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Universal description of the biofilms growth dynamic in logistic model

We study experimental and theoretical dependences of growth dynamics of Pseudomonas aeruginsa biofilms and dynamics of yeast biomass growth. It is revealed that the process of growth of yeast biomass passes into the state of t_{max} three times faster than the formation of biofilm. Analysis of experimental data showed that the biofilm had been continuously growing in the first three days. After the third day, the accumulation of biomass in the biofilm stopped and for the next four days of biofilm observation it remained constant, which indicates competitive mechanisms of interaction. As can be seen, the population is stable at the second stage. Basic growth regimes of proximity with different dynamic characteristics are shown.

The universal description of the biofilms growth dynamic was obtained. Defined parameter of the biological population growth generalized dynamics t uniquely characterized by N* determining parameter and control parameters α and β. The parameter α is determined by the ratio between the radius of individual activity of the population and the characteristic size of the area. The parameter β is determined by competitive interactions, properties of the environment and by cell-to-cell communication. The universal model was proved for Pseudomonas aeruginsa biofilm. The results of the experiments are consistent with the calculated data.*

Introduction. Today, discovery of the biofilm formation process causes interest in microbiologist, biophysics and physicians.

Bacterial biofilm is a complex self-organizing form of bacterial existence. Complex three-dimensional organisation and "social behaviour" phenomena are the specific attributes of bacterial biofilms. Biofilm formation is response function on extracellular impacts of the external environment and in the other hand, on perturbations, produced by microorganisms cells.

Theoretical investigation of nonequilibrium thermodynamic of bacterial biofilms held within the framework of main theory of the biology population models [4-7]. At the same time, methods of the theoretical analysis of the biofilms growth dynamics experimental data represented slightly. Today, there is no theoretically substantiated methods for the generalization of biofilms growth dynamics experimental data.

The aim of this work is development of a theoretically substantiated method of experimental data generalization analysis in the framework of the biology populations general models.

Theory. Any biological population characterized first of all by activity radius and areal size [4, 5]. In the case when activity radius is bigger than areal size, such population can be characterized as well mixed and spatial effects can be ignored in its description. In the opposite case, it is necessary to consider the spatial distribution of the population.

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If, in the first approximation to assume that population has a uniform distribution on the areal, all individuals in population are similar, and population density N(t) - continuously differentiable function, that local population dynamic, growth function F(N) can be represented by the next models: linear growth functions (Malthusian type models), quadratic growth functions (logistic model type), cubic growth function (Alle models type) [5, 7].

In the future, for definiteness, we will consider a logistic type of local population dynamic.

Populations with logistic model of growth is defined as follows [4, 6]:

$$F(N)=\frac{dN}{dt}=rN\left(1-\frac{N}{K}\right). \tag{1}$$

In equation (1) parameter r – call Malthusian, and K – environment "capacity".

It is necessary to make some clarification. Usually, a typical form of the function F(t) are not known. Natural approach in conditions of incomplete information about growth function is its representation in the form of a polynomial the minimum necessary extent is an expansion in a Taylor series in the neighbourhood of the equilibrium values of the density. The equation (1) is obtained by assuming the existence of a series expansion with integral exponent. This assumption is valid for well mixed populations.

In general, *Pseudomonas aeruginosa* growth law of logistic population written in the form:

$$F(N)=rN\left(1-\left(\frac{N}{K}\right)^{\alpha}\right). \tag{2}$$

It is clear, that when $\alpha = 1$ we see a logistic law.

To further it is expedient to write a *Pseudomonas aeruginosa* growth law in the next way:

$$f(N)=\frac{1}{N}\frac{dN}{dt}=r\left(1-\left(\frac{N}{K}\right)^{\alpha}\right), \tag{3}$$

$f(N)$ function describes the dependence of the relative growth rate, called the Malthusian population function.

Connection with the Malthusian function and Malthusian parameter is determined by:

$$f(N)_{N\to 0}=r. \tag{4}$$

In what follows, for the generalized analysis experimental data of density of population growth $N(t)$ appropriate to introduce a generalized Malthusian function.

$$\varphi(N)=\frac{1}{r}f(N)_{N\to 0}. \tag{5}$$

In biological populations dynamic models Malthusian parameter is defined as $r = n - m$, where n – "natural birth rate" and m – "natural death rate" [5, 6]. We introduce by analogy with "birth-death" Malthusian parameter for bacterial biofilms as a ratio between "lifetime" of bacterial cells in the biofilm and a "lifetime" of bacterial cells in the planctonic culture.

Precise, theoretically substantiated methods of Malthusian parameter calculation for biofilm is not exist. Therefore, subsequently, in the analysis of experimental data, Malthusian parameter of biofilm will count according to the definition (4).

To calculate the function $N(t)$ that characterized a biofilm growth dynamic, integrating the equation (3) we obtain:

$$\int_{N_0}^{N} \frac{dN}{N\left(1-\left(N/K\right)^{\alpha}\right)} = r\int_{t_0}^{t} dt. \tag{6}$$

When $\alpha = 1$, the equation (6) is solved analytically [3]. When α takes a fractional value, analytical to solved (6) is impossible. So, cut and dried equation, that describes biofilm growth dynamic is recorded like:

$$t - t_0 = \frac{1}{r}\int_{N_0}^{N} \frac{dN}{N\left(1-\left(N/K\right)^{\alpha}\right)}. \tag{7}$$

In equation (7) N_0 and t_0 are arbitrarily small nonzero coordinates of a point on the phase diagram, that describe biofilm growth dynamic, for which is determined a Malthusian parameter r.

For comparative analysis of the biofilms growth dynamics, obtained under different conditions, spend a similarity transformation equations (3) and (7). We introduce the following dimensionless variables:

$$t^* = \frac{t}{t_{\max}}, \quad N^* = \frac{N}{N_{\max}}. \tag{8}$$

t_{max} and N_{max} parameters are the coordinates of a point on the phase diagram, that determining completion of the biofilm formation.

We will rewrite equations (3) and (7) in coordinates (8):

$$f(N^*) = \frac{1}{N^*}\frac{dN^*}{dt^*} = t_{\max} r\left(1-\left(\frac{N^* N_{\max}}{K}\right)^{\alpha}\right) \tag{9}$$

and

$$t^* = t_0^* + \frac{1}{r t_{\max}}\int_{N_0^*}^{N^*} \frac{dN^*}{N^*\left(1-\left(N^* N_{\max}/K\right)^{\alpha}\right)}. \tag{10}$$

Let us analyze the equations (9) and (10). On the basis of equilibrium thermodynamics, we can show the feasibility of the following approximations: ($t_{max}r$) and (N_{max}/K) values of the order of unity. However, a rigorous proof of this approximation is beyond the scope of this paper. So, subsequently, we will evaluate a values of ($t_{max}r$) and (N_{max}/K) by experimental data.

Can also be suggested, that in a first approximation, a certain contribution to the integral in the right part of equation contribute a member $\left(N^* N_{\max}/K\right)^{\alpha}$. t^* value increase with increasing of this member. So, in a first approximation, we can write the condition of dynamic similarity of the biofilm formation process (formally, biological population increasing process) in the next way:

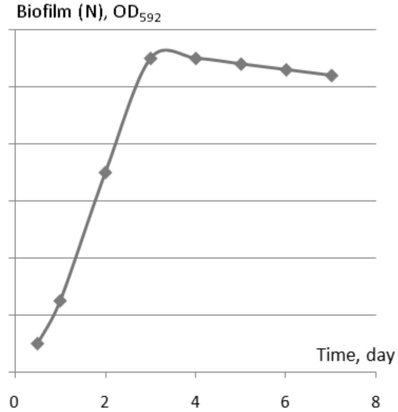

Fig. 1. *Pseudomonas aeruginosa* biofilm growth dynamic

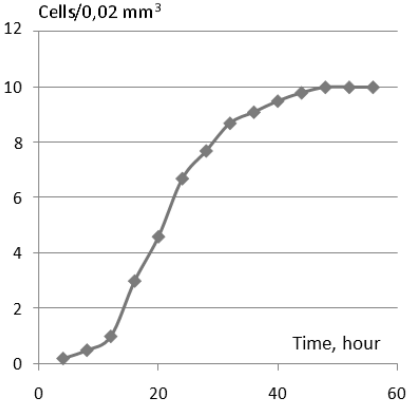

Fig. 2. Yeast biomass growth dynamic

$$\tau^* = S\,[(\beta N^*)^{\alpha}]. \tag{11}$$

In formula (11) S – similarity function; β – depends on the value of ($t_{max}r$) and (N_{max}/K) and determined experimentally.

Results and discussion. To check the adequacy of the conditions of similarity (11) we examined two thermodynamic systems - biofilm growth dynamic (Fig. 1) and yeast biomass growth dynamic (Fig. 2) [1].

It should be noted that yeast biomass growth process passes to state τ_{max} in three times faster than a biofilm formation.

We begin analysis of experimental data with consideration of the biofilm growth dynamic of *Pseudomonas aeruginosa*. Study of the dynamics of biofilm formation during the week showed, that a biofilm was continuously growing at first three days. After the third day biomass accumulation into the biofilm stopped and on the next four days of observation biofilm mass were permanent [2].

The calculation of maltusian function $f(N)$ for biofilm growth dynamic (Fig. 1) were performed by numerical differentiation method (Stirling interpolation formula) [3].

On Fig. 3 there is a dependence of $g = 1 - \varphi(N^*)$ from N^*. Fig. 3 shows that this dependence does not meet the logistic law for which the graph of $[1 - \varphi(N^*)]$ from N^* should be strictly straight line segment. On Fig. 3 there is a schedule of the $\ln[1 - \varphi(N^*)]$ from $\ln N^*$ dependence. This graph is a generalized logistic function which is expressed by equations (3). On the basis of numerical analysis graphical representation of the equation (3) as a $\ln[1 - \varphi(N^*)]$ from $\ln N^*$ we took the equations:

$$\varphi(N^*) = 1 - 1.68(N^*)^{1.58}, \quad 0 < N^* \le 0.3; \tag{12}$$

$$\varphi(N^*) = 1 - 0.96(N^*)^{0.73}, \quad 0.4 \le N^* < 1.0. \tag{13}$$

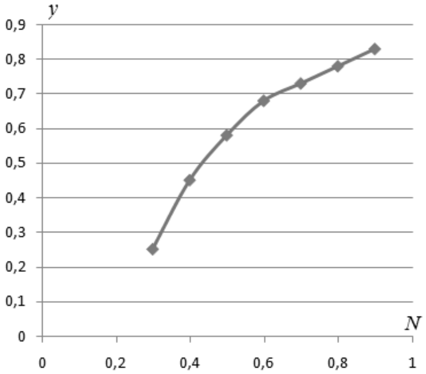

Fig. 3. Dependence of $g = 1 - \varphi(N^*)$ from N^*. $1 - \varphi(N^*) = y$

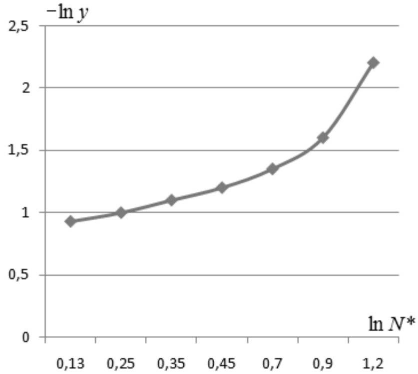

Fig. 4. Dependence of $\ln[1 - \varphi(N^*)]$ from $\ln N^*$. $\ln[1 - \varphi(N^*)] = \ln y$

Equations (12) and (13) allow us to calculate the generalized Malthusian function of the biofilm with a minimum relative deviation $\pm\sigma = 7.8$ %.

Analysis, spent in the same sequence for yeast biomass growth dynamic, show the same deviations from the logistic law. However, in this case, the $\ln[1 - \varphi(N^*)]$ from $\ln N^*$ dependence is a straight line segment over the entire range $0 < N^* < 1$, and is written as follows:

$$\varphi(N^*) = 1 - 1.1(N^*)^{0.78} \tag{14}$$

Equation (14) allows us to calculate generalized Malthusian function of the yeasts dynamics growth with a maximum deviation $\pm\sigma = 7.3$ %. Now, spend the calculation time required to reach an arbitrary state N* for a biofilm formation process and yeasts growth with equation (7).

For a biofilm growth dynamic equation (7) written as follows:

$$t = 0.5\left(1 - \int_{0.05}^{N^*} \frac{dN^*}{N^*\left(1-\left(1.39N^*\right)^{0.73}\right)}\right) \qquad \text{for } 0 < N^* \le 0.3 \tag{15}$$

$$t = t_{0.3} + 0.5\int_{0.03}^{N^*} \frac{dN^*}{N^*\left(1-\left(0.04N^*\right)^{0.73}\right)} \qquad \text{for } 0.4 < N^* \le 1.0 \tag{16}$$

For yeasts biomass growth dynamic:

$$t = 6 + 3.33\int_{0.33}^{N^*} \frac{dN^*}{N^*\left(1-\left(1.13N^*\right)^{0.71}\right)} \qquad \text{for } 0.03 < N^* \le 1.0 \tag{15}$$

The integration is carried out numerically by Newton-Cotes quadrature formulas [3]. The maximum relative deviation in the calculation according to the equations (15), (16), (17) $\pm\sigma = 9.8$ %.

Now, consider the similarity of the dynamic behaviour of the *P. aeruginosa* biofilm and yeasts biomass defined by the formula (11). There is a dependence graph

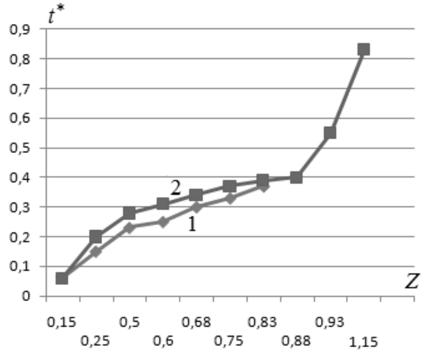

Fig. 5. Universal dependence of yeasts biomass (1) and *P.aeruginosa* biofilm (2) growth.

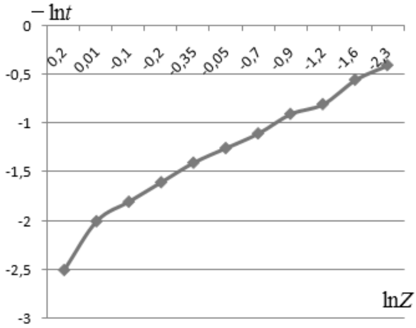

Fig. 6. Universal dependence of yeasts biomass and *P.aeruginosa* biofilm growth in logarithmic coordinates

of t^* from $Z = (\beta N^*)^\alpha$ on the Fig. 5, where α and β are determined as a parameters of the equations (15), (16), (17). From Fig. 5 it is clear that similarity conditions defined by the formula (11) performed well enough. However, dependence ln t^* from lnZ (Fig. 6) has a singular point, as shown by further analysis. There is a dependence of ln t^* from ln Z on Fig. 6, where Z = 0,55 is a breakpoint. Thus, the formula of similarity (11) must be written as follows:

$$t^* = 0.36\, Z^{0.65}\,,\ \ 0 < Z \le 0.55; \qquad (18)$$

$$t^* = 0.62\, Z^{1.56}\,,\ \ 0.55 \le Z < 1.2 \qquad (19)$$

Formulas (18) and (19) allow to calculate the universal characteristic of the biopopulations growth dynamics with maximum relative deviation ± σ = 9.7 %.

Conclusions:

In this paper we have developed a universal description of the biofilms growth logistic dynamic. The dynamics of growth takes place in two stages. On a second stage population is stable α>1. It was shown the essential closeness growth regimes with different dynamic characteristics.

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Джоу Хуюі, Драган Г. С., Кутаров В.В., Галкін М.Б. Філіпова Т.О.

Универсальний опис динаміки росту біоплівки в логістичній моделі

АНОТАЦІЯ

Вивчаються експериментальні та теоретичні залежності динаміки росту біоплівок Pseudotonas aeruginsa і динаміки росту біомаси дріжджів. Виявлено, що процес зростання біомаси дріжджів переходить в стан tmax в три рази швидше, ніж утворення біоплівки. Аналіз експериментальних даних показав, що біоплівка безперервно зростає в перші три дні. Після третього дня накопичення біомаси в біоплівки припинилося і протягом наступних чотирьох днів спостереження біоплівки було постійним, що вказує на конкурентні механізми взаємодії. Як видно, на другому етапі населення стабільно. Показані основні режими зростання близькості з різними динамічними характеристиками.

*Отримано універсальний опис динаміки росту біоплівки. Визначений параметр узагальненої динаміки росту біологічної популяції t * однозначно характеризується визначальним параметром N * і параметрами управління* α *і* β*. Параметр α визначається відношенням між радіусом індивідуальної активності популяції і характерним розміром площі. Параметр* β *визначається конкурентними взаємодіями, властивостями середовища і зв'язком між осередками. Універсальна модель була доведена для біоплівки Pseudotonas aeruginsa. Результати експериментів узгоджуються з обчисленими даними.*

Джоу Хуюи, Драган Г. С., Кутаров В.В., Галкин Н.Б. Филипова Т.О.

Универсальное описание динамики роста биопленки в логистической модели

АННОТАЦИЯ

Изучаются экспериментальные и теоретические зависимости динамики роста биопленок Pseudotonas aeruginsa и динамики роста биомассы дрожжей. Выявлено, что процесс роста биомассы дрожжей переходит в состояние tmax в три раза быстрее, чем образование биопленки. Анализ экспериментальных данных показал, что биопленка непрерывно растет в первые три дня. После третьего дня накопление биомассы в биопленке прекратилось и в течение следующих четырех дней наблюдения биопленки было постоянным, что указывает на конкурентные механизмы взаимодействия. На втором этапе население стабильно. Показаны основные режимы роста близости с различными динамическими характеристиками.

Получено универсальное описание динамики роста биопленки. Определенный параметр обобщенной динамики роста биологической популяции t однозначно характеризуется определяющим параметром N* и параметрами управления* α *и* β*. Параметр* α *определяется отношением между радиусом индивидуальной активности популяции и характерным размером площади. Параметр* β *определяется конкурентными взаимодействиями, свойствами среды и связью между ячейками. Универсальная модель была доказана для биопленки Pseudotonas aeruginsa. Результаты экспериментов согласуются с вычисленными данными.*