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# Development and application of phase reduction and averaging methods to nonlinear oscillators 

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## Introduction

Oscillatory systems are common in nature and man-made equipments. The behavior of such systems is usually described by nonlinear differential equations.

The oscillations in the conservative systems with infinite number of close periodic solutions are well investigated in theoretical physics, since this problem arises when considering the motion of planets. Whereas the oscillators containing limit cycles when in the neighborhood of a periodic solution there are no other such solutions, have been considered only for the last century. Such oscillators can be encountered e.g. in electronics, robotics, lasers, chemical reactions, biological systems and economical models. A great interest about limit cycle oscillators has been boosted in the last two decades with the development of neuroscience. It considers the mechanism of suppression and activation of the neuron, and control of synchronization and desynchronization in the neural networks.

In nonlinear dynamics one may obtain the analytical results by means of linearization of underlying equations around the specific solution. In the case of the limit cycle, such linearization is described by the Floquet theory, which was formulated at the end of the 19th century. However, the main achievement has been made by I. Malkin in the middle of the 20th century, when the phase reduction method was formulated. Later, it was rediscovered by A. Winfree, who investigated the biological rhythms. The method is based on the idea that one is dealing only with a scalar phase instead of all the system variables. Such an approach enables to obtain analytical results for a weakly perturbed limit cycle oscillator or for several coupled oscillators with a weak interaction.

In biological systems, in lasers and electronics, one often has to deal with the delay effect, when the system dynamics depends not only on the current value of dynamic variables but also on their delayed values. Such systems are described by delayed differential equations which are infinite-dimensional, in contrast to ordinary differential equations. Therefore, it is convenient to perform a phase reduction of these systems since an infinite-dimensional system is reduced to a system with a single dimension. In this work we will pay attention to this issue.

The dynamical systems with an irregular behavior, called as chaotic systems, are hard to predict but relatively easy to control. One of the recent problems in the control theory is stabilization of the unstable periodic orbits embedded in a chaotic attractor. For solving this problem, K. Pyragas proposed in 1992 a control method using the delayed feedback. This method showed itself as very attractive in various experimental situations. Here the controlled orbits are described by equations with delay, and thus the phase reduction method such systems is also relevant since it may show whether the orbit is stabilizible, and reveal the other properties of the orbit.

Another significant problem in nonlinear dynamics is the treatment of systems under a high frequency external force. The frequency is high in comparison with the intrinsic system frequencies. The vibrational mechanics is a field of science devoted to mechanical systems subject to high frequency perturbations. The high frequency of the external force can drastically change the system's behavior. For example, the classical problem of the vibrational mechanics is the stabilization of the upside-down position of a rigid pendulum by vibrating its pivot up and down with a quite small amplitude. The stabilization can be achieved if the amplitude and the frequency satisfy some conditions. Another example - a sand spilled on an inclined plane, which is moved by high frequency force. The sand can start climb up if the angle of the plane, the frequency and the amplitude satisfy some conditions. These crazy experimental results can be explained by the mathematical analysis of the system's equations. Here the phase reduction is not the appropriate tool for the theoretical analysis, since oscillator changes it's behavior drastically. Therefore, here it is more useful to apply the averaging method which is based on the eliminating of the fast oscillating terms in order to get the equations determining the system behavior averaged over the period of high frequency oscillations.

For patients with Parkinson's disease, when the illness can't be removed by drugs, there is applied a surgical procedure called deep brain stimulation. The electrode is implanted directly into the brain and the high frequency electrical current stimulates some parts of the brain. From the experiments we know that this leads to the positive results - involuntary movements are decreased or they disappear absolutely. But still it is not clear what happens with the synchronized neurons, which are responsible for the unwanted movement, under the high frequency electrical current. Therefore here we need to use the averaging method in order to analyze the system's dynamical equations.

## The main goals of the research work

1. To introduce an effective algorithm for a computation of phase response curves of oscillating systems described by the ordinary differential equations.
2. To extend the phase reduction method for the oscillators described by the delay-differential equations.
3. To investigate a weakly mismatched extended time-delayed feedback control scheme using the phase reduction tools.
4. To develop an algorithm for the construction of a control matrix which is able to stabilize periodic orbits with a topological restriction for the standard time-delayed feedback control method.
5. To investigate an influence of the high frequency stimulation on the sustained neuronal spiking using the averaging method.

## Scientific novelty

1. A numerical algorithm is developed for the computation of the phase response curve based on the forward integration of the linearized equation for the deviation from limit cycle.
2. The phase reduction theory is extended to the systems described by the delaydifferential equations.
3. The weakly mismatched time-delayed feedback control method is investigated by the phase reduction tools.
4. An algorithm for the construction of the control matrix of the time-delayed feedback control method which is able to stabilize periodic orbits with a topological restriction is proposed.
5. Based on the averaging method a mechanism of suppression of sustained neuronal spiking under high-frequency stimulation is explained.

## Scientific statements

1. For the oscillators described by ordinary differential equations the phase response curve can be computed by the forward integration of the linear equation
for the deviation.
2. An infinite dimensional system of the delay-differential equations of the weakly perturbed limit cycle oscillator can be reduced to a single scalar equation for the oscillator's phase.
3. A profile of the phase response curve of a periodic orbit stabilized by the timedelayed feedback control algorithm does not depend on the control matrix.
4. A period of the orbit stabilized by the weakly mismatched time-delayed feedback control can be estimated using the phase reduction method.
5. An unstable orbit with the topological restriction can be stabilized by the standard time-delayed feedback method provided the control matrix is chosen appropriately.
6. The sustained neuronal spiking can be suppressed by the high frequency stimulation, and the mechanism of the suppression can be explained by the averaging method.

## List of publications

## Scientific papers

[A1] V. Novičenko and K. Pyragas, Computation of phase response curves via a direct method adapted to infinitesimal perturbations, Nonlinear Dyn. 67, 517-526 (2012)
[A2] V. Novičenko and K. Pyragas, Phase reduction of weakly perturbed limit cycle oscillations in time-delay systems, Physica D 241, 1090-1098 (2012)
[A3] V. Novičenko and K. Pyragas, Phase-reduction-theory-based treatment of extended delayed feedback control algorithm in the presence of a small time delay mismatch, Phys. Rev. E 86, 026204 (2012)
[A4] K. Pyragas and V. Novičenko, Time-delayed feedback control design beyond the odd-number limitation, Phys. Rev. E 88, 012903 (2013)
[A5] K. Pyragas, V. Novičenko and P. Tass, Mechanism of suppression of sustained neuronal spiking under high-frequency stimulation, Biol. Cybern. 107, 669684 (2013)

## International conferences

[A6] V. Novičenko and K. Pyragas, Phase response curves for systems with time delay, 7th European Nonlinear Dynamics Conference (Rome, 2011.07.24-29). Proceedings of the rth European Nonlinear Dynamics Conference
[A7] V. Novičenko and K. Pyragas, Phase response curves for systems with time delay, XXXI Dynamics Days Europe (Oldenburg, 2011.09.12-16). Abstracts and list of participants, p. 197
[A8] V. Novičenko and K. Pyragas, Analytical expression for the period of orbits stabilized by extended delayed feedback control, The 5th International Conference (CHAOS 2012) on Chaotic Modeling, Simulation and Applications (Athens, 2012.06.12-15). Book of Abstracts, p. 111
[A9] V. Novičenko and K. Pyragas, Analytical properties of autonomous systems controlled by extended time-delay feedback in the presence of a small time delay mismatch, XXXIII Dynamics Days Europe (Madrid, 2013.06.03-07). Book of Abstracts, p. 145
[A10] K. Pyragas and V. Novičenko, Beyond the odd number limitation: Control matrix design for time delayed-feedback control algorithm, XXXIII Dynamics Days Europe (Madrid, 2013.06.03-07). Book of Abstracts, p. 251

## Local conferences

[A11] V. Novičenko and K. Pyragas, Spontaniniụ neurono osciliacijų slopinimo mechanizmas veikiant aukštadažne stimuliacija, Fiziniu ir technologijos mokslu tarpdalykiniai tyrimai (Vilnius, 2011.02.08). Pranešimu santraukos
[A12] V. Novičenko and K. Pyragas, Spontaniniụ neurono osciliacijų slopinimo mechanizmas veikiant aukštadažne stimuliacija, 39-oji Lietuvos nacionaline fizikos konferencija (Vilnius, 2011.10.6-8). Programa ir pranešimu tezės, p. 149
[A13] V. Novičenko and K. Pyragas, Valdymo matricos konstravimas uždelsto grižtamojo ryšio valdymo algoritmui, 40-oji Lietuvos nacionaliné fizikos konferencija (Vilnius, 2011.06.10-12). Programa ir pranešimu tezés, p. 242

## Acronyms

PRC - phase response curve
UPO - unstable periodic orbit
DDE - difference differential equation
ODE - ordinary differential equation

TDFC - time-delayed feedback control
ETDFC - extended time-delayed feedback control
MIMO - multiple-input multiple-output
RHS - right-hand side
LHS - left-hand side
PFC - proportional feedback control
FE - Floquet exponent
FM - Floquet multiplier
HFS - high frequency stimulation
HH - Hodgkin-Huxley

## Personal contribution of the author

The author of the thesis has performed most of the analytical derivations of the equations as well as numerical simulations.

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## 1. The work structure And CONTENT

The doctoral thesis contains 124 pages. There are 28 figures. The work includes introduction, three chapters, conclusions and the bibliography.

### 1.1 Introduction

In the introduction there is formulated the relevance of the work, the main goals, scientific novelty and scientific statements.

### 1.2 Phase reduction

The chapter "Phase reduction" contains the basics of the Floquet's theory, the basic concepts of the phase reduction, the overview of the phase response curve and it's computation [A1], the derivation of phase reduced equation, the examples where the phase reduction method is useful, two derivations (the first one "heuristic" and the second one more rigorous mathematically) of the phase reduction of weakly perturbed limit cycle oscillations in time-delay systems [A2,A6, A7].

### 1.2.1 Phase response curve

The section "Phase response curve and it's computation" contains overview of the three algorithms for the computation of the phase response curve. The algorithm "adaptation of the direct method to infinitesimal perturbations" is presented in Ref. [A1].

Adaptation of the direct method to infinitesimal perturbations. Let a dynamical system be defined by ordinary differential equations

$$
\begin{equation*}
\dot{\mathbf{x}}=\mathbf{f}(\mathbf{x}) \tag{1.1}
\end{equation*}
$$

where $\mathbf{x}=\left(x_{1}, x_{2}, \ldots, x_{n}\right)^{T}$ represents the vector of state variables in an $n$ dimensional phase space, ${ }^{T}$ represents transpose operation. Suppose that the system has an exponentially stable limit cycle with a period $T: \mathbf{x}_{c}(t+T)=\mathbf{x}_{c}(t)$. To adapt the direct method to the infinitesimal perturbations we employ the variational equation

$$
\begin{equation*}
\delta \dot{\mathbf{x}}=D \mathbf{f}\left(\mathbf{x}_{c}(t+\varphi)\right) \delta \mathbf{x} \tag{1.2}
\end{equation*}
$$

that describes the dynamics of infinitesimal deviations from the limit cycle. Here $\mathbf{x}_{c}(t+\varphi)$ is the limit cycle solution of the system (1.1) with the initial condition $\mathbf{x}_{0}=\mathbf{x}_{c}(\varphi)$ that represents the point on the limit cycle with the phase $\varphi$. Note, that Eq. (1.2) can be integrated together with Eq. (1.1), since they both are stable. Thus contrary to the adjoint method [1, 2, 3] here we do not need any numerical interpolation of the Jacobian in Eq. (1.2).

To obtain the $j$-th component of the phase response curve (PRC) at the phase $\varphi$ we choose the initial condition for the variational equation (1.2) as $\delta x_{k}(0)=\delta_{j k}$, where $\delta_{j k}$ is the Kronecker delta. This means that the initial vector $\delta \mathbf{x}(0)$ has all zero components except $j$ that is equal to one. Let's now integrate Eq. (1.2) for an integer number $p$ of periods and obtain $\delta \mathbf{x}(p T)$. Due to the stability of the limit cycle the vector $\delta \mathbf{x}(p T)$ becomes parallel to the velocity vector $\mathbf{V}(\varphi) \equiv \dot{\mathbf{x}}(\varphi)=\mathbf{f}\left(\mathbf{x}_{c}(\varphi)\right)$ as $p \rightarrow \infty$. The $j$-th component of the $\operatorname{PRC} z_{j}(\varphi)$ by definition is equal to the phase shift of the perturbed trajectory at the point $\mathbf{x}_{c}(\varphi)$, i.e., $\lim _{p \rightarrow \infty} \delta \mathbf{x}(p T)=$ $\mathbf{V}(\varphi) z_{j}(\varphi)$. Alternatively, this equality can be written as follows

$$
\begin{equation*}
z_{j}(\varphi)=\lim _{p \rightarrow \infty} \frac{\mathbf{V}^{T}(\varphi) \delta \mathbf{x}(p T)}{\mathbf{V}^{T}(\varphi) \mathbf{V}(\varphi)} \tag{1.3}
\end{equation*}
$$

This expression allows us to compute the PRC by a simple forward integration of the variational equation (1.2) together with Eq. (1.1) that defines the limit cycle solution. However, this algorithm can be improved.

To compute the PRC at different phases $\varphi$ of the limit cycle we define the $n \times n$ fundamental matrix $\boldsymbol{\Phi}_{\varphi}(t)$ governed by the differential equation

$$
\begin{equation*}
\dot{\boldsymbol{\Phi}}_{\varphi}(t)=D \mathbf{f}\left(\mathbf{x}_{c}(t+\varphi)\right) \mathbf{\Phi}_{\varphi}(t) \tag{1.4}
\end{equation*}
$$

with the initial condition $\boldsymbol{\Phi}_{\varphi}(0)=\mathbf{I}_{n}$, where $\mathbf{I}_{n}$ is the $n \times n$ identity matrix. The PRC computation requires the knowledge of the fundamental matrix for a given $\varphi$ at $t=T$, i.e., $\mathbf{\Phi}_{\varphi}(T)$. Let us split the period $T$ into $N$ equal intervals $\Delta t=T / N \equiv \Delta \varphi$ and define $N$ nodal points $\mathbf{x}_{c}\left(\varphi_{i}\right)$ on the limit cycle with the equally spaced phases $\varphi_{i}=i \Delta \varphi, i=0, \ldots, N-1$. Let us also denote $\boldsymbol{\Phi}_{\varphi_{i}}(t) \equiv \boldsymbol{\Phi}_{i}(t)$. To determine
$\boldsymbol{\Phi}_{i}(T)$ for any nodal point, it suffices to integrate Eq. (1.4) in small time intervals $t \in[0, \Delta \varphi]$ between the neighbors nodal points and obtain a sequence of the auxiliary matrices $\boldsymbol{\Phi}_{0}(\Delta \varphi), \boldsymbol{\Phi}_{1}(\Delta \varphi), \ldots, \boldsymbol{\Phi}_{N-1}(\Delta \varphi)$. Then the desired matrix $\boldsymbol{\Phi}_{i}(T)$ at any nodal point $i$ can be computed as a product of the above matrices:

$$
\begin{equation*}
\boldsymbol{\Phi}_{i}(T)=\boldsymbol{\Phi}_{i-1}(\Delta \varphi) \ldots \boldsymbol{\Phi}_{0}(\Delta \varphi) \boldsymbol{\Phi}_{N-1}(\Delta \varphi) \ldots \boldsymbol{\Phi}_{i}(\Delta \varphi) \tag{1.5}
\end{equation*}
$$

We now describe the procedure of determination of the PRC at the $i$-th nodal point from the known matrix $\boldsymbol{\Phi}_{i}(T)$. To simplify the description we omit the index $i$ in the expressions presented below, but we keep in mind that they are valid for any phase $\varphi$.

Using the fundamental matrix $\boldsymbol{\Phi}(T)$, the deviation $\delta \mathbf{x}(p T)$ in Eq. (1.3) can be presented in the form:

$$
\begin{equation*}
\delta \mathbf{x}(p T)=\boldsymbol{\Phi}^{p}(T) \delta \mathbf{x}(0) \tag{1.6}
\end{equation*}
$$

We should remind that all components of the initial perturbation $\delta \mathbf{x}(0)$ are equal to zero, except the $j$-th component, which is equal to one. It means that here we deal with the $j$-th component of the PRC. To simplify expression (1.6) we use the method of spectral decomposition based on the Floquet theory. We suppose that the fundamental matrix is nonsingular and define its right $\mathbf{R}_{k}$ and left $\mathbf{L}_{k}$ eigenvectors:

$$
\begin{align*}
& \boldsymbol{\Phi}(T) \mathbf{R}_{k}=\mu_{k} \mathbf{R}_{k},  \tag{1.7}\\
& \mathbf{L}_{k}^{T} \boldsymbol{\Phi}(T)=\mu_{k} \mathbf{L}_{k}^{T}, \tag{1.8}
\end{align*}
$$

where $\mu_{k}, k=1, \ldots, n$ are the Floquet multipliers of the limit cycle. They satisfy the characteristic equation

$$
\begin{equation*}
\operatorname{det}\left[\boldsymbol{\Phi}(T)-\mu \mathbf{I}_{n}\right]=0 \tag{1.9}
\end{equation*}
$$

One of the multiplies that describes an evolution of small deviations along the limit cycle is equal to one, $\mu_{1}=1$. The absolute values of other multipliers of the stable limit are less than one:

$$
\begin{equation*}
\left|\mu_{n}\right|<\left|\mu_{n-1}\right|<\ldots<\left|\mu_{2}\right|<1 . \tag{1.10}
\end{equation*}
$$

The left and right eigenvectors corresponding to different multipliers are orthogonal to each other:

$$
\begin{equation*}
\mathbf{L}_{k}^{T} \mathbf{R}_{l}=0, \quad \text { when } l \neq k \tag{1.11}
\end{equation*}
$$

We now expand the initial perturbation $\delta \mathbf{x}(0)$ in terms of the right eigenvectors

$$
\begin{equation*}
\delta \mathbf{x}(0)=c_{1} \mathbf{R}_{1}+\ldots+c_{n} \mathbf{R}_{n} \tag{1.12}
\end{equation*}
$$

and substitute this expression into Eq. (1.6). Due to the inequalities (1.10) the equation 1.6 in the limit of large $p$ transforms to:

$$
\begin{equation*}
\lim _{p \rightarrow \infty} \delta \mathbf{x}(p T)=\lim _{p \rightarrow \infty} \sum_{k=1}^{n} \mu_{k}^{p} c_{k} \mathbf{R}_{k}=c_{1} \mathbf{R}_{1} \tag{1.13}
\end{equation*}
$$

The right eigenvector corresponding to the first multiplier $\mu_{1}=1$ can be chosen equal to the velocity vector, $\mathbf{R}_{1}=\mathbf{V}$, since $\mathbf{V}$ satisfies an obvious equality $\boldsymbol{\Phi}(T) \mathbf{V}=\mathbf{V}$. Then substituting Eq. (1.13) into Eq. (1.3) we obtain that the PRC is equal to the first coefficient in the expansion (1.12):

$$
\begin{equation*}
z_{j}=c_{1} . \tag{1.14}
\end{equation*}
$$

We now multiply Eq. 1.12 by the left eigenvector $\mathbf{L}_{1}^{T}$ and due to the orthogonality property (1.11) we obtain $\mathbf{L}_{1}^{T} \delta \mathbf{x}(0)=c_{1} \mathbf{L}_{1}^{T} \mathbf{R}_{1}$. Substituting $\mathbf{R}_{1}=\mathbf{V}$ and using Eq. (1.14) we get:

$$
\begin{equation*}
z_{j}=\frac{\mathbf{L}_{1}^{T} \delta \mathbf{x}(0)}{\mathbf{L}_{1}^{T} \mathbf{V}} \tag{1.15}
\end{equation*}
$$

Since the initial perturbation $\delta \mathbf{x}(0)$ has only $j$-th nonzero component the numerator in this equation can be simplified to $\mathbf{L}_{1}^{T} \delta \mathbf{x}(0)=\mathbf{L}_{1}[j]$, where $\mathbf{L}_{1}[j]$ is the $j$-th component of the vector $\mathbf{L}_{1}$. Thus we obtain the final equation for the PRC vector in the form:

$$
\begin{equation*}
\mathbf{z}(\varphi)=\frac{\mathbf{L}_{1}(\varphi)}{\mathbf{L}_{1}^{T}(\varphi) \mathbf{V}(\varphi)} \tag{1.16}
\end{equation*}
$$

This equation constitutes the basis of our algorithm. We see that the problem of PRC computation reduces to the problem of evaluation of the left eigenvector $\mathbf{L}_{1}$ that satisfies the matrix equation $\mathbf{L}_{1}^{T}\left[\boldsymbol{\Phi}(T)-\mathbf{I}_{n}\right]=0$. Because the determinant of this system is equal to zero, the value of one of components of the vector $\mathbf{L}_{1}^{T}$ can be assigned arbitrarily. We choose the first component equal to one, $\mathbf{L}_{1}^{T}[1]=1$. Then the other components $\mathbf{L}_{1}^{T}[2: n]$ are obtained by solving the reduced system of $n-1$ linear equations:

$$
\begin{equation*}
\mathbf{L}_{1}^{T}[2: n]\left\{\boldsymbol{\Phi}(T)[2: n ; 2: n]-\mathbf{I}_{n-1}\right\}=-\boldsymbol{\Phi}(T)[1 ; 2: n] . \tag{1.17}
\end{equation*}
$$

Here $\boldsymbol{\Phi}(T)[2: n ; 2: n]$ is a submatrix of the matrix $\boldsymbol{\Phi}(T)$ formed by removing the first row and the first column of the original matrix.

We use Eq. 1.16) to evaluate the PRC for the phases at the nodal points $\varphi_{i}=$ $i \Delta \varphi$, where the values of the fundamental matrix $\boldsymbol{\Phi}_{i}(T)$ are defined. The nodal points do not need to be taken very densely. The values of the PRC between the nodal points can be interpolated.

To summarize our algorithm we list the main steps:
Step 1. Define $n$ nodal points on the limit cycle with equally spaced phases $\varphi_{i}=$ $i \Delta \varphi$ and compute the auxiliary matrixes $\boldsymbol{\Phi}_{i}(\Delta \varphi)$ by integrating Eqs. (1.4) and (1.1) in the interval $t \in[0, \Delta \varphi]$ for different $\varphi=\varphi_{i}$.

Step 2. At each nodal point, evaluate the fundamental matrix $\boldsymbol{\Phi}_{i}(T)$. To this end, multiply the auxiliary matrixes $\boldsymbol{\Phi}_{i}(\Delta \varphi)$ in different sequences, as prescribed by Eq. (1.5).

Step 3. Solve the linear system (1.17) to determine the left eigenvector $\mathbf{L}_{1}\left(\varphi_{i}\right)$ and using Eq. (1.16) evaluate $\mathbf{z}\left(\varphi_{i}\right)$ at each nodal point.

We have tested our algorithm for a variety of dynamical systems. Here we present the results for two dynamical systems, namely the Morris-Lecar [4] and the Hindmarsh-Rose [5 neuron models. For neuron models, only the first component of the PRC vector is of interest, since perturbations are usually applied only to the first equation that describes the dynamics of the membrane potential. Therefore, in all figures presented below we show only the curve $z_{1}(\varphi)$.

The equations of the Morris-Lecar model are [4]:

$$
\begin{align*}
C \dot{V}= & -g_{C a} m_{\infty}(V)\left(V-V_{C a}\right)-g_{K} \omega\left(V-V_{K}\right) \\
& -g_{l}\left(V-V_{l}\right)+I_{0},  \tag{1.18}\\
\dot{\omega}= & \phi\left[\omega_{\infty}(V)-\omega\right] / \tau_{\omega}(V),
\end{align*}
$$

where

$$
\begin{align*}
m_{\infty}(V) & =0.5\left\{1+\tanh \left[\left(V-V_{1}\right) / V_{2}\right]\right\} \\
\omega_{\infty}(V & =0.5\left\{1+\tanh \left[\left(V-V_{3}\right) / V_{4}\right]\right\}  \tag{1.19}\\
\tau_{\omega}(V) & =1 / \cosh \left[\left(V-V_{3}\right) /\left(2 V_{4}\right)\right] .
\end{align*}
$$

The values of the parameters are: $C=5.0 \mu \mathrm{~F} / \mathrm{cm}^{2} ; g_{C a}=4.0 \mu \mathrm{~S} / \mathrm{cm}^{2} ; g_{K}=$ $8.0 \mu \mathrm{~S} / \mathrm{cm}^{2} ; g_{l}=2.0 \mu \mathrm{~S} / \mathrm{cm}^{2} ; V_{C a}=120 \mathrm{mV} ; V_{K}=-80 \mathrm{mV} ; V_{l}=-60 \mathrm{mV}$; $V_{1}=-1.2 \mathrm{mV} ; V_{2}=18.0 \mathrm{mV} ; V_{3}=12.0 \mathrm{mV} ; V_{4}=17.4 \mathrm{mV} ; \phi=1 / 15 \mathrm{~s}^{-1}$; $I_{0}=40 \mu \mathrm{~A} / \mathrm{cm}^{2}$. In Fig. 1.1 we show the membrane potential and the PRC for the Morris-Lecar neuron model.

We tested our algorithm for a complex limit cycle that appears in the HindmarshRose neuron model in the bursting regime. The equations of the Hindmarsh-Rose


Figure 1.1: The membrane potential (a) and the first component of the PRC (b) for the Morris-Lecar neuron model. The number of the nodal points is $N=100$.
model are [5]:

$$
\begin{align*}
\dot{x} & =y+a x^{2}-x^{3}-z+I, \\
\dot{y} & =1-b x^{2}-y,  \tag{1.20}\\
\dot{z} & =r\left[s\left(x-x_{R}\right)-z\right] .
\end{align*}
$$

The values of the parameters corresponding to the bursting regime are: $a=3$; $I=1.3 ; b=5 ; r=0.001 ; s=4 ; x_{R}=-1.6$. The results are presented in Fig. 1.2.,


Figure 1.2: The membrane potential (a) and the first component of the PRC (b) for the Hindmarsh-Rose neuron model. The number of the nodal points is $N=1000$.

### 1.2.2 Phase reduction for the systems with time delay

Here we present the phase reduction method for a general class of weakly perturbed time-delay systems exhibiting periodic oscillations [A2,A6,A7]. The section "Phase reduction for the systems with time delay" contains two derivations of the phase reduced equation and the numerical examples.

The derivation of the phase reduction via approximation of the DDE system by using ODEs. Consider a weakly perturbed limit-cycle oscillator described by a system of difference differential equations (DDEs):

$$
\begin{equation*}
\dot{\mathbf{x}}(t)=\mathbf{f}(\mathbf{x}(t), \mathbf{x}(t-\tau))+\varepsilon \boldsymbol{\psi}(t) \tag{1.21}
\end{equation*}
$$

Here $\mathbf{x}=\left(x_{1}, x_{2}, \ldots, x_{n}\right)^{T}$ is an $n$-dimensional vector, $\tau$ is a delay time, and $\varepsilon \boldsymbol{\psi}(t)=$ $\varepsilon\left(\psi_{1}(t), \psi_{2}(t), \ldots, \psi_{n}(t)\right)^{T}$ represents a small time-dependent perturbation, where $\varepsilon \ll 1$ is a small parameter. We suppose that for $\varepsilon=0$ the system has a stable limit cycle $\mathbf{x}_{c}(t)$ with a period $T: \mathbf{x}_{c}(t)=\mathbf{x}_{c}(t+T)$.

Physically, the time-delay feedback in system (1.21) can be implemented via a delay line, which can be modeled by an advection equation. Thus Eq. (1.21) can be rewritten in a mathematically equivalent form as follows:

$$
\begin{align*}
\dot{\mathbf{x}}(t) & =\mathbf{f}(\mathbf{x}(t), \boldsymbol{\xi}(\tau, t))+\varepsilon \boldsymbol{\psi}(t),  \tag{1.22a}\\
\frac{\partial \boldsymbol{\xi}(s, t)}{\partial t} & =-\frac{\partial \boldsymbol{\xi}(s, t)}{\partial s}, \quad \boldsymbol{\xi}(0, t)=\mathbf{x}(t), \tag{1.22b}
\end{align*}
$$

where $\boldsymbol{\xi}$ is a vector variable of the advection equation and $s \in[0, \tau]$ is a space variable. We take the delay line of the length $\tau$ and the velocity of the wave equal to unity such that the signal at the input of the delay line $\boldsymbol{\xi}(0, t)=\mathbf{x}(t)$ is delayed at the output by the amount $\tau: \boldsymbol{\xi}(\tau, t)=\mathbf{x}(t-\tau)$.

Now we descretize the space variable of the advection equation by dividing it into $N$ equal intervals $s_{i}=i \tau / N, i=0, \ldots, N$ and approximate the space derivative of Eq. 1.22b by a finite difference $[\partial \boldsymbol{\xi}(s, t) / \partial s]_{s=s_{i}} \approx\left[\boldsymbol{\xi}\left(s_{i}, t\right)-\boldsymbol{\xi}\left(s_{i-1}, t\right)\right] N / \tau$. Denoting $\mathbf{x}_{0}(t)=\mathbf{x}(t)$ and $\mathbf{x}_{i}(t)=\boldsymbol{\xi}(i \tau / N, t) \approx \mathbf{x}(t-i \tau / N), \quad i=1, \ldots, N$ we get a system of $n \times(N+1)$ ODEs

$$
\begin{align*}
\dot{\mathbf{x}}_{0}(t) & =\mathbf{f}\left(\mathbf{x}_{0}(t), \mathbf{x}_{N}(t)\right)+\varepsilon \boldsymbol{\psi}(t),  \tag{1.23a}\\
\dot{\mathbf{x}}_{1}(t) & =\left[\mathbf{x}_{0}(t)-\mathbf{x}_{1}(t)\right] N / \tau,  \tag{1.23b}\\
& \vdots \\
\dot{\mathbf{x}}_{N}(t) & =\left[\mathbf{x}_{N-1}(t)-\mathbf{x}_{N}(t)\right] N / \tau, \tag{1.23c}
\end{align*}
$$

which approximate Eqs. (1.22) as well as the time-delay system (1.21). For $N \rightarrow \infty$, the system of Eqs. (1.23) transforms to Eqs. (1.22) and thus its solution approaches the solution of the time-delay system (1.21), $\mathbf{x}_{0}(t) \rightarrow \mathbf{x}(t)$. We emphasize that for any finite $N$, Eqs. (1.23) represent the finite ODE system, and we can utilize the results of phase reduction theory presented in previous subsection. The system (1.23) can be rewritten in the form of the ODEs

$$
\begin{equation*}
\dot{\mathbf{y}}(t)=\mathbf{g}(\mathbf{y}(t))+\varepsilon \boldsymbol{\phi}(t) \tag{1.24}
\end{equation*}
$$

by using the notations:

$$
\begin{gather*}
\mathbf{y}(t)=\left(\begin{array}{c}
\mathbf{x}_{0}(t) \\
\mathbf{x}_{1}(t) \\
\vdots \\
\mathbf{x}_{N}(t)
\end{array}\right), \quad \mathbf{g}(t)=\left(\begin{array}{c}
\mathbf{f}\left(\mathbf{x}_{0}(t), \mathbf{x}_{N}(t)\right) \\
{\left[\mathbf{x}_{0}(t)-\mathbf{x}_{1}(t)\right] N / \tau} \\
\vdots \\
{\left[\mathbf{x}_{N-1}(t)-\mathbf{x}_{N}(t)\right] N / \tau}
\end{array}\right), \\
\boldsymbol{\phi}(t)=\left(\begin{array}{c}
\boldsymbol{\psi}(t) \\
0 \\
\vdots \\
0
\end{array}\right) \tag{1.25}
\end{gather*}
$$

In these notations, the Jacobian of the unperturbed system (1.23) reads:

$$
D \mathbf{g}(t)=\left(\begin{array}{ccccc}
\mathbf{A}(t) & 0 & 0 & \cdots & \mathbf{B}(t)  \tag{1.26}\\
N / \tau & -N / \tau & 0 & \cdots & 0 \\
0 & N / \tau & -N / \tau & \cdots & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & 0 & \cdots & -N / \tau
\end{array}\right)
$$

where $\mathbf{A}(t)=\left[D_{1} \mathbf{f}\left(\mathbf{x}_{0}, \mathbf{x}_{N}\right)\right]_{\mathbf{x}=\mathbf{x}_{c}(t)}$ and $\mathbf{B}(t)=\left[D_{2} \mathbf{f}\left(\mathbf{x}_{0}, \mathbf{x}_{N}\right)\right]_{\mathbf{x}=\mathbf{x}_{c}(t)}$ are $T$-periodic $n \times n$ Jacobian matrices estimated on the limit cycle of the system. The symbols $D_{1}$ and $D_{2}$ denote the vector derivatives of the function $\mathbf{f}$ with respect to the first and second argument, respectively. The adjoint equation for this system takes the form:

$$
\left(\begin{array}{c}
\dot{\mathbf{z}}_{0}(t)  \tag{1.27}\\
\dot{\mathbf{z}}_{1}(t) \\
\dot{\mathbf{z}}_{2}(t) \\
\vdots \\
\dot{\mathbf{z}}_{N}(t)
\end{array}\right)=\left(\begin{array}{ccccc}
-\mathbf{A}^{T}(t) & -N / \tau & 0 & \cdots & 0 \\
0 & N / \tau & -N / \tau & \cdots & 0 \\
0 & 0 & N / \tau & \cdots & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
-\mathbf{B}^{T}(t) & 0 & 0 & \cdots & N / \tau
\end{array}\right)\left(\begin{array}{c}
\mathbf{z}_{0}(t) \\
\mathbf{z}_{1}(t) \\
\mathbf{z}_{2}(t) \\
\vdots \\
\mathbf{z}_{N}(t)
\end{array}\right)
$$

and the initial condition reads:

$$
\begin{equation*}
\sum_{i=0}^{N} \mathbf{z}_{i}^{T}(0) \dot{\mathbf{x}}_{c i}(0)=1 . \tag{1.28}
\end{equation*}
$$

Since the perturbation in system (1.23) is applied only to the first equation 1.23a the function $\phi$ has only the first nonzero component [cf. Eq. (1.25)]. Thus the phase
equation for the system 1.23 transforms to:

$$
\begin{equation*}
\dot{\varphi}(t)=1+\varepsilon \mathbf{z}_{0}^{T}(\varphi(t)) \boldsymbol{\psi}(t) . \tag{1.29}
\end{equation*}
$$

Equations (1.27), (1.28) and (1.29) represent the phase reduced description for the system (1.23) that approximates the solution of the DDE 1.21. To derive the exact phase reduced equations for 1.21 we have to take the limit $N \rightarrow \infty$ in Eqs. (1.27), (1.28) and (1.29).

Now our aim is to transform Eqs. (1.27) to the form of a difference differential equation for large $N$. This is an inverse problem to that, we have applied to derive Eqs. (1.23) from Eq. (1.21). Since the system (1.27) is similar to Eqs. (1.23) we guess that this transformation can be achieved by the following substitutions: $\mathbf{z}_{0}(t)=\mathbf{z}(t)$ and

$$
\begin{equation*}
\mathbf{z}_{i}(t)=\frac{\tau}{N} \mathbf{B}^{T}\left(t+\tau-\frac{(i-1) \tau}{N}\right) \mathbf{z}\left(t+\tau-\frac{(i-1) \tau}{N}\right), \quad i=1, \ldots, N \tag{1.30}
\end{equation*}
$$

Inserting these expressions into Eqs. (1.27), for $\mathbf{z}(t)$ we derive (in the limit $N \rightarrow \infty$ ) a difference-differential equation of advanced type:

$$
\begin{equation*}
\dot{\mathbf{z}}^{T}(t)=-\mathbf{z}^{T}(t) \mathbf{A}(t)-\mathbf{z}^{T}(t+\tau) \mathbf{B}(t+\tau), \tag{1.31}
\end{equation*}
$$

where $\mathbf{A}(t)$ and $\mathbf{B}(t)$ are $T$-periodic Jacobian matrices defined as the vector derivatives of the function $\mathbf{f}$ with respect to the first $\left(D_{1}\right)$ and second $\left(D_{2}\right)$ argument, estimated on the limit cycle of the unperturbed system (1.21):

$$
\begin{align*}
\mathbf{A}(t) & =D_{1} \mathbf{f}\left(\mathbf{x}_{c}(t), \mathbf{x}_{c}(t-\tau)\right)  \tag{1.32a}\\
\mathbf{B}(t) & =D_{2} \mathbf{f}\left(\mathbf{x}_{c}(t), \mathbf{x}_{c}(t-\tau)\right) \tag{1.32b}
\end{align*}
$$

The initial condition for Eq. (1.31) is obtained from Eq. (1.28) by taking the limit $N \rightarrow \infty$ :

$$
\begin{equation*}
\mathbf{z}^{T}(0) \dot{\mathbf{x}}_{c}(0)+\int_{-\tau}^{0} \mathbf{z}^{T}(\tau+\vartheta) \mathbf{B}(\tau+\vartheta) \dot{\mathbf{x}}_{c}(\vartheta) d \vartheta=1 \tag{1.33}
\end{equation*}
$$

Finally, the phase equation for the DDE system (1.21) derived from Eq. (1.29) in the limit $N \rightarrow \infty$ takes the form:

$$
\begin{equation*}
\dot{\varphi}(t)=1+\varepsilon \mathbf{z}^{T}(\varphi(t)) \boldsymbol{\psi}(t) . \tag{1.34}
\end{equation*}
$$

Equations (1.31), (1.32), (1.33) and (1.34) form the complete system for a phase reduced description of weakly perturbed limit-cycle oscillations defined by the time-
delay system (1.21). Note that the original problem formulated by the DDE (1.21) is defined in an infinite-dimensional phase space, while here we have reduced this problem to a single equation (1.34) for the scalar phase variable $\varphi$. The perturbed phase dynamics is completely determined by the $\operatorname{PRC} \mathbf{z}(\varphi)$ that satisfies the adjoint Eq (1.31) with the initial condition (1.33).

Direct derivation of phase reduced equations for DDE system. In this subsection the same equations are derived more rigorously, without using any approximation of the DDE by the ODEs. We apply the phase reduction procedure directly to the DDE system and do not appeal to the known theoretical results from the ODE systems.

Numerical examples. The subsection contains several numerical examples (Mackey-Glass system [6] and phase-locked loop system [7]) of the application of the phase reduction for the systems with time-delay.

### 1.3 Application of the phase reduction in controlling chaos

The chapter "Application of the phase reduction in controlling chaos" contains overview of time-delayed feedback control, the phase response curve for the orbits stabilized by time-delayed feedback control, extended time-delayed feedback control scheme with mismatched delay [A3,A8,A9], overview of the odd-number limitation, algorithm of constructing of the control matrix in order to avoid the odd-number limitation [A4,A10] and examples of successful stabilization of an unstable periodic orbit in the systems (Lorenz and Chua systems) possessed the limitation.

### 1.3.1 Extended time-delayed feedback control in the presence of a small time delayed mismatch

The extended time-delayed feedback control (ETDFC) algorithm has been originally introduced for a dynamical system with a scalar control variable [8]. Here we consider the very general version of this algorithm applied to a multiple-input multiple-output (MIMO) system:

$$
\begin{align*}
\dot{\mathbf{x}}(t) & =\mathbf{f}(\mathbf{x}(t), \mathbf{u}(t))  \tag{1.35a}\\
\mathbf{s}(t) & =\mathbf{g}(\mathbf{x}(t))  \tag{1.35b}\\
\mathbf{u}(t) & =\mathbf{K}\left[(\mathbf{I}-\mathbf{R}) \sum_{j=1}^{\infty} \mathbf{R}^{j-1} \mathbf{s}(t-j \tau)-\mathbf{s}(t)\right] . \tag{1.35c}
\end{align*}
$$

Here $\mathbf{x}(t) \in \mathbb{R}^{n}$ denotes the state vector of the system, $\mathbf{u}(t) \in \mathbb{R}^{k}$ is a control vectorvariable ( $k$-dimensional input) and $\mathbf{f}(\mathbf{x}, \mathbf{u})$ is a nonlinear vector function that defines the dynamical laws of the system and the input properties of the control variable. Equation 1.35 b defines an $l$-dimensional output signal $\mathbf{s}(t)$, which is related with the $n$-dimensional state vector $\mathbf{x}$ through a vector function $\mathbf{g}: \mathbb{R}^{n} \rightarrow \mathbb{R}^{l}$. Equation (1.35c) gives the ETDFC relation between the output vector-variable $\mathbf{s}$ and the control vector-variable $\mathbf{u}$. The diagonal $l \times l$ matrix $\mathbf{R}=\operatorname{diag}\left(R_{1}, \ldots, R_{l}\right)$ defines a set of memory parameters $R_{m}$, which generally can be different for the different components $s_{m}$ of the output signal. However, we assume that the delay time $\tau$ for all components is the same. To provide the convergence of the infinite sum in Eq. (1.35c) we require that $\left|R_{m}\right|<1$ for $m=1, \ldots, l$. The control $k \times l$ matrix $\mathbf{K}$ defines the transformation of the output variable $\mathbf{s}(t)$ to the control (input) variable $\mathbf{u}(t)$ and $\mathbf{I}$ denotes an $l \times l$ identity matrix.

We suppose that the control-free $(\mathbf{K}=0)$ system has an unstable $T$-periodic orbit $\mathbf{x}_{c}(t)=\mathbf{x}_{c}(t+T)$ that satisfies the equation $\dot{\mathbf{x}}_{c}(t)=\mathbf{f}\left(\mathbf{x}_{c}(t), 0\right)$. The aim of the ETDFC signal (1.35c) is to stabilize this orbit. If we take the delay time equal to the UPO period, $\tau=T$ and if the stabilization will be successful, then $\mathbf{s}(t-j \tau)=\mathbf{s}(t)$, $\sum_{j=1}^{\infty} \mathbf{R}^{j-1}=(\mathbf{I}-\mathbf{R})^{-1}$ and the control variable vanishes $\mathbf{u}=0$. This means that the control law 1.35 c ) applied to a MIMO system 1.35 a is noninvasive.

Our aim is to analyze the situation when the delay time differs from the period of UPO, $\tau \neq T$. We assume that the control parameters are chosen such that for $\tau=T$ the stabilization is successful, and the controlled system demonstrates stable periodic oscillations with the period $\Theta=T$. If we detune slightly the delay time $\tau$ then the system still remains in the regime of stable periodic oscillations, but the period $\Theta$ of these oscillations will be changed $\Theta \neq T$. We are seeking to derive an analytical expression for the period $\Theta$ in the dependence of the system parameters using the general formulation of the problem defined by Eqs. (1.35).

Now we consider the system (1.35) assuming that $\tau=T$ and the parameters of the control $\mathbf{K}$ and memory $\mathbf{R}$ matrices are chosen such that the stabilization of the target UPO is successful. Then $\mathbf{x}=\mathbf{x}_{c}(t)$ is the stable periodic solution of the system (1.35). We are interested how this solution will change in the presence of small perturbations. To this end, we add to the r.h.s. of Eq. 1.35a a small perturbing term $\varepsilon \boldsymbol{\psi}(t)$ and taking into account that $\tau=T$ rewrite the system (1.35)
as follows:

$$
\begin{align*}
\dot{\mathbf{x}}(t) & =\mathbf{f}\left(\mathbf{x}(t), \mathbf{u}_{0}(t)\right)+\varepsilon \boldsymbol{\psi}(t)  \tag{1.36a}\\
\mathbf{s}(t) & =\mathbf{g}(\mathbf{x}(t))  \tag{1.36b}\\
\mathbf{u}_{0}(t) & =\mathbf{K}\left[(\mathbf{I}-\mathbf{R}) \sum_{j=1}^{\infty} \mathbf{R}^{j-1} \mathbf{s}(t-j T)-\mathbf{s}(t)\right] \tag{1.36c}
\end{align*}
$$

Here $\boldsymbol{\psi}(t)=\left(\psi_{1}(t), \ldots, \psi_{n}(t)\right)^{T}$ is a time-dependent $n$-dimensional vector and $\varepsilon$ is a small parameter, $|\varepsilon| \ll 1$. To distinguish the case $\tau=T$ we have marked the control variable by the zero subscript.

The description of weakly perturbed stable limit cycle oscillations defined by Eqs. (1.36) can be essentially simplified by using the phase reduction method. The dynamics of the weakly perturbed ETDFC system (1.36) can be reduced to the phase dynamics as follows:

$$
\begin{equation*}
\dot{\varphi}(t)=1+\varepsilon \mathbf{z}^{T}(\varphi(t)) \boldsymbol{\psi}(t) \tag{1.37}
\end{equation*}
$$

Here $\varphi(t)$ is a scalar variable that defines the phase of oscillations and $\mathbf{z}$ is an infinitesimal PRC of the system. The PRC satisfies the adjoint equation:

$$
\begin{align*}
\dot{\mathbf{z}}^{T}(t)= & -\mathbf{z}^{T}(t) \mathbf{A}_{0}(t)+\mathbf{z}^{T}(t) \mathbf{W}(t) \mathbf{K} \mathbf{V}(t) \\
& -\sum_{j=1}^{\infty} \mathbf{z}^{T}(t+j T) \mathbf{W}(t) \mathbf{K}(\mathbf{I}-\mathbf{R}) \mathbf{R}^{j-1} \mathbf{V}(t), \tag{1.38}
\end{align*}
$$

where

$$
\begin{align*}
\mathbf{A}_{0}(t) & =D_{1} \mathbf{f}\left(\mathbf{x}_{c}(t), 0\right)  \tag{1.39a}\\
\mathbf{W}(t) & =D_{2} \mathbf{f}\left(\mathbf{x}_{c}(t), 0\right)  \tag{1.39b}\\
\mathbf{V}(t) & =D \mathbf{g}\left(\mathbf{x}_{c}(t)\right) \tag{1.39c}
\end{align*}
$$

are the $T$-periodic matrices. The matrix $\mathbf{A}_{0}(t)$ is the Jacobian matrix of the controlfree system estimated on the UPO $\mathbf{x}_{c}(t)$, where $D_{1}$ is the vector derivative of the function $\mathbf{f}(\mathbf{x}, \mathbf{u})$ with respect to the first argument. The symbol $D_{2}$ in the definition of the matrix $\mathbf{W}(t)$ denotes the vector derivative of the function $\mathbf{f}(\mathbf{x}, \mathbf{u})$ with respect to the second argument. The matrix $\mathbf{V}(t)$ represents the vector derivative of the function $\mathbf{g}(\mathbf{x})$ that relates the output variable $\mathbf{s}$ with the state variable $\mathbf{x}$. Equation (1.38) is derived taking into account that the multiple delay times in our case are: $\tau_{j}=j T, j=1, \ldots, \infty$.

To find the PRC of the system we have to solve Eq. 1.38) with the requirement of the periodicity $\mathbf{z}(t+T)=\mathbf{z}(t)$. It is easy to see that for any $T$-periodic $\mathbf{z}(t)$ function the last two terms in Eq. 1.38) vanish, since $\sum_{j=1}^{\infty} \mathbf{z}^{T}(t+j T) \mathbf{W}(t) \mathbf{K}(\mathbf{I}-$ $\mathbf{R}) \mathbf{R}^{j-1} \mathbf{V}(t)=\mathbf{z}^{T}(t) \mathbf{W}(t) \mathbf{K V}(t)$. Therefore, the PRC of controlled system also satisfies the adjoint equation of the control-free system:

$$
\begin{equation*}
\dot{\mathbf{z}}^{T}(t)=-\mathbf{z}^{T}(t) \mathbf{A}_{0}(t) \tag{1.40}
\end{equation*}
$$

This equation is independent of the control $\mathbf{K}$ and memory $\mathbf{R}$ matrices. It means that the profile of the PRC of the controlled system is invariant with respect to the variation of $\mathbf{K}$ and $\mathbf{R}$. However, the amplitude of the PRC does depend on these matrices.

In the following, we denote the PRC of an UPO of the control-free system as $\boldsymbol{\rho}(t)$ and treat it as a basic PRC. Then the $\operatorname{PRC} \mathbf{z}(t)$ of the controlled system for any choice of ( $\mathbf{K}, \mathbf{R}$ ) we can express through this basic PRC:

$$
\begin{equation*}
\mathbf{z}(t)=\alpha(\mathbf{K}, \mathbf{R}) \boldsymbol{\rho}(t) \tag{1.41}
\end{equation*}
$$

The proportionality coefficient $\alpha(\mathbf{K}, \mathbf{R})$ can be obtained from the initial condition, which for our system takes the form

$$
\begin{equation*}
\mathbf{z}^{T}(0) \dot{\mathbf{x}}_{c}(0)+\sum_{j=1}^{\infty} j \int_{-T}^{0} \mathbf{z}^{T}(\vartheta) \mathbf{B}_{j}(\vartheta) \dot{\mathbf{x}}_{c}(\vartheta) d \vartheta=1, \tag{1.42}
\end{equation*}
$$

where

$$
\begin{equation*}
\mathbf{B}_{j}(\vartheta)=\mathbf{W}(\vartheta) \mathbf{K}(\mathbf{I}-\mathbf{R}) \mathbf{R}^{j-1} \mathbf{V}(\vartheta) . \tag{1.43}
\end{equation*}
$$

The PRC of the UPO of the control-free system is a periodic function $\boldsymbol{\rho}(t)=\boldsymbol{\rho}(t+T)$ that satisfies the following equation and initial condition:

$$
\begin{align*}
\dot{\boldsymbol{\rho}}^{T}(t) & =-\boldsymbol{\rho}^{T}(t) \mathbf{A}_{0}(t),  \tag{1.44a}\\
\boldsymbol{\rho}^{T}(0) \dot{\mathbf{x}}_{c}(0) & =1 \tag{1.44b}
\end{align*}
$$

An infinite sum in Eq. (1.42) can be determined analytically $\sum_{j=1}^{\infty} j \mathbf{R}^{j-1}=(\mathbf{I}-\mathbf{R})^{-2}$ and then this equation simplifies to:

$$
\begin{equation*}
\mathbf{z}^{T}(0) \dot{\mathbf{x}}_{c}(0)+\int_{-T}^{0} \mathbf{z}^{T}(\vartheta) \mathbf{W}(\vartheta) \mathbf{K}(\mathbf{I}-\mathbf{I})^{-1} \mathbf{V}(\vartheta) \dot{\mathbf{x}}_{c}(\vartheta) d \vartheta=1 \tag{1.45}
\end{equation*}
$$

Now we substitute Eq. (1.41) into Eq. 1.45) and taking into account Eq. 1.44b
obtain the expression for the above coefficient of proportionality:

$$
\begin{equation*}
\alpha(\mathbf{K}, \mathbf{R})=\left[1+\sum_{r=1}^{k} \sum_{p=1}^{l} \frac{K_{r p} C_{p r}}{1-R_{p}}\right]^{-1} \tag{1.46}
\end{equation*}
$$

Here we introduced an $l \times k$ matrix $\mathbf{C}$ whose elements are defined by a double sum of the following integrals:

$$
\begin{equation*}
C_{p r}=\sum_{i=1}^{n} \sum_{s=1}^{n} \int_{-T}^{0} \rho_{i}(\vartheta) W_{i r}(\vartheta) V_{p s}(\vartheta) \dot{x}_{c s}(\vartheta) d \vartheta \tag{1.47}
\end{equation*}
$$

The matrix C captures all inherent properties of the controlled system that define the variation of the PRC amplitude in response to the variation of the matrices (K, R).

Now we consider Eqs. 1.35 without external perturbation but suppose that $\tau \neq T$. Our aim is to derive an analytical expression for the period $\Theta$ of the stabilized orbit in the case of a small time delay mismatch.

We represent the delay time in the form $\tau=T+\varepsilon$, where

$$
\begin{equation*}
\varepsilon=\tau-T \tag{1.48}
\end{equation*}
$$

is a small mismatch. Substituting this expression for $\tau$ in Eq. (1.35c) and expending it with respect to $\varepsilon$ we get

$$
\begin{equation*}
\mathbf{u}(t)=\mathbf{u}_{0}(t)-\varepsilon \mathbf{K}(\mathbf{I}-\mathbf{R}) \sum_{j=1}^{\infty} j \mathbf{R}^{j-1} D \mathbf{g}(\mathbf{x}(t-j T)) \dot{\mathbf{x}}(t-j T) \tag{1.49}
\end{equation*}
$$

Here $\mathbf{u}_{0}(t)$ is a non-mismatched part of the control variable defined by Eq. 1.36 c . The remaining terms in Eq. (1.49) represent the mismatched part of the control variable. Now substituting Eq. 1.49 into Eq. 1.35a) and expanding it with respect to $\varepsilon$ up to the first-order terms, we reveal that the system (1.35) transforms exactly to the form (1.36) with

$$
\begin{equation*}
\boldsymbol{\psi}(t)=-D_{2} \mathbf{f}(\mathbf{x}(t), \mathbf{u}(t)) \mathbf{K}(\mathbf{I}-\mathbf{R}) \sum_{j=1}^{\infty} j \mathbf{R}^{j-1} D \mathbf{g}(\mathbf{x}(t-j T)) \dot{\mathbf{x}}(t-j T) \tag{1.50}
\end{equation*}
$$

When considering the phase dynamics of the stabilized orbit $\mathbf{x}_{c}(t)$ we can substitute in Eq. 1.50) $\mathbf{x}(t)=\mathbf{x}_{c}(t)$ and treat $\boldsymbol{\psi}(t)$ as an external perturbation (c.f. [10]). Then taking into account the periodicity of $\mathbf{x}_{c}(t)$ Eq. (1.50) simplifies to

$$
\begin{equation*}
\left.\boldsymbol{\psi}(t)=-\mathbf{W}(t) \mathbf{K}(\mathbf{I}-\mathbf{R})^{-1} \mathbf{V}(t)\right) \dot{\boldsymbol{\xi}}(t) \tag{1.51}
\end{equation*}
$$

The solution of the phase Eq. (1.37) has the form $\varphi=t+\mathcal{O}(\varepsilon)$ and therefore, it can be alternatively written as

$$
\begin{equation*}
\dot{\varphi}(t)=1+\varepsilon \mathbf{z}^{T}(\varphi) \boldsymbol{\psi}(\varphi)+\mathcal{O}\left(\varepsilon^{2}\right) . \tag{1.52}
\end{equation*}
$$

The period $\Theta$ of the target orbit in the presence of a small time delay mismatch can be estimated as follows:

$$
\begin{equation*}
\Theta=\int_{0}^{T} \frac{d \varphi}{1+\varepsilon \mathbf{z}^{T}(\varphi) \boldsymbol{\psi}(\varphi)}+\mathcal{O}\left(\varepsilon^{2}\right)=T-\varepsilon \int_{0}^{T} \mathbf{z}^{T}(\varphi) \boldsymbol{\psi}(\varphi) d \varphi+\mathcal{O}\left(\varepsilon^{2}\right) \tag{1.53}
\end{equation*}
$$

The integral in this equation can be expressed through the coefficient $\alpha(\mathbf{K}, \mathbf{R})$ introduced above:

$$
\begin{equation*}
\int_{0}^{T} \mathbf{z}^{T}(\varphi) \boldsymbol{\psi}(\varphi) d \varphi=\alpha(\mathbf{K}, \mathbf{R})-1 \tag{1.54}
\end{equation*}
$$

This result follows from Eqs. (1.41, (1.51), 1.46) and 1.47). Substituting Eq. (1.54) into Eq. (1.53) and using Eqs. (1.46) and (1.48) we obtain finally the following analytical expression for the period $\Theta=\Theta(\mathbf{K}, \mathbf{R}, \tau)$ :

$$
\begin{equation*}
\Theta=T+(\tau-T) \frac{\sum_{r=1}^{k} \sum_{p=1}^{l} K_{r p} C_{p r} /\left(1-R_{p}\right)}{1+\sum_{r=1}^{k} \sum_{p=1}^{l} K_{r p} C_{p r} /\left(1-R_{p}\right)}+\mathcal{O}\left((\tau-T)^{2}\right) . \tag{1.55}
\end{equation*}
$$

The main equation derived in Ref. [9] is the special case of Eq. (1.55). If we take the zero memory matrix $\mathbf{R}=0$ and assume that the control matrix has only one nonzero element $K_{11}=K$ then Eq. (1.55) transforms to the main equation from Ref. [9] with $\kappa=-1 / C_{11}$.

### 1.3.2 Time-delayed feedback control design beyond the oddnumber limitation

Let us consider an uncontrolled dynamical system $\dot{\mathbf{x}}(t)=\mathbf{f}(\mathbf{x}(t))$ with $\mathbf{x}(t) \in \mathbb{R}^{n}$ and $\mathbf{f}: \mathbb{R}^{n} \rightarrow \mathbb{R}^{n}$ and assume that it has an unstable $T$-periodic orbit $\mathbf{x}(t)=\mathbf{x}_{c}(t)=$ $\mathbf{x}_{c}(t+T)$, which we seek to stabilize by the time-delayed feedback control of the form

$$
\begin{equation*}
\dot{\mathbf{x}}(t)=\mathbf{f}(\mathbf{x}(t))+\mathbf{K}[\mathbf{x}(t-\tau)-\mathbf{x}(t)], \tag{1.56}
\end{equation*}
$$

where $\mathbf{K}$ is an $n \times n$ control matrix and $\tau$ is a positive delay time. A necessary condition for the stability of the periodic solution $\mathbf{x}_{c}(t)$ of the controlled system (1.56) is given by Hooton's and Amann's theorem [11. To formulate this theorem let us assume that $\tau$ slightly differs from $T$. Then the controlled system (1.56) has a periodic solution close to $\mathbf{x}_{c}(t)$ with a new period $\Theta$. Generally, the period $\Theta$
differs from $\tau$ and $T$; it is a function of $\mathbf{K}$ and $\tau, \Theta=\Theta(\mathbf{K}, \tau)$, which satisfies $\Theta(\mathbf{K}, T)=T$. Hooton's and Amann's theorem claims, that the periodic solution $\mathbf{x}_{c}(t)$ is an unstable solution of the controlled system (1.56) if the condition

$$
\begin{equation*}
(-1)^{m} \lim _{\tau \rightarrow T} \frac{\tau-T}{\tau-\Theta(\mathbf{K}, \tau)}<0 \tag{1.57}
\end{equation*}
$$

holds. Here $m$ is a number of real Floquet multipliers (FMs) larger than unity for the periodic solution $\mathbf{x}_{c}(t)$ of the uncontrolled system. The criterion (1.57) differs from Nakajima's theorem version by the factor $\beta=\lim _{\tau \rightarrow T}(\tau-T) /(\tau-\Theta)$ [12]. It follows that the necessary (but not the sufficient) condition for the TDFC to stabilize a UPO with an odd number $m$ is $\beta<0$. This condition predicts correctly the location of the transcritical bifurcation, which provides successful stabilization of the UPO in the example of Fiedler et al. [13, 11].

The criterion (1.57) can be rewritten in a more handy form. Using previous equation (1.46) we get

$$
\begin{equation*}
\beta=\alpha^{-1}(\mathbf{K})=1+\sum_{i j}^{n} K_{i j} C_{i j}, \tag{1.58}
\end{equation*}
$$

where $K_{i j}$ is the $i, j$ element of the control matrix and

$$
\begin{equation*}
C_{i j}=\int_{0}^{T} \rho_{i}(t) \dot{x}_{c j}(t) d t \tag{1.59}
\end{equation*}
$$

Here $\dot{x}_{c j}(t)$ denotes the $j$-th component of derivative of the periodic orbit and $\rho_{i}(t)$ is the $i$-th component of the PRC of the uncontrolled orbit.

In what follows, we present a practical recipe for designing the control matrix when a target UPO of dynamical system has a single $m=1$ real FM larger than unity. Any control matrix can be written in the form $\mathbf{K}=\kappa \tilde{\mathbf{K}}$, where $\kappa$ is a scalar control gain and $\tilde{\mathbf{K}}$ is a matrix with at least one element equal to -1 or 1 and other elements in the interval $[-1,1]$. We can satisfy Hooton's and Amann's necessary condition $\beta<0$ for any given matrix $\tilde{\mathbf{K}}$ if we choose the control gain as

$$
\begin{equation*}
\kappa>\kappa^{*} \equiv-\left(\sum_{i j}^{n} \tilde{K}_{i j} C_{i j}\right)^{-1} \tag{1.60}
\end{equation*}
$$

However, this condition is not sufficient for the successful control. Without loss of the generality we assume that the threshold $\kappa^{*}$ is positive, since this can be always achieved by appropriate choice of the sign of the matrix $\tilde{\mathbf{K}}$. We obtain additional conditions for $\tilde{\mathbf{K}}$ by using a relationship between the Floquet multipliers of the TDFC and proportional feedback control (PFC) systems [14]. Consider the PFC
problem derived from Eq. (1.56) by replacing the time-delay term $\mathbf{x}(t-\tau)$ with $\boldsymbol{\xi}(t)$ and representing the control matrix as $\mathbf{K}=g \tilde{\mathbf{K}}$

$$
\begin{equation*}
\dot{\mathbf{x}}(t)=\mathbf{f}(\mathbf{x}(t))+g \tilde{\mathbf{K}}\left[\mathbf{x}_{c}(t)-\mathbf{x}(t)\right] . \tag{1.61}
\end{equation*}
$$

The scalar $g$ is a real-valued parameter that defines the feedback gain for the PFC system. The problem of stability of the periodic orbit controlled by proportional feedback is relatively simple. Small deviations $\delta \mathbf{x}(t)=\mathbf{x}(t)-\mathbf{x}_{c}(t)$ from the periodic orbit can be decomposed into eigenfunctions according to the Floquet theory $\delta \mathbf{x}(t)=$ $\exp (\Lambda t) \mathbf{u}(t)$, where $\Lambda$ is the Floquet exponent (FE), and the $T$-periodic Floquet eigenfunction $\mathbf{u}(t)$ satisfies

$$
\begin{equation*}
\dot{\mathbf{u}}(t)+\Lambda \mathbf{u}(t)=\left[D \mathbf{f}\left(\mathbf{x}_{c}(t)\right)-g \tilde{\mathbf{K}}\right] \mathbf{u}(t) \tag{1.62}
\end{equation*}
$$

This equation produces $n$ FEs $\Lambda_{j}, j=1, \ldots, n$ [or FMs $\exp \left(\Lambda_{j} T\right)$ ]. The Floquet problem for the TDFC system (1.56) is considerably more difficult, since it is characterized by an infinity number of FEs. Let us denote the FEs of the periodic orbit controlled by time-delayed feedback by $\lambda$ and the corresponding FMs by $\mu=\exp (\lambda T)$. The Floquet eigenvalue problem for the TDFC system can be presented in a form of Eq. (1.62) with the following replacement of the parameters: $\Lambda \rightarrow \lambda$ and $g \rightarrow \kappa[1-\exp (-\lambda T)]$. Provided the $\mathrm{FM} \exp (\lambda T)$ is real-valued, this property leads to the following parametric equations (c.f. [14])

$$
\begin{equation*}
\lambda=\Lambda(g), \quad \kappa=g[1-\exp (-\Lambda(g) T)]^{-1} \tag{1.63}
\end{equation*}
$$

which allow a simple reconstruction of the dependence $\lambda=\lambda(\kappa)$ for some of branches of FEs of the TDFC system using the knowledge of the similar dependence $\Lambda=\Lambda(g)$ for the PFC system. The dependence $\Lambda=\Lambda(g)$ is obtained by solving the Floquet problem (1.62). Though Eqs. (1.63) are valid only for the real-valued FMs, the examples below show that exactly these branches are most relevant for the stability of the TDFC system.

To demonstrate the advantages of Eqs. (1.63) we refer to the Lorenz system described by the state vector $\mathbf{x}(t)=\left[x_{1}(t), x_{2}(t), x_{3}(t)\right]^{T}$ and the vector field [15]:

$$
\begin{equation*}
\mathbf{f}(\mathbf{x})=\left[10\left(x_{2}-x_{1}\right), x_{1}\left(28-x_{3}\right)-x_{2}, x_{1} x_{2}-8 / 3 x_{3}\right]^{T} . \tag{1.64}
\end{equation*}
$$

We take the standard values of the parameters, which produce the classical chaotic Lorenz attractor and consider the stabilization of its symmetric period-one UPO
with the period $T \approx 1.559$ and the single unstable FM $\mu \approx 4.713$. In Fig. 1.3 we show three typical dependencies of the FEs on the coupling strength for the PFC $\Lambda=\Lambda(g)$ (left-hand column) and the TDFC $\lambda=\lambda(\kappa)$ (right-hand column) systems obtained with different matrixes $\tilde{\mathbf{K}}$. The dependencies $\Lambda=\Lambda(g)$ for the PFC are derived from Eq. 1.62 . We plot only two branches of the FEs, originated from the unstable FE of the free system (red dashed curve) and from the trivial FE (blue solid curve crossing the origin). The branch corresponding to the negative FE of the free system does not influence the stability of the TDFC. The dependencies $\lambda=\lambda(\kappa)$ for the TDFC are obtained using the transformation (1.63). We see that the case (a)-(b) provides successful control for the PFC but it is unsuccessful for the TDFC. The case (c)-(d) is again unsuccessful for the TDFC; here two real FEs coalesce in the positive region and produce a pair of complex conjugate FEs with the positive real part, which grows with the increase of $\kappa$. Finally, the case (e)-(f) is potentially successful for the TDFC; here the branch of unstable FE (which results from two branches of the PFC system) decreases monotonically with the increase of $\kappa$ and becomes negative for $\kappa>\kappa^{*}$.

Now we show that the threshold $\kappa^{*}$ obtained from the FEs of the PFC system and transformation (1.63) coincides with the definition (1.60) derived from Hooton's and Amann's criterion. The values $\lambda(\kappa)$ of the TDFC system with $\kappa$ close to the threshold $\kappa^{*}$ result from the values of the trivial FE $\Lambda_{0}(g)$ of the PFC system with $g$ close to zero. To derive an expression for $\kappa^{*}$ we expand the dependence $\Lambda_{0}(g)$ for the trivial FE in Taylor series

$$
\begin{equation*}
\Lambda_{0}(g) T=a g+b g^{2}+O\left(g^{3}\right) \tag{1.65}
\end{equation*}
$$

Substituting (1.65) into (1.63) and taking the limit $g \rightarrow 0$ we get $\kappa^{*}=a^{-1}$. An expression for the coefficient $a$ can be derived by applying the perturbation theory to Eq. (1.62). To this end we write the trivial eigenmode in the form $\mathbf{u}(t)=$ $\mathbf{u}_{0}(t)+g \mathbf{u}_{1}(t)+O\left(g^{2}\right)$. Substituting this expansion and (1.65) into (1.62), we get in zero approximation $\dot{\mathbf{u}}_{0}(t)=D \mathbf{f}\left(\mathbf{x}_{c}(t)\right) \mathbf{u}_{0}(t)$. The solution of this equation is $\mathbf{u}_{0}(t)=\dot{\mathbf{x}}_{c}(t)$. In the first order approximation, we obtain

$$
\begin{equation*}
\dot{\mathbf{u}}_{1}(t)=D \mathbf{f}\left(\mathbf{x}_{c}(t)\right) \mathbf{u}_{1}(t)-(\tilde{\mathbf{K}}+\mathbf{I} a / T) \dot{\mathbf{x}}_{c}(t) \tag{1.66}
\end{equation*}
$$

where $\mathbf{I}$ is the identity matrix. Multiplying Eq. 1.66) on the LHS by $\boldsymbol{\rho}^{T}(t)$ and summing it with Eq. 1.44a) multiplied on the RHS by $\mathbf{u}_{1}(t)$, we get:

$$
\begin{equation*}
\frac{d}{d t}\left(\boldsymbol{\rho}^{T}(t) \mathbf{u}_{1}(t)\right)=-\boldsymbol{\rho}^{T}(t)(\tilde{\mathbf{K}}+\mathbf{I} a / T) \dot{\mathbf{x}}_{c}(t) \tag{1.67}
\end{equation*}
$$



Figure 1.3: Three typical scenarios for the dependence of the FEs of the Lorenz system on the feedback gain for PFC (left-hand column) and TDFC (right-hand column) at differen matrixes $\tilde{\mathbf{K}}$ : (a) and (b) $[0,0,0 ; 0,1,0 ; 0,0,0]$; (c) and (d) $[0,0,0 ;-1,0,0.3 ; 0,0,0] ;$ (e) and (f) $[0,0,0 ;-1,0,0.5 ; 0,0,0]$. In (a), (c) and (e), blue solid and red dashed curves represent trivial and unstable FEs (both real-valued) for PFC, respectively. In (b), (d) and (f), the corresponding curves show reconstructed values of FEs for TDFC. $\kappa^{*}$ is a threshold control gain, reconstructed from a segment of the trivial FE of the PFC system with $g$ close to zero. Green dotted curves in (c) and (e) show real parts of complex conjugate FEs, which cannot be transformed to TDFC by Eqs. (1.63). Green dotted curve in (d) shows the real part of complex conjugate FEs emerged from coalescence of two real FEs of the TDFC system.

We integrate this equation over the period $T$ and obtain $a=-\int_{0}^{T} \boldsymbol{\rho}^{T}(t) \tilde{\mathbf{K}} \dot{\mathbf{x}}_{c}(t) d t$, which means that the value $a^{-1}$ coincides with the threshold $\kappa^{*}$ defined in (1.60).

A relation of the coefficient $a$ with the matrix $\tilde{\mathbf{K}}$

$$
\begin{equation*}
a=-\sum_{i j}^{n} \tilde{K}_{i j} C_{i j} \tag{1.68}
\end{equation*}
$$

provides an alternative way to estimate the coefficients $C_{i j}$.
Apart from Hooton's and Amann's condition 1.60, the successful control requires that the derivative $d \lambda / d \kappa$ at the threshold $\kappa=\kappa^{*}$ to be negative [see Fig. 1.3(f)]. Substituting (1.65) into (1.63) we get

$$
\begin{equation*}
\left.\frac{d \lambda}{d \kappa}\right|_{\kappa=\kappa^{*}}=\lim _{g \rightarrow 0} \frac{d \Lambda_{0} / d g}{d \kappa / d g}=\frac{2 a}{T\left(1-2 b / a^{2}\right)}<0 . \tag{1.69}
\end{equation*}
$$

The parameter $a$ is positive by assumption of the positiveness of $\kappa^{*}$. Then this
condition simplifiers to

$$
\begin{equation*}
1-2 b / a^{2}<0 \tag{1.70}
\end{equation*}
$$

By extending the above perturbation theory for Eq. (1.62) up to the second order terms with respect to $g$, we derive the following expression for the coefficient $b$ :

$$
\begin{equation*}
b=-\frac{a}{T} \int_{0}^{T} \boldsymbol{\rho}^{T}(t) \mathbf{u}_{1}(t) d t-\int_{0}^{T} \boldsymbol{\rho}^{T}(t) \tilde{\mathbf{K}} \mathbf{u}_{1}(t) d t \tag{1.71}
\end{equation*}
$$

This allows us to write the relation of the coefficient $b$ with the matrix $\tilde{\mathbf{K}}$ in the quadratic form

$$
\begin{equation*}
b=\sum_{i j k l}^{n} \tilde{K}_{i j} \tilde{K}_{k l} D_{i j k l} \tag{1.72}
\end{equation*}
$$

with coefficients $D_{i j k l}=D_{k l i j}$. These coefficients can be obtained in a similar way as the coefficients $C_{i j}$ by taking specific forms of the matrix $\tilde{\mathbf{K}}$ and estimating $b$ from the dependence $\Lambda_{0}(g)$ of the trivial FE for small $g$.

Finally, we can summarize our algorithm as follows: (i) choose the structure of the matrix $\tilde{\mathbf{K}}$ with only several nonzero elements in such a way as to make possible the coalescence of the positive and trivial Floquet branches of the PFC system [like in Fig. (1.3) (c) or (e)]; (ii) for the given structure of the matrix $\tilde{\mathbf{K}}$, estimate the relevant coefficients $C_{i j}$ and $D_{i j k l}$; (iii) choose the values of nonzero elements of the matrix $\tilde{\mathbf{K}}$ such as to satisfy condition 1.70 ; (iv) compute the threshold $\kappa^{*}$ and satisfy condition 1.60 .

### 1.4 Control of neuron's oscillations via high frequency stimulation

The chapter "Control of neuron's oscillations via high frequency stimulation" contains the overview of the averaging method, general description of the analysis of a stimulated neuron, analysis of Hodgkin-Huxley (HH) neuron model under high frequency stimulation (HFS) and analysis of sub-thalamic nucleus neuron model under high frequency stimulation [A5].

Hodgkin-Huxley neuron model. The HH model subject to HFS reads [16]:

$$
\begin{align*}
C_{m} \dot{v} & =-I_{L}-I_{K}-I_{N a}+I_{0}+I_{1} \cos (2 \pi f t)  \tag{1.73a}\\
\dot{m} & =\alpha_{m}(v)(1-m)-\beta_{m}(v) m  \tag{1.73b}\\
\dot{h} & =\alpha_{h}(v)(1-h)-\beta_{h}(v) h  \tag{1.73c}\\
\dot{n} & =\alpha_{n}(v)(1-n)-\beta_{n}(v) n \tag{1.73d}
\end{align*}
$$

Here $C_{m}=1 \mu \mathrm{~F} / \mathrm{cm}^{2}$ is the membrane capacitance, and $v$ is the membrane potential measured in mV . The leak, $N a^{+}$and $K^{+}$currents are given by the following expressions

$$
\begin{align*}
I_{L} & =g_{L}\left(v-v_{L}\right)  \tag{1.74a}\\
I_{K} & =g_{K} n^{4}\left(v-v_{K}\right)  \tag{1.74b}\\
I_{N a} & =g_{N a} m^{3} h\left(v-v_{N a}\right) \tag{1.74c}
\end{align*}
$$

The parameters are: $\left(v_{L}, v_{K}, v_{N a}\right)=(10.6,-12,115) \mathrm{mV},\left(g_{L}, g_{K}, g_{N a}\right)=(0.3,36$, 120) $\mathrm{mS} / \mathrm{cm}^{2}$. The rate parameters defining the dynamics of the gating variables $m$, $h$ and $n$ measured in $\mathrm{ms}^{-1}$ are the following functions of the membrane potential:

$$
\begin{align*}
\alpha_{m}(v) & =(2.5-0.1 v) /[\exp (2.5-0.1 v)-1]  \tag{1.75a}\\
\beta_{m}(v) & =4 \exp (-v / 18)  \tag{1.75b}\\
\alpha_{h}(v) & =0.07 \exp (-v / 20),  \tag{1.75c}\\
\beta_{h}(v) & =1 /[\exp (3-0.1 v)+1]  \tag{1.75d}\\
\alpha_{n}(v) & =(0.1-0.01 v) /[\exp (1-0.1 v)-1]  \tag{1.75e}\\
\beta_{n}(v) & =0.125 \exp (-v / 80) . \tag{1.75f}
\end{align*}
$$

We apply a direct current $I_{0}=20 \mu \mathrm{~A} / \mathrm{cm}^{2}$ in order to destabilize the resting state of the neuron and induce self-sustained periodic spiking. The dynamics of the membrane potential in the absence of stimulation $\left(I_{1}=0\right)$ is shown in Fig. 1.4(a). The neuron fires with the period $T \approx 11.57 \mathrm{~ms}$ or characteristic frequency $\nu=$ $1 / T \approx 86.4 \mathrm{~Hz}$. The subsequent Figs. $1.4(\mathrm{~b})$-(d) show the influence of chargebalanced high-frequency stimulation, which is modeled by the harmonic current $I_{1} \cos (2 \pi f t)$.

As seen from Figs. 1.4(a)-(d), an increase of the simulation intensity $I_{1}$ from zero to $400 \mu \mathrm{~A} / \mathrm{cm}^{2}$ induces drastic changes in the HH neuron dynamics. For small stimulation intensities, the low-frequency periodic spiking is only slightly modulated
by the high-frequency oscillations. The increase of the stimulation intensity leads to an increase of the modulation amplitude. When the stimulation intensity reaches a certain threshold $I_{1} \approx 379 \mu \mathrm{~A} / \mathrm{cm}^{2}$ the neuronal sustained spiking suddenly disappears. In Fig. 1.4 (d) we see that for $I_{1}=400 \mu \mathrm{~A} / \mathrm{cm}^{2}$ the membrane potential displays only high-frequency oscillations of moderate amplitude around a constant value close to the resting potential.


Figure 1.4: Influence of the high-frequency stimulation on the HH neuron dynamics (a)-(d) and spectrum (e)-(h). Blue and red curves represent the solutions of the original Hodgkin-Huxley model (1.73) and the averaged equations (1.78), 1.80), respectively. Here we show the post-transient dynamics for the initial conditions $(v, m, h, n)=(0,0,0,0)$. (a) and (e) $I_{1}=0$; (b) and (f) $I_{1}=200 \mu \mathrm{~A} / \mathrm{cm}^{2}$; (c) and (g) $I_{1}=300 \mu \mathrm{~A} / \mathrm{cm}^{2}$; (d) and (h) $I_{1}=400 \mu \mathrm{~A} / \mathrm{cm}^{2}$.

The effect of suppression of self-sustained spiking is particularly remarkable in the spectrum of the membrane potential shown in Fig. 1.4 (e)-(h). When the stimulation amplitude exceeds the threshold value, the low-frequency part of the spectrum related to the neuronal self-oscillations vanishes, and only a narrow, stimulationrelated 5 kHz line remains.

To clarify the effect of suppression of low-frequency oscillations we apply the averaging method. If the period of stimulation is much less than all characteristic times of the Hodgkin-Huxley neuron, an approximate solution of Eqs. (1.73) can be
presented in the form:

$$
\begin{align*}
v(t) & \approx \bar{v}(t)+A \sin (2 \pi f t)  \tag{1.76a}\\
m(t) & \approx \bar{m}(t)  \tag{1.76b}\\
h(t) & \approx \bar{h}(t)  \tag{1.76c}\\
n(t) & \approx \bar{n}(t) \tag{1.76d}
\end{align*}
$$

where

$$
\begin{equation*}
A=\frac{I_{1}}{2 \pi f C_{m}} \tag{1.77}
\end{equation*}
$$

is the main parameter defining an action of the HFS. This parameter is proportional to the ratio of the amplitude $I_{1}$ to the frequency $f$ of HFS. Thus the effect of HFS to the neuron dynamics is completely determined by this ratio. From Eqs. (1.76) we see that the high-frequency "vibrational" component is added only to the membrane potential. The slow variables marked by bars describe the dynamics of the system averaged over the period of stimulation and satisfy the equations:

$$
\begin{align*}
C_{m} \dot{\bar{v}}= & -g_{l}\left(\bar{v}-v_{l}\right)-g_{K} \bar{n}^{4}\left(\bar{v}-v_{K}\right) \\
& -g_{N a} \bar{m}^{3} \bar{h}\left(\bar{v}-v_{N a}\right)+I_{0}  \tag{1.78a}\\
\dot{\bar{m}}= & \bar{\alpha}_{m}(\bar{v}, A)(1-\bar{m})-\bar{\beta}_{m}(\bar{v}, A) \bar{m}  \tag{1.78b}\\
\dot{\bar{h}}= & \bar{\alpha}_{h}(\bar{v}, A)(1-\bar{h})-\bar{\beta}_{h}(\bar{v}, A) \bar{h}  \tag{1.78c}\\
\dot{\bar{n}}= & \bar{\alpha}_{n}(\bar{v}, A)(1-\bar{n})-\bar{\beta}_{n}(\bar{v}, A) \bar{n} \tag{1.78d}
\end{align*}
$$

Formally, these equations are similar to the original Eqs. (1.73), but the HFS term is eliminated in Eq. 1.73a). The price one has to pay for this elimination is that the rate coefficients $\bar{\alpha}_{X}, \bar{\beta}_{X}(X=m, h, n)$ now depend not only on the membrane potential $\bar{v}$ but also on the stimulation parameter $A$. They are determined by averaging the original rate coefficients as follows

$$
\begin{align*}
\bar{\alpha}_{X}(\bar{v}, A) & =\frac{1}{2 \pi} \int_{0}^{2 \pi} \alpha_{X}(\bar{v}+A \sin \tau) d \tau  \tag{1.79a}\\
\bar{\beta}_{X}(\bar{v}, A) & =\frac{1}{2 \pi} \int_{0}^{2 \pi} \beta_{X}(\bar{v}+A \sin \tau) d \tau \tag{1.79b}
\end{align*}
$$

If the parameter $A$ is not very large, the averaged rate coefficients can analytically be estimated by the Taylor expansion

$$
\begin{align*}
\bar{\alpha}_{X}(\bar{v}, A) & \approx \alpha_{X}(\bar{v})+(1 / 4) A^{2} \alpha_{X}^{\prime \prime}(\bar{v})  \tag{1.80a}\\
\bar{\beta}_{X}(\bar{v}, A) & \approx \beta_{X}(\bar{v})+(1 / 4) A^{2} \beta_{X}^{\prime \prime}(\bar{v}) \tag{1.80b}
\end{align*}
$$

Following the terminology of the vibrational mechanics we refer to the terms in which $A$ appears [the last terms in Eqs. (1.80] as "vibrational forces". The double prime in these equations denotes the second derivative of a function. The vibrational forces are responsible for the changes in the slow component of the neuron dynamics induced by HFS. The solutions of the averaged equations shown in Fig. 1.4 by red curves are in good agreement with the solutions of the original Eqs. (1.73) (blue curves).


Figure 1.5: Bifurcation diagrams of the HH neuron under HFS. (a) shows the bifurcation diagram obtained from the averaged Eqs. 1.78), 1.80). The red line shows the resting potential $\bar{v}_{0}$. The unstable part is depicted by a dashed line. The solid dots and open circles represent the stable and unstable limit cycles, respectively. The symbol "subH" denotes the point of the subcritical Hopf bifurcation, and "dc" marks the double-cycle bifurcation. (b) and (c) show the maxima of the membrane potential obtained from the original Eqs. 1.73 ) for increasing and decreasing values of the stimulation parameter $A=I_{1} /\left(2 \pi f C_{m}\right)$, respectively. The horizontal axis displays the values of the parameter $A$ for fixed $f=5 \mathrm{kHz}$ and varying $I_{1}$.

The results of a global phase space analysis of the averaged equations are summarized in the bifurcation diagram shown in Fig. 1.5(a). When varying the stimulation parameter $A$ the system experiences jumps and hysteresis. For $A=0$, there is an unstable fixed point and the stable limit cycle is responsible for the neuron sustained spiking. When $A$ is increased to the value $A_{d c} \approx 15.17 \mathrm{mV}$, a double-cycle bifurcation (the point at which the stable limit cycle collides with an unstable limit cycle) takes place, and the system jumps to a stable fixed point. This explains the death of self-oscillations. If we now decrease $A$, the system remains in the stable resting state up to the value $A=A_{\text {subH }}$ and then jumps back to the stable limit cycle. In the interval $A_{s u b H}<A<A_{d c}$, the system is bistable; depending on initial
conditions it may approach either the stable fixed point or the stable limit cycle.
In Figs. 1.5(b)-(c) we show the bifurcation diagrams (the maxima of the membrane potential $v$ ) obtained from the original HH equations for increasing and decreasing values of the stimulation parameter $A$. Comparing these results with those presented in Fig. 1.5 (a), we can conclude that the averaged equations correctly predict and explain the bifurcations and the hysteresis observed in the original HH equations. We see that the jumps of the amplitude of the membrane potential are related to the subcritical Hopf and double-cycle bifurcations in the averaged equations. The small amplitudes of the membrane potential correspond to a stable resting state of the averaged dynamics.

## MAIN RESULTS AND CONCLUSIONS

The dissertation is devoted to the analysis of dynamical properties of nonlinear oscillators in the presence of strong and weak perturbations as well as developing analytical and numerical tools for such an analysis. Weakly perturbed oscillators are analyzed by a phase reduction method. The most part of the dissertation deals with this approach. Strong perturbations considered in the dissertation represent highfrequency signals, when the frequency is considerably greater than the reciprocal of characteristic time scale of the oscillator. In this case the method of averaging is employed. Two main problems analyzed by these tools are (i) time-delayed feedback control algorithm and (ii) dynamics of neuron under high-frequency stimulation.

The phase reduction method is a mathematical tool to analyze weakly perturbed nonlinear oscillators. The system's equations can be reduced to a single scalar equation that describes the dynamics of the phase variable. An important characteristic of the limit cycle oscillator resulting from the phase reduction procedure is its phase response curve. It describes the phase shift of the oscillator in response to a perturbing pulse at each phase of the oscillator. In this work we present a new numerical algorithm for computation of the phase response curve. In contrast to the standard algorithm, our algorithm does not require any backward integration and it is easier to program since a necessity of numerical interpolation for the Jacobian matrix is avoided.

The classical phase reduction theory is usually formulated for a weakly perturbed limit cycle oscillator described by the ordinary differential equations. In this work we have developed a phase reduction procedure for a general class of weakly perturbed time-delay systems exhibiting periodic oscillations. Here the main result is that the equation for the phase has the same form as in the classical case. Only the phase response curve must be computed differently.

The time delayed feedback control is a standard method for the stabilization of unstable periodic orbits in chaotic systems. The control signal is formed from a difference between the current state of the system, and the state of the system delayed by one period of a target orbit. Thus the controlled system is described by
equations with time delay. We analyze these equations and show that the profile of the phase response curve of the controlled orbit does not depend on the control matrix. Using this property, we derive an analytical expression for a period of the stabilized orbit in the case of a slightly mismatched time delay.

Time delayed feedback control has some restrictions. One of them is so-called odd-number limitation. Usually it is difficult to stabilize periodic orbit in the autonomous system, when it possesses an odd number of positive Floquet multipliers larger than unity. Using phase reduction method and additional analysis we present an algorithm for constructing the control matrix in the delayed feedback control scheme. We show that the algorithm works well for the Lorenz and Chua systems.

The last problem analyzed in the dissertation concerns the dynamics of neurons under high frequency stimulation. We study neuron's equations with the highfrequency external force by the averaging method. The derived averaged equations show that for some values of the stimulation parameters the stable limit cycle disappears and the unstable resting state becomes stable. Based on the analysis of the averaged equations we derive the criteria for the suppression of sustained neuronal spiking and explain the efficiency of the deep brains stimulation procedure for the patients with the Parkinson disease.

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## SANTRAUKA

Išnagrinėta fazinė redukcija sistemoms, aprašomoms paprastomis diferencialinėmis lygtimis. Pasiūlytas naujas fazės atsako funkcijos skaičiavimo algoritmas, kurio pagrindinis privalumas tas, kad tiesinė lygtis dèl nuokrypio integruojama ì priekí. Tai suteikia du pranašumus prieš standartinį jungtinės lygties algoritmą. Pirma, fazès atsako funkcija gaunama tokiu tikslumu, kokiu yra sprendžiamos diferencialinès lygtys, tuo tarpu jungtinès lygties metode prie bendros paklaidos prisideda interpoliavimo paklaida. Antra, algoritmo greitis nepriklauso nuo ribinio ciklo stabilumo stiprio, tuo tarpu standartinio algoritmo skaičiavimo trukmé esmingai padidėja, kai ribinis ciklas yra silpnai stabilus.

Fazinės redukcijos metodas išplėstas sistemoms, aprašomoms lygtimis su delsa. Gaunama lygtis dèl vieno skaliarinio kintamojo. Tai reiškia, kad be galo dimensinė lygtis su delsa redukuojama ị viendimensinę lygtị dèl fazės. Lygtis dèl fazės visiškai sutampa su analogiška lygtimi klasikiniame fazinės redukcijos metode. Tik fazės atsako funkcija skaičiuojama kitaip. Tai reiškia, kad visi rezultatai gauti iš klasikinės fazinės redukcijos (optimalios formos radimas, silpnai sujungtų osciliatorių sinchronizacijos analizė) lengvai perkeliami it sistemas, aprašomas lygtimis su delsa.

Fazinés redukcijos metodas pritaikytas uždelsto griž̌tamojo ryšio valdomoms sistemoms tirti. Tokioms sistemoms pastebėta ir aprašyta ìdomi fazės atsako funkcijos savybė: jei sistema yra valdoma uždelstuoju (arba išplėstiniu uždelstuoju) grįžtamuoju ryšiu, tai orbitos fazės atsako funkcijos forma nepriklauso nuo valdymo parametrų. Ši savybė panaudota silpnai išderintos išplėstiniu uždelstuoju grižtamuoju ryšiu valdomos sistemos periodo skaičiavimui. Periodas yra svarbus eksperimentinėse realizacijose, nes jis lengvai stebimas ir iš jo galima paskaičiuoti tikslesnị delsos laiką, norint minimizuoti arba panaikinti išderinimą.

Aprašytas ir pritaikytas algoritmas, leidžiantis tinkamai parinkti valdymo matricą, norint stabilizuoti orbitą su nelyginio skaičiaus topologiniu ribojimu, naudojant uždelsto grižztamojo ryšio valdymo schemą. Algoritmas remiasi ankščiau išdėstyta fazės atsako funkcijos savybe bei kitomis sistemos savybėmis, kurias galima pamatyti valdant orbitą proporciniu grizztamuoju ryšiu. Nors algoritmas negarantuoja
sėkmingos stabilizacijos visais atvejais, jo efektyvumas buvo pademonstruotas standartinėms sistemoms, kurių, kaip buvo manoma, nę̇manoma stabilizuoti uždelstojo gričztamojo ryšio metodu. Tai turi praktinę svarbą, nes daugelis eksperimentinių sistemų turi aprašytą topologinị ribojimą.

Darbe detaliai išnagrinėtas neurono veikimas išoriniu aukštu dažniu. Neurono savưjų osciliaciju slopinimo mechanizmas ir is jo plaukiantys rezultatai neblogai sutampa su realiuose klinikiniuose eksperimentuose gautais duomenimis. Šio mechanizmo supratimas leidžia kurti sudėtingesnius bet efektyvesnius neuronų stimuliavimo algoritmus, kurių tikslas yra panaikinti sinchronizaciją tarp neuronų kuo mažesne signalo galia. Ateityje, apjungiant šią neurono analizę su fazinės redukcijos metodu, gal būt pavyks pasiekti geresnių rezultatu, kurie turės praktinės naudos.

