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PECULIARITIES OF BACTERIAL CHEMOTAXIS IN A CYLINDRICAL PORE

The process of bacterial redistribution in a cylindrical pore filled with an attractant has been considered. The attractant concentration decreases linearly along the pore, and the redistribution of bacteria occurs due to their diffusion (the motion of bacteria along the gradient of their concentration) and chemotaxis (the motion of bacteria along the gradient of attractant concentration). The influence of a spatial confinement on the bacterial distribution in the pore is analyzed. It is shown that if the pore wall is "repelling" for bacteria, the spatial confinement can change the bacterial distribution. In particular, as the pore radius decreases, the chemotaxic effect becomes weaker. The non-uniformity of a bacterial distribution in the system is estimated. The chemotaxis sensitivity function (the deviation of the ratio between the local average bacterial concentration and the average bacterial concentration over the whole system from unity) is calculated, and its dependence on the attractant concentration at the system ends and on the pore size is determined.

K e y w o r d s: chemotaxis, attractant, bacterium, diffusion, cylindrical pore.

1. Introduction

The chemotaxis problem is an important direction of researches in modern biophysics [1–5]. The chemotaxis phenomenon arises because some bacteria can "feel" the presence of certain substances, which are called attractants. If there is an attractant in the system, bacteria become redistributed in accordance with the gradient of attractant concentration. Therefore, by affecting the attractant distribution, it is possible to control the bacterial distribution. In this process, besides the attractant concentration gradient, other factors play an important role, for example, the total attractant concentration and the way how the bacteria are introduced into the system.

There are different approaches to study the bacterial chemotaxis theoretically [6–11]. One of them consists in simulating the behavior of separate bacteria. In particular, for today, we know the following algorithm of the bacterial behavior in a medium with an attractant [6]:

• every bacterium moves uniformly in a straight line within a certain time interval;

• this kind of motion continues until a tumbling; i.e. the bacterium stops and randomly changes the direction of its motion;

• the tumbling frequency depends to the amount of an attractant registered by the bacterial receptors during the motion; the higher the amount of the registered attractant, the lower is the tumbling frequency.

This algorithm is applicable, if the behavior of separate bacteria is studied and a further statistical averaging of their trajectories and spatial distribution is carried out (see, e.g., work [6] and the references therein).

Although this approach is quite acceptable, it has disadvantages. In particular, it is often required to know analytical expressions for the distribution function of bacteria and for other parameters of the system. In this case, more appropriate is the approach that is based on the application of non-linear differential equations of the diffusion type. It was substantiated in works [12–14] and is commonly accepted today.

However, the task of studying the chemotaxis is not trivial even in its simplest formulation. The general problem includes a separate important case: the chemotaxis of bacteria in a porous medium [15–18]. On the one hand, this case directly concerns real systems, thus being challenging. On the other hand, when solving this problem, we face certain difficulties of the mathematical origin. In this work, we propose a mathematical model that describes specific features in the behavior of bacteria located in a system with the geometry of a cylindrical pore. This research is methodologically based on a series of our previous studies [19–21] carried out for one- and two-dimensional systems and is their continuation. But, unlike the cited works, we consider a spatially confined three-dimensional system: a cylinder that is finite along its main axis.

2. Mathematical Model

Let us consider a three-dimensional system, which is a finite cylinder with radius R and length L filled with bacteria and an attractant. The coordinate z is reckoned along the cylinder axis, so that $0 \le z \le L$; for the radial distance ρ from the cylinder axis, $0 \le \rho \le R$. The boundary conditions are assumed to be independent of the azimuthal angle, so that the sought functional dependences do not depend on this coordinate.

Our approach is based on an expression for the bacterial flux $\mathbf{j}_b$. We suppose that this expression contains two terms. One of them is associated with the bacterial concentration gradient in the system (the diffusion term), and the other with the attractant concentration gradient (the term describing the chemotaxis). Denoting the space-time distribution of bacteria by $b(t, z, \rho)$ and the stationary spatial distribution of attractant by $c(z, \rho)$, we write the bacterial flux $\mathbf{j}_b$ as follows:

$$\mathbf{j}_b = -D\boldsymbol{\nabla} b(t, z, \rho) + k\frac{b(t, z, \rho)\boldsymbol{\nabla} c(z, \rho)}{(a_0 + c(z, \rho))^2}. \quad (1)$$

Here, $\boldsymbol{\nabla}$ is the gradient operator, D the diffusion coefficient, and k and a_0 are phenomenological parameters of the model.

In the second term, which is directly associated with the chemotaxis, the numerator includes the product of the bacterial concentration $b(t, z, \rho)$ and the attractant concentration gradient $\boldsymbol{\nabla} c(z, \rho)$, because we proceed from the assumption that the chemotaxis-related bacterial flux component is proportional to the attractant gradient and the bacterial concentration. The presence of a denominator in this term is explained by the experimental fact (see, e.g., work [6]) that the growth of the attractant concentration results in the saturation of the bacterial receptor sensitivity, so that the attractant gradient effect decreases. As was shown in works [19, 21], the choice of the term associated with chemotaxis in the presented form [see Eq. (1)] makes it possible to correctly describe the chemotaxis effect not only at the qualitative level, but also at the quantitative one.

Knowing the general expression for the bacterial flux $\mathbf{j}_b$ and the attractant distribution $c(z, \rho)$, we can determine the space-time distribution of bacteria in the system using the continuity equation

$$\frac{\partial b}{\partial t} + \operatorname{div} \mathbf{j}_b = 0, \quad (2)$$

provided that the bacteria do not reproduce themselves or die. Let us consider a stationary case where the distribution of bacteria has stabilized and does not depend on the time, $b = b(z, \rho)$. In addition, the attractant concentration does not depend on the radial coordinate ρ, so that $c = c(z)$ and the attractant concentration gradient is directed along the z-axis. Under all those conditions, Eq. (2) gives rise to the following equation determining the spatial distribution of bacteria:

$$\frac{\partial^2 b}{\partial \rho^2} + \frac{1}{\rho}\frac{\partial b}{\partial \rho} + \frac{\partial^2 b}{\partial z^2} - \frac{k}{D}\frac{d}{dz}\left[\frac{b}{(a_0 + c)^2}\frac{dc}{dz}\right] = 0. \quad (3)$$

This equation should be complemented by boundary conditions. Furthermore, it is also necessary to determine the spatial distribution of the attractant in the system, $c(z)$.

As to the attractant, we assume that its concentrations at system's ends (the left end $z = 0$ and the right end $z = L$) are known, and the concentration is higher at the left end, i.e. $c(0) = C_0 > c(L) = C_1$. In

this case, the spatial distribution of the attractant linearly varies with the coordinate z and is determined by the following formula:

$$c(z) = C_0\left(1 - \frac{z}{L}\right) + C_1\frac{z}{L}. \tag{4}$$

The mode of introducing bacteria into the system consists in that the bacterial concentration is given at the right end,

$$b(z = L) = B_0, \tag{5}$$

and there is no bacterial flux through the left end,

$$\left[\frac{\partial b}{\partial z} - \frac{k}{D}\frac{b}{(a_0 + c)^2}\frac{dc}{dz}\right]_{z=0} = 0. \tag{6}$$

We also assume that there are no bacteria at the cylindrical surface ($\rho = R$), i.e. their concentration equals zero here:

$$b(z, \rho = R) = 0. \tag{7}$$

This condition corresponds to a situation where the cylindrical (pore) surface is "repulsive" for the bacteria.

3. Chemotaxis Sensitivity Function

Now, we have all information required to calculate the spatial distribution of bacteria $b(z, \rho)$. However, in practice, the point of interest is not a local value of the bacterial concentration, but its averaged value over a certain region. In this case, it is convenient to experimentally measure the amount of bacteria at a certain "cross-section" of the cylindrical pore. For example, if we are interested in a "cross-section" of the thickness Δz, which is located at the distance z from the left end of the cylindrical pore, then the average concentration of bacteria in this region, $\bar{B}(z)$, can be calculated as follows:

$$\bar{B}(z) = \frac{2}{R^2\Delta z}\int\limits_{z}^{z+\Delta z} dz' \int\limits_{0}^{R} d\rho b(z', \rho)\rho. \tag{8}$$

In the limit $\Delta z \to 0$ (the "cross-section" thickness vanishes), this formula reads

$$\bar{B}(z) = \frac{2}{R^2}\int\limits_{0}^{R} \rho b(z, \rho) d\rho. \tag{9}$$

The corresponding average concentration of bacteria in the system equals

$$\bar{B} = \frac{2}{R^2 L}\int\limits_{0}^{L} dz \int\limits_{0}^{R} d\rho b(z, \rho)\rho. \tag{10}$$

In the simplest way, the concentration of bacteria can be measured at system's ends. As was already marked above, the bacterial concentration at the right end ($z = L$) is fixed. Therefore, the matter of interest is the concentration of bacteria at the left end ($z = 0$). Let us introduce the following numerical parameter:

$$F = \frac{\bar{B}(0)}{\bar{B}} - 1, \tag{11}$$

which characterizes the deviation of the ratio between the average bacterial concentrations at the left end and throughout the system from unity. Expression (11) defines the chemotaxis sensitivity function F, which numerically characterizes the non-uniformity in the bacterial distribution [6, 19–21]. The case $F = 0$ means that the average concentration of bacteria at the left end of the system is equal to the average concentration over the whole system. The larger the chemotaxis sensitivity function, the higher is the deviation of the average concentration of bacteria at the left end from the average concentration of bacteria in the system. Negative values of the chemotaxis sensitivity function mean that the average concentration of bacteria at the left end is lower than the average concentration of bacteria in the system. The chemotaxis sensitivity function is the ultimate goal of our study.

4. Bacterial Distribution

While solving the problem of bacterial distribution, let us nondimensionalize the variables and introduce some new notations. In particular, we put $\rho = rR$, $z = xL$, and $c(z) = a_0\gamma(x)$, and denote $C_1 = \xi C_0$ ($0 \le \xi \le 1$) and $C_0 = a_0 \times 10^p$. Then the attractant distribution in terms of dimensionless variables is given by the formula

$$\gamma(x) = 10^p(1 - x(1 - \xi)). \tag{12}$$

In essence, the parameter p determines the attractant concentration at the left end ($\gamma(0) = 10^p$), and

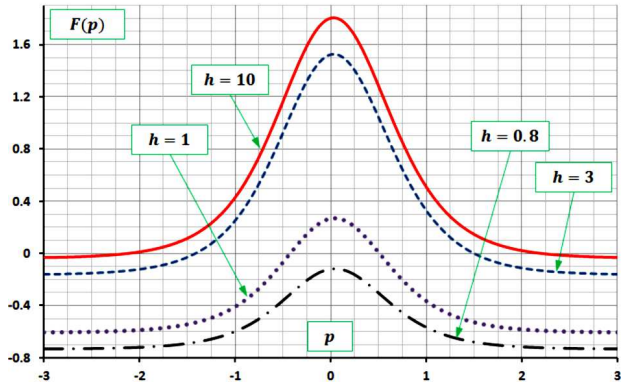

Fig. 1. Chemotaxis sensitivity function $F(p)$ at various values of the parameter $h = 10$ (solid curve), 3 (dashed curve), 1 (dotted curve), and 0.8 (dash-dotted curve)

the parameter ξ the attractant concentration ratio between the right and left pore ends ($\gamma(1) = \xi\gamma(0)$).

By putting $b(z,\rho) = B_0 m(x,r)$, $h = \frac{R}{L}$, and $\lambda = \frac{k}{Da_0}$, we obtain the following equation in dimensionless variables, which describes the distribution of bacteria in the system:

$$\frac{\partial^2 m}{\partial r^2} + \frac{1}{r}\frac{\partial m}{\partial r} + h^2\frac{\partial^2 m}{\partial z^2} - \lambda h^2 \frac{d}{dz}\left[\frac{m\frac{d\gamma(x)}{dx}}{(1+\gamma(x))^2}\right] = 0. \tag{13}$$

The function $m(x,r)$ has to satisfy the following boundary conditions:

$$\left[\frac{\partial m}{\partial z} - \lambda\frac{m(x,r)\frac{d\gamma}{dx}}{(1+\gamma(x))^2}\right]_{z=0} = 0, \tag{14}$$

$$m(x=1,r) = 1, \tag{15}$$

$$m(x,r=1) = 0. \tag{16}$$

The solution is sought in the form of a series

$$m(x,r) = \sum_{n=1}^{\infty} m_n(x) J_0(\mu_n r), \tag{17}$$

where $J_0(u)$ is the Bessel function of the zeroth order, and μ_n $(n = 1,2,...)$ are its zeros ($J_0(\mu_n) = 0$). The function $m_n(x)$ has to satisfy the equation

$$m_n''(x) - \left(\frac{\mu_n}{h}\right)^2 m_n(x) - \lambda\frac{d}{dz}\left[\frac{m_n(x)\gamma'(x)}{(1+\gamma(x))^2}\right] = 0, \tag{18}$$

where the prime denotes the derivative. The boundary conditions for the function $m_n(x)$ are as follows:

$$m_n'(0) + \frac{\lambda(1-\xi)10^p}{(1+10^p)^2} m_n(0) = 0, \tag{19}$$

$$m_n(1) = \frac{2}{\mu_n J_1(\mu_n)}, \tag{20}$$

where $J_1(u)$ is the Bessel function of the first order.

Thus, we have to find the functions $m_n(x)$ and, afterward, calculate the chemotaxis sensitivity function using the formula

$$F = \frac{\sum\limits_{n=1}^{\infty} m_n(0)\frac{J_1(\mu_n)}{\mu_n}}{\sum\limits_{n=1}^{\infty}\int\limits_0^1 m_n(x)dx\frac{J_1(\mu_n)}{\mu_n}} - 1. \tag{21}$$

5. Influence of Boundary Conditions and Spatial Confinement

The solutions $m_n(x)$ can be calculated only numerically. Another important factor is the implicit dependence of the chemotaxis sensitivity function (21) on the parameters p and h, because the solutions $m_n(x)$ depend on them. Actually, the matter concerns the dependence of the chemotaxis sensitivity function on the attractant concentration at system's ends and on the ratio between the linear pore dimensions.

The dependence $F(p)$ of the chemotaxis sensitivity function on the parameter p, which determines the attractant concentrations at system's ends, was calculated for the parameters $\xi = 0.75$ and $\lambda = 40$. The latter value is close to that which can be obtained on the basis of information concerning the actual bacterial parameters (see, e.g., work [6]). The calculations were performed for various values of the parameter h; in particular, $h = 10$, 3, 1, and 0.8. The parameter p was varied within the interval $-3 \le p \le 3$. The results of calculations for the dependence $F(p)$ are shown in Fig. 1.

The dependence $F(p)$ is dome-shaped (like those obtained for one- and two-dimensional systems [6, 19–21]). The dependence of this type can be explained as follows. At a given p-value, the dimensionless concentration gradient equals $\gamma'(x) = (\xi - 1) \times 10^p$. Hence, when the parameter p increases, the attractant concentration gradient grows by magnitude. Therefore, the non-uniformity in the bacterial distribution (and, hence, the chemotaxis sensitivity function) also increases at first. However, together with an increase of

the attractant gradient, the total amount of the attractant in the system also increases. At a certain moment, the sensitivity of a bacterial receptor achieves the saturation, and the bacteria cease to "feel" the attractant gradient. The bacterial distribution becomes more uniform, and the chemotaxis sensitivity function decreases. In particular, at $h = 10$, the chemotaxis sensitivity function increases from zero to a certain maximum value and then vanishes. For larger values of the parameter h, the dependence $F(p)$ does not change qualitatively. However, if the parameter h decreases, then the following effect is observed: the peak height in the chemotaxis sensitivity function profile decreases, and the function itself shifts downward into the region of negative values. This is a result of the spatial confinement, because smaller values of the parameter h mean a reduction of the pore radius with respect to the pore length. Furthermore, this effect is a direct result of zero boundary conditions at the cylindrical surface. As was marked above, such conditions correspond to the situation where the cylindrical surface is "repulsive" for the bacteria. Therefore, the chemotaxis becomes suppressed, and this effect is stronger for smaller pore radii.

The dependence $F(h)$ of the chemotaxis sensitivity function on the ratio h between the pore radius and the pore length is depicted in Fig. 2. The calculation was carried out for the parameter $p = 0$. As was expected, the chemotaxis sensitivity function grows with the parameter h at small h and afterward saturates. A significant deviation from the saturation value is observed only if the pore radius is comparable with or smaller than the pore length.

6. Results and Conclusions

Hence, a phenomenological model for the chemotaxis phenomenon is proposed in this work. The model allows this phenomenon to be studied and a distribution of bacteria in a cylindrical pore with an attractant to be determined. A situation close to probable experimental conditions is considered: the attractant concentration is fixed at the pore ends; the bacterial concentration is fixed at one end, and the average bacterial concentration is registered at the other end. For this configuration of the system, the chemotaxis sensitivity function is calculated, which gives some insight into the non-uniformity of a bacterial distribution over the system.

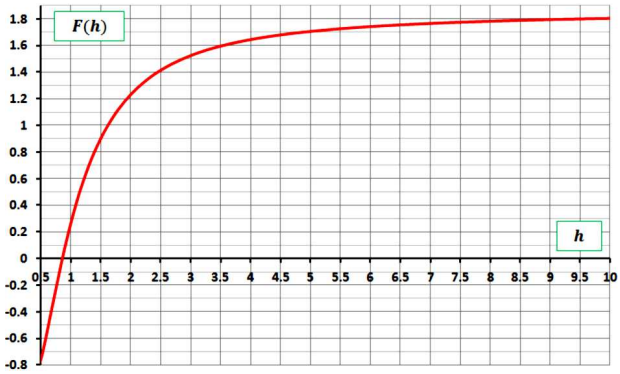

Fig. 2. Chemotaxis sensitivity function $F(h)$ at $p = 0$

Two qualitative effects are obtained, which result from the spatial confinement and the peculiarities in the spatial distribution of an attractant. In particular, the dome-shaped dependence of the chemotaxis sensitivity function on the attractant concentration at the pore end (more exactly, a parameter that determines the concentration at the pore end) is the same as the behavior of this quantity in one- and two-dimensional systems with bacteria and an attractant. At the same time, a reduction of the extremum magnitude and a shift of the chemotaxis sensitivity function into the region with negative values, as the pore radius decreases, take place owing to the spatial confinement of the system and the specific boundary conditions at the lateral pore surface. Therefore, the spatial confinement can be a factor that weakens the processes associated with the chemotaxis.

The results obtained in this work are in agreement with available experimental and theoretical data. They can be useful when processing experimental results obtained for the chemotaxis in capillary systems and porous media.

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ОСОБЛИВОСТІ ХЕМОТАКСИСУ
БАКТЕРІЙ У ЦИЛІНДРИЧНІЙ ПОРІ

Р е з ю м е

В статті розглядається процес перерозподілу бактерій в циліндричній порі за наявності атрактанту. Концентрація атрактанту лінійно зменшується вздовж пори. Перерозподіл бактерій відбувається за рахунок дифузії та за рахунок хемотаксису (рух бактерій у напрямку градієнта атрактанту). В статті з'ясовується питання про вплив просторового обмеження на характер розподілу бактерій в системі. За умови, що бокові стінки пори є "відштовхуючими" для бактерій, показано, що наявність просторового обмеження приводить до зміни характеру розподілу бактерій. Зокрема, зі зменшенням радіуса пори ефект від хемотаксису зменшується. Для оцінки неоднорідності розподілу бактерій у системі розраховується функція чутливості хемотаксису (відхилення від одиничного значення відношення середньої концентрації бактерій в певній області до середньої концентрації бактерій по всій системі). Знайдено залежність функції чутливості хематаксису від концентрації атрактанту на границях системи та від її лінійних розмірів.