

# Comparing Methods for Estimating Parameters in a System of Baroreflex Control over Mean Arterial Pressure

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**Abstract**—An original method is proposed for reconstructing the parameters of an oscillator operating in periodic modes with delayed feedback. It is compared to other methods by analyzing the time series of a system of biological nature in the presence of dynamic and measurement noises. Our method has advantages in analyzing data sensitive to measurement noise.

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## INTRODUCTION

Self-oscillators with delayed feedback are widely used in radiophysical and optical systems [1, 2]. Many objects found in nature can be described using differential equations with delay arguments. Systems with delayed feedback play a special role in, e.g., the modeling of many biological objects [3, 4].

Knowledge of the structure of an object under study, formalized as a mathematical model, offers a number of possibilities to a researcher that allow him to predict a system's behavior over time and as a result of changes in the governing parameters [5]. In addition, information on the structure of a model equation enables us to solve the problem of reconstructing the parameters of a system using its time series, often helping to avoid direct invasive measurements that are sometimes impossible or associated with ethical problems. The development of such approaches is therefore of particular importance in acquiring fundamental knowledge of animate objects and solving applied problems of medical diagnostics.

However, the problem of reconstructing parameters is complicated, since there is no universal method of reconstruction that allows the dynamic reconstruction of any system. As a rule, this problem can be solved by using methods aimed at narrow groups of systems and considering features of the structure of specific objects, formalized in mathematical models.

The problem of reconstructing biological systems of practical importance is often associated with additional challenges driven by the periodic dynamics of many such systems. The reconstruction of parameters is in this case complicated by the simplicity of their oscillation modes, which provide very little information on a studied system. In such cases, methods of reconstruction that proved to be useful in analyzing

chaotic systems [6] are either inapplicable or of limited applicability. In full-scale experiments, researchers also inevitably deal with data distorted by noises of various natures.

The aim of this work was to explore the applicability of known approaches and our approach to reconstructing the parameters of systems with delayed periodic time series in presence of noises. Our object of study was the system of baroreflex control over mean arterial pressure, which is essential in physiology and medicine [3].

## METHODS OF RECONSTRUCTION

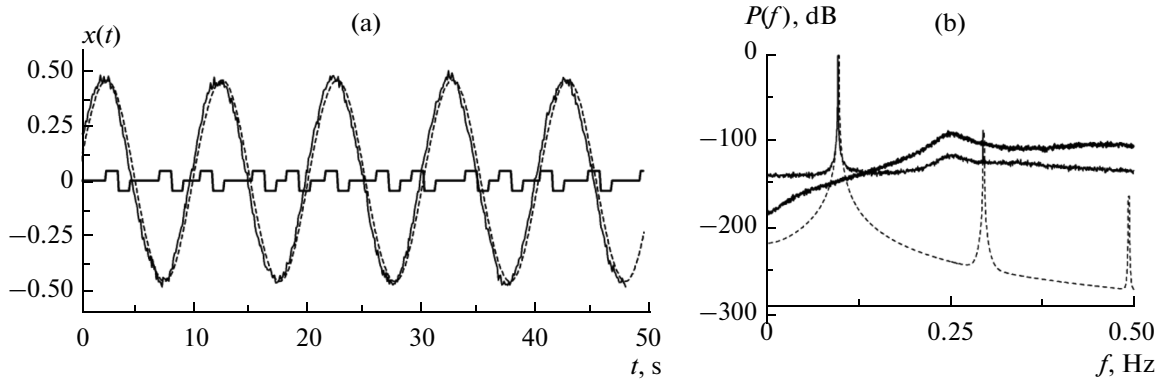
This work considers methods aimed at reconstructing the parameters of a delayed-feedback oscillator (DFO) described by the model equation

$$\varepsilon_0 \dot{x}(t) = -x(t) + f(x(t - \tau_0)), \quad (1)$$

where  $\tau_0$  is the delay time,  $\varepsilon_0$  is the time lag, and  $f$  is a nonlinear function.

A key step in reconstructing delay systems is determining delay time  $\tau_0$ . As a rule, minor mistakes made in estimating  $\tau_0$  lead to rapid growth of the error in estimating the rest of a system's parameters [7]. In this work, we used the accuracy of estimating delay time as a criterion for the efficiency of the compared approaches, taking one unit of discrete time as admissible error. If  $\tau_0$  is reconstructed precisely, other parameters can be reconstructed using our method.

We compared five methods: our original method, based on the use of an additional synchronous response system [8]; estimating the autocorrelation function (ACF); constructing the statistics of extreme value distributions  $N(\tau)$  [6]; analyzing informational entropy  $I(\tau)$  [9]; calculating the fill factor of a system's



**Fig. 1.** (a) Time series, (b) power spectra. Dashed line denotes system (1) with no noise; fine lines, 10% dynamic noise and 4% measurement noise; bold lines, 10% dynamic noise.

trajectory in three-dimensional space,  $V(\tau)$  [10]; and estimating the smoothness of a system's projected path in a two-dimensional space,  $L(\tau, \varepsilon)$  [11].

The method we propose for reconstructing delay time is based on the use of an additional synchronous response system. Time series  $x(t)$  of a system is delivered to the input of the auxiliary system, which is structured similar to the one being studied but has a feedback loop broken by a subtractor. At the subtractor output, difference between signals  $z(t) = x(t) - v(t)$ , where  $v(t)$  is the signal at the output of the auxiliary system's lag element. If the parameters of the auxiliary system are identical to those of the one being studied, dispersion  $D$  of difference signal  $z(t)$  is determined only by noises. When there is no noise, it is equal to 0. If the parameters differ, dispersion value  $z(t)$  will be high. A similar approach was used in building the chaotic system for transmitting secret information proposed in [12].

To solve the problem of reconstruction, nonlinear function  $f$  is parameterized using set of parameters  $\bar{a}$ . Parameters  $\bar{a}$ ,  $\tau$ , and  $\varepsilon$  are determined by minimizing the target function, dispersion  $D(\tau; \varepsilon; \bar{a})$  of the signal at the output of the auxiliary system's subtractor.

### OUR STUDIED SYSTEM

As our object of study, we selected the system of baroreflex control over mean arterial pressure proposed in [3]. The model equation for this system, formed on the basis of results from physiological experiments, is written with nonlinear function  $f$ :

$$f(x) = k \left( \frac{r^*}{1 + \alpha e^{-\beta x}} - \frac{r^*}{1 + \alpha e^{\beta x}} \right). \quad (2)$$

Parameters  $\alpha = 1$ ,  $\beta = 2$ ,  $r^* = 1$ , and  $k = -1.65$  proposed in [3] were selected in approximating the dependency obtained as a result of experimental studies in vitro. With this set of parameters, the nonlinear function has a sigmoid form. When  $\tau = 3.6$  s and  $\varepsilon = 2$  s (values typical of people with no health issues [3]), the system displays periodic oscillations with periods of about 10 seconds, which corresponds to physiological obser-

ventions. To obtain the time series, Eq. (3) was numerically integrated using the Euler method with a step of 0.1 s. The model system and its power spectra are shown in Fig. 1.

The study of real systems is always complicated by dynamic and measurement noises. In our numerical modeling, we therefore examined the applicability of methods for reconstruction with dynamic and measurement noises of various intensities. Statistical analysis of the results required the processing of 100 events at each fixed value of noise intensity. The intensity of added noise is in this work presented as the percentage of the mean-square deviations of a random process and an autonomous system.

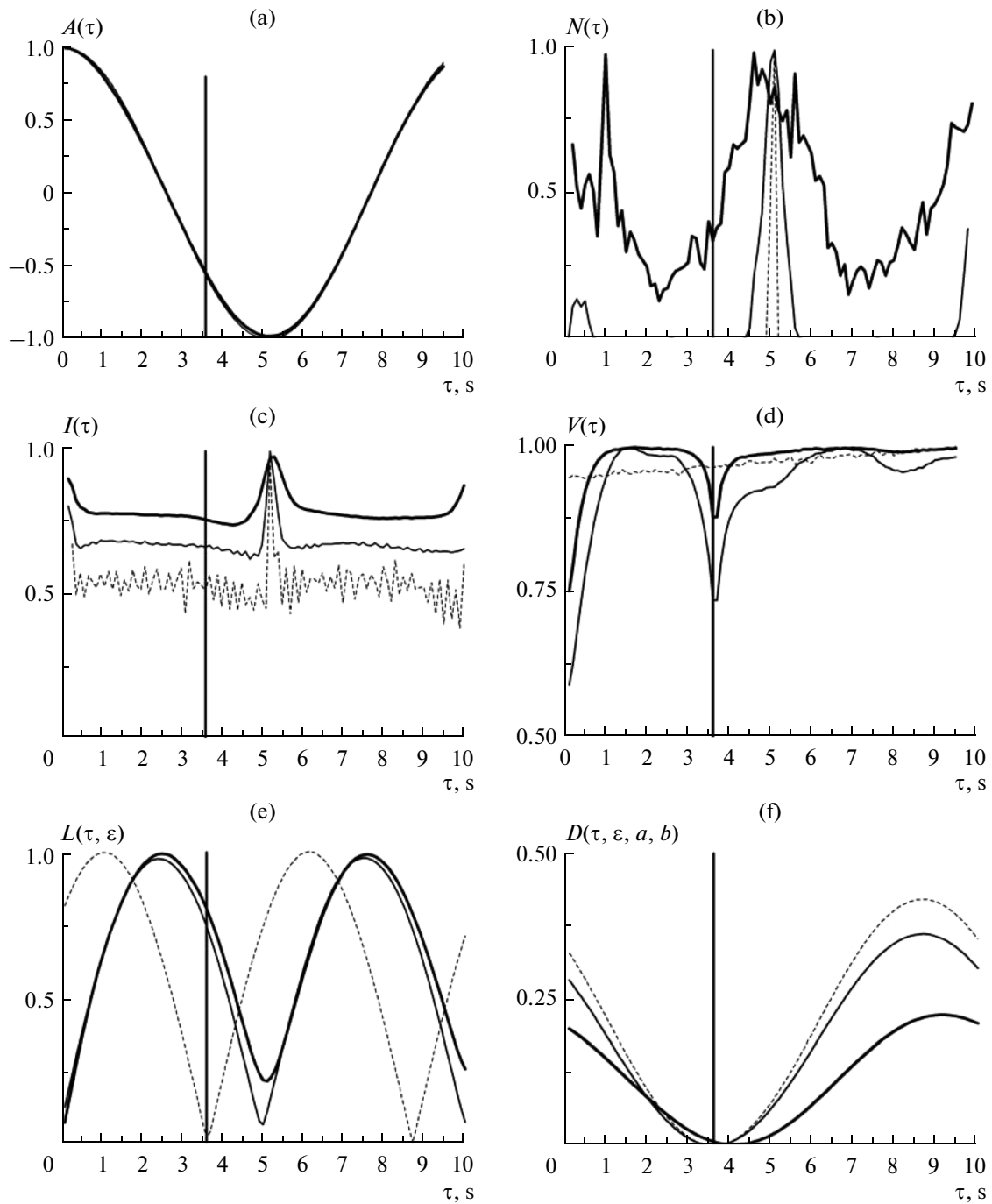
In contrast to measurement noises, the impact of broadband noise on a system's dynamics can in some cases make it easier to reconstruct parameters by shifting the path away from the attractor. Such modes provide more information about a system than periodical modes. Random process  $y(t)$  affects a system's dynamics in the manner

$$\varepsilon_0 \dot{x}(t) = -x(t) + f(x(t - \tau_0)) + y(t). \quad (3)$$

Random process  $y(t)$  was a sequence of bipolar rectangular impulses 2 s in duration, while the immediate period changed randomly in the interval of 3 to 5 s. Such parameters of the exciting signal correspond to physiological tests with forced breath or the mechanical stimulation of a group of carotid baroreceptors [13]. Other types of impact were used as well in the course of our studies: a harmonic signal, a periodic sequence of impulses, and white noise. However, exclusive use of a random sequence of bipolar rectangular impulses with a low ratio proved to be the one most effective in reconstructing the delay time of system (3).

### RESULTS FROM NUMERICAL MODELING

The applicability of methods was compared using an autonomous system of baroreflex control for reconstructing parameters affected by a random sequence of impulses and exposed to measurement noises. We used events as long as 36 000 intervals (360 significant peri-

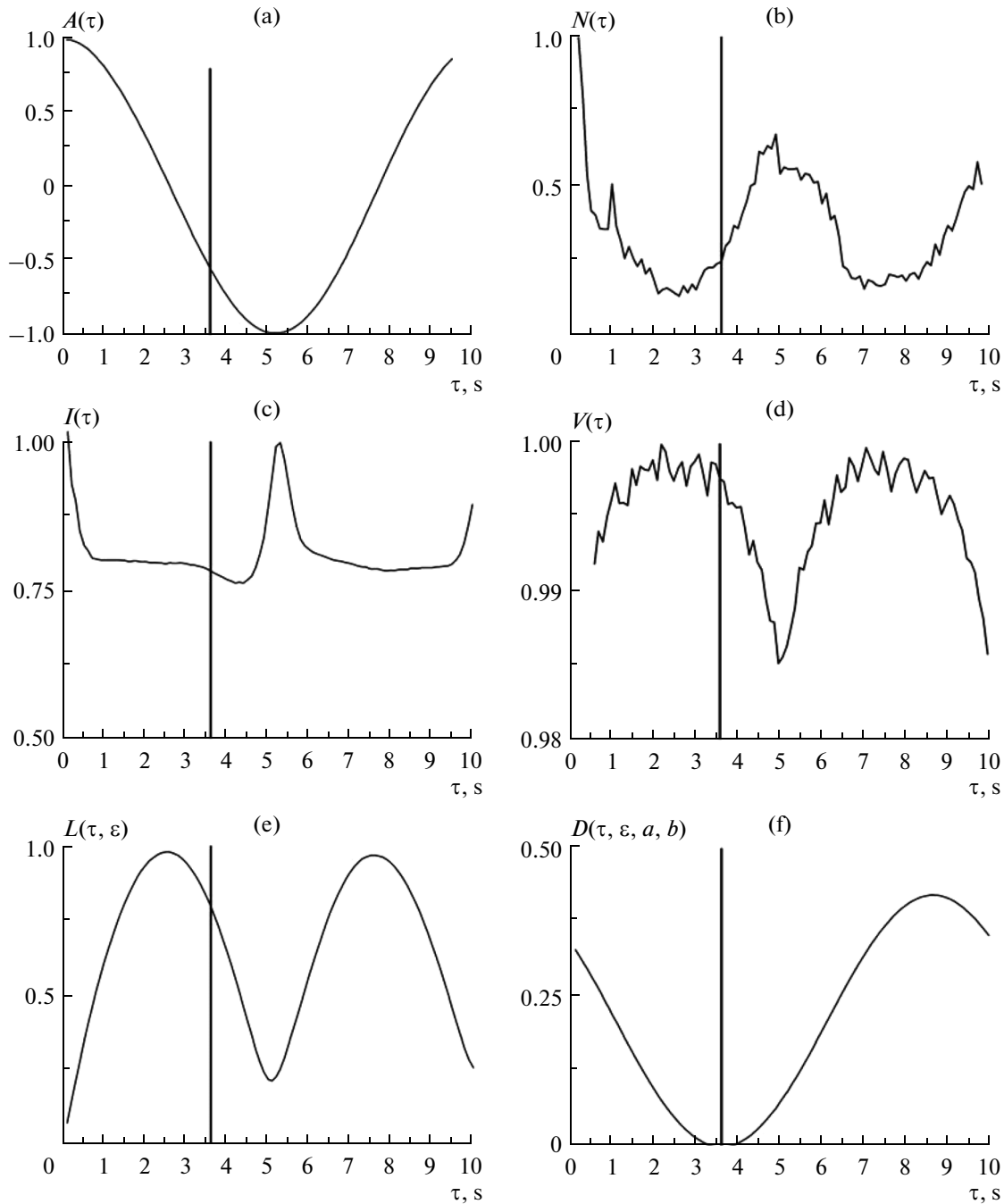


**Fig. 2.** Restoration of  $\tau_0$  using (a) ACF; (b)  $N(\tau)$ ; (c)  $I(\tau)$ ; (d)  $V(\tau)$ ; (e)  $L(\tau, \varepsilon)$ ; (f) the auxiliary system. Dashed line denotes no noise; fine lines, 10% dynamic noise; bold lines 50% dynamic noise. Vertical line denotes  $\tau_0 = 3.6$  s.

ods) in our analysis; this corresponded to a recorded length of 1 hour and was the virtual limit of possibilities when conducting an experiment in vivo.

The results from reconstructing  $\tau_0$  obtained for a system with no noises and systems with 10 and 50% dynamic noises are presented in Fig. 2. Methods based on building an ACF, on calculating the statistics of extreme value  $N(\tau)$  distributions, and on estimating

informational entropy  $I(\tau)$  turn out to be inapplicable by displaying extrema on the graphs at times close to half of the characteristic period. The methodology based on calculating fill factor  $V(\tau)$  allows us to reconstruct the delay time correctly with a probability of 0.99 when there is dynamic noise with intensities of 5–50%. The results from numerical modeling show that the method is inaccurate with regard to the selected size of a free parameter



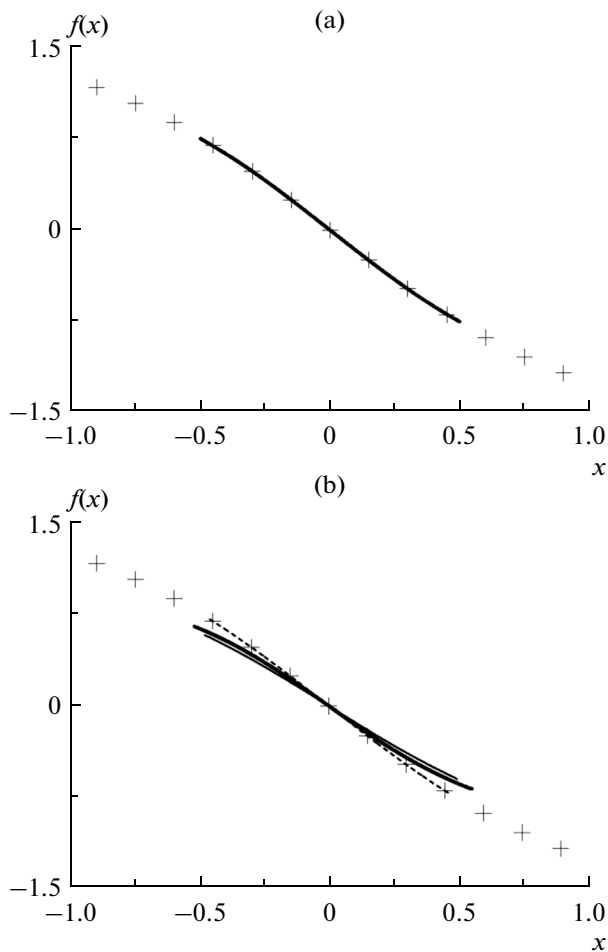
**Fig. 3.** Restoration of  $\tau_0$  with 4% measurement noise and 10% dynamic noise, using (a) ACF; (b)  $N(\tau)$ ; (c)  $I(\tau)$ ; (d)  $V(\tau)$ ; (e)  $L(\tau, \varepsilon)$ ; (f) the auxiliary system. The vertical line denotes  $\tau_0 = 3.6$  s.

(cube face size  $\delta$ ) when  $\delta < 0.007$ . In our calculations, we used fixed value  $\delta = 0.0035$ .

The method based on estimating smoothness  $L(\tau, \varepsilon)$  allows precise reconstruction of the delay time only if there are no noises, although in this case, events with lengths of 10 characteristic periods are sufficient. The approach we propose is based on the use of an auxiliary system and allows correct reconstruction of the delay time with a probability of 0.99 when there is

0–10% dynamic noise. The method of forming the statistics of extreme value distributions starts to reveal the local minimum value at the correct delay time with levels of dynamic noise starting at 75%. As the level of external impact grows, however, the minimum value does not become absolute even if the length of an event reaches 10000 significant periods.

When analyzing experimental data, time series events generally include measurement noises. Figure 3



**Fig. 4.** Results from reconstructing function (2) using (a) the auxiliary system; (b)  $L(\tau, \varepsilon)$ . The dashed line indicates no noise; the fine line, 4% measurement noise and 10% dynamic noise; the bold line, 50% dynamic noise. Crosses denote function (2).

shows the results from reconstructing the delay time when there are both dynamic and measurement noises. If there is even 1% dynamic noise, the methods based on calculating  $V(\tau)$  and  $L(\tau, \varepsilon)$  allow correct determination of the delay time with probabilities no higher than 0.5% at any level of dynamic noise. Among the other approaches, methods based on using an auxiliary system with synchronous response display the best resistance to measurement noises, allowing the correct determination of  $\tau_0$  with 0.99 probability when there are both dynamic (up to 10%) and measurement (up to 4%) noises.

We used our method and the approach based on estimating smoothness of projection  $L(\tau, \varepsilon)$  to restore time lag  $\varepsilon$  and nonlinear function  $f$ . When using an auxiliary system, the nonlinear function is parameterized as

$$f(t) = a_0 \operatorname{th}(b_0 t), \quad (4)$$

where  $a_0$  and  $b_0$  are parameters. Such approximation allows precise description of function (2) with sigmoid form using only two free parameters.

The step size was 0.1 when determining parameters  $\tau$  and  $\varepsilon$ . With no noises, the reconstruction of system (1) parameters is possible using both methods (Figs. 4a and 4b, dashed line). The result from least-squares approximation with function (4), reconstructed in the tabular form of a nonlinear function with the current parameters, yields  $a = -1.65$  and  $b = 1.00$ . These values of  $a$  and  $b$  coincide with the result from approximating direct dependency (2) with function (4) using the least-squares technique.

Analysis of a noise-free event using the auxiliary system allows correct reconstruction of values  $\tau = 3.6$  s and  $\varepsilon = 2.0$  s. The reconstructed parameters of the nonlinear function are  $a = -2.3$  and  $b = 0.6$ .

With 10% dynamic noise and 4% measurement noise, the auxiliary system allows us to determine the values of parameters  $\tau = 3.6$  s,  $\varepsilon = 2.0$  s,  $a = -1.4$ , and  $b = 1.2$  (Fig. 4a, fine line). At such levels of noise, the method based on calculating  $L(\tau, \varepsilon)$  does not allow reconstruction of the delay time, leading to a rapid increase in the error of determining other parameters. However, if the delay time is determined in advance using the auxiliary system or by calculating the fill factor, the estimated smoothness of projection at fixed value  $\tau = 3.6$  s produces  $\varepsilon = 1.3$  s,  $a = -1.2$ , and  $b = 1.1$  (Fig. 4b, fine line).

With 50% dynamic noise and no measurement noise, these methods do not allow reconstruction of the delay time. For both methods, we therefore used  $\tau = 3.6$  s, determined earlier by calculating the fill factor. Reconstruction of parameters using the auxiliary system in this case yields  $\varepsilon = 2.0$  s,  $a = -1.4$ , and  $b = 1.2$  (Fig. 4a, bold line). The technique that uses minimization of  $L(\tau, \varepsilon)$  allows us to obtain  $\varepsilon = 1.5$  s,  $a = -1.0$ , and  $b = 1.5$  (Fig. 4b, bold line).

## CONCLUSIONS

The aim of this work was to determine the possibilities and explore the applicability of the proposed method and several others used to reconstruct the parameters of oscillators operating in the periodic mode with delayed feedback and described by model equation (1). The methods were compared by analyzing periodic time series of a model system for the baroreflex control of mean arterial pressure [3], with both dynamic and measurement noises of different intensities.

We showed that methods based on estimating the autocorrelation function, information entropy, and statistics of extreme value distributions cannot be used to estimate the delay time of oscillators operating in the periodic mode with delayed feedback.

The method we propose, which uses an auxiliary system with a synchronous response, demonstrated

the best resistance to measurement noises when determining  $\tau$ .

Fill-factor calculations allow us to reconstruct the delay of dynamic noises over the broadest range and is inferior to our approach in terms of resistance to measurement noise.

Determining the smoothness of a system's projected path turns out to be the least demanding to the length of an event when there is no noise, but it shows high sensitivity to noise of various natures.

We also showed that when there is noise, we can reconstruct the value of time lag  $\varepsilon$  and nonlinear functions only using the proposed approach, which is based on using the auxiliary system. At high levels of dynamic noise, it is best to make a preliminary estimate of  $\tau$  by calculating the fill factor.

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