Reconstructing Effective Phase Connectivity of Oscillator Networks from Observations

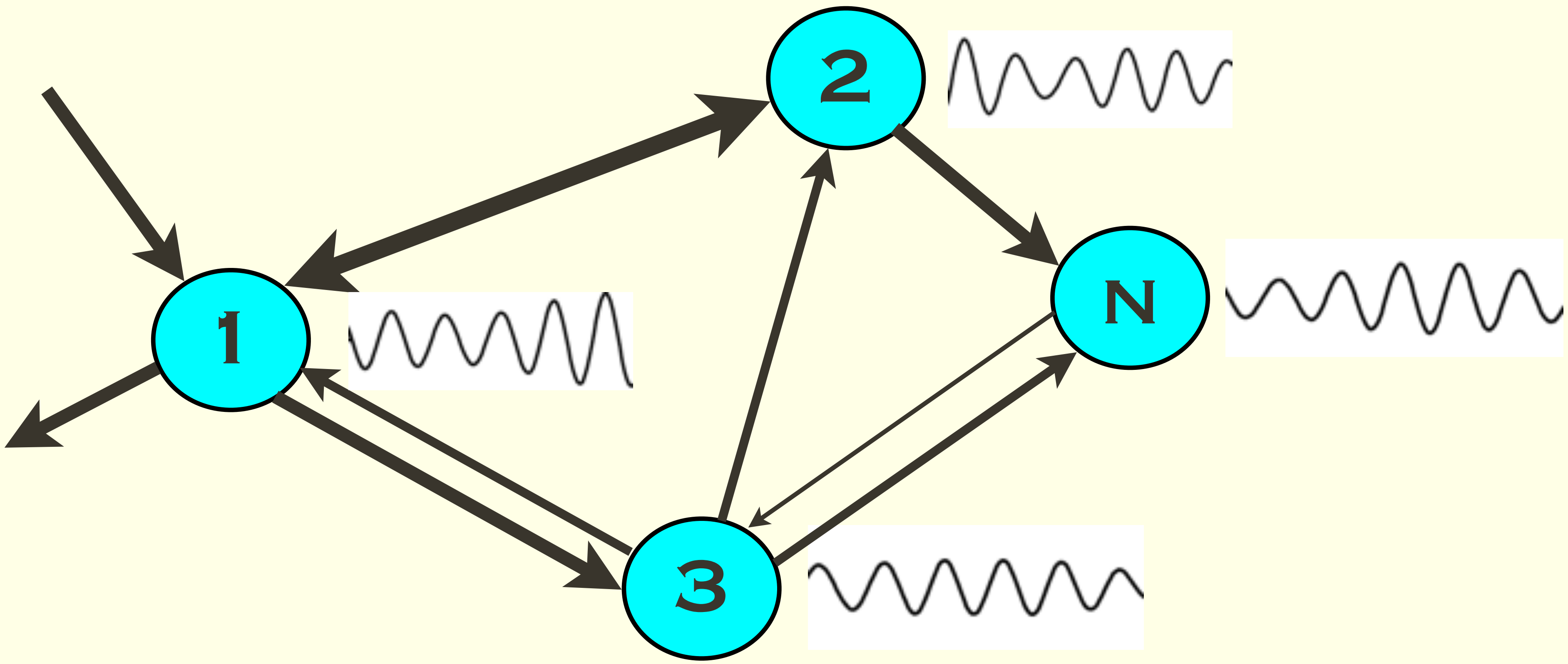
Björn Kralemann

Arkady Pikovsky

Michael Rosenblum

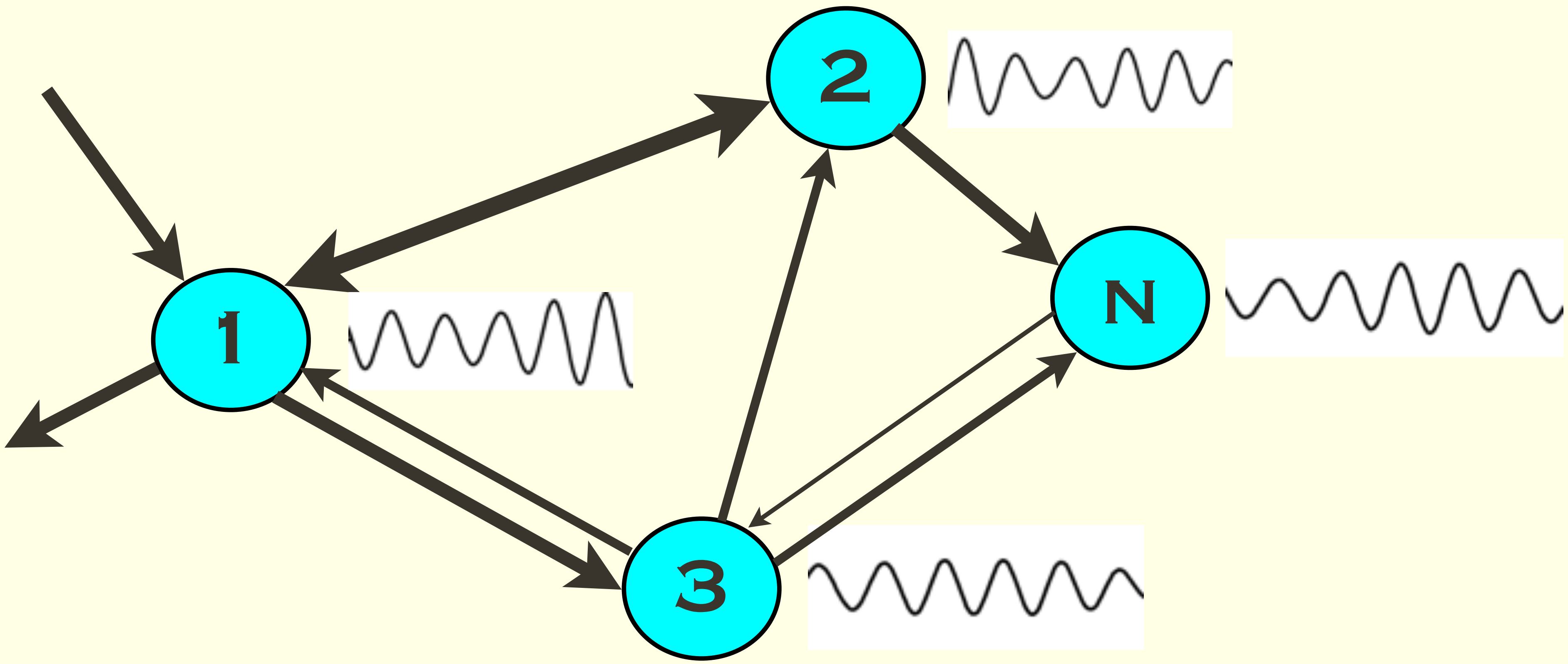
Institute of Physics and Astronomy, Potsdam University, Germany

Formulation of the problem



- Data: we have oscillatory signals coming from several ***weakly coupled self-sustained oscillators***
- Our goal: to say as much as possible about the systems and their interaction
- Particular problem: to reconstruct ***directional connectivity***
- What kind of connectivity do we detect?
  - this will be discussed in detail later

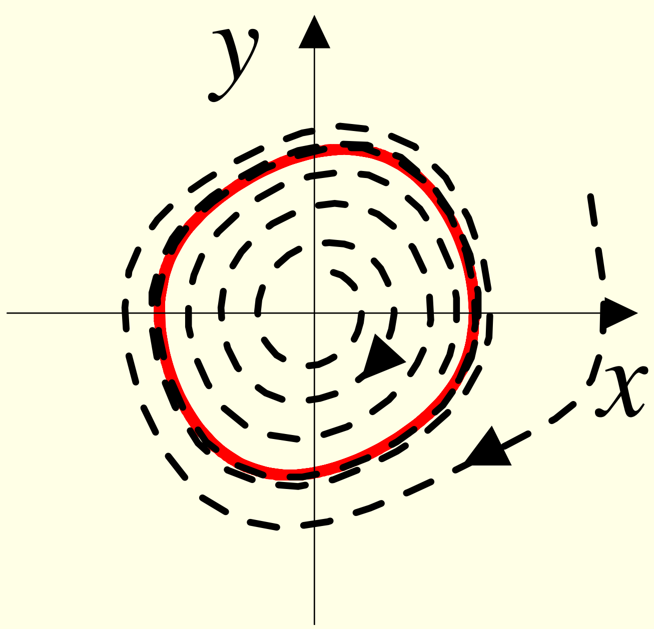
General problem

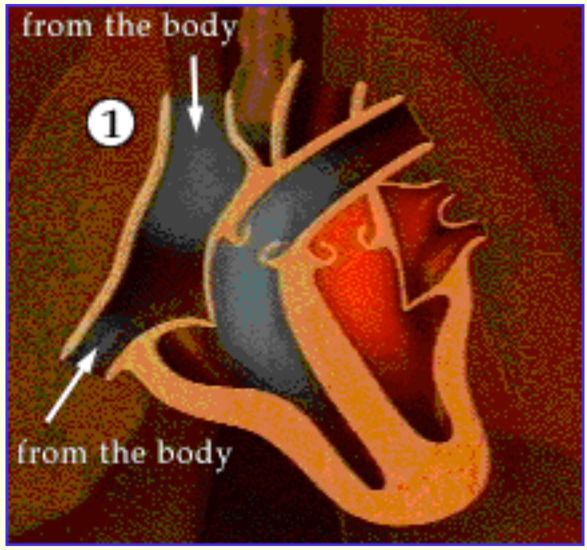


- Data: we have oscillatory signals coming from several ***weakly coupled self-sustained oscillators***

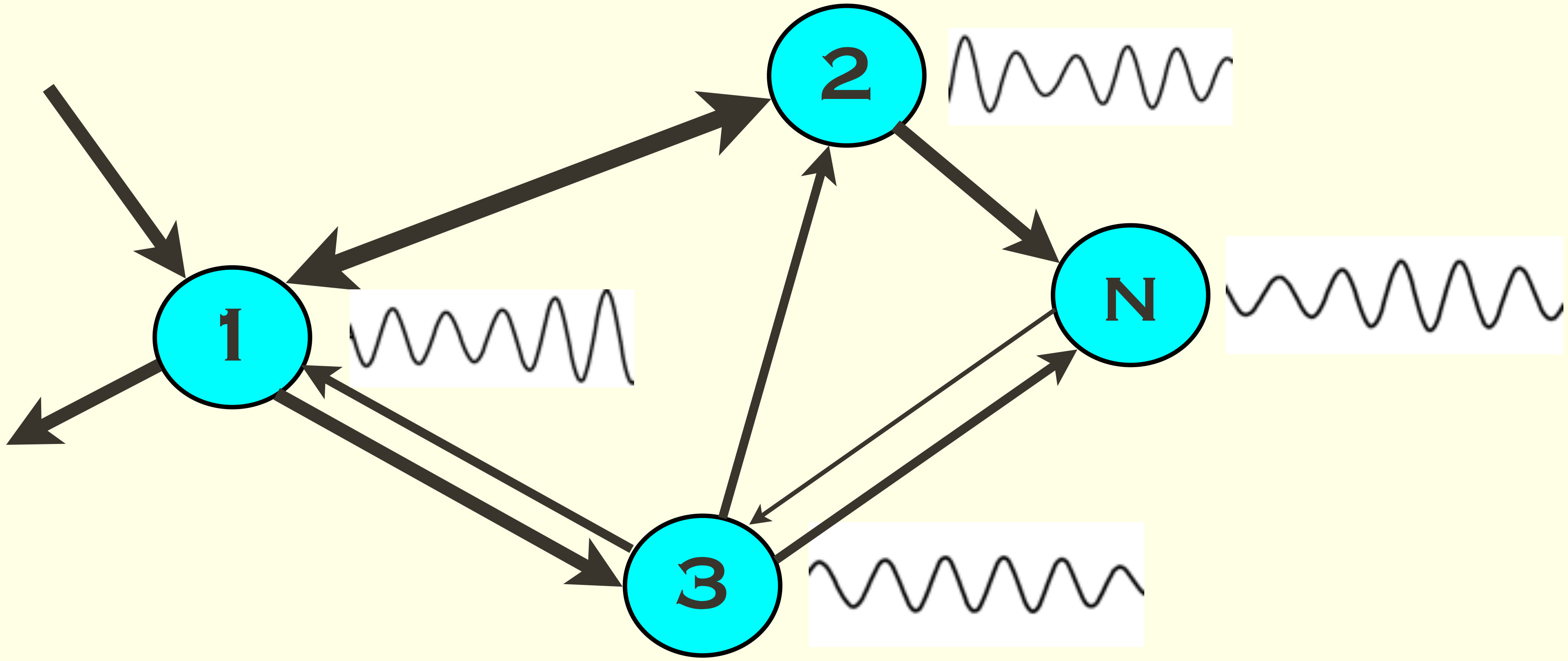
Active oscillators, systems generating endogenous rhythms

Dissipative nonlinear systems, limit cycle in the phase space





Formulation of the problem



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- Our goal: to say as much as possible about the systems and their interaction
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Our approach: we quantify the interaction by reconstructing the model of phase dynamics from data

Key idea: invariant (with respect to observables) model reconstruction

Example: we analyze cardio-respiratory interaction; electrocardiogram and arterial pulse are different observables of the same system: hence, they should yield similar results!!

Content of the talk

- Phase dynamics of coupled oscillators (summary of the theory)

- From scalar time series to phase in two steps
  - from time series to **protophase**
  - **protophase-to-phase** transformation

- Two coupled oscillators:
  - coupling functions and phase response curves
  - application to cardio-respiratory interaction in healthy humans

- Small networks: directed connectivity via triplet analysis

- Summary and **link to software**

Phase dynamics of two coupled oscillators (see, e.g., Kuramoto, 1984)

autonomous frequencies

coupling functions

phases

Phase equations $$\boxed{\frac{d\varphi_{1,2}}{dt} = \omega_{1,2} + q_{1,2}(\varphi_{1,2}, \varphi_{2,1})}$$

can be derived from the full equations by means of a perturbation approach, i.e. in the weak coupling approximation

In typical cases $$q_1(\varphi_1, \varphi_2) = Z_1(\varphi_1) I_2(\varphi_2)$$

phase response curve (PRC)

forcing

Important remark I

Phase equations can be analytically derived in the
weak coupling approximation

However, they are valid as long as the motion is quasiperiodic.
Even if they cannot be derived, they can be obtained from data!

As long as the systems remain asynchronous and not chaotic,
the phase space trajectory lies on the torus $\longrightarrow$
the motion can be parameterized by two phases

Hence, validity of our approach goes beyond the weak coupling approximation!

Important remark II

Phase equations are valid also for transients, not only for steady state

Hence, our approach does not require stationarity of the data!

Simplest case: two oscillators
Phase dynamics equations

$$\frac{d\varphi_{1,2}}{dt} = \omega_{1,2} + q_{1,2}(\varphi_{1,2}, \varphi_{2,1})$$

Phase equations can be reconstructed, e.g. by fit,

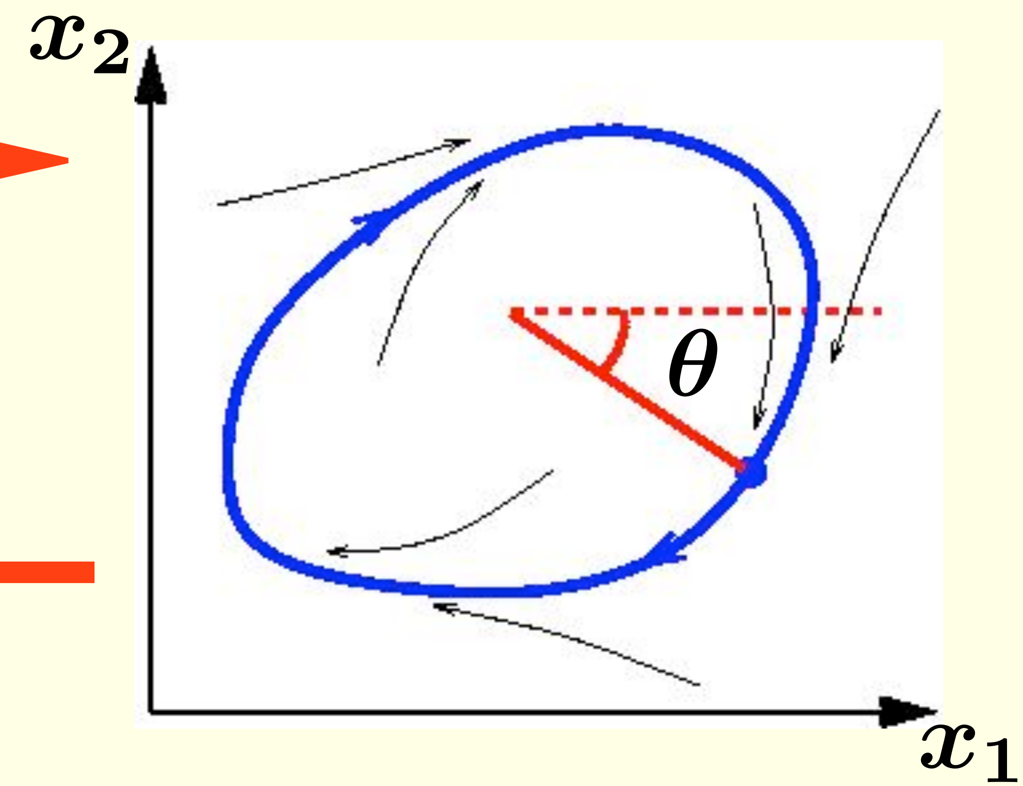
but we need to know phases $\varphi_1(t), \varphi_2(t)$

How to obtain phases from scalar times series?

Protophase of an autonomous oscillator

Limit cycle in the phase space

Equations $\dot{\mathbf{x}} = \mathbf{G}(\mathbf{x})$



Protophase θ

Protophase is a variable along the limit cycle, such that

- it grows monotonically, but generally not uniformly, i.e. $\dot{\theta} = f(\theta)$
- gains 2π with each rotation
- depends on the choice of observables, embedding, etc, i.e. is not invariant

From protophase to phase

Phase is a variable along the limit cycle, such that

- it ***grows uniformly***, $\dot{\varphi} = \omega = \text{const}$
- gains $\mathbf{2\pi}$ with each rotation
- does not depend on the choice of observables, embedding, etc, i.e. is invariant

Phase can be obtained from a protophase by a simple transformation $\theta \;\rightarrow\; \varphi(\theta)$:

$$\frac{d\varphi}{dt} = \omega \quad \Rightarrow \quad \frac{d\varphi}{d\theta}\frac{d\theta}{dt} = \omega \quad \Rightarrow \quad \frac{d\varphi}{d\theta} = \frac{\omega}{\dot{\theta}}$$

or, in integral form: $\quad \varphi = \omega \int_0^\theta \frac{d\theta}{\dot{\theta}}$

From time series to phase in two steps

1. From an oscillatory signal a protophase can be obtained, e.g., by means of the Hilbert Transform, via linear interpolation between marker events, or by other ***ad hoc*** techniques.

   Important remark: choice of the optimal protophase is yet an unsolved problem!

2. Phase is obtained from the protophase by means of the transformation $\theta \rightarrow \varphi(\theta)$

How to perform this transformation for noisy data?

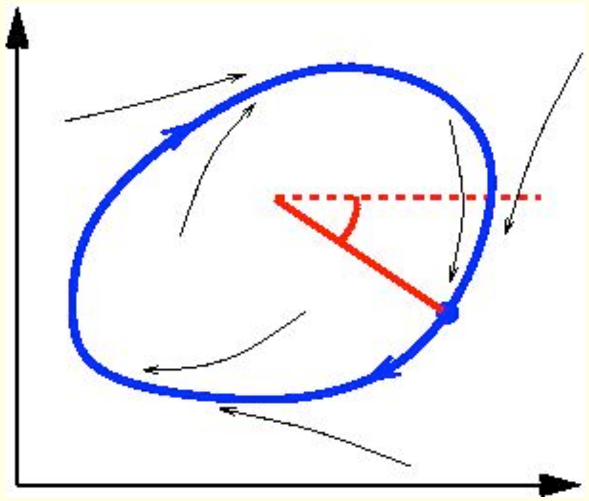
Protophase-to-phase transformation for noisy data

For noise-free system we have: $$\frac{d\varphi}{d\theta} = \frac{\omega}{\dot{\theta}}$$

For noisy data we average the r.h.s.:

$$\frac{d\varphi}{d\theta} = \omega \left\langle \frac{dt}{d\theta}(\theta) \right\rangle_{\theta} = \sigma(\theta)$$

$(2\pi)^{-1}\sigma(\theta)$ is the probability density function of θ



Estimation of the probability density is a standard problem of data analysis, e.g., it can be written as an integral along the trajectory (Kralemann et al., Phys. Rev. E, 2008)

Transformation function $\sigma(\theta)$

With $\sigma(\theta) = \sum_n S_n e^{in\theta}$ the final transformation reads

$$\boxed{\varphi = \int_0^\theta \sigma(\theta')d\theta' = \theta + 2\sum_{n=1}^{\infty} \mathrm{Im}\left[\frac{S_n}{n}(e^{in\theta} - 1)\right]}$$

For a time series of N points Θ_k,

the Fourier coefficients of $\sigma(\theta)$ are:

$$\boxed{S_n = N^{-1}\sum_{k=1}^{N} e^{-in\Theta_k}}$$

Notice: this is a one-to-one transformation, not a filter

Why is the transformation $\theta \to \varphi$ important?

True equation in terms of phases $$\frac{d\varphi_1}{dt} = \omega_1 + q_1(\varphi_1, \varphi_2)$$

Equation in terms of protophases

small term

$$\frac{d\theta_1}{dt} = \omega_1 + f(\theta) + \hat{q}_1(\theta_1, \theta_2)$$

1. Generally not small
2. Has no physical meaning
3. Masks the term we need!

Why is the transformation $\theta \rightarrow \varphi$ important?

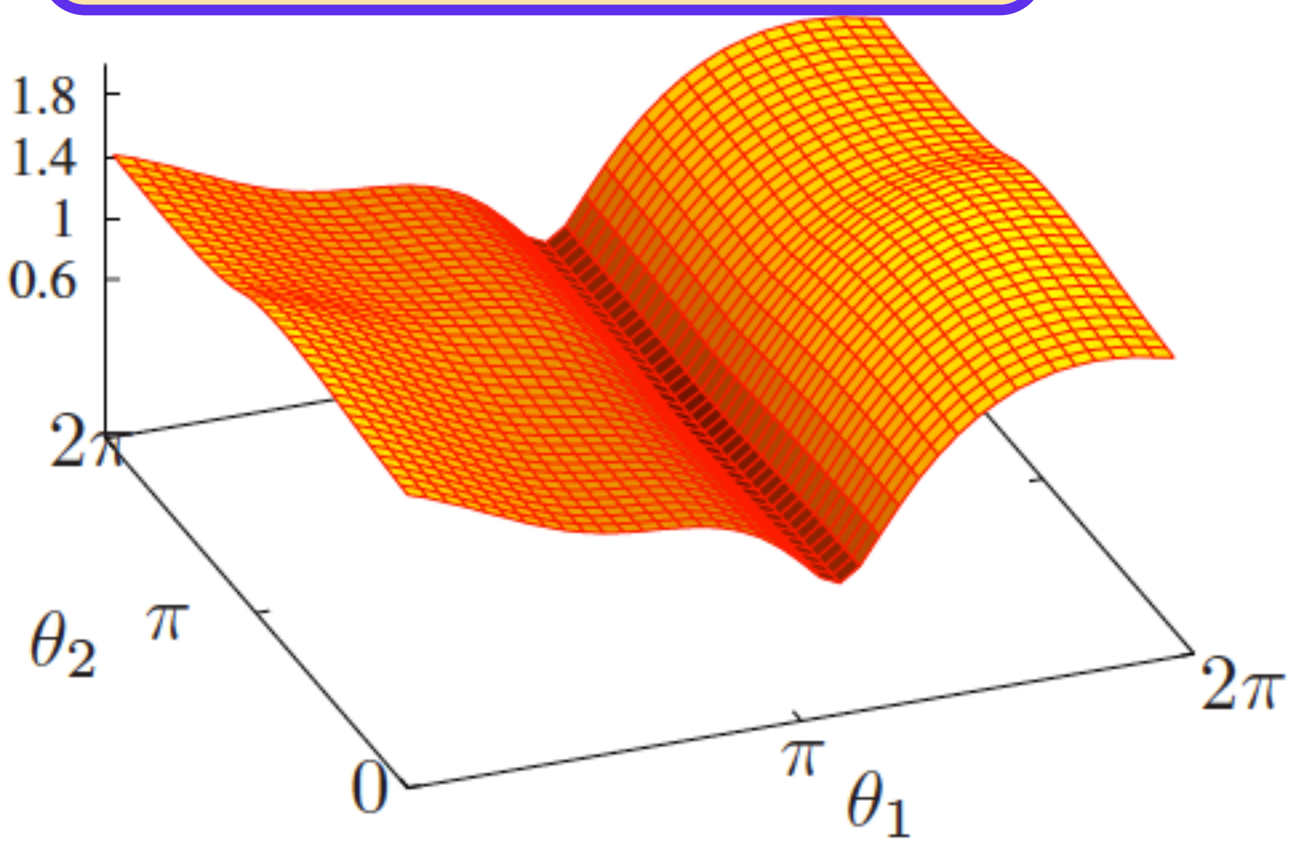
Simple, but illustrative example

$$\dot{\varphi}_1 = \omega_1 + \varepsilon_1 \sin(\varphi_2 - \varphi_1 - \beta_1)$$

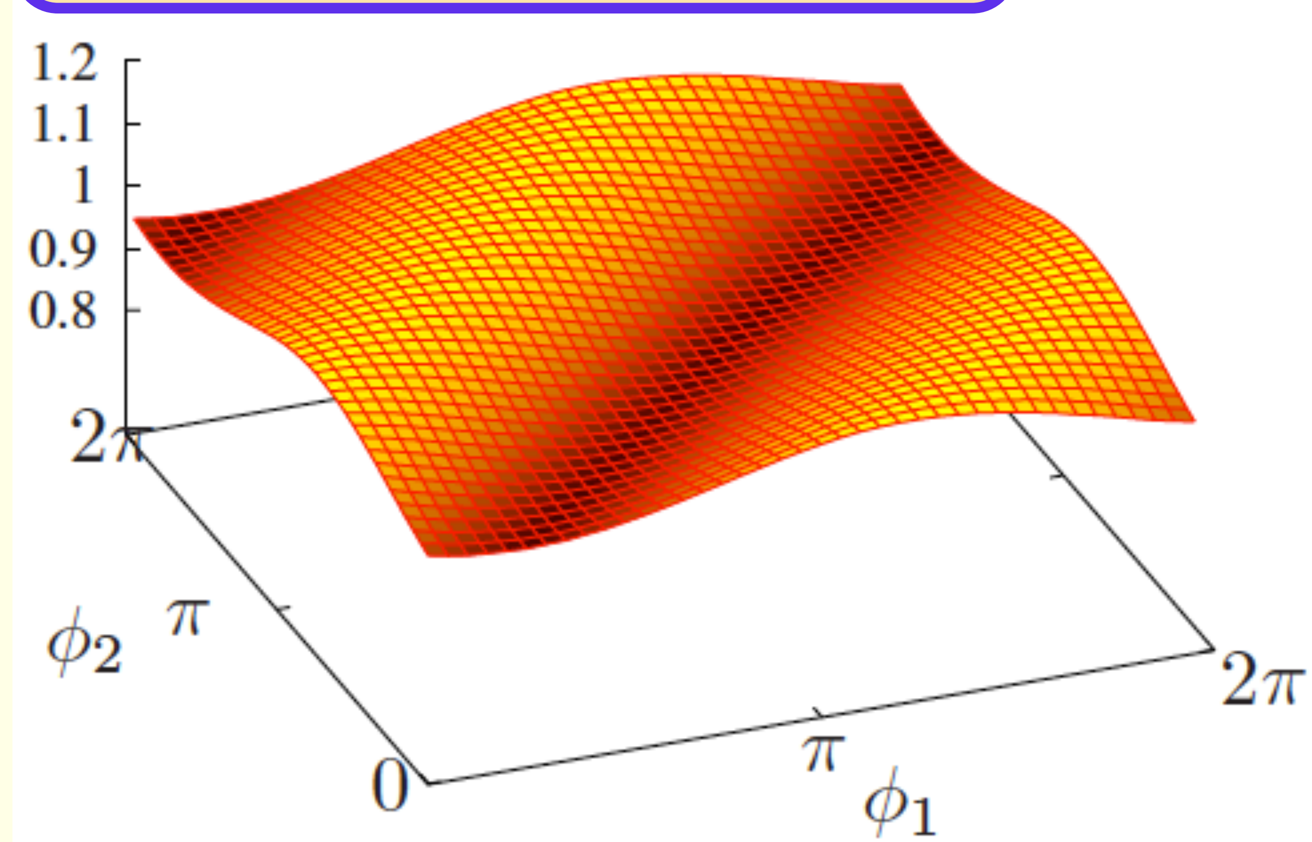
$$\dot{\varphi}_2 = \omega_2 + \varepsilon_2 \sin(\varphi_1 - \varphi_2 - \beta_2)$$

Protophases are distorted phases, this imitates nonlinearity in measurements: $\theta_{1,2} = \varphi_{1,2} + \frac{1}{2}\sin(\varphi_{1,2}) + \frac{1}{10}\cos(2\varphi_{1,2})$

Function of protophases



Function of phases



Why is the transformation $\theta \to \varphi$ important?

Even more simple example!

Data from two **nonidentical** and **uncoupled** Hindmarsh-Rose neurons (different values of the injected current)

Protophases via the Hilbert Transform

Synchronization index (phase locking value, mean phase coherence, ...)

- from protophases $\gamma = \left| \langle e^{i(\theta_1 - \theta_2)} \rangle \right| \approx \mathbf{0.13}$

- from phases $\gamma = \left| \langle e^{i(\theta_1 - \theta_2)} \rangle \right| \approx \mathbf{0.02}$

Phase equations for two coupled oscillators

$$\frac{d\varphi_{1,2}}{dt} = \omega_{1,2} + q_{1,2}(\varphi_{1,2}, \varphi_{2,1})$$

- Fourier-based technique: function $q_{1,2}(\varphi_{1,2}, \varphi_{2,1})$

  is 2π - periodic with respect to its arguments; it can be found by LMS fitting

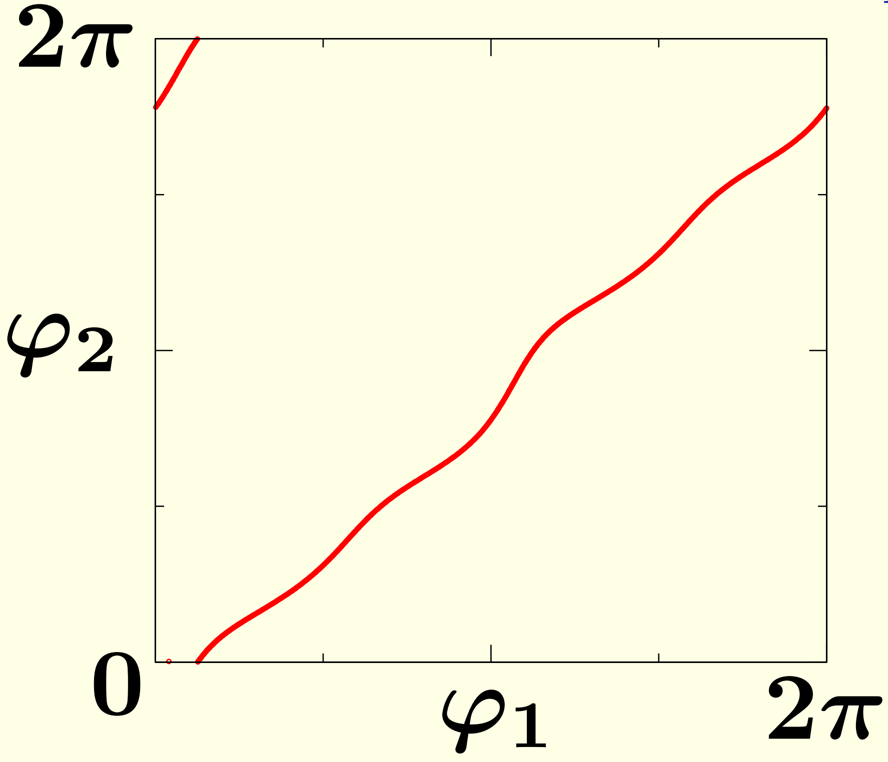
$$\omega_{1,2} + q_{1,2} = \sum_{l_1,l_2} \mathcal{F}^{(1,2)}_{l_1,l_2} \exp\left(il_1\varphi_1 + il_2\varphi_2\right)$$

- Kernel function estimation technique
- Bayesian technique (W. Penny et al., 2009)

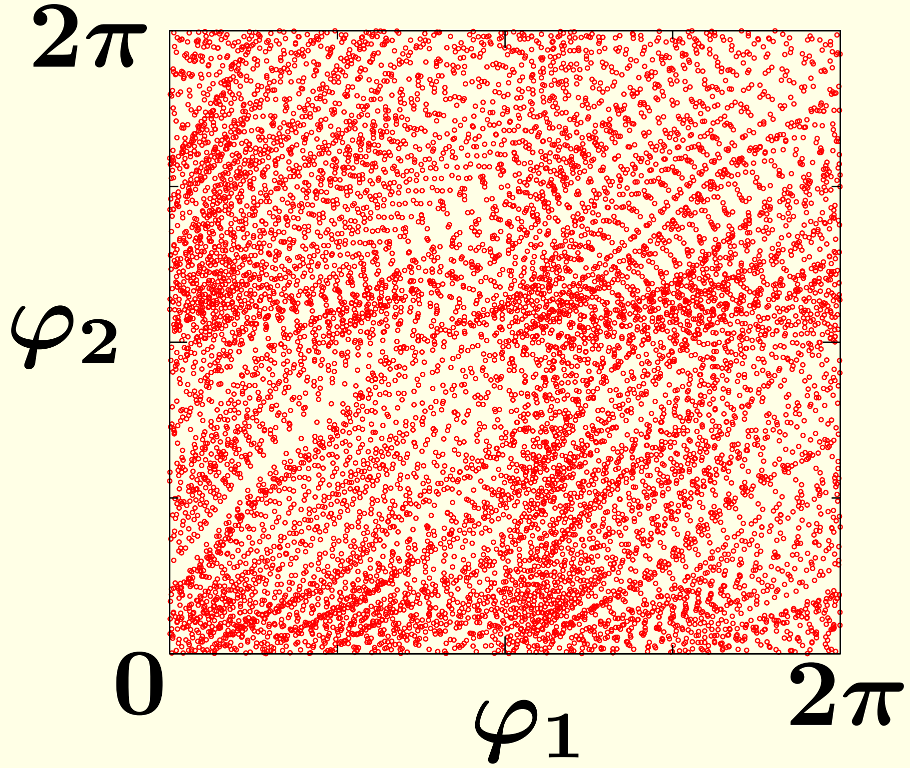
The approach works if the systems do not synchronize

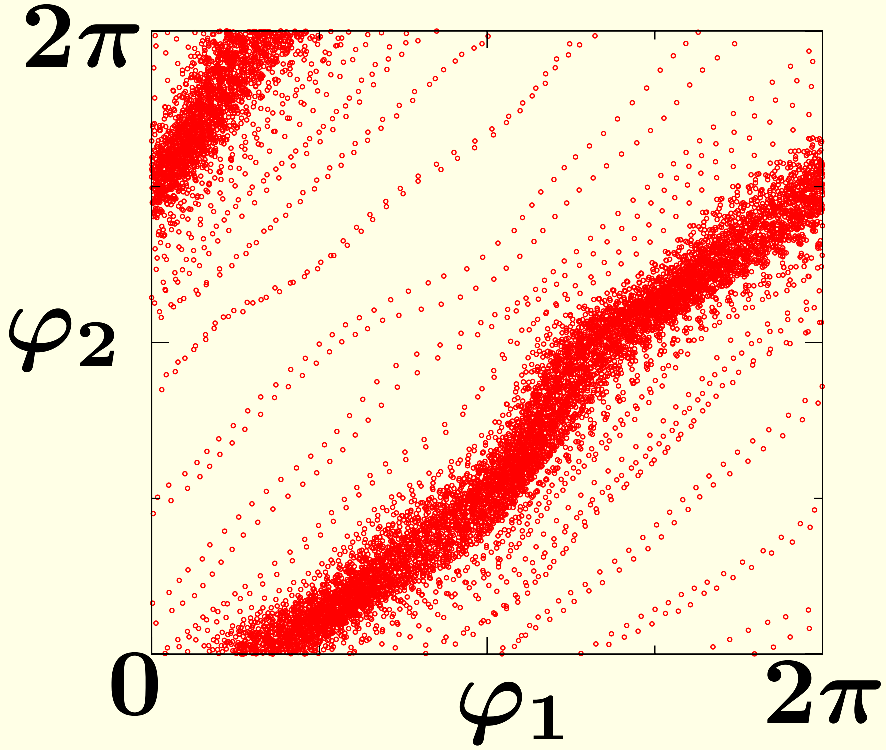
Impact of synchrony

synchrony,
reconstruction not possible



no synchrony,
easy reconstruction





close to synchrony,
long record required

Cardio-respiratory interaction in healthy humans

nature COMMUNICATIONS
DOI: 10.1038/ncomms3418

In vivo cardiac phase response curve elucidates human respiratory heart rate variability

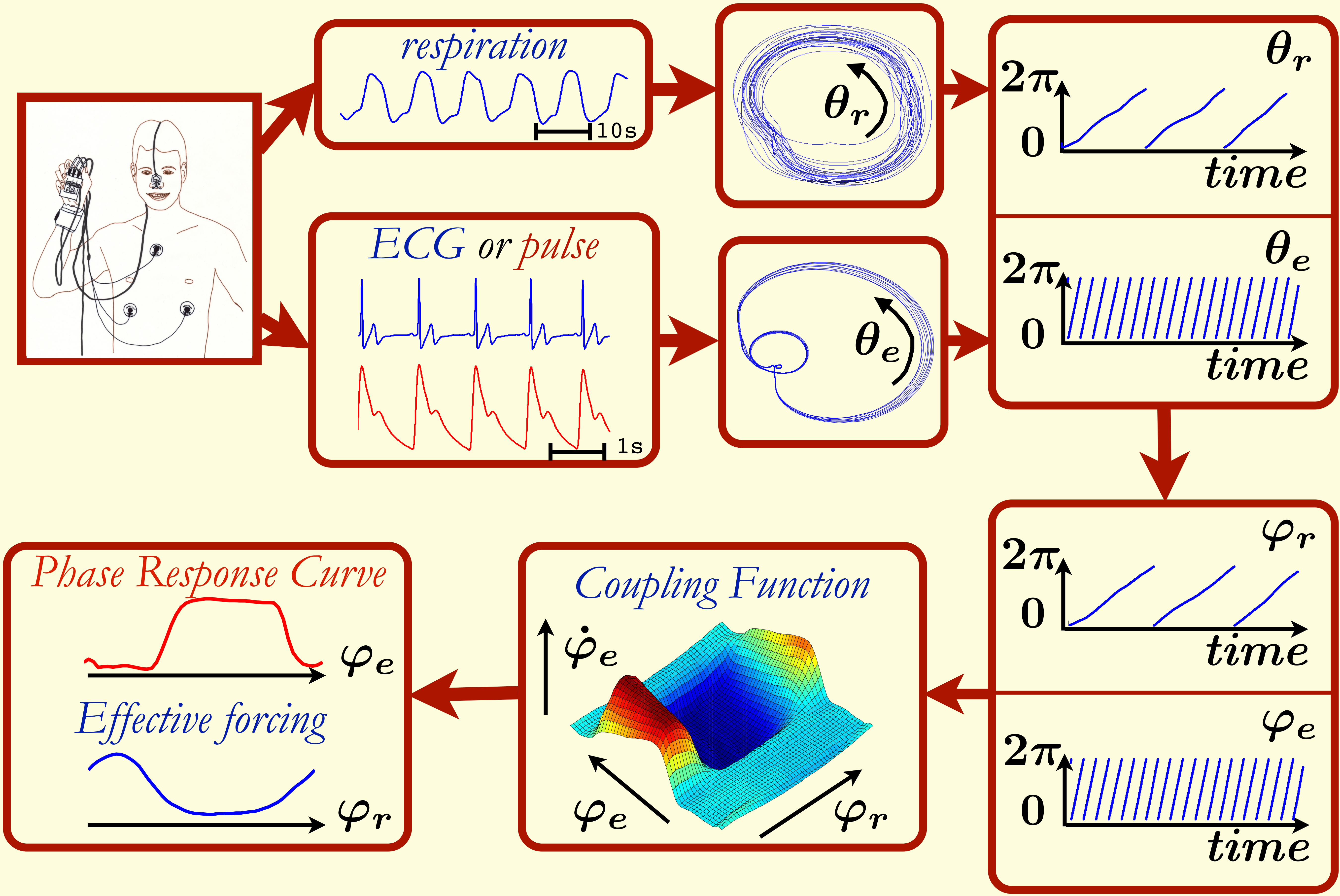
Björn Kralemann[1], Matthias Frühwirth[2], Arkady Pikovsky[3], Michael Rosenblum[3], Thomas Kenner[4], Jochen Schaefer[5] & Maximilian Moser[2,4]

Subjects: 7 females, 10 males; age between 27 and 51, av. 36

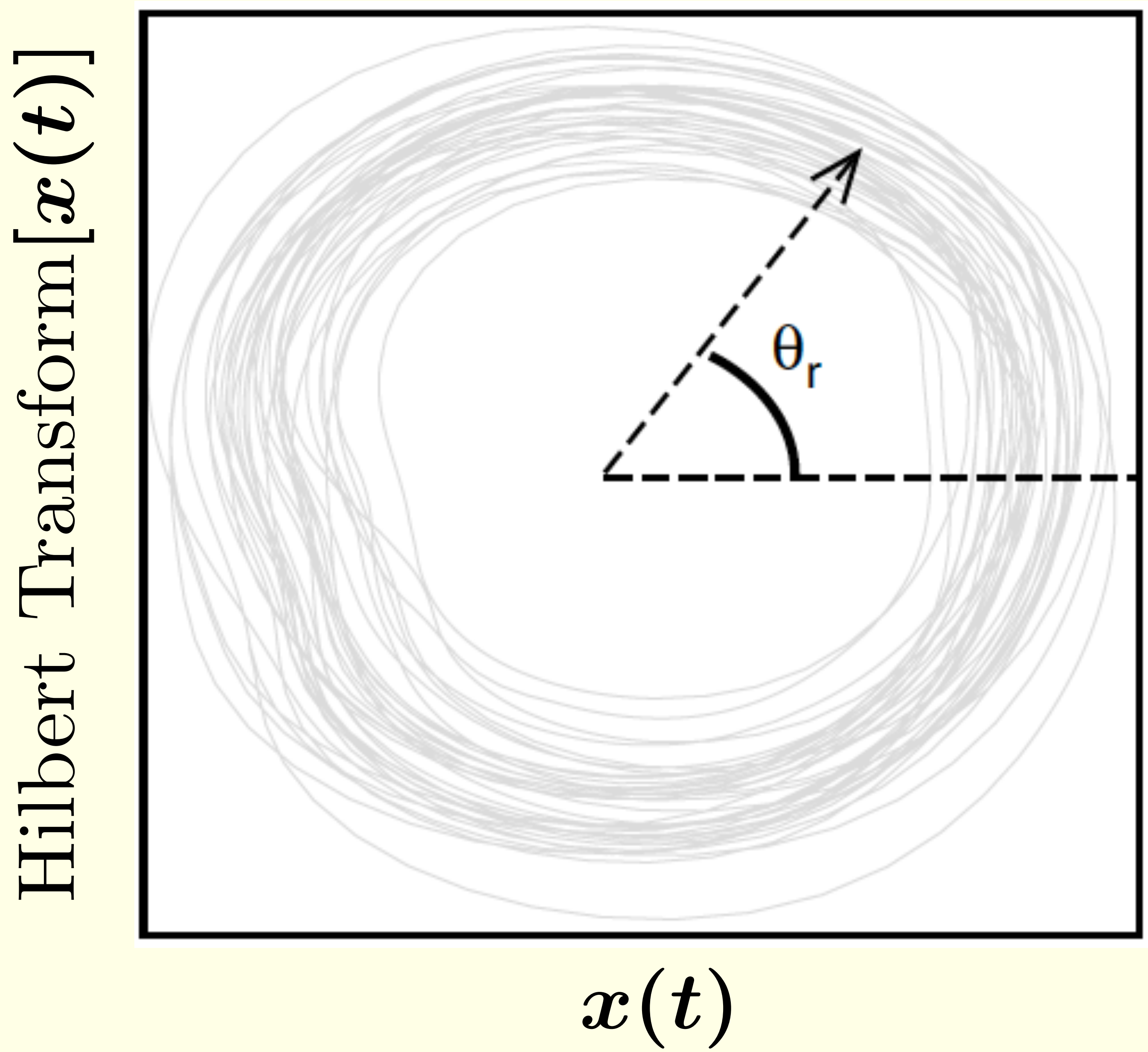
Recordings: chest-wall ECG (1kHz, 16 bit)
arterial pulse (piezoresistive pressure sensors at wrists)
nasal respiratory flow (high-speed thermistor)

Conditions: supine position in rest, 2x420s, break 12 min standing

The approach at a glance



Respiratory protophase

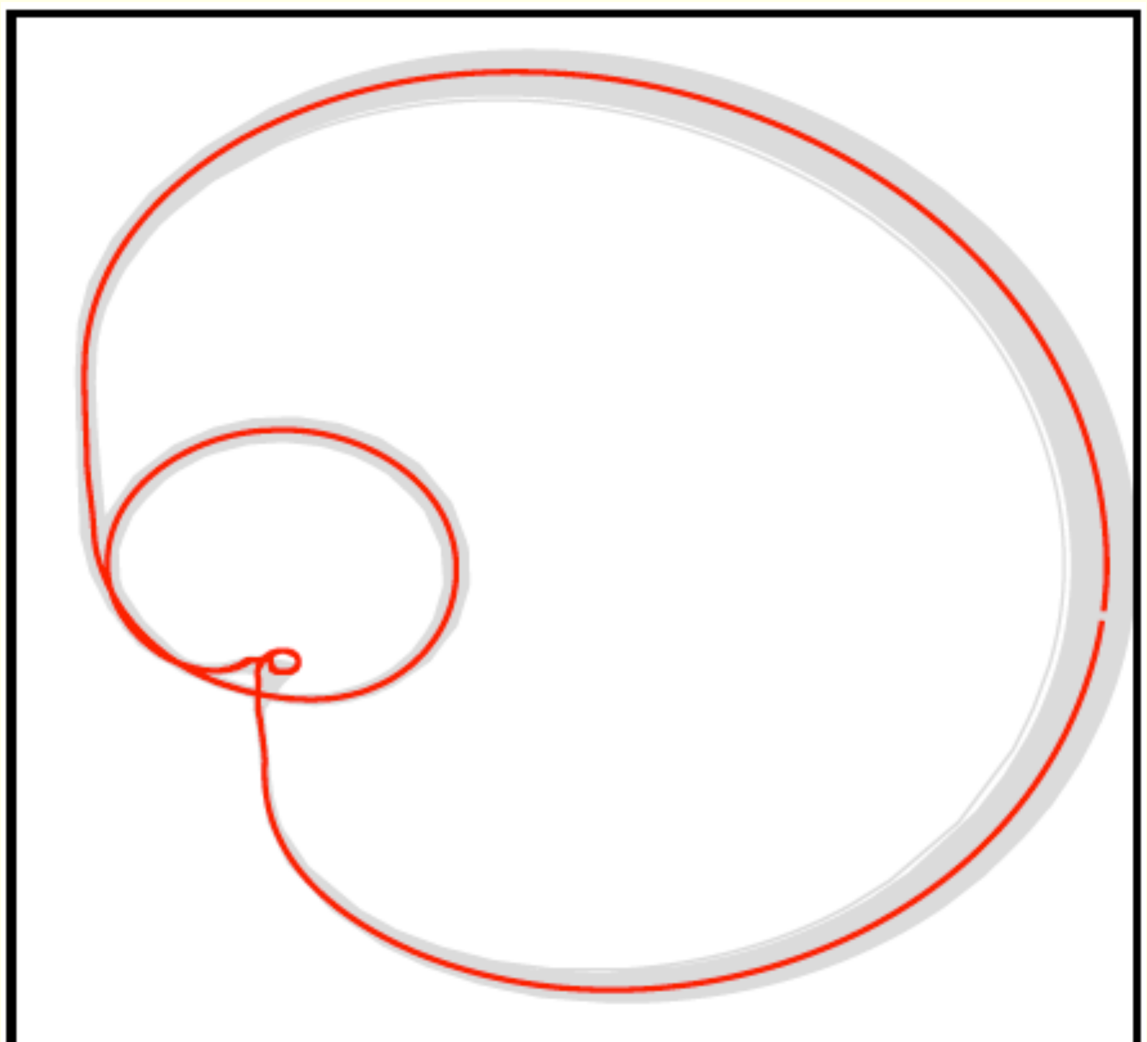


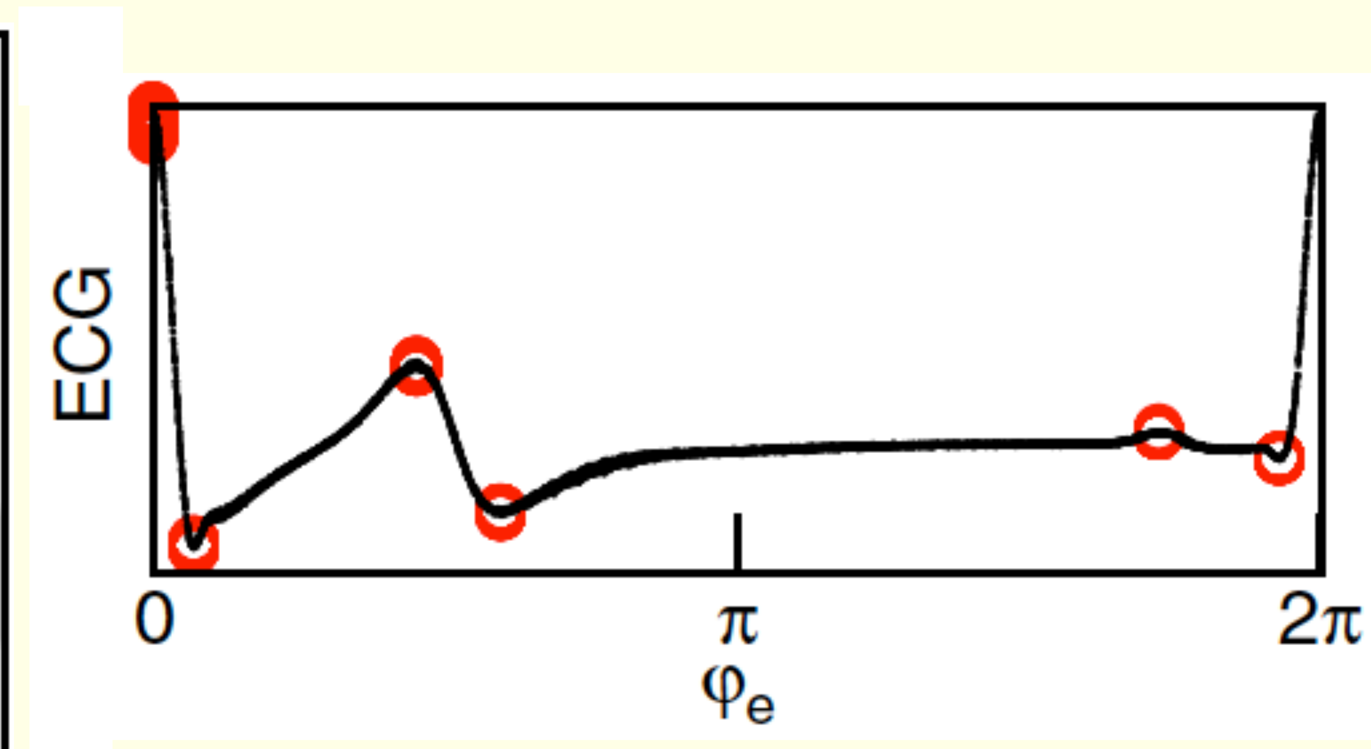
Protophase of the ECG signal in three steps

1. First protophase estimate via 6 markers (maxima of R, T, P waves, minima of Q, S and of the wave after T; linear interpolation between the markers)

2. Construction of the **average cycle**

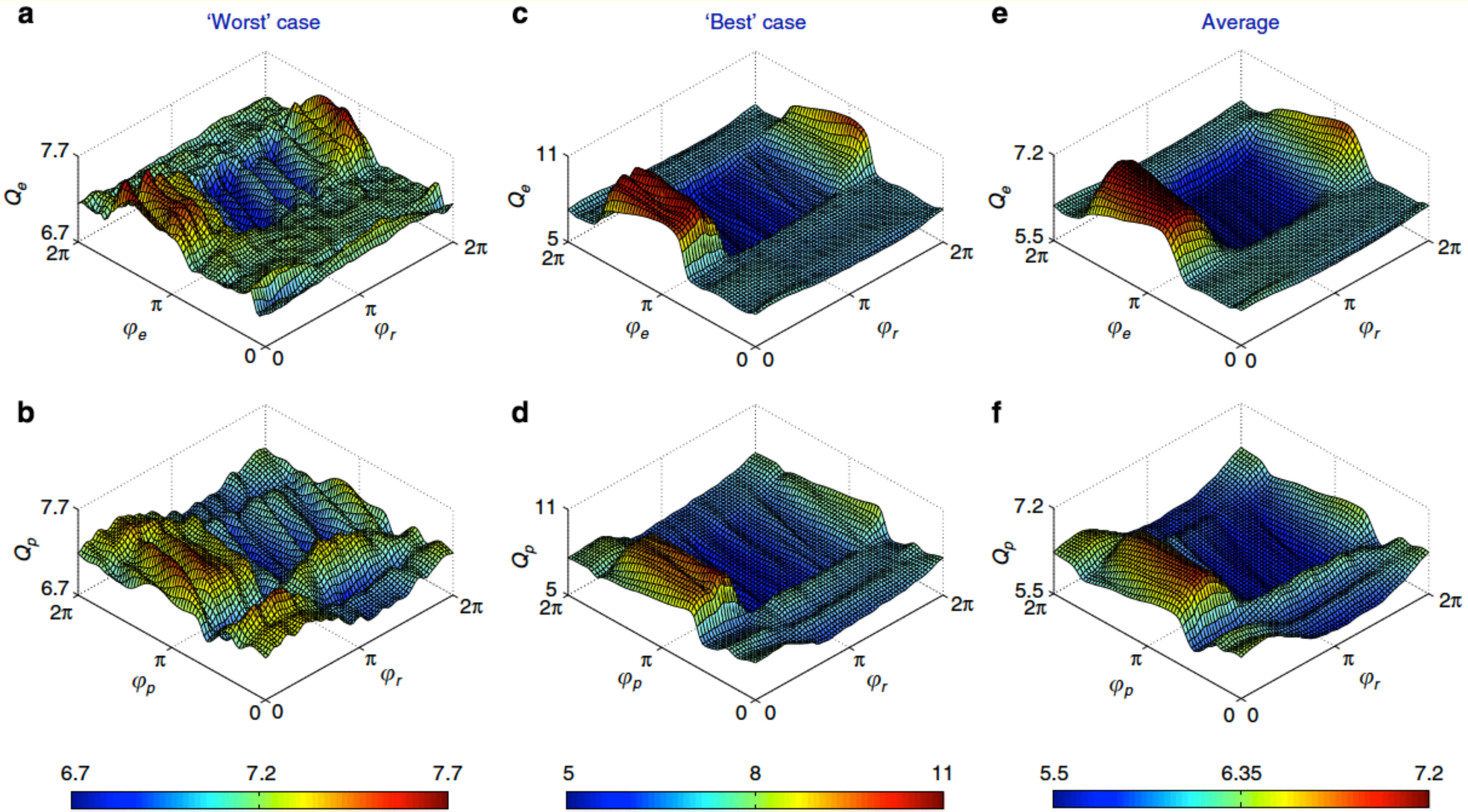
3. Projection of the trajectory on the average cycle with the help of an optimization strategy





similar approach for **arterial pulse** signal

Main result: the coupling functions $Q = \omega + q(\varphi_1, \varphi_2)$

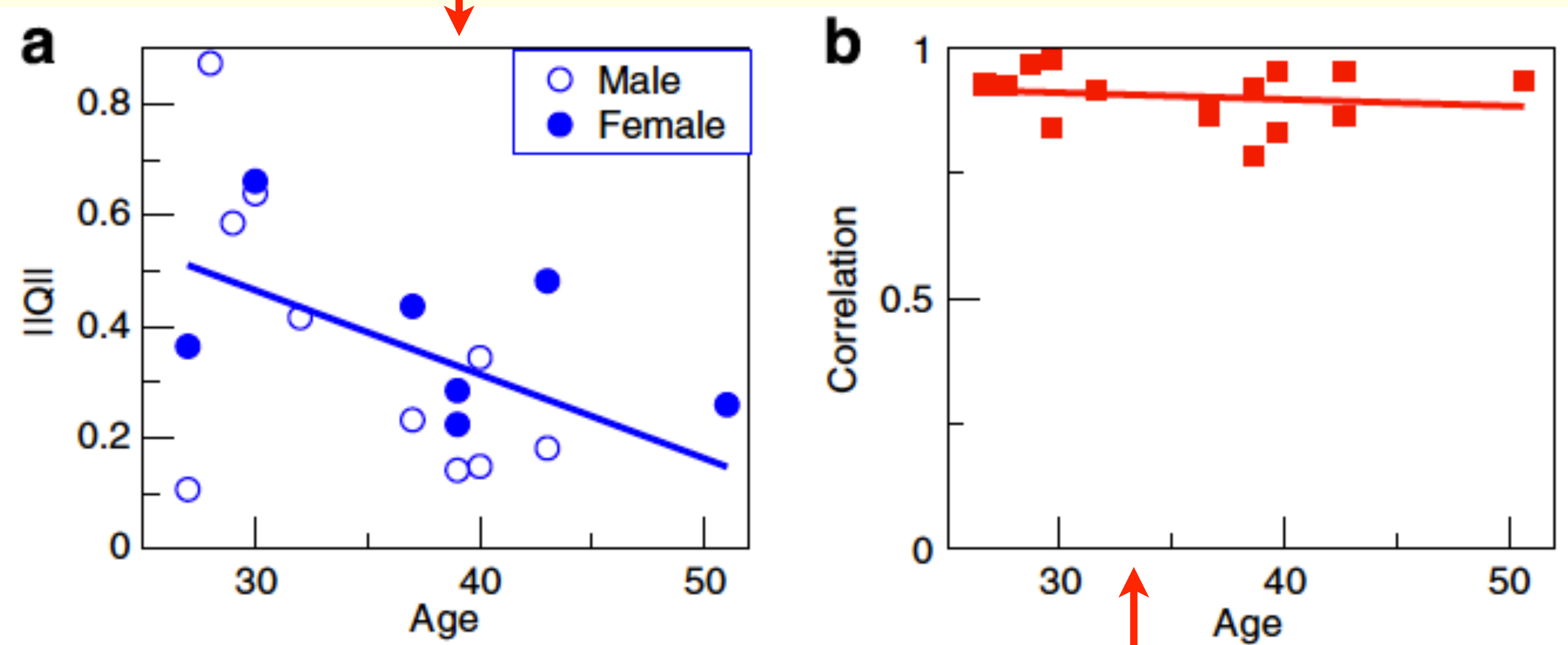


Top (a, c, e): from respiration and ECG,
bottom: from respiration and arterial pulse

Similarity indicates invariant reconstruction

Example of an application: age dependence

Norm of the coupling function vs age: indication for decrease of interaction



Correlation of the function with the average one: independence of the shape on the age

Phase response curves

In typical cases $$q_1(\varphi_1, \varphi_2) = Z_1(\varphi_1) I_2(\varphi_2)$$

phase response curve (PRC) forcing

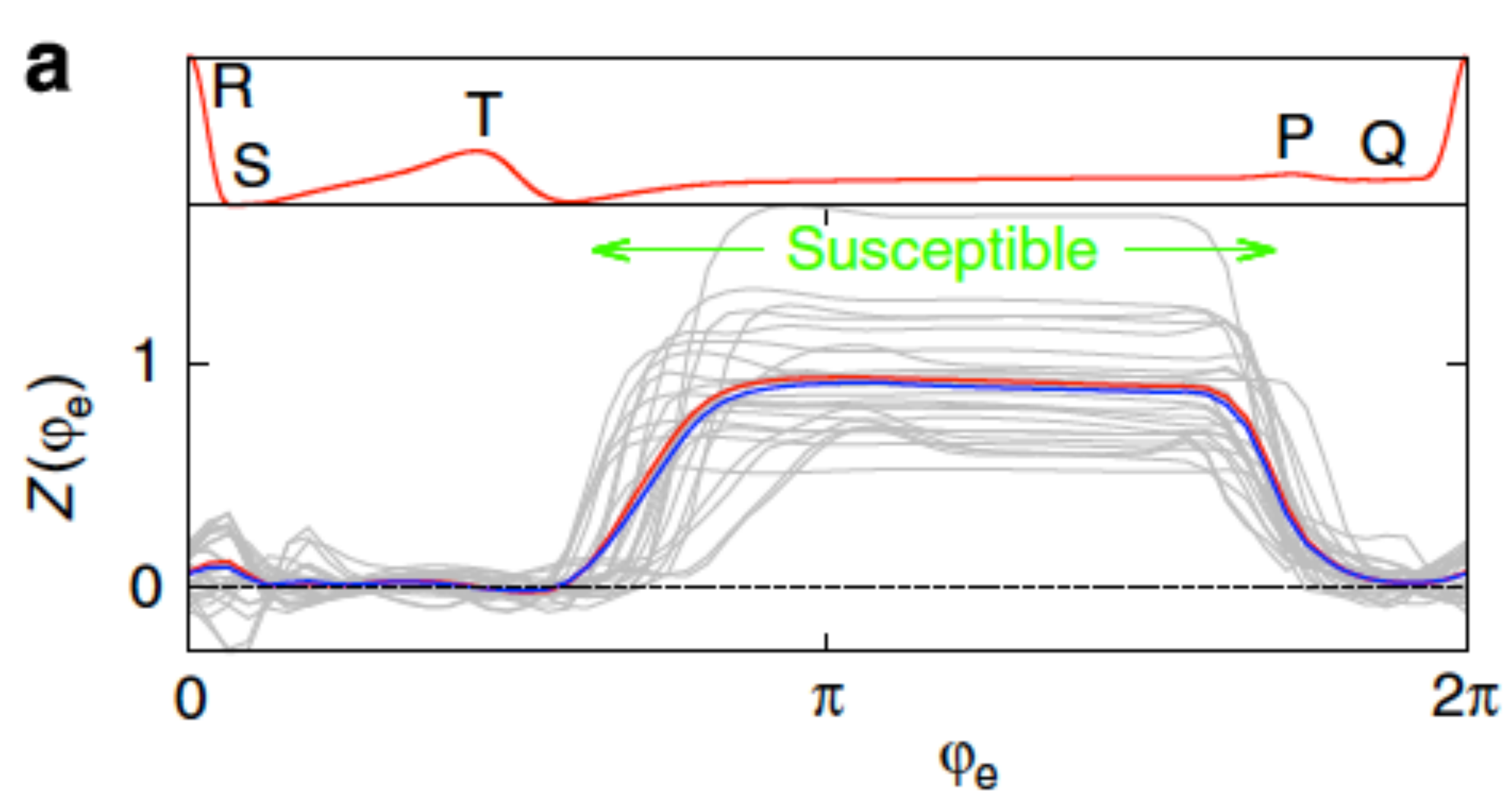
PRC quantifies response (phase shift) of an oscillator to a perturbation.

Traditional approach to PRC determination: repeated stimulation of an isolated oscillator by short pulses

We obtain PRC from a passive observation of the system under free-running conditions

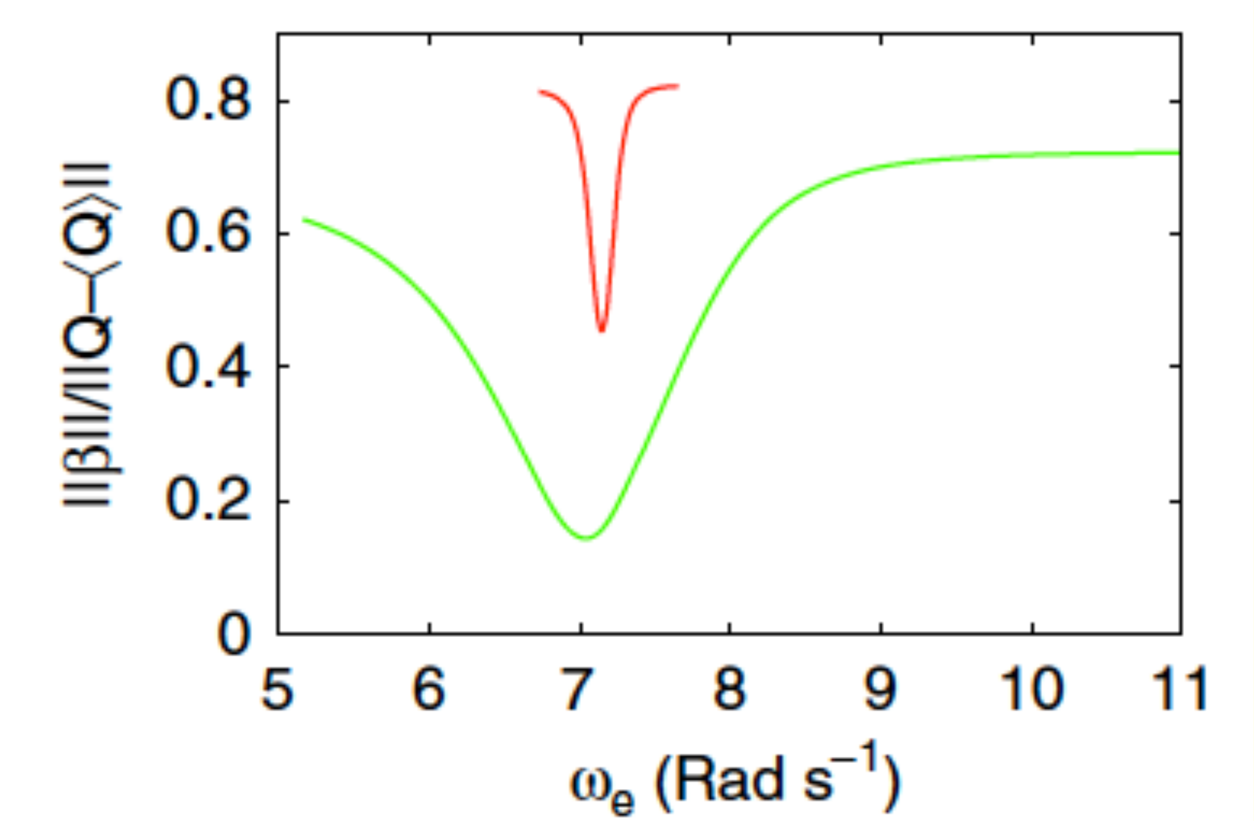
Approach: decomposition of the coupling function into a product

Phase response curves



Blue: average of individual PRCs

Red: decomposition of the average coupling function



The relative decomposition error

$$\beta = Q_e - \omega_e - ZI$$

Quantification of the heart rate variability (HRV)

- Analysis of HRV is an important tool in physiology and medicine
- Respiratory component of HRV (respiratory sinus arrhythmia, RSA) represents the influence of the autonomic nervous system
- With the instantaneous phase and frequency of the cardiac oscillators we obtain a continuous description of the HRV
- We decompose HRV into RSA-HRV and non-RSA-HRV

Decomposition of HRV

Approach: If there were only cardiac and respiratory oscillators:

$$\dot{\varphi}_e = Q_e(\varphi_e, \varphi_r)$$

However, these oscillators are not isolated, hence:

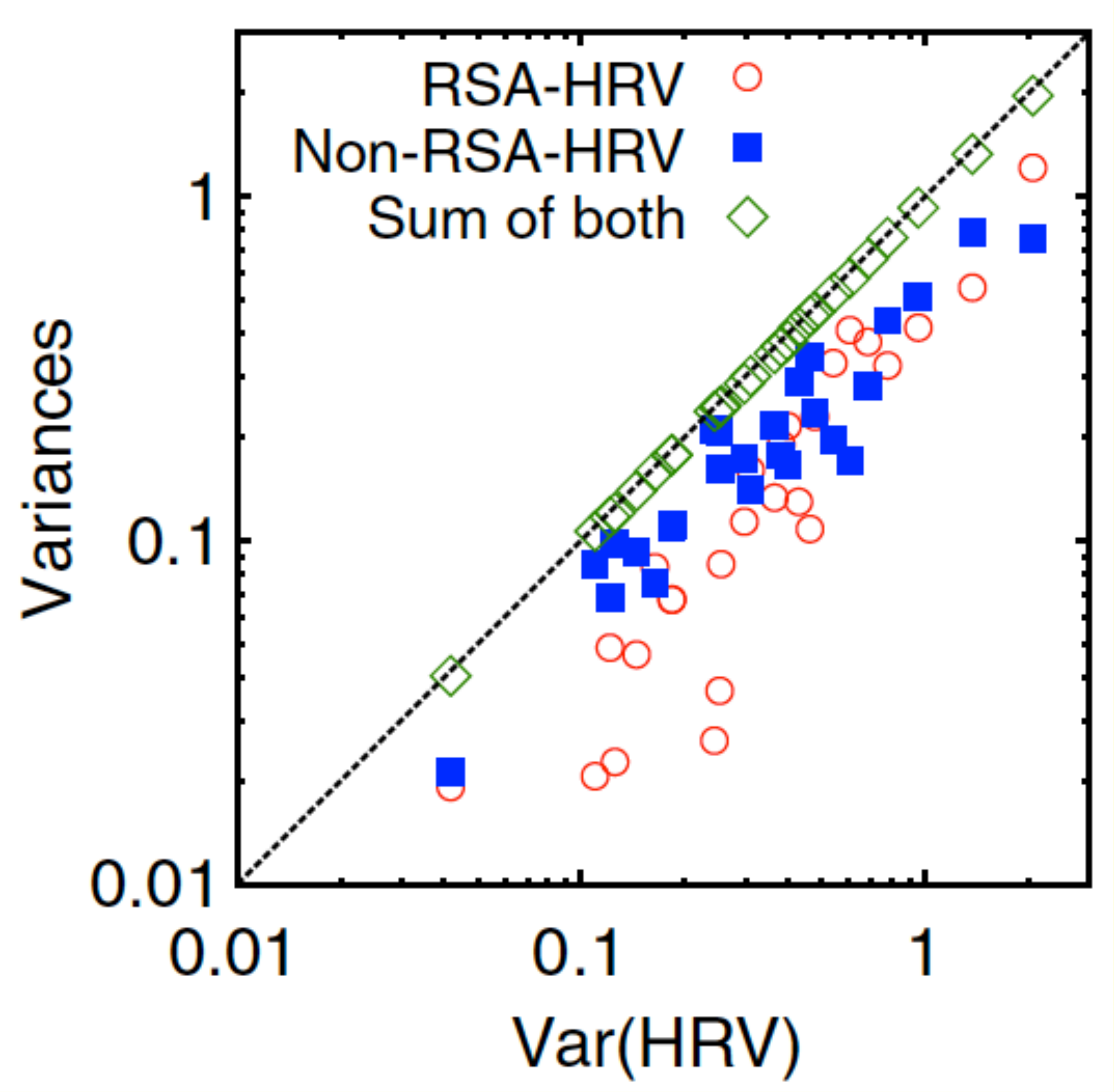
$$\dot{\varphi}_e = Q_e(\varphi_e, \varphi_r) + \xi(t)$$

Intrinsic noise and effect of other systems

With the help of the reconstructed model $Q_e(\varphi_e, \varphi_r)$ we obtain decomposition

$$\boxed{\dot{\varphi}_e(t) = \dot{\varphi}_{e,RSA}(t) + \dot{\varphi}_{e,nonRSA}(t)}$$

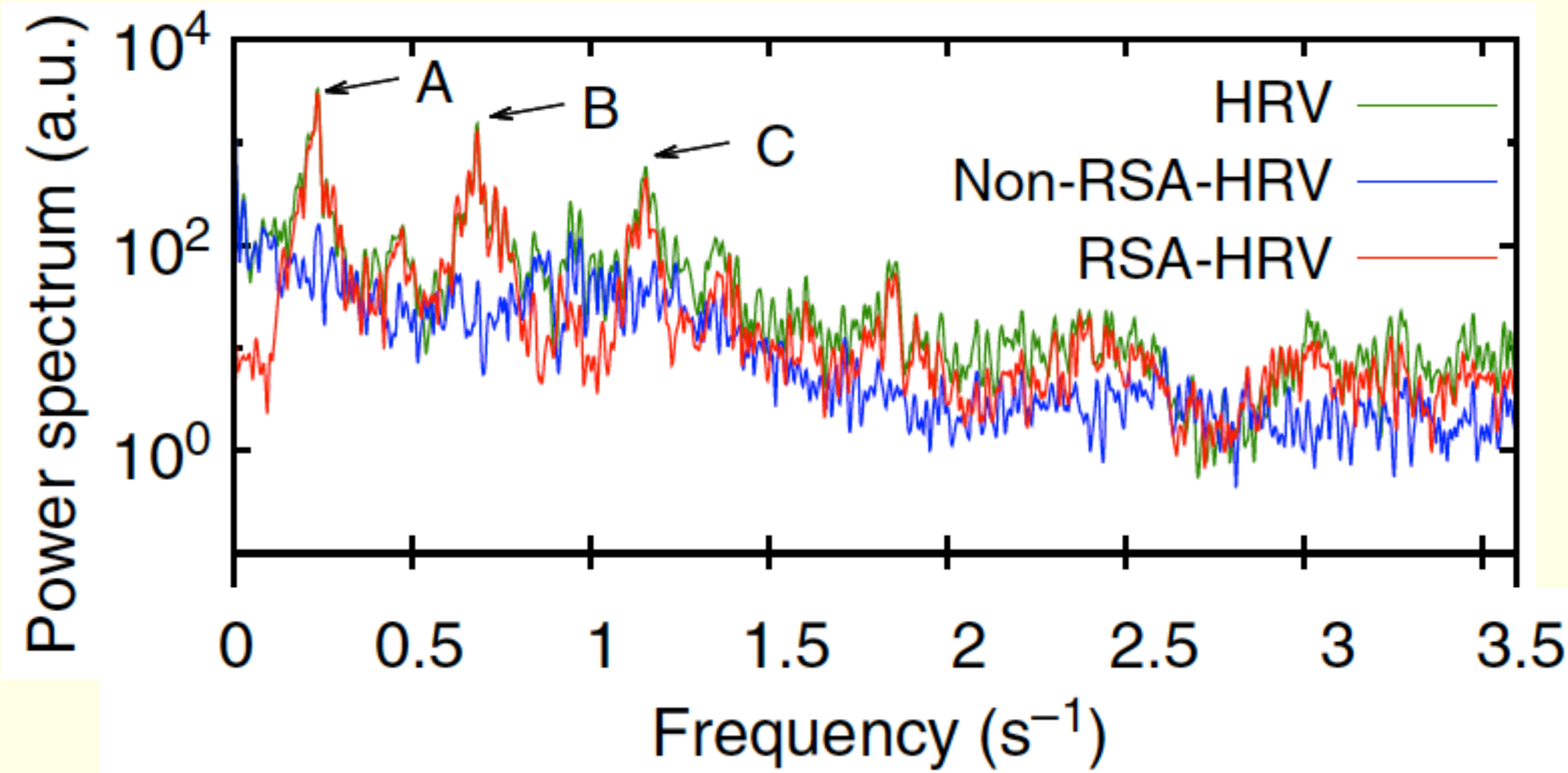
Quality of the decomposition



Var(RSA-HRV)+Var(non-RSA-HRV) ≈ Var(HRV)

→ components are almost uncorrelated

HRV decomposition: power specrum



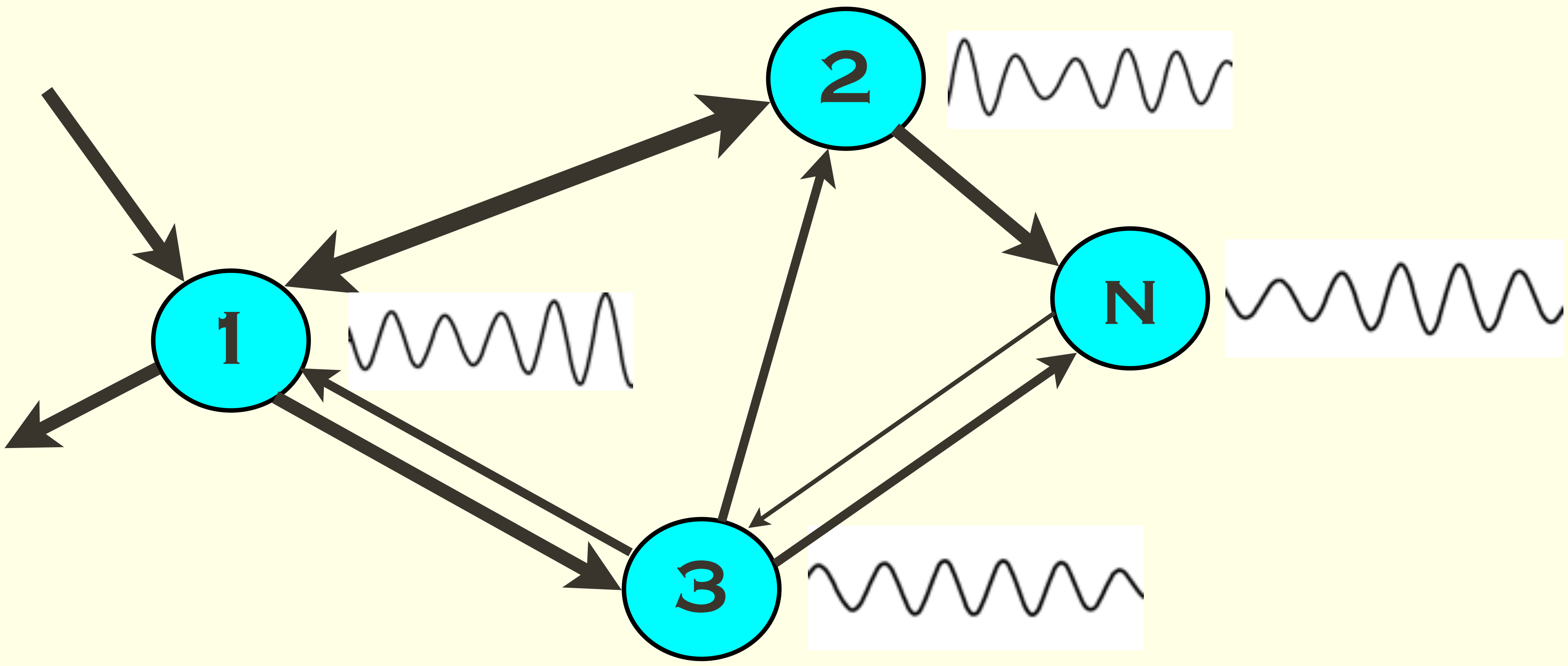
An example of strong RSA: Var(RSA-HRV) $\approx$ 0.67 Var(HRV)

Spectral peaks: **A,** corresponds to respiration, $\mathbf{0.23}$ Hz

B,C are side-bands of the heart rate,

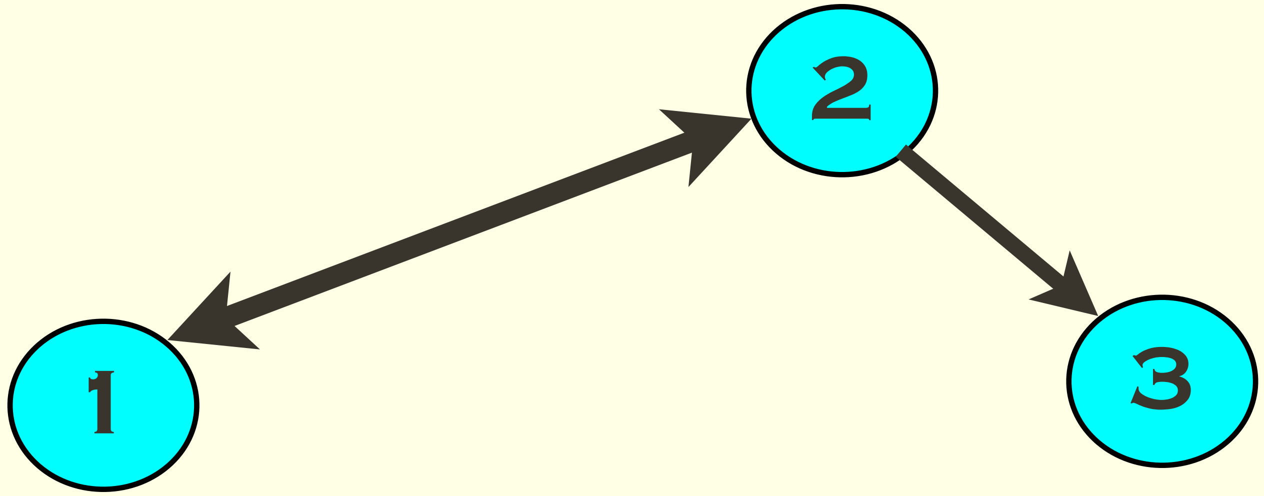
$\mathbf{0.92 \pm 0.23}$ Hz

Connectivity of an Oscillator Network



- Data: we have oscillatory signals coming from several ***weakly coupled self-sustained oscillators***
- Problem: to reconstruct ***directional connectivity***
- What kind of connectivity do we detect?
  Structural vs effective vs functional connectivity

Structural connectivity



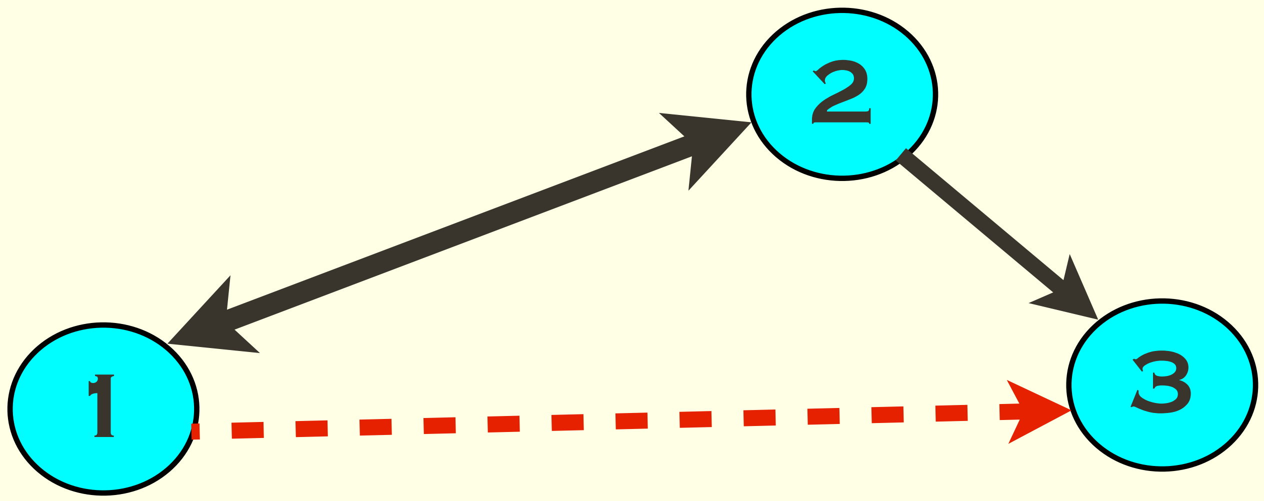
- Real physical connection: resistor, optical fiber...
  Biological system: anatomical connection, e.g., via synapses

- Mathematically, e.g., for the 2nd node:

$$\dot{\mathbf{x}}_2 = \underbrace{\mathbf{G}_2(\mathbf{x}_2)}_{\text{autonomous dynamics}} + \varepsilon \underbrace{\mathbf{H}_2(\mathbf{x}_2, \mathbf{x}_1)}_{\text{coupling function}}$$

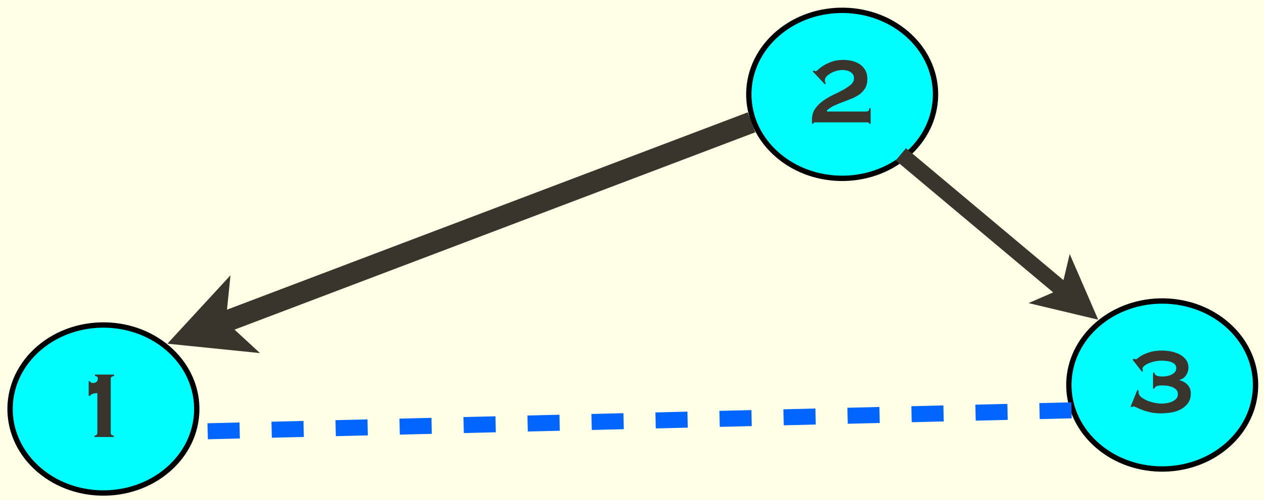
Remark: “coupling” = “physical connection”

Effective phase connectivity



- Nodes 1 and 3 are not physically connected, but phase dynamics of node 3 may depend on the state of node 1. Then, nodes 1, 3 are ***effectively connected*** (unidirectionally)
- Structural connectivity $\neq$ effective phase connectivity

Functional connectivity



- Nodes 1 and 3 are not physically connected, but they may be correlated or synchronized due to the common drive 2

  $\Longrightarrow$ Nodes 1, 3 are functionally connected

- Notice: (1) functional connection is not directed

  (2) functional connectivity is only loosely related to the structural and effective ones

We quantify the

effective phase connectivity

by reconstructing the model of phase dynamics from data

Namely, we perform:

- Protophase estimation
- Protophase-to-phase transformation
- Reconstruction of coupling functions
- Analysis of coupling functions

Network of coupled oscillators

- Individual oscillator: $\dot{\mathbf{x}}_k = \mathbf{G}_\mathbf{k}(\mathbf{x}_\mathbf{k})$
  - limit cycle, parameterized by phase φ_k
  - phase grows linearly with time: $\dot{\varphi}_k = \omega_k = \text{const}$
- A network of N coupled oscillators

$$\dot{\mathbf{x}}_k = \mathbf{G}_\mathbf{k}(\mathbf{x}_\mathbf{k}) + \varepsilon \mathbf{H}_k(\mathbf{x}_1, \mathbf{x}_2, \ldots)$$

- If $\mathbf{x}_l$ enters the equation for $\mathbf{x}_k$ then there is a direct structural connection $l \to k$
- If $\mathbf{H}_k = \sum_{j \neq k} \mathbf{H}_{kj}(\mathbf{x}_\mathbf{k}, \mathbf{x}_\mathbf{j})$ then coupling is pairwise
- If there are terms $\mathbf{H}_{kjl}(\mathbf{x}_\mathbf{k}, \mathbf{x}_\mathbf{j}, \mathbf{x}_\mathbf{l})$: cross-coupling

Weak coupling: Phase description

- Weak coupling, no synchrony: motion on the ***N-torus*** in the phase space of the full system
- This motion can be parameterized by *N* phases:

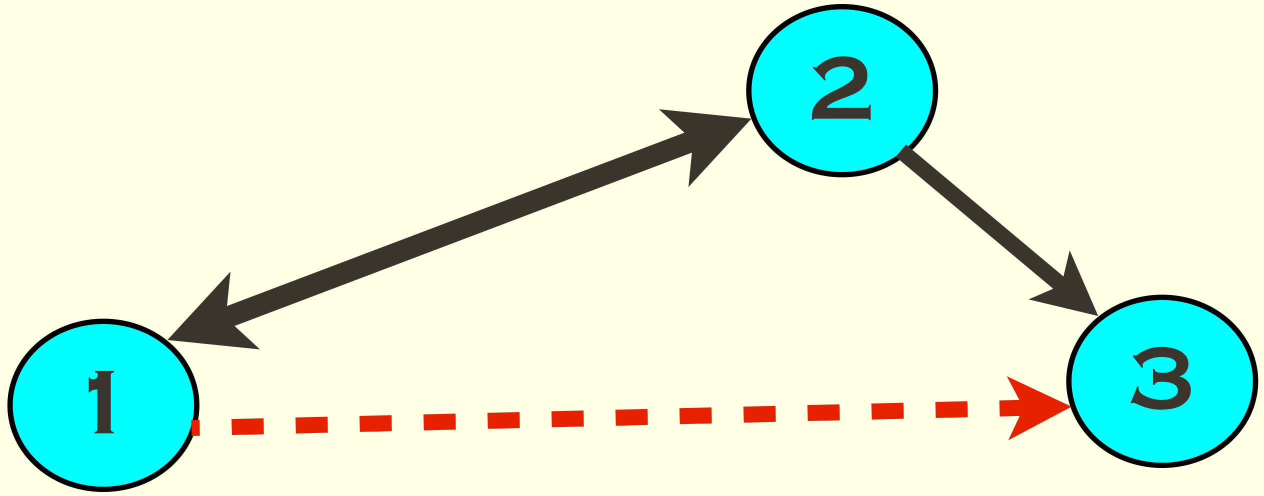
$$\dot{\varphi}_k = \omega_k + q_k(\varphi_1, \varphi_2, \ldots), \quad k = 1, \ldots, N$$

- New coupling functions q_k can be obtained by a perturbative reduction (Kuramoto 84):

$$q_k(\varphi_1, \varphi_2, \ldots) = \varepsilon q_k^{(1)}(\varphi_1, \varphi_2, \ldots) + \varepsilon^2 q_k^{(2)}(\varphi_1, \varphi_2, \ldots) + \ldots$$

- Pairwise coupling in the full system:
  - first-order approximation: pairwise terms like $\varepsilon q_{kl}^{(1)}(\varphi_k, \varphi_l)$
  - high-order approximation: ***terms, depending on many phases***, not only on the phases of directly coupled nodes

Effective phase connectivity



- Nodes 1 and 3 are not physically connected, but phase dynamics of node 3 may depend on the state of node 1. Then, nodes 1, 3 are ***effectively connected*** (unidirectionally)

$$\dot{\varphi}_3 = \omega_3 + \varepsilon q_3^{(1)}(\varphi_2, \varphi_3) + \varepsilon^2 q_3^{(2)}(\varphi_1, \varphi_2, \varphi_3)$$

- Structural connectivity $\neq$ effective phase connectivity

There is no effective phase connection 3 $\longrightarrow$ 1 !

Coupling functions and quantification of interaction

We reconstruct the coupling functions in terms of Fourier coefficients, using LMS fit:

$$\frac{d\varphi_k}{dt} = \omega_k + q_k(\varphi_1, \varphi_2, \ldots, \varphi_N)$$

$$= \sum_{l_1,\ldots,l_N} \mathcal{F}^{(k)}_{l_1,\ldots,l_N} \exp\left(il_1\varphi_1 + il_2\varphi_2 + \ldots + l_N\varphi_N\right)$$

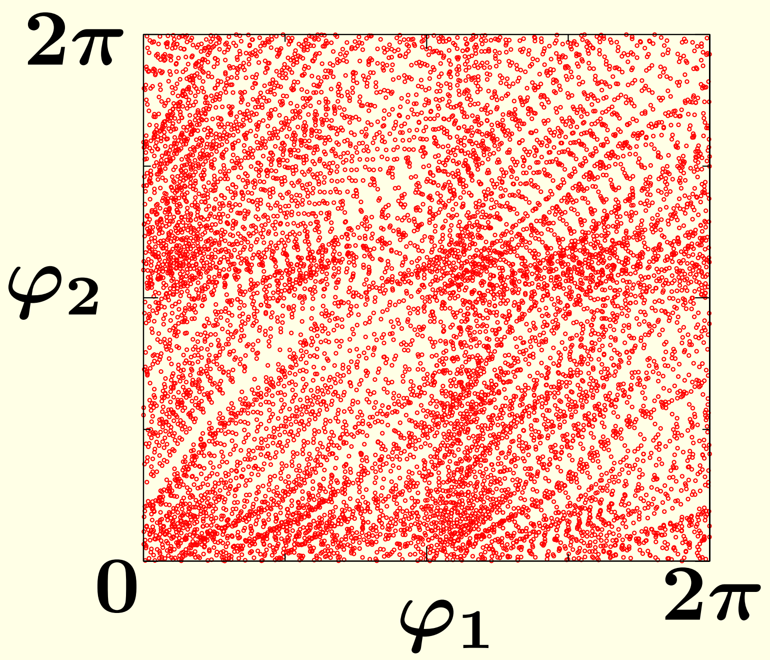
Norm of the coupling function q_k quantifies effect of the rest of the network on oscillator k

Action of particular oscillator $j \to k$

Partial norm $$\mathcal{N}^2_{k\leftarrow j} = \sum_{l_k,l_j\neq 0} \left|\mathcal{F}^{(k)}_{0,\ldots,l_k,0,\ldots,l_j,0,\ldots}\right|^2$$

Numerical problem

- Two coupled oscillators: to reconstruct the coupling function we need enough data points to cover the square
  $0 < \varphi_{1,2} \leq 2\pi$



- Three coupled oscillators: we need enough data points to cover the cube $0 < \varphi_{1,2,3} \leq 2\pi$
- *N* coupled oscillators: we need enough data points to cover the hypercube.... It is not feasible!

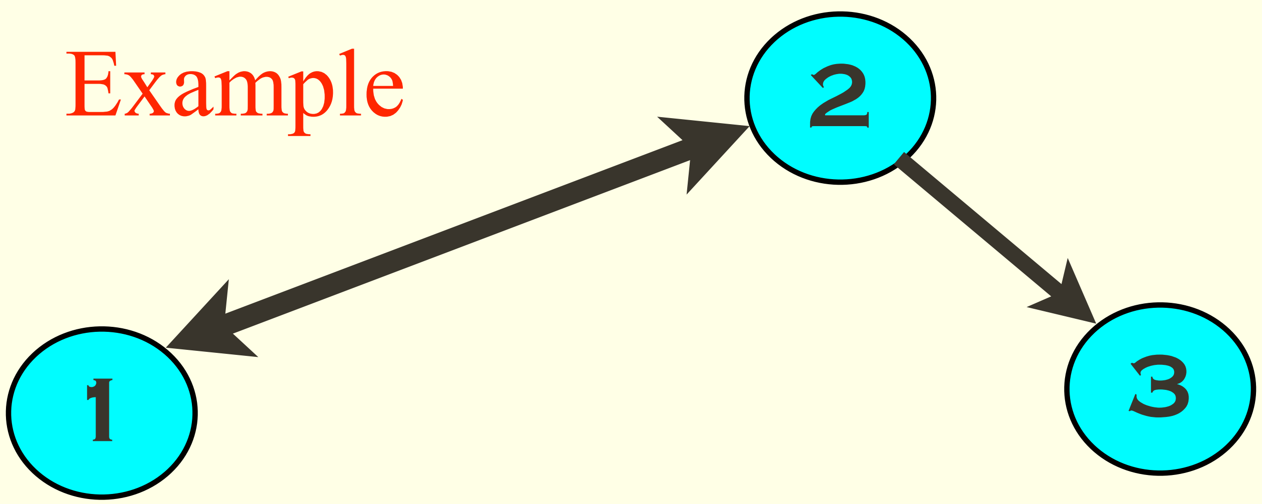
Typically: pairwise analysis. We suggest an analysis by triplets.

Partial phase dynamics

Pairwise analysis: we fit the function of two phases, ignoring all others: $\dot{\varphi}_k = \omega_k + q_{kj}(\varphi_j, \varphi_k)$

Norm $\mathcal{P}_{k\leftarrow j} = ||q_{kj}||$ quantifies link $k \leftarrow j$

Example



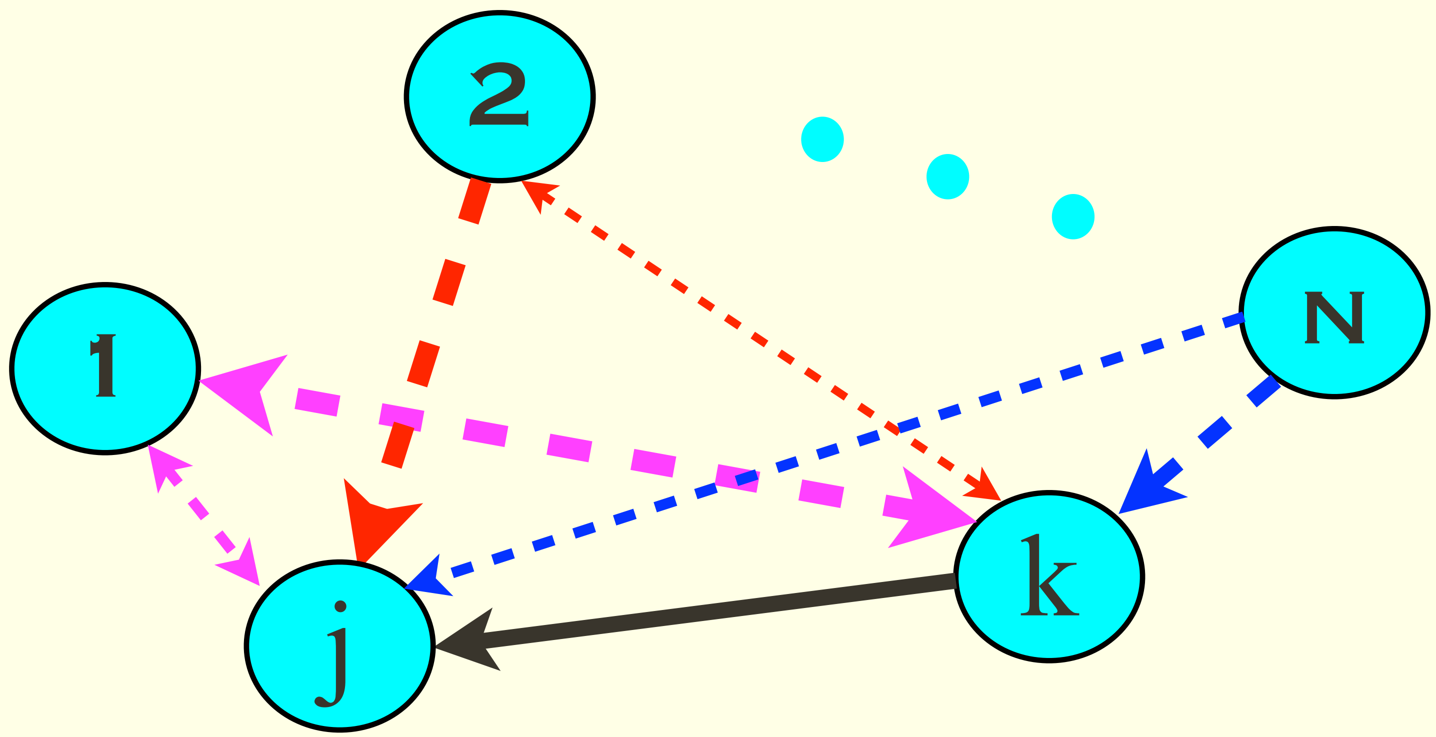
Pairwise analysis yields spurious connection $\mathbf{1} \rightarrow \mathbf{3}$

Triplet analysis yields correct connectivity (Kralemann et al 2011)

What to do for networks with ***N*>3**?

Triplet analysis of networks with *N*>3

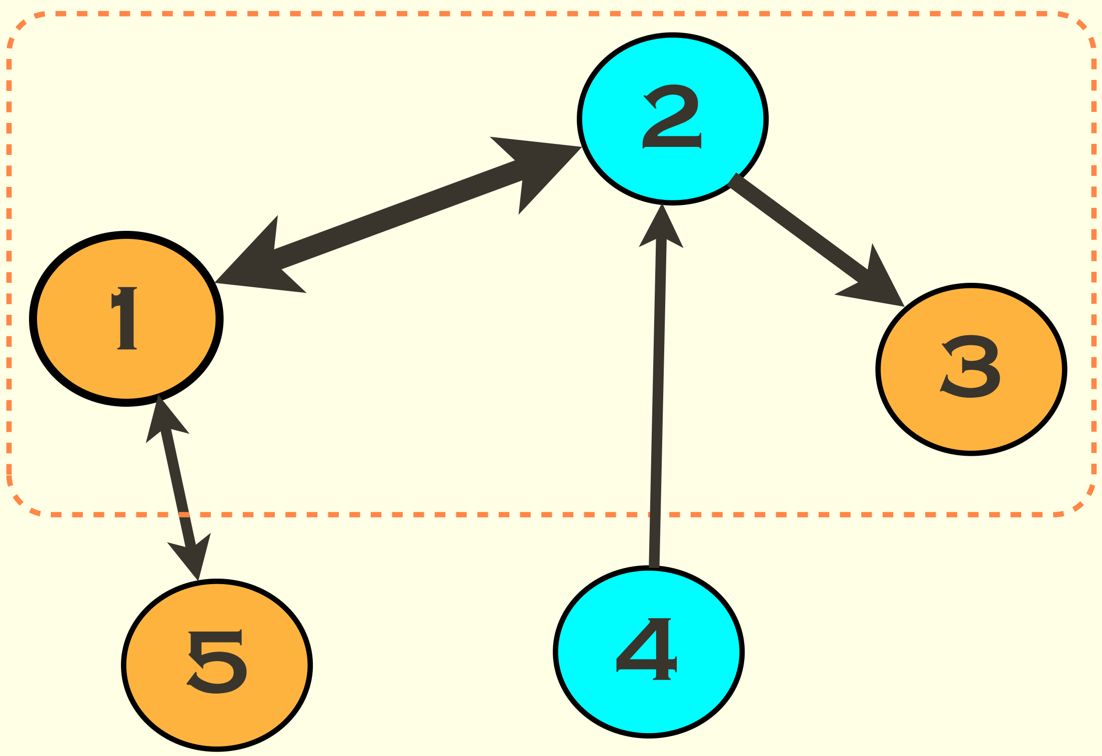
We reconstruct $\dot{\varphi}_j = \omega_j + q_{jkl}(\varphi_j, \varphi_k, \varphi_l)$ for all l



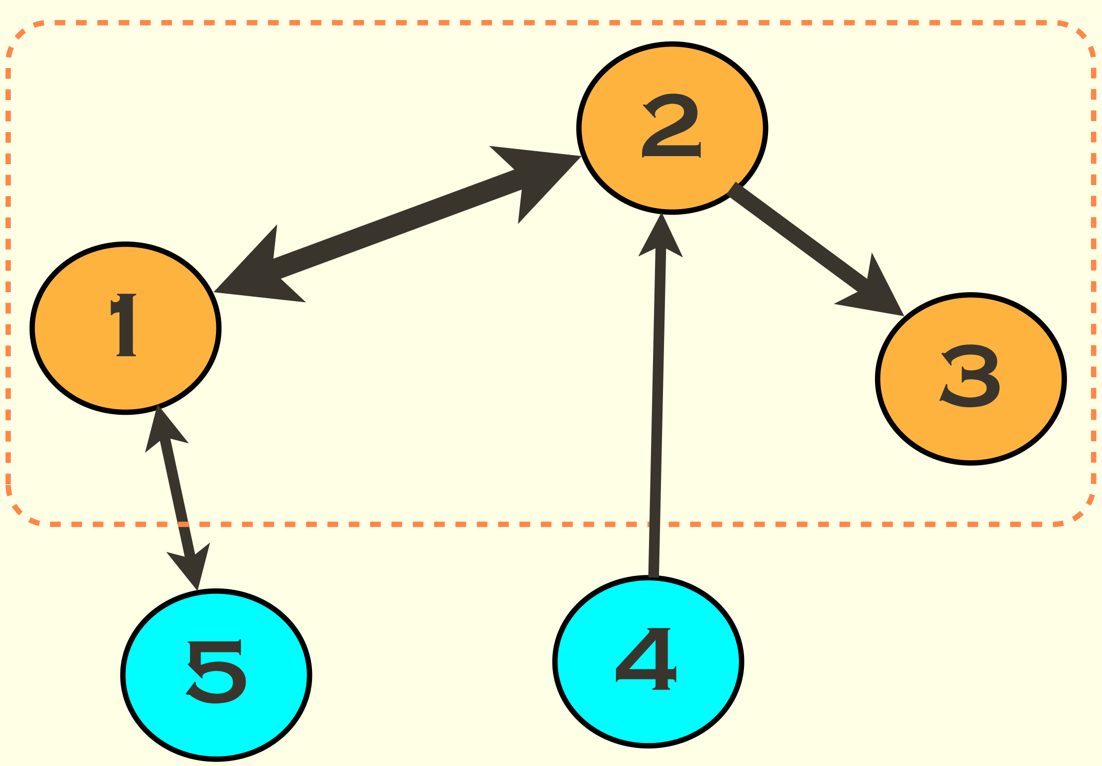
From each triplet we obtain partial norm: $\tilde{\mathcal{T}}^2_{j\leftarrow k}(l) = \sum_{l_j, l_k \neq 0} \left| \mathcal{F}^{(j)}_{l_j, l_k, 0} \right|^2$

We suggest to take $\mathcal{T}_{j\leftarrow k} = \min_l \tilde{\mathcal{T}}_{j\leftarrow k}(l)$ as the final triplet-based measure of the binary effective connectivity

Triplet analysis of networks with N>3



Triplet {1,3,5} yields spuriously large term $\mathbf{1} \rightarrow \mathbf{3}$, because $\boldsymbol{\varphi_1}, \boldsymbol{\varphi_3}$ are correlated due to node 2



Triplet {1,2,3} correctly explains correlation of $\boldsymbol{\varphi_1}, \boldsymbol{\varphi_3}$ and yields a small value for the link $\mathbf{1} \rightarrow \mathbf{3}$

Example: three van der Pol oscillators

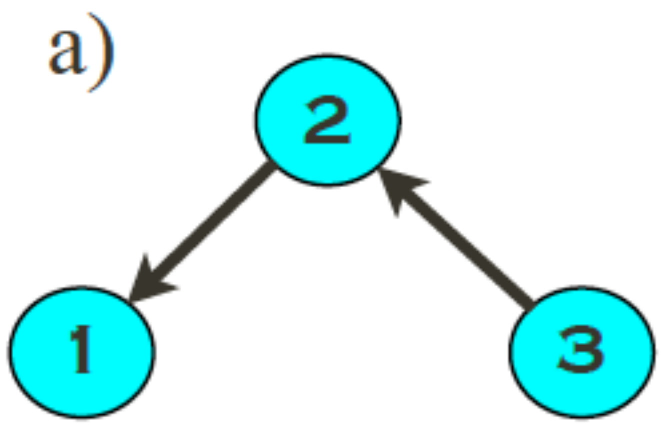
$$\ddot{x}_1 - \mu(1 - x_1^2)\dot{x}_1 + \omega_1^2 x_1 = \varepsilon[\sigma_{12}(x_2 + \dot{x}_2) + \sigma_{13}(x_3 + \dot{x}_3)] \,,$$
$$\ddot{x}_2 - \mu(1 - x_2^2)\dot{x}_2 + \omega_2^2 x_2 = \varepsilon[\sigma_{21}(x_1 + \dot{x}_1) + \sigma_{23}(x_3 + \dot{x}_3)] \,,$$
$$\ddot{x}_3 - \mu(1 - x_3^2)\dot{x}_3 + \omega_3^2 x_3 = \varepsilon[\sigma_{31}(x_1 + \dot{x}_1) + \sigma_{32}(x_2 + \dot{x}_2)] \,.$$

Parameters: $\varepsilon = 0.2$ $\mu = 0.5$

$\omega_1 = 1$ $\omega_2 = 1.3247$ $\omega_3 = 1.75483$

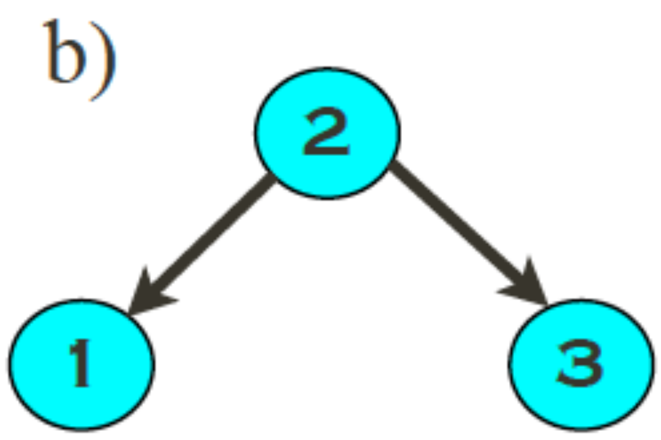
Connectivity matrix: $\sigma_{i,j} = 0$ or 1

Example, N=3, results



(a)	Osc_1	Osc_2	Osc_3
Osc_1		**0.103 , 0.104**	0.018 , 0.024
Osc_2	0.002 , 0.009		**0.095 , 0.095**
Osc_3	0.001 , 0.001	0.001 , 0.001	

$\mathcal{N}_{3\leftarrow 2}, \mathcal{P}_{3\leftarrow 2}$



(b)	Osc_1	Osc_2	Osc_3
Osc_1		**0.113 , 0.113**	0.003 , 0.016
Osc_2	0.001 , 0.001		0.001 , 0.001
Osc_3	0.005 , 0.020	**0.092 , 0.092**	

$\mathcal{N}_{3\leftarrow 1}, \mathcal{P}_{3\leftarrow 1}$

Random oscillator network, *N*=5

$$\ddot{x}_k - \mu(1 - x_k^2)\dot{x}_k + \omega_k^2 x_k = \varepsilon \sum_l \sigma_{kl}(x_l \cos\Theta_{kl} + \dot{x}_l \sin\Theta_{kl})$$

σ_{kl}: random asymmetric connection matrix of zeros and ones

Fixed number of incoming connections (two)

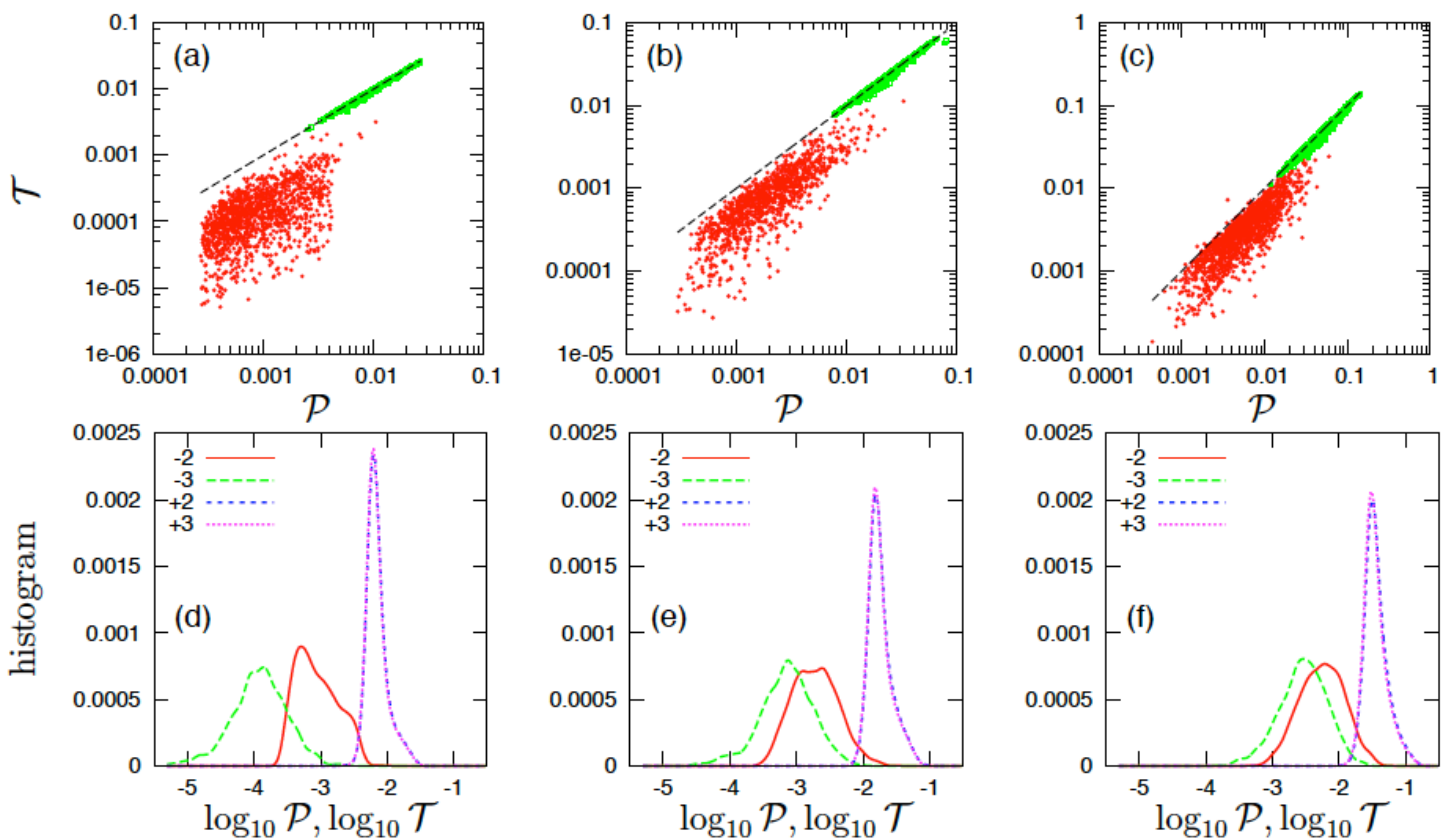
Frequencies are taken from a uniform distribution between 0.5 and 1.5

Θ_{kl} are taken from a uniform distribution between 0 and 2π

States with high degree of synchrony are excluded

Random oscillator network, *N*=5, results

Existing connection in green, non-existing connections in red



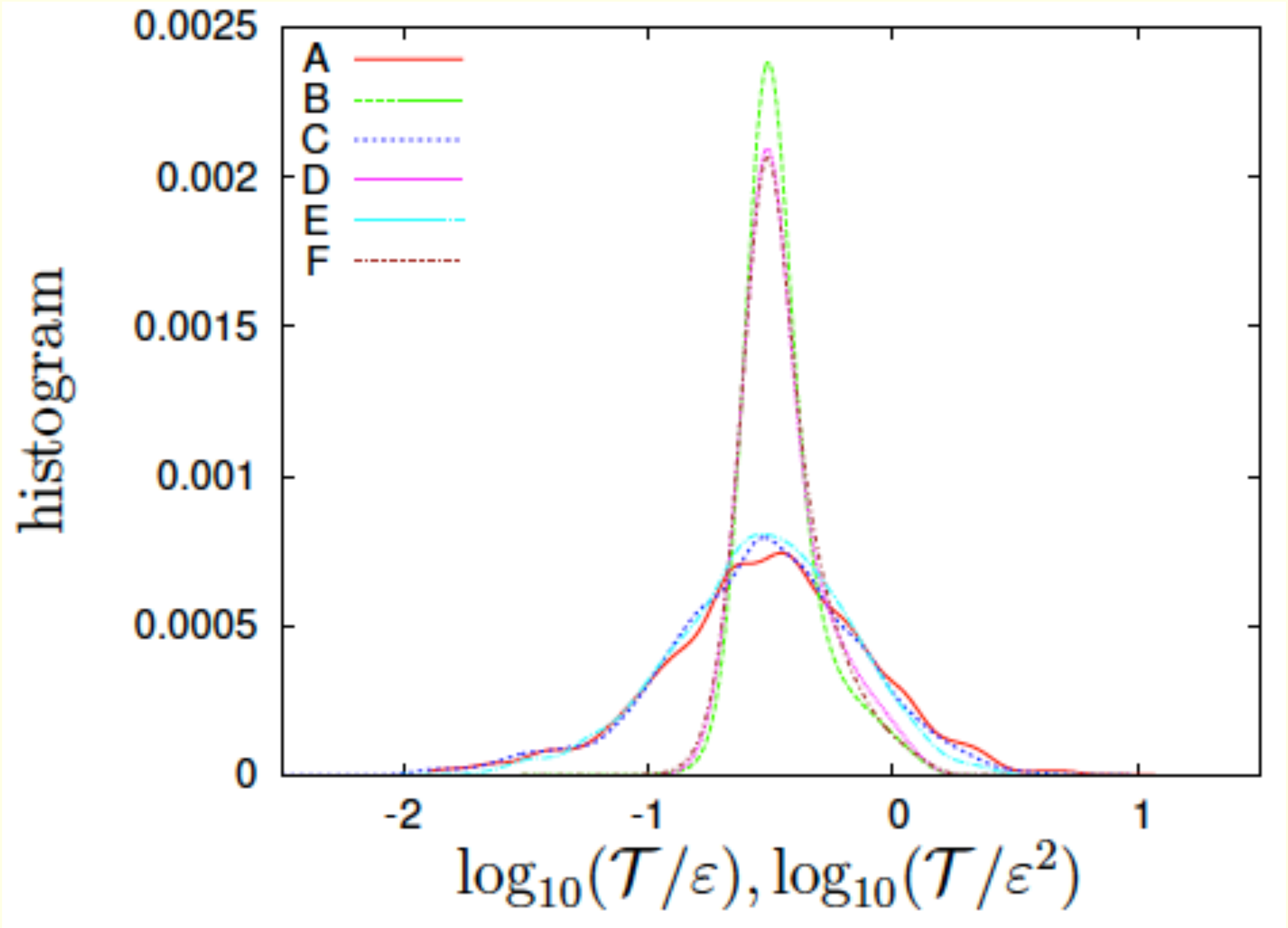
$\varepsilon = \mathbf{0.02}$ $\varepsilon = \mathbf{0.05}$ $\varepsilon = \mathbf{0.1}$

Random oscillator network, *N*=5, results

Rescaled distributions:

Norms of existing links are divided by ε

Norms of non-existing links are divided by ε^2



A,C,E: non-existing links

B,D,F: existing links

A,B: $\varepsilon = 0.02$ C,D: $\varepsilon = 0.05$ E,F: $\varepsilon = 0.1$

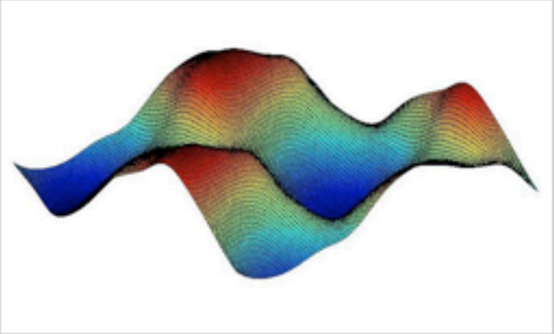
Results confirm our conjuncture that terms, describing indirect phase coupling, appear in the 2nd order of phase approximation

Conclusions

- Protophase-to-phase transformation
- Invariant reconstruction of phase equations for a network
- PRC from passive observation
- Characterization of directional couplings via partial norms
- Triplet analysis
- We detect effective phase connectivity, which is close but not equivalent to the structural connectivity

References

- B. Kralemann et al, Phys Rev E, 76, p. 055201, 2007,
  B. Kralemann et al, Phys Rev E, 77, p. 066205, 2008
  (Phases vs protophases, invariant reconstruction for two coupled oscillators)
- B. Kralemann, A. Pikovsky, and M. Rosenblum, Chaos, 21, p. 025104, 2011 (Analysis of networks)
- B. Kralemann et al, Nature Communications, 4:2418, 2013
  (Cardio-respiratory interaction)
- B. Kralemann et al, arXiv:1402.4331, New J Phys, in press
  (triplet analysis of networks)



DAMOCO: Data Analysis with Models Of Coupled Oscillators

MATLAB Toolbox for multivariate time series analysis

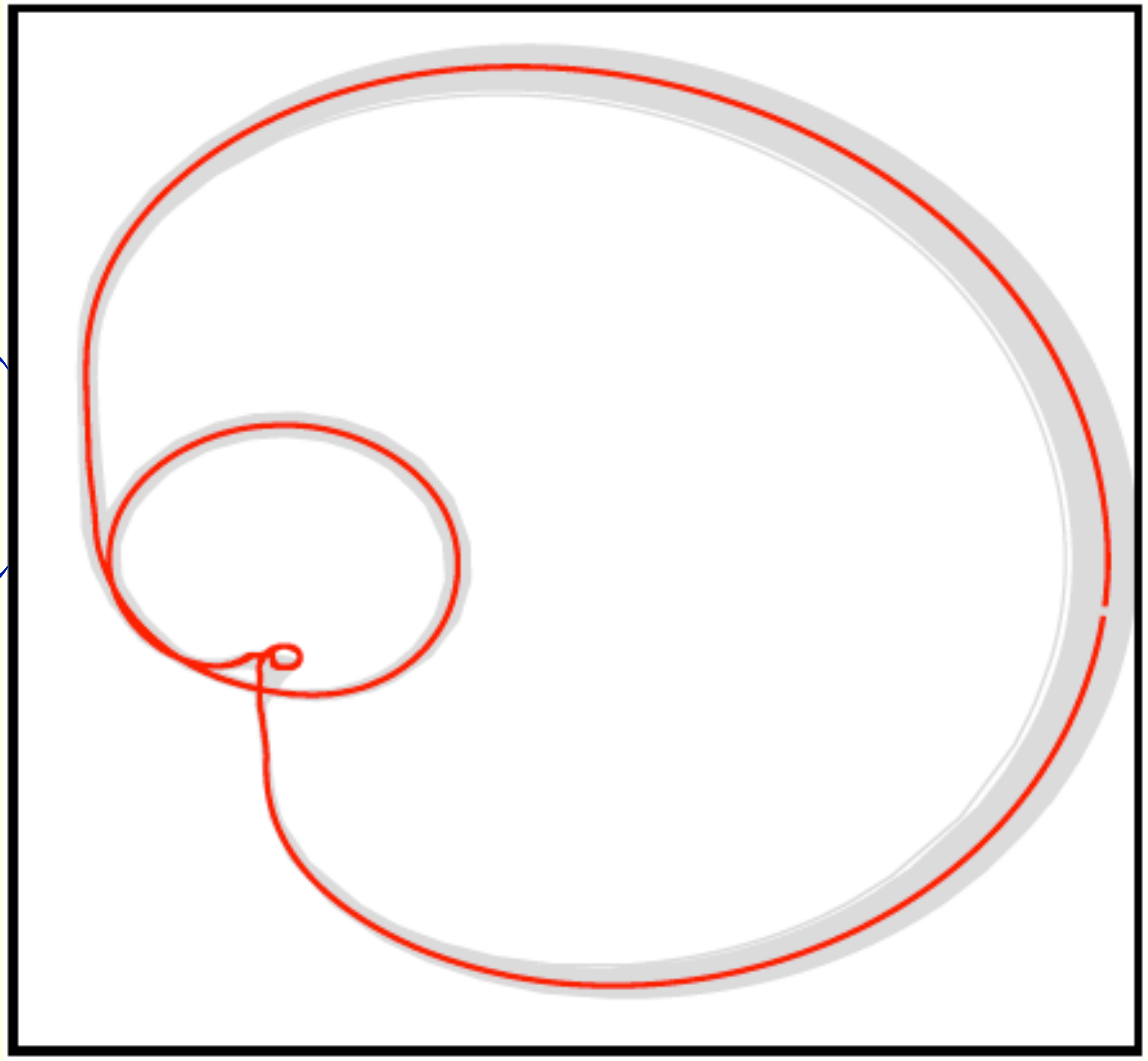
Björn Kralemann, Michael Rosenblum, Arkady Pikovsky

Version 2.0 (2014)

Software for data analysis can be downloaded from:
www.stat.physik.uni-potsdam.de/~mros/damoco2.html

Protophase of the ECG signal in three steps

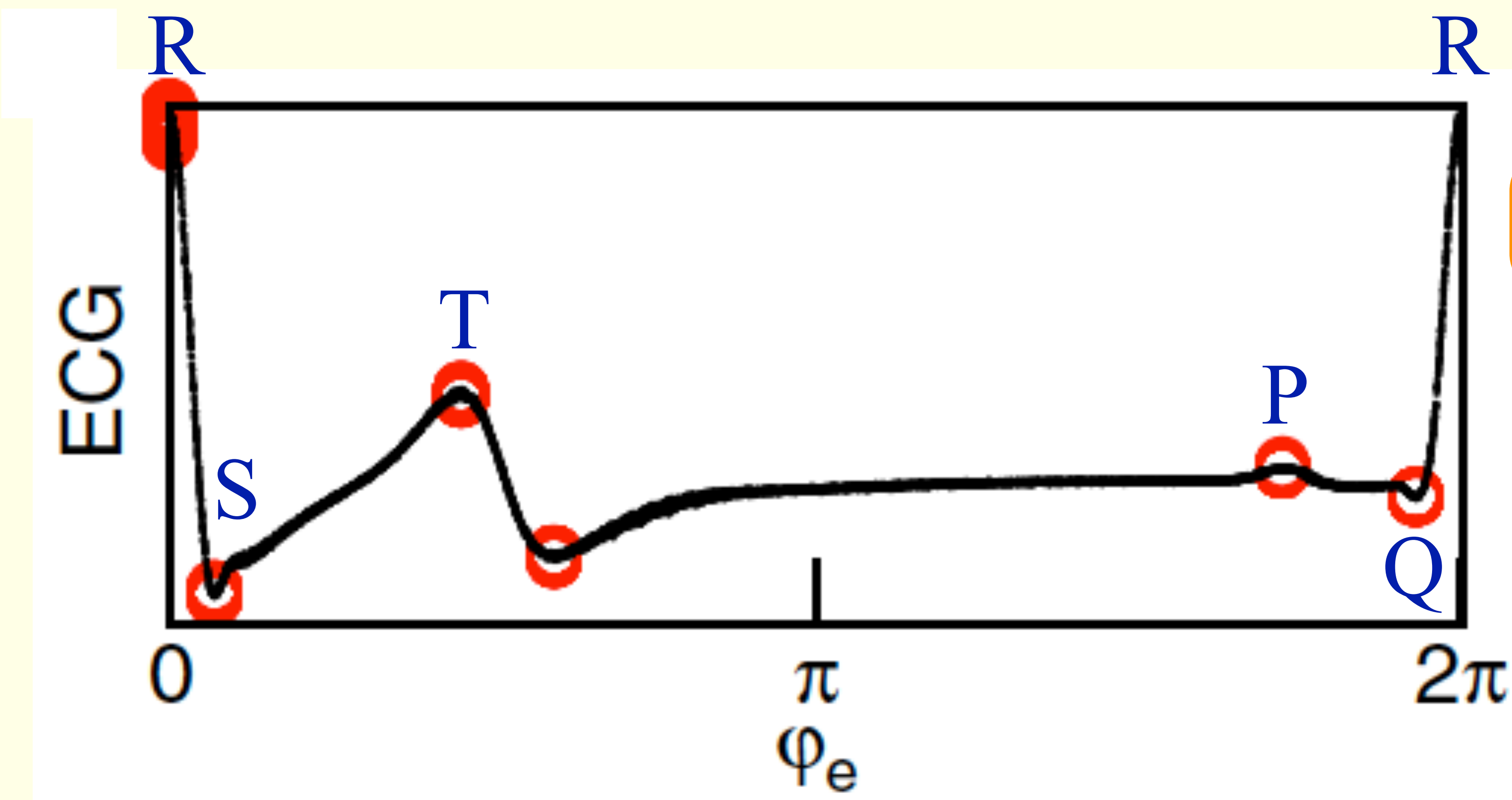
1. First protophase estimate via 6 markers events
2. Construction of the **average cycle** in the Hilbert plane
3. Projection of the trajectory on the average cycle



similar approach for **arterial pulse** signal (three marker events)

Protophase of the ECG step by step

1. First protophase estimate via 6 marker events
   - maxima of R, T, P waves
   - minima of Q, S and of the wave after T
   - protophase of the R-peak is set to zero
   - protophases of other markers are assigned according to their average position within the cycle
   - linear interpolation between the markers $\longrightarrow \hat{\theta}_e$



overlap of all cycles

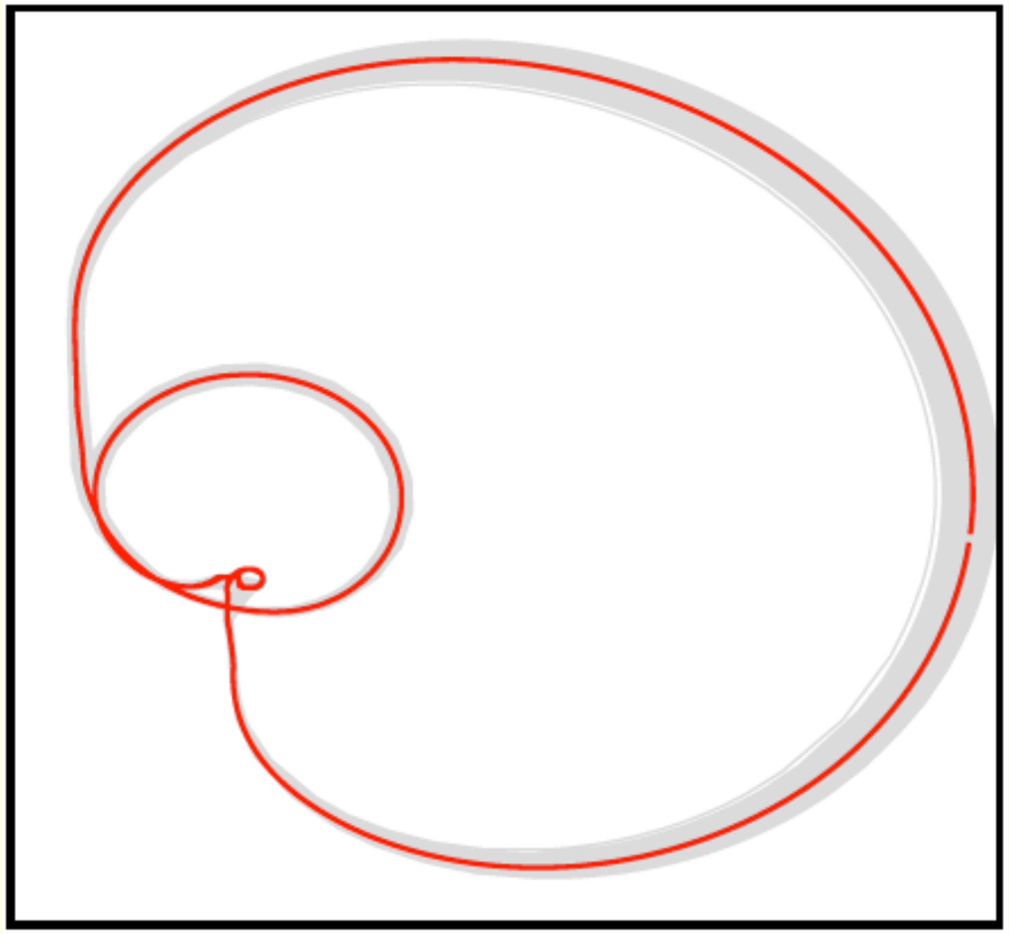
Protophase of the ECG step by step

2. Construction of the **average cycle** $z_{ac}(\psi)$

Analytic signal $z(t) = x(t) + \mathrm{i}\,\mathrm{HT}[x(t)]$

$$z_{ac}(\psi) = \sum_{0}^{80} H_n e^{\mathrm{i}n\psi}$$, where Fourier coefficients are

$$H_n = \frac{1}{\hat{\theta}_e(T)} \int_0^{\hat{\theta}_e(T)} z(\hat{\theta}_e) e^{-\mathrm{i}n\psi} \mathrm{d}\hat{\theta}_e = \frac{1}{T} \int_0^{T} z(t) e^{-\mathrm{i}n\hat{\theta}_e} \frac{\mathrm{d}\hat{\theta}_e}{\mathrm{d}t} \mathrm{d}t$$



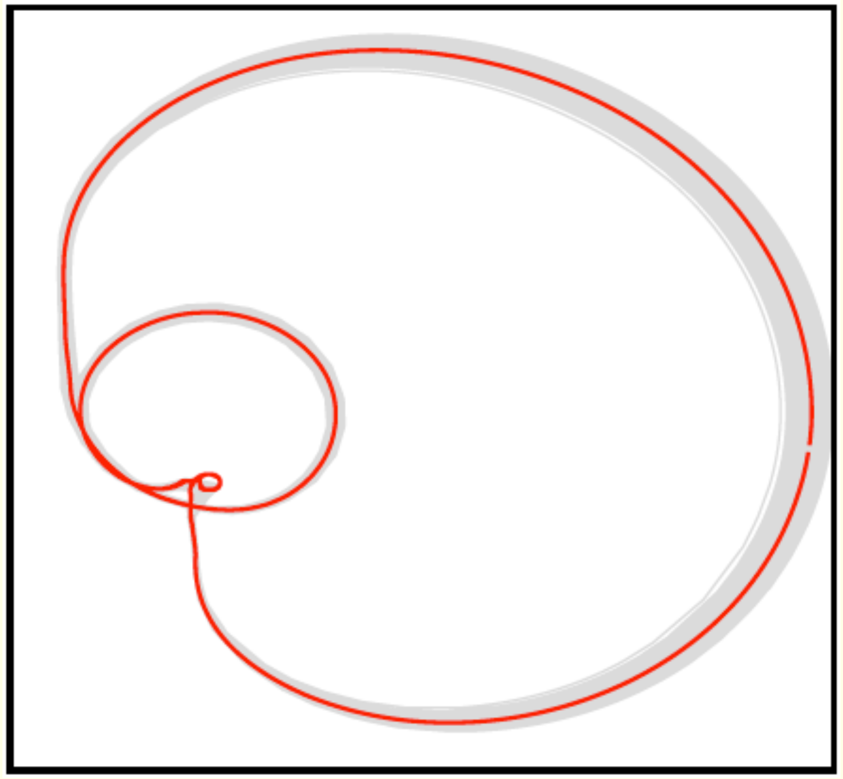
Protophase of the ECG step by step

3. Projection of the trajectory on the average cycle with the help of an optimization strategy

Namely, we look for a point $\boldsymbol{z_{ac}(\psi_0)}$ using minimization

$$\min_{\psi_0}\left\{\left|z(t)-z_{ac}(\psi_0)\right|^2+\alpha\left|e^{i\hat{\theta}_e(t)}-e^{i\psi_0}\right|^2\right\}$$

cost function



Finally, $\boldsymbol{\theta_e(t)=\psi_0}$

How to test and tune the average cycle technique?

1. Generate test phases $\hat{\varphi}_e, \hat{\varphi}_r$ from the **known** phase model $\hat{q}$
2. Generate the test ECG, using the average cycle from a particular record as:

$$\mathcal{E}(t) = \mathrm{Re}\left[z_{ac}(\hat{\varphi}(t))\right]$$

   and add some amplitude modulation and noise.

3. Reconstruct the coupling function q and compare it with $\hat{q}$
4. Do it for different parameters and look for optimal values