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Kinetic model of microorganisms aggregation at absorbing immobilisation on nozzles in continuous and intermittent action machines

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***Abstract*— The problem of biological cells aggregation is one of the fundamental in biology, biophysics and biochemistry. In real-world application particularly in biotechnological processes of number of productive industries: microbiological, food, pharmaceutical, it is necessary to solve application tasks of preventing, reducing or regulating the intensity of cell-cell adhesion, as well as impact assessment of this phenomenon on the course of a technological process. In solving problems connected with the aggregation processes, two sections of process theoretical study: microkinetic and kinetic are used. This paper presents the development, derivation and study of mathematical methods for solving kinetic equations describing the evolution of cell distribution function and agglomerates in the mass for given probability of their collision and sticking, which is included in the range of problems of the coagulation kinetic theory. Equations are proposed that allow to solve a wide broad agenda on the biological cells agglomeration in the processes implemented in machines of intermittent and continuous action of ideal displacement and mixing at experimentally obtained coagulation and fragmentation (decay) coefficients.**

Keywords*— processes, aggregation, biological cells, microorganisms, immobilization, adsorption, kinetic model.

I. INTRODUCTION

The use of immobilized microorganisms was one of the most important achievements in the field of practical biotechnology, including for food and pharmaceutical industries [1]. At the same time, a method of sorption on the developed surfaces of insoluble carriers that hold cells due to adsorption nonspecific and biospecific effects has found mainstreaming use. [2,3,4].

II. METHODS AND MATERIALS

The exceptional importance of using this method in continuous flow bioreactors consists in practically only one possibility of creating a given difference in the movement speeds of production substrate and microorganisms cells in the flow along the machine [5]. In addition, the microorganisms immobilisation creates the possibility of obtaining multienzyme systems that carry out multistage continuously operating processes without exogenous cofactors, is a condition for improvemen and extension of time of fixed cells biological activity compared to intact ones [6,7]. Other positive effects of using cells adsorption on solid carriers are known [1,8].

However, cells efficiency in the layer's depth is extremely limited because of the possibility of their direct contact with reagents of the production substrate, which decreases as the carrier approaches. The decrease in mass transfer intensity for this reason is due to the high density of the structure of the layers, especially formed by single cells [9,10,11].

It is possible to increase the efficiency of reagents interaction by obtaining more rarefied macrolayer of sorbed cells by building it largely from blocks of cells aggregated before adsorption and thus achieving a microporous structure. First, confirm that you have the correct template for your paper size. This template has been tailored for output on the A4 paper size. If you are using US letter-sized paper, please close this file and download the Microsoft Word, Letter file.

III. RESULTS AND DISCUSSION

Methods development for aggregating microbial cells, taking into account the required intensity of this process, occupies an important place in industrial bioreactors. Meanwhile, in a number of situations it becomes necessary to solve applied problems of preventing or reducing cell adhesion intensity and assessing the influence of this phenomenon on the course of a particular technological process.

The adhesion of biological cells and their aggregates to various surfaces in a fluid flow plays an important role in biotechnological processes. For example, the selective adhesion of yeast cells to the surfaces of solid insoluble packing elements in fermentation machines and biogenerators of plants for continuous champagnization of wine [7].

Cell agglomerates formed in flow bioreactors with laminar flow of a suspension significantly affect the hydrodynamics of the relative fluid-cell phase movements, which reduces the efficiency of the biochemical process and requires leveling measures [5,15,16].

Consequently, microorganisms aggregation can play both positive and negative role in various biotechnological processes. Therefore, this process should be subject to theoretical and experimental studies of previous developments or upgrades of machines devices, as well as the size, shape, location, and materials of the elements of the contact adsorbing nozzle.

The interaction of biological cells between them, with other biological objects and elements of special devices of

the machine is determined by the action of both ordinary surface forces [2,12,13] and specific biochemical forces [4,9]. The process of coagulation and aggregation involves the collision or close movement of biological cells relative relative to one another.

Detailed analysis of this kind of movement requires consideration of cell shape dynamics and macroscopic irregularities near the point of contact. Apparently, that significant hydrodynamic forces acting between surfaces almost touching each other should cause deformation of non-rigid biological cells. However, small unicellular microorganisms with a well-developed surface, such as, for example, yeast cells, are satisfactorily approximated by an elastic solid model [10], since in the active state they have a shape close to spherical or elliptical one and have a well-developed cytoskeletal structure. Consequently, for the mathematical description of such biological cells agglomeration, the usual theory of coagulation in disperse systems can be used [10,14]. The problem of coagulation and agglomeration processes in biology, biophysics, and biochemistry should be divided into microkinetic and kinetic theories. Microkinetic theory studies the movement of biological cells until they crash, as well as the processes of collision and adhesion of the colliding cells in order to determine the probability of elementary acts of coagulation in unit time in a given volume. The conclusion, research and development of mathematical methods for solving kinetic equations describing the evolution of the mass distribution function of agglomerates for a given probability of their collision and sticking are included in the range of problems in the kinetic theory of biological cells coagulation of microorganisms. This paper deals mainly with issues related to the kinetic theory of coagulation.

IV. CONCLUSION

It is advisable to apply the Smoluchowski-Mezlak kinetic theory [14,17,18 for the mathematical description of conglomerates formation of biological cells, including the option of their decay.

Discrete spectrum. In this representation, the system of kinetic equations has the form:

$$\frac{\partial}{\partial t}n_k = S\{n_k\} + D\{n_k\}, \qquad k = 1,2,3,\ldots, \qquad (1)$$

where $S\{n_k\}$ and $D\{n_k\}$ - Smoluchowski and Melzak operators:

$$S\{n_k\} = \frac{1}{2}\sum_{i+j=k} G(i,j)n_i n_j - \sum_{i=1}^{\infty} G(i,k)n_i n_k \quad , \qquad (2)$$

$$D\{n_k\} = \sum_{i=k+1}^{\infty} n_i \gamma(i,k) - \frac{n_k}{k}\sum_{i=1}^{k-1} i\gamma(k,i) \quad , \qquad (3)$$

n_k - the number of agglomerates consisting of k cells per unit volume at a given time t; $G(i,j)$ - probability of collision and sticking of agglomerates mass $x_o i$ and $x_o j$ per unit time volumetrically of the bioreactor; $\gamma(k,i)$ - probability of agglomerate breakdown of k x_o mass, в результате as a result of which a "fragment " of i x_o mass is formed, x_o- mass of one cell.

A. Continuum spectrum

In the transition from a discrete spectrum to a continuous one, formal transformations should be made:

$$x_o k = x \quad , \qquad n_k = n(k,t) \to f(x,t)dx \quad ,$$
$$\sum(\ldots) \to \int(\ldots)dx \quad .$$

In this case, the system of equations (1) is transformed into a quasilinear integro-differential equation:

$$\frac{\partial}{\partial t} f(x,t) = S\{f(x,t)\} + D\{f(x,t)\} \quad , \qquad (4)$$

where

$$S\{f(x,t)\} = \frac{1}{2}\int_{x_1+x_2=x} G(x_1,x_2)f(x_1,t)f(x_2,t)dx_1 -$$
$$-\int_0^{\infty} G(x,S)f(x,t)f(S,t)dS \quad , \qquad (5)$$

$$D\{f(x,t)\} = \int_x^{\infty} \gamma(S,x)f(S,t)dS - \frac{1}{x}\int_0^x S\gamma(x,S)f(x,t)dS \qquad (6)$$

B. Stationary spectrum formation

If there are two competing processes, such as coagulation and disintegration of agglomerates, a stationary spectrum can be formed. From the kinetic equations (1) and (4) for a steady process, if it exists, it follows that $\frac{\partial}{\partial t}n_k = \frac{\partial}{\partial t}f(x,t) = 0$. These conditions, in particular, are satisfied if the following relations take place:

$$G(i,k-i)n_i n_{k-i} = n_k \gamma(k,i) \qquad (7)$$

- for discrete spectrum.

$$G(S,x-S)f(S)f(x-S) = f(x)\gamma(x,S) \qquad (8)$$

- for continuum spectrum.

C. Example

Suppose $G(S,x-S) = G_0 S^{\alpha}(x-S)^{\alpha}$, $\gamma(x,S) = \frac{\gamma_0 S^{\beta}(x-S)^{\beta}}{x^{\gamma_1 - 1}}$, where $\beta = \alpha + \gamma_1 - 1$. In this case for $f(x)$ function from relation (8) we get the gamma distribution:

$$f(x) = \frac{M_0 b^{\gamma_1+1}}{\Gamma(\gamma_1+1)} x^{\gamma_1-1} e^{-bx} \quad , \qquad (9)$$

where $\Gamma(x)$ - gamma-function from x;

$$\frac{\gamma_1}{b} = M_0/N \quad , \quad M_0 = x_0 N_0 \quad , \quad N = M_0/\langle x \rangle \quad , \qquad (10)$$

$$(\gamma_1+1)/\gamma_1 = \langle x^2\rangle / \langle x\rangle^2 \quad , \quad \langle x\rangle = \int_0^\infty xf(x)dx \Big/ N \quad ,$$

$$N = \int_0^\infty f(x)dx \quad M = \int_0^\infty xf(x)dx \quad , \quad \langle x^2\rangle = \int_0^\infty x^2 f(x)dx \Big/ N \quad .$$

For the mathematical description of the process under consideration in the machine of continuous action of ideal mixing, the right parts of equations (1) and (4) must be added, respectively, to the following terms:

$$\frac{1}{\tau}[n_{ok} - n_k(t)] \text{ и } \frac{1}{\tau}[f_o(x,t) - f(x,t)], \qquad (11)$$

where $\tau = V/Q$, V – machine working volume, Q – volume flux at the machine input; n_{ok} and $f_o(x,t)$ - values of these quantities at machine input.

In its structure, equation (4) is a quasilinear integro-differential equation with a lag of argument. It can be converted to an equivalent differential equation of infinitely high order, but without argument lag:

$$\frac{\partial}{\partial t}\Phi(x,t) = \sum_{k=1}^{\infty} \frac{1}{k!} \cdot \frac{\partial k}{\partial x^k}(A_k + B_k)\Phi(x,t) \quad , \qquad (12)$$

где $\Phi(x,t) = xf(x,t)$,

$$A_k = (-1)^k \int_0^\infty S^k G(x,S) f(S,t) dS \quad B_k = \int_0^x S^k w(x,S,x-S) dS \quad ,$$

$$w(x, x-S, S) = \frac{S}{x}\gamma(x,S) \quad .$$

D. Diffusion approximation

Equation (12), provided that the sum of only the first two terms is preserved under the sign, is simplified to the form:

$$\frac{\partial}{\partial t}\Phi(x,t) = \frac{\partial}{\partial x}U\Phi(x,t) + \frac{1}{2}\frac{\partial^2}{\partial x^2}b\Phi(x,t) \quad , \qquad (13)$$

where $U = A_1 + B_1$, $b = A_2 + B_2$.

Equation (13) is a Fokker-Planck type equation, the methods for solving which are currently well developed.

E. Example

Suppose $U = \alpha x$, $b = \beta x^2$, $\alpha > 0$, $\beta > 0$, α and β may depend on time. In this case, the solution of equation (13) satisfying the initial and boundary conditions:

$$\Phi(x,t)_{t=t_o} = x_o N_o \delta(x - x_o), \ \Phi(\infty, t) = 0,$$

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$$\Phi(x,t) = \frac{N_0 x_0}{\sqrt{2\pi}} \frac{1}{\sigma}\frac{1}{x}\exp\left[-\frac{1}{2\sigma^2}\ln^2\frac{x}{x_0 Z}\right] , \qquad (14)$$

where N_0 - the number of biological cells at the initial time $t = t_o$ of mass x_o , but σ and Z determined by expressions:

$$\sigma^2 = \int_{t_0}^{t} \beta(\tau)d\tau \quad , \quad Z = \exp\left\{-\int_{t_0}^{t}\left[\alpha(\tau) + \frac{1}{2}\beta(\tau)\right]d\tau\right\} \quad ,$$

$\delta(x - x_0)$ - Dirac delta function.

To describe the process under consideration in the machine of continuous action of ideal mixing in the diffusion approximation, a term of the form should be added to the right-hand side of equation (13) $[\Phi_o(x,t) - \Phi(x,t)]/\tau$, where $\Phi_o(x,t)$ - value of function $\Phi(x,t)$ at the machine input.

Finally, if an internal source of biological cells is required, a term of the form should be added to the right side of equation (1) and (4): $J(x_0,t)$, and to equation (13) – $xJ(x_0,t)$ term, where $J(x_0,t)$ - cells number of x_0 mass, originating in a unit of time volumetrically in machine.

From the foregoing it follows that the kinetics of coagulation process and disintegration of agglomerates essentially depends on the specific type of coefficients. $G(k,j)$ and $\gamma(k,j)$.

By convention $G(k,j)$ - symmetric non-negative function of its arguments, i.e $G(k,j) = G(j,k)$. Explicit kind of dependence $G(k,j)$ determined by the mechanism of collision of particles that prevails in the specific situation.

Determination of coagulation and decay coefficients for various collision mechanisms is an independent task. However, for a number of typical processes, such as Brownian coagulation of particles, gradient coagulation, coagulation with a different mechanism in a turbulent flow, etc. Coagulation and decay coefficients are known and contained in review papers and monographs [19, 20,21].

Thus, the proposed equations with known coefficients $G(k,j)$ and $\gamma(k,j)$ allow to solve a wide range of applications for biological cells agglomeration in intermittent and continuous action machines.

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