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ON SOLVING BIOLOGICAL PROBLEM BASED ON FUNCTIONAL-DIFFERENTIAL EQUATIONS OF DELAY TYPE WITH DISCRETE EXPERIMENTAL DATA

Abstract: The article is devoted to modeling the regulatory mechanisms of biological systems based on functional-differential equations with delayed argument with discrete experimental data as a initial conditions. Approximate method for the initial functions on the basis of discrete values of a biological experimental data is considered. Results show that under certain conditions during mathematical description of biological processes by functional-differential equations with delayed argument, we can plan in advance the necessary amount of experiments.

Key words: mathematical model, regulatory mechanisms, biological systems, functional-differential equations, experimental data.

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Introduction

In mathematical modeling of the regulatory mechanisms of complex, interconnected systems, such as living systems, it is very important to choose a class of mathematical equations that have an "native" ability to oscillate modes of solutions, as well as suitable for modeling biosystems in normal conditions, anomalies, and when there is exist sudden activity death [1, 2]. Such equations are functional differential equations with a delayed argument, constructed on the basis of the methods of regulating living systems [3, 4]. Functional differential equations of regulatory mechanisms of biological systems are not integrated and obtaining exact solutions is generally impossible [1-9]. Using methods of qualitative analysis allows us to identify the general

properties of solutions, to determine the characteristic stationary solutions and the existence of periodic solutions. Solutions can be obtained with the required accuracy based on the implementation of the model on a computer [6-10]. To solve the equations of the regulatory mechanisms of biological systems, it is necessary to set the initial conditions on a segment of length h [11-14]. This is rather difficult for models of biological systems due mainly to discreteness of experimental data. As a result of this, the question arises of approximating the initial functions on the basis of discrete values of the variable equations and obtaining approximate solutions for their finite number. Obtaining solutions of differential equations with high accuracy allows us to study the basic laws of the behavior of solutions based on methods of

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qualitative analysis and selective numerical solutions on a computer.

STATEMENT OF A PROBLEM

The use of functional differential equations with a delayed argument in the modeling of biological systems involves an analysis of the general patterns of solutions based on the theory of qualitative analysis and the most accurate assessment of solutions near critical points, where, depending on the values of the parameters, qualitative changes in the behavior of the model can occur. Let $M(m_1,...,m_n)$ be the point of interest to us in the phase space. Then the equations of the regulatory mechanisms of biological systems in an infinitely small neighborhood M can be linearized by expanding the right-hand side in a power series and taking into account only linear deviations from the point M. We introduce small $z_i(t)$

$$X_i(t) = m_i + z_i(t), \qquad i = 1,2,...,n$$

for which the general equations of the regulatory mechanisms of biological systems have the following form:

$$\frac{dz_i(t)}{dt} = A_i^n(M + z(t-h))e^{-\sum_{j=1}^{n}(m_i+z_i(t))} - b_i m_i - b_i z_i(t), \quad (1)$$

where

$$A_i^n(M + z(t-h)) = \sum_{j=1}^{n} \sum_{k_1..k_j=1}^{j} \prod_{m=1}^{j}(m_i + z_i(t-h)).$$

$$1 = 1,2,...,n$$

After consecutive calculations we

$$\frac{dz_i(t)}{dt} = \sum_{j=1}^{n} \alpha_{ij} z_j(t-h) - b_i z_i(t) + q_i, \qquad (2)$$

where α_{ij} $(i,j = 1,2,...,n)$ are constants expressed in terms of parameters (1), and

$$q_i = A_i^n(M)e^{-\sum_{j=1}^{n} m_j} - b_i m_i. \qquad (3)$$

If to replace in (2)

$$u_i(t) = z_i(t)e^{-b_i(t)},$$

then we obtain the following equations in an infinitesimal neighborhood of the point M of the phase space.

$$\frac{du_i(t)}{dt} = \sum_{j=1}^{n} \alpha_{ij} u_j(t-h) + q_i$$
$$i = 1,2,...,n \qquad (4)$$

If M is not an equilibrium of the equations of the regulatory mechanisms of cell communities, then by (3) we have $q_i \neq 0$ $(i = ,2,...,n)$. The considered "biological" problem for differential-delay equations (3) allows, under the indicated conditions, solutions to be obtained from the point values of the desired functions. We study some questions of obtaining approximate solutions of inhomogeneous, linear differential-delay equations with for a limited number of specified point values of the desired functions.

THE PROBLEM DECISION

Let us consider the following equation

$$\frac{du_i(t)}{dt} = a(t)u(t-h) + q(t). \qquad (5)$$

Let the boundary conditions be given in the following form:

$$U(t_0-kh) = U_k. \quad k = 0,1,2,... \qquad (6)$$

here $t_0 = Ph$ and $P > 1$, where P is positive.

We introduce the following notation: let $u_0(t)$ be a solution (5) satisfying the boundary conditions:
$$u(Ph - kh) = u_k, \qquad k = 0,1,2,... .$$

and let $u_p(t)$ be a solution (5) satisfying the following boundary conditions:

$$u(kh) = u_k, \qquad k = 0,1,2,..P$$
$$u(-kh) = 0. \qquad k = 0,1,2,...$$

We consider the behavior of the approximate solution $u_p(t)$ of equation (5) under boundary conditions (6) at $t \geq t_0$. Let $q(t)$ be a continuous function in $(-\infty,\infty)$ and $|/q(t)| < M$, and the function $a(t)$ has in $(-\infty,\infty)$ all derivatives and

$$\left|\frac{d^n a(t)}{dt}\right|_{t \in (-\infty, h)} < N^{n+1}$$

$$n = 0,1,2,..$$
$$|u_k| < L. \quad k = 0,1,2,...$$

Then for $[t_0+kh, t_0+(k+1)h]$ $(k= 0,1,2, ...)$ we obtain:

$$\left|u_0(t) - u_p(t)\right| \leq (1+Mh)^k (e^{Mh} - Mh)\frac{L(Mh)^{p+1}}{(p+1)!}.$$

Indeed, the function $r_p(t) = u_0(t) - u_p(t)$ satisfies the equation

$$\frac{dr_p(t)}{dt} = a(t)r_p(t-h)$$

and the following boundary conditions
$$r_p(kh) = 0, \qquad k = 0,1,2,..P.$$
$$r_p(-kh) = u_{p+k}, \qquad k = 0,1,2,...$$

At $t \in [t_0,t_0+h]$ we have:

$$r_p(t) = \sum_{n=p+1}^{\infty} \frac{u_n\left[\int_0^t a(\theta)d\theta\right]...\left[\int_0^t a(\theta)d\theta\right]}{n!}.$$

Consequently:

$$r_p(t) = \sum_{n=p+1}^{\infty} \frac{L(Mh)^n}{n!} \leq \frac{L(Mh)^{p+1}}{(p+1)!}\left(1 + \frac{Mh}{p+2} + \frac{(Mh)^2}{(p+2)(p+3)} + ...\right)$$

we obtain

$$|r_p(t)| \le \frac{L(Mh)^{p+1}}{(p+1)!}(e^{Mh} - Mh).$$
$$t_0 \le t \le t_0 + h$$

For $[t_0+h, t_0+2h]$ we have:

$$r_p(t) = r_p(t_0 + h) + \int_{t_0}^{t} a(\theta) r_p(\theta - h) d\theta.$$

and

$$|r_p(t)| \le |r_p(t_0)| + Mh \cdot \max |r_p(t-h)| \le (1+Mh)(e^{Mh} - Mh)\frac{L(Mh)^{p+1}}{(p+1)!}$$
$$t_0 + h \le t \le t_0 + 2h$$

Thus, after sequential integration, we obtain:

$$|r_p(t)| \le (1+Mh)^k (e^{Mh} - Mh)\frac{L(Mh)^{p+1}}{(p+1)!}$$

at $[t_0+kh, t_0+(k+1)h]$.

Let us consider approximate solutions for the system of equations

$$\frac{du_i(t)}{dt} = \sum_{j=1}^{n} a_{ij}(t)u_j(t) + q_i(t). \qquad (7)$$

$i = 1,2,...,n$

Let $q_i(t)$ be continuous on $(-\infty,\infty)$ and $|q_i(t)| < N$, $k = 0, \pm 1, \pm 2 \ ...$ and the functions $a_{ij}(t)$ have derivatives of all orders on $(-\infty,\infty)$ and

$$\left|\frac{d^m a_{ij}(t)}{dt^m}\right|_{t \in (-\infty,h)} < M^{n+1}.$$

$i,j = 1,2,...,n$
$m = 0,1,2,..$
Let's also we have

$u_i(t_0-kh) = |U_{ik}| < L.$
$k = 0,1,2,...; \ i = 1,2,...,n; \ t_0 = Ph \ (p>1).$
Then for $[t_0+kh, t_0+(k+1)h] \ (k = 0,1,2,...)$ we obtain:

$$|u_{oi}(t) - u_{pi}(t)| \le (1+nMh)^k (e^{Mh} - Mh)\frac{n^n L(Mh)^{p+1}}{(p+1)!},$$

where u_{0i}, u_{pi} are exact and approximate solutions (7). Since the functions

$$r_{pi}(t) = u_{0i}(t) - u_{pi}(t), \qquad i = 1,2,...,n$$

satisfy the system of equations

$$\frac{dr_{pi}(t)}{dt} = \sum_{j=1}^{n} a_{ij}(t)r_{pi}(t-h)$$

$i = 1,2,...,n$
and the following boundary conditions
$r_{pi}(kh) = 0, \qquad k = 0,1,2,..P.$
$r_{pi}(-kh) = u_{p+ki}, \qquad k = 0,1,2,...$
$i = 1,2,...,n$
we obtain:

$$r_{p_i}(t) = \sum_{n=p+1}^{\infty} \frac{\sum_{l_1l_2...l_j=1}^{n} u_{l_jp+j} B_0^t(p, p+j)}{j!}.$$
$$t_o \le t \le t_o + h$$

Then

$$|r_{p_i}(t)| \le \frac{n^n L(Mh)^{p+1}}{(p+1)!}(e^{Mh} - Mh).$$

Having carried out similar sequential integrations as in the previous case, we have:

$$|r_{p_i}(t)| \le (1+nMh)^k (e^{Mh} - Mh)\frac{n^n L(Mh)^{p+1}}{(p+1)!}.$$

DISCUSSION

These studies show that approximate solutions to the biological problem for differential-delay equations can most effectively be applied in the immediate vicinity of the initial point t_0. If the permissible error of the solution is given in $[t_0, t_0+h]$, then, using the proved inequalities, we can determine the smallest number of boundary conditions necessary for this. This allows for the mathematical description of biological processes by functional-differential equations with delayed argument, under certain conditions, to plan in advance the necessary amount of experimental data.

Indeed, let some biological process be described by the system of differential-delay equations (7) and experimental data can be obtained at the points $t_0, t_0 - h, t_0 - 2h,...$. It is required to determine the required number of experimental points for the mathematical description of the process on the time interval $[t_0, t_0+T]$ up to a certain $\varepsilon > 0$.

The required number of experimental points can be determined from the following relation:
$|r_{pi}(t)| < \varepsilon$
$t \in [mh, (m+1)h], \quad$ где $\ m = [T/h]$
or

$$(1+nMh)^m (e^{Mh} - Mh)\frac{n^n L(Mh)^{p+1}}{(p+1)!} < \varepsilon.$$

By entering the notation

$$k = \frac{(1+nMh)^m (e^{Mh} - Mh)n^n L}{\varepsilon}, \qquad (8)$$

We obtain
$$\frac{(p+1)!}{(Mh)^{p+1}} > k.$$
Keeping in mind, that

$$(p+1)! = \left(\frac{p+1}{e}\right)^{p+1}\sqrt{2\pi(p+1)},$$

we have

$$\left(\frac{p+1}{Mhe}\right)^{p+1} > \frac{k}{\sqrt{2\pi(p+1)}} . \qquad (9)$$

Thus, the required number of experimental points (p) can be determined using the following equation:

$$\sqrt{2\pi(p+1)}\left(\frac{p+1}{Mhe}\right)^{p+1} - k = 0 . \qquad (10)$$

Consider an example. Let the process be described by the following equation

$$\frac{du(t)}{dt} = 9\sin tu(t-1) + q(t) \qquad (11)$$

and it is required to determine the necessary number of experimental points that allow one to obtain solutions on $[t_0, t_0+10]$ with an accuracy of 10^{-4} . We calculate k from (8). Then equation (10) has the form:

$$\sqrt{2\pi(p+1)}\left(\frac{p+1}{Mhe}\right)^{p+1} = \frac{10^{10}(y^9-9)}{10^{-4}} .$$

An analysis of this equation shows that the minimum number of experimental points that make it possible to obtain a solution on $[t_0, t_0+10h]$ with an accuracy of 10^{-4}, is not more than 48.

An important task, when we realizing differential-delay equations on a computer, is to determine the initial functions. In this case, $T = h$ ($m = 1$). Therefore, to estimate the amount of necessary data in order to obtain the initial function with the required accuracy of 10^{-q} , we have

$$\sqrt{2\pi(p+1)}\left(\frac{p+1}{Mhe}\right)^{p+1} = \alpha 10^q ,$$

where

$$\alpha = (1+nMh)^m(e^{Mh} - Mh)n^nL .$$

Then for q we obtain

$$q = \frac{1}{2\alpha}\log(2\pi(p+1)) + \frac{p+1}{\alpha}\log\frac{p+1}{Mhe},$$

which shows a very rapid increase in the degree of accuracy with an increase in the amount of data.

Conclusion

Thus, the studies results for some aspects during applying differential-delay equations for the mathematical description of biological processes show that in many cases when it is impossible to reliably determine continuous experimental curves on the initial segment of length h, effective results can be obtained with using the biological problem formulated above for differential-difference equations with a delayed argument, taking into account the specific character of biological data.

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