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Functional Connectivity in MEG

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MRC CBU, Cambridge

Functional Connectivity Background

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- Much interest in functional connectivity in fMRI
- And yet many neural interactions (e.g, coupled oscillations) occur at a timescale faster than visible by fMRI
- Beyond localization: the same set of brain regions could perform different functions depending on how they interact
- So, real promise of MEG/EEG is functional connectivity?

Talk Overview

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1. Problem of Field Spread (Volume Conduction)

2. Linear vs Nonlinear measures

3. Directed vs Undirected measures

4. Direct vs Indirect measures

5. Generative Models

Field Spread Problem

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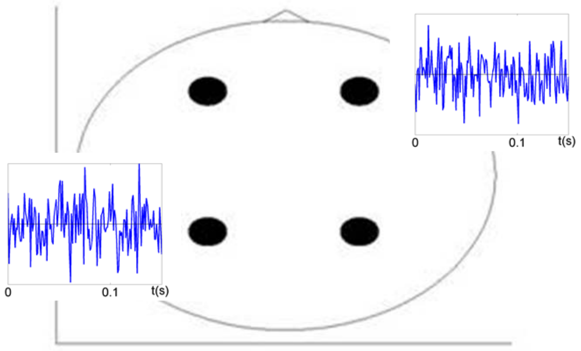
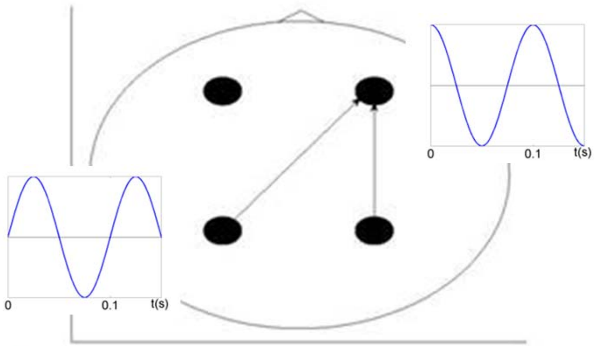
Many (zero-lag) measures of functional connectivity between sensors can be spurious, i.e, reflect activity from single source

No true source connectivity



True source connectivity



Field Spread Problem

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Source reconstruction reduces field spread problem…

…and allows easier comparison with fMRI connectivity

BUT spurious connections between sources can remain (“point-spread”)

Hillebrand et al (2012) Neuroimage

…and field-spread is instantaneous (zero-lag), so some measures of connectivity between sensors are immune to field spread (e.g, time- or phase-lagged measures)

Different Types of Connection

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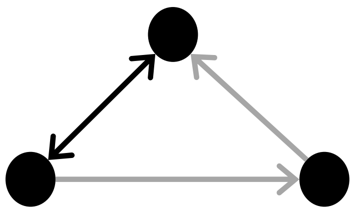
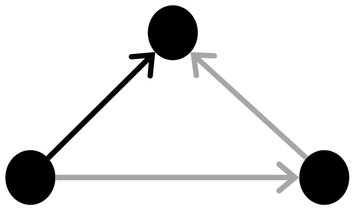
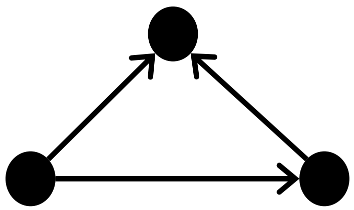
Undirected, Indirect (bivariate)



Directed, Indirect (bivariate)



Directed, Direct (multivariate)
("effective connectivity")



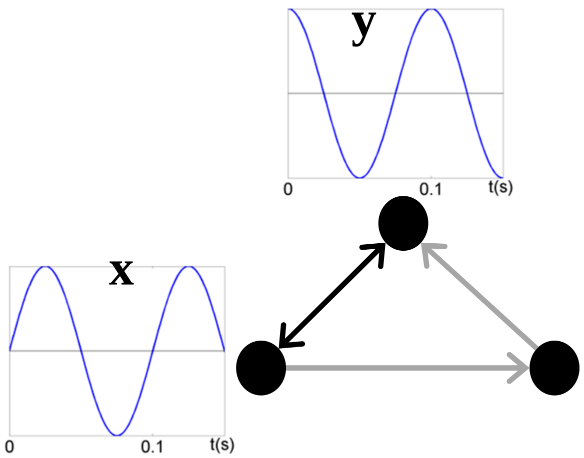
Cross-Correlation

Sensitive to Field-spread (when $l=0$), Undirected, Indirect, Linear

$$c_{xy}(l) = \left\langle \left(x_t - \bar{x}\right)\left(y_{t+l} - \bar{y}\right)\right\rangle_t$$

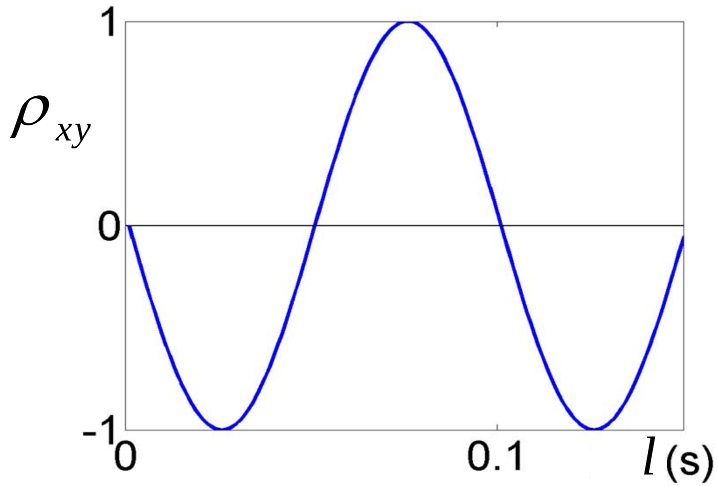
Cross-covariance

l = *"lag"*



$$\rho_{xy}(l) = \frac{c_{xy}(l)}{\sigma_x \sigma_y}$$

Cross-correlation



Coherency
(Fourier transform of cross-covariance)

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Sensitive to Field-spread, Undirected, Indirect, Linear

$$c_{xy}(l) = \left\langle \left(x_t - \bar{x}\right)\left(y_{t+l} - \bar{y}\right) \right\rangle_t$$

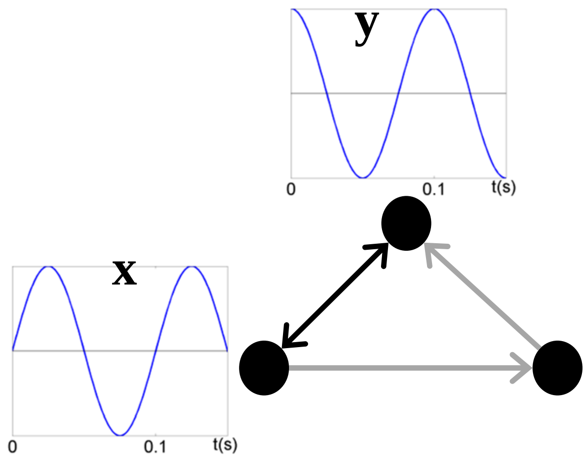
Cross-covariance

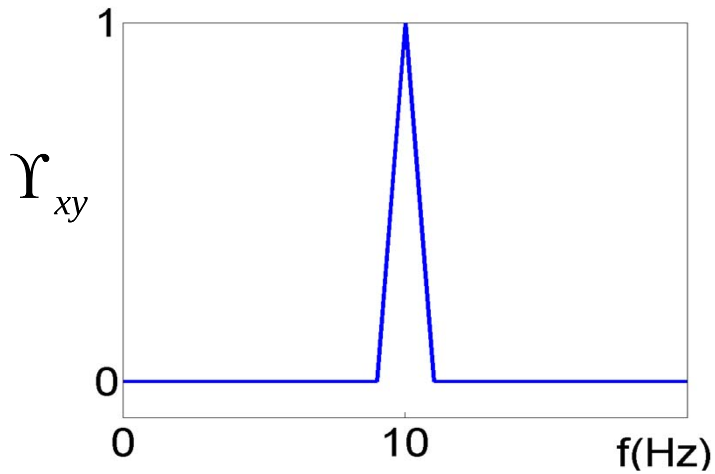
$$C_{xy}(f) = \sum_l c_{xy}(l) e^{-2\pi i.l.f}$$

Coherency

$$\Upsilon_{xy}(f) = \frac{\left|C_{xy}(f)\right|^2}{\left|C_{xx}(f)\right|\left|C_{yy}(f)\right|}$$

(Magnitude-squared) Coherence





Digression on Complex Numbers

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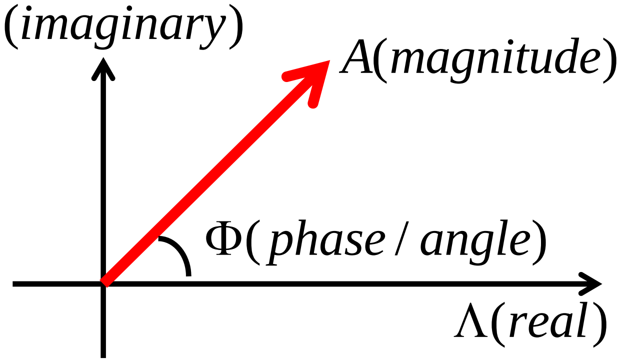
An oscillation of frequency *f* can be represented in terms of amplitude and phase (polar coordinates), which can also be represented by a complex number

$$C(f) = A(f)e^{i\Phi(f)}$$

$$= \Lambda(f) + i\Psi(f)$$



$$A(f) = |C(f)| = \sqrt{\Lambda^2(f) + \Psi^2(f)}$$

$$\Phi(f) = \arctan(\Psi(f) / \Lambda(f))$$

Coherence

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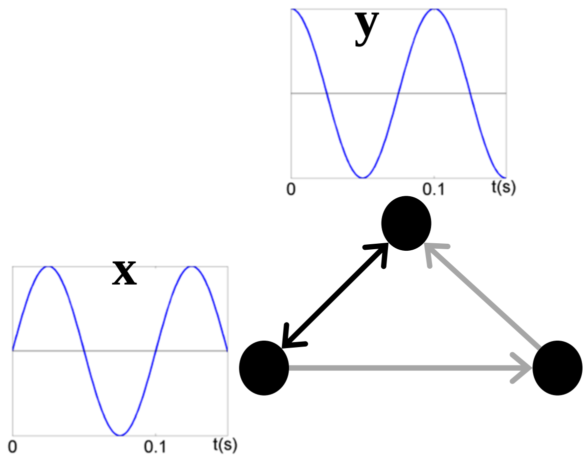
Sensitive to Field-spread, Undirected, Indirect, Linear

$$c_{xy}(l) = \left\langle \left(x_t - \bar{x}\right)\left(y_{t+l} - \bar{y}\right) \right\rangle_t$$

Cross-covariance

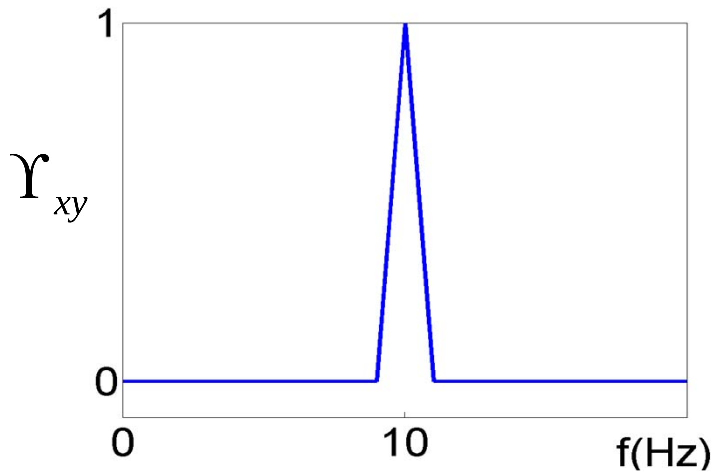


$$C_{xy}(f) = \sum_l c_{xy}(l) e^{-2\pi i.l.f}$$

Coherency

$$\Upsilon_{xy}(f) = \frac{\left|C_{xy}(f)\right|^2}{\left|C_{xx}(f)\right|\left|C_{yy}(f)\right|}$$

(Magnitude-squared) Coherence



Imaginary Coherency

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Immune to Field-spread, Undirected, Indirect, Linear

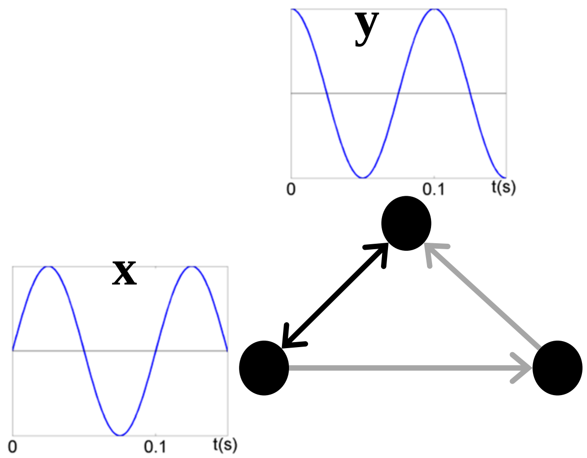
$$c_{xy}(l) = \left\langle \left(x_t - \bar{x}\right)\left(y_{t+l} - \bar{y}\right) \right\rangle_t$$

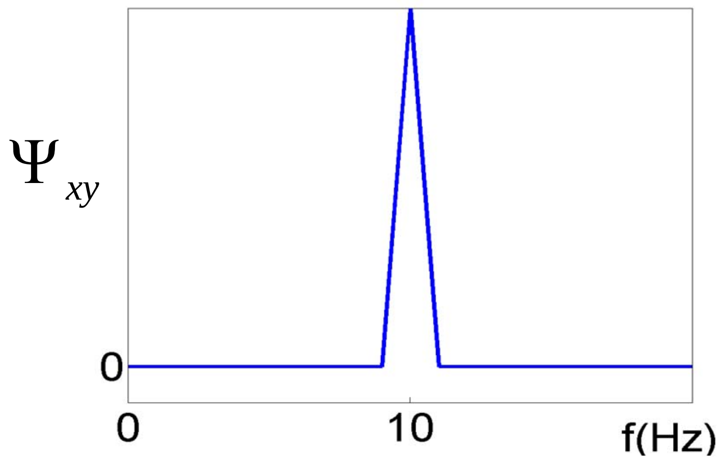
$$C_{xy}(f) = \sum_l c_{xy}(l) e^{-2\pi i.l.f}$$

Coherency

$$\Psi_{xy}(f) = imag(C_{xy}(f))$$

Imaginary Coherency

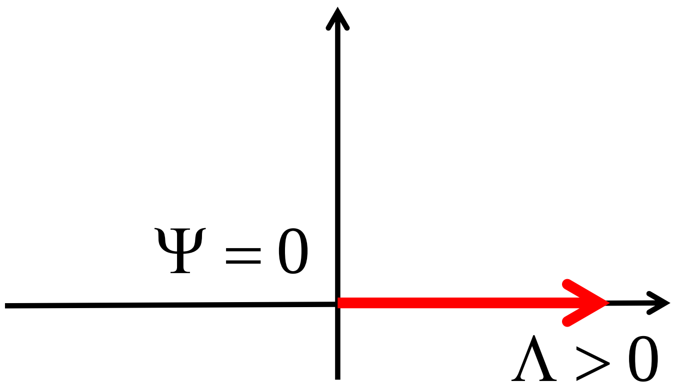


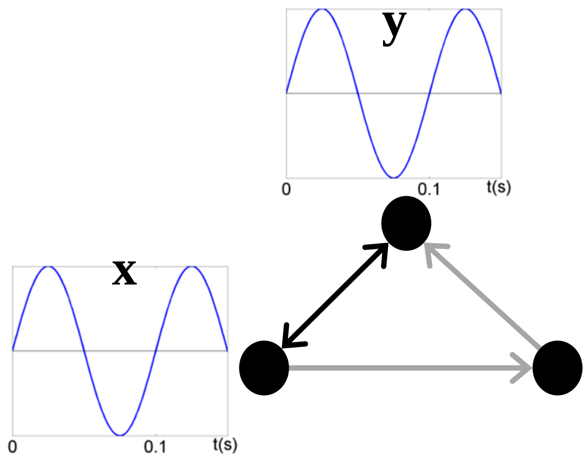


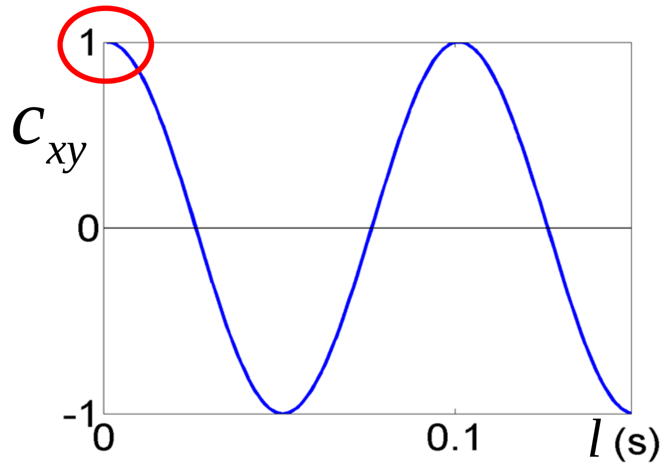
Nolte et al (2004) Clin Neurophys

Imaginary Coherency

A zero imaginary component implies a phase of the coherency of either 0º or 180º, which could be caused by field-spread…







$$\Psi_{xy}(f) = imag(C_{xy}(f))$$

Nolte et al (2004) Clin Neurophys

Imaginary Coherency

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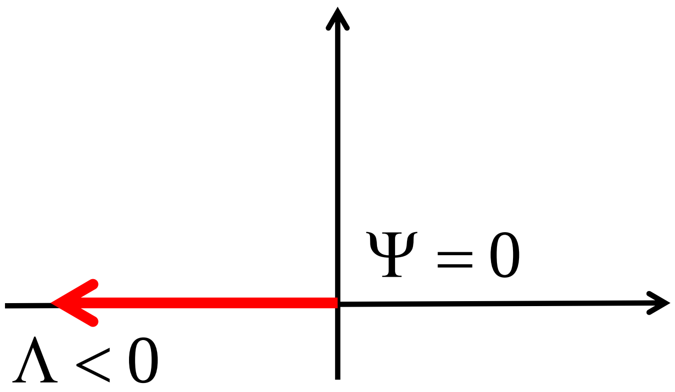
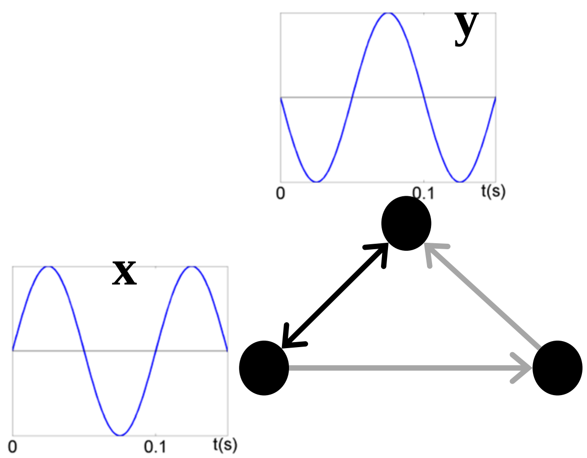
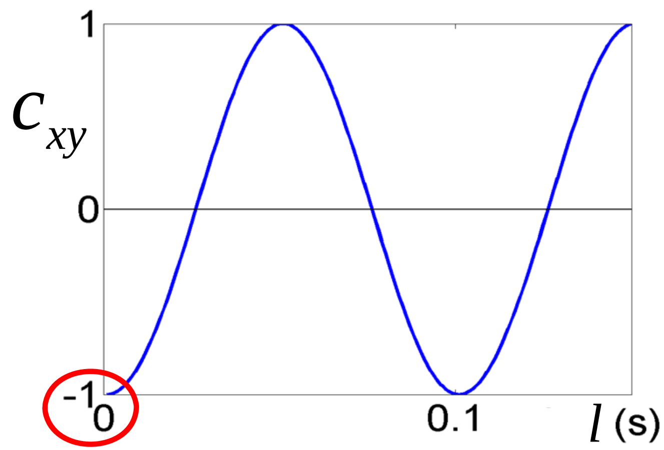
A zero imaginary component implies a phase of the coherency of either 0º or 180º, which could be caused by field-spread…







$$\Psi_{xy}(f) = imag(C_{xy}(f))$$

Nolte et al (2004) Clin Neurophys

Imaginary Coherency

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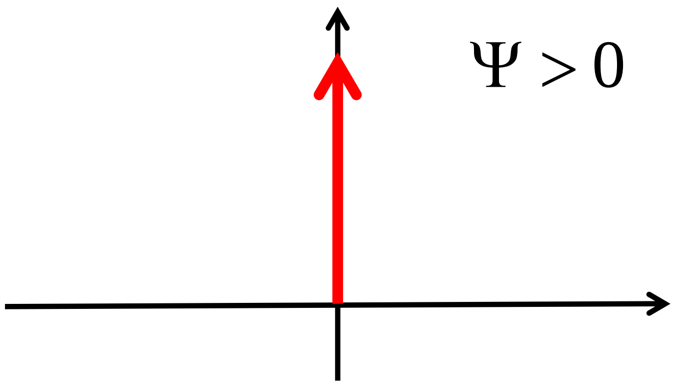
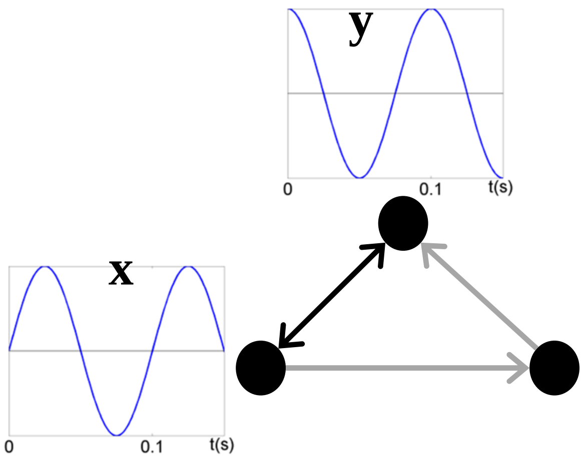
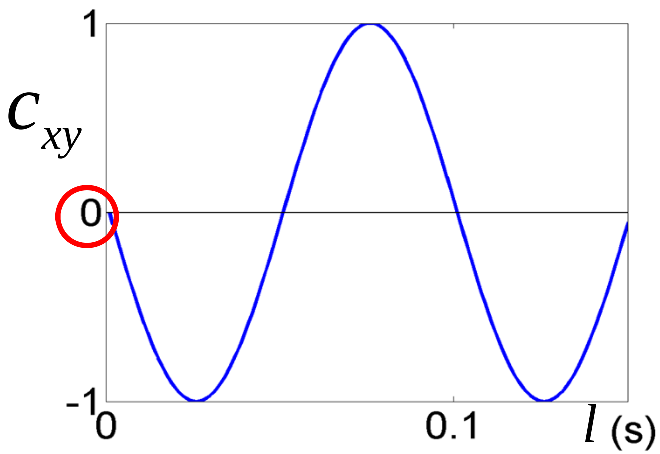
…whereas a NON-zero imaginary component implies a phase of the coherency other than 0º or 180º, which can NOT be caused by field-spread





$$\Psi_{xy}(f) = imag(C_{xy}(f))$$

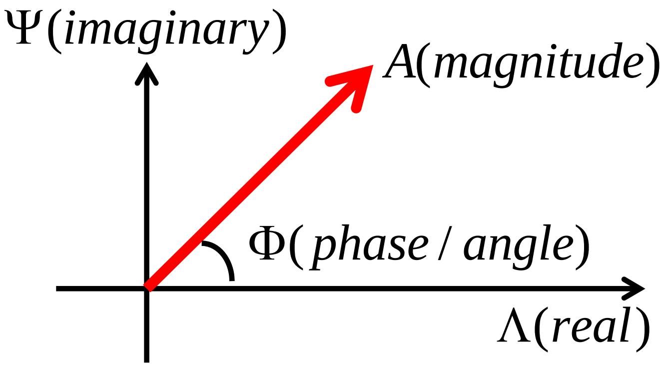


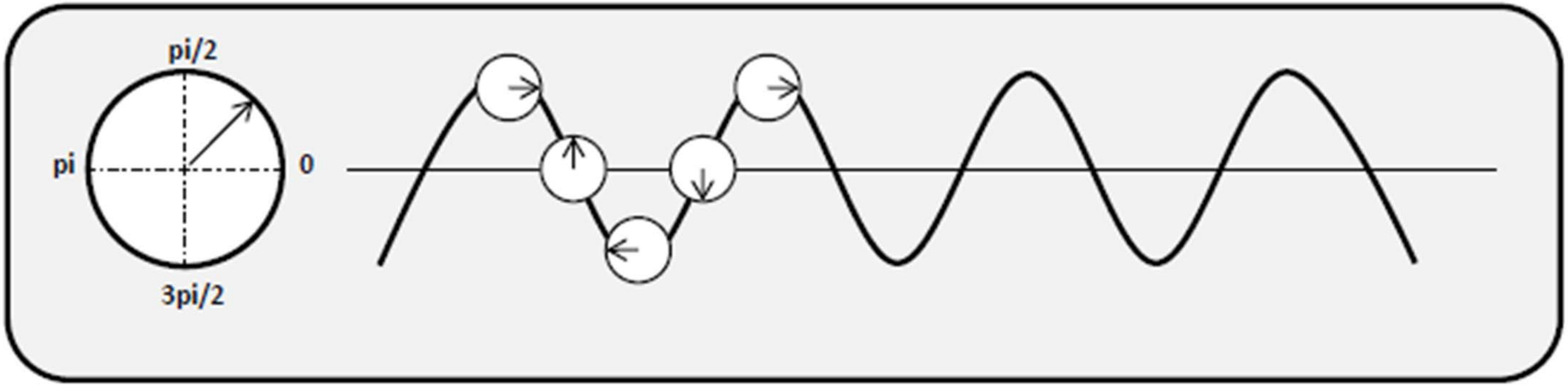
Nolte et al (2004) Clin Neurophys

Digression on Analytic Signals

A signal can be represented analytically in terms of its amplitude and phase over time (within a narrow frequency band) (e.g, using Hilbert transform)

$$x(t, f) = A(t, f)e^{i\Phi(t,f)}$$





Phase-related Measures

Immune to Field-spread, Undirected, Indirect, Linear

$$x(t) = A_x(t)e^{i\Phi_x(t)}$$
$$y(t) = A_y(t)e^{i\Phi_y(t)}$$

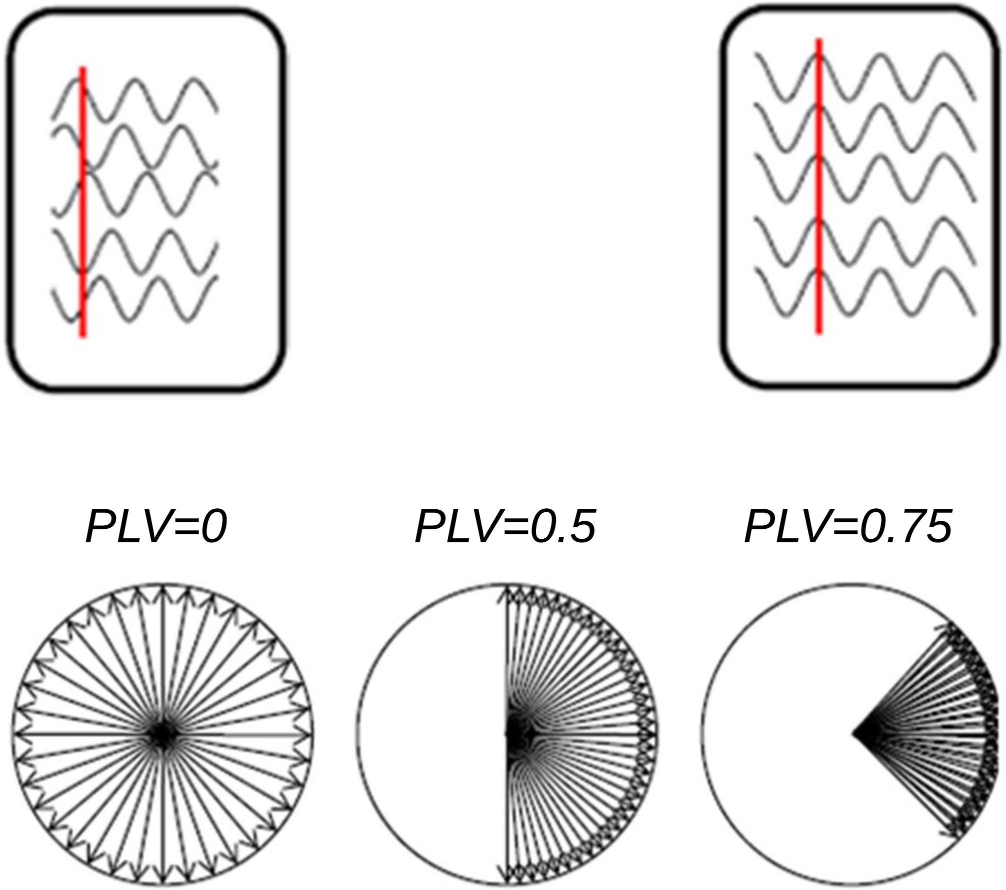
$$\Delta\Phi(t) = \Phi_x(t) - \Phi_y(t)$$

$$PLV = \left\langle e^{i\Delta\Phi(t)} \right\rangle_t$$

Phase-Locking Value

$$PLI = \left\langle sign(\Delta\Phi(t)) \right\rangle_t$$

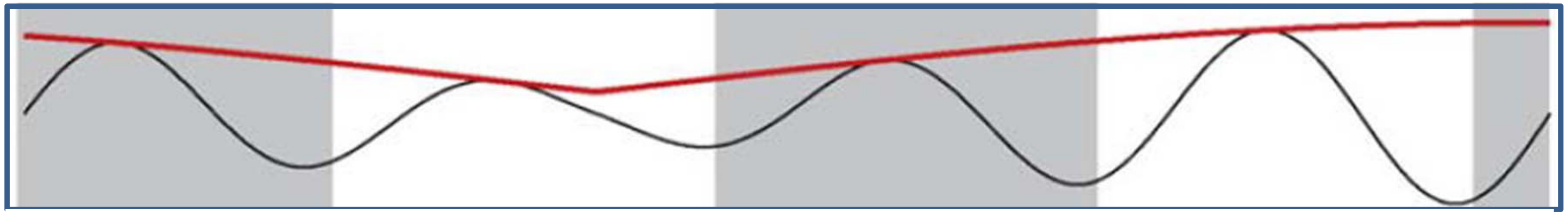
Phase-Lag Index



Stam et al (2007) Human Brain Mapp

More complex coupling

$x(t)$



$y(t)$

Power-Power
$A_x(t) : A_y(t)$

Phase-Phase
$\Phi_x(t) : \Phi_y(t)$

Phase-Freq
$\Phi_x(t) : F_y(t)$

Phase-Power
$\Phi_x(t) : A_y(t)$

Jenson & Colgin (2007) TICS

Talk Overview

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2. Linear vs Nonlinear measures

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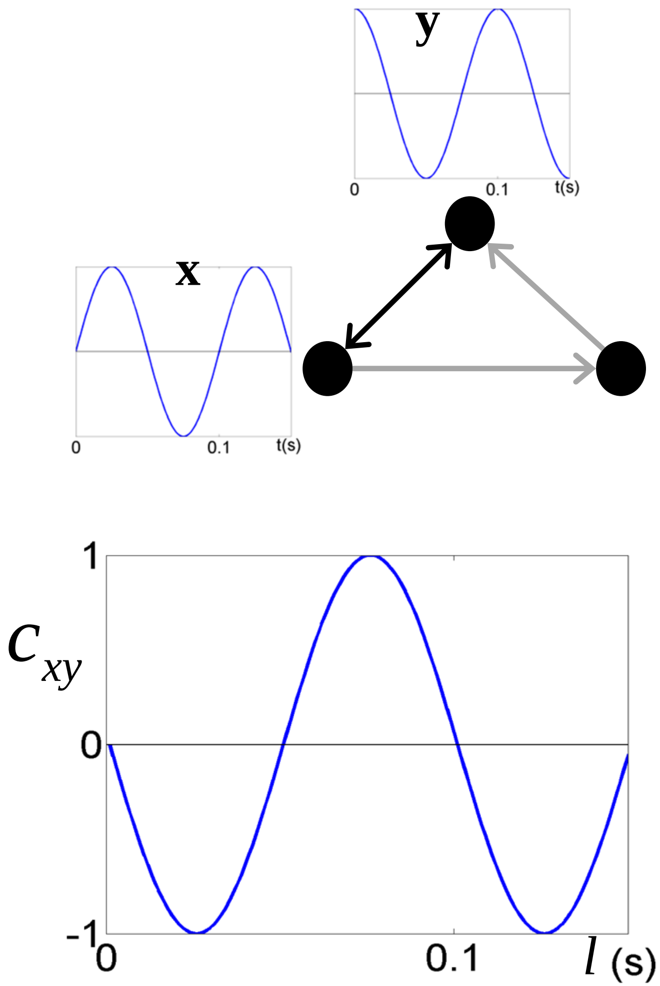
Nonlinear Measures



Nonlinear Measures

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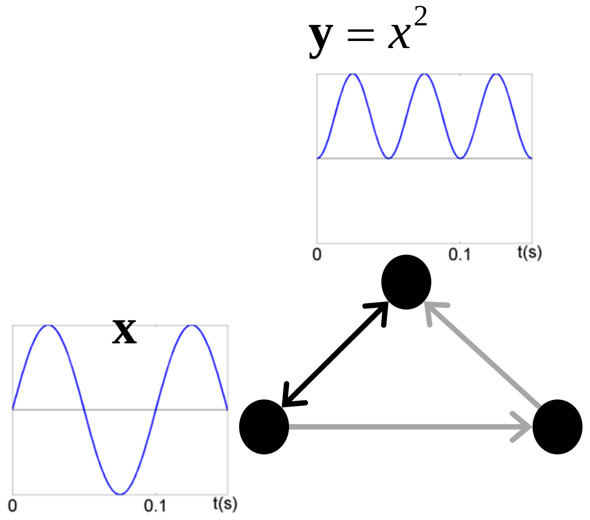
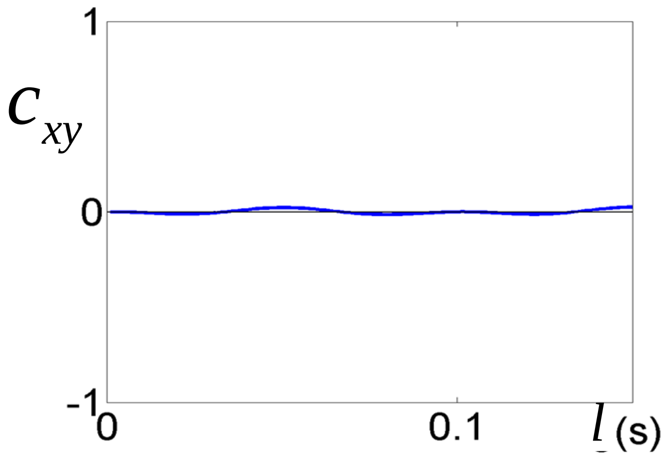
Cross-correlation/coherence insensitive to nonlinear dependencies





Mutual Information

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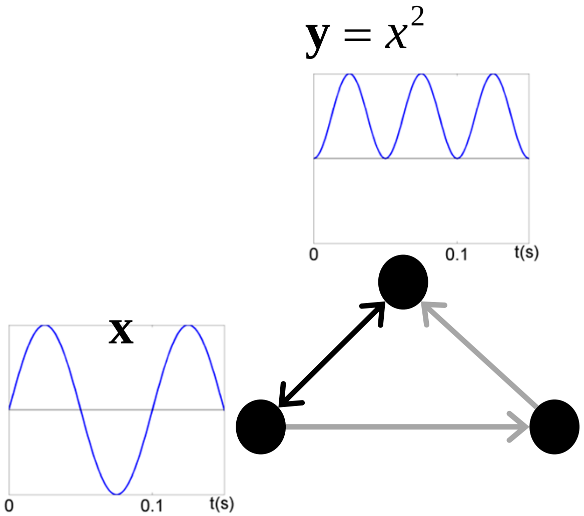
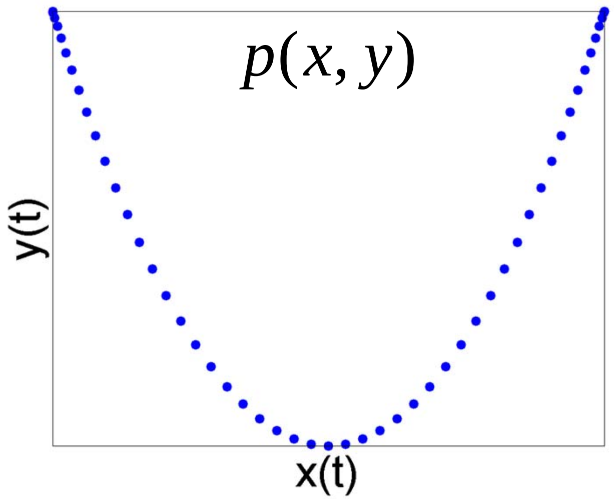
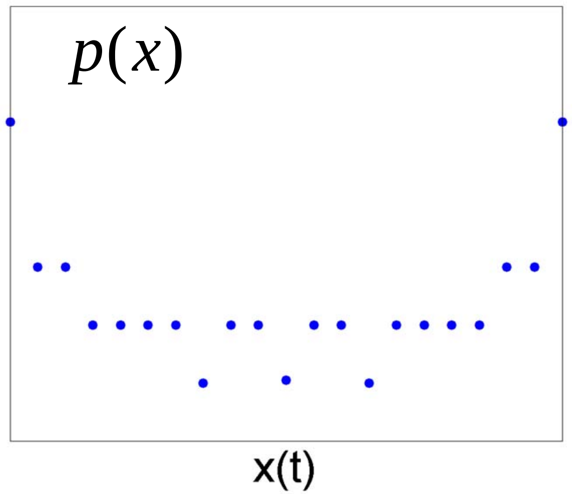
Sensitive to Field-spread, Undirected, Indirect, Nonlinear

$$MI(x,y) = \sum_{x,y} p(x,y) \log\left(\frac{p(x,y)}{p(x)\,p(y)} \right)$$







Mutual Information

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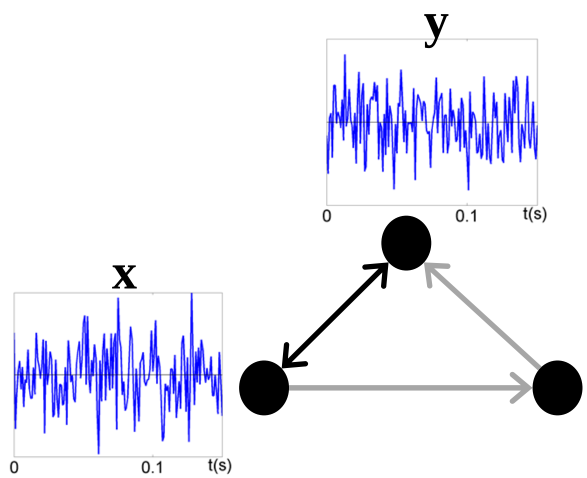
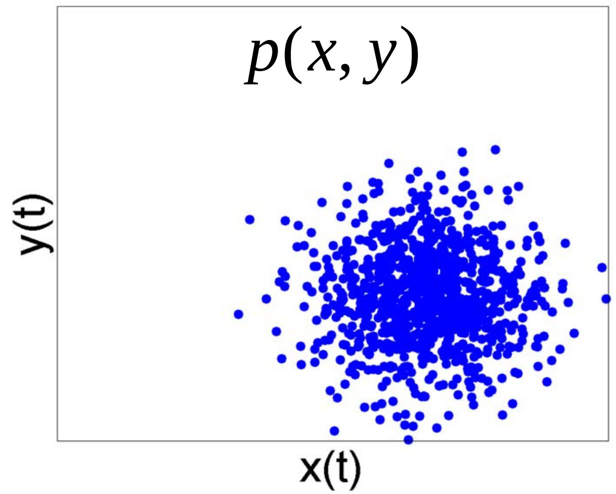
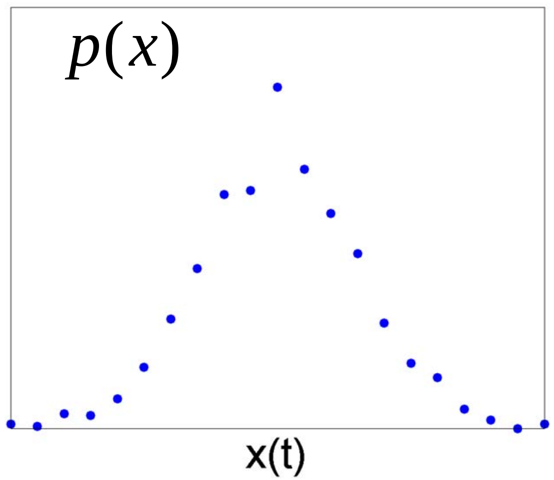
Sensitive to Field-spread, Undirected, Indirect, Nonlinear

$$MI(x,y) = \sum_{x,y} p(x,y) \log\left(\frac{p(x,y)}{p(x)\,p(y)}\right)$$







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Directed Measures

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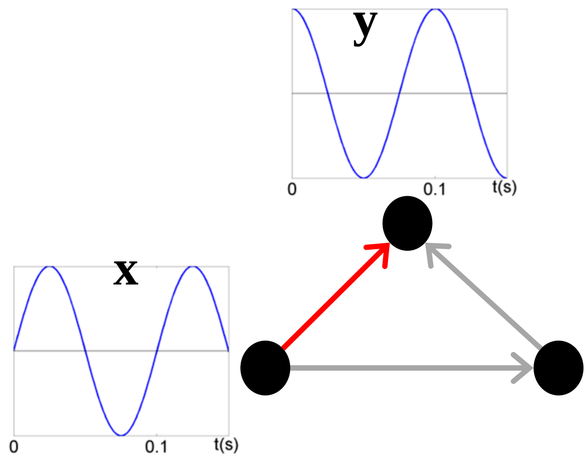
(bivariate) Granger Causality

Immune to Field-spread, Directed, Indirect, Linear

Auto-regressive model to order *p*
(assuming mean-corrected, with residuals *e*)

$$y_y(t) = a_1 y(t-1) + \ldots + a_p y(t-p) + e(t)$$

$$= \sum_{l=1}^{p} a_l y(t-l) + e(t)$$



Augmented model including past values of *x* (to order *q*)

$$y_{y \leftarrow x}(t) = \sum_{l=1}^{p} a_l y(t-l) + \sum_{l=1}^{q} b_l x(t-l) + e(t)$$

If classical F-test shows *b* parameters are non-zero, then *x* “Granger-causes” *y*
(special case of MVAR; see later)

Directed, Nonlinear Measures

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Transfer Entropy (lagged generalisation of mutual information)

Immune to Field-spread, Directed, Indirect, Nonlinear

$$TE_{y \to x}(l) = \sum_{x_{n+l}, x_n, y_n} p(x_{n+l}, x_n, y_n) \log\left(\frac{p(x_{n+l} \mid x_n, y_n)}{p(x_{n+l} \mid x_n)}\right)$$

$$TE_{x \to y}(l) = \sum_{y_{n+l}, y_n, x_n} p(y_{n+l}, x_n, y_n) \log\left(\frac{p(y_{n+l} \mid x_n, y_n)}{p(y_{n+l} \mid y_n)}\right)$$

Schreiber (2000) Phys Rev Letters

Generalised Synchronisation

Sensitive to Field-spread, Directed, Indirect, Nonlinear

$$x_t = [x_t, x_{t+l}, \ldots, x_{t+(m-1)l}]$$

$$y_t = [y_t, y_{t+l}, \ldots, y_{t+(m-1)l}]$$

$$S(x \mid y) = \frac{1}{N} \sum_{t=1}^{N} \frac{D_t(x)}{D_t(x \mid y)}$$

m is the embedding dimension and *l* lag

D is the Euclidean distance between x_t and embedded neighbours

Quian Quiroga et al (2000) Phys Rev E

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Direct Measures

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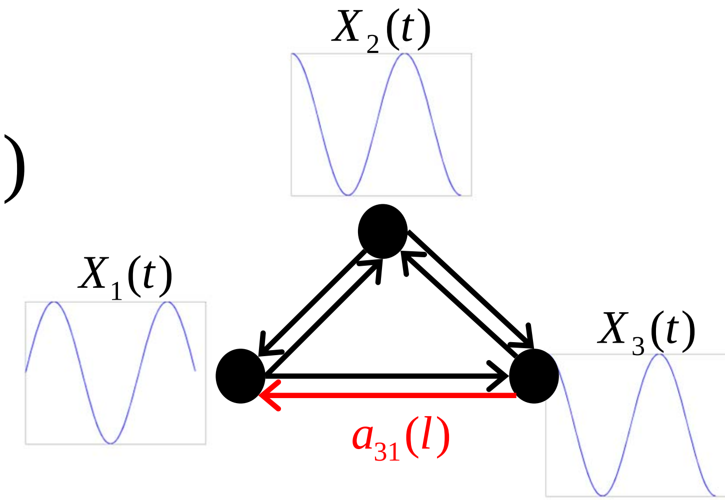
Multivariate Autoregressive Modelling (MVAR)

Immune to Field-spread, Directed, Direct, Linear

$$X_i(t) = \sum_{j=1}^{N} \sum_{l=1}^{p} a_{ij}(l) X_j(t-l) + u_i(t)$$



Various summary measures, eg,
Partial Directed Coherence (PDC):

$$PDC_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\sum_{k=1}^{M} \left|A_{kj}(f)\right|^2}}$$

$$A_{ij}(f) = F(a_{ij}(l))$$

Generalised form of Granger Causality

Though insensitive to true zero-lag dependencies (occur in reality?)

Baccala & Sameshima (2001) Biol Cybernet

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Generative Models

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Immune to Field-spread, Directed, Direct, Nonlinear, model-driven

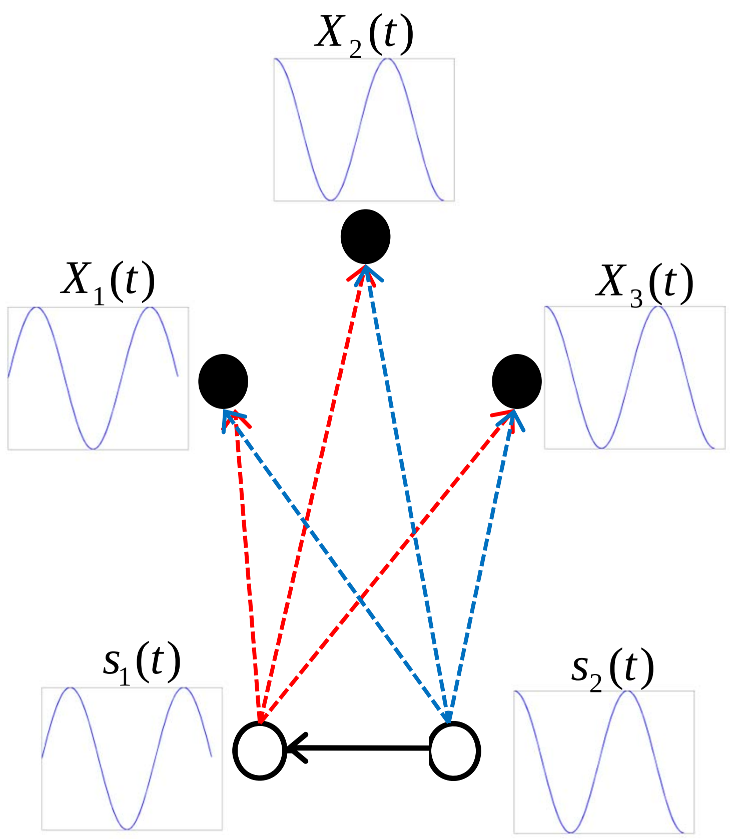
Connectivity modelled between sources

Projected to sensors via headmodel

Typically a handful of sources, and a range of networks fit to data

Bayesian methods for comparing which network model is best

Dynamic Causal Modelling (DCM) is one approach



Chen et al, 2009, Neuroimage

Measure	Immume to Field Spread	Directed	Nonlinear	Direct
Cross-Correlation	Y (l>0)	N	N	N
Coherence	Y (imaginary)	N	N	N
PLV/PLI	Y	N	N	N
Granger (bivariate)	Y	Y	N	N
Mutual Information	N	N	Y	N
Transfer Entropy	Y	Y	Y	N
Generalised Synchrony	N	Y	Y	N
MVAR (eg, PDC)	Y	Y	Y	N
Generative (eg, DCM)	Y	Y	Y	Y

The End