Controlling collective synchrony by pulsatile stimulation

An approach to manipulate brain rhythms?

Michael Rosenblum

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Network Physiology Summer Institute, Como, 25.07.22

Contents of the talk

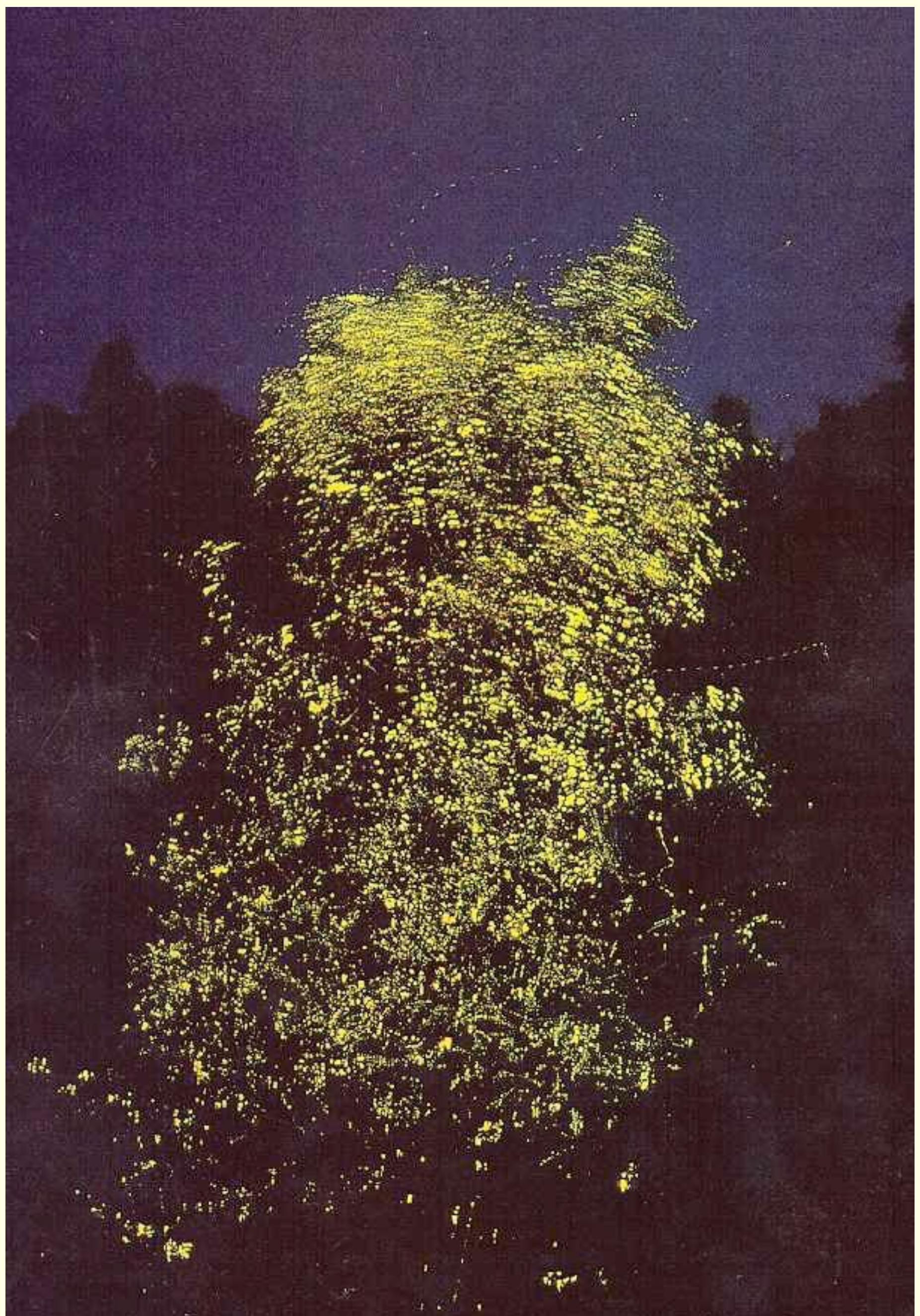
- Ensemble synchrony: a brief introduction
- Motivation: why to control?
- Closed-loop control
- Control by precisely timed pulses: examples
- Discussion and outlook

Fireflies synchrony

Engelbert Kaempfer

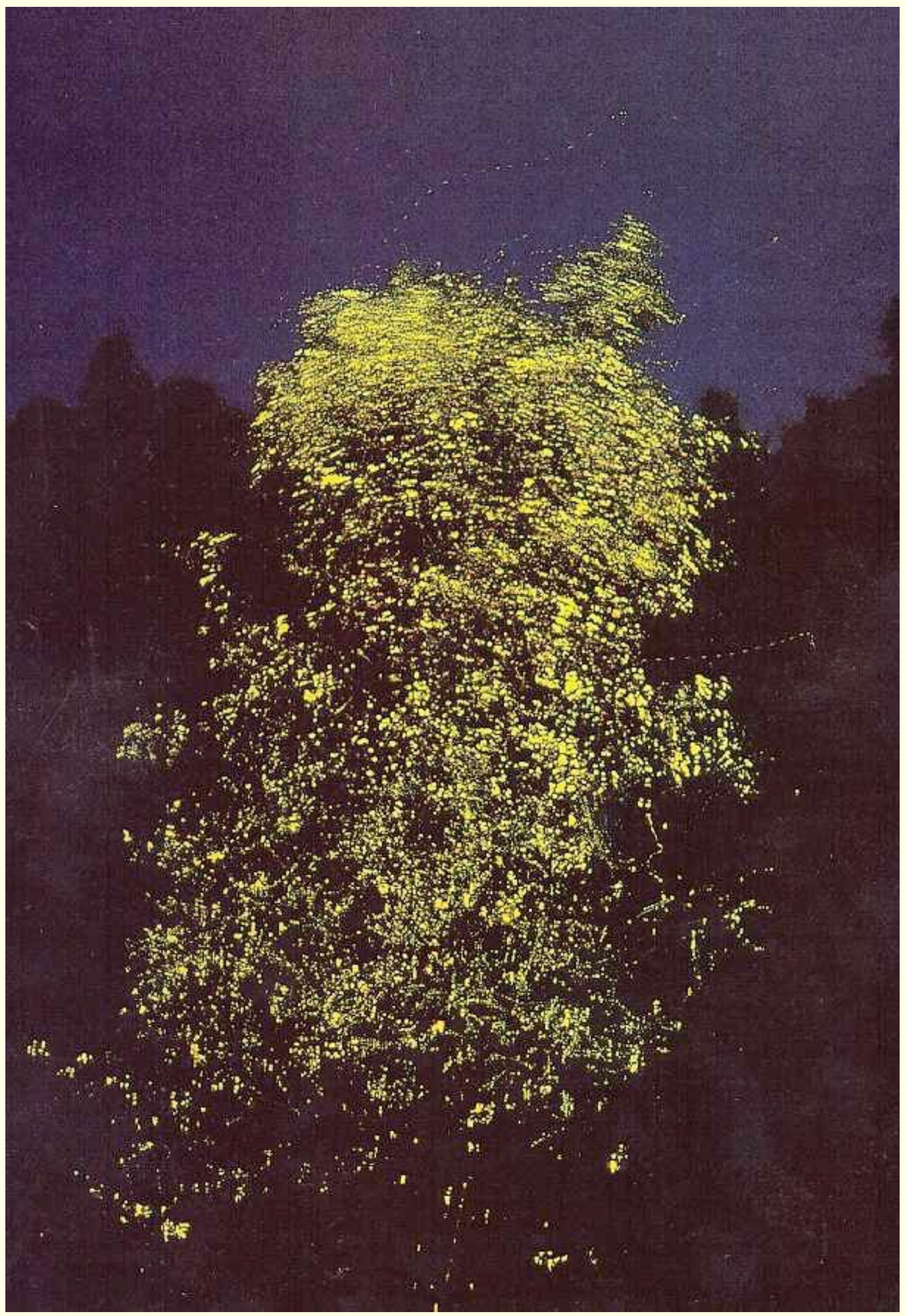
(16.09.1651, Lemgo, Germany - 2.11.1716)

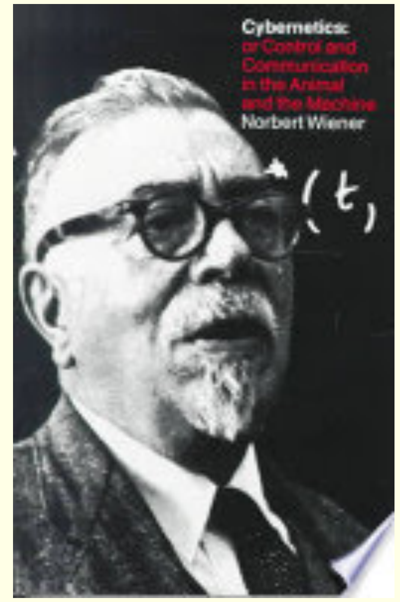
A description of the Kingdom of Siam, 1690



Fireflies "hide their Lights all at once, and a moment after make it appear again with the utmost regularity and exactness."

Fireflies synchrony II





Norbert Wiener

Cybernetics: or the Control and Communication in the Animal and the Machine, 1961

Hypothesis: same "*phenomenon of the pulling together of frequencies*" is responsible for emergence of the brain waves

Metronomes on a moveable support

Idea: B. Daniels, Diploma thesis, Ohio Wesleyan University

Highly interconnected oscillator networks

Typical assumption: all-to-all (global) coupling; each unit equally interacts with all other units

Main effect: emergence of a collective mode (mean field)

Different mechanisms:

- Kuramoto scenario
- Van Vreeswijk scenario
- Quasiperiodic partial synchrony

N all-to-all coupled oscillators: The Kuramoto model

Oscillator, forced by another one: $\dot{\varphi} = \omega + \varepsilon \sin(\varphi_{ext} - \varphi)$

Oscillator, equally forced by $N-1$ oscillators:

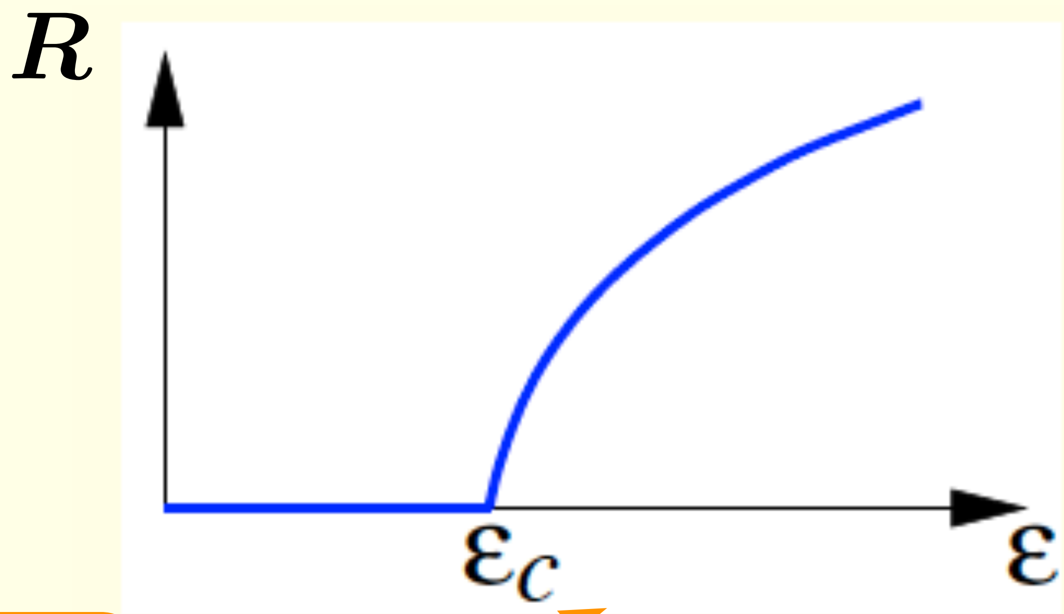
$$\dot{\varphi}_k = \omega_k + \tilde{\varepsilon} \sum_{j=1}^{N} \sin(\varphi_j - \varphi_k)\ , \qquad k = 1, \ldots, N$$

It is convenient to set: $\tilde{\varepsilon} = \varepsilon / N$

$$\boxed{\dot{\varphi}_k = \omega_k + \frac{\varepsilon}{N} \sum_{j=1}^{N} \sin(\varphi_j - \varphi_k)}$$

Yoshiki Kuramoto, *1975, 1984*

Kuramoto scenario



Order parameter (mean field amplitude)

$$R \sim \sqrt{\varepsilon - \varepsilon_c}$$

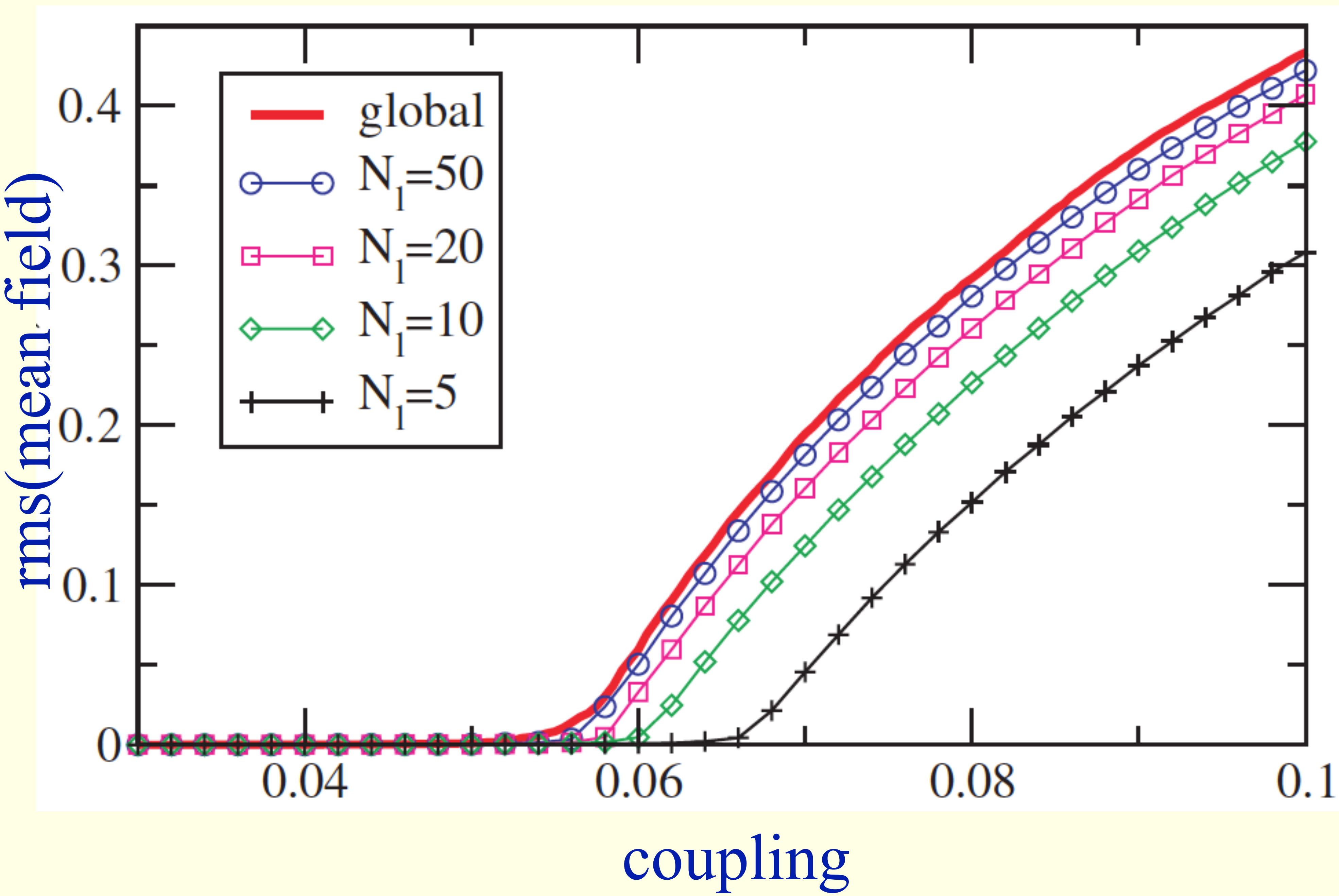
Critical coupling

Main result for a unimodal frequency distribution

Qualitatively similar results for ensembles of periodic or weakly chaotic oscillators

Qualitatively similar results for ensembles of excitatory and inhibitory model neutrons

Highly interconnected neuronal network



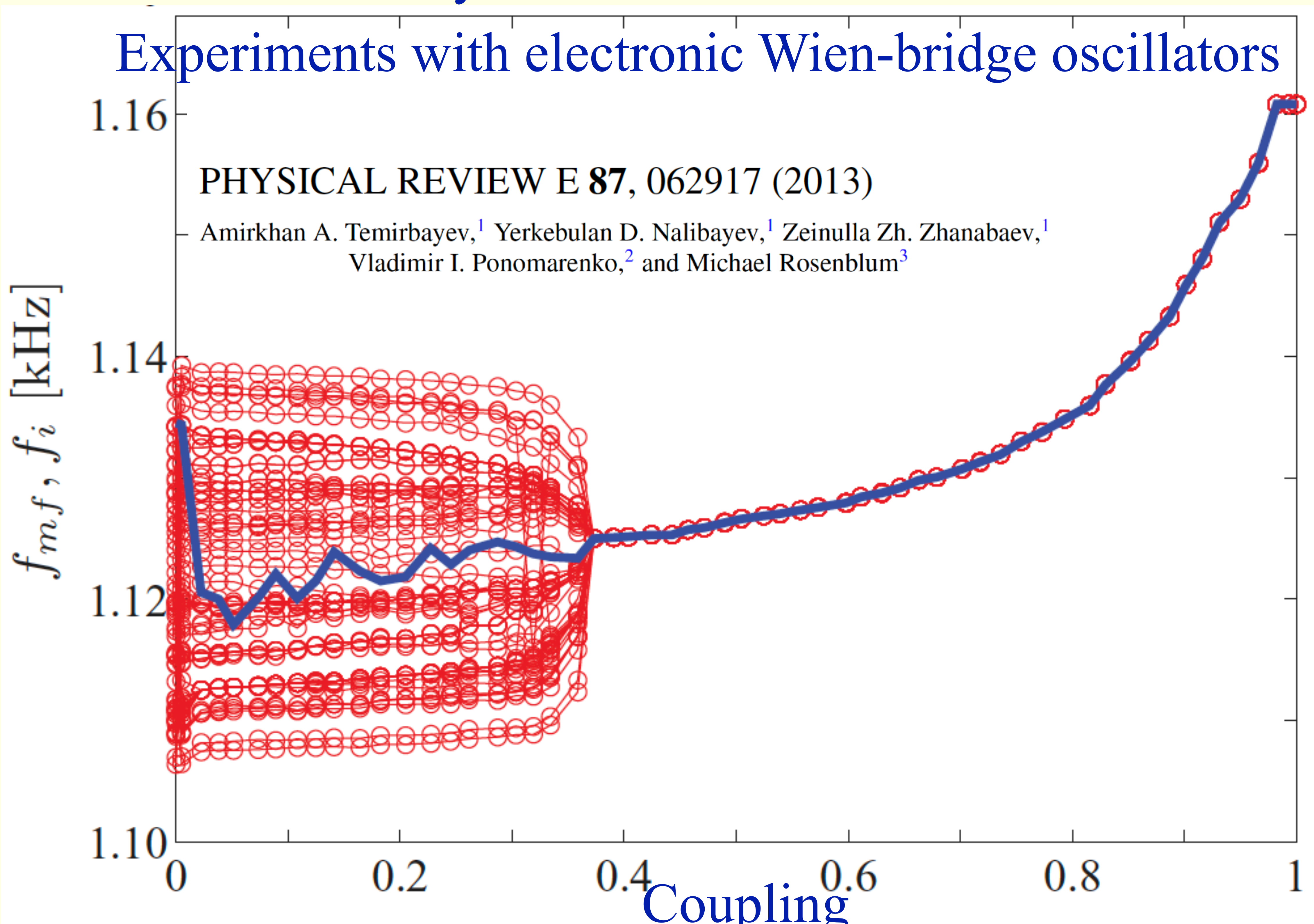
10000 bursting neurons

(Rulkov map model)

Global coupling is a reasonable model of collective neuronal dynamics

Kuramoto scenario

Emergence of a cluster of units synchronized mutually and with the mean field



Van Vreeswijk scenario

PHYSICAL REVIEW E VOLUME 54, NUMBER 5 NOVEMBER 1996

Partial synchronization in populations of pulse-coupled oscillators

C. van Vreeswijk*

The model: coupled integrate-and-fire neurons

$$\frac{dx_i}{dt} = F(x_i) + gE_i(t).$$

Coupling via an α function:

$$E_j(t) \rightarrow E_j(t) + \frac{\alpha^2}{N-1}(t-t_0)e^{\alpha(t_0-t)}.$$

Here t_0 is the time at which oscillator i fires.

Van Vreeswijk model

- There is no synchronous solution
- There is either the asynchronous state or partial synchrony
- Partial synchrony:
  mean field is periodic, individual units are quasiperiodic;
  average firing frequency of a unit $\neq$ mean-field frequency

Self-organized quasiperiodic dynamics

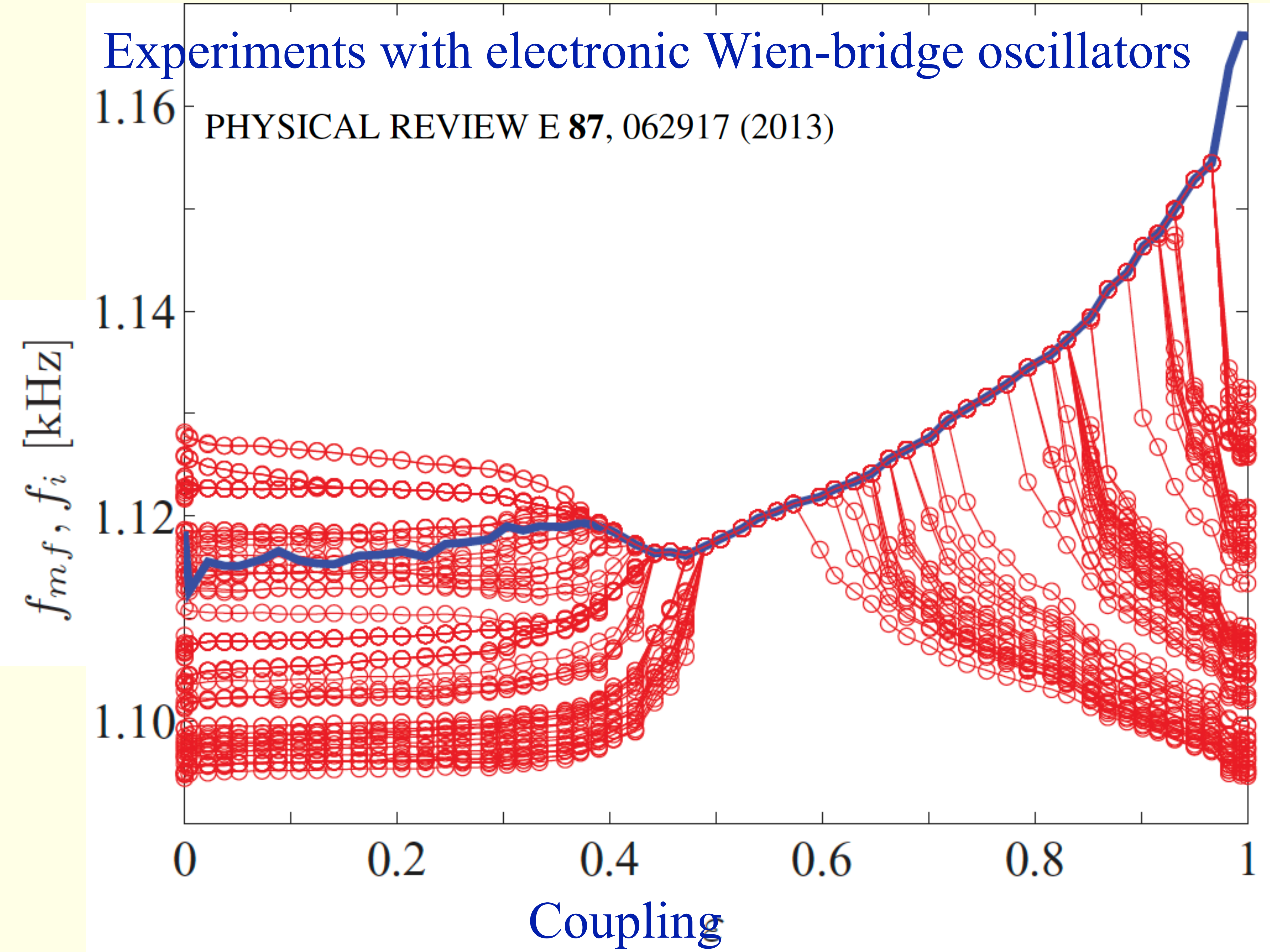
PRL **98,** 064101 (2007) PHYSICAL REVIEW LETTERS week ending 9 FEBRUARY 2007

Self-Organized Quasiperiodicity in Oscillator Ensembles with Global Nonlinear Coupling

Michael Rosenblum and Arkady Pikovsky

- Nonlinear coupling
- Transition from synchronous periodic state to partially synchronous quasiperiodic state (SOQ)
- SOQ: average frequency of units $\neq$ mean-field frequency

Self-organized quasiperiodic dynamics



Why to control collective synchrony?

Neuroscience, **D**eep **B**rain **S**timulation (DBS):

- high-frequency electrical stimulation of a motor-control brain region via implanted microelectrodes
- approved by FDA as a treatment for Parkinson's disease and essential tremor since 1997
- also approved for dystonia (2003), obsessive-compulsive disorder (2009), and epilepsy (2018) (Wikipedia)

Mechanisms of DBS are still a matter of debate

Standard DBS: stimulation with a constant frequency $\sim 120 \div 130$ Hz

Current research: adaptive DBS, also feedback-based

Working hypothesis

Pathological brain rhythm emerges due to an excessive synchrony in a neuronal network

DBS shall be considered as a desynchronization problem

Formulated by Peter Tass

Many approaches: open-loop and closed-loop techniques

Closed-loop control (*in silico only!*)

VOLUME 92, NUMBER 11 PHYSICAL REVIEW LETTERS week ending 19 MARCH 2004

Controlling Synchronization in an Ensemble of Globally Coupled Oscillators

Michael G. Rosenblum and Arkady S. Pikovsky

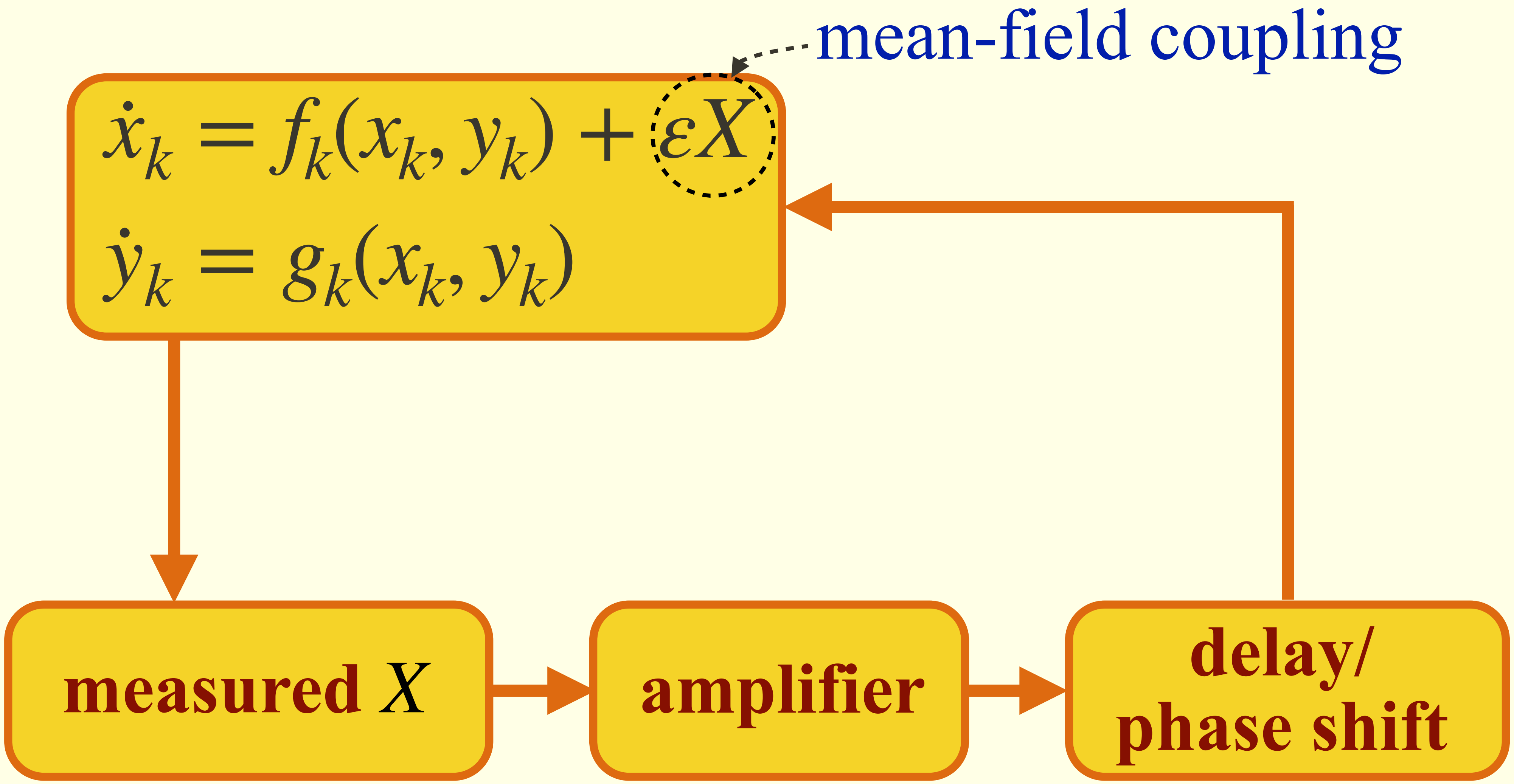
PHYSICAL REVIEW E **70**, 041904 (2004)

Delayed feedback control of collective synchrony: An approach to suppression of pathological brain rhythms

Michael Rosenblum* and Arkady Pikovsky†

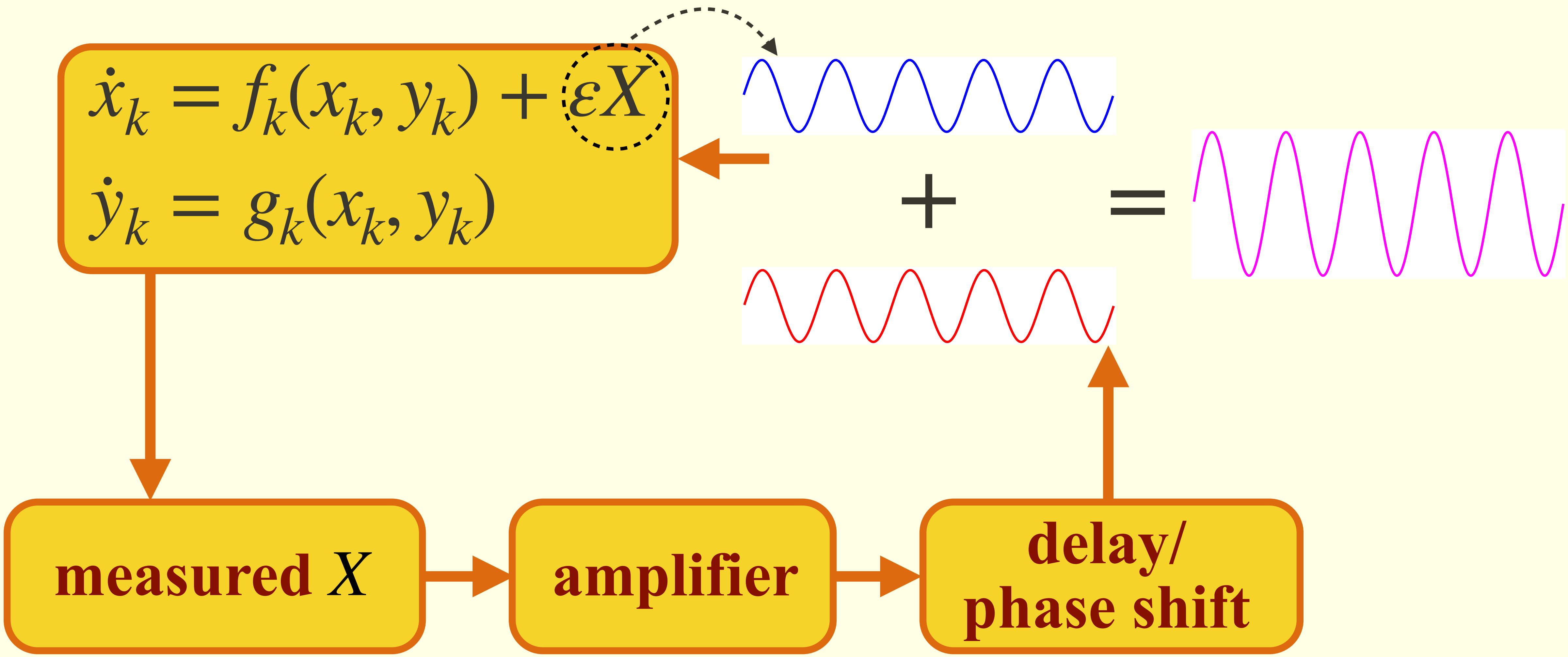
Assumption: we can measure the collective activity (mean field) and stimulate the whole ensemble (or its large part)

Closed-loop control: a simple explanation



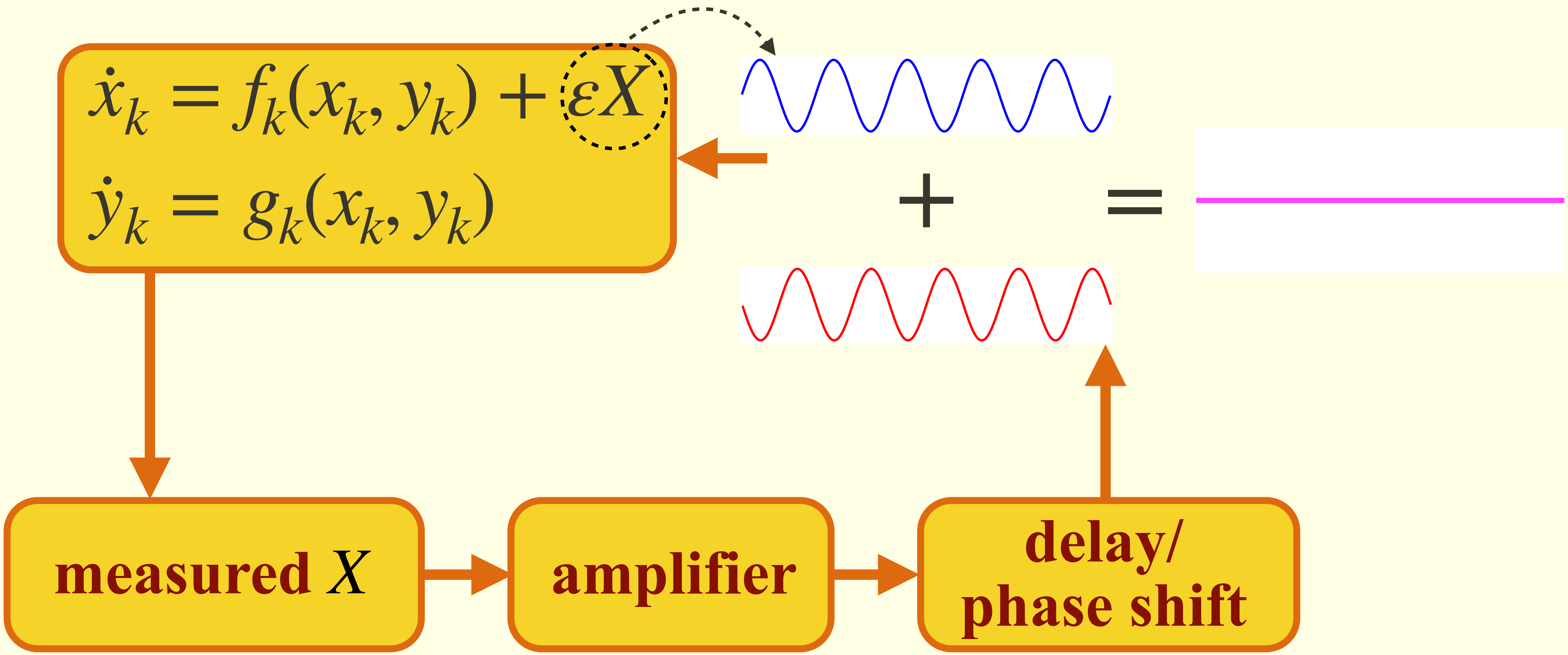
mean field $X = N^{-1} \sum_k x_k$

Closed-loop control: a simple explanation



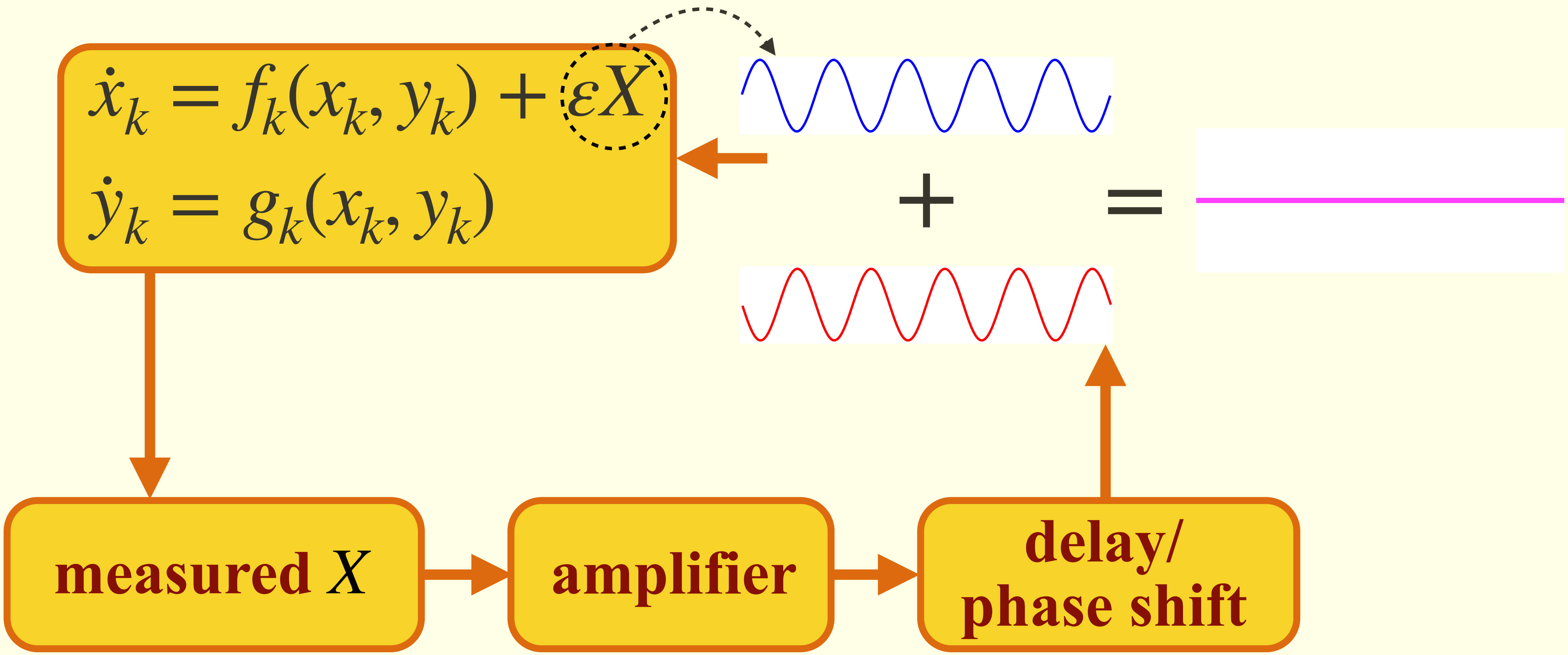
enhancement of synchrony!

Closed-loop control: a simple explanation



suppression of synchrony!

Closed-loop control: a simple explanation



suppression of synchrony!

The problem: we have to find appropriate amplification and proper phase shift without any knowledge of the system

Solution of the problem: adaptive control

CHAOS **23**, 033122 (2013)

Synchrony suppression in ensembles of coupled oscillators *via* adaptive vanishing feedback

Ghazal Montaseri,[1,2] Mohammad Javad Yazdanpanah,[3] Arkady Pikovsky,[2]
and Michael Rosenblum[2]

Solution of the problem: adaptive control

CHAOS 23, 033122 (2013)

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Synchrony suppression in ensembles of coupled oscillators *via* adaptive $\boxed{\text{vanishing}}$ feedback

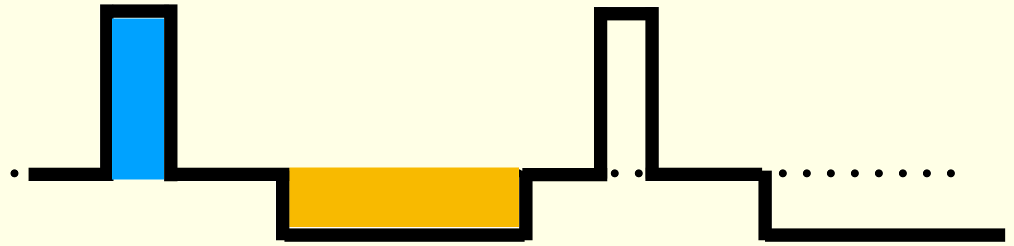
Ghazal Montaseri,[1,2] Mohammad Javad Yazdanpanah,[3] Arkady Pikovsky,[2]
and Michael Rosenblum[2]

Neuroscience application: requirements

- continuous stimulations is not feasible

  → we need a pulsatile-stimulation scheme

- pulses must be **charge-balanced**!



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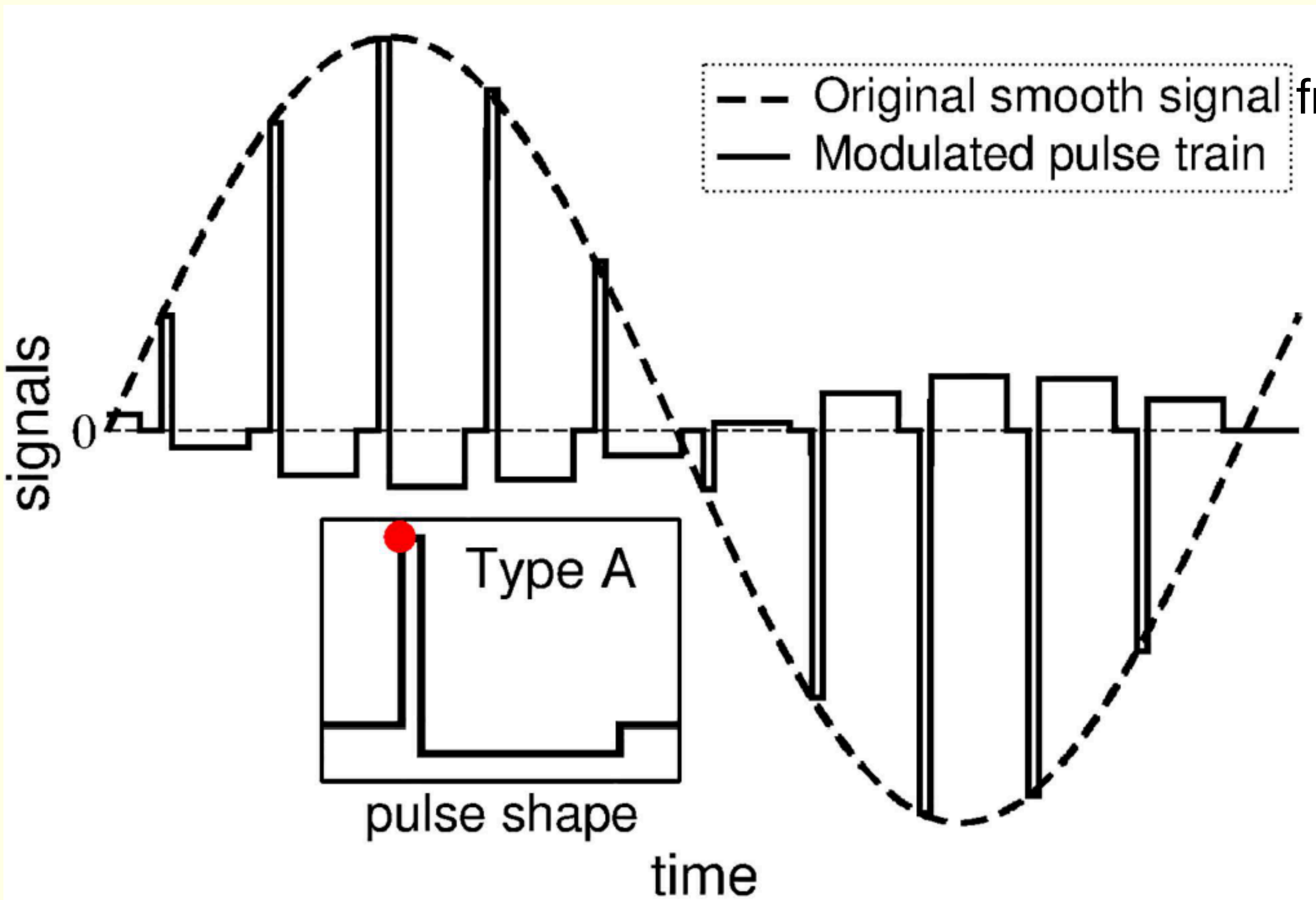
Pulsatile stimulation: a solution

Pulsatile desynchronizing delayed feedback for closed-loop deep brain stimulation

Oleksandr V. Popovych[1]*, Borys Lysyansky[1], Michael Rosenblum[2], Arkady Pikovsky[2], Peter A. Tass[1,3,4]

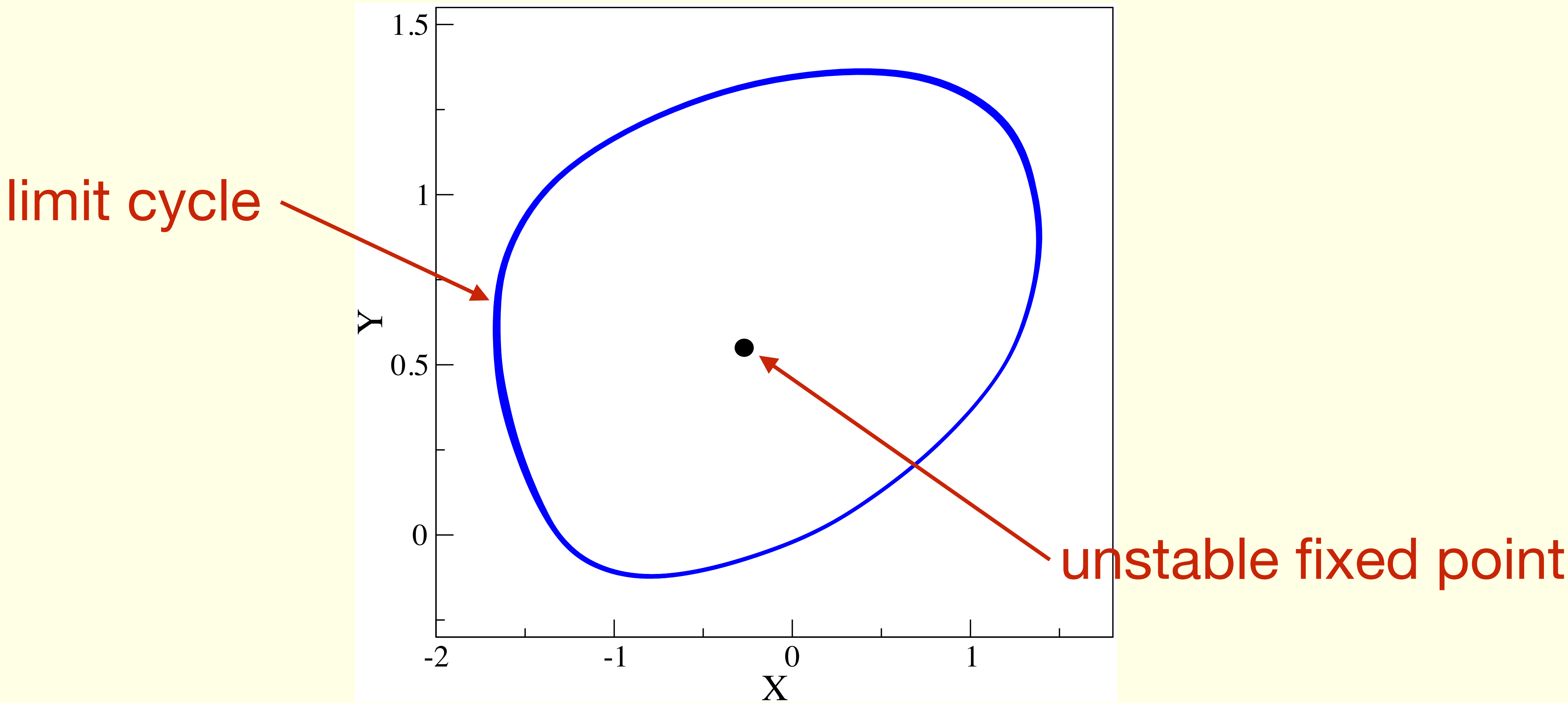
PLOS ONE | DOI:10.1371/journal.pone.0173363 March 8, 2017



from a continuous feedback scheme

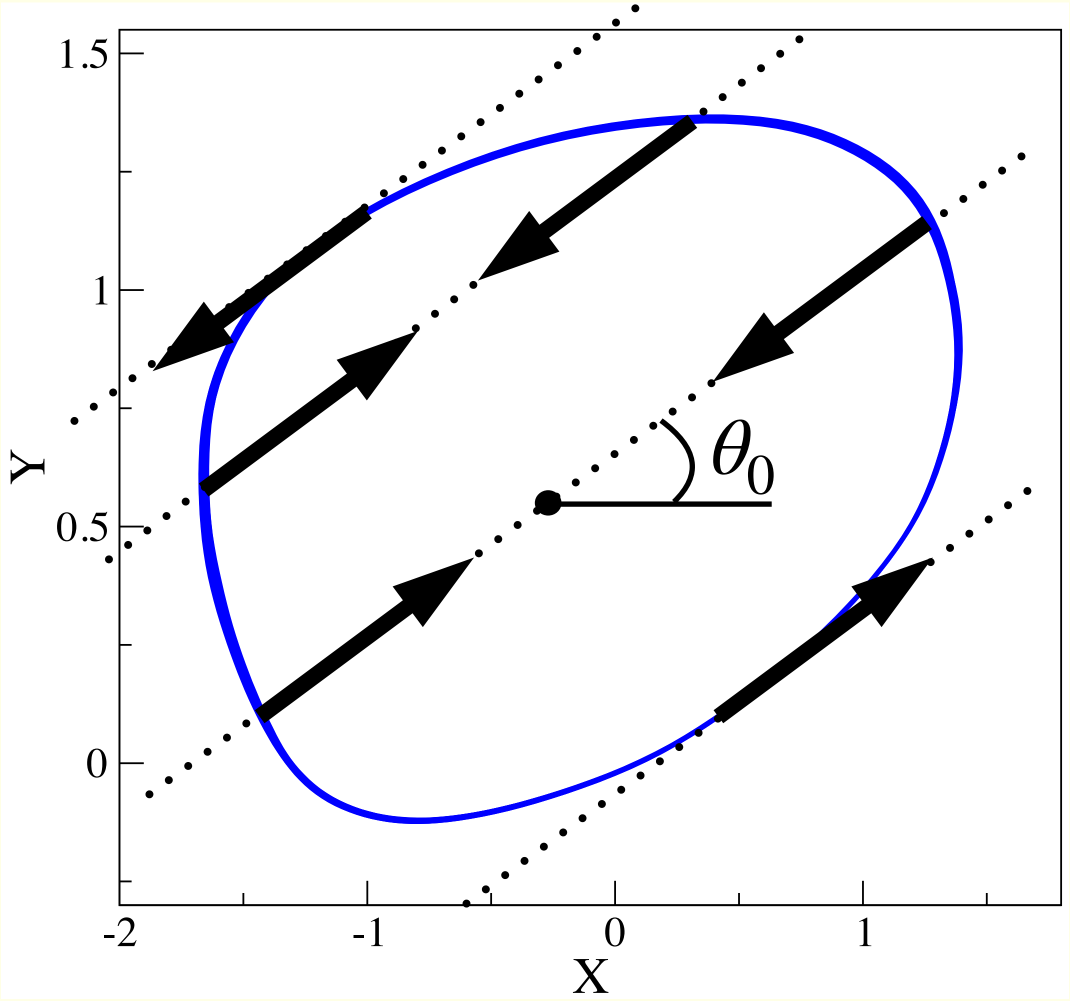
The problem: contemporary DBS equipment cannot alter pulse amplitude so fast

Stimulation by rare pulses: the idea



We want to push the state space point off the limit cycle

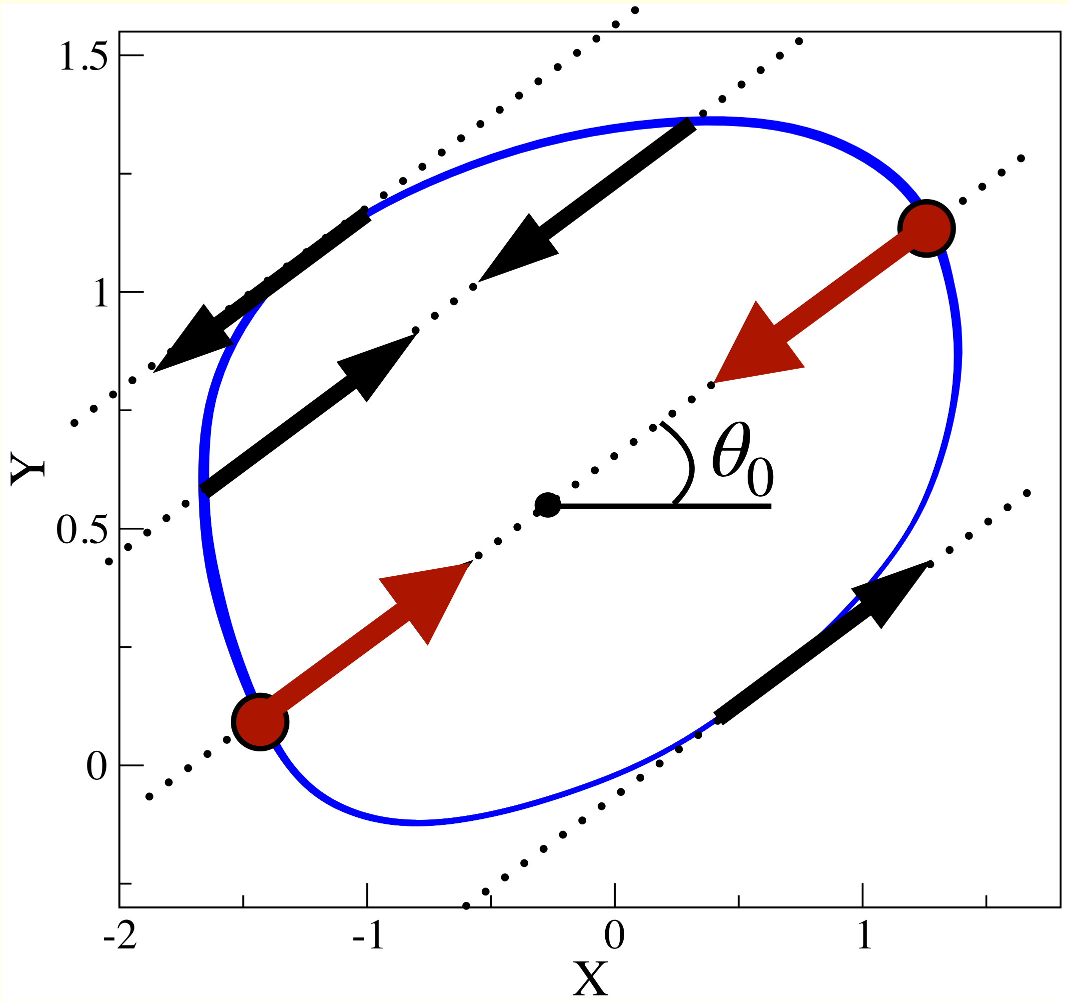
Stimulation by rare pulses: the idea



We want to push the state space point off the limit cycle

The pulses act along some *a priori* unknown direction!

Stimulation by rare pulses: the idea



We want to push the state space point off the limit cycle

There are two favourable phases - let us stimulate only twice per period!

We have to determine phase on the fly

Two models

1 Bonhoeffer-van der Pol oscillators, global coupling

$$\dot{x}_k = x_k - x_k^3/3 - y_k + I_k + \varepsilon X + \cos\psi \cdot P(t)$$

$$\dot{y}_k = 0.1(x_k - 0.8 y_k + 0.7) + \sin\psi \cdot P(t)$$

Parameters I_k have Gaussian distribution with $\bar{I}_k = 0.6$, std$(I_k) = 0.1$

Parameter ψ determines how the pulses act on the system

2 Rössler oscillators, global coupling

$$\dot{x}_k = -\omega_k y_k - z_k + \varepsilon X + \cos\psi \cdot P(t)$$

$$\dot{y}_k = \omega_k x_k + 0.15 y_k + \sin\psi \cdot P(t)$$

$$\dot{z}_k = 0.4 + z_k(x_k - 8.5)$$

Parameters ω_k have Gaussian distribution with $\bar{\omega}_k = 1$, std$(\omega_k) = 0.02$

Phase determination

We follow PHYSICAL REVIEW E **75**, 011918 (2007)

Feedback suppression of neural synchrony by vanishing stimulation

Natalia Tukhlina, Michael Rosenblum, Arkady Pikovsky, and Jürgen Kurths

and introduce a "device" (harmonic oscillator + integrating unit):

$$\ddot{u} + \alpha\dot{u} + \omega_0^2 u = X(t)$$
$$\mu\dot{d} + d = \dot{u}$$

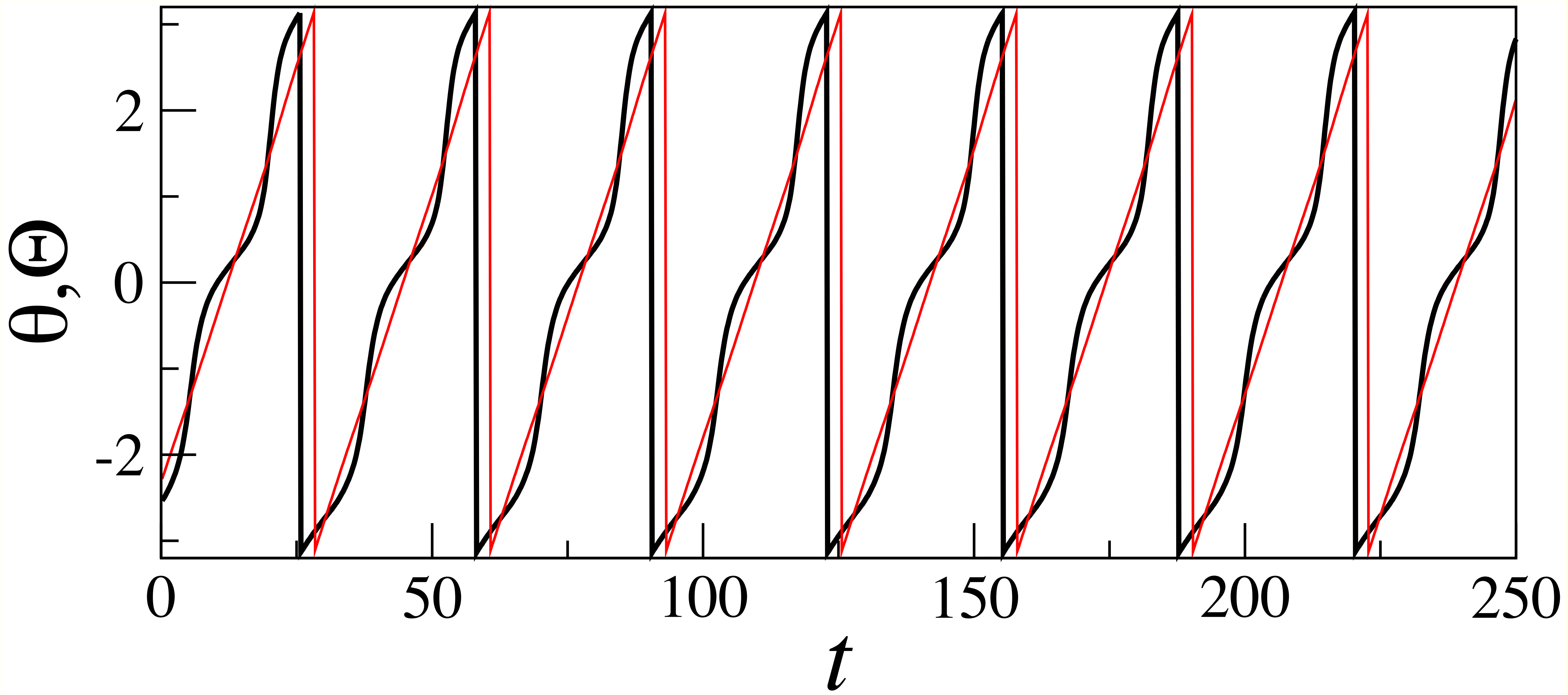
$\omega_0 \approx$ average frequency of $X(t)$

Auxiliary variables $\hat{x} = \alpha\dot{u}$ and $\hat{y} = \alpha\omega_0\mu d$ have zero mean, amplitudes close to that of X, and phases shifted by 0 and $\pi/2$

We obtain phase as $\boxed{\theta = \arctan(\hat{y}/\hat{x})}$

We obtain instantaneous amplitude as $\boxed{a_{in} = \sqrt{\hat{x}^2 + \hat{y}^2}}$

Phase determination: how it works for model 1



$\Theta = \arctan \dfrac{Y - Y_0}{X - X_0}$

$\theta = \arctan \dfrac{\hat{y}}{\hat{x}}$

$$X = N^{-1} \sum_k x_k \, , Y = N^{-1} \sum_k y_k$$

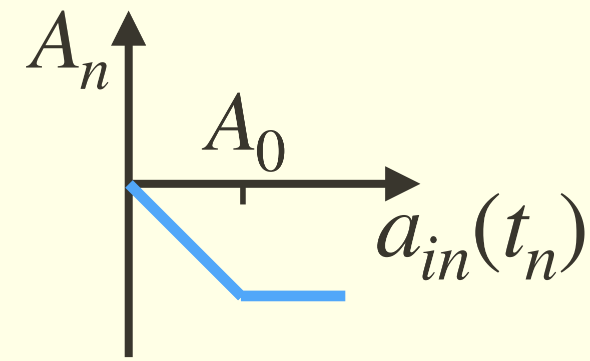
Fixed point coordinates:

$$X_0 \approx -0.27 \, , Y_0 \approx 0.55$$

Phase and amplitude of stimuli

We implement a feedback with the factor $\varepsilon_{fb} < 0$:

The pulse strength A_n is limited: $|A_n| \leq A_0$



Suppose the favourable phase θ_0 is known, then

- we stimulate around θ_0 with pulse strength

$$A_n = A(t_n) = \max(\varepsilon_{fb} a_{in}(t_n), -A_0)$$

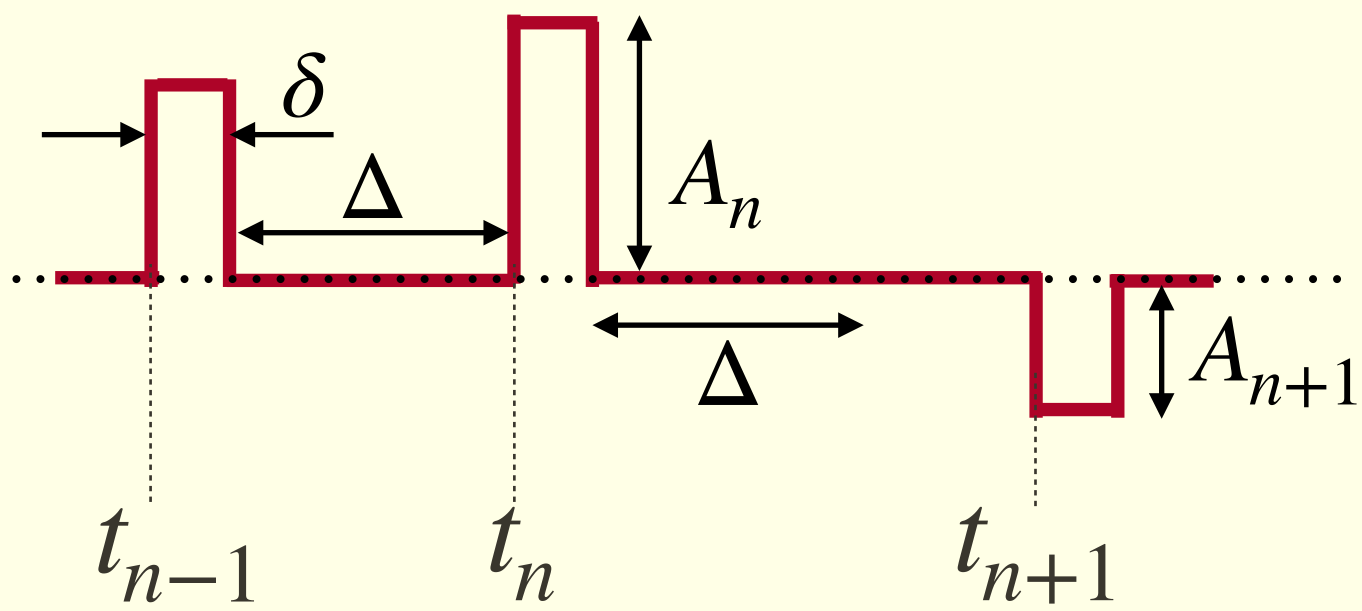
- we stimulate around $\theta_0 + \pi$ with pulse strength

$$A_n = A(t_n) = -\max(\varepsilon_{fb} a_{in}(t_n), -A_0)$$

Practically, we check the conditions $|\theta(t) - \theta_0| < \Theta_{tol}$

$$|\theta(t) - \theta_0 - \pi| < \Theta_{tol}$$

Simple case: rectangular pulses



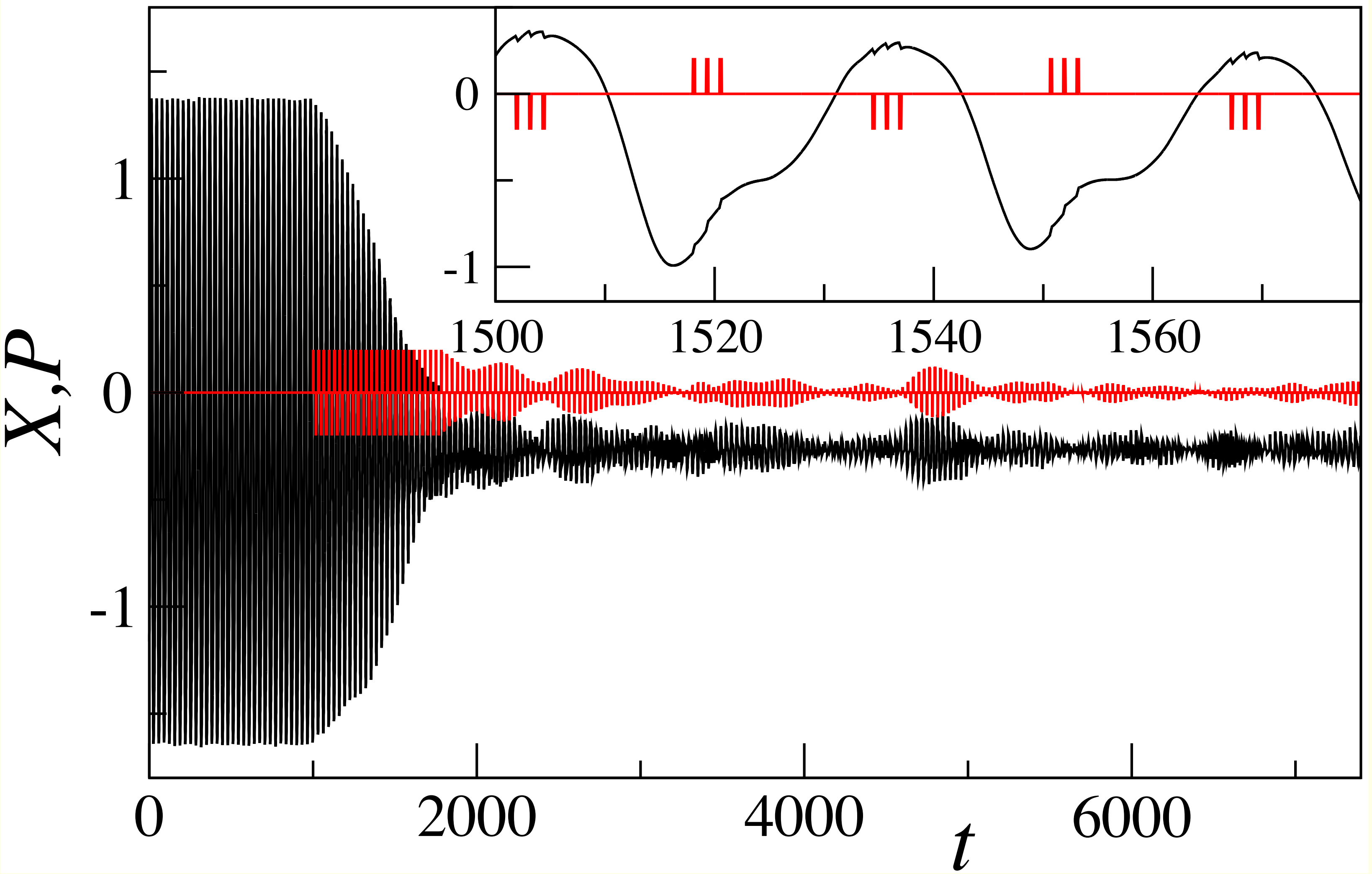
The pulse strength A_n is determined by $a_{in}(t_n)$

Example 1

Rectangular pulses

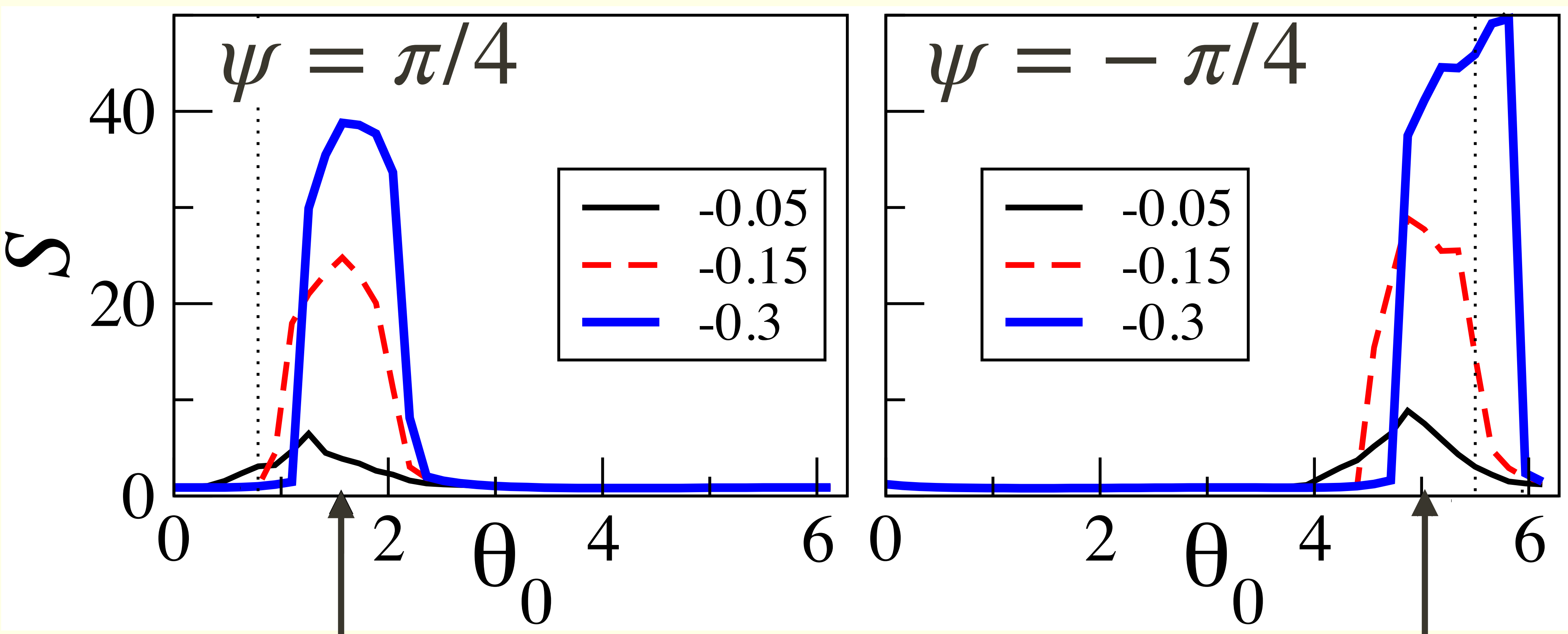
Bonhoeffer-van der Pol model, $\varepsilon = 0.03, \psi = 0$

Stimulation parameters $\theta_0 = 0\,, \varepsilon_{fb} = -\,0.05$



Efficiency of suppression in dependence on choice of θ_0

Suppression coefficient $S = \mathrm{std}(X_{autonomous})/\mathrm{std}(X_{stimulated})$



values detected as optimal by an automated algorithm

Adaptive control

We adapt the technique from

Synchrony suppression in ensembles of coupled oscillators *via* adaptive vanishing feedback

Ghazal Montaseri,[1,2] Mohammad Javad Yazdanpanah,[3] Arkady Pikovsky,[2] and Michael Rosenblum[2]

We adjust $\theta_0, \varepsilon_{fb}$ after each complete cycle according to $\bar{a}$

$\bar{a}$ is average of $a_{in} = \sqrt{\hat{x}^2 + \hat{y}^2}$ over all points **where we do not stimulate**

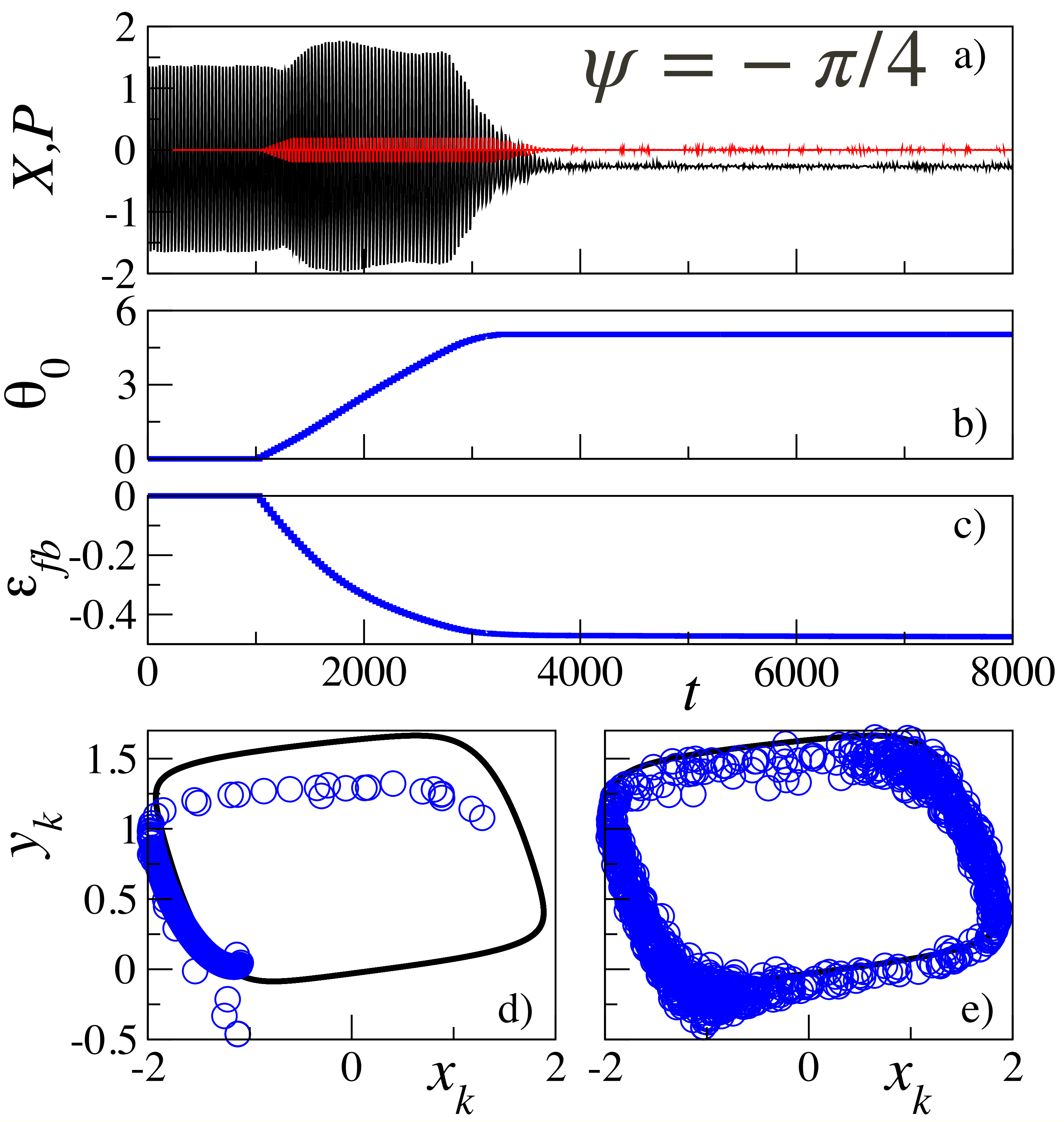
The update rules: $\theta_0 \;\to\; \theta_0 + k_1\bar{a}(1 + \tanh[k_2(\bar{a} - a_{stop})]$

$$\varepsilon_{fb} \;\to\; \varepsilon_{fb} - k_3\bar{a}/\cosh(k_4\varepsilon_{fb})$$

Example 2

$$\theta_0(t_0) = 0$$

$$\varepsilon_{fb}(t_0) = 0$$



Snapshot, autonomous system

Snapshot, stimulated system

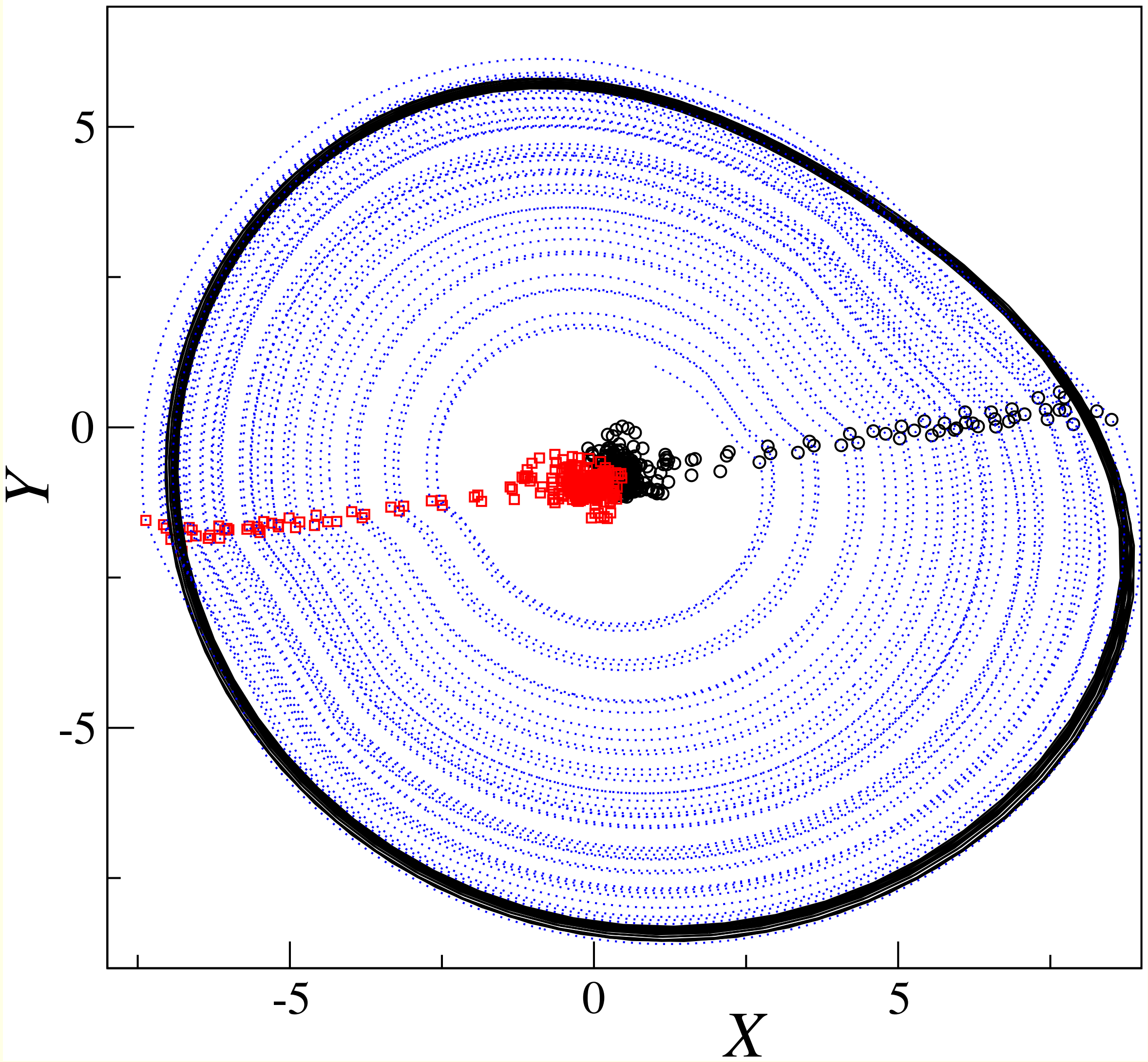
Does it work with chaotic systems? Example 3

Rössler oscillators, coupling $\varepsilon = 0.1$, $\psi = \pi/4$

(Critical coupling of the Kuramoto transition $\varepsilon_{cr} \approx 0.05$)

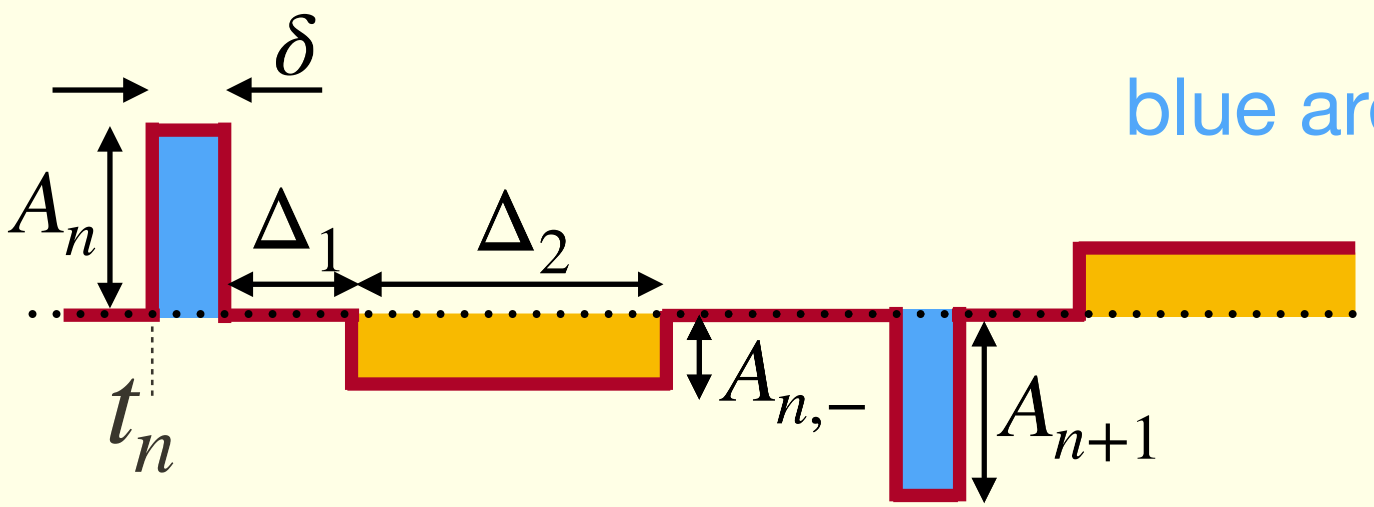
Here we use only two pulses per period, $A_0 = 2$

For strongly coupled system, $\varepsilon = 0.2$, we have to increase $A_0 = 4$ and allow stronger feedback



Charge-balanced stimuli

We tested the following pulse form:



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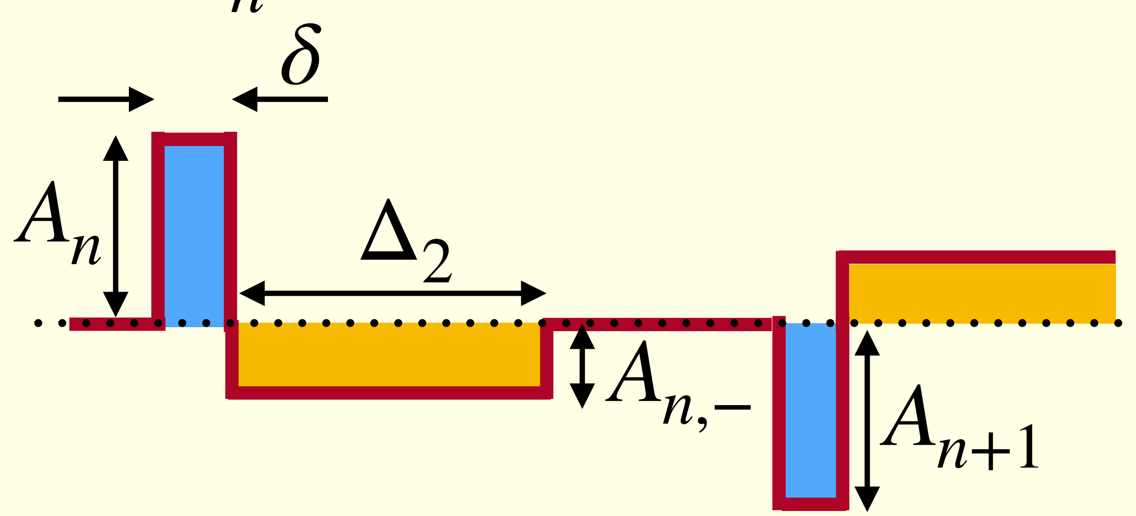
Here δ, Δ_1, Δ_2 are fixed within trial, while A_n varies with each pulse

We set $\Delta_2 = 10\delta$, then $A_{n,-} = -A_n/10$

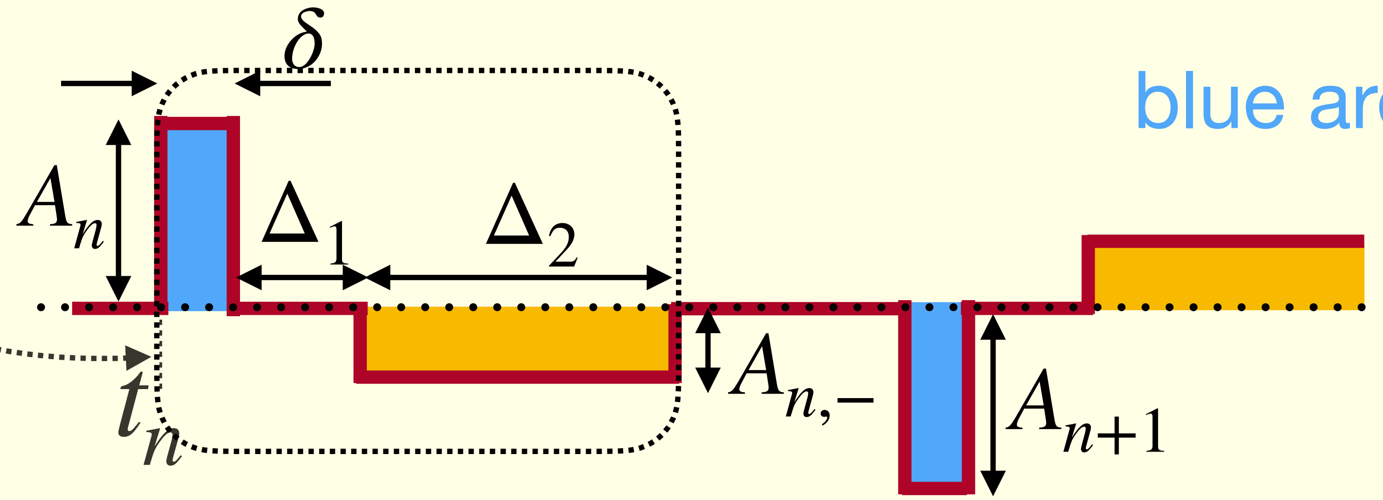
The simplest case $\Delta_1 = 0$
is **inefficient**



We have to choose Δ_1 large enough so that low-amplitude pulse comes in the least sensitive phase

Charge-balanced stimuli

We tested the following pulse form:



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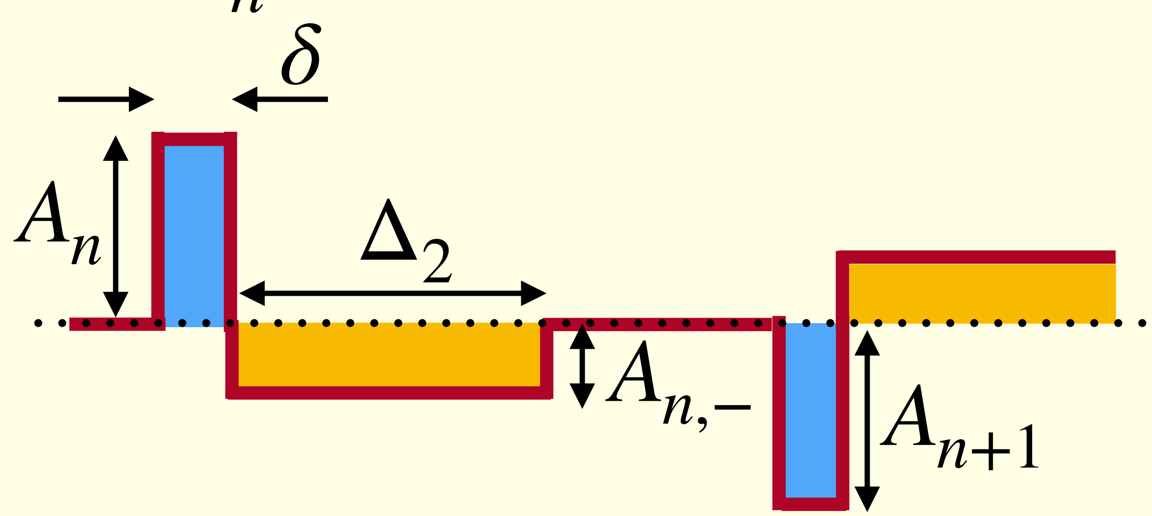

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Charge-balanced stimuli

We tested the following pulse form:

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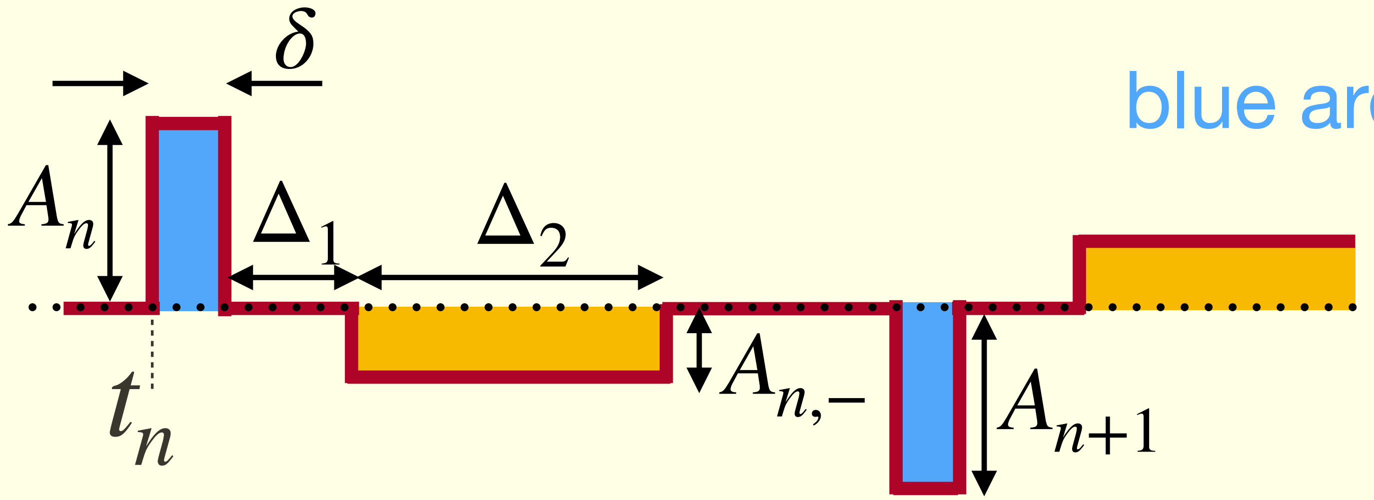

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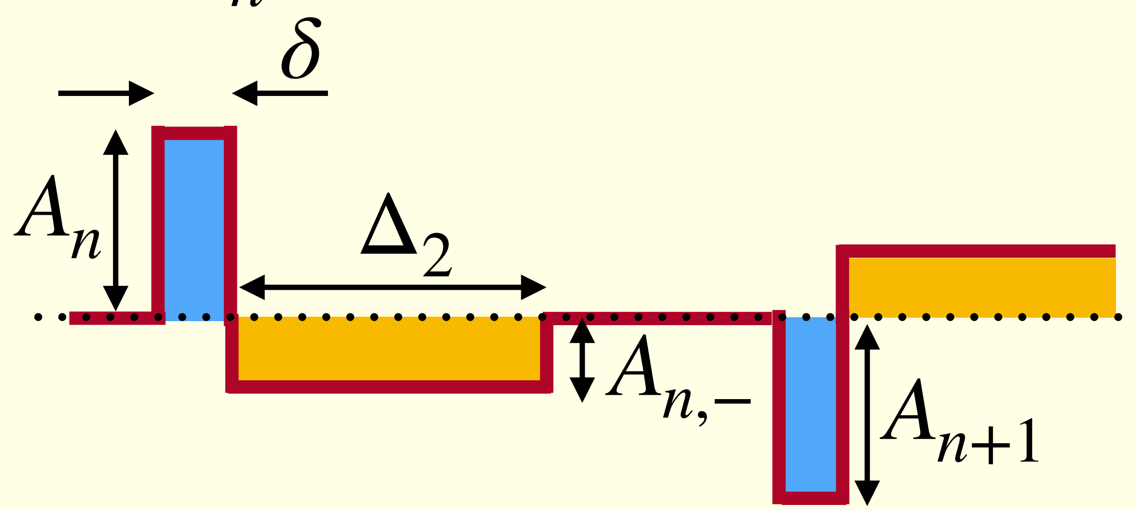
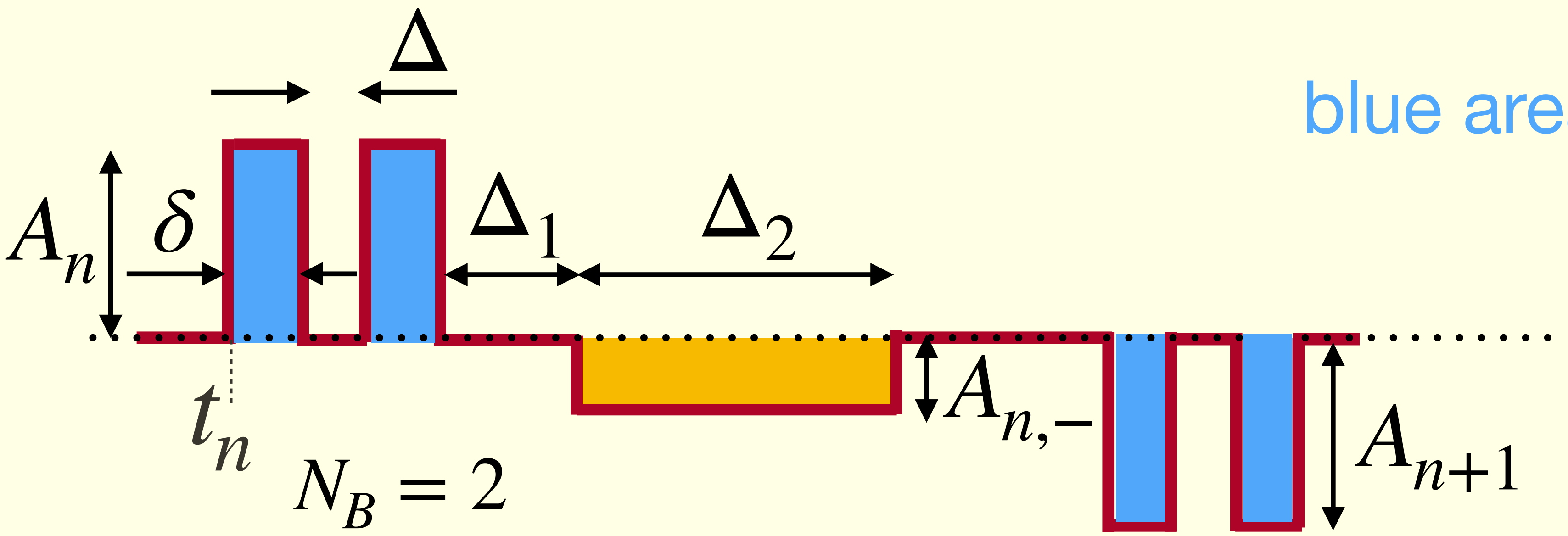


We have to choose Δ_1 large enough so that low-amplitude pulse comes in the least sensitive phase

Charge-balanced pulses II

Most efficient we find the following pulse form:



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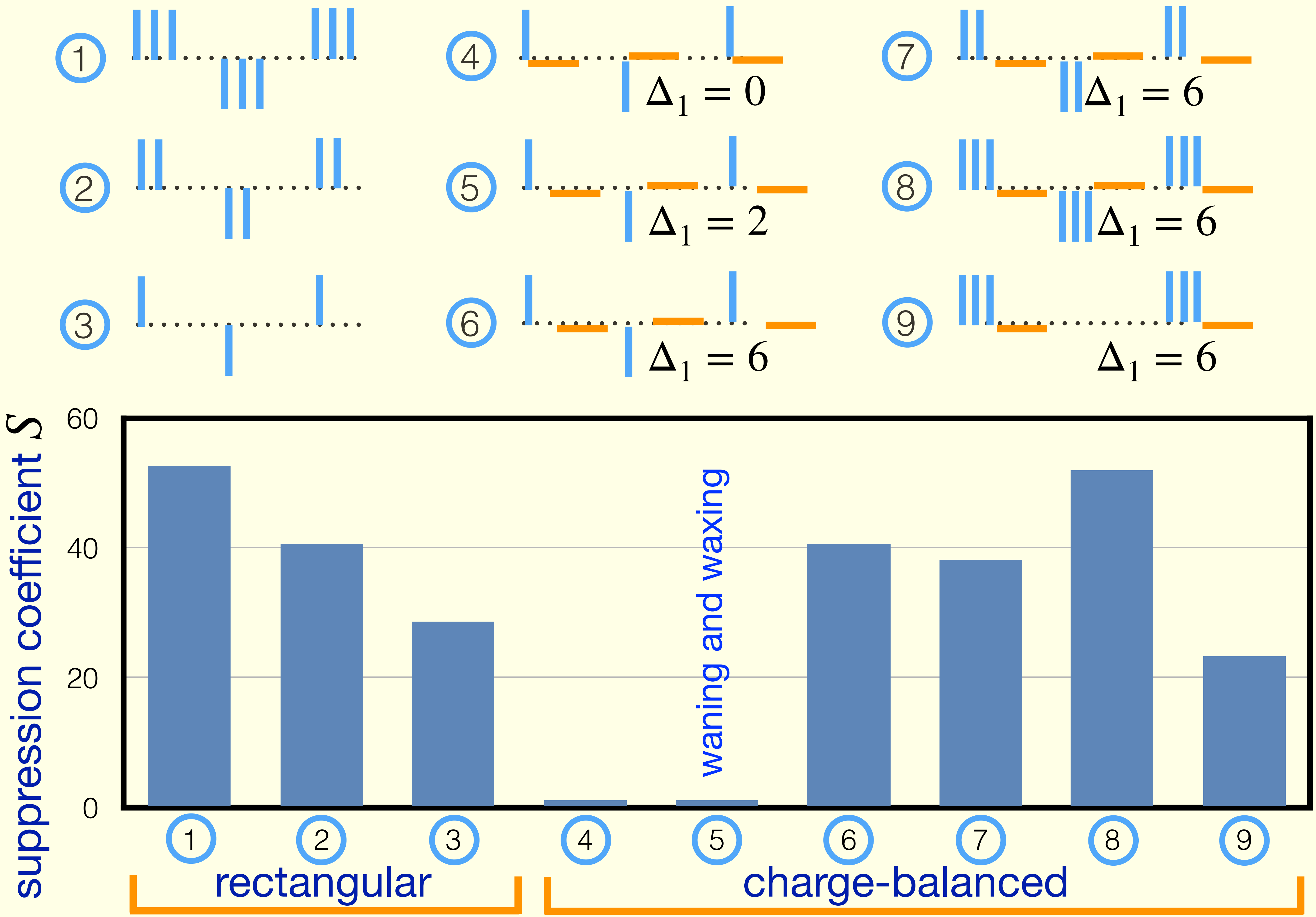
Results: Bonhoeffer-van der Pol model

Rectangular pulses vs. charge-balanced pulses



Summary

- Suppression of synchrony with rare pulses
- Automated tuning of the feedback parameters
- Works for charged-balanced stimuli;
  stimulation and measurement are separated in time
- Enhancement of synchrony is possible as well (but you cannot beat the injection locking approach)

Controlling collective synchrony in oscillatory ensembles by precisely timed pulses

Cite as: Chaos **30**, 093131 (2020); doi: 10.1063/5.0019823
Submitted: 25 June 2020 · Accepted: 1 September 2020 ·
Published Online: 18 September 2020

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Michael Rosenblum[a]

Some important issues

- Optimisation of the pulse's shape

Optimizing charge-balanced pulse stimulation for desynchronization Erik T. K. Mau[a) iD] and Michael Rosenblum[b) iD]

Cite as: Chaos **32**, 013103 (2022); doi: 10.1063/5.0070036

- Real-time phase and amplitude estimation

Scientific Reports | (2021) 11:18037

Michael Rosenblum[1✉], Arkady Pikovsky[1], Andrea A. Kühn[2] & Johannes L. Busch[2]

- Optimisation of the stimulation by machine learning

Reinforcement learning for suppression of collective activity in oscillatory ensembles

Dmitrii Krylov,[1] Dmitry V. Dylov,[1,a) iD] and Michael Rosenblum[2,b) iD]

Cite as: Chaos **30**, 033126 (2020); doi: 10.1063/1.5128909

Outlook

- Algorithms for phase/amplitude estimation with artefacts removal

- Improved adaptation algorithm (both increasing and decreasing θ_0) for suppression in case of slow varying parameters

- The utmost goal: **clinical implementation** in cooperation with Charité – Universitätsmedizin Berlin

RETUNE

CRC TRR 295 Berlin-Würzburg

Transregional Collaborative Research Center for Neuromodulation