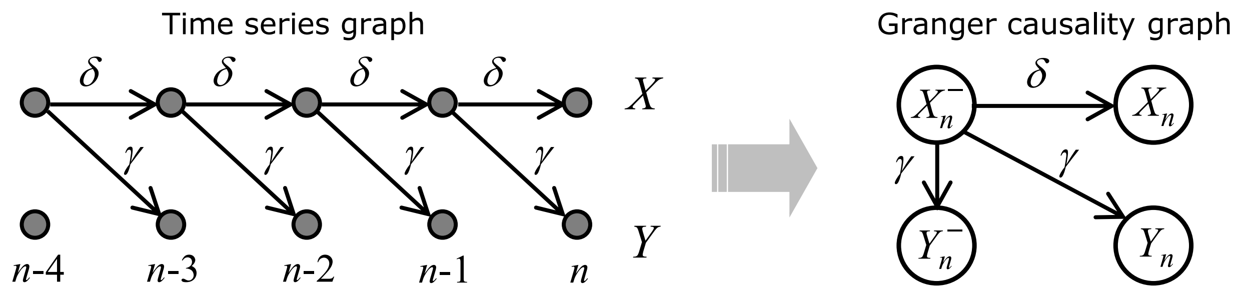
$$S_{Y|X} = \sum_{y_n, y_n^- \in \Omega} p(y_n, x_n^-, y_n^-) \log \frac{p(y_n \mid x_n^-, y_n^-)}{p(y_n, x_n^-)} = H(Y_n \mid X_n^-) - H(Y_n \mid X_n^-, Y_n^-)$$

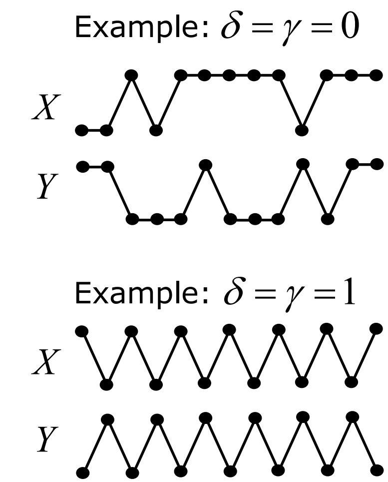
Information contained in the past of Y that can be used to predict its present above and beyond the information contained in the past of X

- The internal information assesses internal dynamics of the target
  - ✓ cSE = 0 whenever internal dynamics are absent
  - ✓ cSE increases with the strength of the internal dynamics
  - ✓ cSE may vary also with the causal interactions from target to driver
  - ✓ The monotonic behavior of cSE with the strength of internal dynamics may be lost when the system approaches the deterministic behavior (cSE=0 if the target is deterministic!)

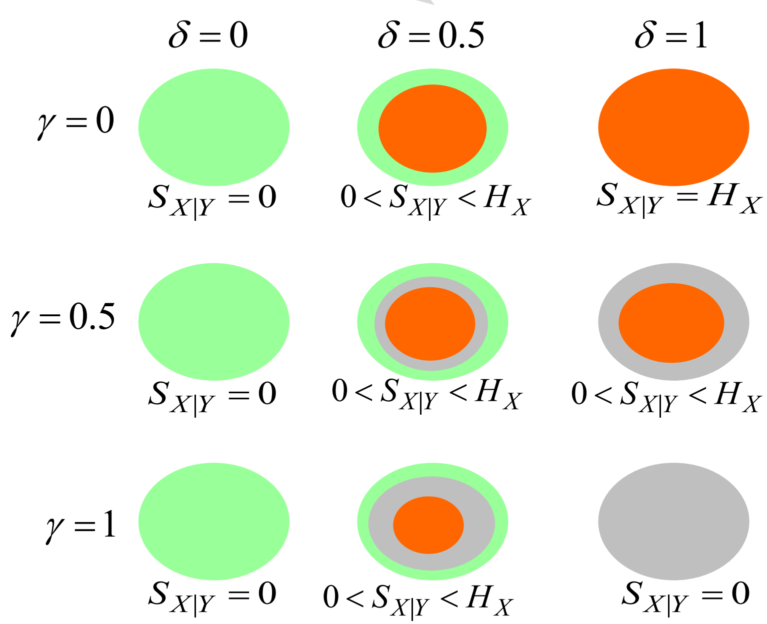
INTERNAL INFORMATION

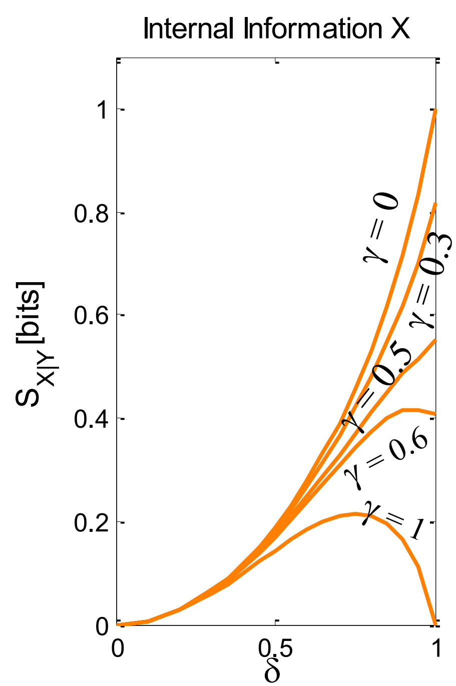
- ***Example**: binary bivariate Markov process* with variable δ and γ

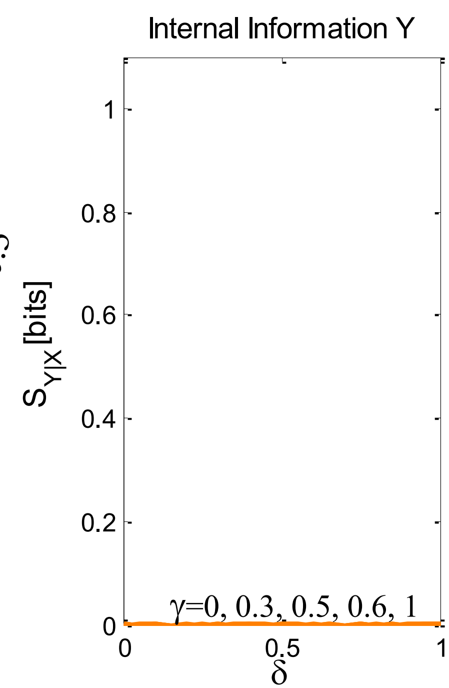




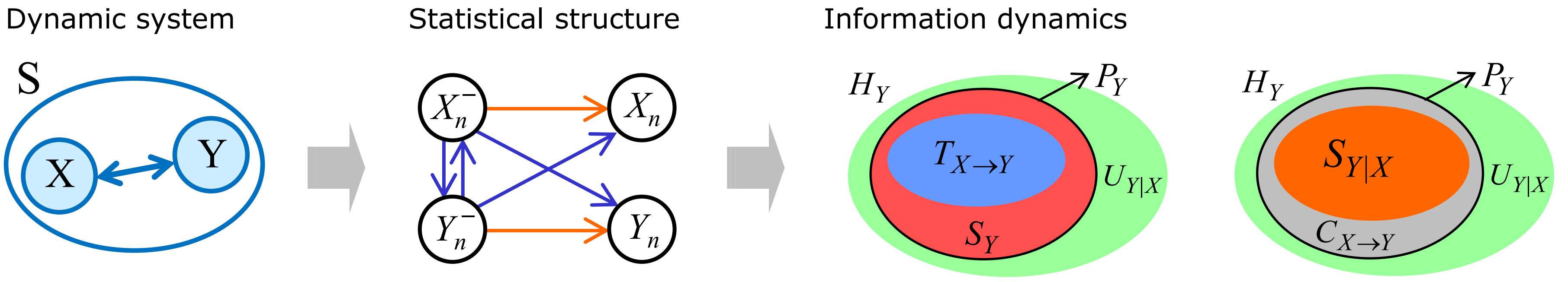
- Internal Information: $S_{X|Y} = H_X - C_{Y\to X} - U_{X|Y}$ $\quad S_{Y|X} = H_Y - C_{X\to Y} - U_{Y|X}$







INFORMATION DYNAMICS: SUMMARY OF MEASURES



- Target system Y :

  - **Predictive information :** *Prediction Entropy (PE)* $P_Y = I(Y_n; X_n^-, Y_n^-)$
    Reflects the whole statistical dependencies about the target process

  - **Information storage :** *Self Entropy (SE)* $S_Y = I(Y_n; Y_n^-)$
    Reflects the statistical dependencies about the target process arising from its own past

  - **Information transfer :** *Transfer Entropy (TE)* $T_{X\to Y} = I(Y_n; X_n^- \mid Y_n^-)$
    Reflects causal interactions from the driver to the target process

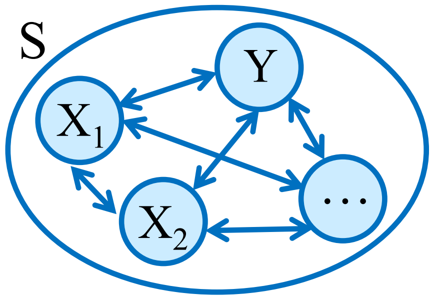
  - **Internal information :** *Conditional Self Entropy (cSE)* $S_{Y|X} = I(Y_n; Y_n^- \mid X_n^-)$
    Reflects internal dynamics in the target process

Full separation of the causal sources of statistical dependence is in general not possible
(e.g., causal connections from X to Y subserve both information storage and information transfer)

INFORMATION DYNAMICS IN FULLY MULTIVARIATE SYSTEMS

- Dynamical System $\mathrm{S}=\{\mathrm{S}_1,\ldots,\mathrm{S}_M\}$
- With reference to a target system Y :

  $\mathrm{X}=\{\mathrm{X}_1,\ldots,\mathrm{X}_{M\text{-}1}\}$ ➡ $\mathrm{S}=\{\mathrm{X}_1,\ldots,\mathrm{X}_{M\text{-}1}, \mathrm{Y}\} = \{\mathrm{X},\mathrm{Y}\}$
- Dynamic Process $S=(X_1,\ldots,X_M, Y) = (X,Y)$



- Information Dynamics - target system Y :

  ❖ **Predictive information :** *Prediction Entropy*

  $$P_Y = I(Y_n; X_{1,n}^-,\ldots,X_{M-1,n}^-, Y_n^-) = I(Y_n; X_n^-, Y_n^-)$$

  ❖ **Information storage :** *Self Entropy*

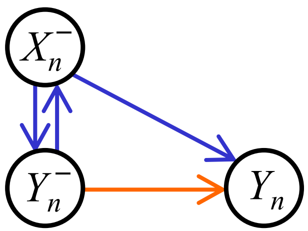
  $$S_Y = I(Y_n; Y_n^-)$$

  ❖ **Internal information :** *Conditional Self Entropy*

  $$S_{Y|X} = I(Y_n; Y_n^- \mid X_{1,n}^-,\ldots,X_{M-1,n}^-) = I(Y_n; Y_n^- \mid X_n^-)$$

  ❖ **Information transfer:** ***Collective*** *Transfer Entropy*

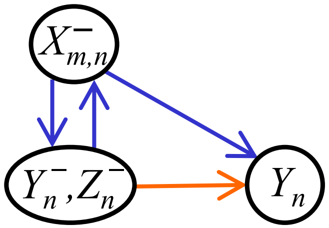
  $$T_{X\rightarrow Y} = I(Y_n; X_{1,n}^-,\ldots,X_{M-1,n}^- \mid Y_n^-) = I(Y_n; X_n^- \mid Y_n^-)$$



❖ **Information transfer from a single driver system to the target system:**

driver system X_m , target system Y ; define $\mathrm{Z}=\mathrm{X}\setminus \mathrm{X}_m$

***Partial Transfer Entropy* (PTE):** $T_{X_m\rightarrow Y|Z} = I(Y_n; X_{m,n}^- \mid Y_n^-, Z_n^-)$



PRACTICAL ESTIMATION OF INFORMATION DYNAMICS

MODEL-BASED ESTIMATION

- Exact Computation under the **assumption of Gaussianity**
  - Generic scalar variable $X \in N(0,\sigma(X)) \Rightarrow f(x) = \frac{1}{\sqrt{2\pi\sigma(X)}} e^{\frac{-x^2}{2\sigma(X)}} \Rightarrow H(X) = -\int f(x) \ln f(x) dx = \frac{1}{2} \ln 2\pi e \sigma(X)$
  - Generic n-dimensional vector variable Y: $H(Y) = \frac{1}{2} \ln (2\pi e)^n \cdot |\Sigma(Y)|$

    Covariance matrix of Y: $\Sigma(Y) = E[YY^T]$
  - ***Conditional entropy:*** $H(X|Y) = H(X,Y) - H(Y) = \frac{1}{2} \ln 2\pi e \frac{|\Sigma(X,Y)|}{|\Sigma(Y)|}$
  - Main result from [Barnett et al, Phys Rev Lett 2009]:

$$\frac{|\Sigma(X,Y)|}{|\Sigma(Y)|} = \left| \sigma(X) - \Sigma(X;Y)\Sigma(Y)^{-1}\Sigma(X;Y)^T \right|$$

$\sigma(X|Y)$ **Partial Variance** *of X given Y*

Variance of the prediction error of a linear regression of X on Y

$$H(X|Y) = \frac{1}{2} \ln 2\pi e \sigma(X|Y)$$

- Any measure of Information Dynamics is a (conditional) mutual information

$$T_{X\to Y} = I(Y_n; X_n^- | Y_n^-) = H(Y_n | Y_n^-) - H(Y_n | X_n^-; Y_n^-) \cong \frac{1}{2} \ln \frac{\sigma(Y_n | Y_n^L)}{\sigma(Y_n | X_n^L, Y_n^L)}$$

approximation of Y_n^- with $Y_n^L = (Y_{n-1}, \ldots, Y_{n-L})$, and of X_n^- with $X_n^L = (X_{n-1}, \ldots, X_{n-L})$

MODEL-BASED ESTIMATION

- Computation of the partial variance

$$\sigma(Y_n|V)=\sigma(Y_n)-\Sigma(Y_n;V)\Sigma(V)^{-1}\Sigma(Y_n;V)^T$$ for $V=Y_n^-$ or $V=(X_n^-,Y_n^-)$

Can be derived from the autocovariance matrix $\Gamma_k=E[S_nS_{n-k}^T]$ of the vector process $S_n=[X_nY_n]^T$

❖ **Vector Autoregressive (VAR) representation of joint multivariate Gaussian processes:**

$$\boldsymbol{S}_n=[X_nY_n]^T=\sum_{k=1}^{p}\mathbf{A}_k\,\boldsymbol{S}_{n-k}+\boldsymbol{\varepsilon}_n$$

$$\boldsymbol{\Gamma}_k=\boldsymbol{E}\left[\boldsymbol{U}_n\boldsymbol{U}_{n-k}^{\boldsymbol{T}}\right]=\sum_{l=1}^{p}\mathbf{A}_l\,\boldsymbol{\Gamma}_{k-l}+\boldsymbol{\delta}_{k0}\boldsymbol{\Lambda}$$

Yule-Walker equations for the covariance of $\boldsymbol{S}_n$ ($\Lambda=\mathrm{E}[\boldsymbol{\varepsilon}_n\boldsymbol{\varepsilon}_n^{\mathrm{T}}]$)

All measures can be computed numerically from the VAR parameters

[L Faes, A Porta, G Nollo, Entropy 2014 (submitted)]

✓ VAR estimation: least squares identification

✓ Model order selection: Bayesian Information Criterion

- Assessment of the statistical significance of Information Dynamics measures

❖ **Fisher F-test** $$F=\frac{\left(\sigma(X_n|X_n^-)-\sigma(X_n|X_n^-,Y_n^-)\right)/p}{\sigma(X_n|X_n^-,Y_n^-)/(N-Mp)}$$

M : number of variables

N : data length

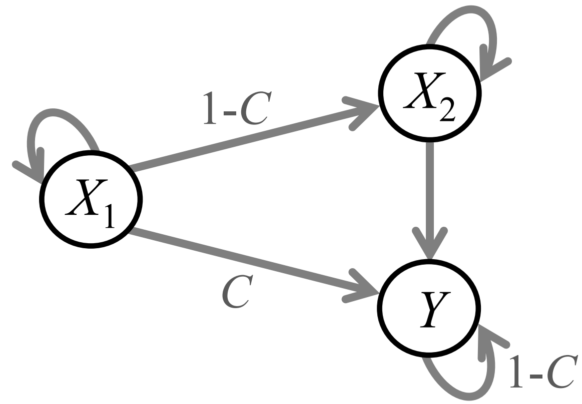
p : model order

[L Faes, S Erla, G Nollo, Comp Math Methods in Medicine 2012]

MODEL-BASED ESTIMATION: EXAMPLE

- Simulated VAR process

$$X_{1,n} = 0.85X_{1,n-1} - 0.36X_{1,n-2} + \chi_n$$
$$X_{2,n} = 0.85X_{2,n-1} - 0.36X_{2,n-2} + (1-C)X_{1,n-1} + \xi_n$$
$$Y_n = (1-C)(0.85Y_{n-1} - 0.36Y_{n-2}) + X_{2,n-1} + CX_{1,n-1} + \nu_n$$



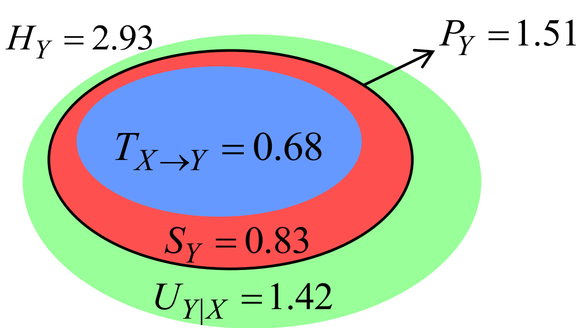
- Computation of information dynamics measures

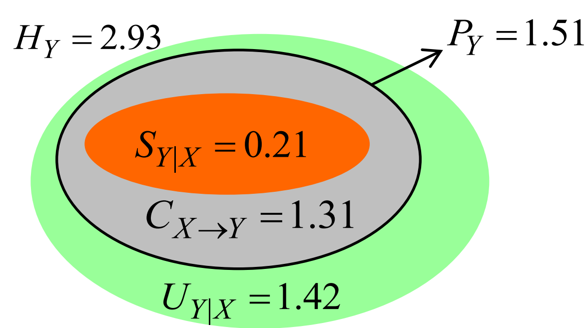
$$X = (X_1, X_2)$$

$$H_Y = \frac{1}{2}\ln 2\pi e\sigma(Y_n) \qquad P_Y \cong \frac{1}{2}\ln\frac{\sigma(Y_n)}{\sigma(Y_n \mid X_n^L, Y_n^L)} \qquad U_{Y|X} \cong \frac{1}{2}\ln 2\pi e\sigma(Y_n \mid X_n^L, Y_n^L)$$

$$S_Y \cong \frac{1}{2}\ln\frac{\sigma(Y_n)}{\sigma(Y_n \mid Y_n^L)} \qquad T_{X\to Y} \cong \frac{1}{2}\ln\frac{\sigma(Y_n \mid Y_n^L)}{\sigma(Y_n \mid X_n^L, Y_n^L)} \qquad C_{X\to Y} \cong \frac{1}{2}\ln\frac{\sigma(Y_n)}{\sigma(Y_n \mid X_n^L)} \qquad S_{Y|X} \cong \frac{1}{2}\ln\frac{\sigma(Y_n \mid X_n^L)}{\sigma(Y_n \mid X_n^L, Y_n^L)}$$

- Example (C=0.2)

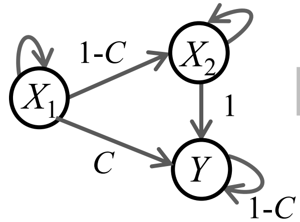




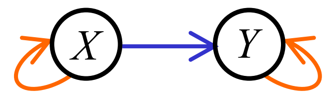
MODEL-BASED ESTIMATION: EXAMPLE

- Simulated VAR process

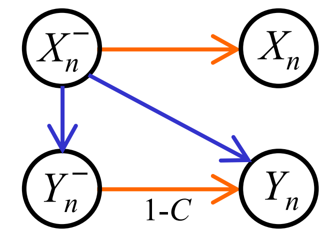
$$X_{1,n} = 0.85X_{1,n-1} - 0.36X_{1,n-2} + \chi_n$$
$$X_{2,n} = 0.85X_{2,n-1} - 0.36X_{2,n-2} + (1-C)X_{1,n-1} + \xi_n$$
$$Y_n = (1-C)(0.85Y_{n-1} - 0.36Y_{n-2}) + X_{2,n-1} + CX_{1,n-1} + \nu_n$$



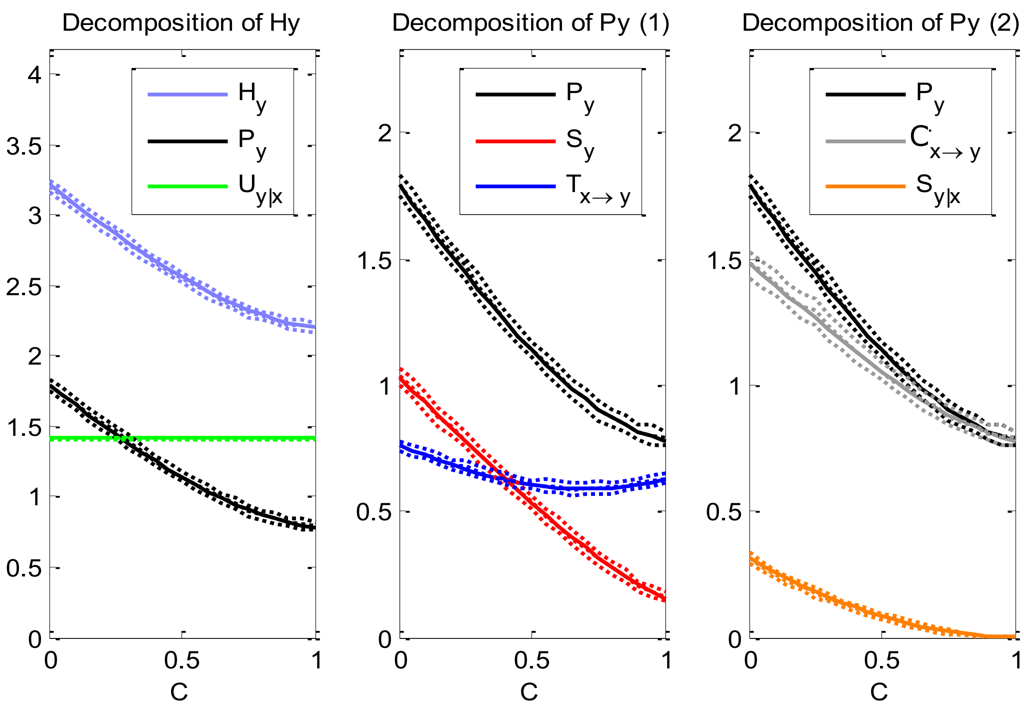
Process graph:



Granger causality graph:



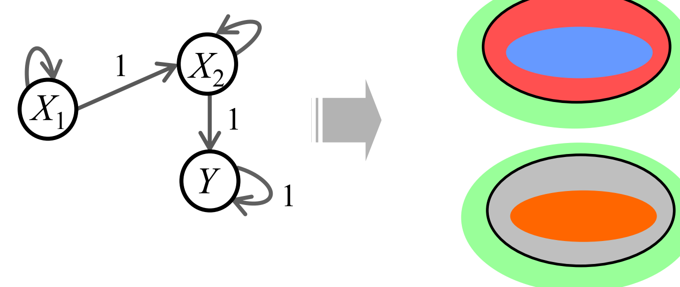
- Computation of information dynamics measures (varying C)



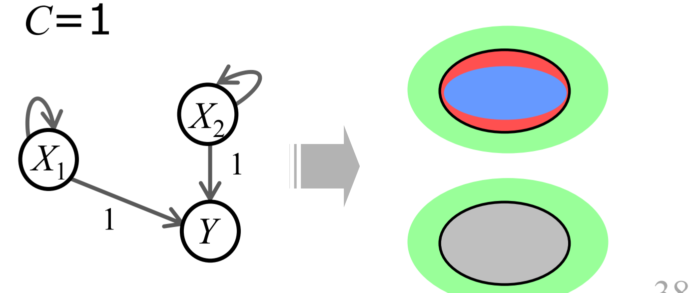
— Theory

--- Estimation: 100 realizations (300 points); least squares VAR identification; L=10

- C=0



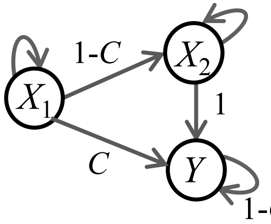
- C=1



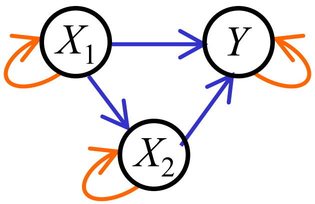
$S_{Y|X} = 0$

MODEL-BASED ESTIMATION: EXAMPLE

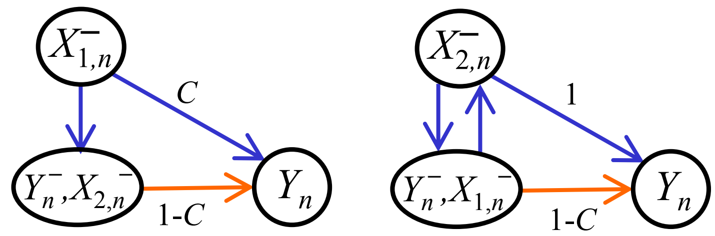
- Simulated VAR process – multivariate analysis



Process graph:

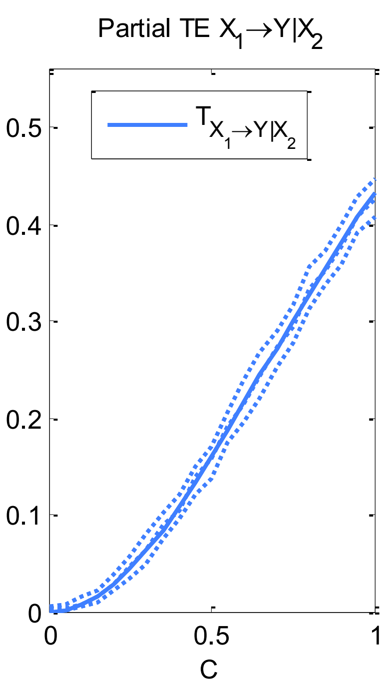


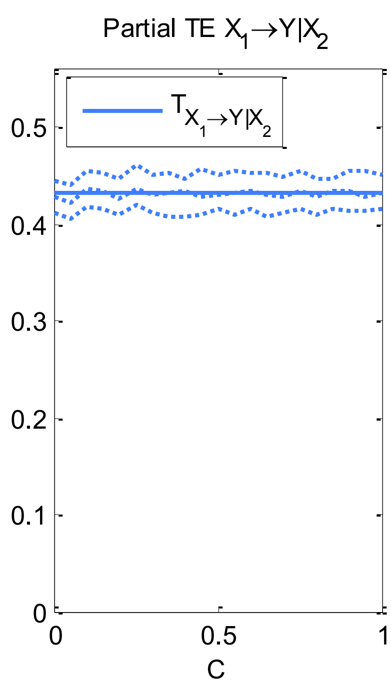
Granger causality graphs:



- Computation of partial transfer entropies

— Theory --- Estimation: 100 realizations (300 points); least squares VAR identification; L=10

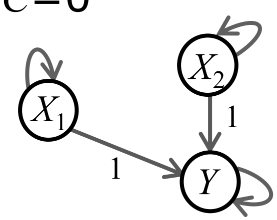




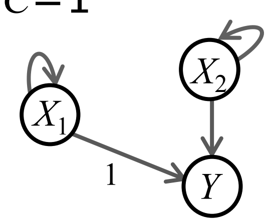
$$T_{X_1\rightarrow Y|X_2} \cong \frac{1}{2}\ln\frac{\sigma(Y_n \mid Y_n^L, X_{2,n}^L)}{\sigma(Y_n \mid X_{1,n}^L, X_{2,n}^L, Y_n^L)}$$

$$T_{X_2\rightarrow Y|X_1} \cong \frac{1}{2}\ln\frac{\sigma(Y_n \mid Y_n^L, X_{1,n}^L)}{\sigma(Y_n \mid X_{1,n}^L, X_{2,n}^L, Y_n^L)}$$

- C=0



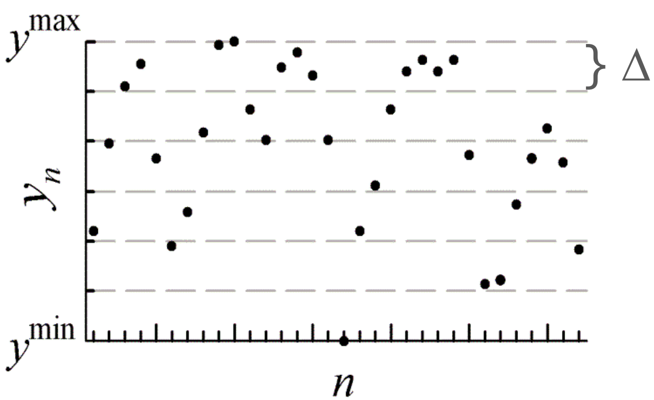
- C=1



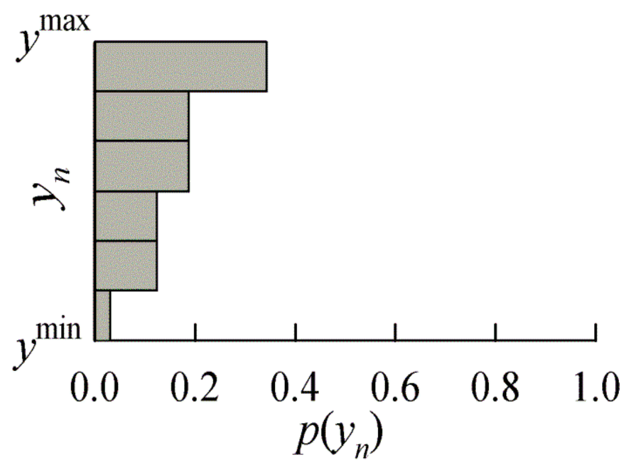
MODEL-FREE ESTIMATION: BINNING

- Histogram method - quantization

Continuous random variable Y
with range $\Delta Q = y^{max} - y^{min}$



Discrete random variable $Y^{(Q)}$
with alphabet $\Omega=\{1,\ldots,Q\}$



- ***Entropy:***

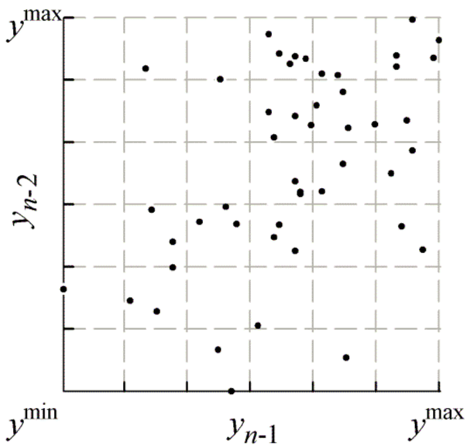
$$p(q) = p(Y_n = q) \cong \frac{N(q)}{N}$$

$$\hat{H}_Y = \hat{H}(Y_n) = -\sum_{q\in\Omega} p(Y_n = q)\log p(Y_n = q)$$

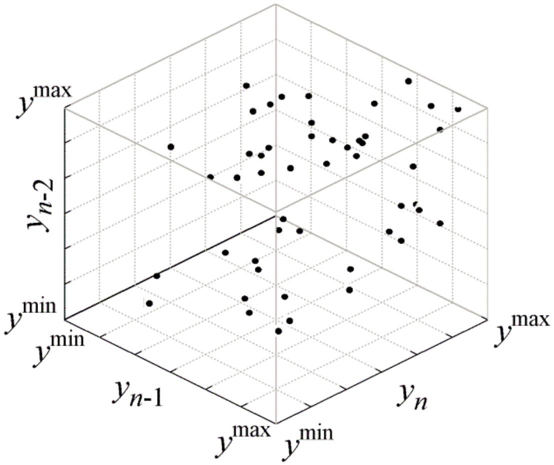
MODEL-FREE ESTIMATION: BINNING

- Histogram method - quantization

Dimension 2: $(Y_{n\text{-}1}, Y_{n\text{-}2})$



Dimension 3: $(Y_n, Y_{n\text{-}1}, Y_{n\text{-}2})$



$$p(Y_{n-1}=q_1, Y_{n-2}=q_2) \cong \frac{N(q_1,q_2)}{N}$$

$$\hat{H}(Y_{n-1}, Y_{n-2})$$

$$p(Y_n=q, Y_{n-1}=q_1, Y_{n-2}=q_2) \cong \frac{N(q,q_1,q_2)}{N}$$

$$\hat{H}(Y_n, Y_{n-1}, Y_{n-2})$$

- ***Conditional entropy:*** $\hat{H}(Y_n \mid Y_{n-1}, Y_{n-2}) = \hat{H}(Y_n, Y_{n-1}, Y_{n-2}) - \hat{H}(Y_{n-1}, Y_{n-2})$

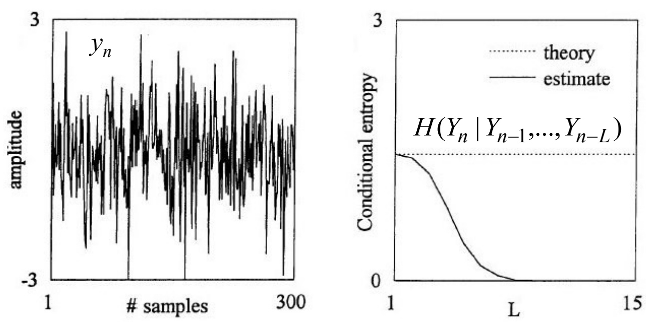
  - ***Information Storage:*** $S_Y = \hat{H}(Y_n) - \hat{H}(Y_n \mid Y_{n-1}, Y_{n-2})$

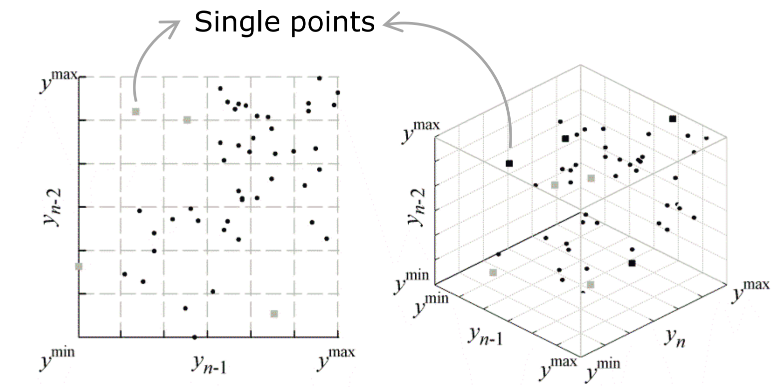
    (approximation of Y_n^- with $Y_n^L = (Y_{n-1}, \ldots, Y_{n-L})$, L=2)

MODEL-FREE ESTIMATION: BINNING

- ESTIMATION BIAS: *Conditional Entropy estimates are biased at increasing the dimension*

Example: white noise
[A Porta et al., Biol. Cyb. 1998]



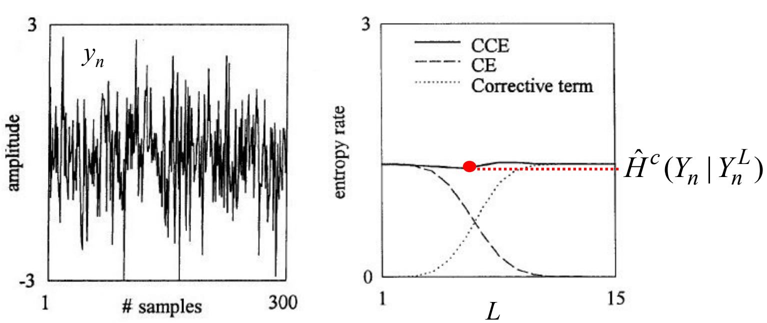


- Solution: CORRECTED CONDITIONAL ENTROPY [A Porta et al., Biol. Cyb. 1998]

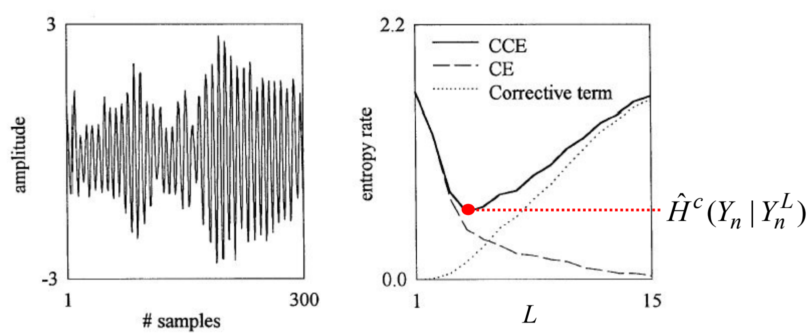
$$\hat{H}^c(Y_n|Y_n^L) = \hat{H}(Y_n|Y_n^L) + n(Y_n^L)\cdot\hat{H}(Y_n)$$

Fraction of single points

- Unpredictable process (white noise):



- Predictable (AR) process:



MODEL-FREE ESTIMATION: APPROXIMATION OF THE SYSTEM PAST

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

  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:***
    [Faes L et al., Phys Rev E 2011]

(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 $I(Y_n; W_n, V_n^{(k-1)})$ → $\min \hat{H}^c(Y_n | W_n, V_n^{(k-1)})$

$$V_n^{(k)} = [\hat{W}_n, V_n^{(k-1)}]$$

(c) Termination

Terminate the procedure when $\hat{W}_n$ does not add significant information to Y_n

minimum of corrected conditional entropy: stop if $\hat{H}^c(Y_n | \hat{W}_n, V_n^{(k-1)}) > \hat{H}^c(Y_n | V_n^{(k-1)})$

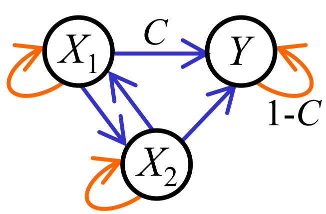
(d) After termination – embedding vector $V_n = [V_n^X, V_n^Y, V_n^Z]$ → $X_n^- \approx V_n^X \quad Y_n^- \approx V_n^Y \quad Z_n^- \approx V_n^Z$

MODEL-FREE ESTIMATION: EXAMPLE

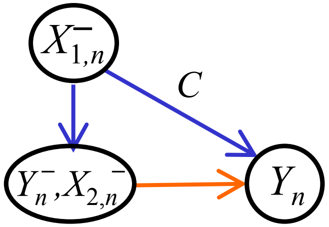
- Coupled deterministic nonlinear Henon systems

$$X_{1,n} = 1.4 - X_{1,n-1}^2 + 0.3X_{1,n-2} + 0.08(X_{1,n-1}^2 - X_{2,n-1}^2)$$
$$X_{2,n} = 1.4 - X_{2,n-1}^2 + 0.3X_{2,n-2} + 0.08(X_{2,n-1}^2 - X_{1,n-1}^2)$$
$$Y_n = 1.4 - [CX_{1,n-1} + (1-C)Y_{n-1}]Y_{n-1} + 0.1X_{2,n-2}$$

Process graph:



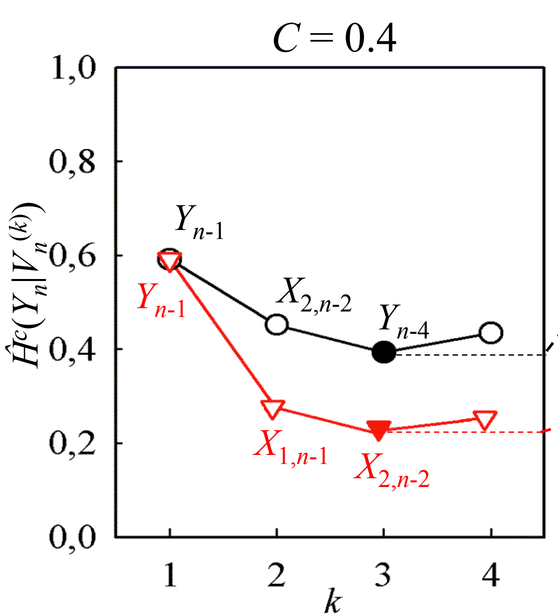
Granger causality graph:



- Computation of partial transfer entropy from X_1 to Y

$$T_{X_1 \to Y|X_2} = H(Y_n | Y_n^-, X_{2,n}^-) - H(Y_n | Y_n^-, X_{2,n}^-)$$

- N=300 samples
- Q=6 quantization levels
- L=10 initial components



❖ First embedding: $\Omega_1 = \{X_{2,n-1},\ldots,X_{2,n-L}, Y_{n-1},\ldots,Y_{n-L}\}$

$$V_1 = V_n^{(3)} = [X_{2,n-2}, Y_{n-1}, Y_{n-4}]$$

Minimum CCE: $H(Y_n | X_{2,n}^-, Y_n^-) \cong \hat{H}^c(Y_n | V_1)$

❖ Second embedding: $\Omega_2 = \{X_{1,n-1},\ldots,X_{1,n-L}, X_{2,n-1},\ldots,X_{2,n-L}, Y_{n-1},\ldots,Y_{n-L}\}$

$$V_2 = V_n^{(3)} = [X_{1,n-1}, X_{2,n-2}, Y_{n-1}]$$

Minimum CCE: $H(Y_n | X_{1,n}^-, X_{2,n}^-, Y_n^-) \cong \hat{H}^c(Y_n | V_2)$

$$\hat{T}_{X_1 \to Y|X_2} = \hat{H}^c(Y_n | V_1) - \hat{H}^c(Y_n | V_2) > 0$$

MODEL-FREE ESTIMATION: EXAMPLE

- Coupled deterministic nonlinear Henon systems

$$X_{1,n} = 1.4 - X_{1,n-1}^2 + 0.3X_{1,n-2} + 0.08(X_{1,n-1}^2 - X_{2,n-1}^2)$$
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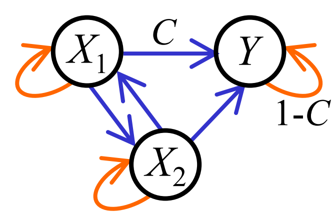
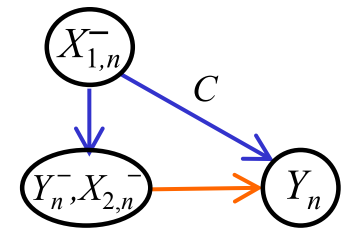
$$Y_n = 1.4 - [CX_{1,n-1} + (1-C)Y_{n-1}]Y_{n-1} + 0.1X_{2,n-2}$$

Process graph:



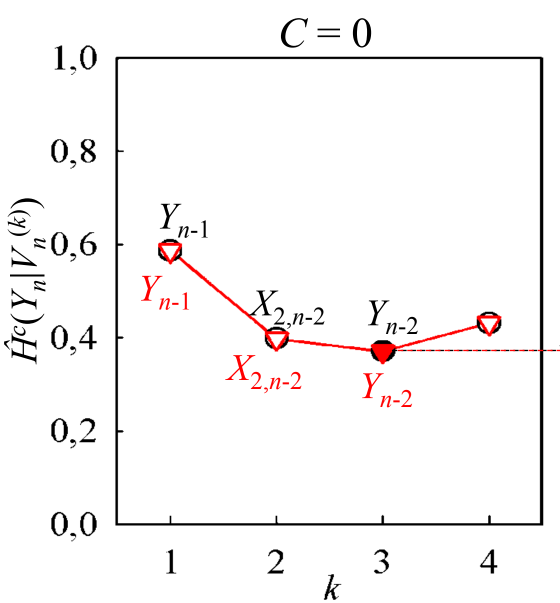
Granger causality graph:



- Computation of partial transfer entropy from X_1 to Y

$$T_{X_1 \to Y|X_2} = H(Y_n \mid Y_n^-, X_{2,n}^-) - H(Y_n \mid Y_n^-, X_{2,n}^-)$$

- *N*=300 samples
- *Q*=6 quantization levels
- *L*=10 initial components



❖ First embedding: $\Omega_1 = \{X_{2,n\text{-}1},\dots,X_{2,n\text{-}L}, Y_{n\text{-}1},\dots,Y_{n\text{-}L}\}$

$$V_1 = V_n^{(3)} = [X_{2,n-2}, Y_{n-1}, Y_{n-2}]$$

Minimum CCE: $H(Y_n \mid X_{2,n}^-, Y_n^-) \cong \hat{H}^c(Y_n \mid V_1)$

❖ Second embedding: $\Omega_2 = \{X_{1,n\text{-}1},\dots,X_{1,n\text{-}L}, X_{2,n\text{-}1},\dots,X_{2,n\text{-}L}, Y_{n\text{-}1},\dots,Y_{n\text{-}L}\}$

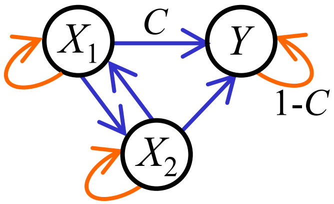
$$V_2 = V_n^{(3)} = [X_{2,n-2}, Y_{n-1}, Y_{n-2}]$$

Minimum CCE: $H(Y_n \mid X_{1,n}^-, X_{2,n}^-, Y_n^-) \cong \hat{H}^c(Y_n \mid V_2)$

$$\hat{T}_{X_1 \to Y|X_2} = \hat{H}^c(Y_n \mid V_1) - \hat{H}^c(Y_n \mid V_2) = 0$$

MODEL-FREE ESTIMATION: EXAMPLE

- Coupled deterministic nonlinear Henon systems



Computation of partial transfer entropy from X_1 to Y

- 100 realizations (varying initial conditions)
- N=300 samples for each realization
- Q=6 quantization levels
- L=10 initial components

- Normalized PTE:

$$\hat{T}^{(n)}_{X_1 \to Y|X_2} = \frac{\hat{H}^c(Y_n|V_1) - \hat{H}^c(Y_n|V_2)}{\hat{H}^c(Y_n|V_1)}$$

- **Significance of coupling** assessed by time-shifted surrogate data:

Original: $x_1,\ldots,x_N \longrightarrow T_{X\to Y}$

Surrogate 1: $x_{L_1+1},\ldots,x_N,x_1,\ldots,x_{L_1}$

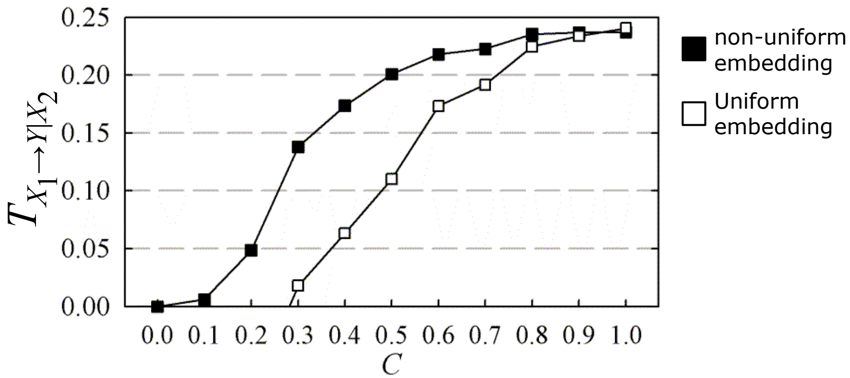
⋮

Surrogate S: $x_{L_S+1},\ldots,x_N,x_1,\ldots,x_{L_S}$

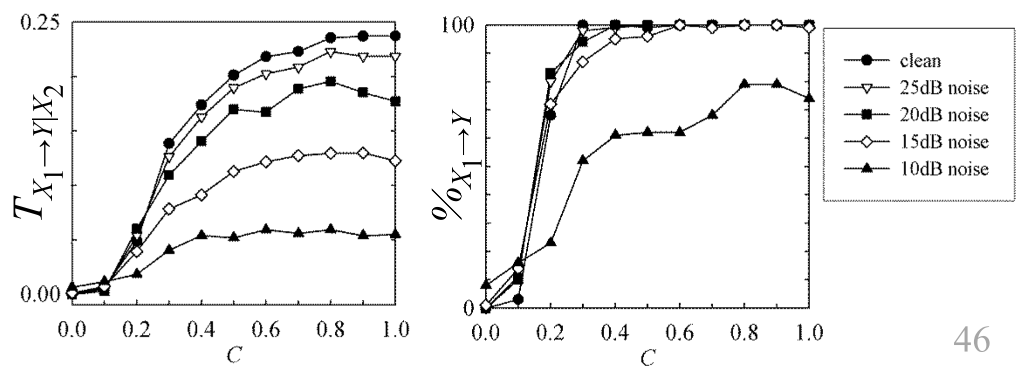
Distribution of $T^{(s)}_{X\to Y}$

$T_{X\to Y}$ *is significant if it exceeds the upper bound of the distribution of* $T^{(s)}_{X\to Y}$

- Clean data:



- Noisy data:

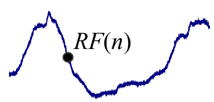


APPLICATION ON PHYSIOLOGICAL SYSTEMS

ASSESSMENT OF CARDIORESPIRATORY INTERACTIONS

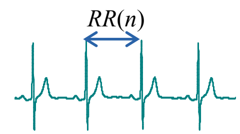
- **Heart rate variability is the result of the interplay of several regulation mechanisms**

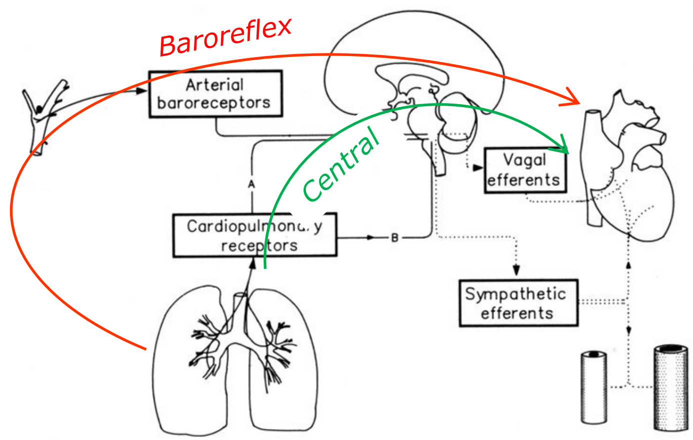
Respiration variability



Respiratory sinus arrhythmia

Heart rate variability





- **Aim: quantifying HRV complexity and how it is reduced by cardiorespiratory interactions**

- **Analysis:** *Information decomposition of cardiorespiratory dynamics*

  Target: cardiac system → *Heart period variability*

  Driver: respiratory system → *Respiration variability*

[Faes L , A Porta, G Nollo: *Information Decomposition in Bivariate Systems: Theory and Application to Cardiorespiratory Dynamics* , Entropy 2014, under revision]

ASSESSMENT OF CARDIORESPIRATORY INTERACTIONS

- **Experimental Protocols**

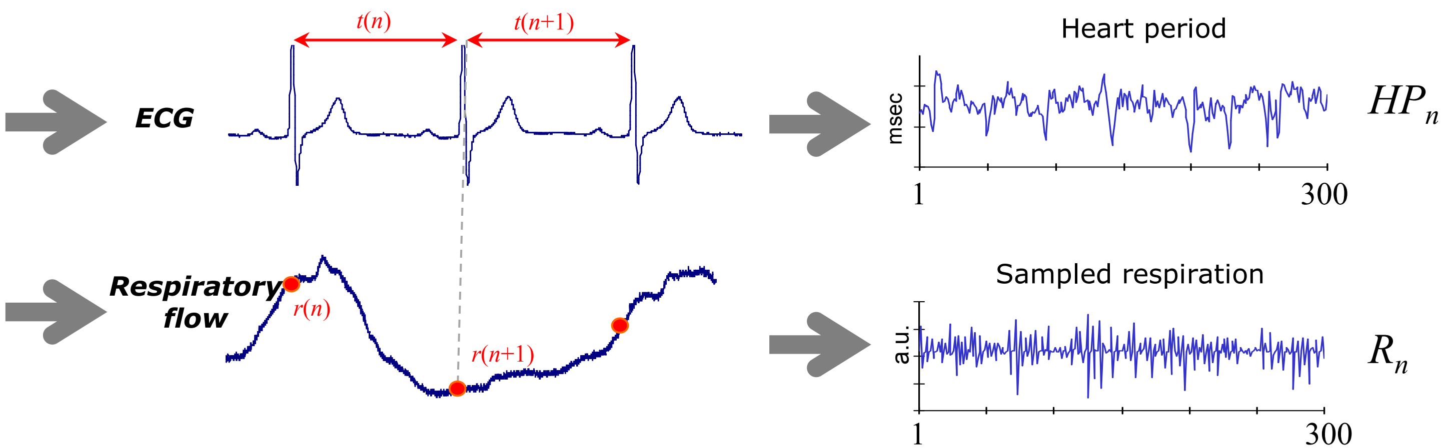
Partial Transfer Entropy (PTE):

❑ ***HEAD-UP TILT***
  - *15 Healthy subjects (8 males, 25±3 years)*
  - *Conditions:* *supine position (SU)*
    60° upright position (UP)

❑ ***PACED BREATHING***
  - *15 Healthy subjects (6 males, 26±3 years)*
  - *Conditions:* *Spontaneous breathing (SP)*
    paced breathing: 10 breaths/min
    15 breaths/min
    20 breaths/min

- **Construction of beat-to-beat variability series**

  - **Cardiac system**
  - **Respiratory system**



- **Analysis: Predictive Information decomposition**

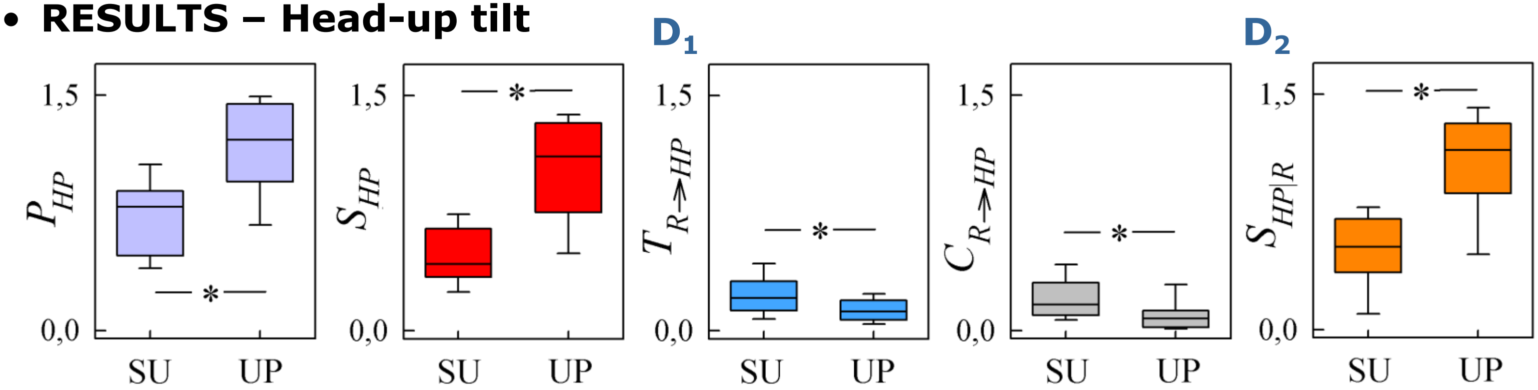
❖ **D1:** $P_{HP} = S_{HP} + T_{R\rightarrow HP}$ *Information Storage* $S_{HP} = I(HP_n; HP_n^-)$ *Information Transfer* $T_{R\rightarrow HP} = I(HP_n; R_n^- \mid HP_n^-)$

❖ **D2:** $P_{HP} = C_{R\rightarrow HP} + S_{HP|R}$ *Cross-Information* $C_{R\rightarrow HP} = I(HP_n; R_n^-)$ *Internal Information* $S_{HP|R} = I(HP_n; HP_n^- \mid R_n^-)$

❖ **Linear model-based analysis** (model order selection with Bayesian Information Criterion)

ASSESSMENT OF CARDIORESPIRATORY INTERACTIONS

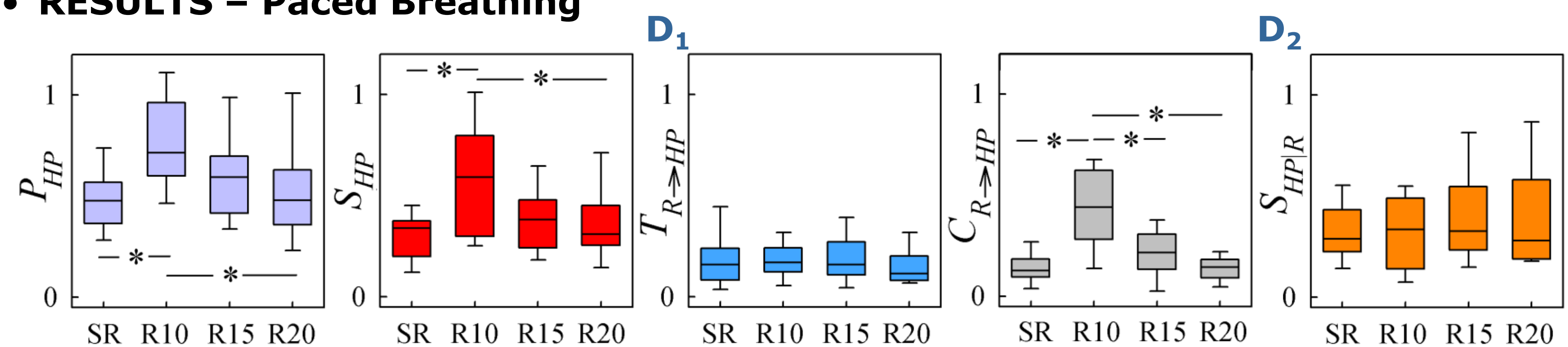
- **RESULTS – Head-up tilt**



- ↑ PE in the upright position
  ↑ Storage, Internal Information: reduced complexity of HP
  ↓ Transfer, Cross Information: reduced respiratory sinus arrhythmia

sympathetic activation and parasympathetic deactivation induced by tilt

- **RESULTS – Paced Breathing**



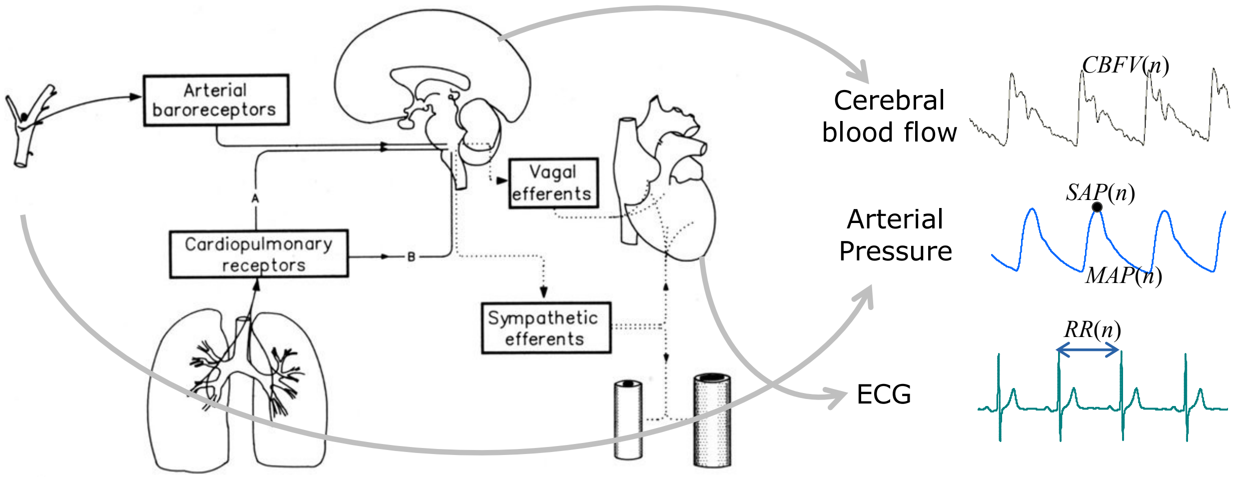
- ↑ PE at slow paced breathing
  D1: ↑ Storage, ↔Transfer
  D2: ↑ Cross-information, ↔Internal information

Unaltered cardiorespiratory coupling and cardiac internal dynamics

Entrainment of low- and high-frequency components of HP variability

CARDIOVASCULAR AND CEREBROVASCULAR DYNAMICS DURING SYNCOPE

- **The variability of heart rate and cerebral blood flow reflect important physiological mechanisms**
  - ✓ Effects of systolic arterial pressure on heart period reflect baroreflex modulation
  - ✓ Effects of mean arterial pressure on cerebral blood flow velocity reflect cerebral auto-regulation



- **Aim: assess cardiovascular and cerebrovascular regulation in postural syncope**

- **Analysis:** *Information decomposition of cardiovascular and cerebrovascular dynamics*

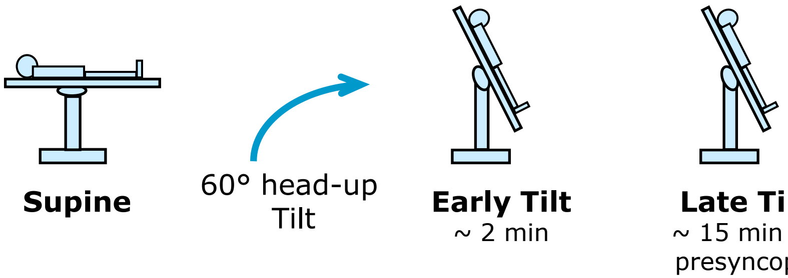
  Cardiac system, Vascular system → *Heart Period variability, Systolic Arterial Pressure variability*

  Cerebral system, Vascular system → *Cerebral Blood Flow variability, Mean Arterial Pressure variability*

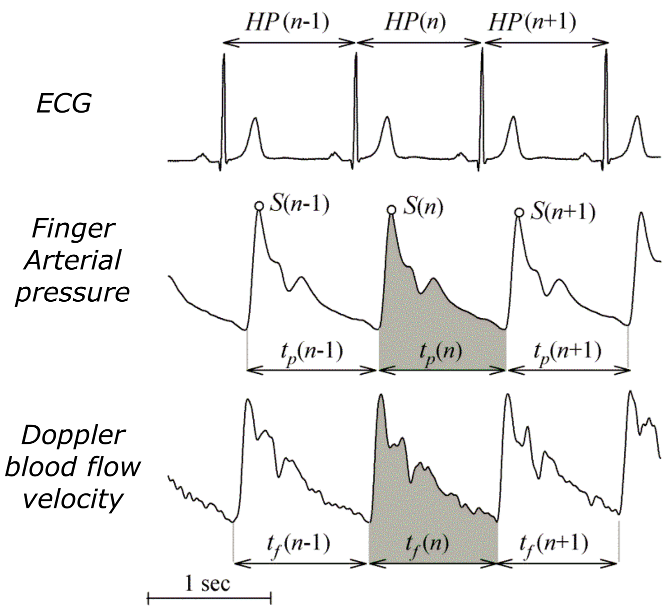
[L Faes, A Porta, G Rossato, A Adami, D Tonon, A Corica, G Nollo, *Investigating the mechanisms of cardiovascular and cerebrovascular regulation in orthostatic syncope through an information decomposition strategy*, Autonomic Neuroscience 2013; 178:76-82]

CARDIOVASCULAR AND CEREBROVASCULAR DYNAMICS DURING SYNCOPE

- **Experimental Protocol**
  - 10 syncope subjects (37±17 years)
  - Three analysis windows, *N*~300 beats each



- **Construction of beat-to-beat variability series**



- Cardiovascular interactions
  - **Cardiac system** → **Process *HP*** (heart period)
  - **Vascular system** → **Process *S*** (systolic arterial pressure)

- Cerebrovascular interactions
  - **Cerebral system** → **Process *FV*** (mean blood flow velocity)
  - **Vascular system** → **Process *P*** (mean arterial pressure)

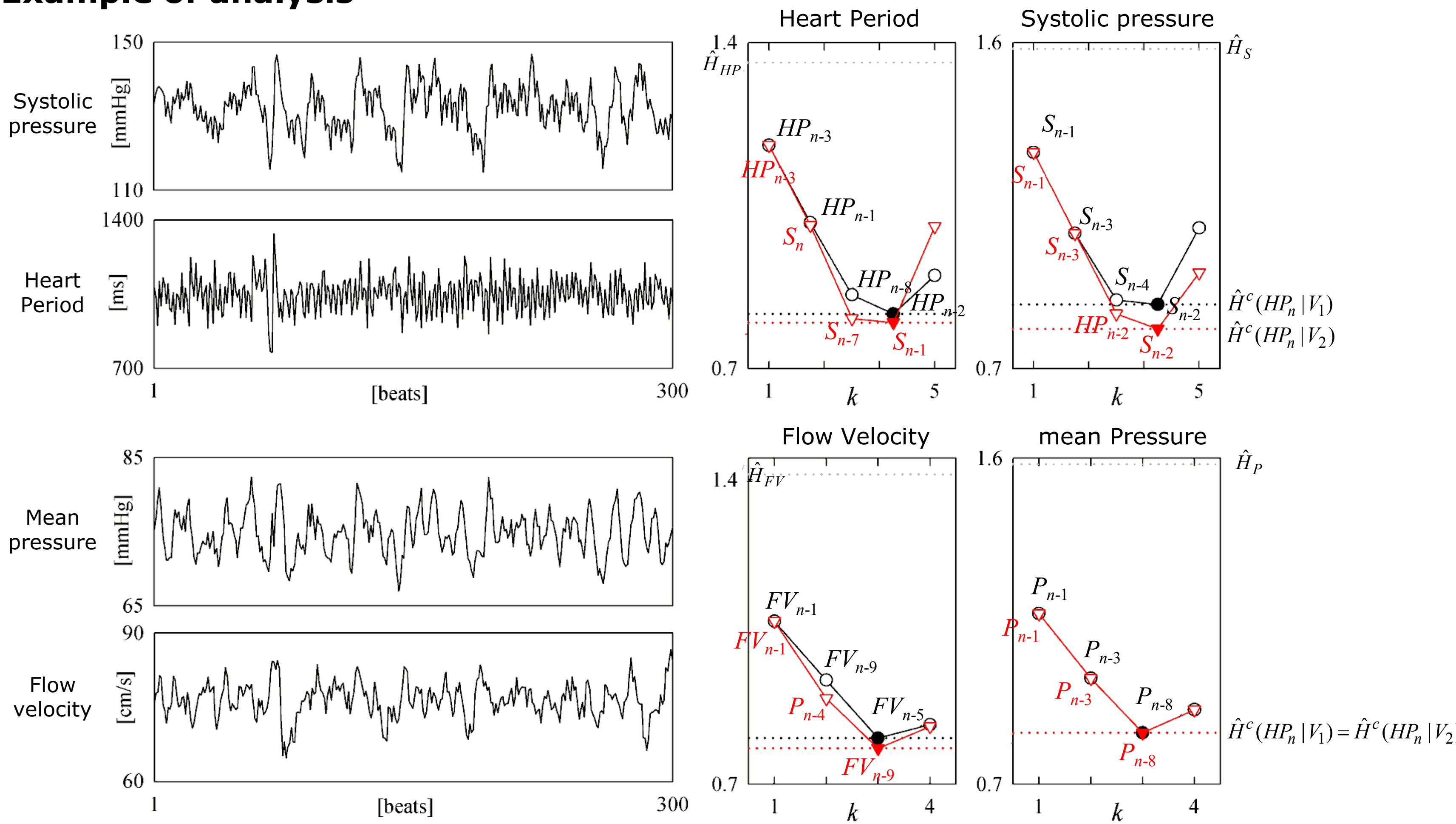
- **Analysis: Entropy decomposition** $H_Y = S_Y + T_{X \to Y} + U_{Y|X}$

Information
Information Storage
Information Transfer
Unexplained Information

  - **model-free analysis** (histogram entropy estimator with NUE (L=10), Q=6 quantization levels

CARDIOVASCULAR AND CEREBROVASCULAR DYNAMICS DURING SYNCOPE

- **Example of analysis**



For each target Y : System Information $H_Y \cong \hat{H}^c(Y_n)$

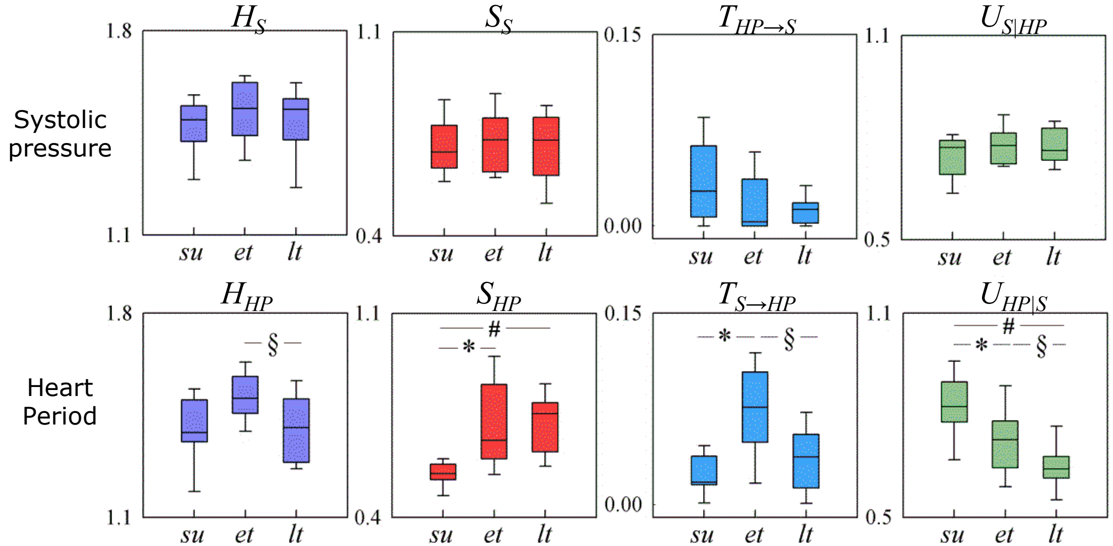
Information Storage $S_Y \cong \hat{H}^c(Y_n) - \hat{H}^c(Y_n|V_1)$

Information Transfer $T_{X \to Y} \cong \hat{H}^c(Y_n|V_1) - \hat{H}^c(Y_n|V_2)$

Unexplained Information $U_{Y|X} \cong \hat{H}^c(Y_n|V_2)$

CARDIOVASCULAR AND CEREBROVASCULAR DYNAMICS DURING SYNCOPE

- **Results – cardiovascular analysis**



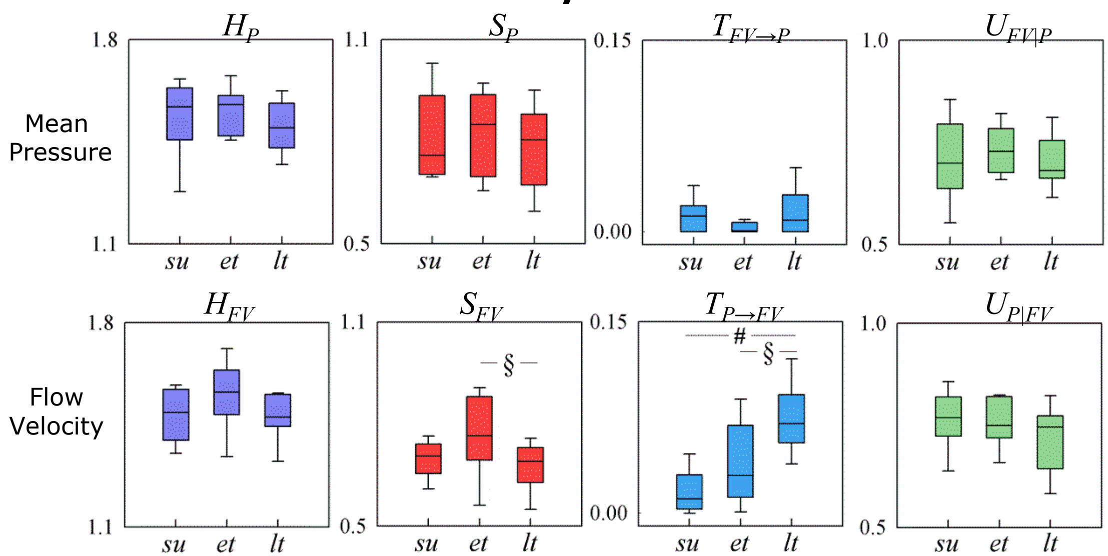
- from *su* to *up*: ↑ Storage HP
  ↑ Transfer S→HP

Tilt-induced sympathetic activation and baroreflex enhancement

- during *late tilt*: ↔ Storage HP
  ↓ Transfer S→HP

impairment of baroreflex regulation

- **Results – cerebrovascular analysis**



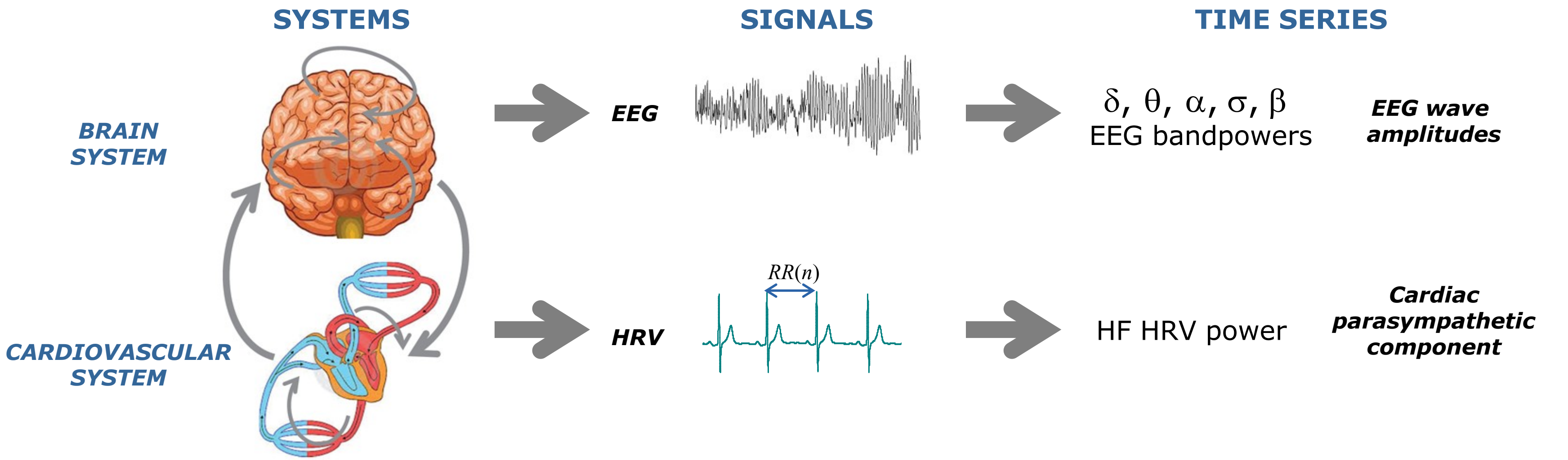
- during *late tilt*:
  ↓ Storage FV
  ↑ Transfer P→FV

lack of cerebral autoregulation

BRAIN – HEART AND BRAIN-BRAIN DYNAMICS DURING SLEEP

- **Sleep has a profound impact on cardiovascular and brain regulation, with its stage organization reflecting autonomic nervous system activity**

- **Aim: investigate the networks of brain-heart and brain-brain interactions during sleep**

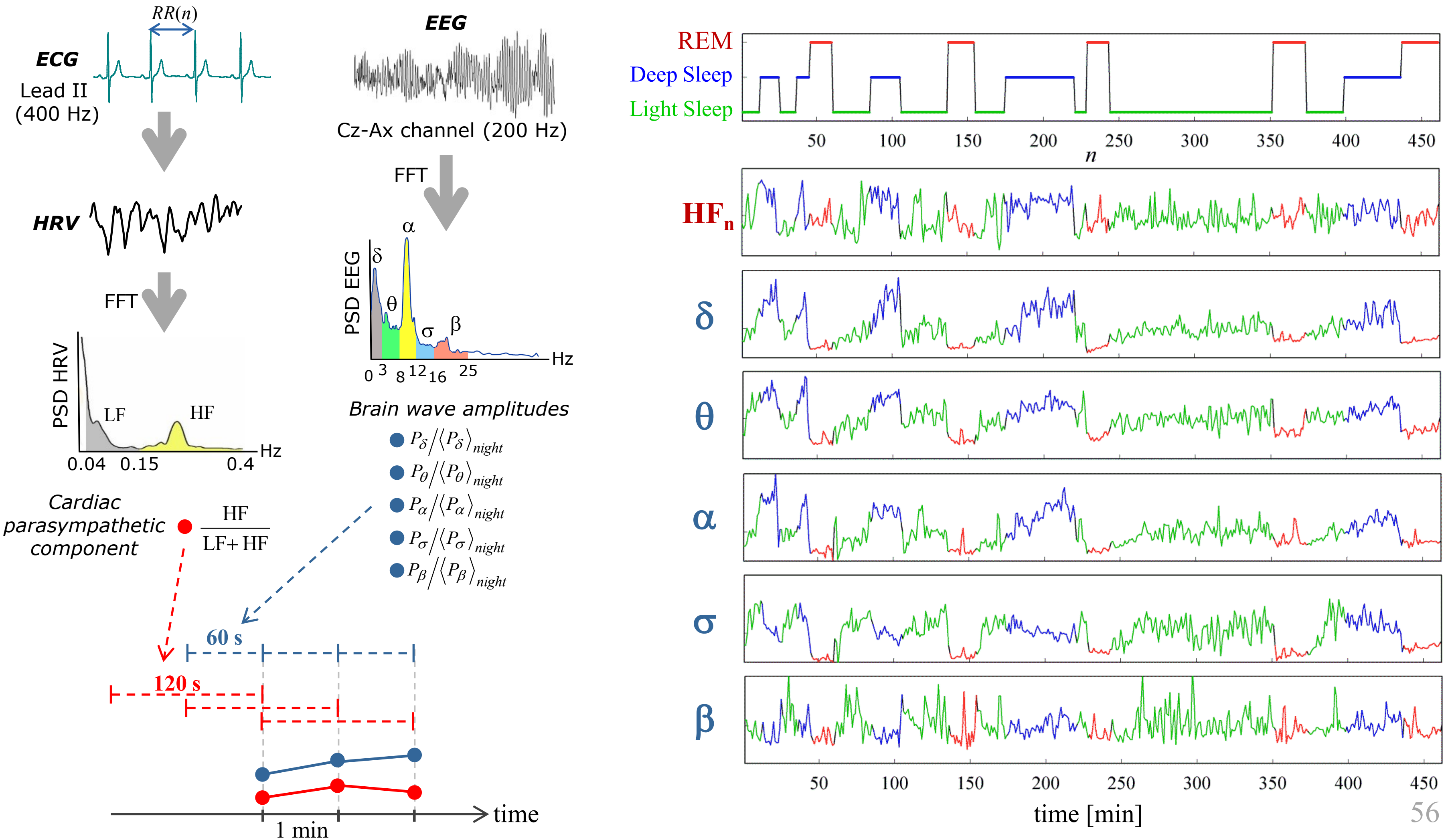


- **Analysis:** *Study of the structure of brain-heart and brain-brain networks*
  - computation of internal information and information transfer

[L Faes, G Nollo, F Jurysta, D Marinazzo, 'Information dynamics of brain-heart physiological networks during sleep', New J Phys 2014; 16:105005]

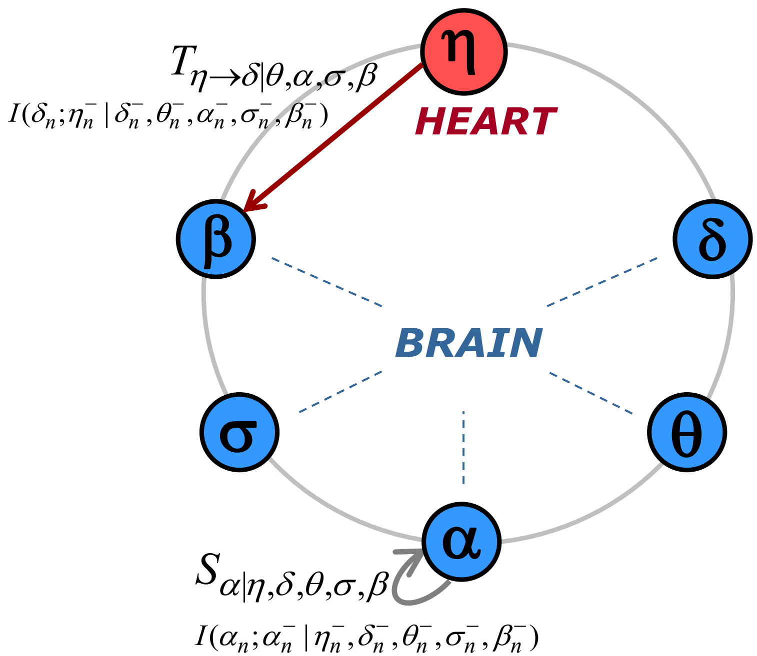
BRAIN – HEART AND BRAIN-BRAIN DYNAMICS DURING SLEEP

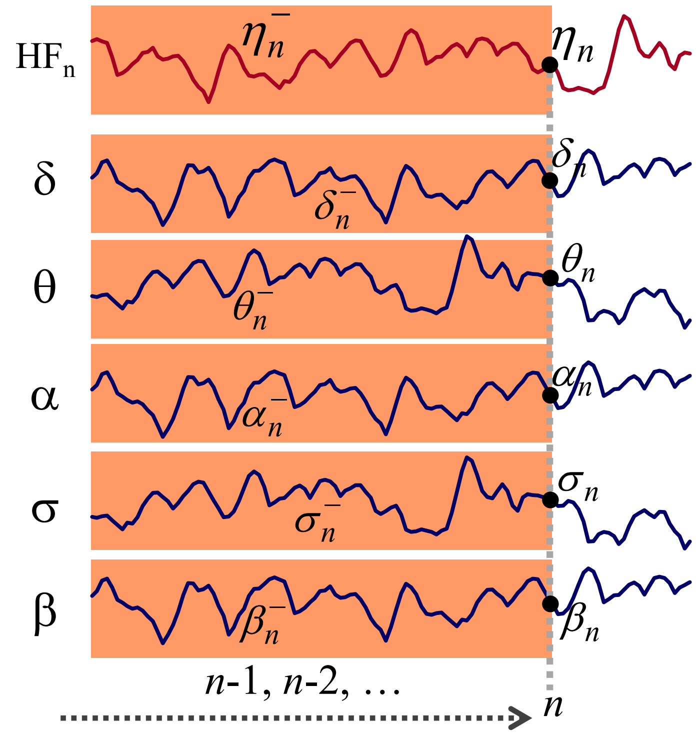
- Protocol: polysomnography from 10 healthy subjects (18-23 yrs)
- Time series measurement:



BRAIN – HEART AND BRAIN-BRAIN DYNAMICS DURING SLEEP

- **NETWORK REPRESENTATION**

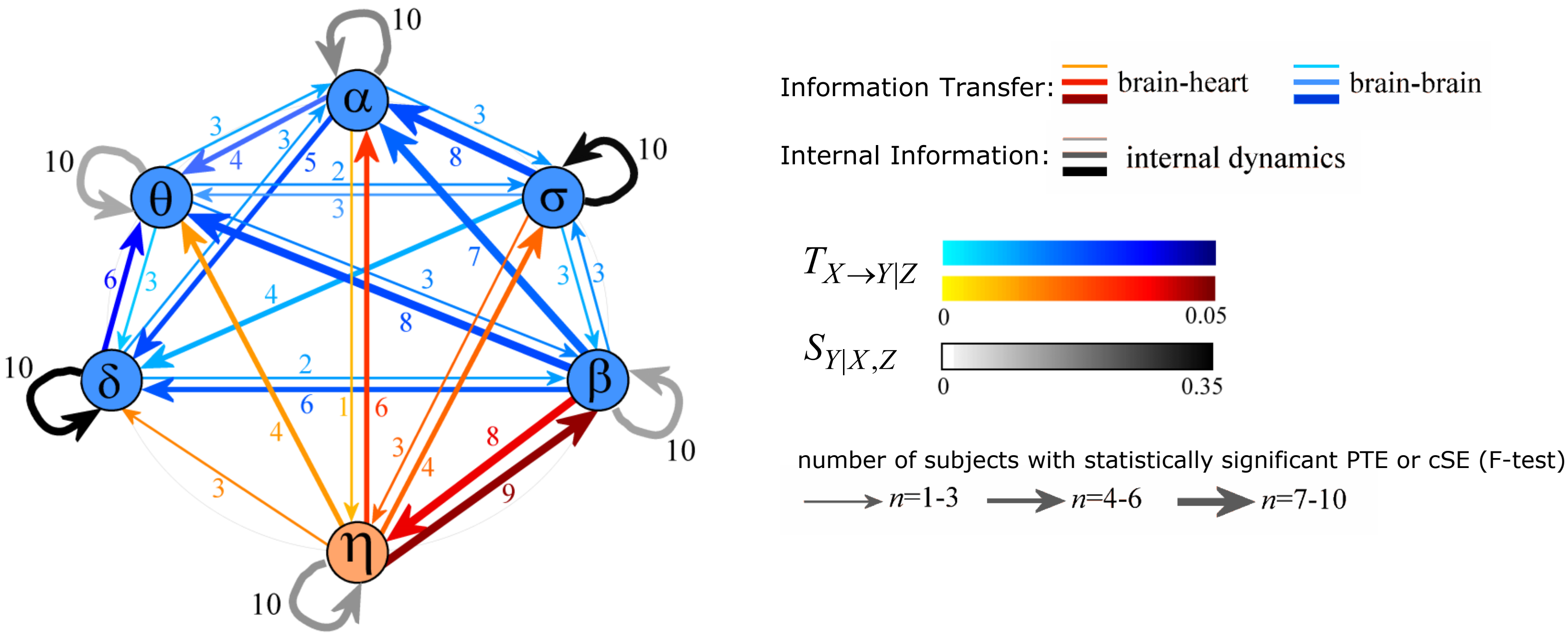




- **Analysis:** driver system X, target system Y ; define $Z=S\setminus\{X,Y\}$
  - ❖ **Internal information :** *Conditional Self Entropy* (cSE) $S_{Y|X,Z} = I(Y_n;Y_n^- \mid X_n^-,Z_n^-)$
  - ❖ **Information transfer:** *Partial Transfer Entropy* (PTE): $T_{X\to Y|Z} = I(Y_n;X_n^- \mid Y_n^-,Z_n^-)$
  - ❖ **Linear model-based analysis** (model order selection with Bayesian Information Criterion)
    (Statistical significance of cSE and PTE with the Fisher F-test)

BRAIN – HEART AND BRAIN-BRAIN DYNAMICS DURING SLEEP

- **RESULTS – Full night analysis**

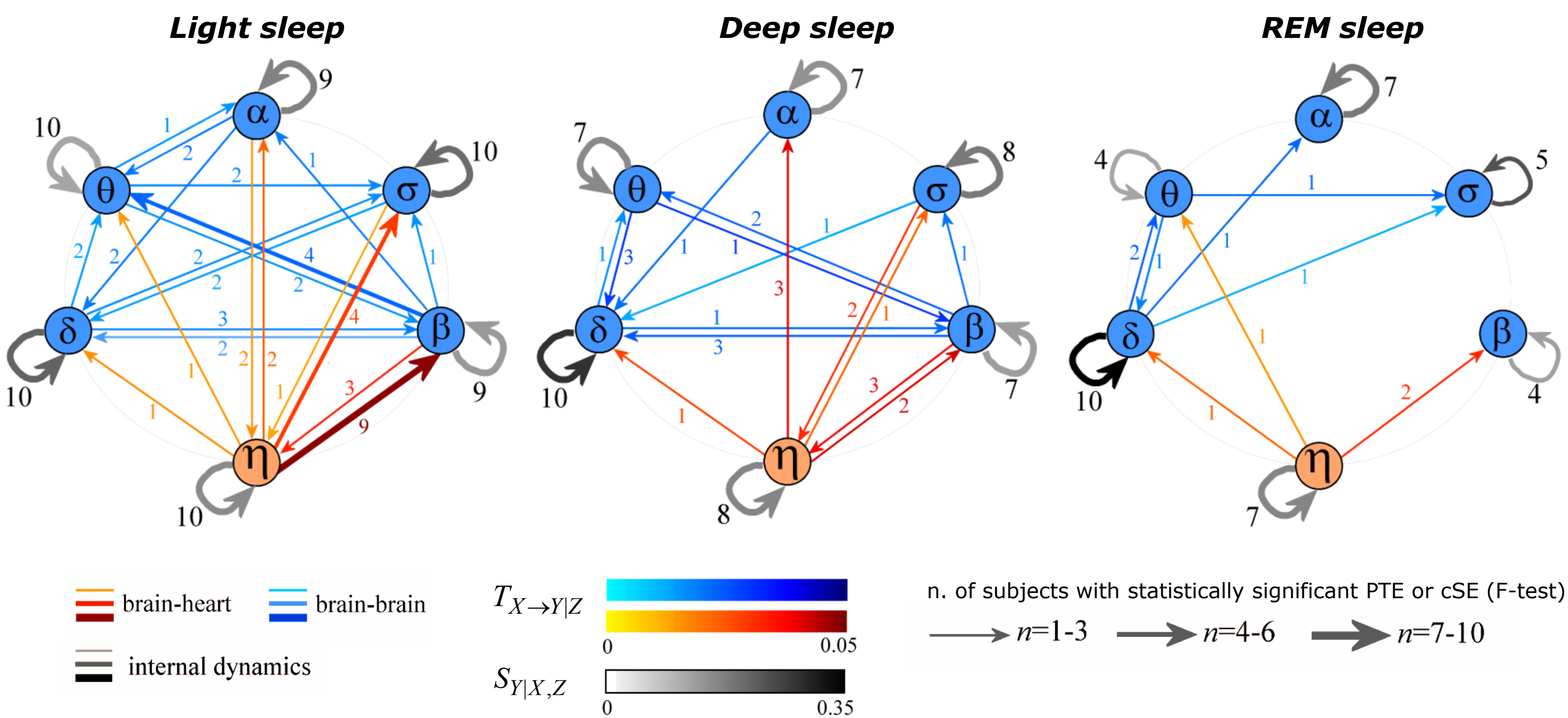


- **Brain - heart interactions**
  - ✓ *Bidirectional between* HF$_n$ *and EEG* β *wave*
  - ✓ *Weaker and unidirectional from heart to brain for* δ, θ, α , σ *EEG waves*
- **Brain - brain interactions** ➔ *Fully connected network with transfer mostly from* β, σ *towards* δ, θ, α
- **Internal dynamics** ➔ *Strong self-dependencies in all rhythms*

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

BRAIN – HEART AND BRAIN-BRAIN DYNAMICS DURING SLEEP

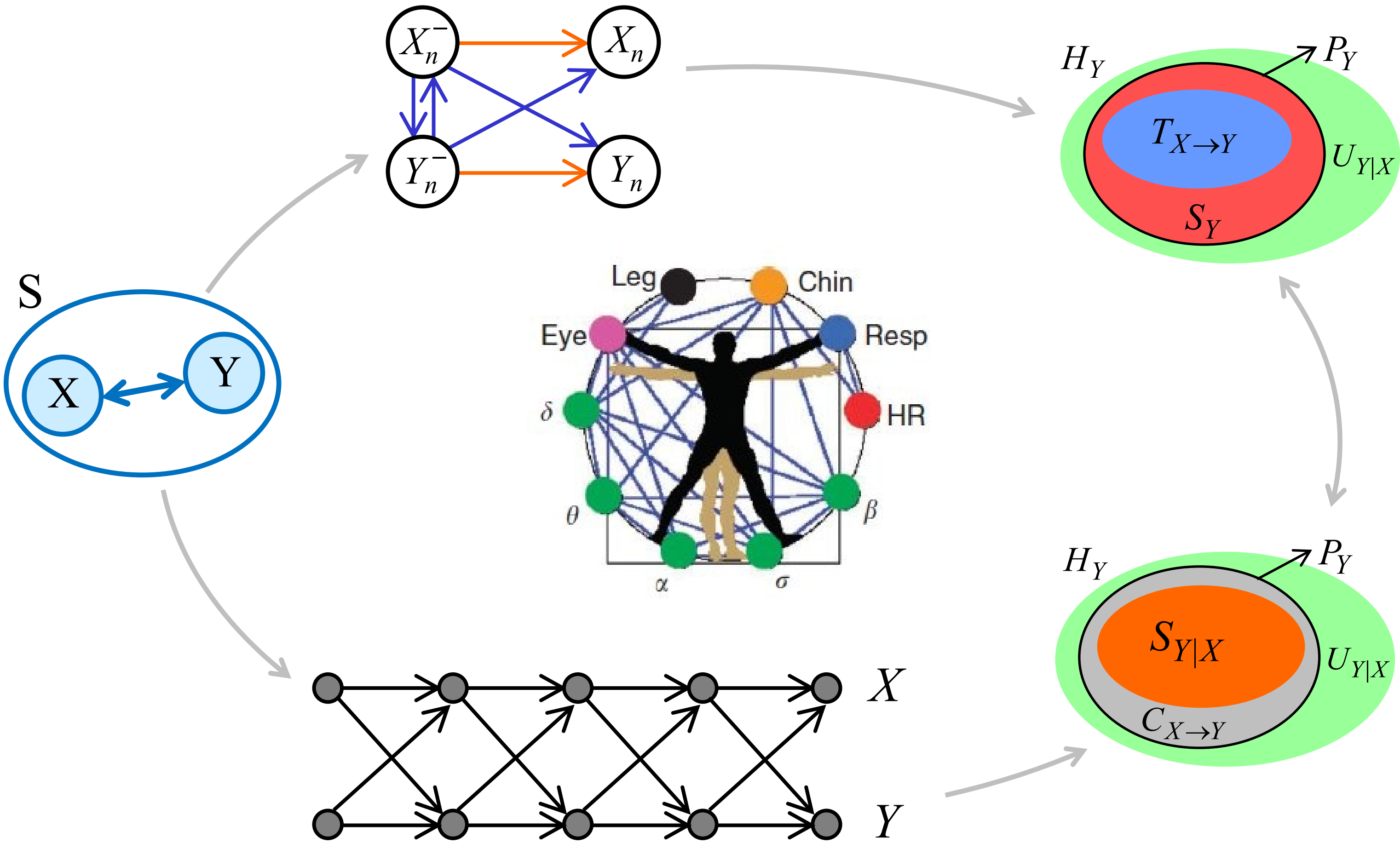
- **RESULTS – stage-specific analysis**



- *Weaker network links, progressively less consistent from light sleep to deep sleep and to REM*
- *Internal dynamics are almost preserved*

The interaction network is sustained by the sleep stage transitions

During single sleep stages the systems are isolated but keep internal activity



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REFERENCES

- 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; ISBN: 978-3-642-54473-6; DOI: 10.1007/978-3-642-54474-3.
- L Faes, D Kugiumtzis, A Montalto, G Nollo, D Marinazzo, 'Estimating the decomposition of predictive information in multivariate systems', Phys Rev E, submitted, 2014.
- L Faes, D Marinazzo, F Jurysta, G Nollo, 'Linear and nonlinear analysis of brain-heart and brain-brain interactions during sleep', Phys. Meas., submitted, 2014.
- 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", submitted, 2014.
- D Widjaja, A Montalto, E Vlemincx, D Marinazzo, L Faes, S Van Huffel, 'Cardiorespiratory information dynamics during mental arithmetic and sustained attention', Phys. Meas., submitted, 2014.
- A Montalto, L Faes, D. Marinazzo, 'MuTE: a MATLAB toolbox to compare established and novel estimators of the multivariate transfer entropy', PLOS ONE 2014; 9(10):e109462 (13 pages).
- L Faes, G Nollo, F Jurysta, D Marinazzo, 'Information dynamics of brain-heart physiological networks during sleep', New J Phys 2014; 16:105005 (20 pages).
- 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 Neurosci 2013; 178:76-82.
- L Faes, D Marinazzo, A Montalto, G Nollo, 'Lag-specific transfer entropy as a tool to assess cardiovascular and cardiorespiratory information transfer', IEEE Trans Biomed Eng 2014; 61(10):2556-2568. DOI: 10.1109/TBME.2014.2323131
- L Faes, G Nollo, A Porta: 'Compensated transfer entropy as a tool for reliably estimating information transfer in physiological time series', Entropy; special issue on "Transfer Entropy", 2013; 15(1):198-219.
- L Faes, G Nollo, A Porta: 'Mechanisms of causal interaction between short-term heart period and arterial pressure oscillations during orthostatic challenge', J Appl Physiol 2013;114:1657-1667.
- L Faes, G Nollo, A Porta: 'Non-uniform multivariate embedding to assess the information transfer in cardiovascular and cardiorespiratory variability series', Comput Biol Med 2012; 42:290-297.
- L Faes, S Erla, G Nollo: 'Measuring connectivity in linear multivariate processes: definitions, interpretation and practical analysis', Comp Math Methods Med, special issue on "Methodological Advances in Brain Connectivity", 2012; 140513:18 pages.
- L Faes, G Nollo, A Porta: 'Information-based detection of nonlinear Granger causality in multivariate processes via a nonuniform embedding technique', Phys Rev E; 2011; 83(5 Pt 1):051112.
- L Faes, G Nollo, A Porta: 'Information domain approach to the investigation of cardio-vascular, cardio-pulmonary and vasculo-pulmonary causal couplings', Front Physiol, Special Issue "Engineering Approaches to Study Cardiovascular Physiology: Modeling, Estimation, and Signal Processing", 2011; 2:80.