

Reconstruction of Network Connectivity from Observations

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Part I: continuous time signals, appropriate for data estimation

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Part II: spike data (point processes)



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- 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

Formulation of the problem: assumptions



- Assumption 1: all units are observed
- Assumption 2: the units are **self-sustained** oscillators
- Assumption 3: the interaction between the units is not too strong
- Assumption 4: signals are good for estimation of phases



- 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? <u>Structural vs effective vs functional</u> connectivity

Structural connectivity

- Real physical connection: resistor, optical fiber... Biological system: anatomical connection, e.g., via synapses
- Mathematically, e.g., for the 2nd node:

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

coupling function

autonomous dynamics

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

 \implies Nodes 1, 3 are functionally connected

Notice: (1) functional connectivity is not directed
 (2) functional connectivity is only loosly 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: $\dot{\mathbf{x}}_k = \mathbf{G}_k(\mathbf{x}_k)$
 - limit cycle, parameterized by phase φ_k
 - phase grows linearly with time: $\dot{\varphi}_k = \omega_k = \mathrm{const}$
- A network of N coupled oscillators

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

- If X_l enters the equation for X_k then there is a direct structural connection $l \to k$
- If $\mathbf{H}_k = \sum_{j \neq k} \mathbf{H}_{kj}(\mathbf{x}_k, \mathbf{x}_j)$ then coupling is pairwise (We consider only this case)
- If there are terms $H_{kjl}(x_k, x_j, x_l)$: 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(φ₁, φ₂,...) = εq_k⁽¹⁾(φ₁, φ₂,...) + ε²q_k⁽²⁾(φ₁, φ₂,...) + ...
- 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)

 φ₃ = ω₃ + εq₃⁽¹⁾(φ₂, φ₃) + ε²q₃⁽²⁾(φ₁, φ₂, φ₃)

• Structural connectivity \neq effective phase connectivity

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

Coupling functions and quantification of interaction

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

$$egin{aligned} rac{darphi_k}{dt} &= \omega_k + q_k(arphi_1,arphi_2,\ldots,arphi_N) \ &= \sum_{l_1,\ldots,l_N} \mathcal{F}_{l_1,\ldots,l_N}^{(k)} \exp\left(il_1arphi_1 + il_2arphi_2 + \ldots + l_Narphi_N) \end{aligned}$$

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

Action of particular oscillator j
ightarrow k

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

Numerical problem

Two coupled oscillators: to reconstruct the coupling function we need enough data points to cover the square 0 < φ_{1,2} ≤ 2π



- Three coupled oscillators: we need enough data points to cover the cube $\ 0 < arphi_{1,2,3} \leq 2\pi$
- 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 $k \leftarrow j$



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

Triplet analysis of networks with *N***>3**

We reconstruct $\dot{\varphi}_j = \omega_j + q_{jkm}(\varphi_j, \varphi_k, \varphi_m)$ for all m



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

We suggest to take $\mathcal{T}_{j\leftarrow k} = \min_{m} \tilde{\mathcal{T}}_{j\leftarrow k}(m)$ 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 $1 \rightarrow 3$, because φ_1, φ_3 are correlated due to node 2



Triplet $\{1,2,3\}$ correctly explains correlation of φ_1, φ_3 and yields a small value for the link $1 \rightarrow 3$

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	
0.003	0.001, 0.001		
		$\mathcal{N}_{3\leftarrow 2}, \mathcal{P}_{3\leftarrow 2}$	

0)	(b)	Osc_1	Osc_2	Osc_3
2	Osc_1	· · · · · · · · · · · · · · · · · · ·	0.113, 0.113	0.003, 0.016
	Osc_2	0.001, 0.001		0.001, 0.001
(1) (3)	Osc_3	0.005, 0.020	0.092, 0.092	

Remark: here $\mathcal{N}_{3\leftarrow 2} = \mathcal{T}_{3\leftarrow 2}$

Random oscillator network, N=5

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

 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 connections in green, non-existing connections in red



Larger networks?

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Distinguishing between direct and indirect directional couplings in large oscillator networks: Partial or non-partial phase analyses?

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inherent to the recording technique. Our findings indicate that particularly in larger networks (number of nodes $\gg 10$), the partialized approach does not provide information about directional couplings extending the information gained with the evolution map approach. *Published by AIP Publishing*. [http://dx.doi.org/10.1063/1.4962295]

Conclusions

- Invariant reconstruction of phase equations for a network
- Characterization of directional couplings via partial norms
- Triplet analysis yields directed connectivity
- We detect effective phase connectivity, which is close but not equivalent to the structural connectivity

References

- B. Kralemann, A. Pikovsky, and M. Rosenblum, Chaos, 21, p. 025104, 2011
- B. Kralemann, A. Pikovsky, and M. Rosenblum, New J Phys, 16 085013, 2014



Software for data analysis can be downloaded from: <u>www.stat.physik.uni-potsdam.de/~mros/damoco2.html</u> Reconstructing networks of pulse-coupled oscillators from spike trains



Rok Cestnik



Complex Oscillatory Systems: Modeling and Analysis Innovative Training Network

European Joint Doctorate



Formulation of the problem



The data we measure are like sequences of spikes

Formulation of the problem II



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>
- 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 $\, arphi_k = \omega_k t \,$



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

A simple model: integrate-and-fire units

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



A simple model: integrate-and-fire units

- Without interaction phases of all oscillators grow as $arphi_k = \omega_k t$
- 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 $Z_j(\varphi)$:



Assumptions

- 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, $\varepsilon_{km} \neq \varepsilon_{mk}$
- Relaxation after pulse stimulation is fast

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(arphi)
 - strength of all incoming connections $\, arepsilon_m, m=2,\ldots,N \,$



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 2π

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

(1)

Phase equation

Phase increase within each inter-spike interval is 2π



Our approach: main idea

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

- 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

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

Thus: • φ_k, ε_i are known \longrightarrow we find Z, ω • φ_k, Z is known \longrightarrow we find ε_i, ω (1)

Our approach: iterative solution Thus: • φ_k, ε_i are known \longrightarrow we find Z, ω • φ_k, Z is known \longrightarrow we find ε_i, ω

First estimate of φ_k, ε_i



Our approach: iterative solution

Thus: • φ_k, ε_i are known \longrightarrow we find Z

• φ_k, Z is known \longrightarrow 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 \longrightarrow we find Z • φ_k, Z is known \longrightarrow we find ε_i

First estimate of φ_k, ε_i

First estimate of Z, ω

Second estimate of φ_k, ε_i

Third estimate of φ_k, ε_i

Second estimate of Z, ω

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 want to estimate strength of the link from unit *m* to unit *1*

We plot the interval length T_k of the first unit vs the phase when the first stimulus from unit *m* arrives within this time interval



First estimate: coupling coefficients Binning and averaging over N_b bins



averaging over s

First estimate: coupling coefficients

Very weak coupling: no dependence Stronger coupling: prominent dependence



First estimate:
$$\varepsilon_m = \langle (\bar{T}_s - \langle \bar{T}_s \rangle)^2 \rangle^{1/2}$$

Next estimates: phases

An example: within T_k there are three incoming stimuli at

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:

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

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

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

Coupling coefficients once again

We want to estimate strength of the link from unit *m* to unit *1*

We plot the interval length T_k of the first unit vs the phase when the first stimulus from unit *m* arrives within this time interval



Coupling coefficients once again



This approach works very good for a rather long time series

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

Numerical tests

Model phase response curves

Type I PRC

Type II PRC



Numerical tests: a remark on normalization Recall the main equation:

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

 ε_i and Z enter it as a product

 ε_i and Z can be arbitrary rescaled

For comparison with the true values we choose scaling factor by minimizing

$$\sum_{i=2}^{N} \left[arepsilon_{i}^{(t)} - c arepsilon_{i}^{(r)}
ight]$$

Numerical tests: a remark on normalization Recall the main equation:

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

 ε_i and Z enter it as a product

 ε_i and Z can be arbitrary rescaled

For comparison with the true values we choose scaling factor by minimizing

$$\sum_{i=2}^{N} \left[\varepsilon_{i}^{(t)} - c \varepsilon_{i}^{(r)} \right]$$
true recovered

Numerical test I

<u>Network size:</u> N = 20

<u>Natural frequencies</u>: uniformly distributed between 1 and 2 $\omega_1 = 1$ (most difficult case)

<u>Coupling coefficients:</u> 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!

<u>Reconstruction</u>: 10 iterations, 10 Fourier harmonics only 200 inter-spike intervals used initial values $\varepsilon_i = 1, \forall i$

Iterative solution: results, coupling strengthType I PRCType II PRC



- true values
- + first iteration
- **X** second iteration
- 10th iteration

Iterative solution: results, PRCType I PRCType II PRC



- true PRC
- ----- first iteration
- ---- second iteration
 - 10th iteration

Iterative solution: results, frequenciesType I PRCType II PRC



true value

Numerical test II: statistical analysis Network size: N = 20Natural frequencies: uniformly distributed between 1 and 2 $\omega_1 = 1$ (most difficult case) <u>Coupling coefficients:</u> sampled from the positive part of a Gaussian distribution with zero mean and std 0.02We exclude the networks where at least two units synchronize! Reconstruction: 10 iterations, 10 Fourier harmonics only 200 inter-spike intervals used

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

We generate and reconstruct 10^5 networks

Numerical test II: statistical analysis

<u>Quality of the reconstruction:</u> we define the corresponding errors

Numerical test II: results, histograms of errors

Type I PRC

Type II PRC



- **- -** first iteration
- ----- third iteration
 - 10th iteration

Numerical test II: results, impact of data length

Type I PRC

Type II PRC



number of inter-spike intervals used

Further tests: impact of network size and noise

Network size from N=10 to 500, with number of spikes $\sim N$

Computational time: $\sim N^4$, in fact, small (minutes on a laptop)

Errors increase linearly with noise intensity

One step towards realistic modelling: Morris-Lecar neurons

$$\begin{split} \dot{V}_i = &I_i - g_l (V_i - V_l) - g_K w_i (V_i - V_k) \\ &- g_{Ca} m_\infty (V_i) (V_{Ca} - V_i) + I_i^{(\text{syn})} , \\ \dot{w}_i = &\lambda (V_i) (w_\infty (V_i) - w_i) , \\ &m_\infty (V) = [1 + \tanh (V - V_1 / V_2)] / 2 , \\ &w_\infty (V) = [1 + \tanh (V - V_3 / V_4)] / 2 , \\ &\lambda (V) = \cosh [(V - V_3) / (2V_4)] / 3 , \end{split}$$

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

Morris-Lecar network: results, coupling strength



Morris-Lecar network: results, PRC



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
- Error of the phase estimation increases with the number of spikes ===> the reconstruction may fail for $\omega_i/\omega \gg 1$
- We need some variability in the drive: the reconstruction may fail for very sparse networks where periodic nodes can be found (however, noise helps here!)

Conclusions II

• Reference: Phys. Rev. E 96, 012209 (2017)

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Thank you for your attention!