APPLIED AND COMPUTATIONAL MATHEMATICS

Original article
DOI: https://doi.org/10.18721/JPM.18212

AN INVERSE PROBLEM OF DIFFERENTIAL EQUATION SYSTEMS IN CONNECTION WITH THE STUDY OF SEMICONDUCTOR MATERIALS AND BIOMEDICINAL PROCESSES

A. P. Golovitskii✉

Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia

✉ alexandergolovitski@yahoo.com

Abstract. This paper puts forward a new method of solving the problem for calculating the unknown and non-measurable parameters, that are included in a system of differential equations, whose solution adequately reproduces the given experimental data, but has no analytical form. The problems of this kind are often found in physical research of semiconductor materials, biomedical processes and in electronics. The novelty lies in the proposed idea of numerical calculations of partial derivatives which has made it possible to adapt the Levenberg – Marquardt method of non-linear approximations for solving the said problem. Our specific examples showed that calculation errors of the parameter values were not more than the experimental errors.

Keywords: inverse problem, differential equation system, indirect measurements, Levenberg–Marquardt method

Funding: The reported study was carried out within the framework of the State Assignment for Fundamental Research (Subject Code FSEG-2023-0016).

Citation: Golovitskii A. P., An inverse problem of differential equation systems in connection with the study of semiconductor materials and biomedical processes, St. Petersburg State Polytechnical University Journal. Physics andMathematics. 18 (2) (2025) 132–143. DOI: https://doi.org/10.18721/JPM.18212

Научная статья
УДК 519.65, 53.088
DOI: https://doi.org/10.18721/JPM.18212

ОБРАТНАЯ ЗАДАЧА СИСТЕМ ДИФФЕРЕНЦИАЛЬНЫХ УРАВНЕНИЙ В СВЯЗИ С ИЗУЧЕНИЕМ ПОЛУПРОВОДНИКОВЫХ МАТЕРИАЛОВ И БИОМЕДИЦИНСКИХ ПРОЦЕССОВ

А. П. Головицкий✉

Санкт-Петербургский политехнический университет Петра Великого, Санкт-Петербург, Россия

✉ alexandergolovitski@yahoo.com

Аннотация. В работе представлен новый метод решения задачи вычисления априори неизвестных и не поддающихся прямым измерениям параметров, входящих в состав систем дифференциальных уравнений, адекватно описывающих имеющиеся экспериментальные данные, но не имеющих аналитической формы решения. Задачи такого рода нередко встречаются при физических исследованиях полупроводниковых материалов, а также в электронике, биофизике и медицинской физике. Новизна заключается в предложенной идее численного расчета частных производных, что позволило применить для решения такой задачи метод нелинейной аппроксимации Левенберга – Марквардта. На

конкретных примерах показано, что погрешность вычисления значений параметров оказывается не больше погрешности экспериментальных данных.

Ключевые слова: обратная задача, система дифференциальных уравнений, косвенные измерения, метод Левенберга −Марквардта

Финансирование: Работа выполнена в рамках Государственного задания на проведение фундаментальных исследований (код темы FSEG-2023-0016).

Ссылка для цитирования: Головицкий А. П. Обратная задача систем дифференциальных уравнений в связи с изучением полупроводниковых материалов и биомедицинских процессов // Научно-технические ведомости СПбГПУ. Физико-математические науки. 2025. Т. 18. № 2. С. 132−143. DOI: https://doi.org/10.18721/JPM.18212

Introduction

Systems of ordinary differential equations (ODEs) with solutions in the form of periodic nonlinear undamped oscillations are widely used for mathematical modeling of physical, chemical and biological self-oscillatory processes [1−4, 10]. Generally, the argument in these solutions is the time *t*.

Real processes in living and nonliving matter commonly include a large number of separate subprocesses or stages, often incredibly complex, especially in complex processes of current flow in semiconductor materials [10] or biological processes [3−6, 13]. Ideally, their model description should include a large number of related variables, which complicates the analysis, leads to ill-posedness of models and instability of model solutions, typically obtained numerically, since it often turns out that analytical solutions to such models do not exist.

In view of the above, models have to be simplified for clarity and stability, the number of variables is reduced; some unimportant reactions (as judged by the researchers) are neglected and others are combined into sets to quantify (albeit incompletely) the influence of those numerous reactions that do not determine the overall qualitative course of the given process.

To preserve the quantitative adequacy of simplified models that include such combined reaction sets, it is necessary to correctly define their rate coefficients acting as de-facto fitting parameters.

Notably, even the rates of individual biochemical reactions or the values of some parameters of new semiconductor materials are also known quite approximately; the data from different authors vary greatly.

Models can include unknown or ill-known parameters. It would be optimal to be able to calculate and refine their values to obtain new quantitative physical information.

If the variables that make up the solution of the ODE system are measured experimentally, it becomes possible to calculate unknown parameters to compare computational and experimental model results. Such an inverse problem of the ODE system can become the basis for indirect experimental measurements, when unknown parameters cannot be measured directly but can be calculated through a known relationship (model) with other measurable quantities and/or variables.

The goal of this paper is to develop a procedure for solving such an inverse problem and test it.

Problem statement

In general, the problem is formulated as follows. Experimental data are available about the variables $u(t_i)$, $v(t_i)$, $w(t_i)$, ... , measured (with an error) at k points in time t_i. There is also a system of ODE:

$$\left.\begin{aligned} \dot{\tilde{u}} &= f(t,\tilde{u},\tilde{v},\tilde{w},...,a,b,c,...) \\ \dot{\tilde{v}} &= g(t,\tilde{u},\tilde{v},\tilde{w},...,a,b,c,...) \\ \dot{\tilde{w}} &= h(t,\tilde{u},\tilde{v},\tilde{w},...,a,b,c,...) \\ &\cdots\cdots\cdots\cdots \end{aligned}\right\}, \qquad (1)$$

with N components of the solution

$$\tilde{u}(t_i, a, b, c, ...), \tilde{v}(t_i, a, b, c, ...), \tilde{w}(t_i, a, b, c, ...), ...$$

It is assumed that system (1) has no analytical solution and that the components of solution (1) can only be found numerically.

Let us also assume that these components can adequately match the experimental data, denoted below as

$$u_i \equiv u(t_i), v_i \equiv v(t_i), w_i \equiv w(t_i), ...$$

Let the initial conditions of all equations (1) be set at the conditional time origin t_0; then the ODE system (1) is the Cauchy problem. It is required to find unknown numerical values of the parameters a, b, c, ... included in system (1), minimizing the functional of sums of square deviations of the solution components in system (1) from the corresponding experimental data:

$$S = \sum_{i=1}^{k} [\tilde{u}(t_i, a, b, c, ...) - u_i]^2 + \sum_{i=1}^{k} [\tilde{v}(t_i, a, b, c, ...) - v_i]^2 + \\ + \sum_{i=1}^{k} [\tilde{w}(t_i, a, b, c, ...) - w_i]^2 + ... \to \min_{a,b,c,...}. \quad (2)$$

The number of sums in the functional S is equal to n, the number of those variables of system (1) for which experimental data were obtained.

Notably, it was found in the course of this study that it is unnecessary to obtain the experimental data for all N variables of system (1). Data on a smaller number of variables $n < N$, and often only on a single variable is sufficient to calculate the parameters with acceptable accuracy.

A problem similar to the one formulated in this section was posed earlier in [5] for the model of the Belousov–Zhabotinsky reaction [6]. The experimental data in [5] were modeled by solving a direct problem; no additional model error was introduced in these data. The parametric search for the minimum S was carried out in [5] using the Hooke–Jeeves method [7], which is a variant of the coordinate descent method [9]. The method is direct, so that inverse problem (2) was actually solved by searching over solutions to direct problem (1). For such methods of solving inverse problems, convergence is guaranteed only in a very small neighborhood of the minimum; it is also characterized by long calculation times and low accuracy of the results. The calculation accuracy for three reaction rates given in [5] turned out to be rather unsatisfactory: 12, 14, and 420%.

Algorithm for solving the problem

An alternative method is proposed in this paper to find the parameters minimizing functional (2), which is close in theory to the Levenberg–Marquardt nonlinear approximation method [11], including elements of gradient descent along with preconditioning and regularization.

Since solution (1) exists but the analytical form of its components

$$\tilde{u}(t_i, a, b, c, ...), \tilde{v}(t_i, a, b, c, ...), \tilde{w}(t_i, a, b, c, ...), ...$$

remains unknown, we are forced to assume a nonlinear dependence of the components on the parameters a, b, c, ... Therefore, to find the latter, it is advisable to apply one of the methods for nonlinear minimization of the functional S.

All such methods are based on linearization of deviations

$$\tilde{u}(t_i, a, b, c, ...) - u_i; \tilde{v}(t_i, a, b, c, ...) - v_i; \tilde{w}(t_i, a, b, c, ...) - w_i; \text{ ... , etc.}$$

of relatively small increments of the parameters da, db, dc, ...

Let us assume that a certain initial set of parameters is known from physical considerations:

$$a_0, b_0, c_0, \ldots \equiv \mathbf{p}_0.$$

Here it makes sense to immediately try to solve system (1) with the initial parameter set $\mathbf{p}_0$, calculate the relative residual of the form

$$\rho_0 = \frac{1}{n}\left\{\frac{\sum_{i=1}^{k}[\tilde{u}(t_i, a_0, b_0, c_0, \ldots) - u_i]^2}{\sum_{i=1}^{k} u_i^2} + \frac{\sum_{i=1}^{k}[\tilde{v}(t_i, a_0, b_0, c_0, \ldots) - v_i]^2}{\sum_{i=1}^{k} v_i^2} + \right.$$
$$\left. + \frac{\sum_{i=1}^{k}[\tilde{w}(t_i, a_0, b_0, c_0, \ldots) - w_i]^2}{\sum_{i=1}^{k} w_i^2} + \ldots\right\}^{1/2} \quad (3)$$

and compare it with the relative experimental error ρ.

If it turns out that $\rho_0 \approx \rho$, we can assume that the required parameters were found. However, this is generally not the case, and $\rho_0 > \rho$. If the value of ρ_0 is excessively higher than the value of ρ, it is worthwhile to refine the initial set by trial and error, varying a_0, b_0, c_0, ... , finding ρ_0 from expression (3) and comparing the values of ρ_0 and ρ.

We should note that the time dependences of some components of solution (1) often take the form of a sequence of narrow pulses with a large duty cycle. Practice shows that reliable convergence is guaranteed when the pulses of solution (1) overlap with the corresponding experimental data by at least 10%.

Next, we expand the deviation in the *i*th position:

$$\tilde{u}(t_i, a_0, b_0, c_0, \ldots) - u_i; \tilde{v}(t_i, a_0, b_0, c_0, \ldots) - v_i; \tilde{w}(t_i, a_0, b_0, c_0, \ldots) - w_i; \quad (4)$$

in the vicinity of a_0, b_0, c_0, ... into a Taylor series with respect to increments of parameters *da*, *db*, *dc*, ..., retaining only the linear terms of the expansion:

$$S = \sum_{i=1}^{k}\left\{\left[\tilde{u}(t_i, a_0, b_0, c_0, \ldots) - u_i + \left.\frac{\partial\tilde{u}(t_i)}{\partial a}\right|_{\mathbf{p}_0} da + \left.\frac{\partial\tilde{u}(t_i)}{\partial b}\right|_{\mathbf{p}_0} db + \ldots\right]^2 + \right.$$
$$+\left[v(t_i, a_0, b_0, c_0, \ldots) - v_i + \left.\frac{\partial\tilde{v}(t_i)}{\partial a}\right|_{\mathbf{p}_0} da + \left.\frac{\partial\tilde{v}(t_i)}{\partial b}\right|_{\mathbf{p}_0} db + \ldots\right]^2 + \ldots\Big\} \quad (5)$$
$$\left. +\left[\tilde{w}(t_i, a_0, b_0, c_0, \ldots) - w_i + \left.\frac{\partial\tilde{w}(t_i)}{\partial a}\right|_{\mathbf{p}_0} da + \left.\frac{\partial\tilde{w}(t_i)}{\partial b}\right|_{\mathbf{p}_0} db + \ldots\right]^2 + \ldots\right\}.$$

Thus, problem (2) turns out to be linearized with respect to the increments *da*, *db*, *dc*, ...

Then, as in the linear least squares method, we should find the partial derivatives

$$\frac{\partial S}{\partial[da]}, \frac{\partial S}{\partial[db]}, \frac{\partial S}{\partial[dc]}, \ldots,$$

equate them to zero and obtain a system of linear algebraic equations (SLAE) with respect to the unknowns *da*, *db*, *dc*, ... :

$$\begin{cases} A_{aa}[da]+A_{ab}[db]+A_{ac}[dc]+\ldots=A_{a0}, \\ A_{ba}[da]+A_{bb}[db]+A_{bc}[dc]+\ldots=A_{b0}, \\ A_{ca}[da]+A_{cb}[db]+A_{cc}[dc]+\ldots=A_{c0}, \\ \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \end{cases} \tag{6}$$

$$\left.\begin{aligned} A_{ab}&=\sum_{i=1}^{k}\left[\left.\frac{\partial\tilde{u}(t_i)}{\partial a}\right|_{p_0}\left.\frac{\partial\tilde{u}(t_i)}{\partial b}\right|_{p_0}+\left.\frac{\partial\tilde{v}(t_i)}{\partial a}\right|_{p_0}\left.\frac{\partial\tilde{v}(t_i)}{\partial b}\right|_{p_0}+\left.\frac{\partial\tilde{w}(t_i)}{\partial a}\right|_{p_0}\left.\frac{\partial\tilde{w}(t_i)}{\partial b}\right|_{p_0}+\ldots\right]; \\ A_{a0}&=-\sum_{i=1}^{k}\left\{\left.\frac{\partial\tilde{u}(t_i)}{\partial a}\right|_{p_0}[\tilde{u}(t_i,a_0,b_0,c_0,\ldots)-u_i]+\left.\frac{\partial\tilde{v}(t_i)}{\partial a}\right|_{p_0}[\tilde{v}(t_i,a_0,b_0,c_0,\ldots)-v_i]+\ldots\right\}. \end{aligned}\right\} \tag{7}$$

The main problem with applying the linearization method to find the parameters of control systems is that, unlike other nonlinear minimization methods (including the Levenberg–Marquardt method), it is impossible to calculate partial derivatives in (7) analytically, since it was initially assumed that system (1) does not have an analytical solution.

In this paper, it is proposed to find derivatives numerically.

Let us define an initial set $\mathbf{p}_0 \equiv a_0, b_0, c_0, \ldots$, and initial conditions of system (1) from the experimental data. We solve system (1) numerically and find the components of the solution

$$\tilde{u}(t_i,a_0,b_0,c_0,\ldots),\ \tilde{v}(t_i,a_0,b_0,c_0,\ldots),\ \ldots\text{, etc.}$$

After that, we define a small increment to parameter a_0, such that $|\delta a| < |a_0|$, and leave all other parameters unchanged. Substituting $a_0 + \delta a$ into system (1) instead of a_0, we solve it with the same initial conditions and find

$$\tilde{u}(t_i,a_0+\delta a,b_0,c_0,\ldots),\ \tilde{v}(t_i,a_0+\delta a,b_0,c_0,\ldots)\ \ldots\text{, etc.}$$

Next, calculating the relation

$$\frac{\tilde{u}(t_i,a_0+\delta a,b_0,c_0,\ldots)-\tilde{u}(t_i,a_0,b_0,c_0,\ldots)}{\delta a}=\frac{\delta\tilde{u}(t_i,a_0,b_0,c_0,\ldots)}{\delta a}, \tag{8}$$

we obtain a numerical equivalent of the partial derivative

$$\left.\frac{\partial\tilde{u}(t_i,a,b,c,\ldots)}{\partial a}\right|_{\mathbf{p}_0}.$$

Partial derivatives $\left.\frac{\partial}{\partial a}\right|_{\mathbf{p}_0}$ for the remaining components of solution (1) are found similarly.

Then a small increment is given to the parameter b_0 and numerical analogues $\left.\frac{\partial}{\partial b}\right|_{\mathbf{p}_0}$, etc., are found similarly.

As a result, the problem of calculating all the elements of SLAE (6) is successfully solved.

The solution to SLAE (6) is a vector

$$d\mathbf{p} \equiv [da, db, dc, \ldots].$$

Ostensibly, problem (2) should be solved iteratively, defining an initial parameter set $\mathbf{p}_0$, constructing and solving a SLAE (6), finding $d\mathbf{p}$ and then $\mathbf{p}_1 = \mathbf{p}_0 + d\mathbf{p}$. After that, it is necessary to check whether the quantity S in Eq. (2) decreases when $\mathbf{p}_1$ is substituted instead of $\mathbf{p}_0$. If it decreases, then $\mathbf{p}_1$ is taken for $\mathbf{p}_0$ and the next iteration begins: system (1) is solved again, SLAE (6) is composed, and so on, until the value of S is stabilized as it decreases monotonically.

So far, everything seems logical, since we describe the well-known Gauss–Newton method for finding the minimum. However, we found in this study that this method is basically unsuitable for solving inverse problems of ODE systems in practice. If this method is used, the value of S often does not decrease at all when the initial approximation is not sufficiently close to the set of parameters giving the minimum, and/or when the matrix A from SLAE (6) is ill-conditioned [12].

Solving inverse problems of ODE systems by the Gauss–Newton method, generally yields $S(\mathbf{p}_1) > S(\mathbf{p}_0)$ instead of $S(\mathbf{p}_1) < S(\mathbf{p}_0)$ at first iteration, and $S(\mathbf{p}_1)$ often turns out to be much larger than $S(\mathbf{p}_0)$. This is because physical considerations often give such a set a_0, b_0, c_0, ... that neither the increments of the parameters da, db, dc, ... , nor the deviations (4) are sufficiently small to neglect the higher terms of series (5). Then all expressions starting from (5) are, strictly speaking, incorrect, i.e., do not correspond to the problem. However, all these expressions would correspond to it if the increments da, db, dc, ... were small.

Therefore, we propose, firstly, the same preconditioning procedure with matrix A as in the Levenberg–Marquardt method [11], called scaling, where matrix A is transformed into matrix R:

$$R = \begin{pmatrix} 1 & r_{ab} & r_{ac} & \cdots \\ r_{ba} & 1 & r_{bc} & \cdots \\ r_{ca} & r_{cb} & 1 & \vdots \\ \vdots & \vdots & \cdots & \ddots \end{pmatrix}, \text{ where } \forall m,n>0\ r_{mn} = \frac{A_{mn}}{\sqrt{A_{mm}A_{nn}}}. \tag{9}$$

It is also necessary to recalculate the elements in the column of free terms of SLAE (6):

$$\forall m>0\ r_{m0} = A_{m0}\Big/\sqrt{A_{mm}}\,. \tag{10}$$

The scaled SLAE replacing SLAE (6) takes the following matrix form

$$Rz = R_0, \tag{11}$$

and the components of its solution z_m (their number is equal to the number of required parameters) are related to the components of the solution of SLAE (6) by

$$\forall m>0\ [d\mathbf{p}]_m = z_m\Big/\sqrt{A_{mm}}\,. \tag{12}$$

SLAE (11) turns out to be much better-posed, and its solution is more stable than that of SLAE (6).

Secondly, to further improve the well-posedness of SLAE and accelerate the convergence of the method, we propose, based on the results from [11], to introduce additional regularization: a positive number μ should be added to the diagonal elements of the matrix R (which is positive definite and whose eigenvalues are all positive). In addition to reducing the condition number of SLAE (12), introducing the coefficient μ, according to Levenberg [11], forcibly makes the increments of the parameters small.

As a result, instead of SLAE (6), we need to solve the following SLAE:

$$(R + I\mu)z = R_0, \tag{13}$$

where I is the identity matrix.

The quantity μ must be refined during the solution of the problem. In the first iteration, it is recommended to take $\mu \approx 0.1–0.3$.

After composing SLAE (6), converting it to form (13) and finding a solution, we should perform inverse scaling of Eq. (12), thus calculating the increments of the required parameters da, db, dc, ... Next, we find

$$\mathbf{p}_1 = \mathbf{p}_0 + d\mathbf{p} \equiv a_0 + da, b_0 + db, c_0 + dc, \ldots = a_1, b_1, c_1, \ \ldots\ .$$

Next, the found values of the parameters a_1, b_1, c_1, ... are inserted into system (1), solved, and the residual ρ_1 is calculated:

$$\rho_1 = \frac{1}{n}\left\{\frac{\sum_{i=1}^{k}[\tilde{u}(t_i,a_1,b_1,c_1,...)-u_i]^2}{\sum_{i=1}^{k}u_i^2}+\frac{\sum_{i=1}^{k}[\tilde{v}(t_i,a_1,b_1,c_1,...)-v_i]^2}{\sum_{i=1}^{k}v_i^2}+\right.$$
$$\left.+\frac{\sum_{i=1}^{k}[\tilde{w}(t_i,a_1,b_1,c_1,...)-w_i]^2}{\sum_{i=1}^{k}w_i^2}+...\right\}^{1/2}. \quad (14)$$

Now we should check whether there will be $\rho_1 \approx \rho$. If that is the case, then the required parameters were found (these are a_1, b_1, c_1, ...), and the problem was successfully solved.

End of calculations.

If $\rho_1 > \rho_0$, the iteration is not counted, the value of μ should be increased (approximately by 1.5 times) and it is necessary to return to the beginning of solution (13). Occasionally, the ratio $\rho_1 > \rho_0$ suddenly appears in the course of calculations after the first iteration. Then the procedure for increasing μ can help restore convergence and stability. If μ has reached an excessively large value (exceeding 2), this indicates an error in the formulation of the problem.

End of calculations.

On the other hand, if $\rho_1 < \rho_0$, but still $\rho_1 > \rho$, then $\mathbf{p}_1$ is taken as $\mathbf{p}_0$ and ρ_1 as ρ_0. Then it is necessary to reduce the quantity μ (multiplying it by 0.6–0.9) and start the next iteration: construct SLAE (6) again, etc.

Iterations are carried out until S stabilizes and ρ_1 becomes approximately equal to ρ.

Example solutions of inverse problems of ODE systems

In this section, two well-known models that can be called classical are considered as examples. The fourth-order Runge–Kutta method with a posteriori error estimation [8, 9] was used in this work to numerically solve system (1).

Brusselator model of autocatalytic reaction (Model I). The Brusselator model [13] was initially created by Prigogine and Lefever as a computational experiment, i.e., to find and establish a reasonable physico-chemical mechanism of periodic biochemical reactions. Subsequently, the model made it possible to study the properties of dissipative structures in various nonlinear systems, including those of a non-chemical nature. The model does not relate to any specific reaction, therefore, the values of all rates of the hypothetical intermediate stages of the reaction were fitting parameters, selected so that the solutions of the model equations exhibited an oscillatory behavior.

The ODE system proposed in the [13] has the following form:

$$\left.\begin{aligned}\dot{x} &= a-(b+1)x+x^2y;\\ \dot{y} &= bx-x^2y\end{aligned}\right\}.$$

The variables $x(t)$ and $y(t)$ are proportional to the concentrations of the substances participating in the reaction and can be measured experimentally. The values of parameters a and b were assumed to be unknown.

The error of the model experimental data for the time functions $x(t)$ and $y(t)$ was taken as about 5% for this example. The starting approximations for the values of parameters a_0 and b_0 were selected by trial and error. As a result, $a_0 = 1.0$; $b_0 = 2.5$ were taken. The deviation of $x_0(t)$ and $y_0(t)$ from the experimental data amounted to 97% (Fig. 1, *a*, *b*).

The results of the algorithm after 18 iterations are shown in Fig. 1, *c*, *d*: the found parameter values were $a = 1.09$; $b = 3.16$; the error did not exceed 1.3% (model values of 1.1 and 3.2), which can be accepted as a good result.

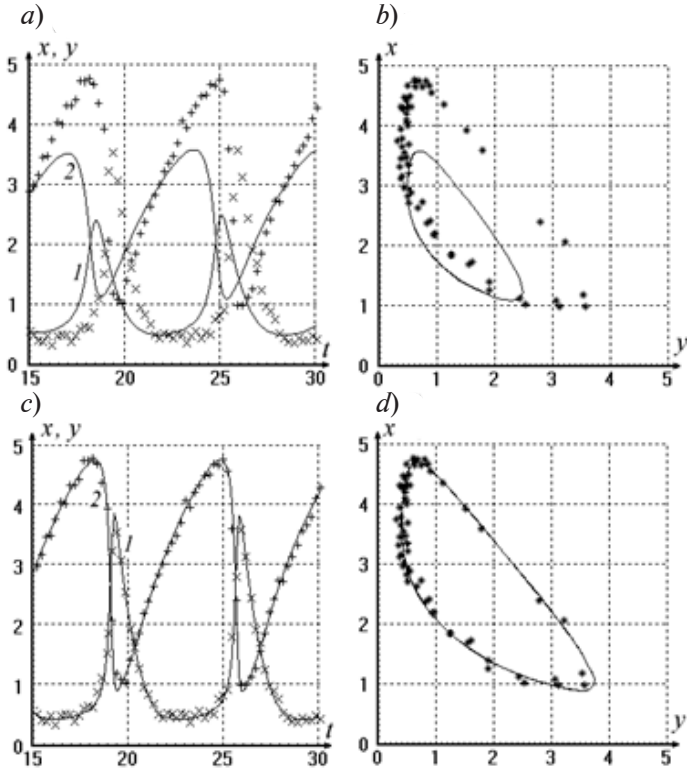

Fig. 1. Solution of inverse problem of ODE system for model I with respect to $x(t)$ (curves *1*) and $y(t)$ (curves *2*); the graphs show the experimental data (symbols) and calculation results (lines): variables calculated from the initial parameter approximations (*a*); limit cycle plotted from the experimental data and from the initial approximations (*b*); variables with optimal values of parameters and experimental data (*c*); limit cycles plotted from variables with optimal values of parameters and from the experimental data (*d*)

The above example shows that if there is experimental data on the time dependence of the concentrations of reagents and products of a particular reaction, it is possible to quantify the rates of the intermediate stages of this reaction (which is the essence of an indirect experiment), establishing the mechanism of their course based on this.

Oregonator model of periodic reaction (Model III). This model was proposed by Field and Noyes in [6] and is a good example of the simplified models mentioned in Introduction. It describes the mechanism of an entire class of reactions such as the Belousov–Zhabotinsky reaction including about 80 different stages. Reducing such a complex reaction to a system of only three equations for the concentrations of the principal reagents, the authors inevitably had to subdivide the entire range of intermediate reactions into a small number of complexes with some effective rates; attempts to refine these reaction rates are still made with varying success [5]. However, the purpose of this example was not to study the reaction itself but to identify the advantages of the algorithm proposed in this paper compared with algorithms used by other authors to solve the inverse problem of the same ODE system.

The corresponding system of equations takes the following form [6]:

$$\left.\begin{aligned} \dot{x} &= a(x + y - qx^2 - xy); \\ \dot{y} &= 2hz - y - xy; \\ \dot{z} &= (x - z)/2 \end{aligned}\right\}. \qquad (15)$$

The initial values of the parameters, selected by trial and error, were:

$$a_0 = 30.0;\ q_0 = 0.005;\ h_0 = 1.0.$$

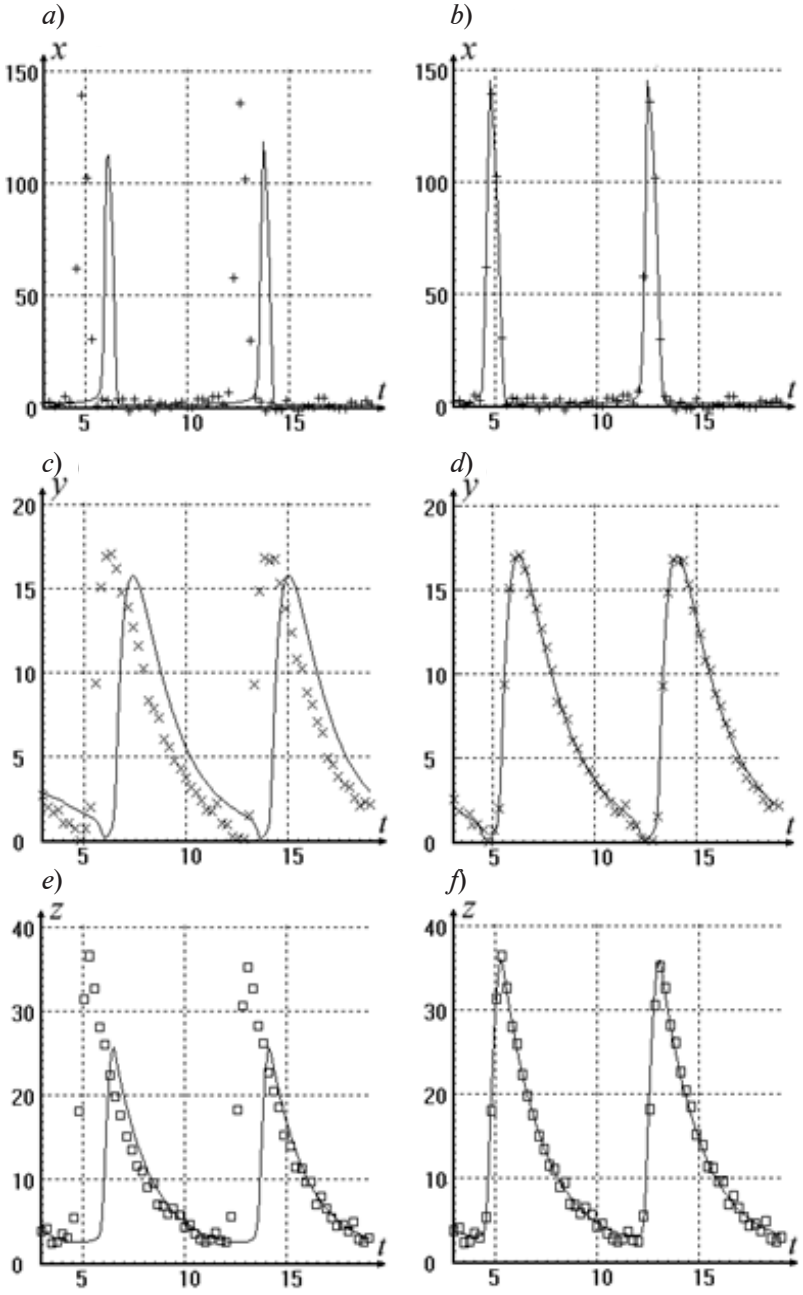

Fig. 2. Example solutions of inverse problem of ODE system (model II): experimental values (symbols) and components of solution of system (15) with initial approximations of parameters (lines) (*a, c, e*); comparison of components of solution of system (15) with optimal values of parameters (lines) found with experimental data (symbols) (*b, d, f*)

The input error of the experimental data was about 5%. The deviation of the initial variables $x_0(t)$, $y_0(t)$ and $z_0(t)$ from the experimental data was 84% (Fig. 2, *a*, *c, e*). The results of the algorithm are shown in Fig. 2, *b*, *d*, *f*. After 21 iterations, we obtained:

$$\boldsymbol{\rho}_1 = 5.17\%;\ a = 34.6;\ q = 0.0059;\ h = 0.758;$$

the deviations of the parameters from the model values ($a = 33.3$; $q = 0.006$; $h = 0.75$) are no more than 3.9%, which can be accepted as a good result.

It is important to note that the accuracy of the results obtained by the method for solving the inverse problem of ODE systems proposed in this paper turned out to be of the same order as

the experimental data (this is also true for Model I) and significantly exceeds the accuracy of the above-mentioned results obtained by the direct Hooke–Jeeves method used in [5] for the same Oregonator model.

Both examples given here show that the presented algorithm for solving the inverse problem of ODE systems without analytical solutions can yield satisfactory accuracy for indirect measurements of the values of the parameters included in these ODE systems.

Results and discussion

If only one parameter a is unknown in the inverse problem of ODE system, then instead of the (rather complex) linearization algorithm presented above, it is advisable to minimize the quantity

$$S = \sum_{i=1}^{k} [\tilde{u}(t_i, a) - u_i]^2 + \sum_{i=1}^{k} [\tilde{v}(t_i, a) - v_i]^2 + \sum_{i=1}^{k} [\tilde{w}(t_i, a) - w_i]^2 + \ldots \to \min_a,$$

using a simpler golden ratio algorithm [9], which, of course, should include the algorithm for solving system (1). It is common to try to avoid iterative solution of the direction problem by searching in the solution of inverse problems, due to the duration of the calculation and the unsatisfactory accuracy of the solutions obtained. However, in the case of a single unknown parameter, the golden ratio method combines fast convergence with good accuracy of the parameter value. On the other hand, the approach proposed in this paper is preferable for two or more parameters, since the golden ratio method turns out to be unsuitable, and other methods for solving inverse problems based on repeatedly solving the direct problem by searching over a multidimensional grid require much time while the accuracy of the results remains mediocre.

There are problems where it is required to calculate not the constant values of the parameters included in the ODE system but an unknown function $f(t)$, which is also part of ODE system (1) not related to the components of its solution. Then, if it is possible (for example, for physical considerations) to represent this function as a dependence on a finite number of parameters $f(t, a, b, \ldots)$, then the proposed method for solving the inverse problem of ODE system can be applied and the numerical values of these parameters can be determined as described above.

It should also be noted that the solutions of ODE systems are very sensitive to parameter values. On the one hand, this complicates the choice of initial parameter values guaranteeing reliable convergence of the method (however, the preconditioning and regularization included in the proposed method significantly improve its convergence). On the other hand, such sensitivity makes it possible to consequently achieve good accuracy in calculating the required parameters even with noticeable errors in the experimental data.

REFERENCES

1. **Frame M.,** Mathematical models in the biosciences. Vol. I, CT, Yale University Press, New Haven, USA, 2021.

2. **Viana M., Espinar J. M.,** Differential equations: A dynamical systems approach to theory and practice (Book Ser. "Graduate Studies in Mathematics". Vol. 212). The American Mathematical Society, Providence, USA, 2021.

3. **Alvey Ch., Alvey D.,** Mathematical biology discrete and differential equations, CRC Press, Boca Raton, FL, USA, 2024.

4. **De Maria E. (Ed.),** Systems biology modelling and analysis: Formal bioinformatics methods and tools, John Wiley & Sons, Inc., Hoboken, New Jersey, USA, 2022.

5. **Ikramov R. D., Mustafina S. A.,** The algorithm of search of rate constants of oscillating reaction to the example of the Belousov–Zhabotinsky reaction, Bashkirskiy Khimicheskiy Zhurnal [Bashkir Chemical Journal]. 22 (1) (2015) 87–91 (in Russian).

6. **Field R. J., Noyes R. M.,** Oscillations in chemical systems. IV. Limit cycle behavior in a model of a real chemical reaction, J. Chem. Phys. 60 (5) (1974) 1877–1884.

7. **Hooke R., Jeeves T. A.,** Direct search solution of numerical and statistical problems, Journal of the ACM. 8 (2) (1961) 212–229.

8. **Städter Ph., Schälte Y., Schmiester L., et al.,** Benchmarking of numerical integration methods for ODE models of biological systems, Sci. Rep. 11 (1; Jan. 29) (2021) 2696.

9. **Kalitkin N. N.,** Chislennyye metody [Numerical methods], Publ. BHV-Petersburg, St. Petersburg, 2011 (in Russian).

10. **Sun Z. Z., Sun Y., Wang X. R., et al.,** Self-sustained current oscillations in superlattices and the van der Pol equation, Appl. Phys. Lett. 87 (18) (2005) 1821100–1821102.

11. **Marquardt D. W.,** An algorithm for least-squares estimation of nonlinear parameters, J. Soc. Indust. Appl. Math. 11 (2) (1963) 431–441.

12. **Yudin N. E.,** Modified Gauss–Newton method for solving a smooth system of nonlinear equations, Comput. Res. Model. 13 (4) (2021) 697–723 (in Russian).

13. **Prigogine I., Lefever R.,** Symmetry breaking instabilities in dissipative systems. J. Chem. Phys. 48 (4) (1968) 1695–1700.

СПИСОК ЛИТЕРАТУРЫ

1. **Frame M.** Mathematical models in the biosciences. Vol. I. New Haven, CT, USA: Yale University Press, 2021. 544 p.

2. **Viana M., Espinar J. M.** Differential equations: A dynamical systems approach to theory and practice. Book series: “Graduate Studies in Mathematics”. Vol. 212. Providence, USA: American Mathematical Society, 2021. 536 p.

3. **Alvey Ch., Alvey D.** Mathematical biology discrete and differential equations. Boca Raton, FL, USA: CRC Press, 2024. 378 p.

4. **De Maria E. (Ed.)** Systems biology modeling and analysis: Formal bioinformatics methods and tools. Hoboken, New Jersey, USA: John Wiley & Sons, Inc., 2022. 464 p.

5. **Икрамов Р. Д., Мустафина С. А.** Алгоритм поиска констант скоростей колебательной реакции на примере реакции Белоусова – Жаботинского // Башкирский химический журнал. 2015. Т. 22. № 1. С. 87–91.

6. **Field R. J., Noyes R. M.** Oscillations in chemical systems. IV. Limit cycle behavior in a model of a real chemical reaction // The Journal of Chemical Physics. 1974. Vol. 60. No. 5. Pp. 1877–1884.

7. **Hooke R., Jeeves T. A.** Direct search solution of numerical and statistical problems // Journal of the Association for Computing Machinery (JACM). 1961. Vol. 8. No. 2. Pp. 212–229.

8. **Städter Ph., Schälte Y., Schmiester L., Hasenauer J., StaporP. L.** Benchmarking of numerical integration methods for ODE models of biological systems // Scientific Reports. 2021. Vol. 11. No. 1. January 29. P. 2696.

9. **Калиткин Н. Н.** Численные методы. Серия: «Учебная литература для вузов (BHV)» СПб.: Изд-во БХВ-Петербург, 2011. 592 с.

10. **Sun Z. Z., Sun Y., Wang X. R., Cao J. P., Wang Y. P., Wang Y. Q.** Self-sustained current oscillations in superlattices and the van der Pol equation // Applied Physics Letters. 2005. Vol. 87. No. 18. Pp. 1821100–1821102.

11. **Marquardt D. W.** An algorithm for least-squares estimation of nonlinear parameters // Journal of the Society for Industrial and Applied Mathematics. 1963. Vol. 11. No. 2. Pp. 431–441.

12. **Юдин Н. Е.** Модифицированный метод Гаусса–Ньютона для решения гладкой системы нелинейных уравнений // Компьютерные исследования и моделирование. 2021. Т. 13. № 4. С. 697–723.

13. **Prigogine I., Lefever R.** Symmetry breaking instabilities in dissipative systems // The Journal of Chemical Physics. 1968. Vol. 48. No. 4. Pp. 1695–1700.

THE AUTHOR

GOLOVITSKII Alexander P.
Peter the Great St. Petersburg Polytechnic University
29 Politechnicheskaya St., St. Petersburg, 195251, Russia
alexandergolovitski@yahoo.com
ORCID: 0000-0003-4292-0959

СВЕДЕНИЯ ОБ АВТОРЕ

ГОЛОВИЦКИЙ Александр Петрович – *доктор физико-математических наук, профессор Высшей инженерно-физической школы Санкт-Петербургского политехнического университета Петра Великого.*
195251, Россия, г. Санкт-Петербург, Политехническая ул., 29
alexandergolovitski@yahoo.com
ORCID: 0000-0003-4292-0959

Received 25.02.2025. Approved after reviewing 04.03.2025. Accepted 04.03.2025.
Статья поступила в редакцию 25.02.2025. Одобрена после рецензирования 04.03.2025. Принята 04.03.2025.