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MODELING OF MICROBIAL SYNTHESIS PROCESSES CONSIDERING INOCULUMS IMMOBILIZATION IN POROUS NANOSTRUCTURED MEDIA

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Abstract. The results of analytical relationships refinement based on the system of differential equations application of material balance for microbiological synthesis batch process are presented. Improved technique for solving the system is based on the definition of *potential energy* batch of microbiological synthesis and *new formula of specific growth rate* of microorganisms' biomass concentration.

1. Introduction

The problem of modeling the production of microbial biomass is merely a special case of the more general problem of modeling any product production process. Indeed, the general problem of modeling the production process of a product expressly or implicitly contains two components: the modeling of the production process of the product itself and modeling of the profit dynamics on the production products sales (the economic component). The framework of the project didn't aim to model the process of microbial biomass sales, that is the economic component was ignored, which is generally a limiting assumption (but only from the point of view of the economy), as the economic component has a significant impact on production.

Results presented below allow simulating the process of production of biologicals in the idealized case, where no restrictions are placed on output. The approach implemented for solving the general problem of modeling the production process (including the economic component), is based on a *new concept in the interpretation of the system of differential equations of material balance* for periodic processes of microbiological synthesis. Typically, the economic component of the manufacturing process modeling for some products is studied within the *theory of production functions* course. Applying this theory is limited by constructing the product manufacturing empirical relationship of time and production predefined factors (see, e.g. [1]). In deeper studies optimization techniques taking into account the constraints on the production factors are used.

Mathematical model of the fermentation process can be written as a system of differential equations of material balance for basic measurement in the output variables experiment: the concentration of microbial biomass, substrates, and metabolic products. Of the material balance differential equations for the entire system, which we do not present here since they are well known [2, 3]; in this paper we are interested only in two equations (explanation will be given below). They are the basic material balance equation:

$$X'(t) = (\mu(t) - \frac{F(t)}{V(t)})X(t) \quad (1)$$

and the equation:

$$V'(t) = F(t). \quad (2)$$

In Equation (1), *X(t) is* the concentration of microbial biomass, *V(t)* is the volume of the cultural liquid in the apparatus (without gas content), *μ(t)* is the specific growth rate of the microorganisms biomass concentration

$$F(t) = \sum_{i=1}^{k} F_{i0}(t) - F_{H_2O} .$$

In this formula, $F_{i0}(t)$ is the volumetric flow rate of the *i*-substrate added to the unit, and F_{H2O} represents the rate of evaporation and drop entrainment. Function *F(t)* is called the flow rate of the nutrient medium. Culture liquid is solution nutrient medium and inoculum.

The remaining equations appearing in the system of differential equations of material balance [2<1] are not informative, as they are special because of physical and chemical constants appearing in these equations. In other words, equations excluded from consideration are simply empirical relationships (in terms of practical use) and there is no need to reproduce them.

Indeed, the physical-chemical "constants", in fact, may be functions of time and other parameters of the fermentation process. When we say that some physical quantity is taken to be constant, it simply means that it is slightly variable (usually meaning a weak variability is not specified). Depending on the equation structure, averaging physical variable quantity can lead to distortion of the physical meaning of a solution. Any record, where there are both an unknown function and physical "constants" that may also depend on other factors of the production process, can't be called "a law", as we get an equation with a variety of not recorded and physically not interpretable factors.

On the other hand, equations (1) and (2) are general in nature and may be useful in studying the growth of production products and in other areas of industry and science. Equations (1) and (2) contain three unknowns:

1. *X(t)* - the microbial biomass concentration,
2. *V(t)* - the volume of the culture liquid in an apparatus,
3. *μ(t)* – the specific growth rate of microorganisms biomass concentration.

It is obvious that the volume of the culture liquid in the *V(t)* apparatus is the fermentation process *potential energy*. All that is needed is to determine the specific growth rate *μ(t)* and we obtain for a microbial biomass production process a physically meaningful law.

Interpretation of material balance equations (1) and (2) for the production process of any product is now obvious. It is suffice to interpret the variable *V(t)* in equation (1) as a potential energy of *production product X(t).* This is the main novelty of the approach proposed and in the study of the microorganisms' biomass production process. Thus, the key to study differential mass balance equation (1) is a formula for a specific growth rate of the microorganisms' biomass concentration.

There are numerous narrowly focused researches, where various physical constants associated with the operation of a fermenter and their influence on the fermentation process are studied with a particular purpose. There is no need in studying the interactions of these physical constants, since the problem of optimizing and increasing the microorganisms biomass production (or optimizing the production of any other product) consists in constructing a mathematical model for the dependence of product production (in this case, the microorganisms' biomass) on time and the predefined industrial unit performance (fermenter). Of course, in the production of mathematical models physical constants can also be present and they have to be determined. However, this is clearly formulated purposeful mathematical problem, which is called the *inverse problem* of the mathematical model of production.

In modern mathematics, the solution of inverse problems received much attention, as many modern technologies in industrial production are based on their solution. It is important to mention that the mathematical model of the production of microbial biomass taking into account the time and performance of the industrial unit is much more difficult than simpler models (1) and (2) that depends only on time.

Onwards we present the technique for solving the simplest inverse problem for a system of differential equations (1) and (2). For solving the inverse problem, we rewrite the formula for the specific growth rate in the following form

$$\mu(t) = \frac{\sigma X'(t)}{X(t)V(t)}, \tag{3}$$

where a constant factor σ is to be determined.

Now the formulation of the inverse problem for equation (1) can be reduced to the classical one. Let the concentration of microbial biomass is known at certain points of time (or each point of time.) It is necessary to determine the volume of the culture liquid in the apparatus (potential energy) and the factor σ, i.e., *the ratio* in equation (1).

On the basis of a new concept in the interpretation of the basic material balance equation (1) the following physical characteristics of the fermentation process were introduced:

- Potential of biomass concentration;
- Deformation of the cultural liquid volume in the apparatus;
- Deformation volume tension of cultural liquid in the apparatus;
- Volume deformation change of the cultural liquid in the apparatus;
- Transport coefficient of the nutrient solution;
- Change in the density of the inoculum;
- *Rate of natural increase in population;*
- *Coefficient of internal struggle in the seed population.*

Some of these physical properties after the corresponding change in terminology can be transferred to any other production product.

As a graphic illustration, the results of a natural experiment regarding the concentration of microbial biomass, which were specially interpolated with a polynomial, are shown. The scale factors in graphic pictures were chosen arbitrarily. It is important to note that this interpretation of the proposed method of microbiological synthesis modeling batch is also possible for describing periodic processes of any product production.

2. Specific growth rate and the physical principles of the fermenter operation

The volume of the cultural liquid in the device V is the potential energy of the fermentation process. Changing the potential energy of a system when moving from an arbitrary position P_0 in an arbitrary position P_1 is gives the work

$$A = V(t_0) - V(t_1).$$

Solving the system of equations (1) and (2) relative to the volume of the cultural liquid in the apparatus and at $V(t_0) = c_0$, we find (using formula (3)) that

$$V(t) = \frac{c_0 C_0 - c_1 C_1}{C_0 - C_1} + \frac{C_0 C_1 (c_1 - c_0)}{C_0 - C_1} \frac{1}{X(t)}. \quad (4)$$

The specific growth rate of microorganism biomass concentration can be written as

$$\mu(t) = \frac{X'(t)}{\frac{C_0 C_1 (c_1 - c_0)}{c_0 C_0 - c_1 C_1} + X(t)}.$$

Graphical representation of the specific growth rate is shown in Fig. 1.

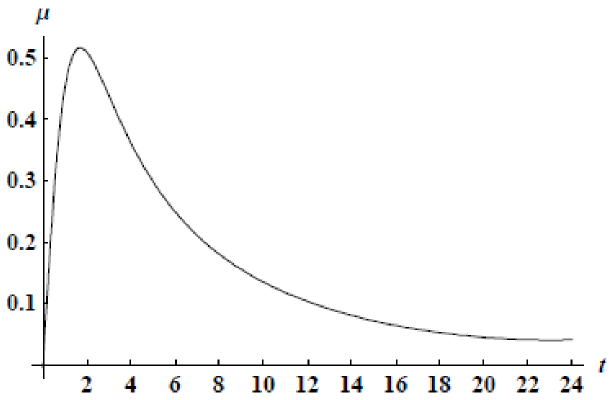


Fig. 1. Specific growth rate.

Consumption of nutrient medium F can also be expressed in terms of the microorganism biomass concentration at certain points of time as

$$F(t) = \frac{C_0 C_1 (c_0 - c_1)}{C_0 - C_1} \frac{X'(t)}{X(t)^2}.$$

The time interval where the concentration of microorganisms' biomass is a monotonic non-decreasing function and the consumption of the nutrient medium is negative, since $C_0 < C_1$, aand $X'(t) \geq 0$. In other words, the nutrient medium is consumed.

Note that the volume of cultural liquid in the apparatus is a monotonic non-increasing function, if the concentration of microorganism biomass is a monotonic non-decreasing function:

$V(t_1) \geq V(t_2)$, if $t_1 < t_2$.

Now the work of the fermenter can be rewritten as

$$\mathrm{A} = V(t_0) - V(t_1) = -\int_{t_0}^{t_1} F(\xi) d\xi = \frac{C_0 C_1 (c_1 - c_0)}{C_0 - C_1} \int_{t_0}^{t_1} \frac{X'(\xi)}{X(\xi)^2} d\xi. \quad (5)$$

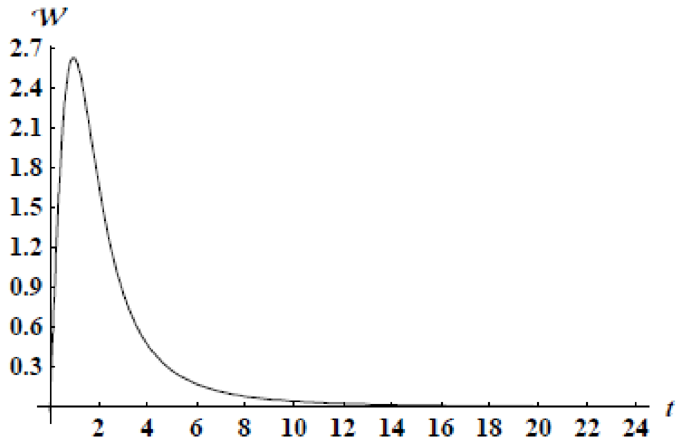
Formula (5) allows us to introduce new physical concepts. External force (in absolute value), acting on a volume of cultural liquid is

$$F(t) = \frac{C_0 C_1 (c_1 - c_0)}{C_0 - C_1} \frac{1}{X(t)^2}. \quad (6)$$

Potential biomass concentration W is the quantity characterizing the change (strain) state volume of cultural liquid in the apparatus, which is numerically equal to the consumption of nutrient medium with the opposite sign

$$W = \frac{C_0 C_1 (c_1 - c_0)}{C_0 - C_1} \frac{X'(t)}{X(t)^2}. \tag{7}$$

Graphical representation of potential biomass concentration is shown in Fig. 2.



Fig, 2. Potential biomass concentration.

Potential biomass concentration is the potential energy density a fermenter, and can be expressed as $\mathrm{A} = \int_{t_0}^{t_1} W(\xi)\mathrm{d}\xi.$ Let's call the function $\frac{X'(t)}{X(t)^2} = \frac{C_0 - C_1}{C_0 C_1 (c_1 - c_0)} W(t)$ strain deformation volume of cultural liquid in the apparatus. Let's call the value $\frac{C_0 - C_1}{C_0 C_1 (c_1 - c_0)}$ change in the deformation volume of the cultural liquid in the apparatus. The energy that effects on changing the volume of the cultural liquid in the apparatus internally is spent by chemical reactions that are formed under the influence of external forces (stirrer speed, feed rate of oxygen, temperature, pH, etc.)

Let us denote the stock of chemical energy per unit mass of the cultural liquid by *Q(t)*. Internal forces chemical reactions energy can be spent both to increase biomass concentration (microorganisms particles detach - the growth of microorganisms "living tissue"), and to decrease the concentration of biomass (microorganisms accession particles - withering away microorganisms "living tissue"). Chemical energy is spent on the construction of microorganisms living tissue, and the external forces are spent on transportation nutrient medium to the microorganisms living tissue and under favorable conditions, there is a growth of biomass.

Thus, if the deformation strain is a negative value, we can talk about conditional accession of certain amount of biomass as a result of the aging process of microorganism healthy cells because of adverse growth conditions.

Time t_0 is the occurrence of this event corresponds to the solution of the equation

$$X'(t_0) = 0. \tag{8}$$

Loss of potentially possible biomass equals

$$X(t_0) - X(t), t \geq t_0. \tag{9}$$

At time chemical energy is expended just to build living tissue microorganisms, and the external forces are spent only on transportation nutrient medium to the microorganism living tissue and due to the adverse conditions growth of biomass stops. If the nutrient medium is limited, the process of metabolism (aging and biomass decomposition) can begin. If the deformation strain is a positive value, then we can talk about the "microorganism disconnect particles" i.e. biomass growth.

3. Transporting the nutrient medium and the density of the seed culture

Growth of the seed culture is characterized by varying the concentration of biomass *X(t).* Nutrient medium transporting coefficient and the density of the seed culture in the time interval $0 \le t \le t_0$ is described by

$$k_3(t) = \nu \frac{\dfrac{C_0 C_1 (c_1 - c_0)}{C_0 - C_1}}{X(t)^2} - 3\gamma_1 \frac{X'(t)}{X(t)^2} = \nu \mathrm{F}(t) - 3\gamma_1 \frac{C_0 - C_1}{C_0 C_1 (c_1 - c_0)} W(t).$$

Graphical representation of the transporting coefficient is shown in Fig. 3.

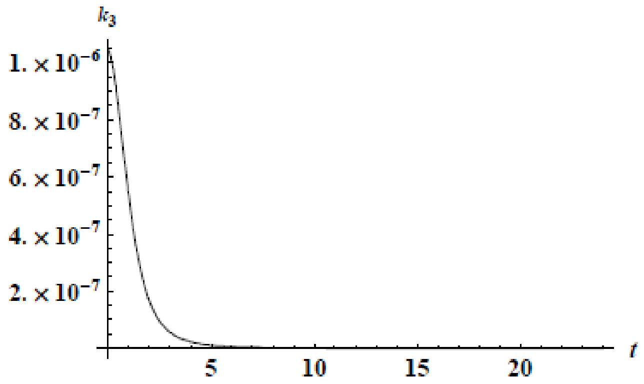


Fig. 3. Transporting coefficient.

From the balance equation we find simple law of the seed culture density change (Fig. 4):

$$\gamma(t) = \gamma_1 + \frac{\gamma_0 - \gamma_1 X(0)^3}{X(t)^3},$$

where γ_0 is the seed culture density at the starting moment of time.

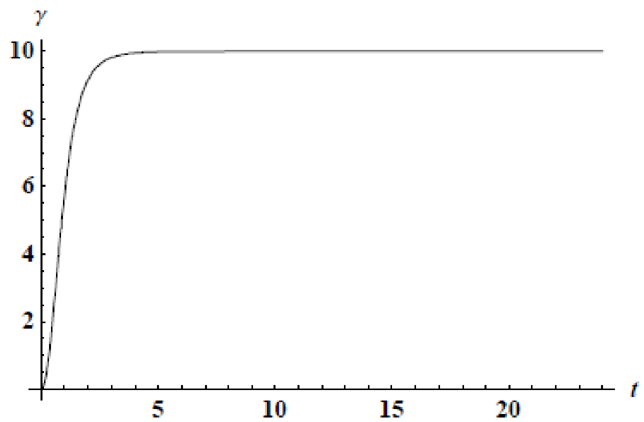


Fig. 4. Seed culture density.

4. Natural population increase and internal struggle coefficient in the seed population

In 1838 demographer P. Verhulst, based on the results of A.-L.-ZH. Ketle, his teacher and the famous Belgian statistics scientist, proposed a model for population growth, which was rediscovered in 1920 by Americans R. Perle and L. Reed. The model was named Verhulst-Pearl logistic growth model. The following is a description of *a general* Verhulst-Pearl law, and its output is based on the decision of the general Riccati equation with constant coefficients ($h \neq 0$):

$$y'(t) = fy(t)^2 + gy(t) + h.$$

Classical Verhulst-Pearl law is based on a solution of the simpler Riccati equation (h = 0):

$$y'(t) = fy(t)^2 + gy(t).$$

The solution of this equation was proposed by Verhulst [4-5], to describe *only* the microorganism-population-growth dynamics. As it was explained later (more than a hundred years later), this equation is of fundamental importance, and scenarios predicted within this equation were found in the description of some turbulent flow properties, as well as in research on laser physics, hydrodynamics and chemical reactions kinetics.

The essence of the Verhulst-Pearl law is that it expresses the concentration of microorganism biomass *X(t)* as a time function and only two physical values: the natural increase rate in population and the inner struggle coefficient in the seed culture population. That's enough to express all of the gained above dependences (e.g., the specific growth rate and the volume of cultural fluid in the apparatus) in terms of time, the natural increase rate in population and the coefficient of internal struggle in the seed population. Such representation simplifies qualitative study of the microorganism-biomass-concentration-behavior dynamics *X(t)* bringing it down to a foreseeable level. In some studies, the number of parameters is limited to one, i.e. to natural increase rate in population, considering it constant at a certain time interval. In the derivation of the *generalized* Verhulst-Pearl law the number of living microorganisms *Y(t)* in the colony inoculum is taken proportional to the biomass concentration $Y(t) = \wp X(t)$.

It is assumed that the seed colony exists in the real natural conditions i.e. competition within a population, the lack of space and food, transmission of infection because of density, etc. Thus, it is necessary to find an expression for the law of living microorganisms' total number changing in the colony seed.

Let's assume first, that the colony lives in ideal conditions, has unlimited resources and power is not suppressed by other species. Due to the natural processes of birth and death, the number of colony's living organisms varies over time: the increase is proportional to the number of adult members. Let *Y(t)* is the number of organisms at time *t*, and *Y(t + Δt)* is the number of living microorganisms at time *t + Δt*. Then for a time interval *Δt*. *Y(t)* function increment will be

$$Y(t+\Delta t) - Y(t) = \Delta Y.$$

For time *Δt* all adult members of the colony (or part of them) produce offspring, and some members of the colony may die. Then

$$\Delta Y = N - M, \tag{10}$$

where *N* is the birth number during the time Δ*t*, *M* is the death number during the time Δ*t*.

The number of births *N* depends on the time length Δ*t* (the greater Δ*t*, the greater *N*) and on the number of parents (the more the adult organisms are, the more offspring they produce), i.e. $N = F(Y, \Delta t)$, where the function F increases together with the increase of Y or Δt and is equal to zero, if one of these variables is equal to zero.

Leaving behind the output process rich in formulas, the required function *Y(t)* (*Verhulst-Pearl generalized law*) is described by

$$Y(t) = \frac{2\eta}{\Bbbk + \sqrt{\Bbbk^2 - 4\eta\lambda}} +$$
$$+\frac{e^{t\sqrt{\Bbbk^2-4\eta\lambda}}\sqrt{\Bbbk^2 - 4\eta\lambda}\left(-2\eta + X(0)(\Bbbk + \sqrt{\Bbbk^2 - 4\eta\lambda})\wp)\right)}{(-2\eta\lambda + (\Bbbk + \sqrt{\Bbbk^2 - 4\eta\lambda})(\Bbbk - X(0)\lambda\wp) + e^{t\sqrt{\Bbbk^2-4\eta\lambda}}\lambda\left(-2\eta + X(0)(\Bbbk + \sqrt{\Bbbk^2 - 4\eta\lambda})\wp)\right)}, \quad (11)$$

$$X(t) = \frac{Y(t)}{\wp}.$$

The law obtained expresses a microorganism biomass concentration through the correction coefficient η, the coefficient of internal struggle, the specific rate of natural increase in population and the proportionality coefficient $\wp$. This formula can be used to obtain other expressions for the specific growth rate and volume of cultural liquid in the apparatus at a *certain time interval*.

Verhulst-Pearl generalized law shows that in the *first approximation* the concentration of microorganism biomass can be considered as a function of time, the correction coefficient η, the coefficient of internal struggle, the specific rate of natural increase in population and the proportionality coefficient $\wp$. Therefore, by these physical values it is possible to examine all qualitative behavior pattern of the microorganism biomass concentration as a function of time. After conducting such a study the task of identifying the physical quantities can be assigned (see the introduction for a discussion of the inadvisability of considering other material balance equations, except (1) and (2)) associated with the work of the fermenter, which significantly affect the *change* in the coefficient internal struggle and a specific rate of natural increase in the concentration of microorganism biomass.

Below there is a sample calculation of the coefficient of self-poisoning and specific rate of natural increase in population. To simplify the calculations, we set η = 0. In the calculation of these coefficients we use the following sample values of biomass concentration of microorganisms first:

KOE = {{0, 7.1×10^7}, {4, 1.1×10^8}, {6, 2×10^8}, {8, 4.1×10^8}, {10, 4.2×10^8}, {12, 5.25×10^8}, {16, 6.3×10^8}, {20, 4.4×10^8}, {24, 2.8×10^8}},

corresponding fermenter operational characteristics are: $Q = 1$, $n = 50$, where Q is the oxygen supply speed and n is the rotational speed of a stirrer. Make *rational interpolation* of sampled values. Interpolation result is shown below

$$\frac{(-3.5973345\times10^{22} + 9.732114\times10^{21}t - 6.543201\times10^{20}t^2 - 1.7285288\times10^{19}t^3 + 3.7620313\times10^{17}t^4)}{(-5.066668\times10^{14} + t(1.888759\times10^{14} + t(-2.5582\times10^{13} + 1.4526134\times10^{12}t - 3.161519\times10^{10}t^2)))}.$$

Let's build the physical and mathematical model for the concentration dependence of microorganism biomass on time and height $2h$ fermenter. In this case, the concentration of microorganism biomass is a function $u(r,t,z)$ and is a solution of the mixed problem for the heat equation as follows: to find the heat propagation law in a circular cylinder of radius R and height $2h$, the initial temperature being equal to U_0 = const, and on the top of cylinder there are heat loses to the environment at a constant temperature U_1 = const.

It is required to solve the equation in the mathematical formulation

$$\partial_t u(r,t,z) = a^2(\partial_{r,r}u(r,t,z) + \frac{1}{r}\partial_r u(r,t,z) + \partial_{z,z}u(r,t,z)) + F(t),$$

with the following initial condition and boundary conditions on the lateral surface and the top of cylinder

$$u(r,0,z) = U_0, 0 \le r \le R, -h \le z \le h,$$

$$\partial_r u(r,t,z)_{r=R} = 0, -h \le z \le h, t > 0,$$

$$\partial_z u(r,t,z)_{z=h} = -q(u(r,t,h) - U_1), 0 \le r \le R, t > 0.$$

The presence of energy sources within the cylinder due to the fermenter with density *F(t)* is assumed.

The inverse problem is to determine the physical constants a^2, q and energy density *F(t)*, since the constants U_0 and U_1 we believe to be known. In calculating the coefficients a^2, q and energy density *F(t) sample values* obtained on the basis of *rational interpolation* are used. The average value of the direct problem (the variables *r and z*) as found by sampling the coefficients a^2, q and energy density *F(t)* is written below

$$mu(t) = 1.7620624\times10^{15} - 1.7620623\times10^{15}E^{-0.03622471t} - 6.386975\times10^{13}t + 1.1575347\times10^{12}t^2$$
$$-1.3979759\times10^{10}t^3 + 1.2588722\times10^8 t^4 - 862721.0397513t^5 + 3664.2611215t^6.$$

The average value of the *mu(t)* direct problem and sample data are shown in Fig. 5.

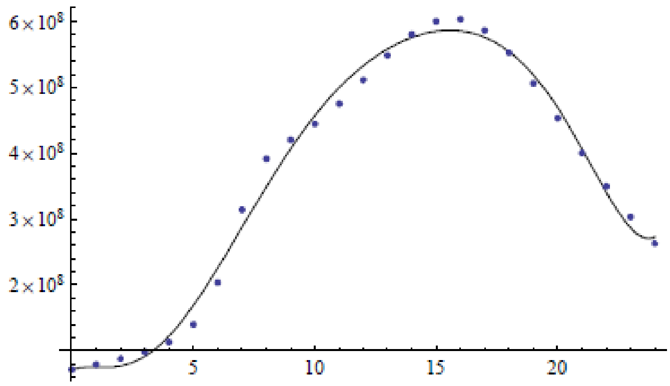


Fig. 5. Average value of the *mu(t)* direct problem and sample data.

Now we use the Verhulst-Pearl law to calculate the average specific rate of natural increase in population k. To do this, we remove the sample data with functions *mu(t)* with a time step of 1 hour and apply the least squares method to estimate parameters in a nonlinear Verhulst-Pearl model. Find average values $\lambda = 1.11018\times10^{-9}$ and $\Bbbk = 0.602537$. Then we write the Verhulst-Pearl law.

$$\frac{7.03781\times10^{15}E^{0.602537t}}{5.27863\times10^8 + 1.48746\times10^7 E^{0.602537t}}.$$

Apparent discrepancies between Verhulst-Pearl law and sample values in Fig. 6 may indicate two main reasons: first, the coefficient of specific rate of natural increase in the population *essentially depends on the time* and, second, the sample data were obtained with errors. There is, of course, a third possibility; it is incorrectly calculated local extremum. One reason for this may be defined limit of $\eta = 0$.

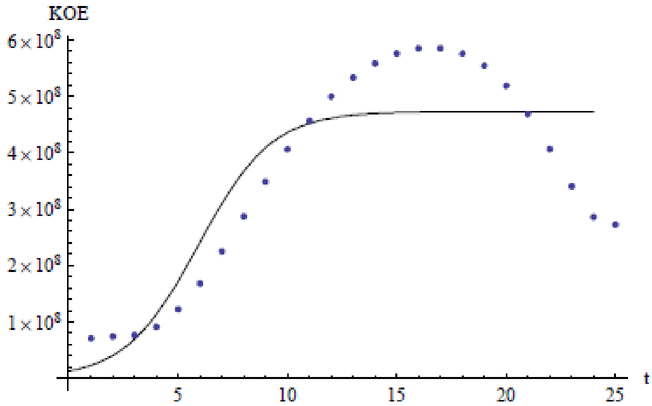


Fig. 6. Sample values and the Verhulst-Pearl law.

In the main applications the coefficient of specific rate of natural increase in the population essentially depends on time. This fact is also valid for this example. Rationale is given below. Based on the average specific rate of natural increase in population we find the coefficient of self-poisoning or internal struggle in the population of seed. To achieve this, it is sufficient to solve the equation

$$mu'(t) = \Bbbk mu(t) - \lambda(t)\wp mu(t)^2,$$

regarding unknown *λ(t)*, where *mu(t)* is the average value of the heat conduction direct problem. The results are presented in Fig. 7.

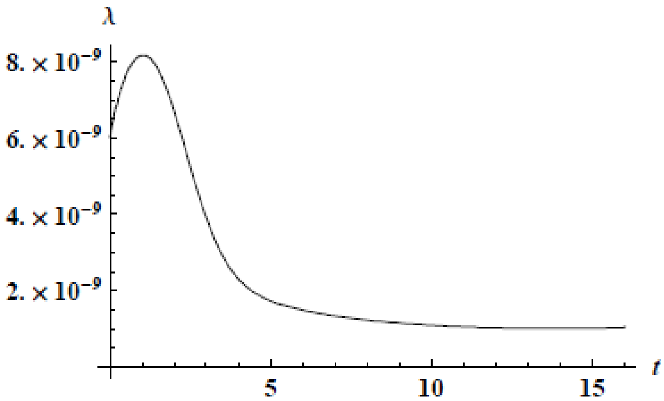


Fig. 7. *Inner struggle* coefficient $\lambda(t)$.

On the other hand, if we average internal struggle coefficient, that is, i.e. put $\lambda = 1.11018 \times 10^{-9}$, then according to the formula

$$\Bbbk(t) = \frac{mu'(t)}{mu(t)} + \lambda \wp mu(t)$$

we can find specific rate of natural increase in the population rate as a function of time. Type of this formula is similar to the *classical* formula for recording the specific growth rate. In many applications (including this example) value $\lambda \wp mu(t)$ can be neglected (because of the smallness of the coefficients λ, ℘) and then the coefficient of specific rate of natural increase in population approximately coincides with the *classical* definition of specific growth rate. In this interpretation of the coefficients of equation

$$X'(t) = \Bbbk(t)X(t) - \lambda \wp X(t)^2$$

sample values of *mu(t)* and Verhulst-Pearl law will meet each other with sufficient accuracy. We do not give graphic factor of specific rate of natural increase in the population depending on the time as *visually* its graphic will coincide with the Fig. 1 for the specific growth rate in our definition (3).

Let's consider the same task, but under different fermenter operating characteristics: $Q = 0.3$, $n = 89$, where Q is an oxygen supply rate, and n is a stirrer rotational speed. There is no sample data for the mentioned performance values. There are only the following samples

KOE(*time*)={7.1×10^7, 1.1×10^8, $2.\times10^8$, 4.1×10^8, 4.2×10^8, 5.25×10^8, 6.3×10^8, 4.4×10^8, 2.8×10^8},
KOE(*time*)={1.7×10^7, 2.7×10^7, 6.5×10^7, 2.3×10^8, 2.4×10^8, 3.1×10^8, 3.4×10^8, 3.1×10^8, 4.2×10^8},
KOE(*time*)={1.5×10^7, 1.9×10^7, 4.6×10^7, 1.9×10^8, 1.9×10^8, 2.8×10^8, 2.9×10^8, 2.9×10^8, 2.9×10^8},
KOE(*time*)={1.3×10^7, 2.1×10^7, 5.1×10^7, 7.4×10^7, 7.5×10^7, 8.9×10^7, 9.5×10^7, 1.2×10^8, 3.6×10^8},
KOE(*time*)={1.5×10^7, 2×10^7, 6.2×10^7, 3.1×10^8, 3.2×10^8, 3×10^8, 3.2×10^8, 3×10^8, 3×10^8},
KOE(*time*)={4.7×10^7, 7.5×10^7, 9.5×10^7, 1.3×10^8, 1.4×10^8, 1.5×10^8, 4.1×10^8, 5×10^8, 4.4×10^8},

obtained for the time points 0, 4, 6, 8 , 10, 12, 16, 20, and 24 for six values performance equals {Q, n} = {1,50}, {0.7,50}, {0.5,50} {0,3,50}, {0.5,70} , {0.5,100}.

KOE concentration dependence as a function of time and performance Q, n should be found with the usage of special polynomial interpolation using the Maclaurin expansion, as the solution of the *inverse problem* for the physical and mathematical KOE model depending on the time, and performance of Q, n is quite difficult (even in the direct problem original formulation). Result of interpolation is denoted by the letter $g(t, Q, n)$. Using the function $g(t, Q, n)$, we form a set of sample values in the time interval [0, 24] with a time step of 1 hour: Sample data=(I, $g(I$,0.3/89)), I = 0,1,2,…,24 .

KOE initial value is equal to 6.82913×10^6. We use the sample data and the Verhulst-Pearl law in its simplest form to calculate the average value of the specific rate of natural increase in population $\Bbbk$. Parameter estimation in Verhulst-Pearl nonlinear model leads to the following results (see Fig. 8)

$$\Bbbk = 0.3358649,\ \lambda = 5.2084522\times10^{-6},\ \rho = 0.0005167\,.$$

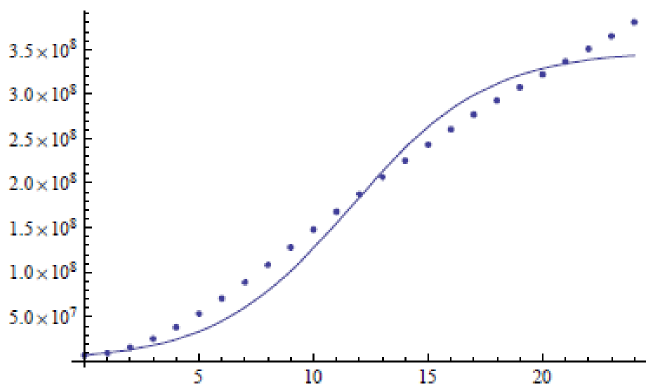


Fig. 8. Graph for Verhulst-Pearl law and sample values.

From the differential equation (11) for η = 0, as above, we find the coefficient of self-poisoning or internal struggle in the seed population.

$$\lambda(t)=\frac{(0.0001706(-4.45222+t)(-0.547357+t)(1442.84+(-68.6843+t)t))}{((1241.94+(-61.9011+t)t)^2(2.79385+t(0.126719+t))^2)}.$$

The results are presented in Fig. 9.

In this example the assumption of a constant specific rate of natural increase in population does not lead to some distortions in the interpretation of experimental data by Verhulst-Pearl law. This fact means that periodic fermentation process is still in its formative stages.

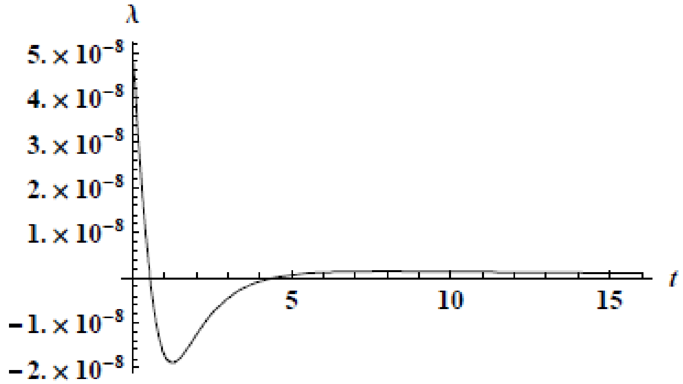


Fig. 9. Internal *struggle coefficient.*

4. Conclusions

To increase the efficiency and versatility of developed fermentation processes physical and mathematical modeling, following enhancements are included in the models developed:

1. The concepts of potential energy and kinetic energy of the periodic production processes have been introduced; developed and implemented software methods of mathematical modeling.

2. Analytical dependences between the main observable variables in the system of differential equations of material balance have been obtained.

3. A generalization of the Verhulst-Pearl law has been produced. This branch of research may even enter into the development framework of *nanotechnologies* to increase industrial and a decrease in microorganism biomass output and fermentation time decrease, since the change in the organizational structure of nano-objects causes a change in the coefficient of internal struggle and the specific rate of natural increase in the concentration of microorganism biomass.

It is important to note that the results obtained are of general nature and can be used not only in the description of the microbiological processes , but also in industry (see [2<1]), or in baking (see [2]), yet in various fields of natural sciences, even in the economy (see [1<3], for example.) In relation to the economy the main conclusion is the following: *the speed of capital movement* is the main component of earnings growth (*ceteris paribus*).

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