Inferring network properties via phase dynamics modelling with application to Network Physiology

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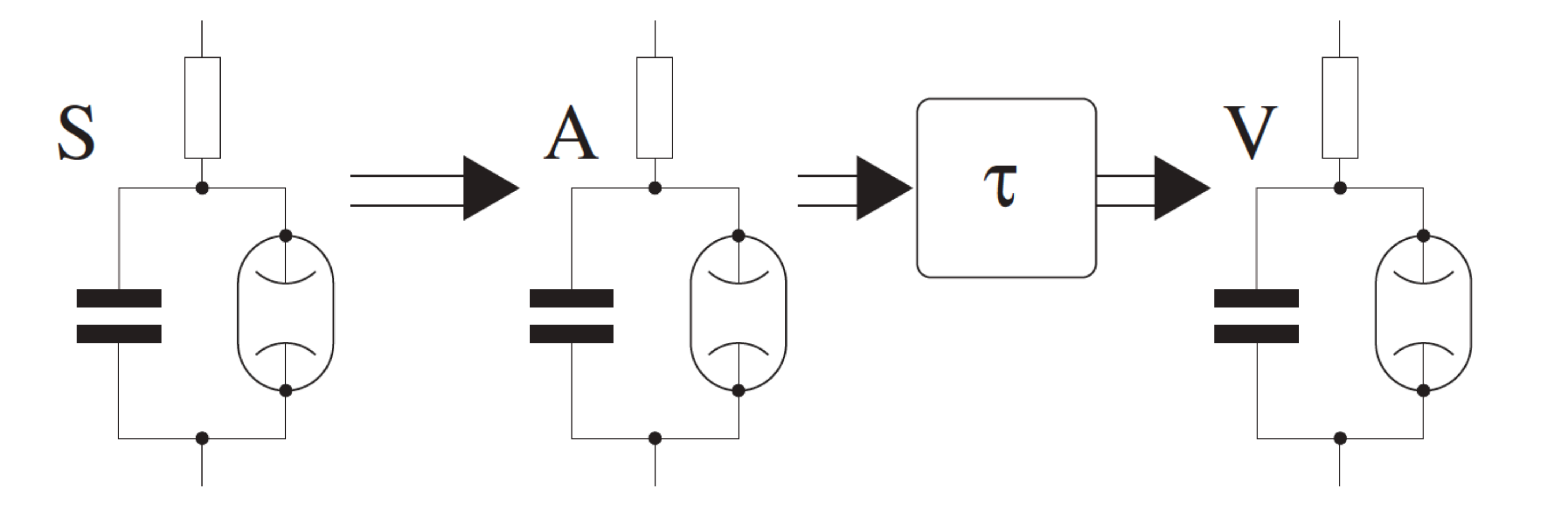
Network Physiology Summer Institute, Como, 31.07.19

Oscillatory networks as models for living systems

sino-atrial node

atria

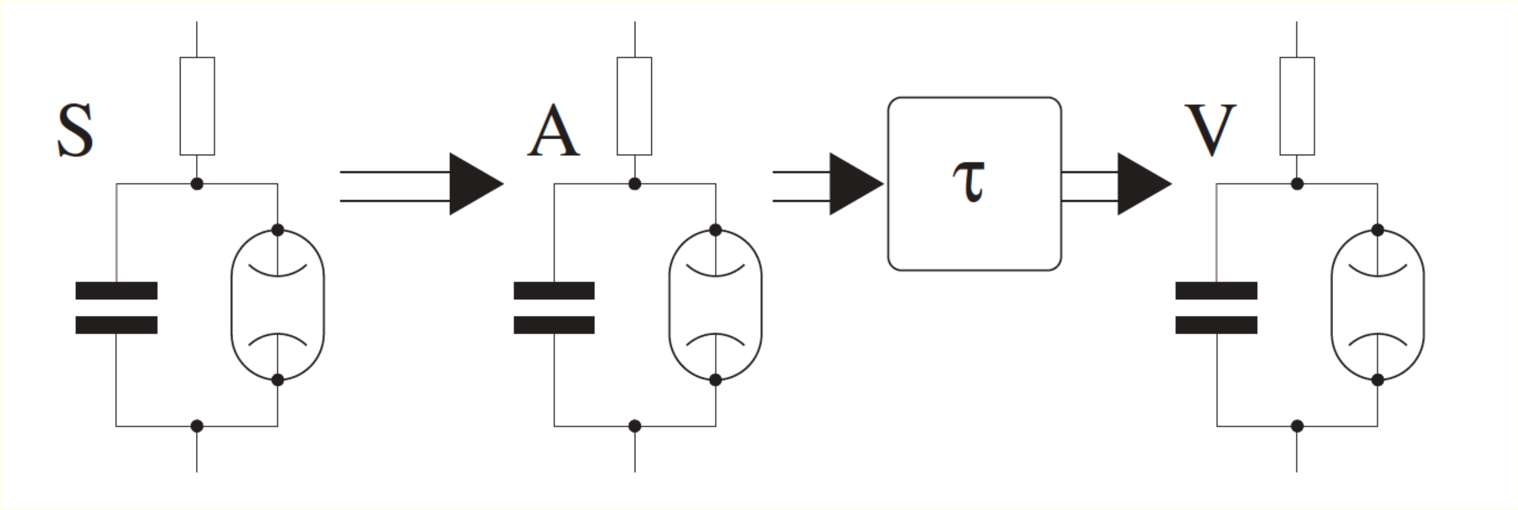
ventricles

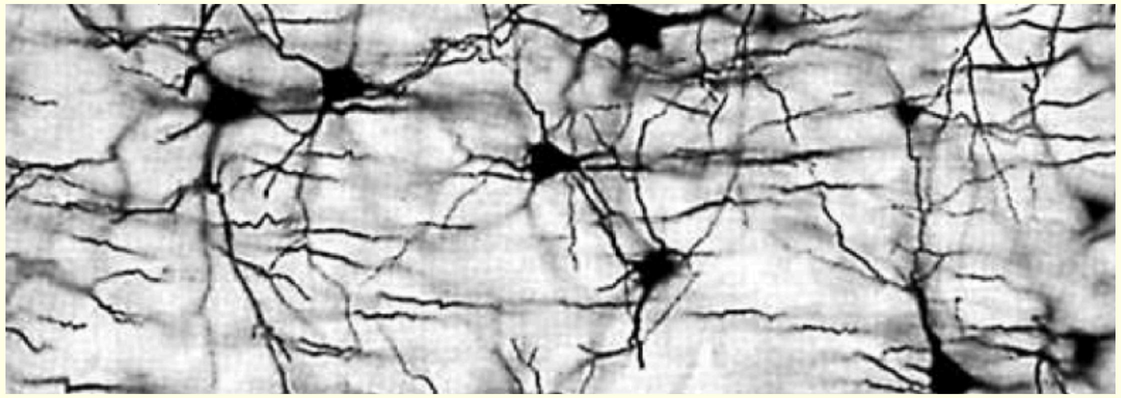


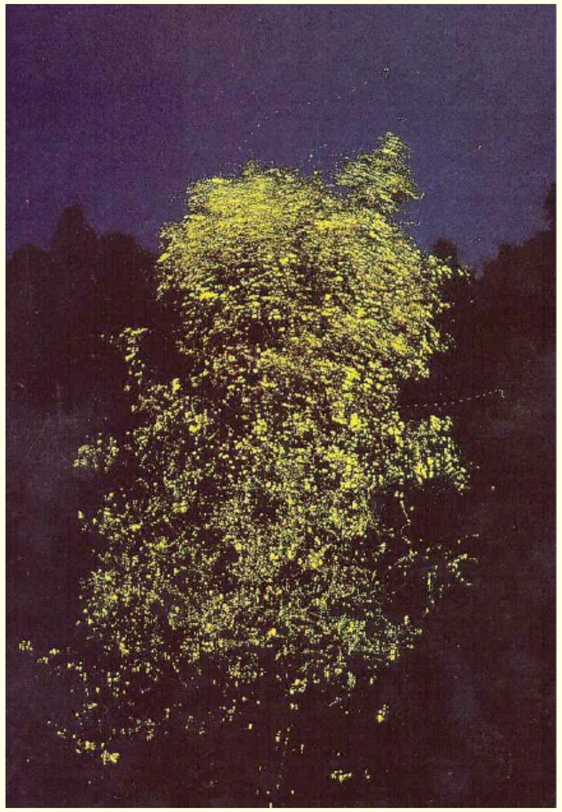
Electrical model of the heart: three coupled relaxation oscillators

van der Pol and van der Mark, 1928

Oscillatory networks as models for living systems

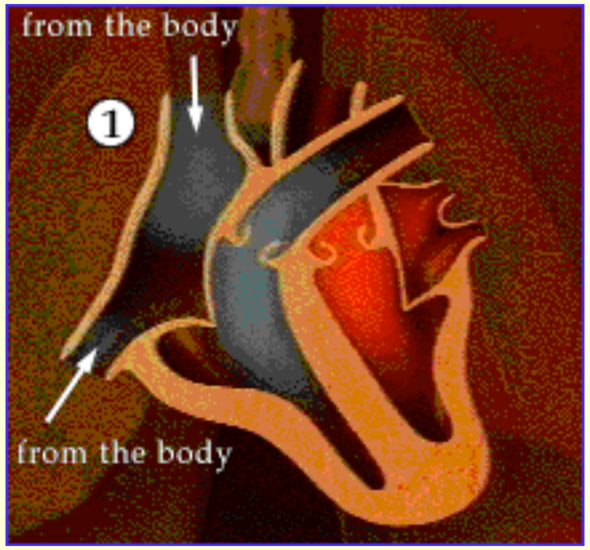






We consider networks of self-sustained oscillators

Self-sustained oscillators



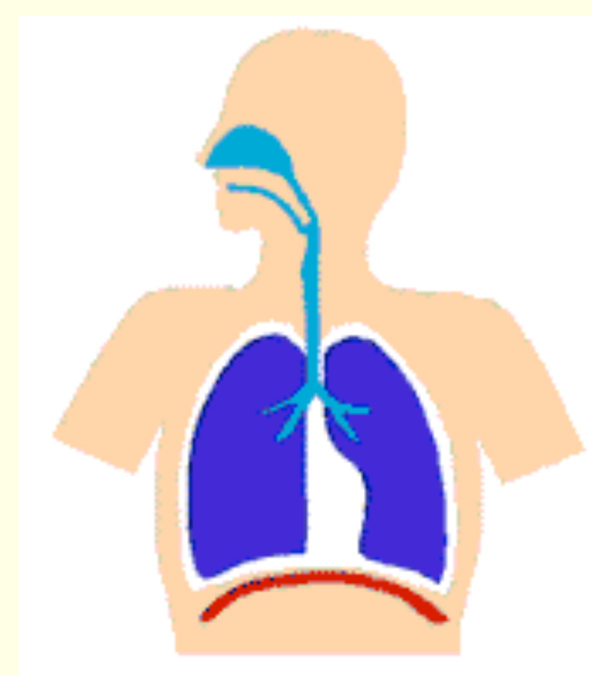
Active oscillators

Biology: systems generating **endogenous** rhythms

Systems of this class:

1. generate stationary oscillations without periodic forces
2. are dissipative nonlinear systems
3. are described by autonomous differential equations
4. are represented by a limit cycle in the phase space

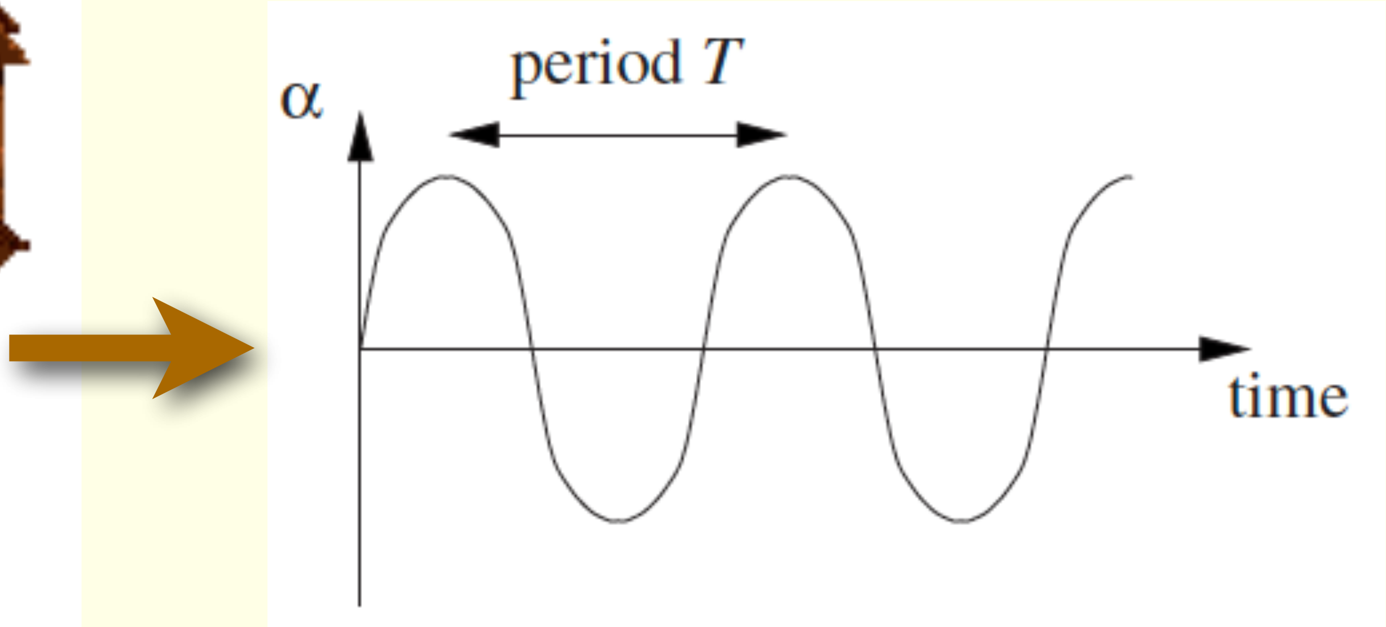
Self-sustained oscillators: Examples

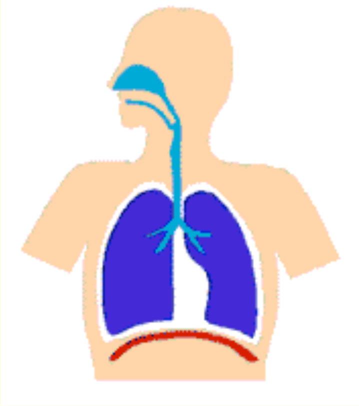


Animated images: www.netanimations.net

Self-sustained oscillators: Examples

1 periodic oscillators





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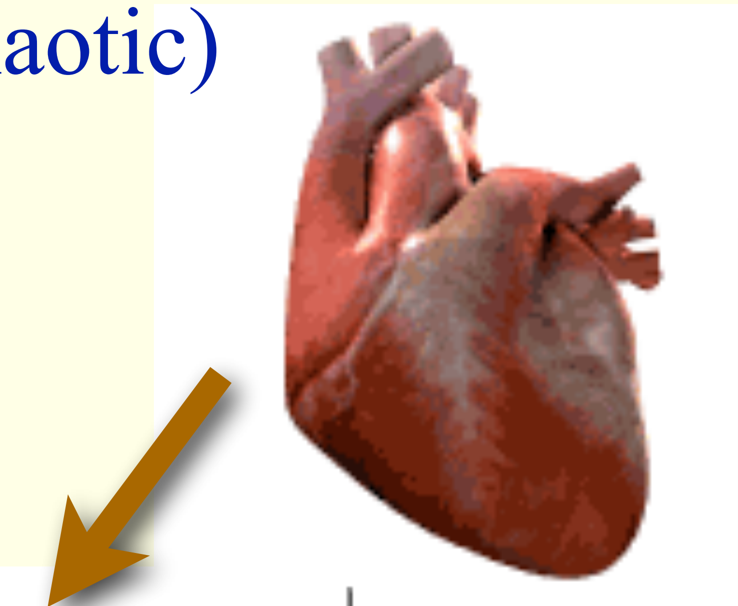
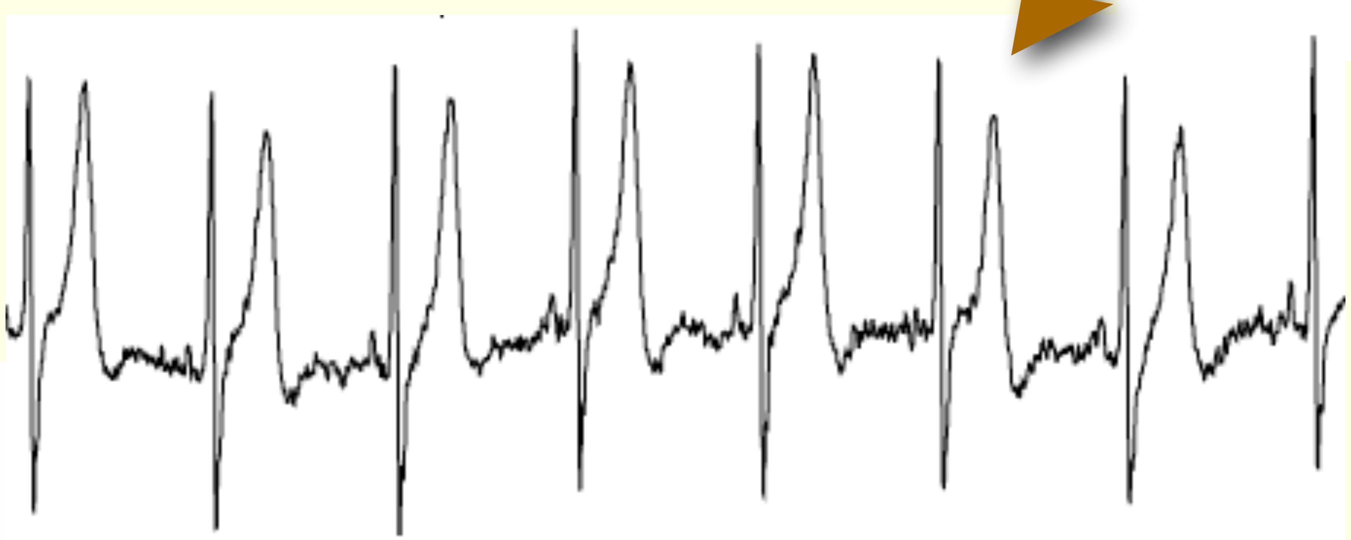
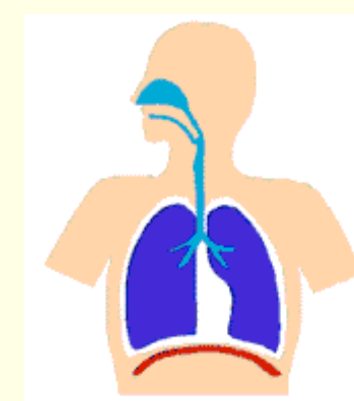
Self-sustained oscillators: Examples

2 Irregular oscillators (noisy/chaotic)







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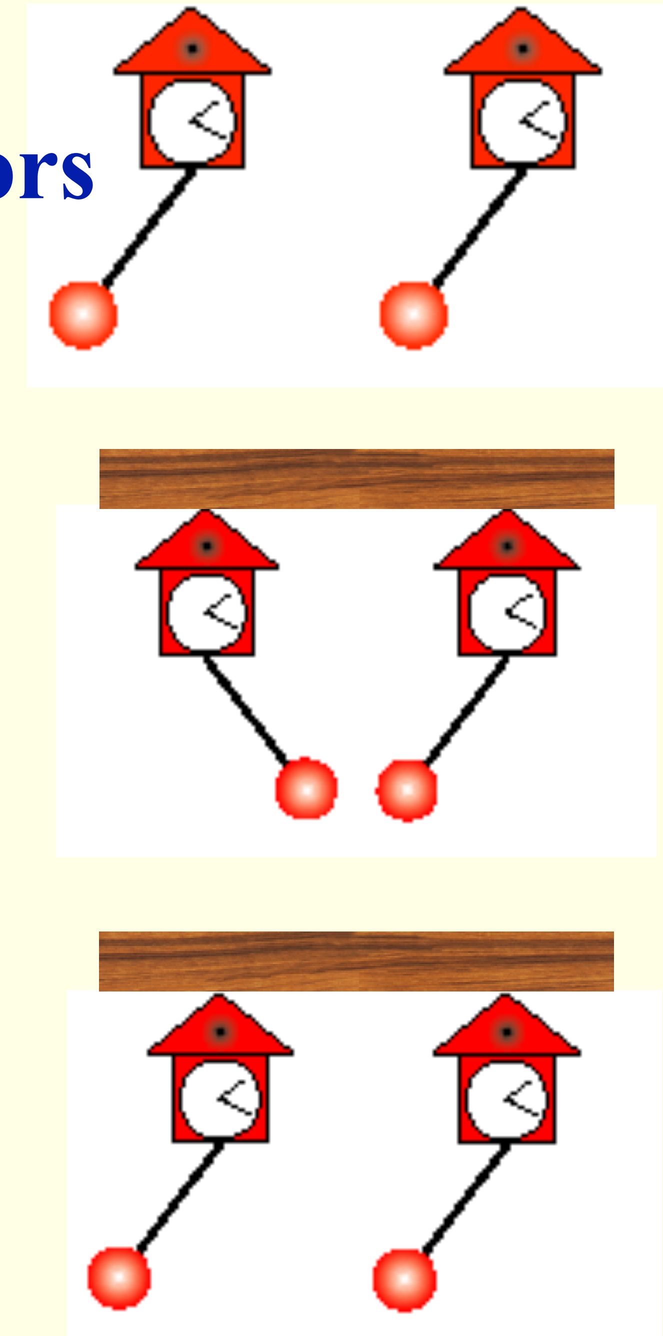
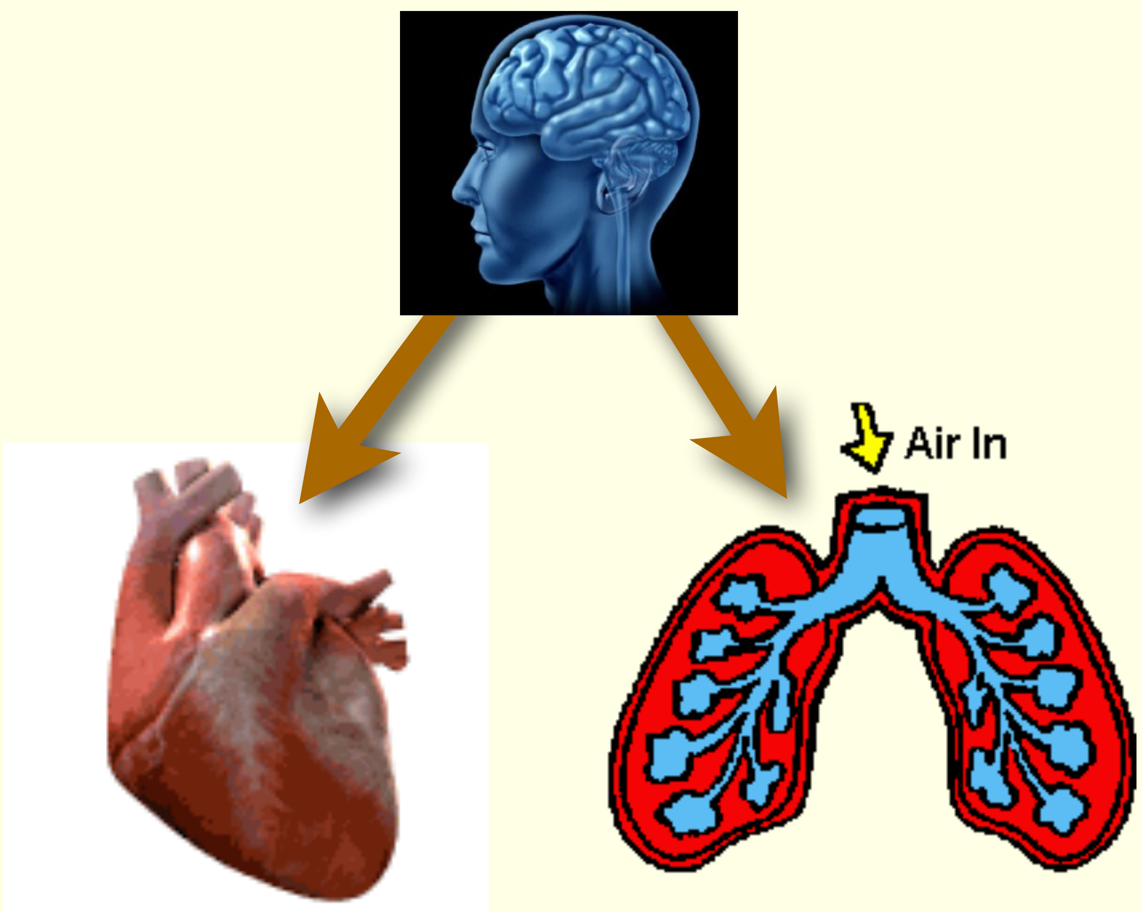
Main effect: Synchronization

1 It is a property of **self-sustained oscillators**

2 It appears due to their **interaction**





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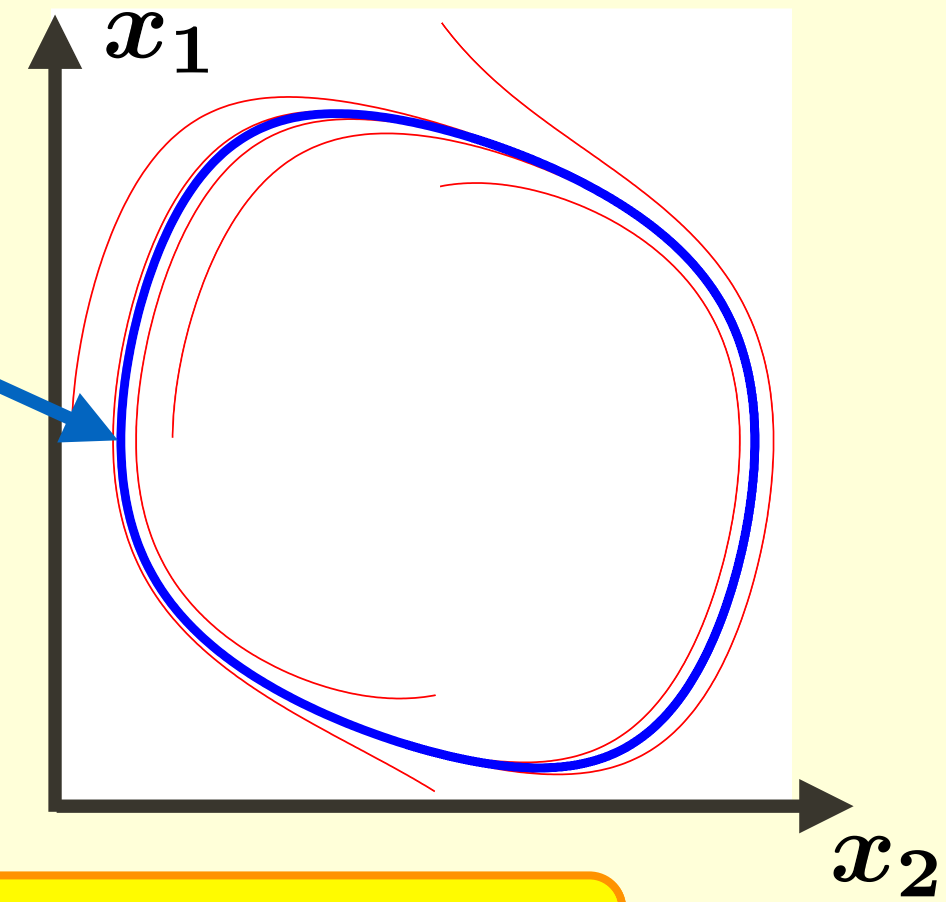
Self-sustained oscillator: limit cycle and phase

Stable limit cycle: an attractive closed curve in the phase space



Phase is a variable that describes the motion along the **limit cycle**

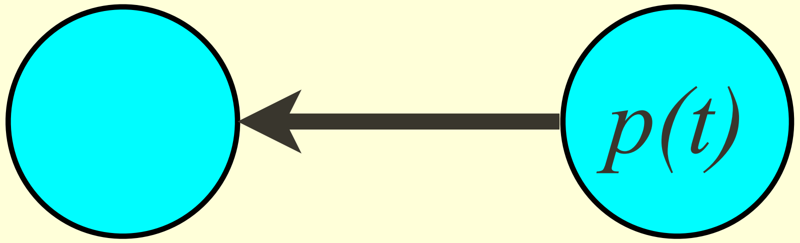
Phase is defined to obey the condition $\dot{\varphi} = \omega = 2\pi/T$

and can be introduced:

1. on the limit cycle

2. in the basin of attraction of the limit cycle

Phase dynamics: the phase sensitivity function



Suppose the oscillator is driven by **weak** perturbation *p(t)*

Then

$$\dot{\varphi} = \omega + Z(\varphi)p(t)$$

Phase Sensitivity function, or Phase Response Curve (PRC)

Phase dynamics equation in the **Winfree form**

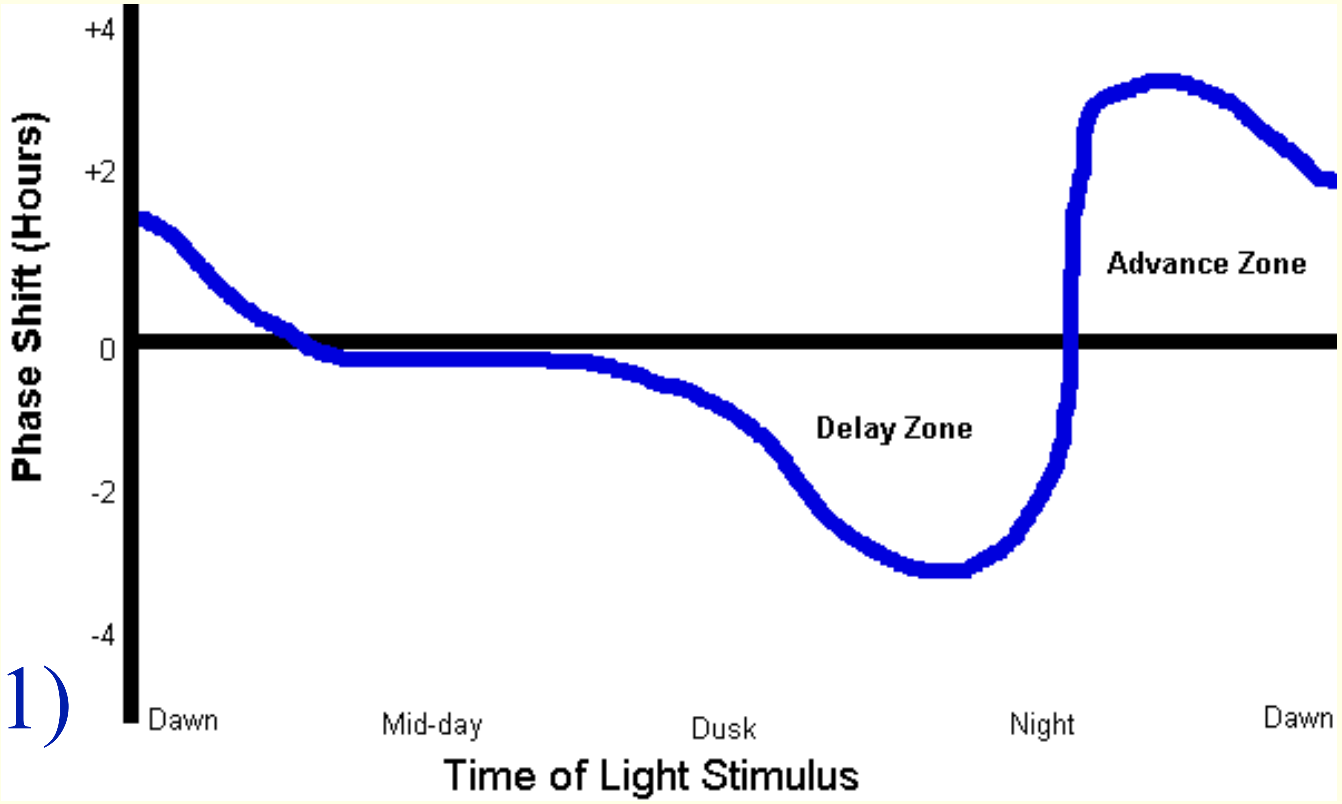
Phase response curve (PRC)

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

Example: human circadian cycle

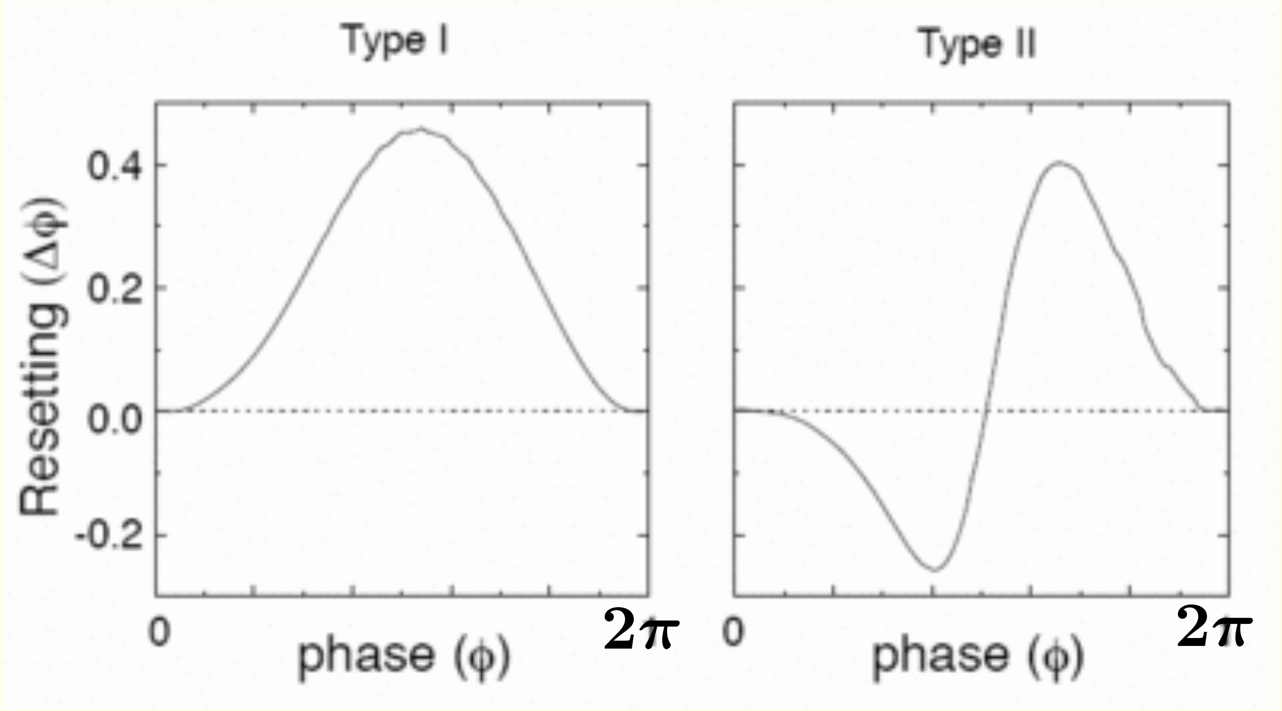
- *Delay region: evening light shifts sleepiness later* and
- *Advance region: morning light shifts sleepiness earlier*.

(Wikipedia; Kripke & Loving, 2001)

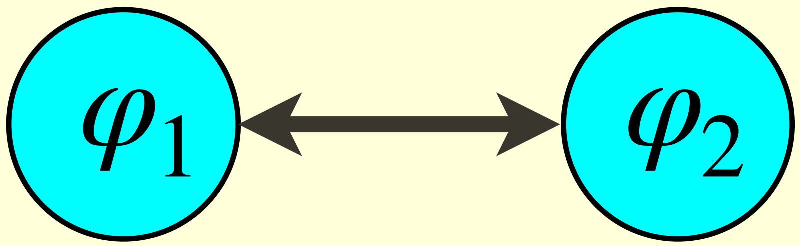


Example: neural PRCs

(Scholarpedia)



Phase dynamics: the coupling function



Consider two coupled oscillators

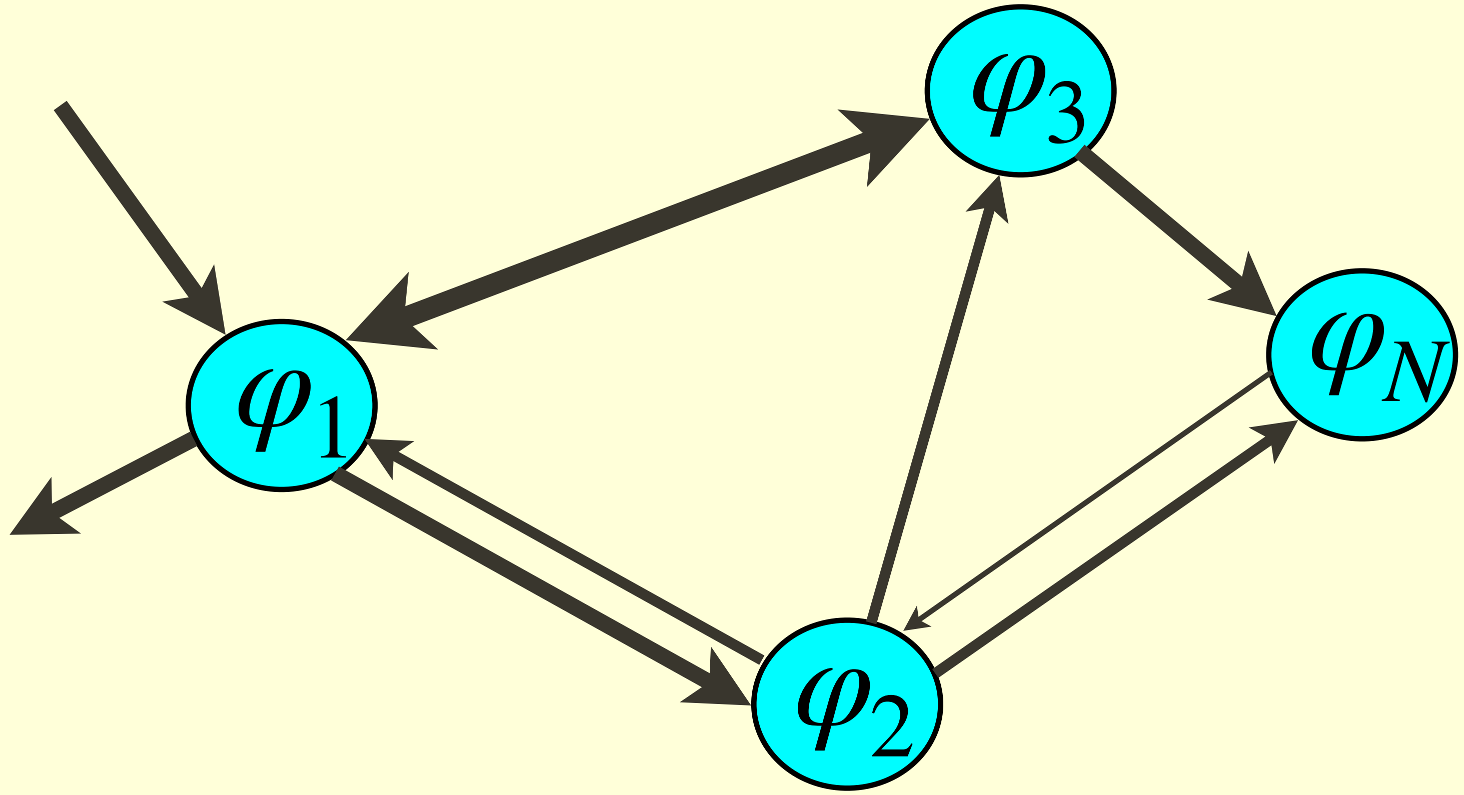
Then $$\dot{\varphi}_1 = \omega_1 + Q(\varphi_1, \varphi_2)$$

Coupling function

Notice: Phase dynamics equation can be analytically derived only in the limit of weak coupling

However: this equation is generally valid for quite strong coupling and the coupling function can be obtained numerically or **reconstructed from data**

Phase dynamics: the coupling function II



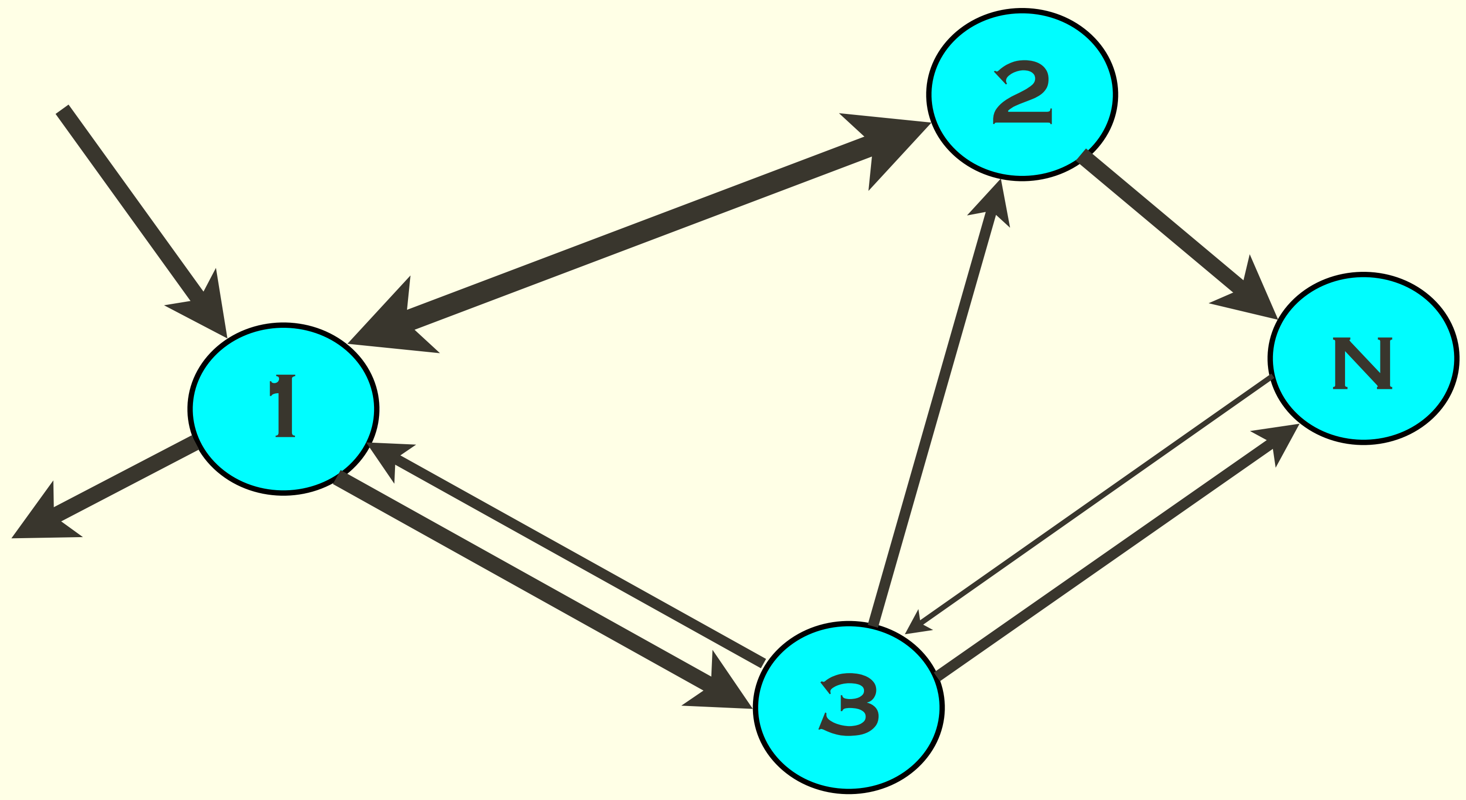
Consider an oscillatory network

- Pairwise coupling in the full system:
  - first-order approximation: pairwise terms, like

$$\dot{\varphi}_1 = \omega_1 + Q_{12}(\varphi_1, \varphi_2) + Q_{13}(\varphi_1, \varphi_3) + \dots$$

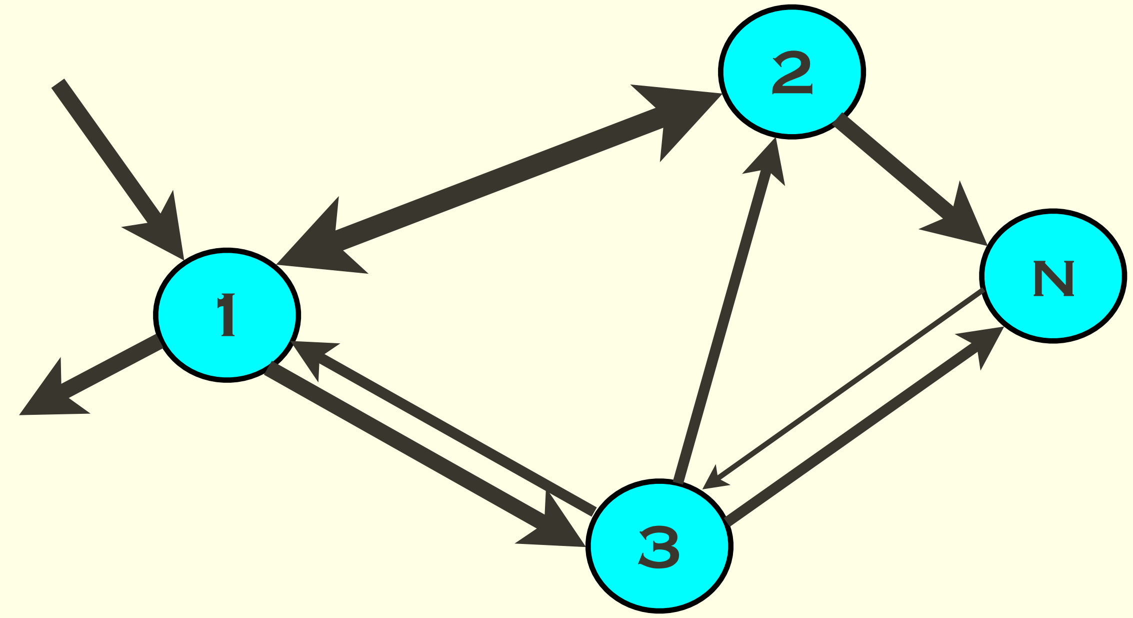
  - high-order approximation: ***terms, depending on many phases***, not only on the phases of directly coupled nodes

Formulation of the problem



- Data: we have signals measured from all units
- Assumption 1: the units are **self-sustained** oscillators
- Assumption 2: the interaction between the units is not too strong (phase modelling is justified)

Formulation of the problem II

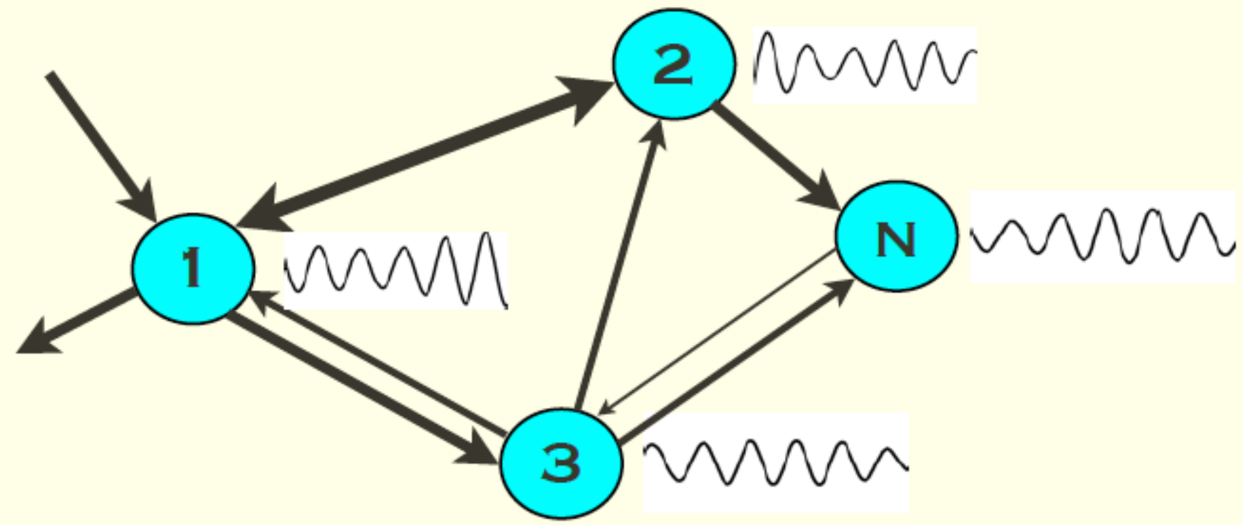


- Synchronization analysis: quantification of the strength of the interaction (degree of the phase locking)
- Connectivity analysis: recovery of the **directed** connectivity via reconstruction of phase dynamics from data
- Model reconstruction: estimation of some parameters of the interacting units

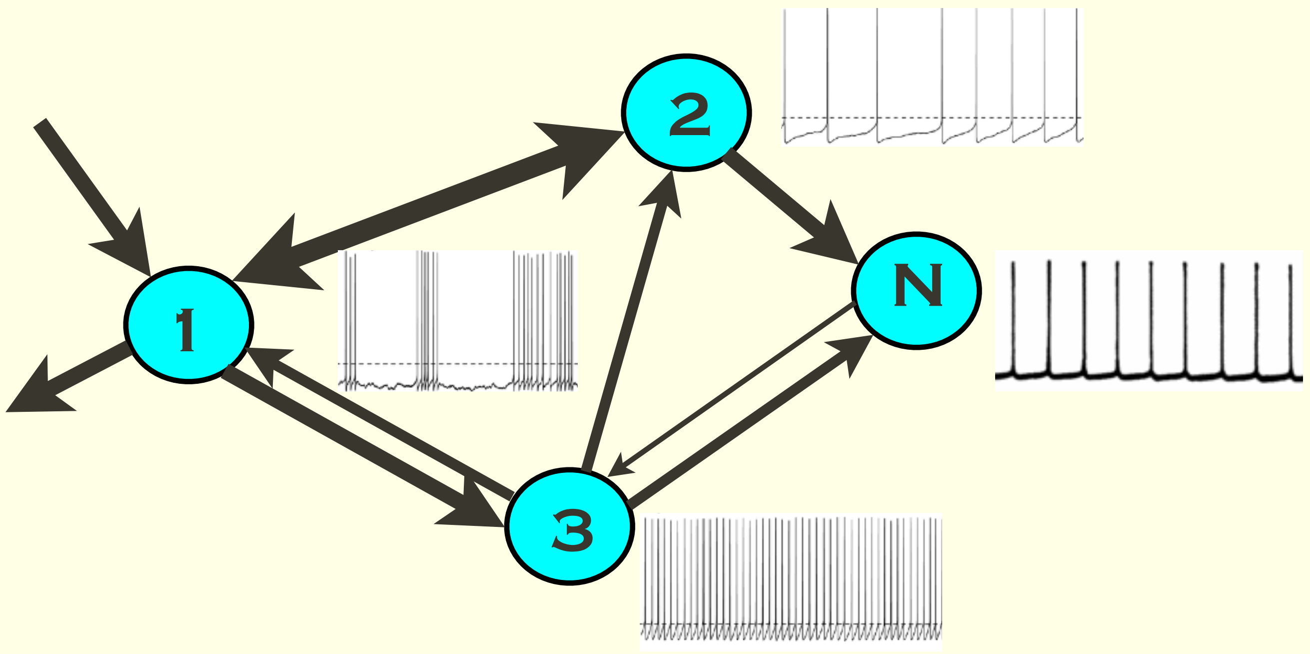
To solve these tasks we have to consider separately two cases

Formulation of the problem III

Case 1: oscillatory signals suitable for phase estimation from time series

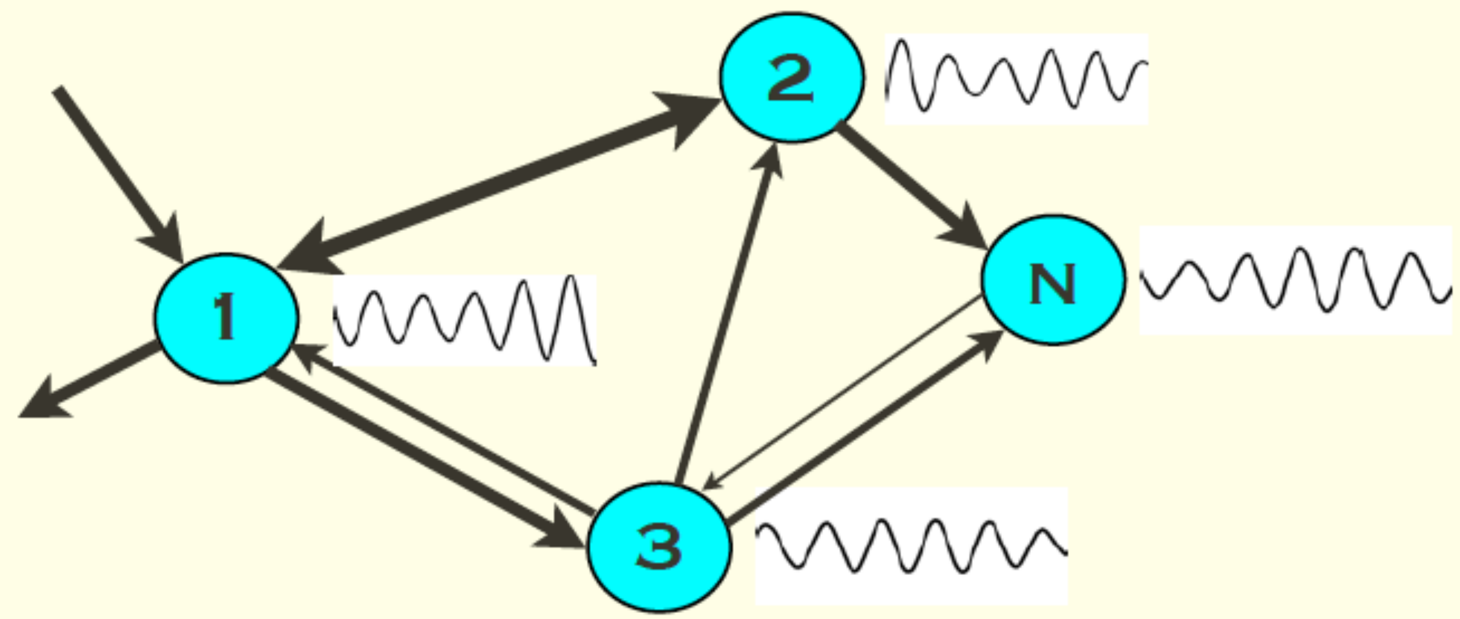


Case 2: pulse-like signals, only times of spikes can be reliably measured



How to treat case 1

- Estimate phases from time series, e.g. via the Hilbert Transform



- Compute numerically derivatives $\dot{\varphi}$
- Construct phase dynamics equations, e.g. $\dot{\varphi}_1 = \omega_1 + Q_1(\varphi_1, \varphi_2, \ldots)$ by fit (kerned density estimation, l.m.s. fit for Fourier harmonics, etc)
- Analyse norms of all coupling functions to recover connectivity

How to recover connectivity

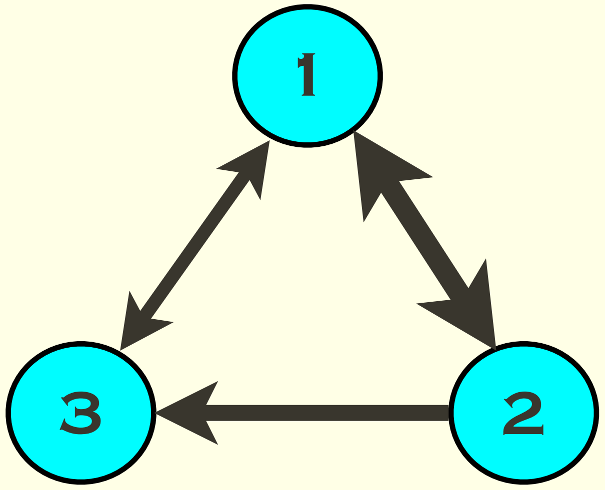
- Two oscillators: $\dot{\varphi}_1 = \omega_1 + Q_1(\varphi_1, \varphi_2)$

$$\dot{\varphi}_2 = \omega_2 + Q_2(\varphi_2, \varphi_1)$$

Strength of the connection $2 \to 1$ is given by norm $\|Q_1\|$

Strength of the connection $1 \to 2$ is given by norm $\|Q_2\|$

- Three oscillators:



$$\dot{\varphi}_1 = \omega_1 + Q_1(\varphi_1, \varphi_2, \varphi_3)\ , \ldots$$

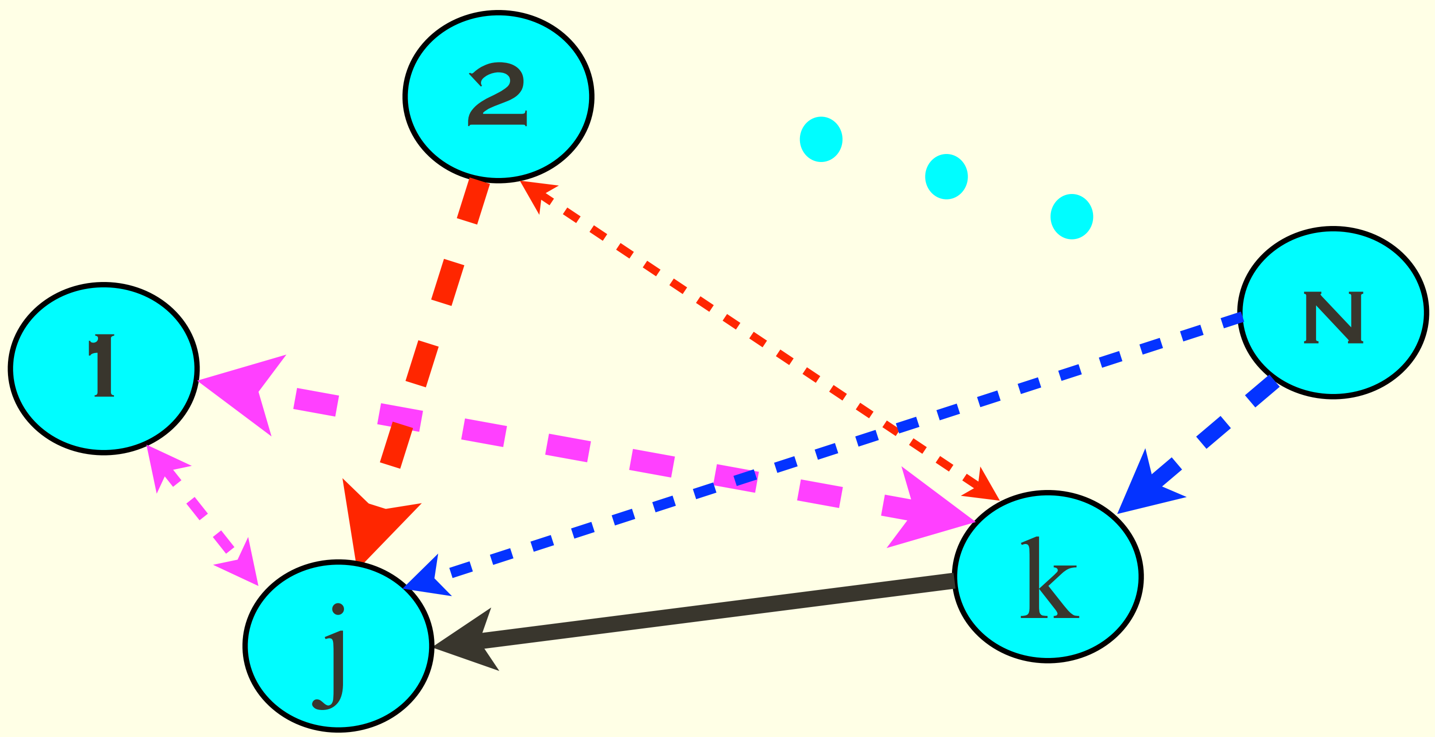
Strength of the links is quantified by **partial norms,** e.g. for the link $2 \to 1$

$$\mathcal{N}^2_{1\leftarrow 2} = \sum_{l_1, l_2 \neq 0} \left| F_{l_1, l_2, 0} \right|^2 ,$$ where F are Fourier coefficients

$$Q_1(\varphi_1, \varphi_2, \varphi_3) = \sum_{l_1, l_2, l_3} F_{l_1, l_2, l_3} \exp[i(l_1\varphi_1 + l_2\varphi_2 + l_3\varphi_3)]$$

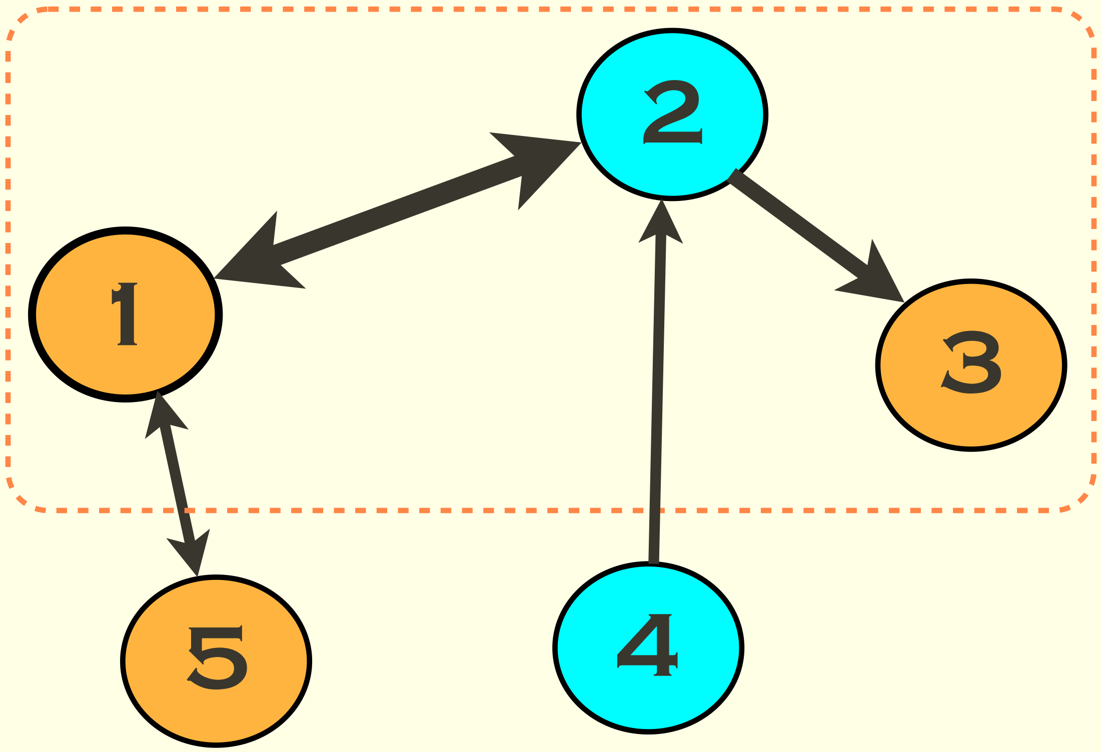
How to recover connectivity II

- More than three oscillators: use triplet analysis!

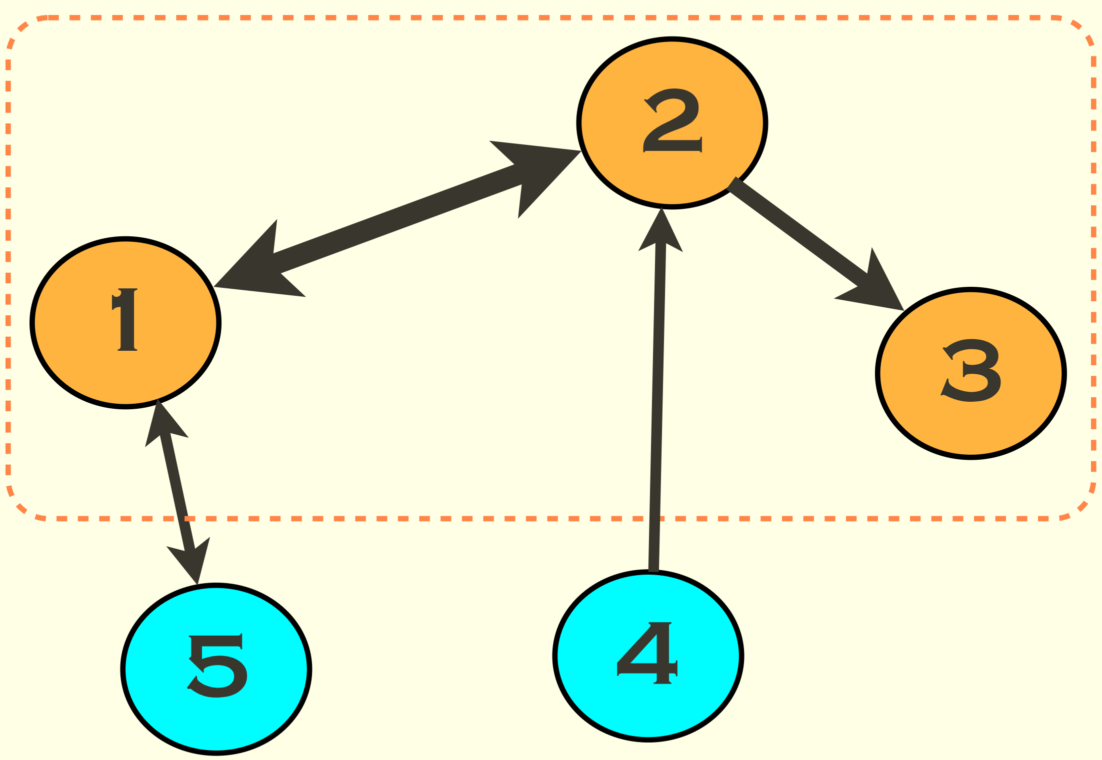


Compute partial norms for the desired link from all possible triplets and take the minimal value for the strength of the connection

Triplet analysis: why does it work?



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

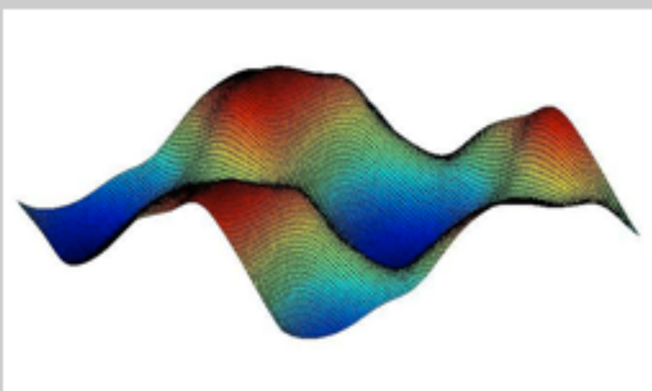


Triplet $\{1,2,3\}$ correctly explains correlation of $\boldsymbol{\varphi_1}, \boldsymbol{\varphi_3}$ and yields a small value for the link $\mathbf{1} \to \mathbf{3}$

Intermediate summary

- Network of oscillatory units can be reconstructed if the signals are good for phase estimation
- There is a number of technical details - see original publications
- Matlab toolbox:

www.stat.physik.uni-potsdam.de/~mros/damoco2.html



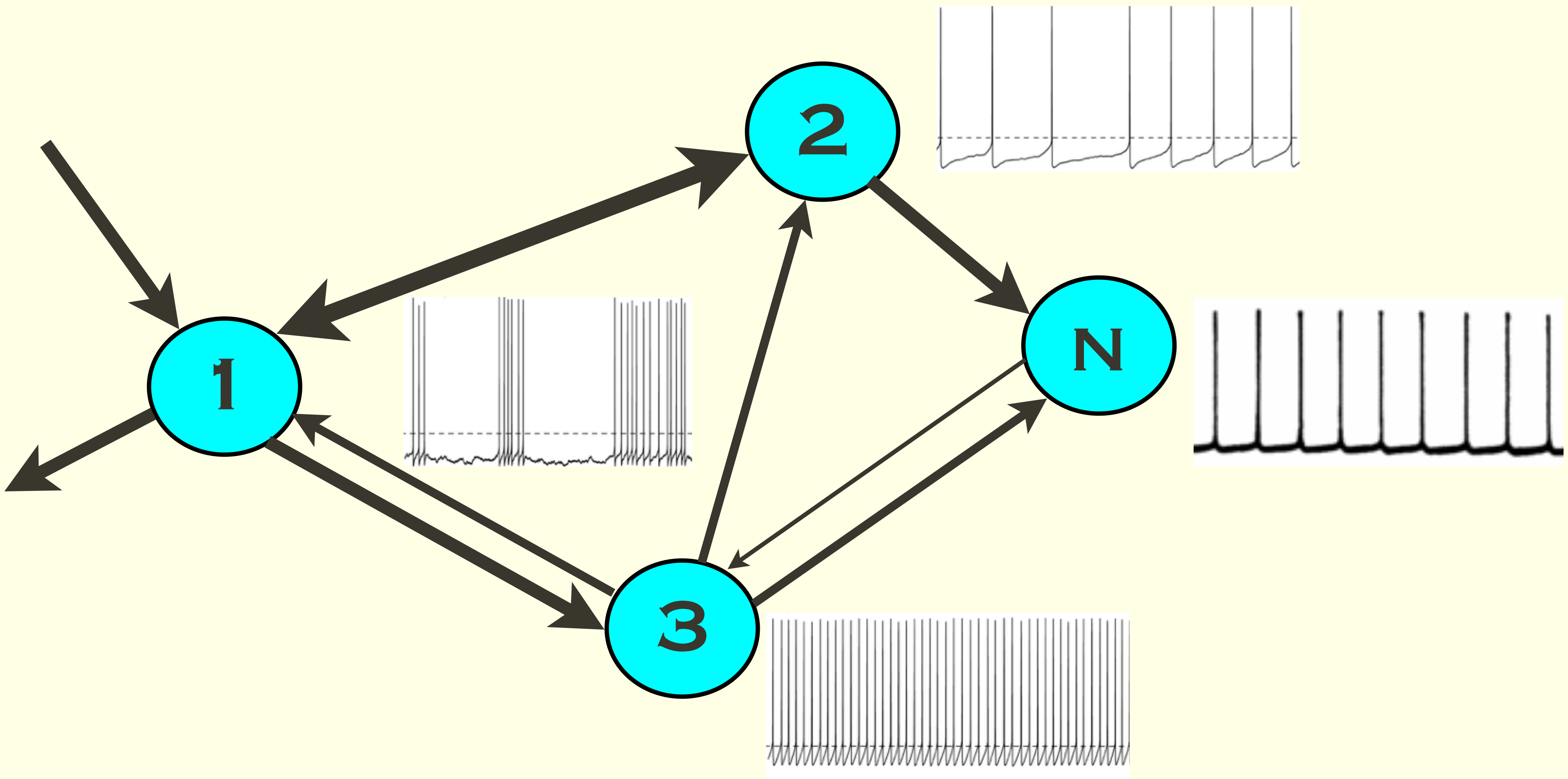
DAMOCO: Data Analysis with Models Of Coupled Oscillators

MATLAB Toolbox for multivariate times series analysis

Björn Kralemann, Michael Rosenblum, Arkady Pikovsky

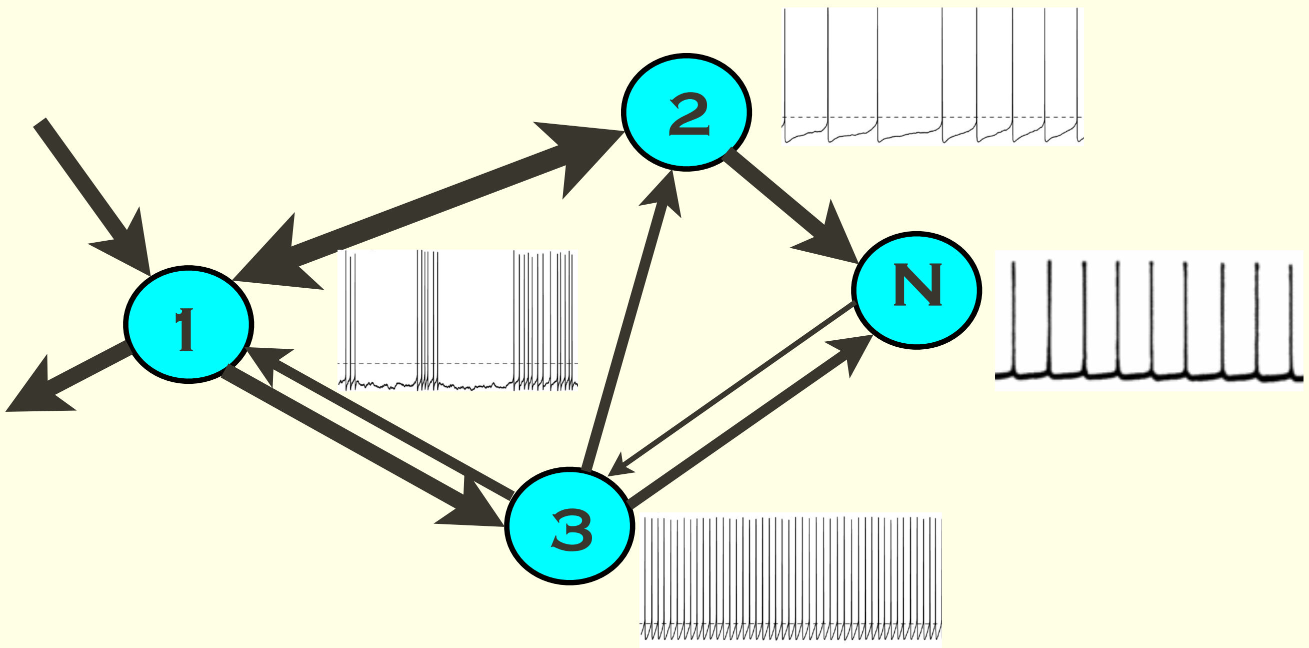
- B. Kralemann et al, New Journal of Physics, **16,** 085013, 2014
- B. Kralemann et al, Nature Communications, **4,** p. 2418, 2013
- B. Kralemann et al, Chaos, 21, 025104, 2011
- … and references therein

Case 2: Reconstructing networks of pulse-coupled oscillators from spike trains



The data we measure are like **sequences of spikes**

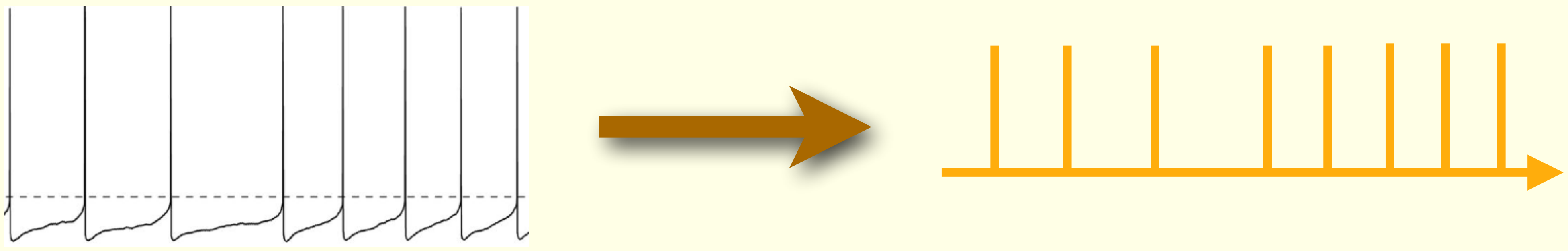
Formulation of the problem



The data we measure are like **sequences of spikes**

→ we can reliably detect only times of spikes

→ we reduce the data to **point processes**



Assumptions about the network

- Weak interaction: phase description is justified
- PRC of a unit is the same for all incoming connections
  <u>PRCs of different units can differ!</u>

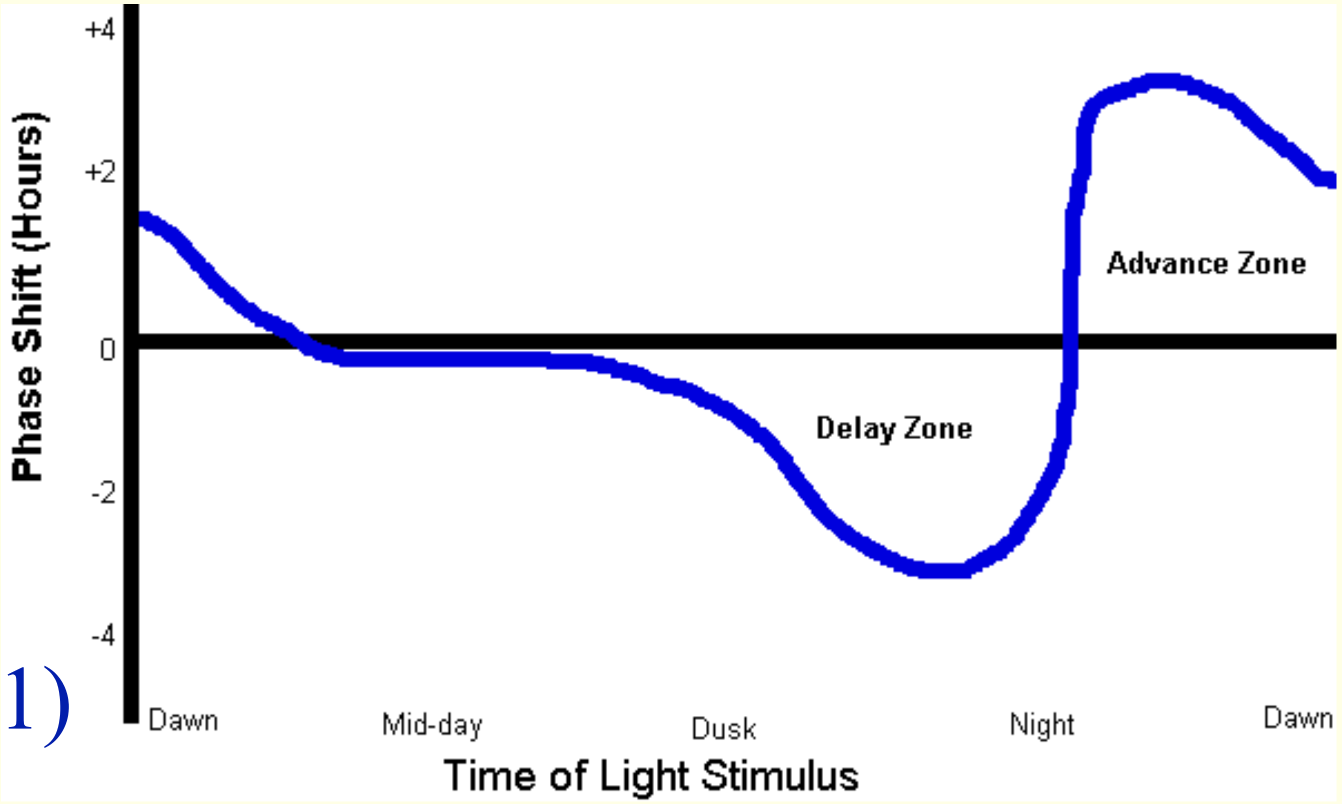
Phase response curve (PRC)

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

Example: human circadian cycle

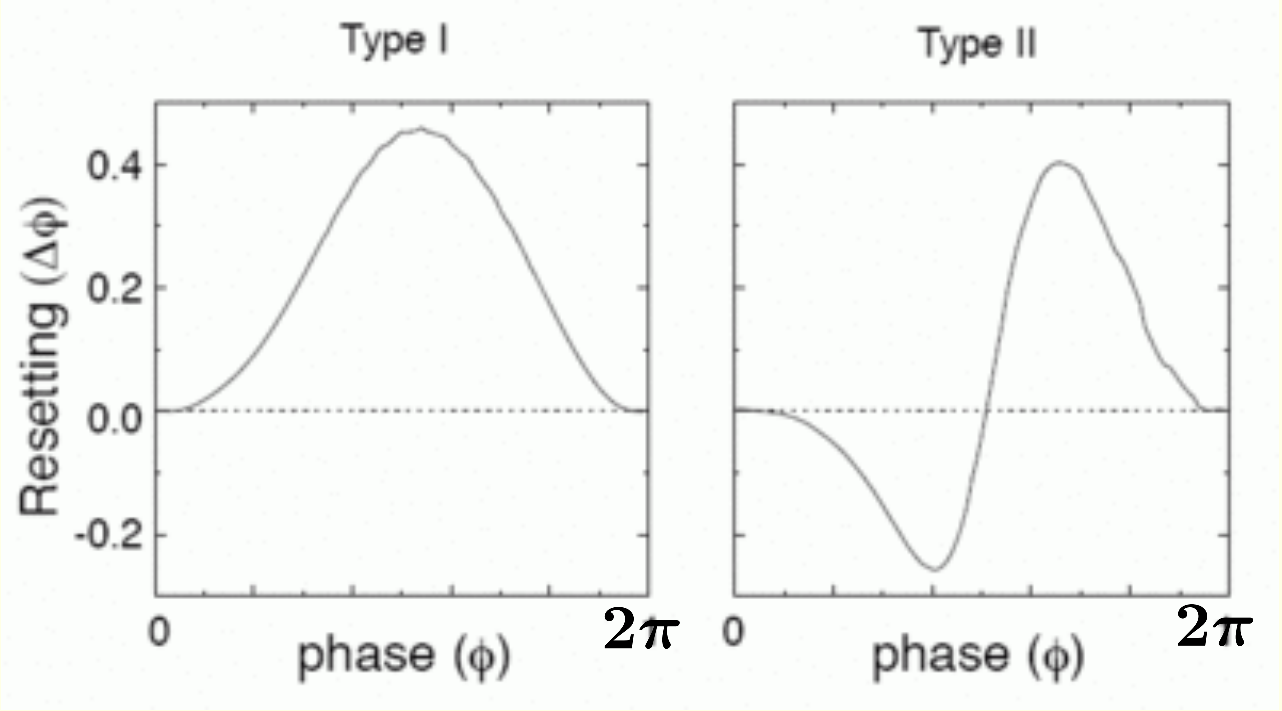
- *Delay region: evening light shifts sleepiness later* and
- *Advance region: morning light shifts sleepiness earlier*.

(Wikipedia; Kripke & Loving, 2001)



Example: neural PRCs

(Scholarpedia)



Assumptions about the network

- Weak interaction: phase description is justified

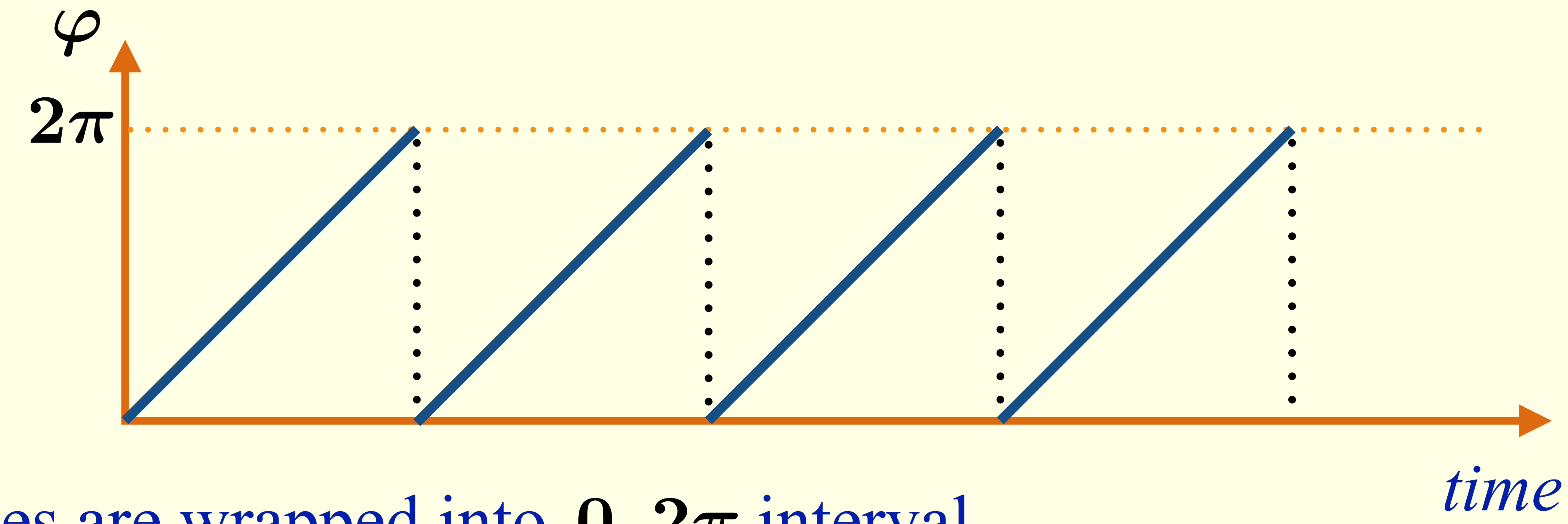
- PRC of a unit is the same for all incoming connections
  <u>PRCs of different units can differ!</u>

- Coupling is bidirectional but generally asymmetric,
  $\varepsilon_{km} \neq \varepsilon_{mk}$

  ↑ strength of the link from m to k

A simple model: integrate-and-fire units

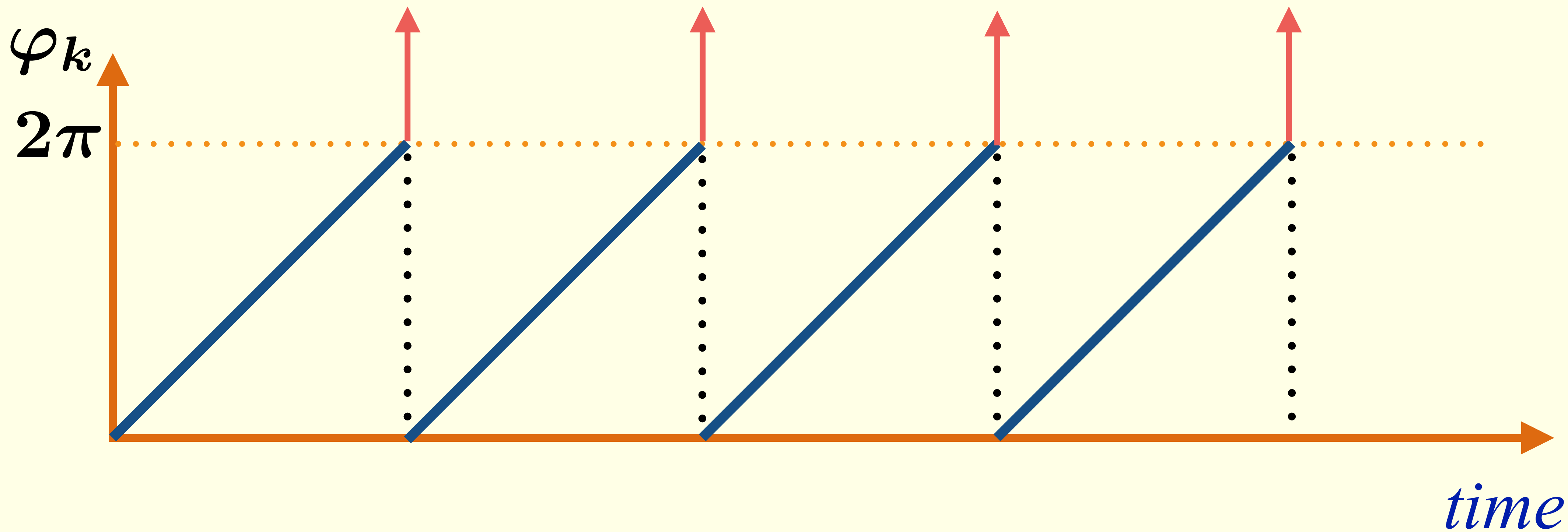
- Without interaction phases of all oscillators grow as $\varphi_k = \omega_k t$



phases are wrapped into $0, 2\pi$ interval

A simple model: integrate-and-fire units

- Without interaction phases of all oscillators grow as $\varphi_k = \omega_k t$
- When phase of the oscillator k attains $\varphi_k = 2\pi$,
  it **issues a spike**

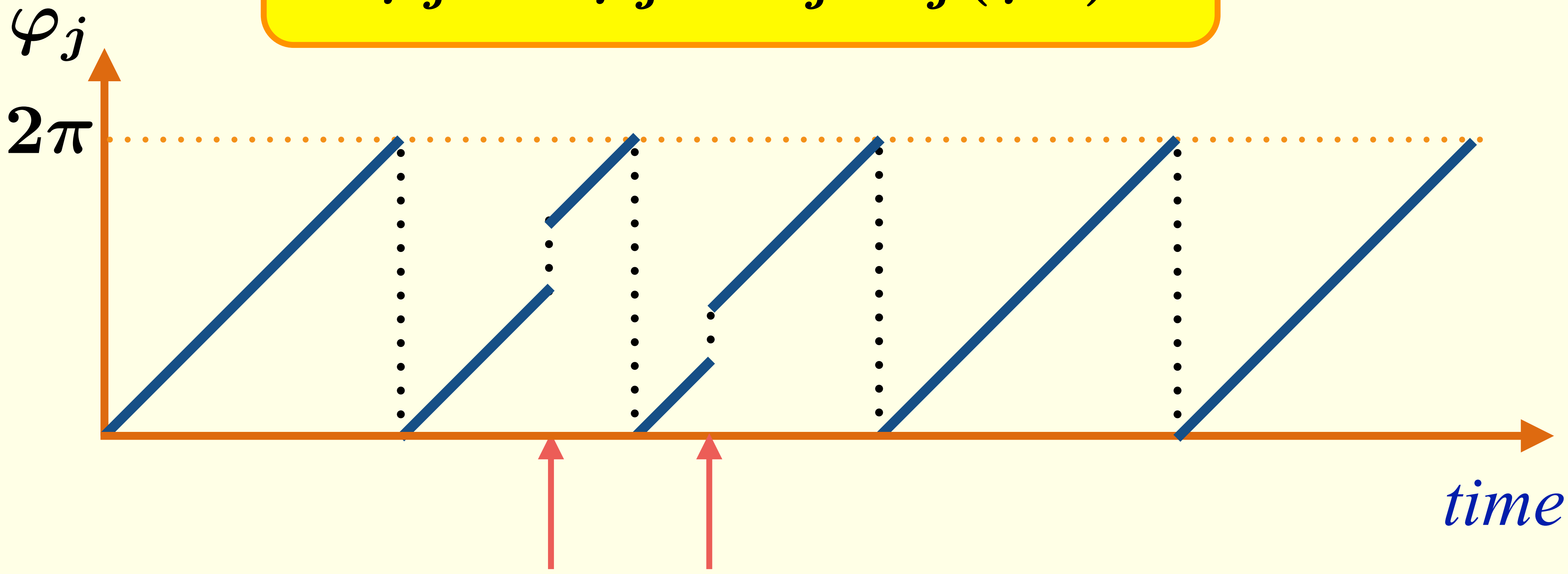


spikes affect all units with incoming connections from unit k

A simple model: integrate-and-fire units

- Without interaction phases of all oscillators grow as $\varphi_k = \omega_k t$
- When phase of the oscillator ***k*** attains $\varphi_k = 2\pi$, it **issues a spike**
- When unit *j* **receives** a spike from unit *k*, its phase is instantaneously reset according to its PRC $Z_j(\varphi)$:

$$\varphi_j \to \varphi_j + \varepsilon_{jk} Z_j(\varphi_k)$$



Our approach: iterative solution

- We choose one oscillator (let it be the first one) and consider its all incoming connections ε_{1m}

- For this oscillator, we recover:
  - its frequency
  - its PRC
  - strength of all incoming connections

- We achieve this in several iterative steps

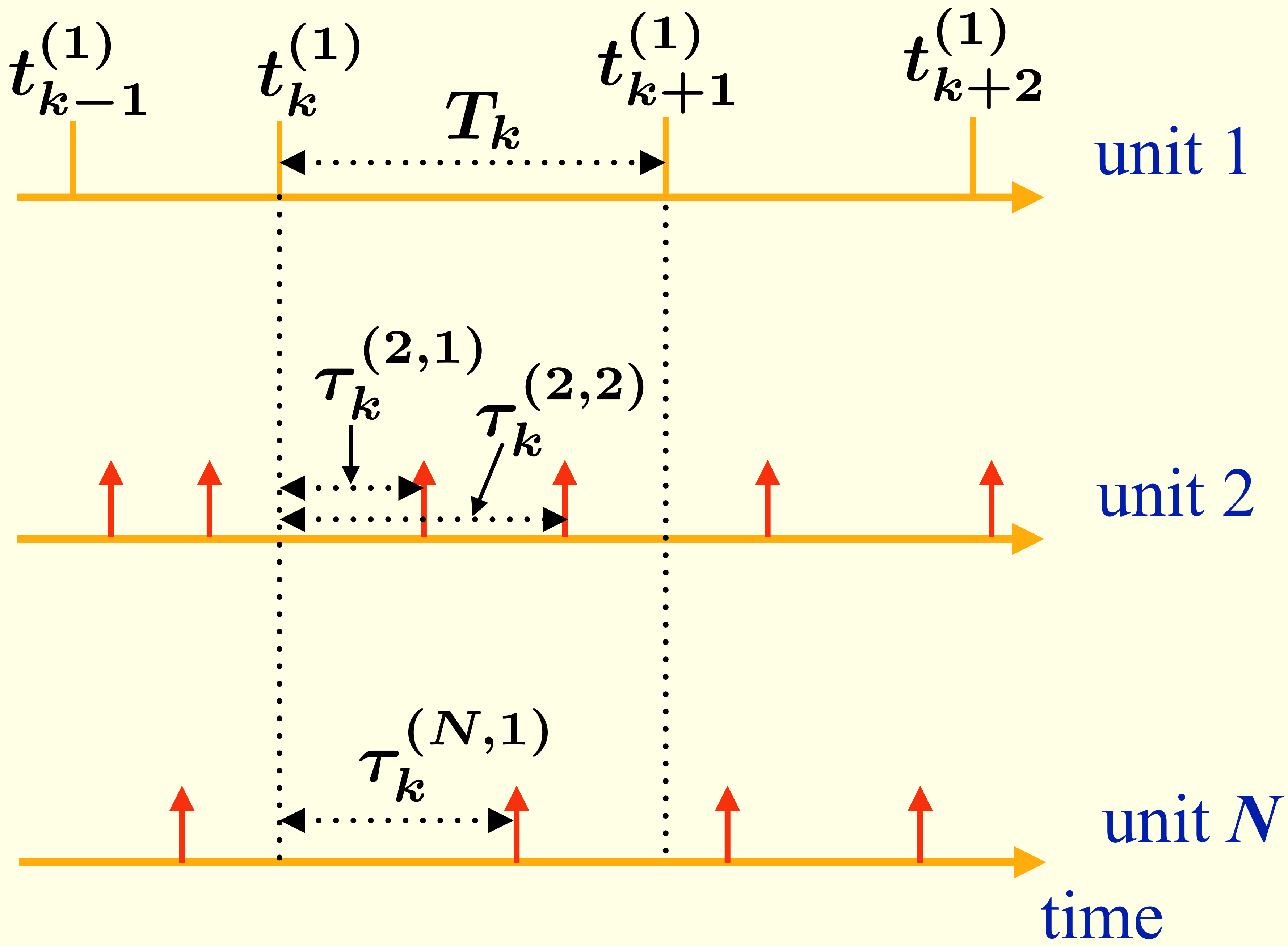
- Then we repeat the procedure for all other units

Our approach: Notations

- Since we choose the first oscillator, we simplify notations by omitting one index

- For this oscillator, we recover:
  - its frequency ω
  - its PRC $Z(\varphi)$
  - strength of all incoming connections $\varepsilon_m, m = 2, \ldots, N$

Notations II



When the spike at $\tau_k^{(i,l)}$ arrives, the phase of the first unit is

$$\varphi(t_k^{(1)} + \tau_k^{(i,l)}) = \varphi_k^{(i,l)}$$

Phase equation

Phase increase within each inter-spike interval is $\mathbf{2\pi}$

$$\omega T_k + \sum_{i=2}^{N} \varepsilon_i \sum_{l=1}^{n_k(i)} Z(\varphi_k^{(i,l)}) = 2\pi \qquad (1)$$

Phase equation

Phase increase within each inter-spike interval is 2π

Network size

Number of stimuli from unit *i*

inter-spike interval

natural frequency

$$\omega T_k + \sum_{i=2}^{N} \varepsilon_i \sum_{l=1}^{n_k(i)} Z(\varphi_k^{(i,l)}) = 2\pi \quad (1)$$

PRC

strength of incoming connections

Phase of the first unit when it receives the ***l***-th spike from unit ***i***, within the inter-spike interval number ***k***

Our approach: main idea

$$\omega T_k + \sum_{i=2}^{N} \varepsilon_i \sum_{l=1}^{n_k(i)} Z(\varphi_k^{(i,l)}) = 2\pi \qquad (1)$$

- Suppose we know phases and coupling coefficients; then we represent the PRC as a finite Fourier series; thus, we obtain *M* linear equations (1), where *M* is the number of inter-spike intervals; for long time series it can be solved, e.g., by LMS fit
- Suppose, vice versa, that we know phases and PRC; then we obtain a linear system to find coupling coefficients ε_j

Our approach: main idea

$$\omega T_k + \sum_{i=2}^{N} \varepsilon_i \sum_{l=1}^{n_k(i)} Z(\varphi_k^{(i,l)}) = 2\pi \qquad (1)$$

Thus:

- $\boldsymbol{\varphi_k, \varepsilon_i}$ are known → we find $\boldsymbol{Z, \omega}$
- $\boldsymbol{\varphi_k, Z}$ are known → we find $\boldsymbol{\varepsilon_i, \omega}$

Our approach: iterative solution

Thus:

- φ_k, ε_i are known → we find Z, ω
- φ_k, Z is known → we find ε_i, ω

First estimate of φ_k, ε_i → First estimate of Z, ω

Our approach: iterative solution

Thus:

- φ_k, ε_i are known → we find Z
- φ_k, Z is known → we find ε_i

First estimate of φ_k, ε_i

→ First estimate of Z, ω

→ Second estimate of φ_k, ε_i

Our approach: iterative solution

Thus:

- φ_k, ε_i are known → we find Z
- φ_k, Z is known → we find ε_i

First estimate of φ_k, ε_i

→ First estimate of Z, ω

→ Second estimate of φ_k, ε_i

→ Second estimate of Z, ω

→ Third estimate of φ_k, ε_i

→ …

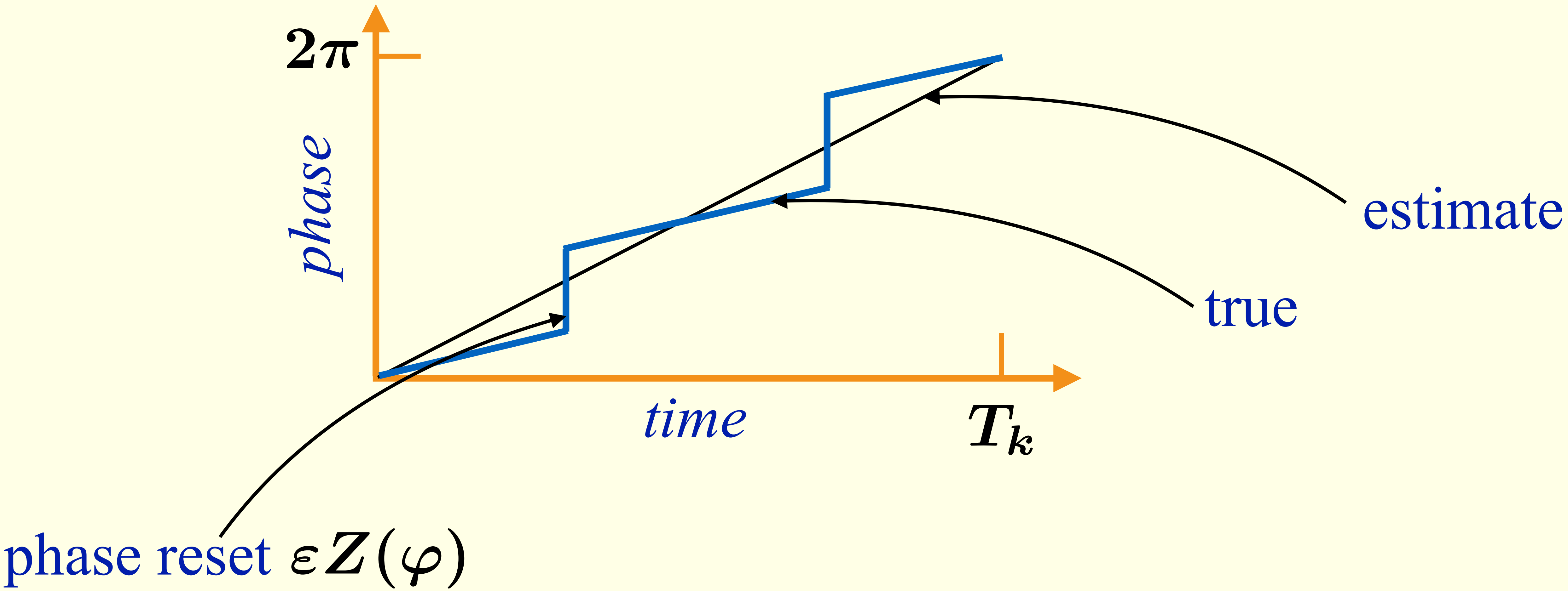
It looks like a fairy tale…

… but it works very good!

Baron Munchausen is a fictional German nobleman created by the German writer Rudolf Erich Raspe in his 1785 book Baron Munchausen's Narrative of his Marvellous Travels and Campaigns in Russia.

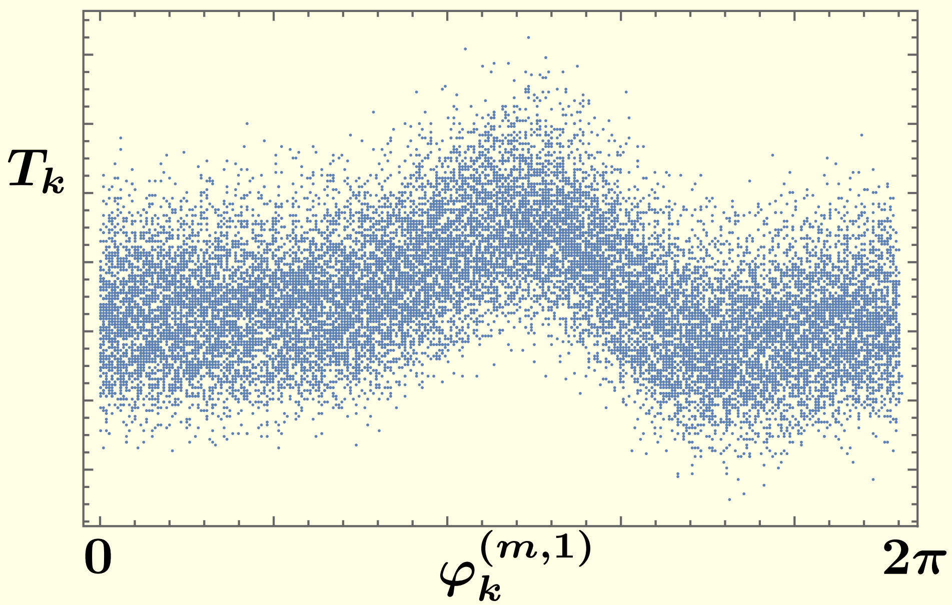
First estimate: phases

Initial estimate: proportionally to time $\varphi_k^{(i,l)} = 2\pi\tau_k^{(i,l)}/T_k$



Error of the initial estimate is of the order of $\varepsilon Z(\varphi)$

First estimate: Coupling coefficients



We have suggested an approach that works very good for a rather long time series, but we rarely use it, because

numerical tests demonstrate that iterations converge to the correct value even for random assignment of initial values ε_i!

Next estimates: phases

An example: within T_k there are three incoming stimuli at

$$\tau_k^{(i,1)} < \tau_k^{(m,1)} < \tau_k^{(n,1)}$$

1st stimulus: $\varphi_k^{(i,1)} = \omega\tau_k^{(i,1)}$

2nd stimulus: $\varphi_k^{(m,1)} = \omega\tau_k^{(m,1)} + \varepsilon_i Z(\varphi_k^{(i,1)})$

3rd stimulus: $\varphi_k^{(n,1)} = \omega\tau_k^{(n,1)} + \varepsilon_i Z(\varphi_k^{(i,1)}) + \varepsilon_m Z(\varphi_k^{(m,1)})$

At the end of the interval:

$$\psi = \omega T_k + \varepsilon_i Z(\varphi_k^{(i,1)}) + \varepsilon_m Z(\varphi_k^{(m,1)}) + \varepsilon_n Z(\varphi_k^{(n,1)})$$

Our quantities are not precise → generally $\psi \neq 2\pi$

→ we rescale all estimated phases by $2\pi/\psi$

Next estimates: phases

At the end of the interval:

$$\psi = \omega T_k + \varepsilon_i Z(\varphi_k^{(i,1)}) + \varepsilon_m Z(\varphi_k^{(m,1)}) + \varepsilon_n Z(\varphi_k^{(n,1)})$$

Our quantities are not precise → generally $\psi \neq 2\pi$

→ we rescale all estimated phases by $2\pi/\psi$

Thus, for each interval we can compute mismatch $\psi_k - 2\pi$

→ Standard deviation of $\psi_k - 2\pi$ provides a measure for

quality of the reconstructed model

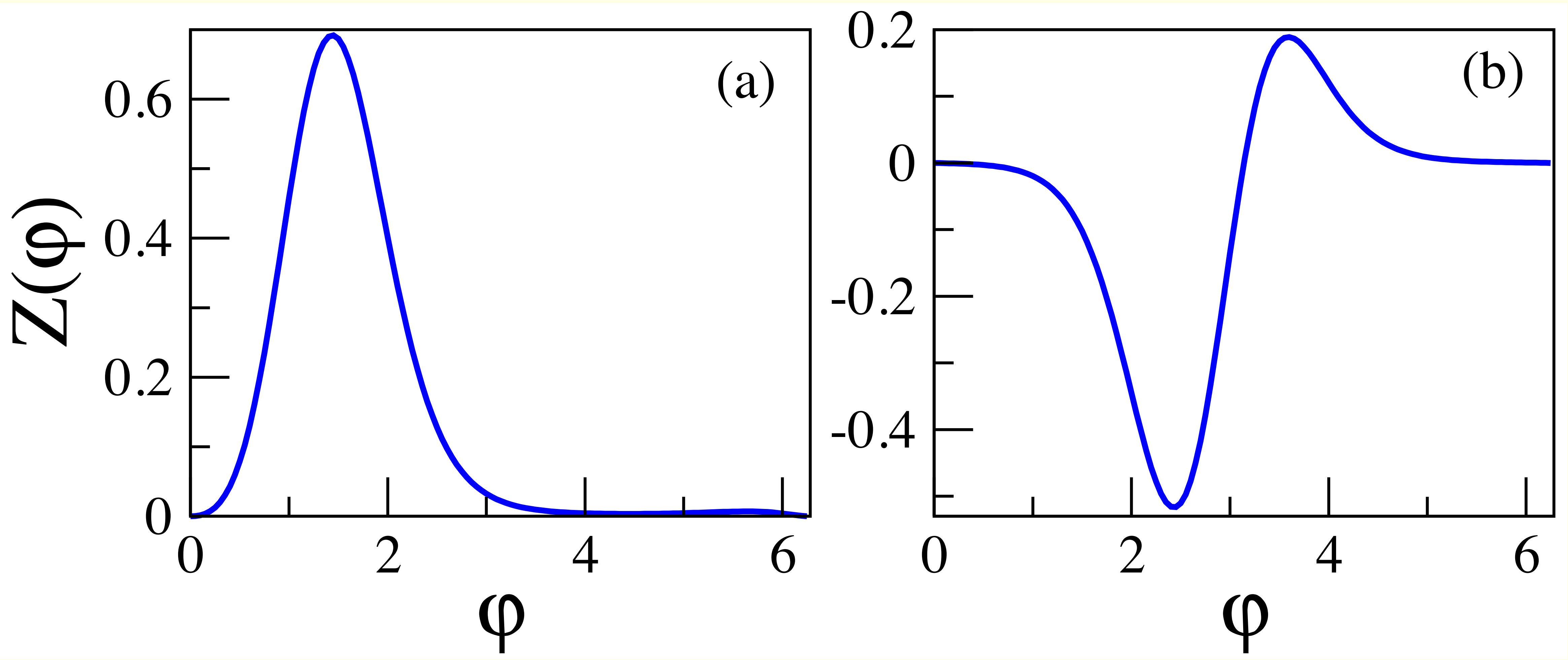
We use this measure to monitor convergence of our procedure!

Numerical tests

Model phase response curves

Type I PRC

Type II PRC



Numerical test I

Network size: $N = 20$

Natural frequencies: uniformly distributed between 1 and 2

$\omega_1 = 1$ (most difficult case)

Coupling coefficients: sampled from the positive part of a Gaussian distribution with zero mean and std 0.02

We exclude the networks where at least two units synchronize!

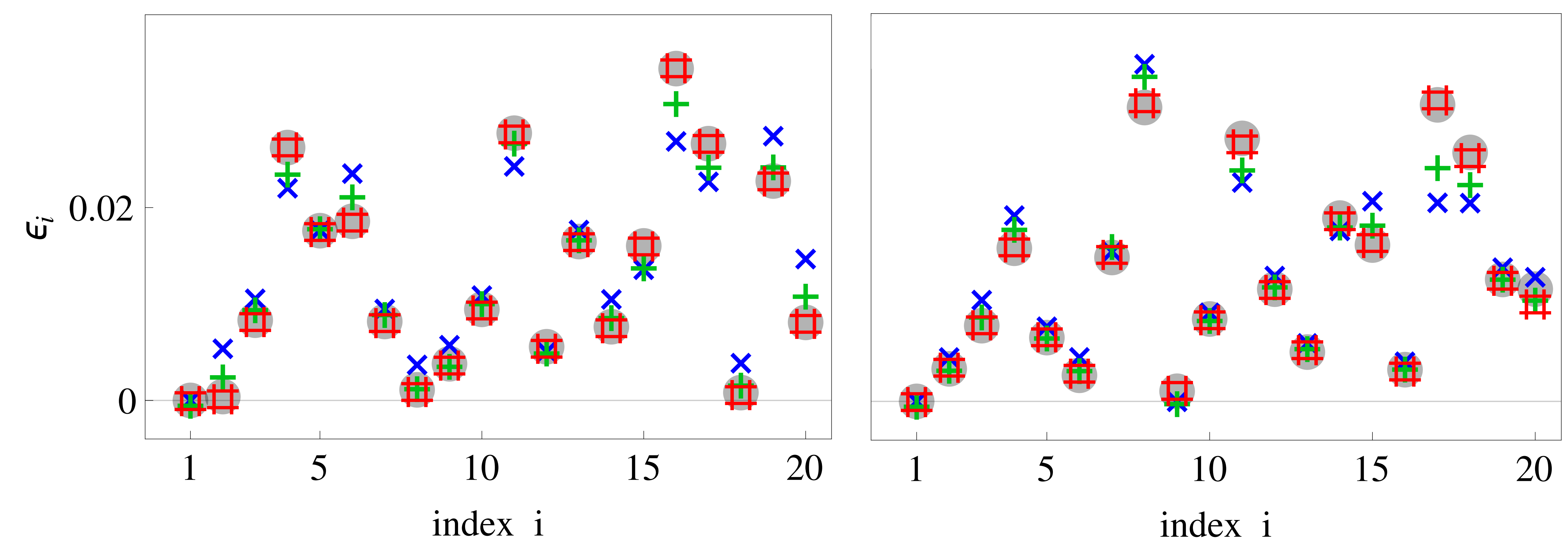
Reconstruction: 10 iterations, 10 Fourier harmonics

only 200 inter-spike intervals used

initial values $\varepsilon_i = 1, \ \forall i$

Iterative solution: results, coupling strength

Type I PRC　　Type II PRC



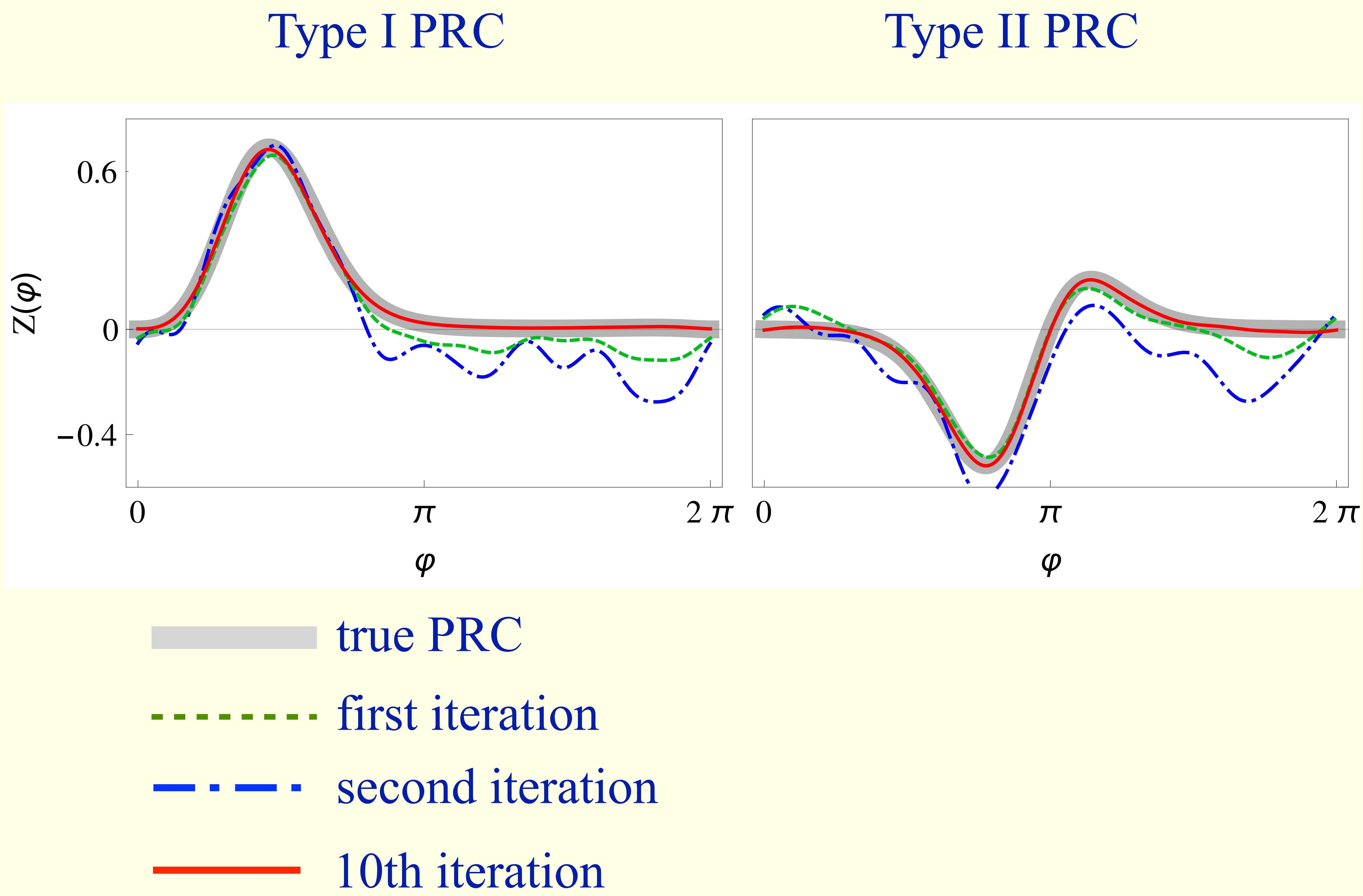
true values

first iteration

second iteration

10th iteration

Iterative solution: results, PRC



One step towards realistic modelling: Morris-Lecar neurons

$$\dot{V}_i = I_i - g_l(V_i - V_l) - g_K w_i (V_i - V_k)$$

$$- g_{Ca} m_\infty(V_i)(V_{Ca} - V_i) + I_i^{(\mathrm{syn})} ,$$

$$\dot{w}_i = \lambda(V_i)(w_\infty(V_i) - w_i) ,$$

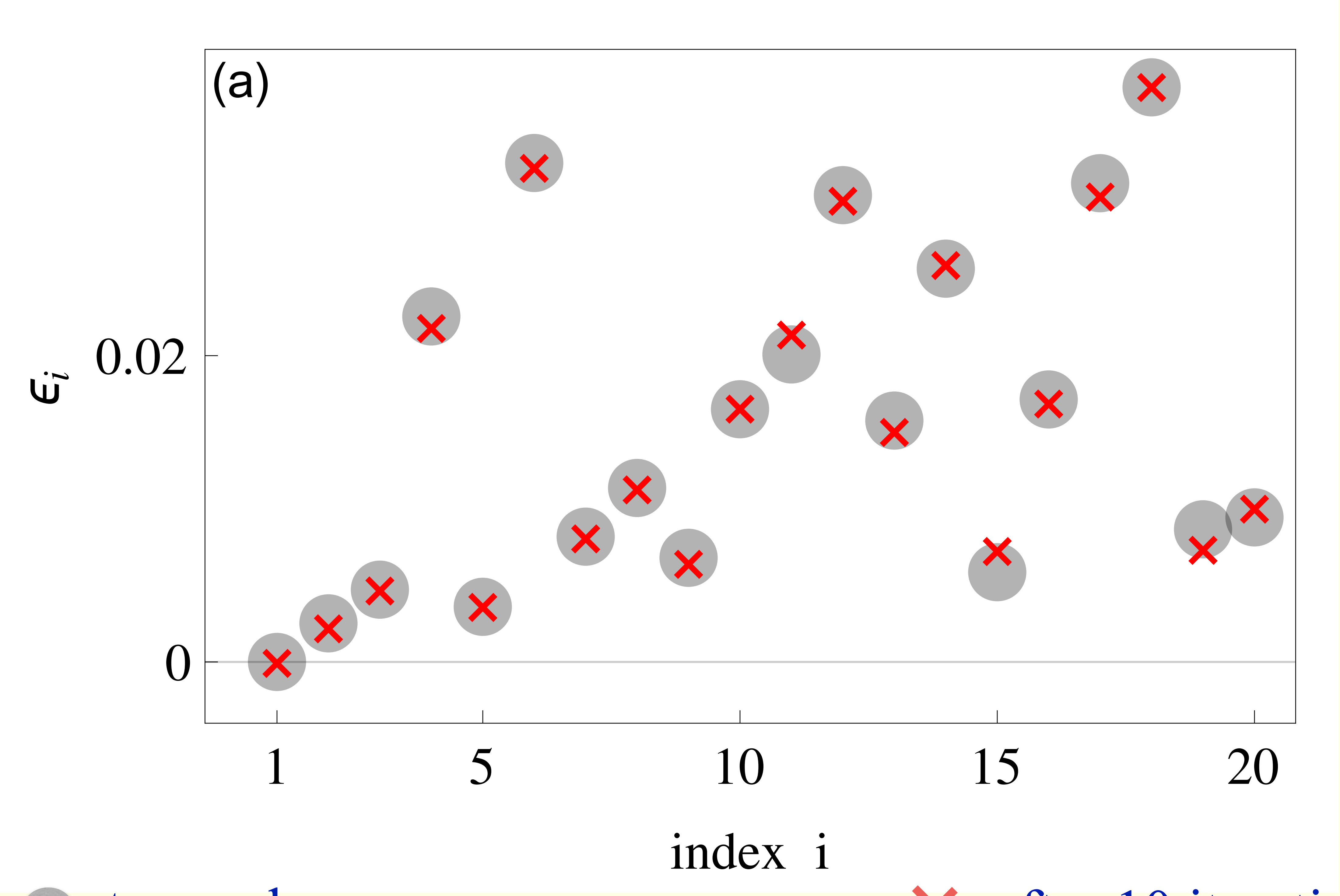
$$m_\infty(V) = [1 + \tanh (V - V_1/V_2)]/2 ,$$

$$w_\infty(V) = [1 + \tanh (V - V_3/V_4)]/2 ,$$

$$\lambda(V) = \cosh [(V - V_3)/(2V_4)]/3 ,$$

with synaptic coupling $I_i^{(\mathrm{syn})} = [V_{\mathrm{rev}} - V_i] \sum_{k,k\neq i} \frac{\varepsilon_{ik}}{1 + \exp[-(V_{\boldsymbol{k}} - V_{\mathrm{th}})/\sigma]}$

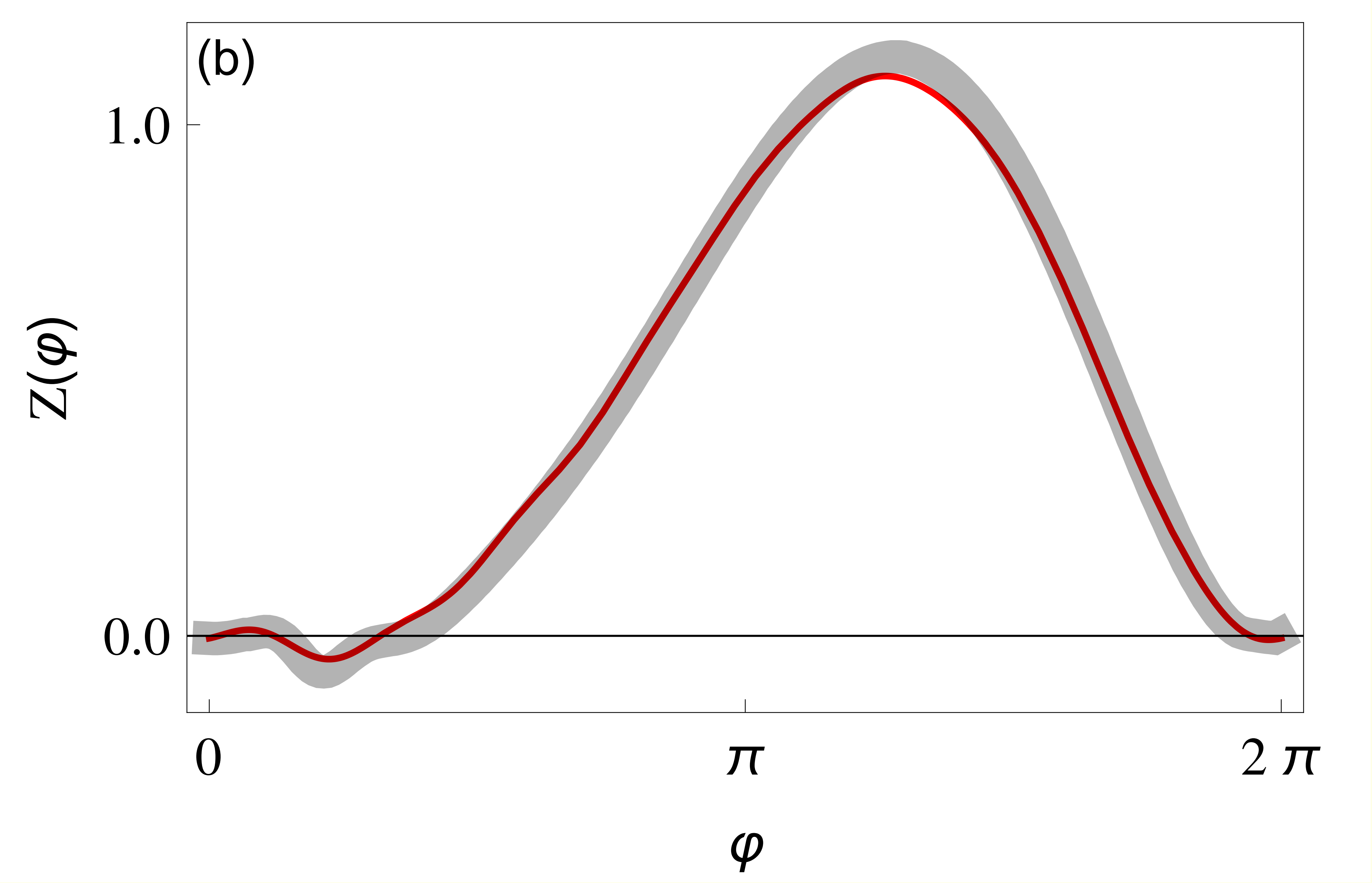
Morris-Lecar network: results, coupling strength



true value after 10 iterations

only 200 inter-spike intervals are used!

Morris-Lecar network: results, PRC

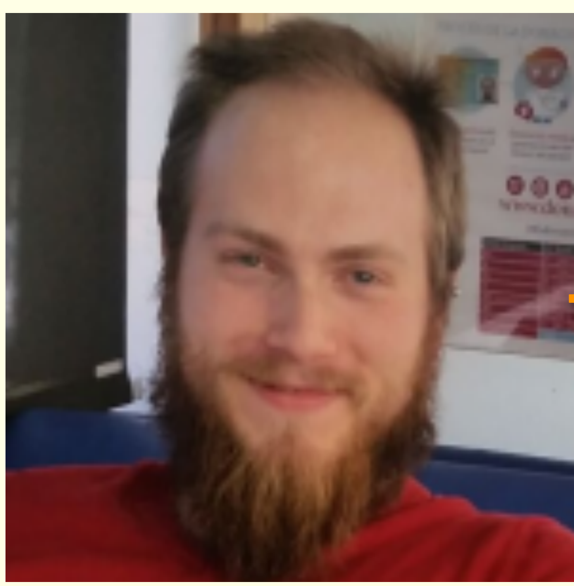


true PRC

10th iteration

Conclusions

- Robust reconstruction of the network structure already for several hundreds of spikes; works if the network does not synchronize
- If the coupling is not weak enough: the network reconstruction remains correct, the PRC is amplitude-dependent
- We need some variability in the drive: noise helps here!



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Reconstructing networks of pulse-coupled oscillators from spike trains

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