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MATHEMATICAL MODELING OF CRITICAL PHENOMENA IN BIOMEDICAL SYSTEMS

Abstract. The methods of mathematical modeling of critical phenomena in multicomponent systems, which have the prospect of use in modern biomedical and gene technologies, are considered. The proposed method involves modeling the studied system by systems of equations containing potential functions of the system state using a differential topological approach. The purpose of the modeling is to determine the stability spaces, bifurcations and spaces of simultaneous coexistence of several phases of the studied system. The simulation results can be used to analyze the stability of the studied system under different operating conditions.

Keywords: mathematical modeling, phase coexistence spaces, differential topological approach, theory of catastrophes.

Relevance of research. Modern methods of mathematical modeling make it possible to effectively solve a wide range of theoretical and practical problems of studying the stability of the states of multicomponent systems, which have the prospect of being used in modern biomedical and genetic technologies [1 – 7]. A special place in the current epidemiological crisis in the world is occupied by studies aimed at studying the stability of new drugs, viruses and other objects that are complex multicomponent systems or exist as part of systems [8]. In this regard, the study of the problem of self-organized and orderly structures in multicomponent compounds used in medicine and biosystems is of great interest. Fields of application of modern biomedical technologies, which include multicomponent compounds, on the one hand, require high stability of work in various external conditions. On the other hand, the phase states of viruses and other biosystems under different conditions of existence are interesting. Assessments of the state of multicomponent systems make it possible to predict the probability of loss of stability in relation to fluctuations in composition and external conditions and the appearance of metastable or unstable states. Modern methods of computer modeling make it possible to analyze such special states, build appropriate models based on the differential-topological approach, and predict the behavior of multicomponent systems. The involvement of computer modeling for the analysis of the processes of appearance of ordered structures that are self-organized, allows calculating multidimensional phase diagrams that take into account the possibility of the existence of bifurcation spaces, critical spaces and spaces of coexistence of phases of different orders. In this regard, a mathematical model is proposed, which, based on the formation of potential functions describing the energy state of the system, makes it possible to create a basis for the following description of the processes of the emergence of self-organized ordered structures [1, 4]. Modeling of such processes opens up the possibility not only of the purposeful synthesis of new systems in biomedical engineering, when the conditions correspond to the unstable state of the system, but also opens perspectives (in understanding the problem of self-organized formation of ordered structures) for the analysis of the stability of biosystems and multicomponent compounds under various conditions of existence and operation. Therefore, performing an analysis of the possibility of the existence of bifurcation spaces, critical spaces, and spaces of coexistence of phases of different orders to describe the processes of self-organization is a relevant component of the general analysis of the phase diagram of the state of a multicomponent biosystem or compound.

Solving the problems of mathematical modeling of processes that lead to critical phenomena in multicomponent systems is associated with a number of fundamental difficulties of both a design and computational nature. In this sense, it should be noted first of all: the limited amount of experimental data on the occurrence of multidimensional phases, the non-stationary and non-linear nature of the studied functions that model the expression for the free energy of the system; the complexity of the topology of the modeling area spaces; limited data for determining energy parameters of interaction between parts of the system; the unwieldyness of higher-order derivative expressions and, as a result, the complexity of constructing and analyzing block matrices of partial derivative components. It is natural that qualitative solving of the problems of mathematical modeling of the processes of occurrence and forecasting of critical phenomena in multicomponent biosystems, taking into account the above-mentioned problems, is possible only on the basis of the use of modern modeling approaches and the development of new methods that allow solving the problems of predicting the behavior of complex, multicomponent systems.

The practical application of known methods of mathematical modeling of processes that cause loss of stability in biosystems is limited by the lack of consideration of the possibility of the appearance of several simultaneously coexisting phases, insufficient efficiency and universality of these systems, which is caused by the action of a complex of contradictions:

– with the recent significant increase in the capabilities of modern tools, the reduction of their cost, the distribution of free software and the expansion of its fields of application in mathematics, a significant amount of theoretical work in the field of mathematical modeling, there is a lack of development of a mathematical apparatus for the analysis of determinants of multidimensional matrices, which is extremely necessary for the analysis of higher derivatives of multicomponent functions;

– with the existing software for solving computer algebra problems, which allows obtaining analytical expressions of complete derivatives of multidimensional functions, there are no means of an analytical approach to solving nonlinear differential equations;

– in the presence of models that describe the states of biosystems, it is impossible to use these models as primary ones in the process of improving existing modeling systems and adapting them to predict critical phenomena;

– with the existing amount of experimental data on determining the properties of biosystems, there is a limitation of data on the interaction parameters between individual components of the system;

– with the growing needs of modern biomedical engineering to expand the range of applied problems to be solved, there is a limitation of opportunities in choosing effective models in specific cases of analyzing the stability of a particular system.

Expanding the capabilities of modern equipment for researching the structure of biosystems enables the observation and study of processes of formation of coexisting phases, which leads to interest in their mathematical formalization based on a differential topological approach [4]. The differential topological approach, based on the analysis of determinants of matrices of partial derivatives of multidimensional functions, makes it possible to build such mathematical models that make it possible to obtain zero contours of determinants in the space of concentrations of components of compounds synthesized in biomedicine, according to temperature and other intersections, and this, in its in turn, ensures a high level of adequacy of the nature of the observed physical phenomena: the presence of spaces corresponding to the stability of the system and its loss; limits of phase equilibrium; spaces of coexistence of phases of different orders; appearance of metastable states under certain conditions; existence of spaces where biosystems exist and spaces where they cannot exist; the occurrence of the composition ordering effect.

A wide range of fundamental theoretical works and practical studies of domestic and foreign scientists devoted to the study of critical phenomena in multicomponent systems is known (for example, the works of: I. Prigozhin, A.G. Khachaturyan, G.F. Voronin, K. Onabe, D.De Fontaine, P. Henoc, Cann J.W., Hillard J.E. and others), as well as the use of models of complex physical phenomena that can cause the loss of stability of multicomponent systems, including those based on the differential topological approach (in particular, the works of K. Okada, A.K. Singh, A. Laugier, K. Karkkainen). In addition, at the present time, there are more and more works that involve mathematical methods for predicting the properties of systems in biomedical and genetic engineering [2, 3, 5, 7, 8]. However, the issues of building mathematical models for predicting the appearance of spaces of coexistence of several phases at the same time, ordering and appearance of spaces of coexistence of phases of different orders, especially those observed in biosystems and multicomponent compounds synthesized according to modern medical technologies, as well as instrumental software tools that allow you to implement the specified classes of models.

The above-mentioned tasks determine the relevance of involvement in forecasting the states of multicomponent compounds, biosystems, and natural biosystems synthesized by genetic and biotechnologies, and necessitate the development of methodological foundations for the construction of modeling systems for the formation of spaces of coexistence of phases of different orders in multicomponent systems based on model support in the form of systems of equations and inequalities between the values of the determinants of the matrices of partial derivatives of the free energy of the system, as well as automated complexes for solving applied problems of mathematical modeling and forecasting of the specified critical phenomena.

Modification of the properties of multicomponent compounds and biosystems, according to the phase transformations of the specified type, can undergo both during synthesis and during existence in various external conditions. The successful and purposeful use of these effects for multicomponent compounds and biosystems requires appropriate theoretical analysis and experimental research. This situation leads to the need for special research and modeling of phase formation processes that occur under different conditions of existence of biosystems and the use of multicomponent compounds in medical technologies.

The aim of the study. The purpose of the research is to create models and a method of numerical modeling of the processes of emergence in multicomponent systems of spaces of phase coexistence based on the provisions of the theory of catastrophes and the application of a differential topological approach, as well as the development of computer modeling tools that provide effective solutions to applied problems in research and practical use of a wide class of technological processes of synthesis of multicomponent compounds in biomedical technologies and prediction of their behavior during operation under external conditions.

To achieve the research goal, the following tasks are solved:

– the analysis and systematization of existing experimental and calculation data is carried out regarding the appearance of effects associated with the appearance of composition ordering in multicomponent systems and the appearance of spaces for the coexistence of phases of different orders.

– developed mathematical methods for calculating the spaces of coexistence of phases of order two, three and four in three- and four-component compounds within the framework of a model that takes into account the interactions between the components of the first two coordination spheres of the systems and the model that takes into account the interactions between the components of the first three coordination spheres;

– developed software that implements the proposed mathematical models;

– a method of numerical modeling of the processes of emergence in multicomponent systems of spaces of phase coexistence has been developed.

Basic research materials. The equations of state forming the basis of the model were built on some n-dimensional concentration space [1, 4, 6]. A situation in which one stable state of the system coexists with another stable state was considered a criterion for determining the spaces of phase coexistence. The process of the emergence of such a space is a phase transition of the first kind according to Maxwell's principle. In this case, two or more global minima of the system state function will have the same depth. Within the investigated phase space, under certain conditions, bifurcation subspaces can appear in which a stable phase can become unstable. Critical spaces of order 2 can arise under conditions where two different phases become identical. Critical spaces of order 3 and 4 are formed, respectively, in the presence of three or four identical phases.

According to the provisions of Tom’s theory of catastrophes and the generalization of Landau’s theory of phase transitions to the case of an n-dimensional concentration space, the conditions for the existence of regions of a stable phase were obtained [1, 4]:

$$\frac{dF}{dX} = 0; \quad \frac{d^2F}{dX^2} > 0 \tag{1}$$

and first-order instability regions or bifurcation spaces according to the conditions:

$$\frac{dF}{dX} = \frac{d^2F}{dX^2} = 0; \quad \frac{d^3F}{dX^3} > 0\,. \tag{2}$$

The condition for the existence of a critical space of the second order:

$$\frac{dF}{dX} = \frac{d^2F}{dX^2} = \frac{d^3F}{dX^3} = 0; \quad \frac{d^4F}{dX^4} > 0\,. \tag{3}$$

The condition for the existence of a critical space of the third order:

$$\frac{dF}{dX} = \frac{d^2F}{dX^2} = \ldots = \frac{d^5F}{dX^5} = 0; \quad \frac{d^6F}{dX^6} > 0\,. \tag{4}$$

The condition for the existence of a critical space of the fourth order:

$$\frac{dF}{dX} = \frac{d^2F}{dX^2} = \ldots = \frac{d^7F}{dX^7} = 0; \quad \frac{d^8F}{dX^8} > 0\,. \tag{5}$$

In conditions (1)–(5), F is a function simulating the free energy of the system, X is the concentration of the corresponding components.

For practical implementation, the work developed models of 3- and 4-component systems, taking into account the interaction between the components of different coordination spheres. The practical interpretation of calculated results becomes more useful when the spaces of phase coexistence on the phase diagrams of ternary systems are specified through the concentrations of binary components, i.e. through the concentrations of pairs of components of X_{AC} and X_{BC}, where the symbols A, B and C denote the components of the corresponding species. At the same time, at each point of the concentration space, it is necessary to demand a normalization condition, according to which the sum of the concentrations of pairs must be equal to one:

$$X_{\mathrm{AC}} + X_{\mathrm{BC}} = 1\,. \tag{6}$$

For a graphical representation of the locations of the zero contours of the free energy derivatives and the spaces of phase coexistence in four-component systems of the type $A_xB_{1-x}C_yD_{1-y}$ on the cross-section of the existence of solid solutions of the state diagram, it was proposed to write the expressions for the concentrations of binary components through the concentration parameters x and y ($0 < x < 1$, $0 < y < 1$):

$$X_{AC} = (1-x)(1-y),\ X_{AD} = (1-x)y,\ X_{BC} = x(1-y),\ X_{BD} = xy.. \tag{7}$$

The free energy of the system was presented in the paper as the sum of the contributions of the free energy for the binary components of the system, the free energy of the ideal mixture of the system components, without taking into account the interaction between the components and the components taking into account the deviation of the free energy from the energy of the ideal system [1, 4]:

$$F = \frac{1}{2}\sum_{i=1}^{2} F_i + F^{id} + \Delta F^{ex}\,. \tag{8}$$

where F_i is the free energy for pure binary components; F^{id} – free energy of an ideal system without taking into account the interaction of components; ΔF^{ex} – deviation of the value of free energy from the energy of an ideal system.

Conclusion

According to the provisions of Tom's theory of catastrophes, as well as the generalization of Landau's theory of phase transitions to the case of an *n*-dimensional concentration space, a mathematical model of critical phenomena in multicomponent compounds was built.

In accordance with the proposed mathematical model of critical phenomena and on the basis of a differential topological approach, a method was developed and its algorithm for predicting the occurrence of critical spaces and spaces of phase coexistence of different orders in multicomponent systems was implemented.

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