

COMPUTER MODELING OF BIOTECHNOLOGICAL PROCESSES AND SYSTEMS

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Abstract. The article presents the fundamentals of computer modeling of biotechnological processes. The kinetics of microorganism growth is studied depending on reducing substances and temperature. The physical laws that determine the processes associated with heat propagation, the Fourier law and Newton's equation, which describes the surface temperatures of a solid and a flow, are formulated. The analysis of reducing substances, heat exchange and concentration of microorganisms is considered based on a mathematical model of the fermentation process.

Key words: biotechnology, heat exchange, thermal conductivity, secondary metabolism products, reducing substances, specific growth rate of microorganisms, limiting factors, metabolic processes, enzymatic reaction, nutrients, convective heat transfer, isothermal surface.

Biotechnological processes involve living cells, subcellular structures or enzymes and their complexes isolated from cells. This affects the processes of mass exchange (exchange of substances between different phases - transfer of oxygen from the gaseous phase to the liquid) and heat exchange (redistribution of thermal energy between the interacting phases). Therefore, one of the most important mechanisms of the apparatus is the mixing system, which ensures uniformity of conditions in the apparatus. The biotechnological process creates aerobic conditions required for the cultivation of microorganisms. Therefore, in certain cases, it is necessary to supply oxygen and remove the resulting gaseous products of a different kind, primarily CO₂. Aeration systems are often very complex in design, since they must ensure a balance between the consumption of O₂ and its supply in the required quantities, taking into account the fact that the need for oxygen is not the same at different stages of cultivation. The article discusses aspects of computer modeling of biotechnological processes and systems. The paper presents a classification of mathematical models, their structure, properties and basic definitions that help to determine the goals and objectives of computer modeling and its role in the study of complex biotechnological systems. The paper presents ideas about the main stages of computer modeling. Particular attention is paid to fundamental models of microorganism growth, accumulation of metabolic products and

changes in substrate concentration during biotechnological processes. The influence of various environmental factors on the kinetics of these processes is assessed. The basis of the modern cybernetic approach to solving problems of analysis and synthesis of biotechnological objects is systems analysis. The essence of systems analysis is determined by its strategy, which is based on general principles applicable to solving any systems problem. Computer modeling itself is the process of constructing a model of a real object and setting up computational experiments on this model in order to either study the behavior of this system or evaluate the efficiency of various algorithms for its functioning, using computational logical algorithms implemented on computers. Thus, the process of computer modeling includes both the construction of a model and its application to solve a given problem: analysis, research, optimization or synthesis (design) of biotechnological processes, devices and systems.

In the process of computer modeling, the researcher deals with three objects: a system, a mathematical model, and a computer program that implements the algorithm for solving the model equations. The traditional scheme of computer modeling as a single process of constructing and studying a model with appropriate software support can be presented as a set of stages.

Microbiological synthesis is a process that occurs with the participation of microorganisms and is accompanied by the formation of biomass. The target product of biosynthesis is either the biomass itself or various substances produced by microorganisms during their life activity. The main stages of the biosynthesis process - the growth of microorganisms and the accumulation of biomass - occur in devices that most often operate periodically.

In gas or liquid flows, the transfer of matter is carried out both due to direct contact of molecules and their interaction, and due to the transfer of matter by liquid particles - conglomerates of molecules - moving from one point of a given environment to another. The influence of one or another mechanism is mainly determined by the hydrodynamic conditions of the process. The mechanism of transfer within each phase is directly related to the hydrodynamics of a single-phase flow, while the mechanism of transfer across the phase interface is related to the hydrodynamics of a two-phase flow. Therefore, in the macro transfer of matter, the vortex motion of the liquid is of great importance, since vortices are carriers of energy and matter in the flow. During the movement of the liquid, some physical quantities change, by which the process of movement itself can be assessed. A change in a physical quantity can generally occur both at a given point over time and when moving from one point in space to another. Numerous experimental and theoretical studies expand and deepen our understanding of the process. However, despite significant success, at all levels of mathematical modeling there remain a number of important unsolved research

problems. At the kinetic level, the kinetic model of the process needs to be refined and clarified. It is also necessary to supplement the scheme of biochemical transformations with stages that take into account the regularities of the process. With both periodic and continuous organization of the process, the flow movement has a character. The structure of the flows in the apparatus, i.e. complete displacement, complete mixing or their combination determines the choice of a mathematical model of the process, including equations describing the dynamics, as well as boundary and initial conditions and other characteristics of the process. The compilation of a mathematical model in each particular case is carried out in accordance with the systems approach to the process. The process is divided into elementary stages located in hierarchical order. At the first level of the mathematical model, dependencies are usually located that describe the equilibrium conditions, as well as the nature of biochemical transformations. At the second hierarchical level, the patterns of elementary transfer processes occurring in a single microorganism, in one drop, bubble, etc. are described. The third level corresponds to modeling the process of hydrodynamics, heat and mass exchange phenomena in the entire apparatus, including the dependencies of the second level.

A mathematical model of a technological process is created for a targeted study of the process mechanism as a whole or for studying its individual aspects or phenomena, such as, for example, the transfer of heat, mass, momentum. Therefore, when developing a model, individual processes or phenomena taking place in a specific modeling object are first analyzed.

Mathematical models are a description of processes in a real object using mathematical equations, including differential equations. Computers are currently widely used to implement mathematical models. With the help of computer technology, so-called computer modeling is carried out. In this case, you can easily change the time scale, speed up or slow down the process. With the help of computer technology, you can solve complex equations and predict the course of fermentation processes.

Based on the above, mathematical modeling of any biotechnological process, apparatus or system comes down to assessing the rate of biochemical processes, which is determined by the rate of biochemical activity of micro-objects depending on one or more parameters of the environment that ensures the flow of metabolic processes.

The description of a set of biochemical processes is a biochemical model of the process. The study of biochemical kinetics provides a kinetic model of the process, which describes the dependence of the reaction rates included in the biochemical model on the temperature and concentrations of the reagents.

Meanwhile, during the process, there is a regular change in the kinetic characteristics of growth, biosynthesis of the metabolic product, and consumption of the substrate. All

these changes are subject to certain kinetic dependencies, which are essentially the basis of the theory of the process of cultivating microorganisms and the biosynthesis of metabolic products and are the objects of study of the kinetics of fermentation processes.

The kinetics of biotechnological processes studies the patterns of change in the growth rate of microorganisms and the biosynthesis of metabolic products depending on the current concentrations of substrates, biomass, metabolic products, temperature and pH of the environment. Let us consider the kinetic patterns of biotechnological processes in more detail. The most common equations describe the kinetics depending on the concentration of only one substrate, which is called limiting; other substrates are assumed to be in excess and do not affect the growth rate.

The simplest kinetic model follows from the very definition of the specific rate of change μ of the concentration of substance C and has the form

$$\frac{dC}{dt} = \mu C \quad (1)$$

This model implicitly assumes that the value of μ is constant here, but this is not the case – it strictly depends on the concentration of the substrate. The task is to find this dependence. Depending on the type of microorganism, as well as the substrate, the relationship $\mu(S)$ can have a very different character.

Moser's model has the form

$$\mu = \frac{\mu_m S^K}{K_s + S^K},$$

where K is a new parameter, and $K > 1$.

Andrews' model takes into account inhibition by elevated substrate concentrations and is described by the equation

$$\mu = \frac{\mu_m S}{K_s + S + S^2 / K_i}.$$

This equation differs from the Monod equation by the presence of a quadratic term with a new kinetic parameter in the denominator. The Monod model consists of the enzymatic kinetics of biochemical transformations occurring in cells, and is widely known:

$$\mu = \frac{\mu_m S}{K_s + S},$$

Where μ_m - maximum growth rate when there is no secondary metabolism (waste of microorganisms after consumption of substances) of microorganisms, h^{-1} , K_s - const.

Then formula (1) takes the form

$$\frac{dC}{dt} = \mu_m \frac{S}{K_s + S} C.$$

The Monod model is based when there is no secondary metabolism of microorganisms in the process.

The model which takes into account the inhibition with secondary metabolisms of microorganisms and is described by the equation

$$\mu = \mu_m \frac{k_{ps}}{k_{ps} + S_0 - S}.$$

This model is based on the fact that the consumption of substances by microorganisms is proportional to secondary metabolism.

In this regard, this paper examines the patterns of change in heat transfer in fermentation processes.

Heat transfer is possible in three different ways: conduction, convection and radiation.

Thermal conduction is the transfer of heat during direct contact of bodies (or parts of one body) with different temperatures. This process can be imagined as the spread of heat from particle to particle in the absence of their movement. In its pure form, thermal conductivity is observed in solids, and in liquids and gases - only in the absence of convective currents in them.

Convective heat transfer, possible only in liquids and gases, occurs as a result of the movement of their particles in the volume. Depending on the cause causing the movement of liquid or gas particles, a distinction is made between convective heat exchange with free convection and with forced convection. Free convection involves the movement of particles caused solely by the difference in density of liquid or gas in different parts of the volume they occupy due to the difference in temperature. Convection is called forced when the movement of liquid or gas particles occurs under the action of external forces (pumping, compressors, etc.).

Radiant heat exchange is the process of heat transfer in the form of electromagnetic waves, accompanied by the transformation of thermal energy into radiant energy and vice versa from radiant to thermal energy.

In technology, the above-mentioned methods of heat exchange are rarely encountered in isolation: most often we have to deal with a combination of two or even all three methods in their sequential or simultaneous action. A special place is occupied by heat exchange accompanied by a change in the aggregate state of the bodies participating in this process (evaporation of liquid, condensation of vapors). There are two cases of heat exchange: heat transfer and heat transmission. Heat transfer is the process of heat exchange between a solid body (for example, the wall of an apparatus) and a liquid or gas in contact

with it. Heat exchange between liquids, gases, liquid and gas separated by a wall is called heat transfer.

Let us formulate the physical laws that determine the processes associated with the spread of heat.

Fourier's law. Amount of heat dQ , transferred by heat conduction through the cross-sectional area S isothermal surface of the body during time $d\tau$ is expressed by the basic equation of heat conduction

$$dQ = -\lambda S \frac{dT}{dn} dt, \quad (2)$$

The negative sign on the right side of the equation is a consequence of the temperature drop in the direction of heat transfer. Proportionality coefficient λ in the equation is called the thermal conductivity coefficient, λ [Вт/(м·град)]. It is expressed by the amount of heat transferred in 1 s through 1 m² of the body surface with a temperature gradient of 1 °C per 1 m of the length of the normal to the isothermal surface. The value λ depends on the nature of the substance, being its individual property. Numerical values of λ are determined empirically. The value of λ varies greatly for different substances, and for the same substance it depends on temperature, density, structure, humidity and other factors.

Newton's equation. Heat flow

$$\frac{dQ}{dt} = \alpha (T_c - T) S,$$

Where T_c , T - temperature of the surface of a solid body and flow, respectively; α is the heat transfer coefficient, W/(m² deg).

The heat transfer coefficient α expresses the amount of heat given off by a unit of surface $S=1$ m² per unit of time $t=1$ s with a temperature difference of $(T_s-T)=1$ deg. Note that α is not a constant value, but depends on many parameters, primarily on the hydrodynamic situation near the heat-giving surface.

The amount of heat that must be imparted to a homogeneous body in order to increase its temperature by ΔT is equal to

$$Q = cm\Delta T = c\rho V\Delta T,$$

where c is the specific heat capacity, J/(kg · deg); m is the mass of the body, kg; ρ is the density of the body, kg/m³; V is the volume of the body, m³. The nature of the temperature distribution in biotechnological processes is extremely important when analyzing the processes occurring in it, since temperature is one of the main parameters of the technological process. Firstly, the state of biochemical equilibrium and the maximum achievable degree of growth of microorganisms depend on temperature. Secondly, the rate of biochemical reactions depends on temperature

$$\mu(T) = k_0 \exp \left(-\frac{E}{R} \left(1 - \frac{T}{T^{omn}} \right)^2 \right),$$

Where, k_0 - kinetic constant, h^{-1} ; E - activation energy, $\Delta J / (K \cdot \text{моль})$; T^{omn} - temperature corresponding to the maximum growth rate, K; R - universal gas constant, $R = 8,31 \Delta J / (K \cdot \text{моль})$; T - temperature of the nutrient medium, K.

Violation of uniform temperature distribution in fermentation processes can lead to undesirable side effects, to destructive disturbances of the process.

Temperature distribution by the volume of the apparatus occurs due to the processes occurring in it, the supply of air to the apparatus for which it is necessary to maintain dissolved oxygen in the nutrient medium, heat exchange of the apparatus with the environment, as well as due to the accompanying release of heat by microorganisms. This means that biotechnological processes in the apparatus occur under isothermal conditions. Therefore, to determine heat release in the studied aerobic processes, the method of calculation by secondary indirect parameters is used $\Delta H = 3,38 \cdot \alpha_1$ - Where, a α_1 - stoichiometric coefficient for dissolved oxygen, kg/kg.

The hydrodynamic situation in the apparatus has a significant impact on the nature of the temperature distribution. For example, in an ideal displacement apparatus, all process parameters, including temperature, are the same at any point in the apparatus at a given time. On the contrary, in a displacement reactor, the temperature may be different at different points in the apparatus. The intensity of mixing also affects the intensity of heat exchange in the apparatus.

The mathematical model consists of systems of equations for the material, thermal and final product, of which the first takes into account the change in the amount of substance, the second - the change in the temperature of the nutrient medium, the third - the amount of concentration of microorganisms during the fermentation process.

$$\begin{cases} \frac{\partial S}{\partial t} = D(S_0 - S) - \alpha^S \mu(S, T, C_o) X \\ c\rho \frac{\partial T}{\partial t} = -\frac{\alpha}{l}(T - T_b) - 2\frac{\alpha_{cm}}{r}(T - T_{og}) + \Delta H \cdot \mu(S, T) \cdot X \\ \frac{\partial X}{\partial t} = -DX + \mu(S, T) \cdot X \\ \mu(S, T, C_o) = \mu_m \frac{C_o}{k_0 + C_o} \frac{k_{ps}}{k_{ps} + S_0 - S} \exp \left(-\frac{E}{R} \left(1 - \frac{T}{T^{omn}} \right)^2 \right) \end{cases} \quad (4)$$

with initial conditions

$$T(0) = T_0, S(0) = S_0, X(0) = X_0,$$

Where, X – concentration of microorganism biomass, kg/m^3 ; T_b – air temperature, K ; α , α_{cr} – heat transfer coefficients of the nutrient medium and the apparatus wall from the environment, $\text{Вт}/(\text{m}^2 \cdot K)$; c – specific heat capacity of the nutrient medium, $\text{Дж}/(\text{кг} \cdot K)$; ρ – density of the nutrient medium, kg/m^3 ; l , r – length and radius of the device, m ; D – dilution rate of the nutrient medium, ч^{-1} ; μ , α^S – specific rates of biomass accumulation and consumption of limiting substrates, respectively, ч^{-1} ; S – concentration of limiting substrates, kg/m^3 ; t – time, h .

Computer experiments to study the dynamics of the main variables of the state of the resulting model of a continuous mode for biomass production show that the behavior of the system is divided into two typical periods – some time from the beginning of the calculation, a transient process is observed, after which the system enters a stationary mode of operation.

Thus, the mathematical model of the state of the process allows obtaining significant information about the fermentation process in bioreactors based on the identification of quantitative patterns between the influencing and output parameters, and allows predicting its results under non-stationarity conditions.

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