Dynamical disentanglement in analysis of oscillatory systems
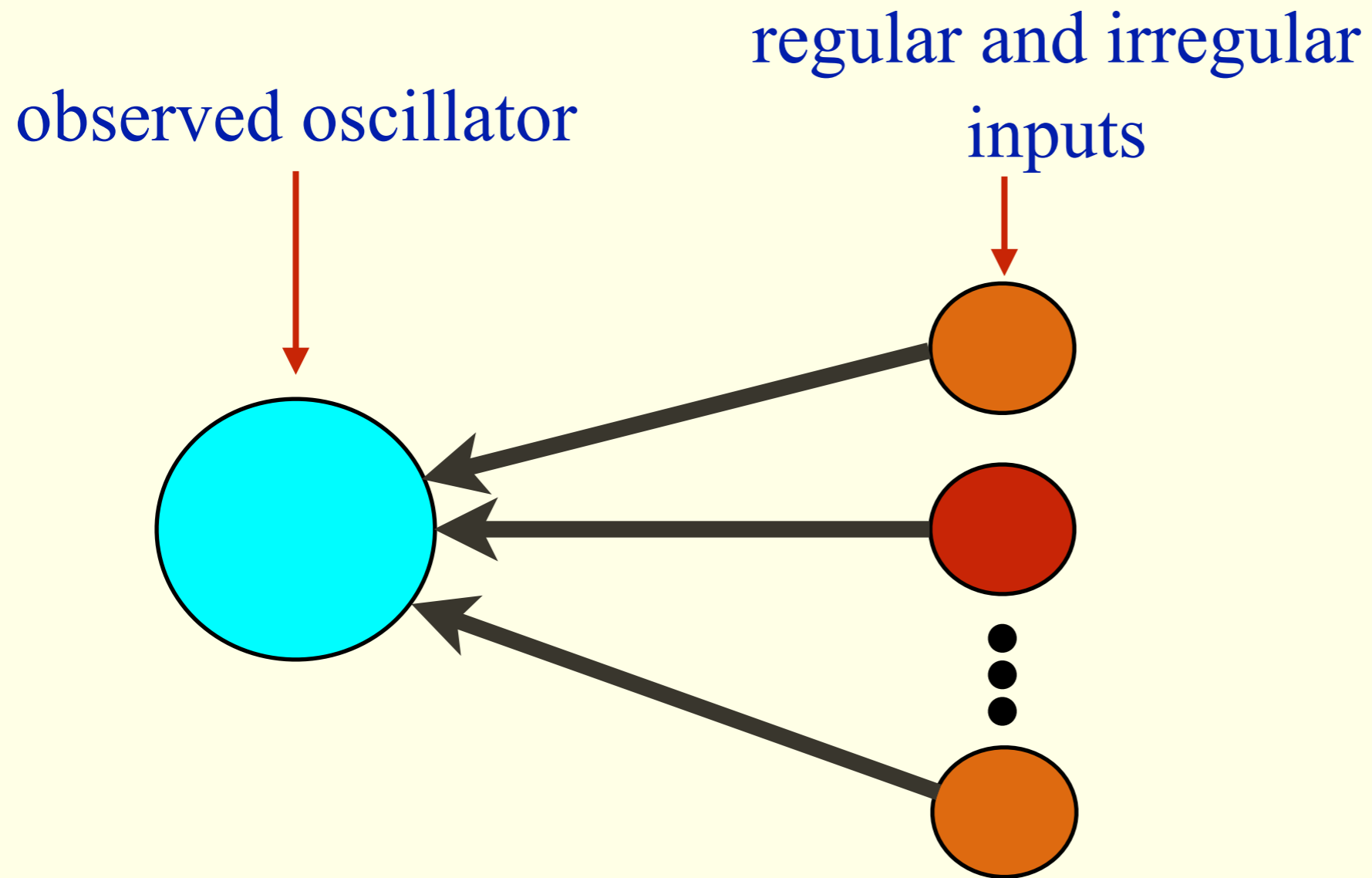
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Dynamical disentanglement

observed oscillator

regular and irregular inputs

Dynamical disentanglement

observed oscillator

regular and irregular inputs

unobserved input

observed input

unobserved input

Dynamical disentanglement

observed oscillator

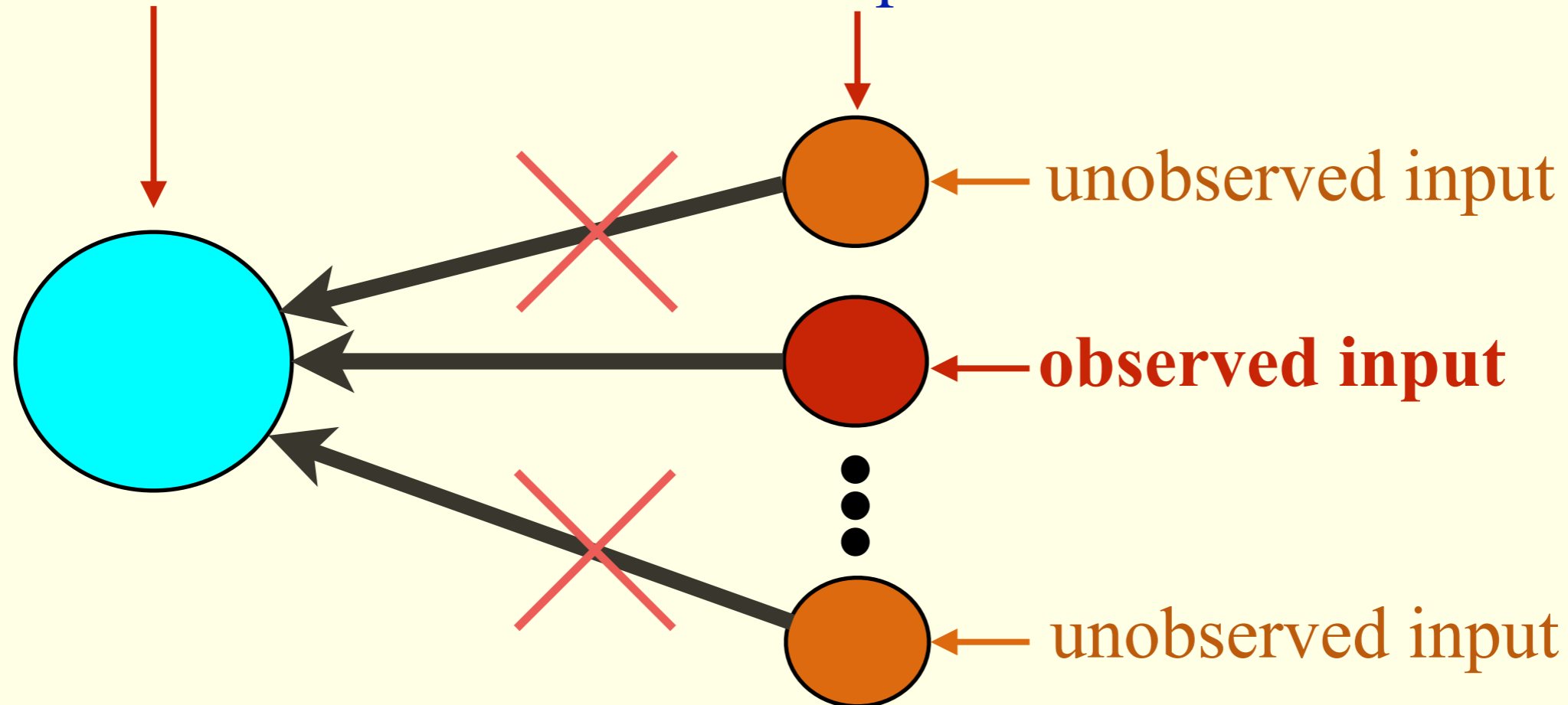regular and irregular inputs

unobserved input

observed input

unobserved input

Question 1: what would be dynamics of the oscillator if there were no observed input?
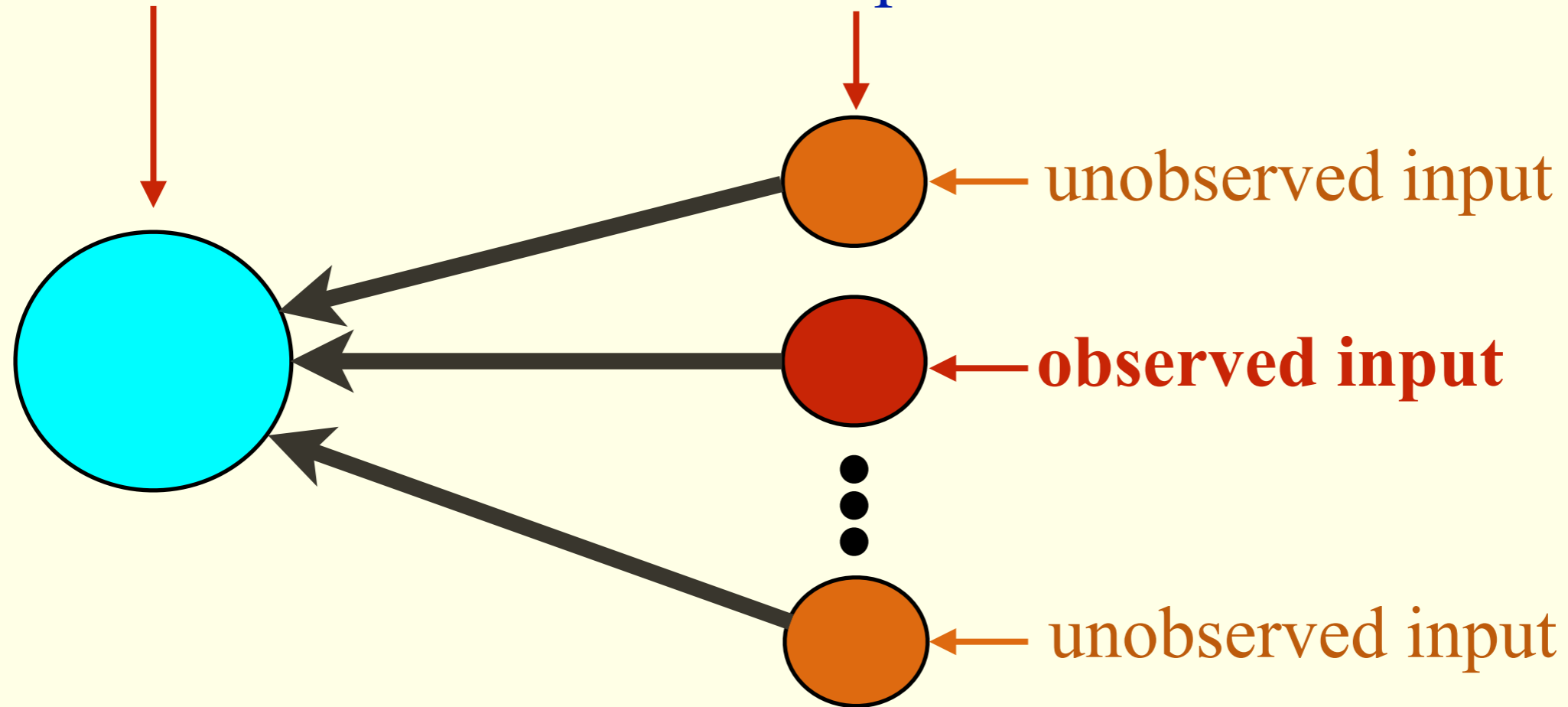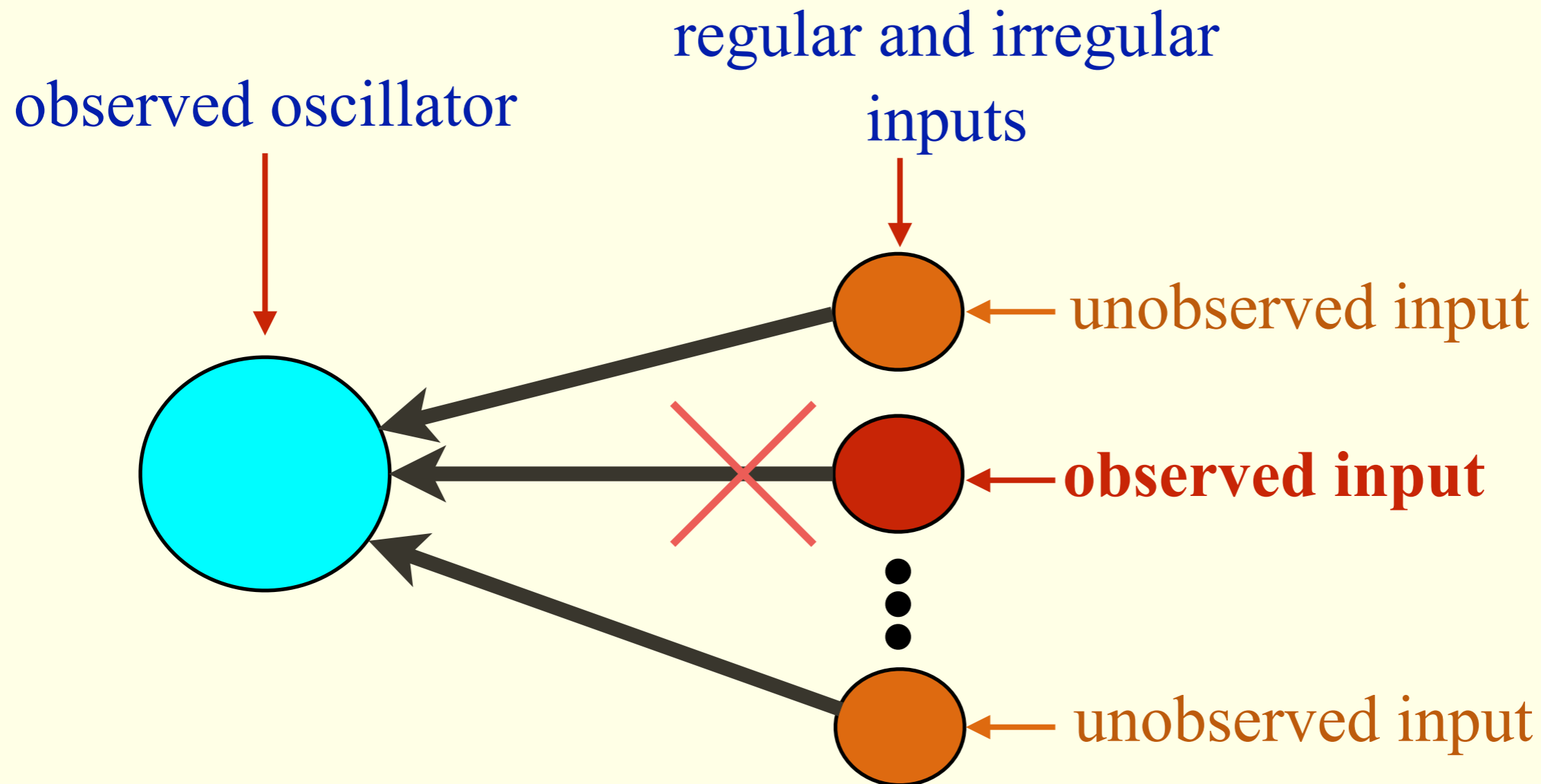
Dynamical disentanglement

observed oscillator

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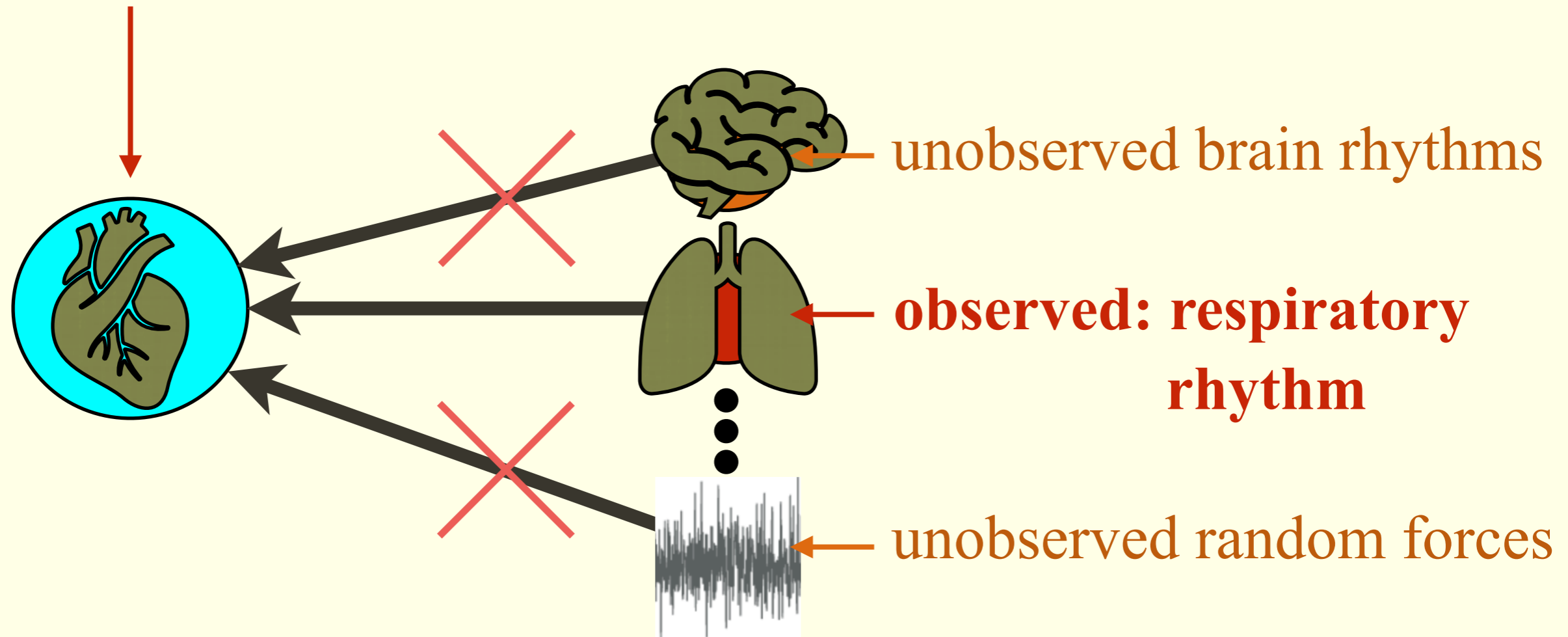
observed input

unobserved input

Question 1: what would be dynamics of the oscillator if there were no observed input?

Question 2: what would be dynamics of the oscillator if there were no other inputs?
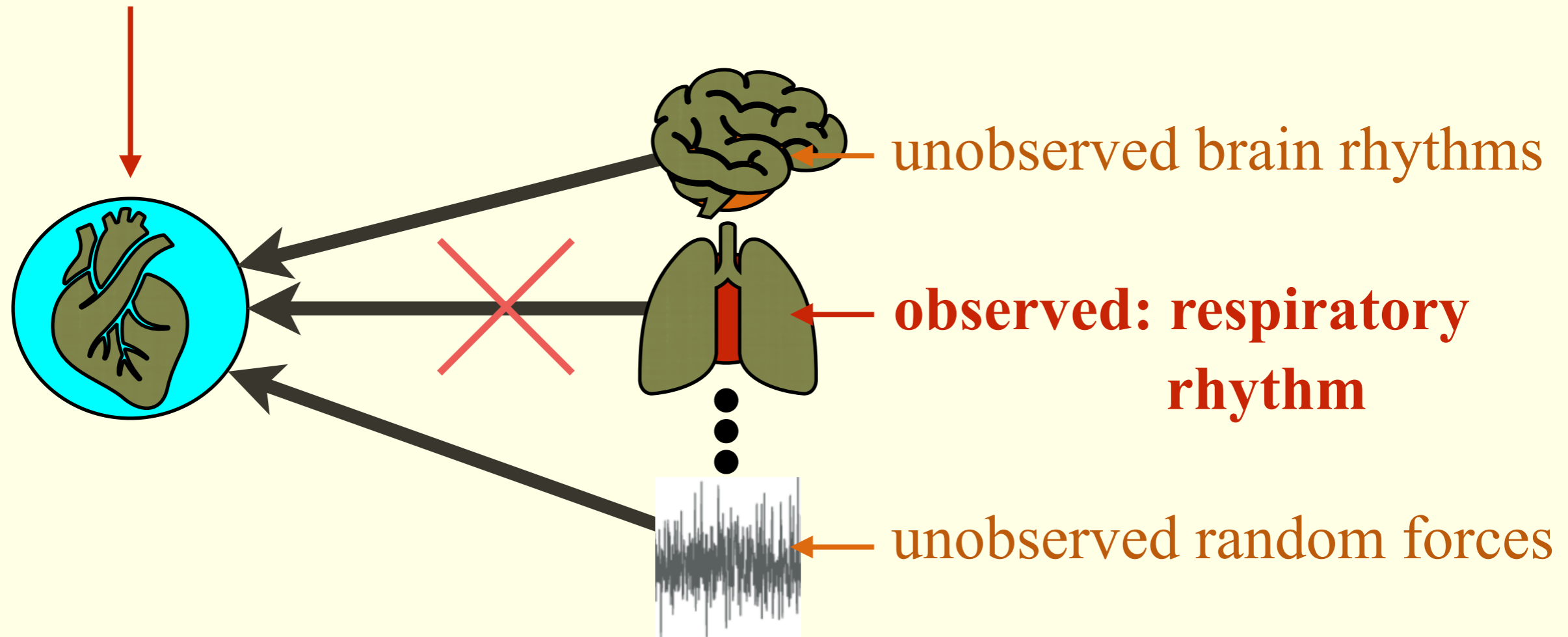
Dynamical disentanglement: an application

observed oscillator

unobserved brain rhythms

observed: respiratory rhythm

unobserved random forces

Question 1: how does the respiratory-related heart rate variability look like?

Dynamical disentanglement: an application

observed oscillator

unobserved brain rhythms

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Question 1: how does the respiratory-related heart rate variability look like?

Question 2: what is the cardiac rhythm variability due to sources other than respiration?

Dynamical disentanglement: an application

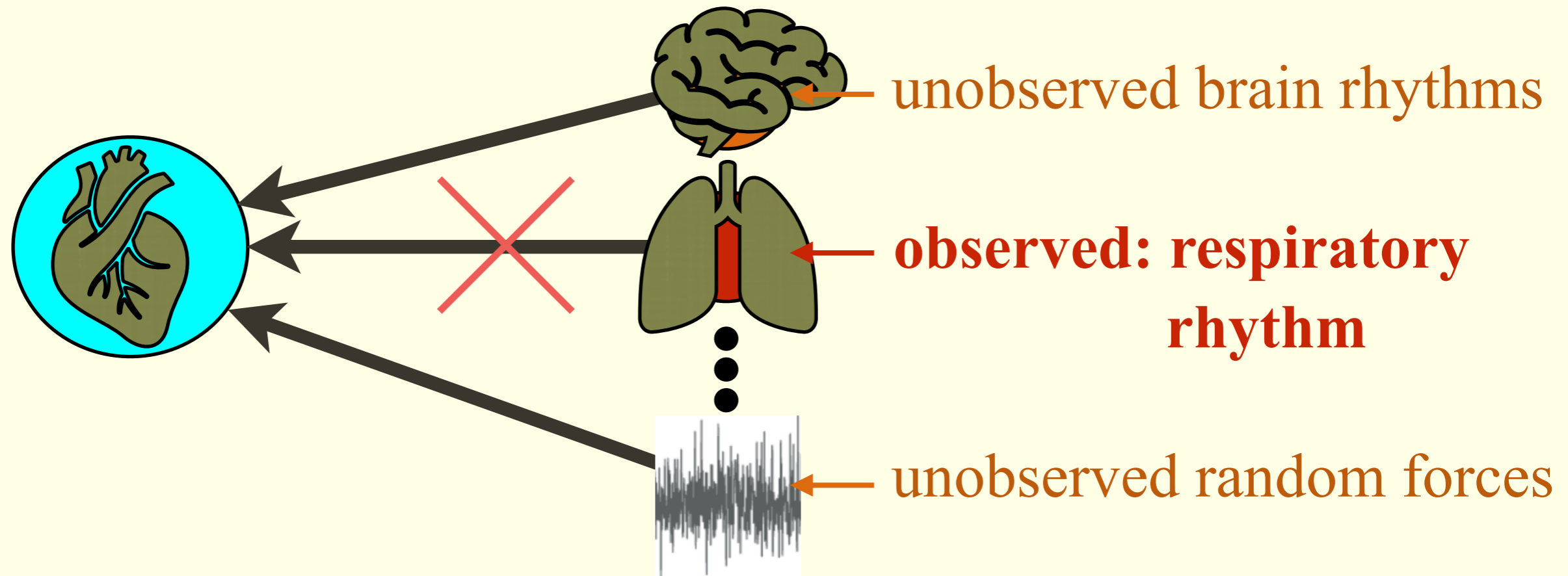unobserved brain rhythms

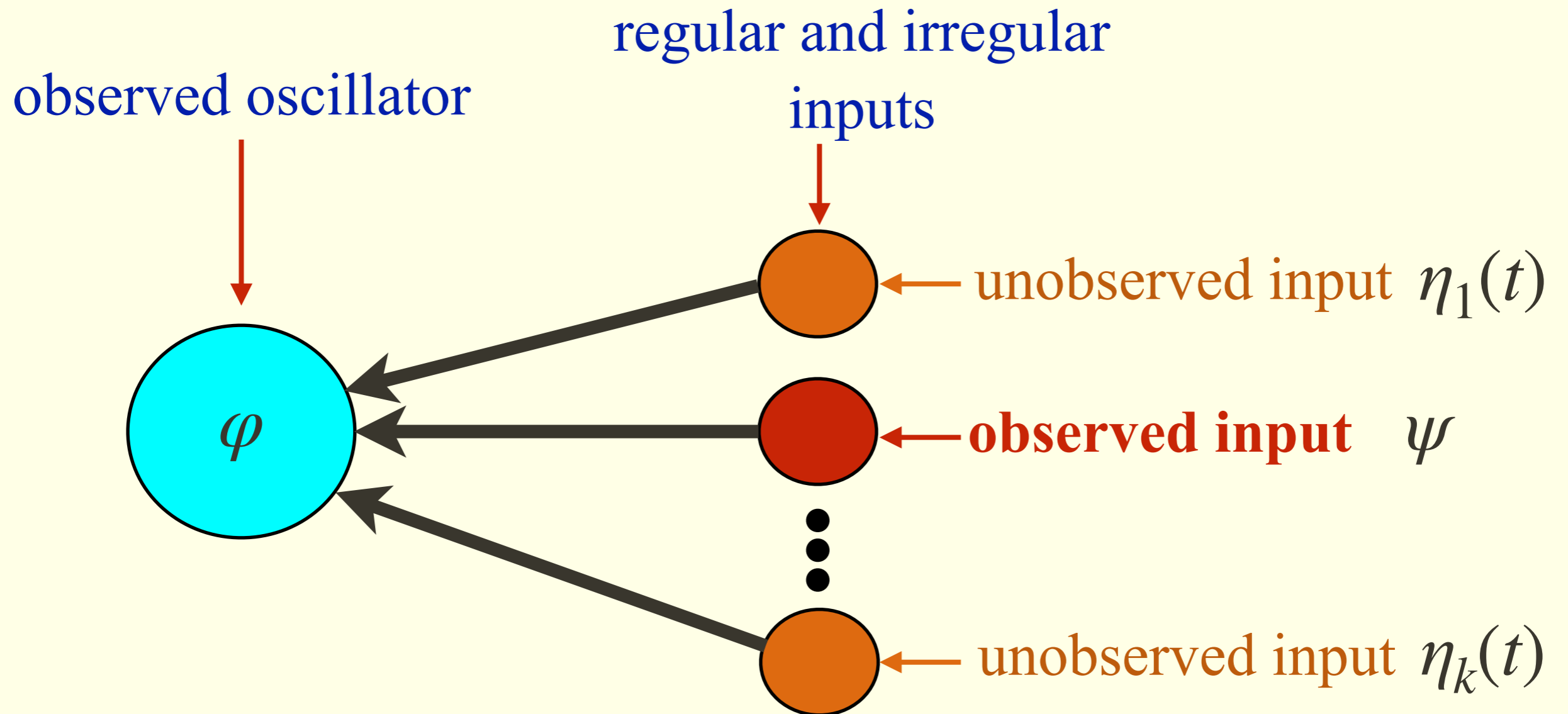**observed: respiratory rhythm**

unobserved random forces

Question 1: how does the respiratory-related heart rate variability look like?

Question 2: what is the cardiac rhythm variability due to sources other than respiration?

Our approach is based on inference of the phase dynamics equation from observations

Dynamical disentanglement

observed oscillator

regular and irregular inputs

unobserved input $\eta_1(t)$

observed input ψ

unobserved input $\eta_k(t)$

Suppose we can reconstruct phase dynamics from observations:

$$\dot{\varphi} = \omega + Q(\varphi, \psi) + \sum_k Q_k(\varphi, \eta_k(t)) = \omega + Q(\varphi, \psi) + \zeta$$

Dynamical disentanglement

Suppose we can reconstruct phase dynamics from observations:

$$\dot{\varphi} = \omega + Q(\varphi, \psi) + \sum_k Q_k(\varphi, \eta_k(t)) = \omega + Q(\varphi, \psi) + \zeta$$

Question 1: what would be dynamics of the oscillator if there were no observed input?

→ we solve equation $\dot{\varphi} = \omega + \zeta$

Question 2: what would be dynamics of the oscillator if there were no other inputs?

→ we solve equation $\dot{\varphi} = \omega + Q(\varphi, \psi)$

Dynamical disentanglement: simple example

Suppose we have noisy Rayleigh oscillator:

$$\ddot{x} - 4(1 - \dot{x}^2)\dot{x} + x = p(t) = \varepsilon \cos(\nu t) + \zeta(t)$$

noise

For weak perturbation $p(t)$ the coupling function reads

$$\dot{\varphi} = \omega + Q(\varphi, \nu t) + Q_N(\varphi, \zeta(t))$$

Deterministic part $\dot{\varphi} = \omega + Q(\varphi, \nu t)$ describes the noise-free system

We use $\varphi, \psi = \nu t$ to infer Q via fit from observations

While fit $\approx$ averaging, the random perturbations are washed out

and we obtain equation $\dot{\varphi} \approx \omega + Q(\varphi, \nu t)$
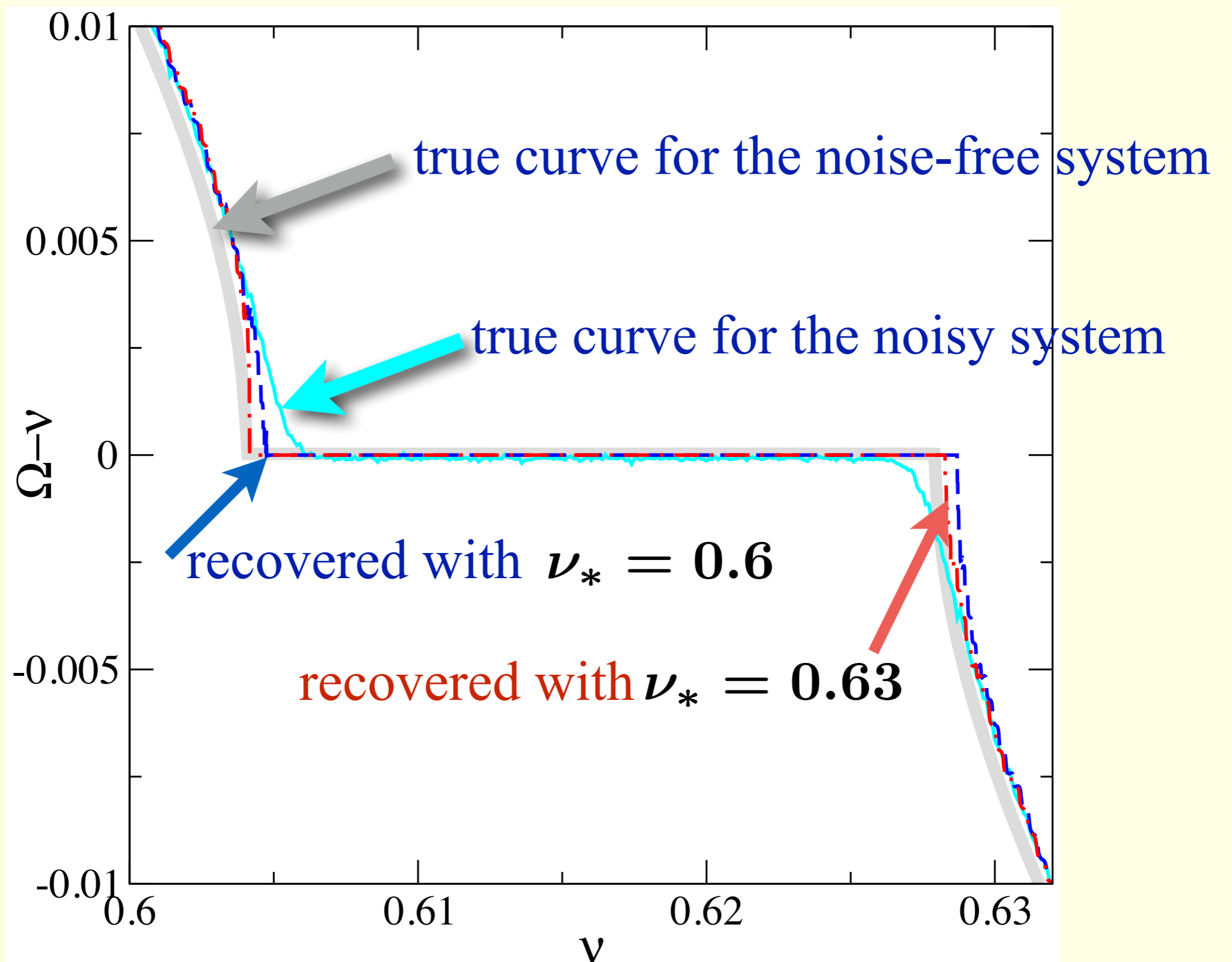
Dynamical disentanglement: simple example

→ We obtain equation $\dot{\varphi} \approx \omega + Q(\varphi, \nu t)$
that describes noise-free system and we can solve it
numerically for different ν to predict domain of locking

→ Thus, we can find the Arnold tongue from a few
measurements of noisy systems
In experiments, phase can be estimated from data,
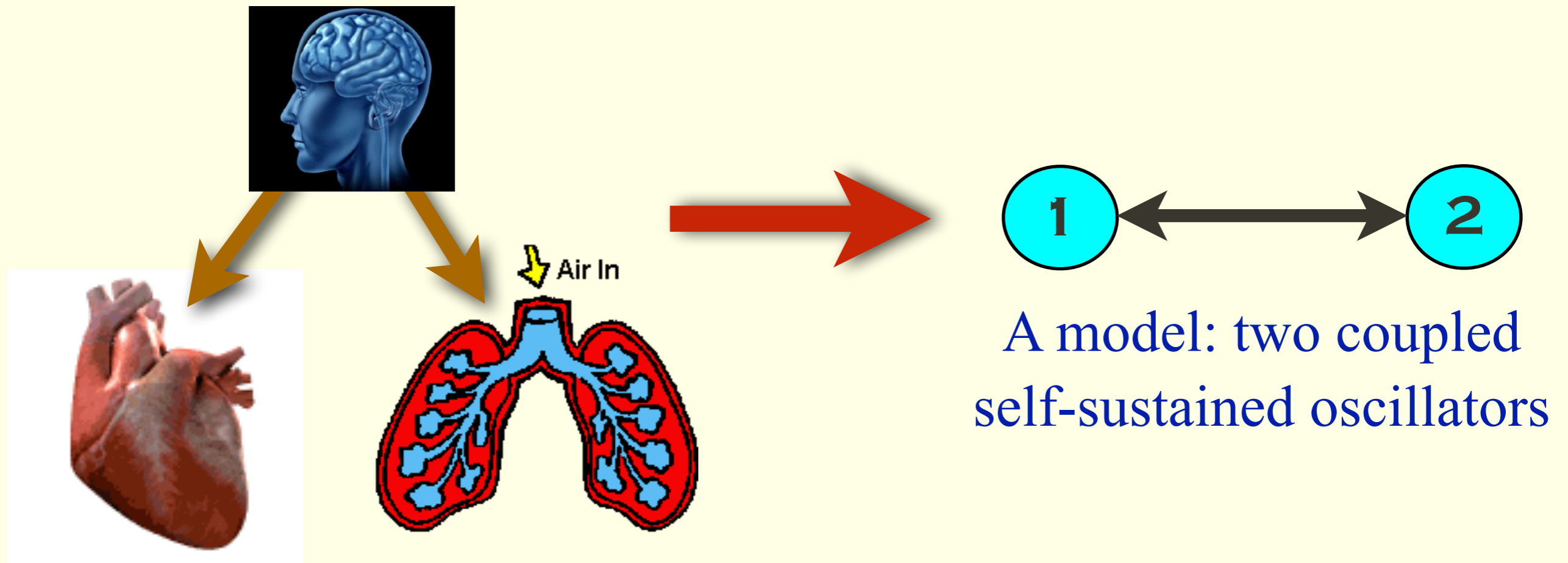e.g., with the help of the Hilbert Transform

It works perfectly for weak noise and quite good for strong one!

Noisy Rayleigh oscillator

true curve for the noise-free system

true curve for the noisy system

recovered with $\nu_* = 0.6$

recovered with $\nu_* = 0.63$

$\varepsilon_* = 0.05$, $D = 0.05$

Main example: cardiorespiratory interaction

A model: two coupled self-sustained oscillators

Analysis: synchronization indices, directionality indices

reconstruction of the phase dynamics model

Our main interest: respiratory-related heart rate variability

Coupled oscillators: phase description

A model: two coupled
self-sustained oscillators

$$\dot{\varphi}_1 = \omega_1 + Q_1(\varphi_1, \varphi_2)$$
$$\dot{\varphi}_2 = \omega_2 + Q_2(\varphi_1, \varphi_2)$$

Coupled oscillators: phase description
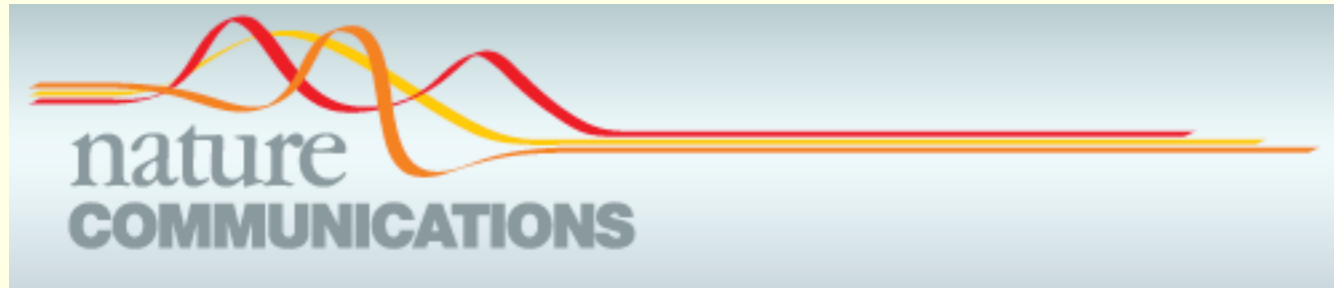

A model: two coupled
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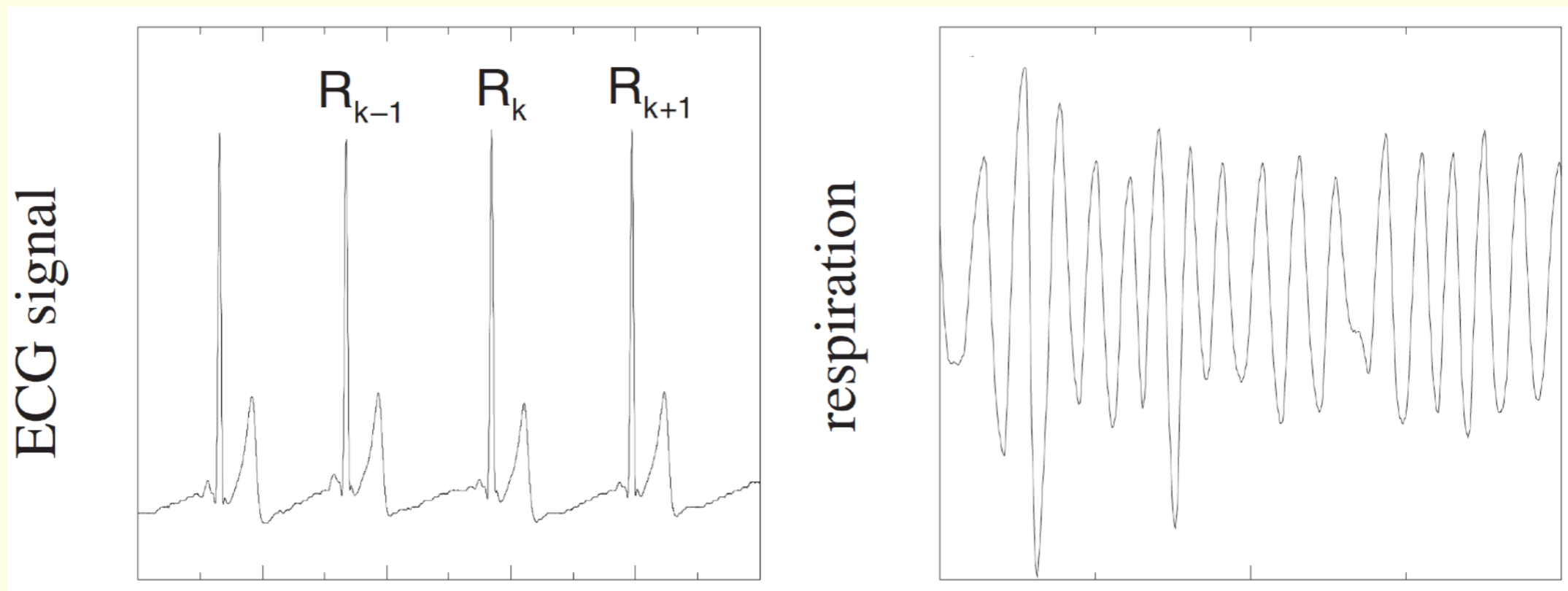coupling functions

These equations can be reconstructed from data

Cardiorespiratory interaction in adults

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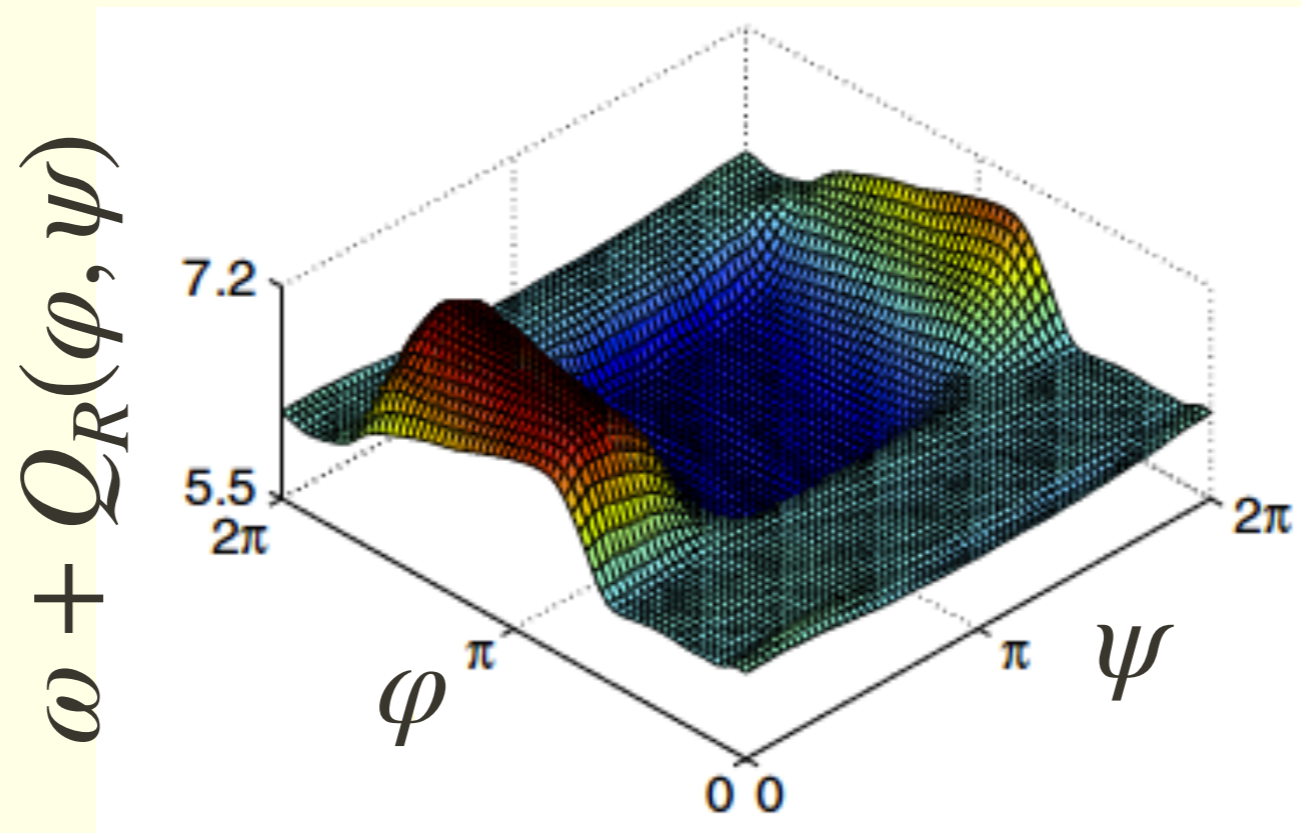
nature
COMMUNICATIONS

Experiments on healthy humans

- Spontaneous respiration, supine position, rest state

- Data: ECG, arterial pulse, respiration

Cardiac dynamics: the coupling function
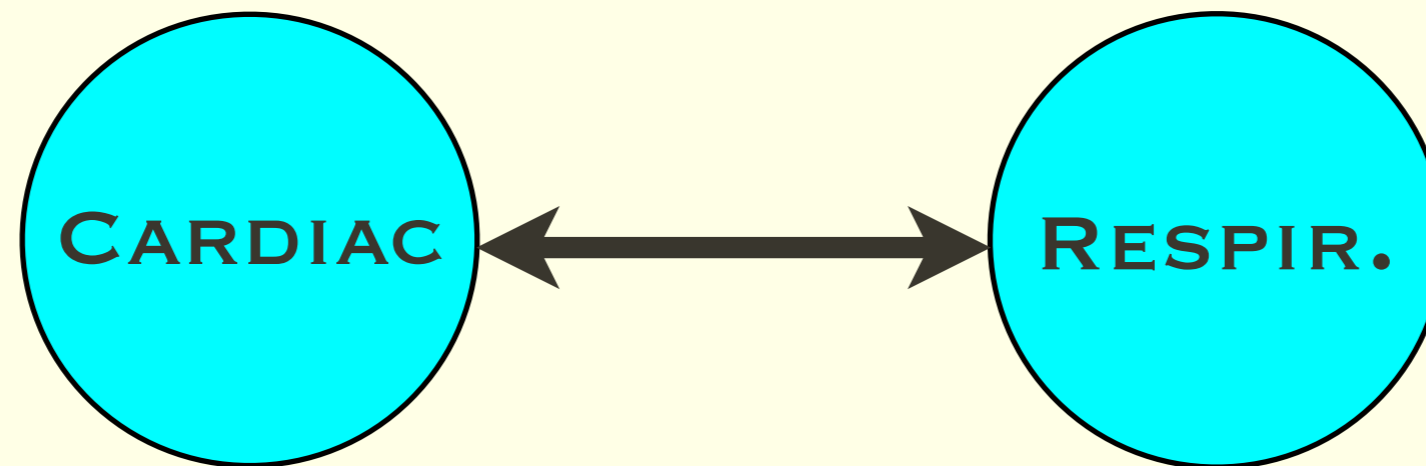

Cardiac phase from ECG

Phase of respiration

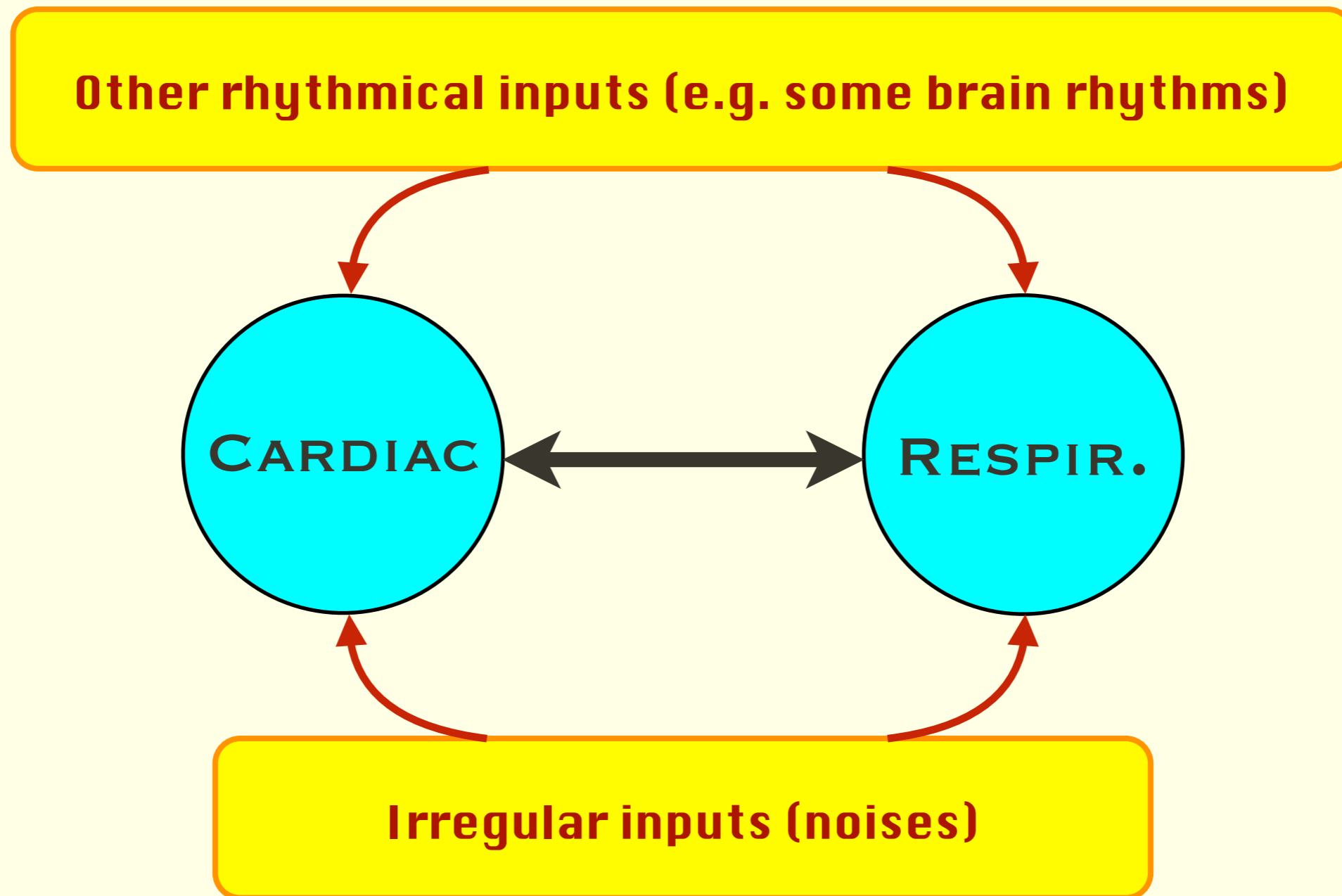$$\dot{\varphi} = \omega + Q_R(\varphi, \psi)$$

stands for 'respiration'

We used the model of two coupled oscillators…

…but it is too simplistic!

Interaction with the environment

Phase dynamics with account of many inputs

Cardiac phase from ECG

Phase of respiration

$$\dot{\varphi} = \omega + Q_R(\varphi, \psi) + \sum_s Q_s(\varphi, \eta_s) + \zeta$$

other inputs

intrinsic fluctuations

For weak inputs we expect to have a sum of coupling functions for different inputs, while for stronger inputs we expect cross-terms

Thus, we have two terms:

$Q_R(\varphi, \psi)$ describes variability due to respiration only

$\xi = \sum_s Q_s(\varphi, \eta_s) + \zeta$ describes effect of everything else except respiration

Phase dynamics with account of many inputs

Thus, we have two terms:

$Q_R(\varphi, \psi)$ describes variability due to respiration only

$$\xi = \sum_s Q_s(\varphi, \eta_s) + \zeta$$ describes effect of everything else
except respiration

Hence, we achieve a decomposition:

$$\dot{\varphi} - \omega = Q_R(\varphi, \psi) + \xi$$

Heart rate variability (HRV)

variability due to respiration (RSA-HRV)

variability due to everything else (non-RSA-HRV)

RSA= respiratory sinus arrhythmia

Phase dynamics with account of many inputs

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Heart rate variability (HRV)

variability due to respiration (RSA-HRV)
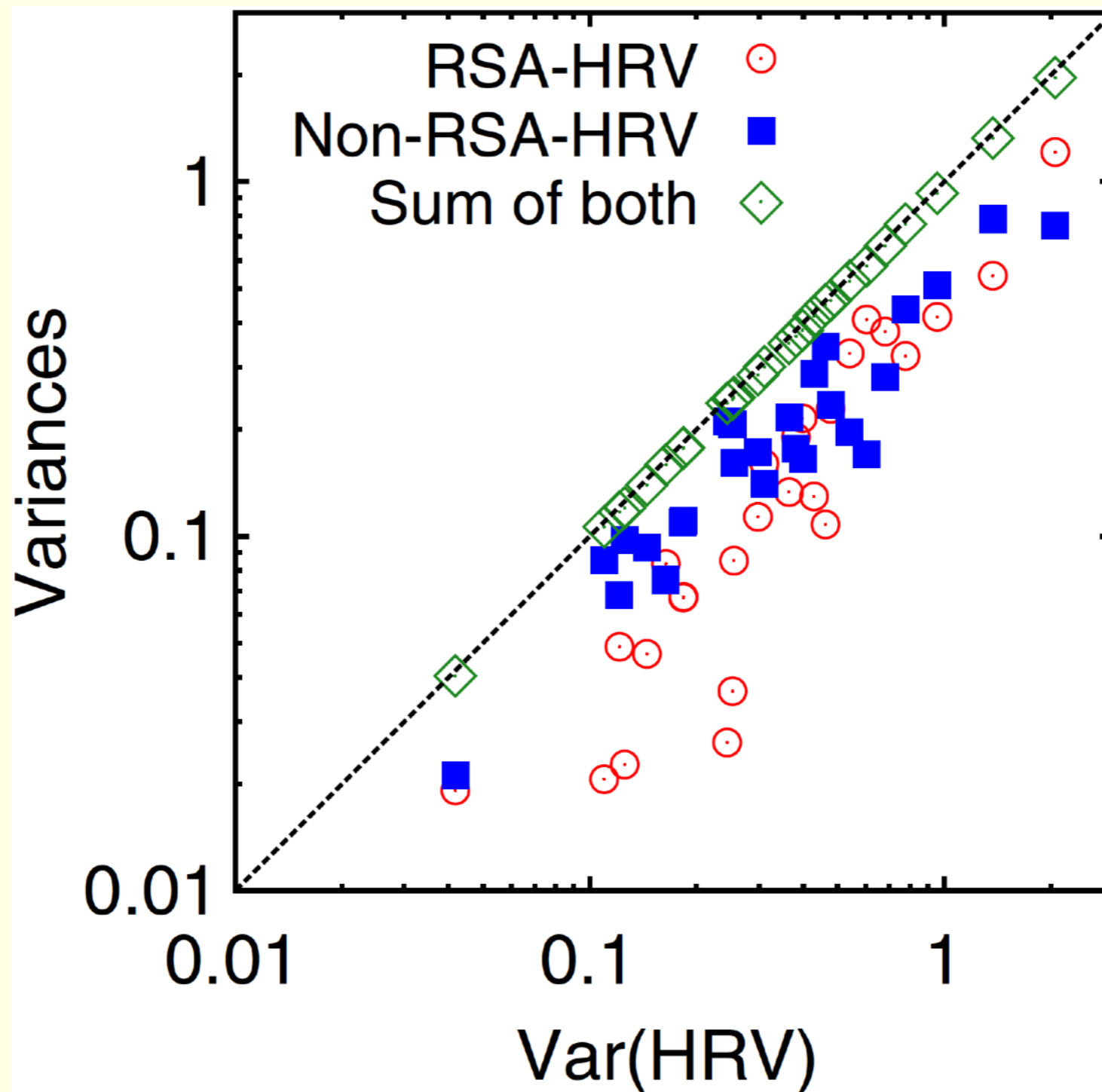
variability due to everything else (non-RSA-HRV)

Practically: we estimate Q_R from time series $\dot{\varphi}_k, \varphi_k, \psi_k$

Then we compute time series $\mu_k = Q_R(\varphi_k, \psi_k)$

Then we compute the rest term $\xi_k = \dot{\varphi}_k - \omega - \mu_k$

Thus, $\dot{\varphi}_k - \omega = \mu_k + \xi_k$

How good is this decomposition?

$$\text{Var(RSA-HRV)}+\text{Var(Non-RSA-HRV)} \approx \text{Var(HRV)}$$

as expected for non-correlated processes

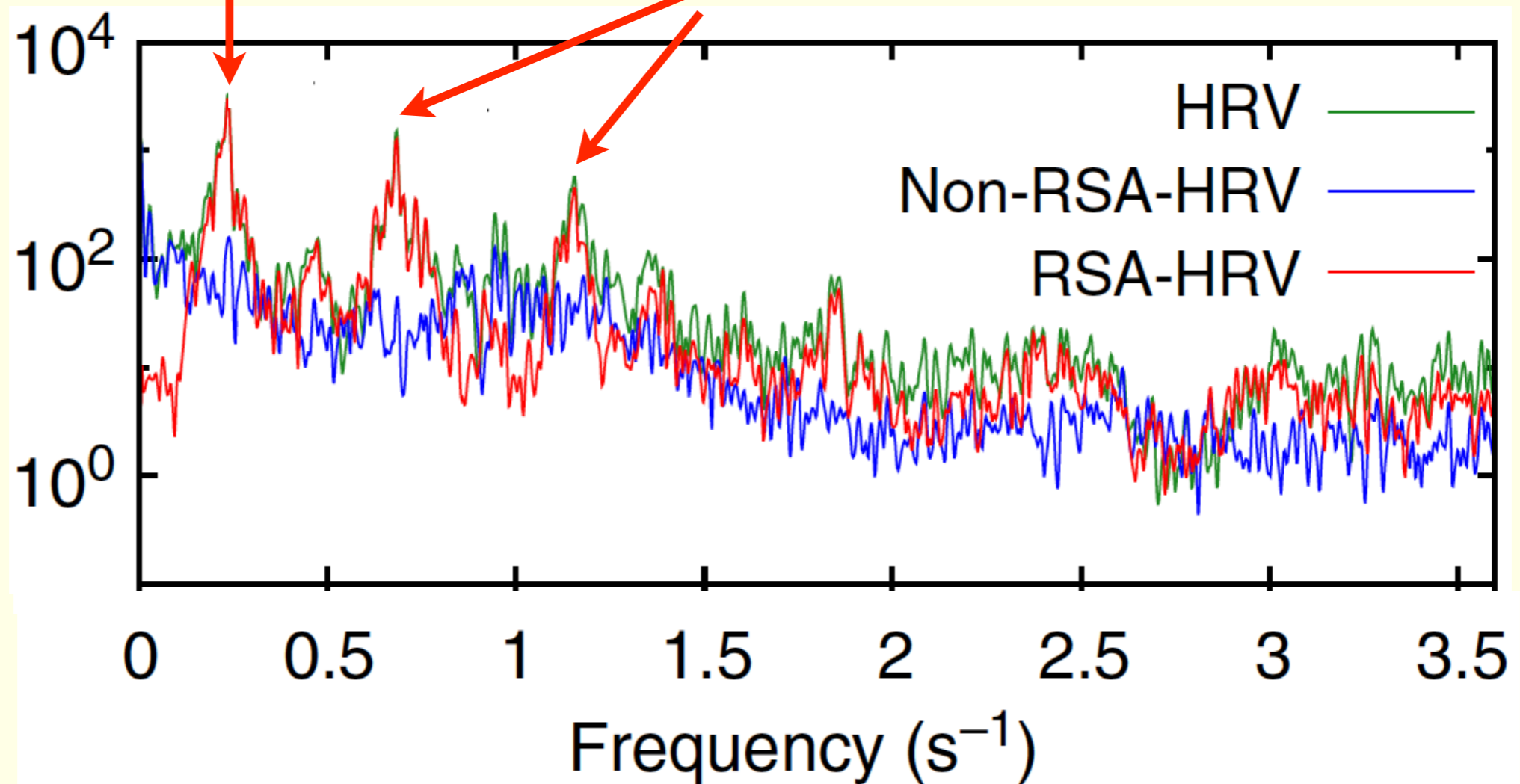# Decomposition: power spectra

Subject with maximal content of respiratory-related component
$$Var(RSA\text{-}HRV) \approx 0.67 \, Var(HRV)$$

respiratory frequency   side-bands of the heart rate

Respiratory-related peaks are well-described by

RSA-HRV component

Summary for this example

Starting with instantaneous phases of cardiac and respiratory systems we disentangled heart rate variability into a component <u>due to respiration</u> and a component <u>due to other factors</u>

However, medical doctors and researchers are used to operate with inter-beat intervals (RR-intervals)

→ We have to generate sequences of RR-intervals for respiratory-related and non-respiratory related components

Phase dynamics with account of many inputs

Cardiac phase from ECG

Phase of respiration

$$\dot{\varphi} = \omega + Q_R(\varphi, \psi) + \xi$$

other inputs and intrinsic fluctuations

Now we introduce two ***new phases:***

φ_R describes effect of respiration (<u>and only respiration!</u>)

and obeys $\dot{\varphi}_R = \omega + Q_R(\varphi_R, \psi)$

φ_{NR} describes effect of everything else <u>except respiration</u>

and obeys $\dot{\varphi}_{NR} = \omega + \xi$

We obtain new phases solving the corresponding equations

(Euler technique)

New RR-intervals

We obtain φ_R, φ_{NR} simulating the corresponding equation

We obtain instants of **respiratory-related R-peaks** from the condition

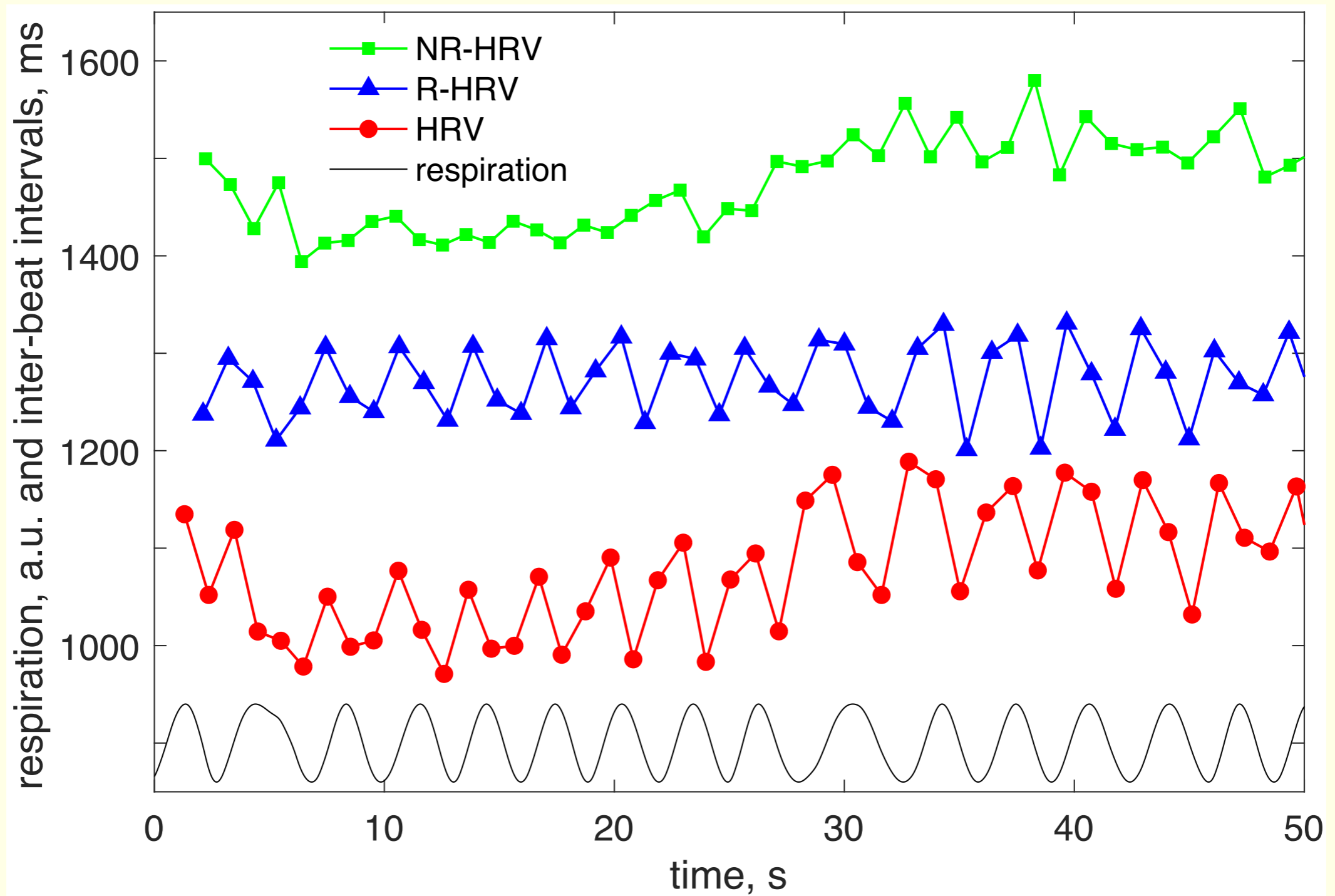$$\varphi_R(t_k^R) = 2\pi k$$

We obtain instants of **non-respiratory-related R-peaks** from the condition

$$\varphi_{NR}(t_k^{NR}) = 2\pi k$$

RR-intervals $t_{k+1}^R - t_k^R$: respiratory-related component of HRV

RR-intervals $t_{k+1}^{NR} - t_k^{NR}$: variability due to all other factors

An example

We suggest to use dynamical disentanglement as a universal preprocessing tool prior to computation of any measures of respiratory sinus arrhythmia (RSA)

Çağdaş Topçu[1,2], Matthias Frühwirth[3], Maximilian Moser[1,3] iD, Michael Rosenblum[2,4,5] iD and Arkady Pikovsky[2,4] iD

Physiological Measurement

A practical algorithm

- The proposed technique operates with <u>time-continuous</u> phases of the cardiac and respiratory systems, $\varphi(t), \psi(t)$

- Computation of $\varphi(t)$ is quite complicated: it requires high-quality measurements and extensive preprocessing

- Hence, we need a practical (maybe approximate) algorithm that would operate only with R-peaks, i.e. with a point process

A practical algorithm

- The proposed technique operates with time-continuous phases of the cardiac and respiratory systems, $\varphi(t), \psi(t)$

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- Hence, we need a practical (maybe approximate) algorithm that would operate only with R-peaks, i.e. with a point process

...and here it is!

Disentanglement from RR-intervals and respiration
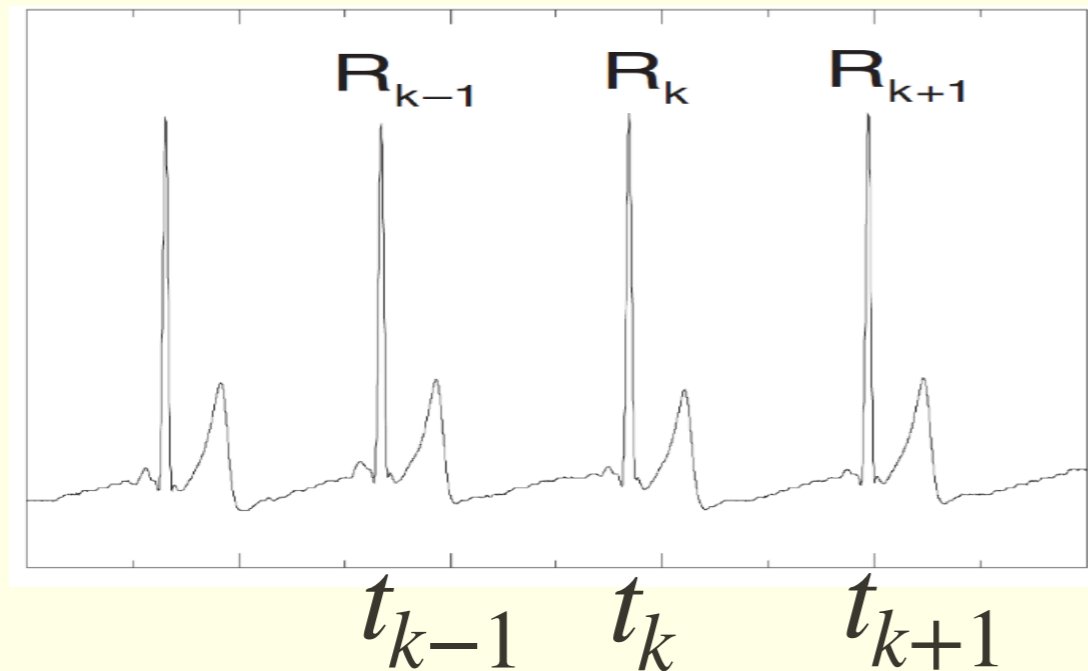
Interbeat intervals $T_k = t_{k+1} - t_k$

Recall the equation

$$\dot{\varphi} = \omega + Q_R(\varphi, \psi) + \xi$$

Consider deterministic part and assume weak coupling, $\| Q_R \| \ll \omega$

$$T_k = \int_0^{2\pi} \frac{d\varphi}{\omega + Q_R(\varphi, \psi)} \approx \frac{2\pi}{\omega} - \frac{1}{\omega^2} \int_0^{2\pi} Q_R(\varphi, \psi) d\phi$$

Respiration is much slower than the heart rate

we approximate $\psi(t)$ by a piece-wise linear function:

$$\psi(t) = \psi(t_k) + \omega_k^{(R)}(t - t_k) \quad \text{FOR} \quad t_k \leq t \leq t_{k+1}$$

Disentanglement from RR-intervals and respiration

$$T_k = \int_0^{2\pi} \frac{d\varphi}{\omega + Q_R(\varphi, \psi)} \approx \frac{2\pi}{\omega} - \frac{1}{\omega^2} \int_0^{2\pi} Q_R(\varphi, \psi) d\phi$$

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$$\psi(t) = \psi(t_k) + \omega_k^{(R)}(t - t_k) \ \text{FOR} \ \ t_k \le t \le t_{k+1}$$

Then

$$\int_0^{2\pi} Q_R(\varphi, \psi) d\varphi = \int_0^{T_k} Q_R[\varphi(t), \psi(t)] dt \approx F(\psi_k, \omega_k^{(R)})$$

$$T_k \approx T - F(\psi_k, \omega_k^{(R)})/\omega^2 \ \text{WITH} \ \ T = 2\pi/\omega$$

Disentanglement from RR-intervals and respiration

$$\int_0^{2\pi} Q_R(\varphi, \psi)d\varphi = \int_0^{T_k} Q_R[\varphi(t), \psi(t)]dt \approx F(\psi_k, \omega_k^{(R)})$$

$$T_k \approx T - F(\psi_k, \omega_k^{(R)})/\omega^2 \quad \text{WITH} \quad T = 2\pi/\omega$$

We introduce mean respiratory frequency $\bar{\omega}$

and represent F as a Taylor-Fourier series:

$$T_k \approx T + \sum_{n=1}^{N_F} \left\{ \left[\sum_{m=0}^{N_T-1} a_{n,m}(\omega_k^{(R)} - \bar{\omega})^m \right] \cos(n\psi_k) + \left[\sum_{m=0}^{N_T-1} b_{n,m}(\omega_k^{(R)} - \bar{\omega})^m \right] \sin(n\psi_k) \right\}$$

N_T, N_F : orders of the Taylor-Fourier series

Disentanglement from RR-intervals and respiration

$$T_k \approx T + \sum_{n=1}^{N_F} \left\{ \left[\sum_{m=0}^{N_T-1} a_{n,m}(\omega_k^{(R)} - \bar{\omega})^m \right] \cos(n\psi_k) + \left[\sum_{m=0}^{N_T-1} b_{n,m}(\omega_k^{(R)} - \bar{\omega})^m \right] \sin(n\psi_k) \right\}$$

Coefficients $a_{n,m}, b_{n,m}$ can be found, e.g., by LMS fit

We obtain a **coupling map** for RR-intervals

$$T_k \approx T + \mathscr{F}\left[\psi(t_k), \dot{\psi}(t_k)\right]$$

We take $\omega_k^{(R)} = \dot{\psi}(t_k)$

Construction of the respiratory-related RR-series

We obtain a **coupling map** for RR-intervals

$$T_k \approx T + \mathscr{F}\left[\psi(t_k), \dot{\psi}(t_k)\right]$$

Now we construct the respiratory-related RR-intervals:

We take $t_1^{(R)} = t_1$

Substituting $\psi(t_1), \dot{\psi}(t_1)$ into the model we obtain T_1 and

$$t_2^{(R)} = t_1^{(R)} + T_1 \qquad \ldots \text{ and so on, to obtain all } t_k^{(R)}$$

and intervals $T_k^{(R)} = t_{k+1}^{(R)} - t_k^{(R)}$

Construction of the non-respiratory-related RR-series

We obtain a **coupling map** for RR-intervals

$$T_k \approx T + \mathscr{F}\left[\psi(t_k), \dot{\psi}(t_k)\right]$$

First, for all original intervals we obtain the rest term (effective noise)

$$\xi_k = T_k - T - \mathscr{F}\left[\psi(t_k), \dot{\psi}(t_k)\right]$$

We start with $t_1^{(NR)} = t_1$ and obtain $t_2^{(NR)} = t_1^{(NR)} + T + \xi_1$

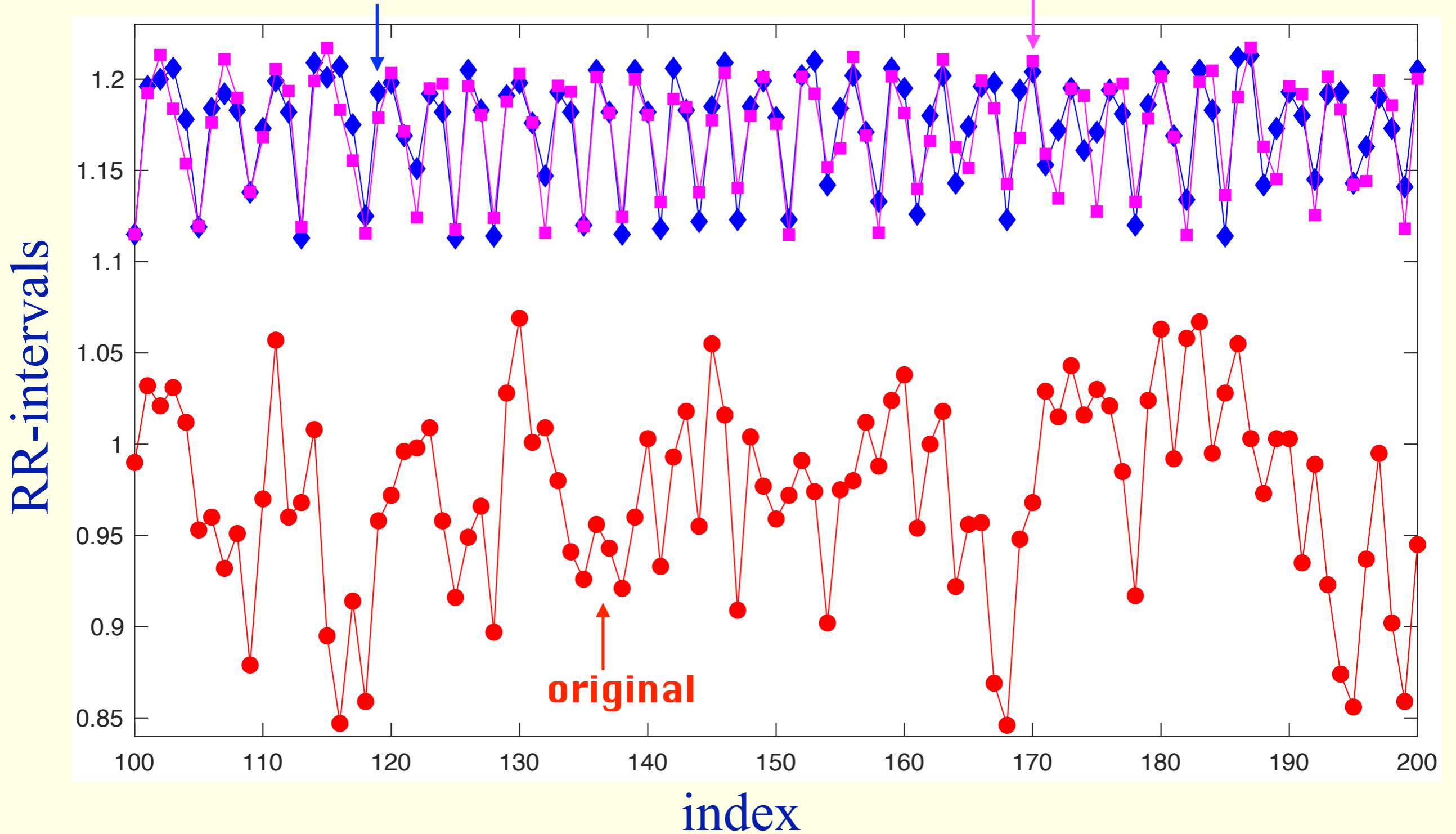Next, if already computed $t_l^{(NR)}$ obeys $t_k < t_l^{(NR)} < t_{k+1}$

then $\quad t_{l+1}^{(NR)} = t_l^{(NR)} + T + \xi_k + \dfrac{\xi_{k+1} - \xi_k}{t_{k+1} - t_k}(t_l^{(NR)} - t_k)$

and $\quad T_k^{(NR)} = t_{k+1}^{(NR)} - t_k^{(NR)}$

Results: real data

disentangled with continuous phase

disentangled using RR-intervals

original

RR-intervals

index

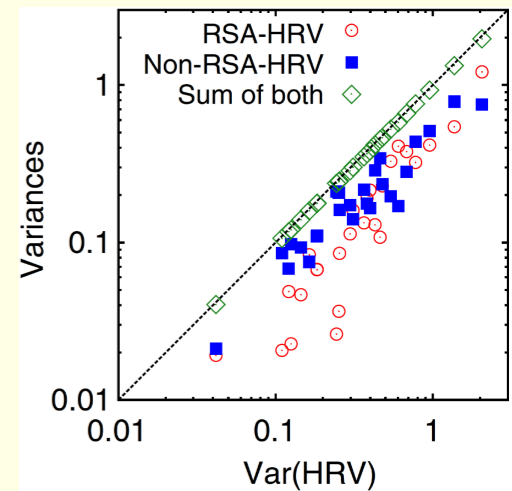# Real data: quality of disentanglement

For continuous phase data we have checked that

$$\text{Var(RSA-HRV)} + \text{Var(Non-RSA-HRV)} \approx \text{Var(HRV)}$$

as expected for non-correlated processes

We now check it for point-process time series of R-peaks, taking the phase to be piece-wise linear between the events,

$$\dot{\varphi}(t) = 2\pi/T_k \ \text{FOR} \ t_k \leq t < t_{k+1}$$

and obtaining

$$\sigma^2 = \text{VAR}(\dot{\varphi}(t)) = \frac{4\pi^2}{T_\Sigma} \sum_{k=1}^{N} \left(\frac{1}{T_k} - \frac{N}{T_\Sigma} \right)^2 T_k, \ T_\Sigma = \sum_k T_k$$

We compute variance for 4 series of intervals:

Real data: quality of disentanglement

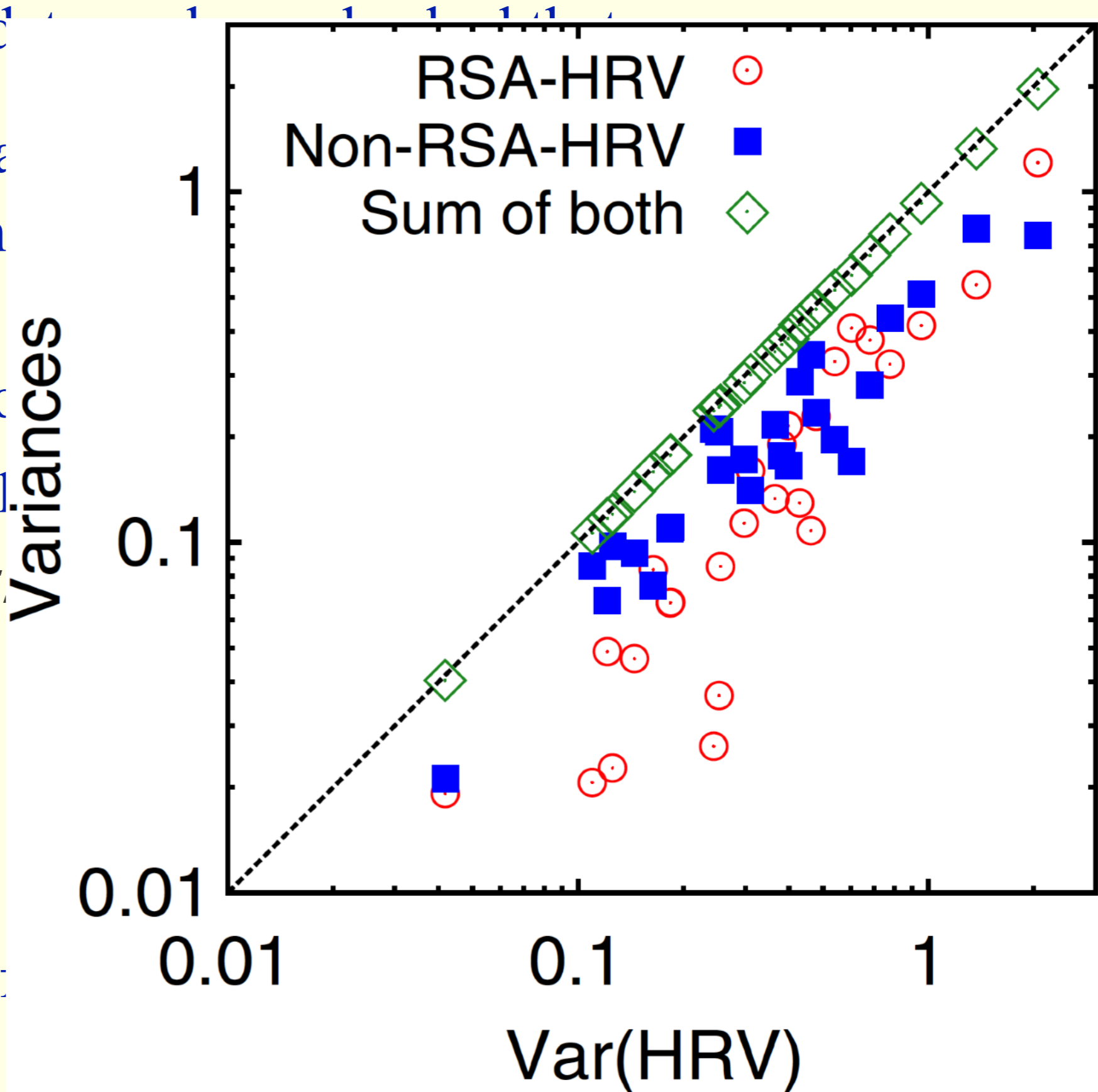For continuous phase d...

Var(RSA-HRV)+Va...

as expected for non...

We now check it for po...

taking the phase to be ...

$$\dot{\varphi}(t) = 2\pi...$$

and obtaining

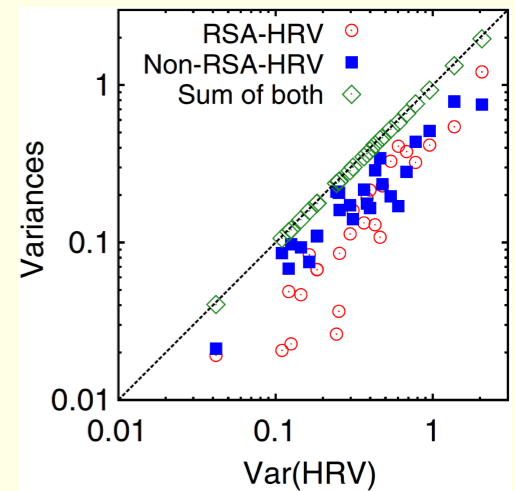$$\sigma^2 = \mathbf{VAR}(\dot{\varphi}(t)) = ...$$

We compute variance ...

Real data: quality of disentanglement

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Real data: quality of disentanglement

$$\dot{\varphi}(t) = 2\pi/T_k \ \text{FOR} \ t_k \leq t < t_{k+1} \qquad \sigma^2 = \text{VAR}(\dot{\varphi}(t))$$
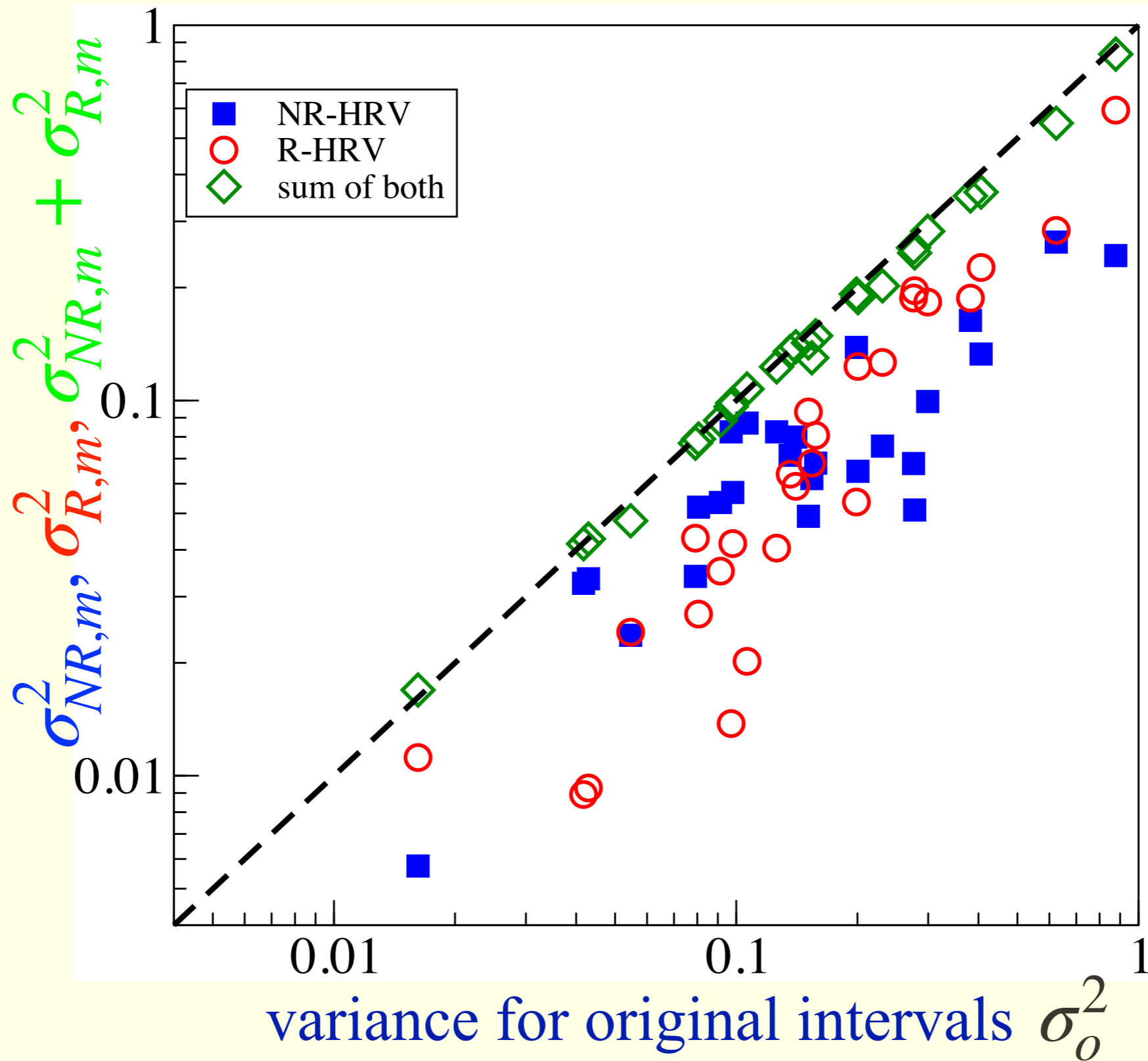
We compute variance for 4 series of intervals:

- variance σ_o^2 for original intervals

- variance $\sigma_{R,c}^2$ for **continuously-cleansed** respiratory-related intervals,

- variance $\sigma_{R,m}^2$ for **map-cleansed** respiratory-related intervals

- variance $\sigma_{NR,m}^2$ for **map-cleansed** non-respiratory-related intervals

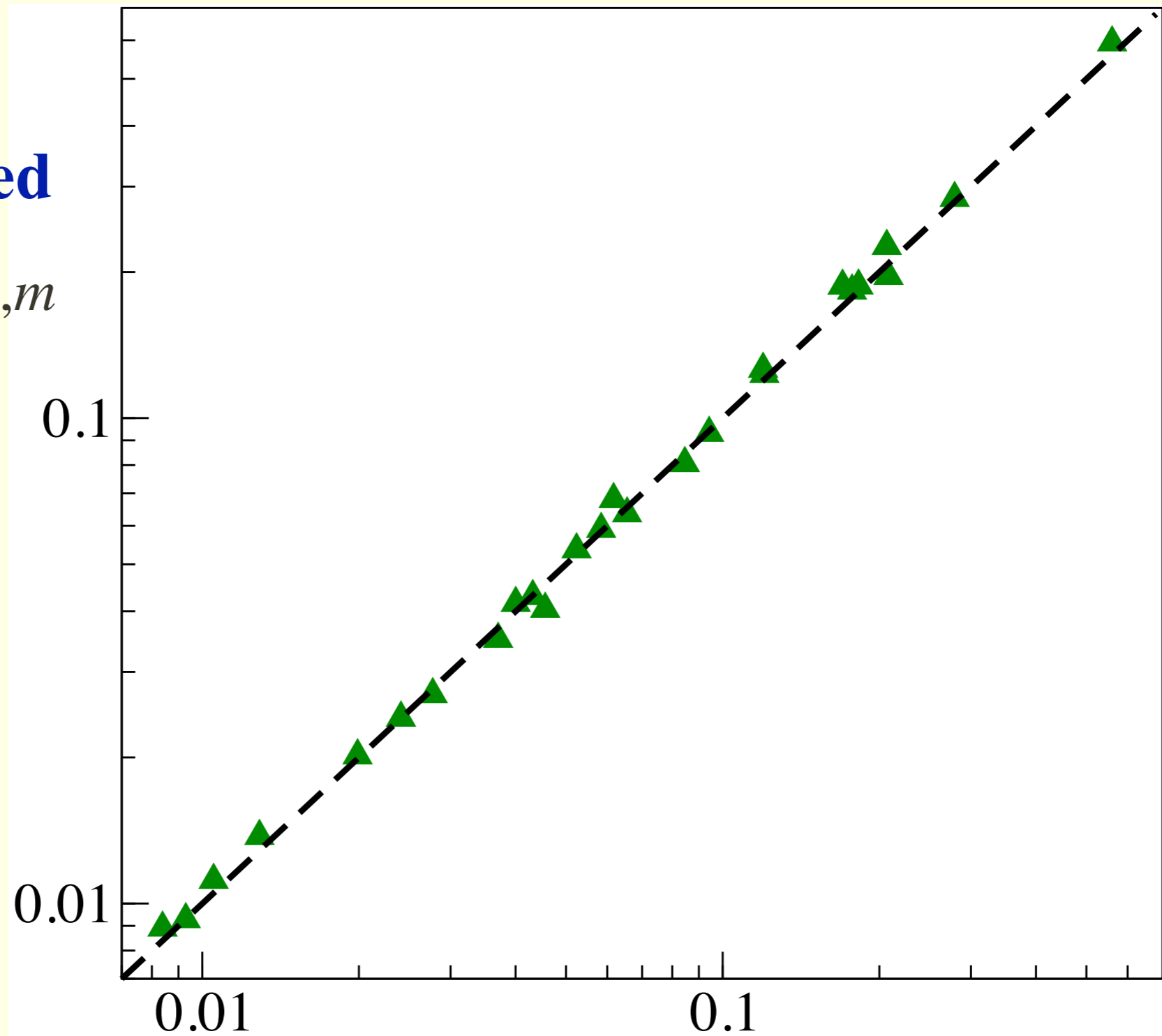We check that: $\sigma_{R,c}^2 \approx \sigma_{R,m}^2$

$$\sigma_{R,m}^2 + \sigma_{NR,m}^2 \approx \sigma_o^2$$

Real data: quality of disentanglement

Real data: quality of disentanglement

variance for **map-cleansed** intervals, $\sigma^2_{R,m}$

variance for **continuously-cleansed** intervals, $\sigma^2_{R,c}$

Conclusions

- Dynamical disentanglement: A tool to extract variability due to a certain rhythm

- Not a usual filter

- Can be used as a universal preprocessing tool in analysis of heart rate variability, in particular for quantification of respiratory sinus arrhythmia

References

- B. Kralemann et al, "*In vivo* cardiac phase response curve elucidates human respiratory heart rate variability", Nature Communications, **4,** p. 2418, 2013

- C. Topçu et al, "Disentangling respiratory sinus arrhythmia in heart rate variability records", Physiological Measurements, **39,** p. 054002, 2018

- M. Rosenblum and A. Pikovsky. "Efficient determination of synchronization domains from observations of asynchronous dynamics", Chaos, **28,** 106301, 2018

- M. Rosenblum et al. "Dynamical disentanglement in an analysis of oscillatory systems: an application to respiratory sinus arrhythmia", submitted