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O.M. VASYLIEV, A.O. SLOBODIANIUK

Taras Shevchenko National University of Kyiv
(60, Volodymyrs'ka Str., Kyiv 01601, Ukraine; e-mail: oleksii@vasyliev.kyiv.ua)

THE CHEMOTAXIS SENSITIVITY FUNCTION FOR A SYSTEM WITH A SPHERICAL GEOMETRY

The problem of determining the chemotaxis sensitivity function, which is used to characterize the heterogeneity of a distribution of bacteria in the system with an attractant, has been solved for a system with spherical geometry. In the presence of an attractant, bacteria are distributed according to the attractant distribution in the system. At the same time, the important role is played by the system geometry, boundary conditions, the attractant injection regime, and the control over the number of bacteria in the system. In particular, a system, where bacteria are distributed over the surface of a sphere, is considered. The attractant concentration in the system is controlled by its fixation at the sphere's poles using a thin capillary. The number of bacteria in the system is considered constant. For such a system, an analytic expression for the chemotaxis sensitivity function is obtained. The obtained results can be useful when predicting the behavior of bacteria in real systems with a complicated geometry and when processing experimental data.

K e y w o r d s: chemotaxis, bacteria, attractant, concentration, distribution.

You can observe a lot by watching.

Yogi Berra

1. Introduction. Laws of Bacterial Movement

The chemotaxis phenomenon consists in that some types of flagellated bacteria (such as *Escherichia coli*) can respond to the distribution of a definite substance called attractant, by moving toward its higher concentrations [1–6]. It is important that the process of bacterial movement in the medium is random. Hence, the corresponding dependences arising between the distributions of bacteria and an attractant are statistical. Furthermore, the sequence of interactions taking place in the course of bacterial movement includes several stages, which significantly complicates its theoretical analysis [7–9].

Bacteria that can feel the presence of an attractant (for example, it can be sugar) in the system detect it in the environment with the help of special receptors. However, the matter is that the size of a bacterium is too small, so the bacterium cannot "determine" the direction of the attractant concentration gradient at such distances. Instead, bacteria use a movement algorithm that actually allows them to eventually move in the direction of increasing attractant concentration. Namely, a bacterium moves uniformly and rectilinearly during a certain time interval, and then randomly changes the direction of

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motion. The stage of changing the direction of motion is called *tumbling*. The key circumstance in this scheme is related to the fact that the tumbling frequency depends on the amount of attractant registered by the bacterium during its movement. The rule is simple: the more the attractant was registered, the lower the tumbling frequency is, and, therefore, the less likely is that the bacterium will change the direction of movement. For example, in the case of one-dimensional movement, a bacterium, in the course of tumbling, either changes or does not change the direction of its movement to the opposite with the same probability of 0.5. This value does not depend on the registered amount of an attractant. However, this amount affects the probability of the tumbling at every time moment: this probability decreases, as the amount of the attractant registered by the bacterium increases. Let A_t denote the event consisting in the occurrence of the tumbling within a certain time interval, and let B_t denote the event consisting in changing the bacterium movement direction. Then the probability of changing a direction of the bacterium movement, $P(B_t)$, is determined as follows:

$$P(B_t) = P(B_t|A_t)P(A_t), \tag{1}$$

where $P(A_t)$ is the probability of the tumbling, and the conditional probability $P(B_t|A_t) = 0.5$ is the probability of changing the direction of movement provided that the tumbling has occurred. As was mentioned above, the probability $P(A_t)$ decreases, if the amount of an attractant registered by the bacterium increases. This means that the probability $P(B_t)$ that the bacterium will change the direction of its movement also decreases.

If the movement is not one-dimensional, then the situation, of course, becomes more complicated, but, at the qualitative level, everything remains the same: a change in the direction of movement during the tumbling occurs randomly (with a uniform distribution of the random vector describing the bacterium movement direction), and the probability of the tumbling depends on the amount of a registered attractant.

Although this simple scheme explains how bacteria, by means of the described algorithm, can determine the regions with the highest attractant concentration, this approach (based on the analysis of stochastic processes) is difficult for applications (at least for obtaining the analytic results). Therefore, alternative approaches are often used.

2. Formulation of the Problem. Phenomenological Model

For practical applications, it is convenient to use the phenomenological model based on a system of nonlinear differential equations of the diffusion type. This model has certain restrictions, but it was used to study various chemotaxis systems and proved itself well [10–14]. The model is based on an approach with a rather long and successful history [15–21].

To formalize the problem, let us introduce the following notations. Let $a(\mathbf{r}, t)$ be the attractant concentration and $b(\mathbf{r}, t)$ be the concentration of bacteria in the system at the point $\mathbf{r}$ at the time t. The change of the attractant distribution in time is described by the diffusion-type equation

$$\frac{\partial a}{\partial t} = D_a \Delta a, \tag{2}$$

where D_a is the diffusion coefficient, and Δ denotes the Laplace operator.

For the flux of bacteria $\mathbf{j}_b(\mathbf{r}, t)$ at the point $\mathbf{r}$ at the time t, the following expression was proposed in the framework of the model [10–14]:

$$\mathbf{j}_b = -D_b \boldsymbol{\nabla} b + \frac{kb\boldsymbol{\nabla} a}{(a_0 + a)^2}. \tag{3}$$

The first term on the right-hand side describes the diffusion process, and the second one is associated with the chemotaxis effect. The parameter D_b is the diffusion coefficient, the parameters k and a_0 are phenomenological, and the gradient operator is denoted by $\boldsymbol{\nabla}$. Then the equation determining the spatio-temporal distribution of bacteria in the system looks like

$$\frac{\partial b}{\partial t} = -\boldsymbol{\nabla} \mathbf{j}_b. \tag{4}$$

In principle, the above equations supplemented with boundary and initial conditions make it possible to determine how the distributions of bacteria and an attractant change in time at every point of the system. However, from a practical viewpoint, the stationary case is of interest, when the distributions of bacteria and an attractant do not change in time. It

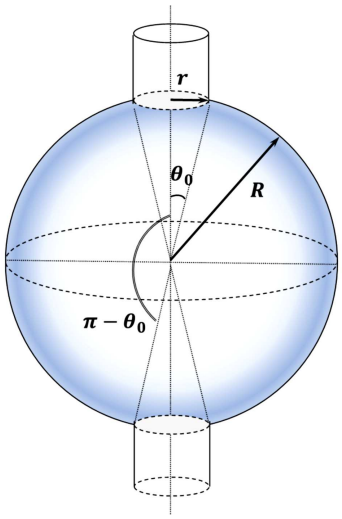

Fig. 1. Geometry of the system. Bacteria and the attractant are distributed over the surface of a sphere. A capillary is used to inject the attractant

is just such situations that are studied and analyzed at the empirical level. As a result, for the attractant distribution, we have

$$\Delta a = 0. \tag{5}$$

The spatial distribution of bacteria is determined as follows:

$$D_b \boldsymbol{\nabla} b + kb \boldsymbol{\nabla} \left(\frac{1}{a_0 + a} \right) = 0. \tag{6}$$

By supplementing Eqs. (5) and (6) with boundary conditions, we obtain a correctly formulated problem.

As was mentioned above, we consider a system with the geometry of a sphere of fixed radius R. Bacteria and the attractant are distributed over the surface of the sphere. The attractant is injected in the following way. A capillary of radius $r \ll R$ passes through the sphere's poles. It is used to control the attractant distribution at the sphere surface in the regions, where they are in contact. The geometry of the system is illustrated in Fig. 1.

We consider a system, where the boundary conditions have radial symmetry. Therefore, the system properties do not depend on the polar angle, but only on the azimuthal angle θ, which is reckoned from the upper pole and varies from θ_0 to $\pi - \theta_0$, where the angle θ_0 determines the direction to the capillary (see Fig. 1) and for which the obvious relation takes place:

$$\sin(\theta_0) = \frac{r}{R}. \tag{7}$$

From Eq. (5), with regard for the explicit expression for the Laplace operator in spherical coordinates, in the case of a fixed radius and no dependence on the polar angle, we obtain the following equation for the attractant distribution:

$$\frac{\partial}{\partial \theta} \left[\sin(\theta) \frac{\partial a}{\partial \theta} \right] = 0. \tag{8}$$

Here, $\theta_0 \leq \theta \leq \pi - \theta_0$, and the following boundary conditions are assumed:

$$a(\theta = \theta_0) = A, \tag{9}$$

$$a(\theta = \pi - \theta_0) = 0. \tag{10}$$

In essence, we assume that the attractant concentration is zero (the attractant is absent) at the capillary boundary in the lower hemisphere (at $\theta = \pi - \theta_0$) and has a maintained constant value A at the capillary boundary in the upper hemisphere (at $\theta = \theta_0$).

The bacterial distribution in the system is determined by the equation

$$D_b \frac{\partial b}{\partial \theta} + kb \frac{\partial}{\partial \theta} \frac{1}{a_0 + a} = 0. \tag{11}$$

This equation is supplemented with an additional relation

$$2\pi R^2 \int\limits_{\theta_0}^{\pi - \theta_0} \sin(\theta) b(\theta) d\theta = B, \tag{12}$$

where B denotes the total number of bacteria in the system.

3. Results. Distribution of Bacteria in the System

Equations (8)–(12) comprise the starting point for obtaining information about the distributions of the attractant and bacteria. In particular, based on Eq. (8) and the boundary conditions (9) and (10), we obtain the following expression for the attractant distribution:

$$a(\theta) = \frac{A}{2} \left[1 + \frac{\ln \frac{1-\cos(\theta)}{1+\cos(\theta)}}{\ln \frac{1-\cos(\theta_0)}{1+\cos(\theta_0)}} \right]. \tag{13}$$

After simple transformations, we determine the relation between the bacterial and attractant distributions,

$$b(\theta) = B_0 \exp\left[-\frac{k}{D_b(a_0 + a(\theta))}\right], \tag{14}$$

where the dependence $a(\theta)$ is given by relation (13), and the constant B_0 can be found from condition (12):

$$B_0 = \frac{B}{2\pi R^2 \int\limits_{\theta_0}^{\pi-\theta_0} \sin(\theta) \exp\left[-\frac{k}{D_b(a_0+a(\theta))}\right] d\theta}. \tag{15}$$

Relations (13)–(15) describe the stationary distributions of the attractant and bacteria in the system. They depend on boundary conditions, namely, on the values of the parameters A and B. Furthermore, we are not interested in the bacterial distribution itself, but in its non-uniformity degree. For this purpose, a special numerical parameter has to be used that would characterize the bacterial distribution behavior.

4. Non-Uniformity of Bacterial Distribution. Chemotaxis Sensitivity Function

As a parameter that characterizes the non-uniformity of the bacterial distribution, we will use the *chemotaxis sensitivity function* $F(S)$. It depends on the region S, where it is determined. A formal definition of this function is that it is the ratio between the average number of bacteria in a certain subregion and the average number of bacteria in the system, minus one [7, 12]:

$$F = \frac{\frac{1}{S}\int\limits_S b dS}{\frac{1}{\Omega}\int\limits_\Omega b d\Omega} - 1, \tag{16}$$

where S denotes the region, where the chemotaxis sensitivity function is determined, and Ω denotes the region occupied by the whole system. Under this definition of the chemotaxis sensitivity function, its zero value corresponds to the situation, when the average concentrations of bacteria in the region S and the system are identical. Its value is positive, if the bacterial concentration in S exceeds the average one, and negative otherwise.

As was mentioned, the chemotaxis sensitivity function F depends on the region S for which the average bacterial concentration is calculated. Usually, it is calculated for the contact region of the system with the capillary through which the attractant is injected. There are two important reasons for that. One of them is associated with the fact that the attractant concentration is the highest in this region; therefore, the bacterial concentration is also the highest. Hence, the value of the chemotaxis sensitivity function for this region makes it possible to evaluate the maximum possible non-uniformity in the bacterial distribution. The other reason is associated with the fact that, in practice, the bacterial concentration can be most easily measured just in this region. Therefore, the theoretical estimates obtained for this region can be useful in the future in the application aspect as well.

If the chemotaxis sensitivity function is calculated for a thin band of thickness $h \ll R$ near the capillary-sphere connection region, then, in the limit $h \to 0$, we obtain the following expression:

$$F(\theta = \theta_0) = 4\pi R^2 \frac{b(\theta = \theta_0)}{B} - 1. \tag{17}$$

Here, we took into account that the total number of bacteria at the sphere surface is constant and equals B. Since the capillary radius $r \ll R$, we also neglected that some part of the sphere surface (at the poles) is covered by the capillary.

In view of Eq. (9), we have $a(\theta = \theta_0) = A$, and, taking Eqs. (14) and (15) into account, we obtain

$$b(\theta = \theta_0) = \frac{B}{2\pi R^2} \frac{\exp\left(-\frac{k}{D_b(a_0+A)}\right)}{\int\limits_{\theta_0}^{\pi-\theta_0} \sin(\theta) \exp\left(-\frac{k}{D_b(a_0+a(\theta))}\right) d\theta}, \tag{18}$$

and, accordingly,

$$F(\theta = \theta_0) = 2\frac{\exp\left(-\frac{k}{D_b(a_0+A)}\right)}{\int\limits_{\theta_0}^{\pi-\theta_0} \sin(\theta) \exp\left(-\frac{k}{D_b(a_0+a(\theta))}\right) d\theta} - 1. \tag{19}$$

We are interested in how the chemotaxis sensitivity function changes, when the boundary conditions change, namely, how the chemotaxis sensitivity function depends on the concentration of the attractant

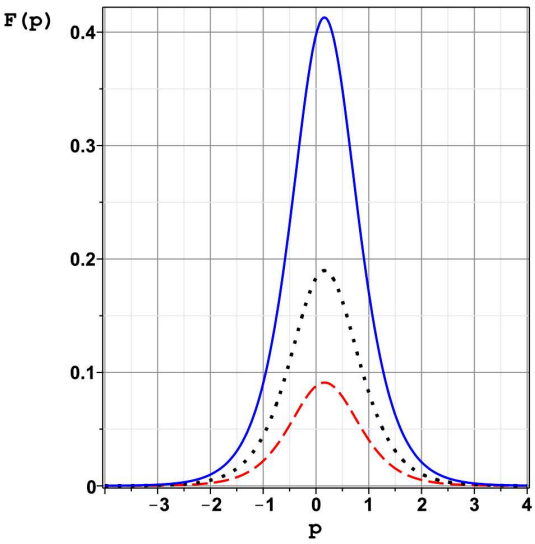

Fig. 2. The chemotaxis sensitivity function $F(p)$ for $\theta_0 = 0.01$ and various $\lambda = 2$ (solid curve), 1 (dotted curve), and 0.5 (dashed curve)

injected into the system through the capillary. The relevant analysis can be implemented only numerically. For this purpose, the required relations should be converted into a dimensionless form.

5. Quantitative Analysis. Influence of Attractant Concentration on Distribution Uniformity

For convenience, denote $\lambda = \frac{k}{D_b a_0}$, and let also $A = a_0 \times 10^p$, where p is a dimensionless parameter. We are interested in the dependence of the chemotaxis sensitivity function F on the parameter p. In so doing, we consider the parameters λ and θ_0 fixed. In the new notation, we have

$$F(p) = \frac{2\exp\left(-\frac{\lambda}{1+10^p}\right)}{\int\limits_{\theta_0}^{\pi-\theta_0} \sin(\theta)\exp\left[-\frac{\lambda}{Z(p,\theta)}\right]\,d\theta} - 1, \tag{20}$$

where

$$Z(p,\theta) = 1 + \frac{10^p}{2}\left[1 + \frac{\ln\frac{1-\cos(\theta)}{1+\cos(\theta)}}{\ln\frac{1-\cos(\theta_0)}{1+\cos(\theta_0)}}\right]. \tag{21}$$

Numerical calculations show that the dependence $F(p)$ is not trivial. Namely, it has a strongly nonlinear dome-shaped character. The peak magnitude increases, as the parameter λ grows. In Fig. 2, this dependence is illustrated for several values of the parameter λ.

6. Conclusions

Based on the proposed model, the chemotaxis sensitivity function F for a system with spherical geometry has been calculated. It is shown that the dependence of this function on the attractant concentration in the region, where the attractant is injected into the system, has a non-linear behavior with a characteristic maximum.

The presence of an extremum in the dependence $F(p)$ has the following explanation. The growth of the parameter p means the growth of the attractant concentration in the region of its injection into the system. In the framework of the considered model, the term responsible for the chemotaxis effect in Eq. (6) depends nonlinearly on the attractant concentration and is proportional to its gradient. Therefore, the common effect depends not only on the magnitude of the attractant concentration gradient, but also on the local concentration value. If the attractant concentration increases, the role of the gradient considerably diminishes. The model scenario agrees well with the behavior of real systems (see, for example, work [7]). Namely, if the attractant concentration increases, the non-uniformity of the bacterial distribution also increases, but, after the receptors of bacteria become saturated, the chemotaxis effect begins to decrease.

The obtained results can be useful while analyzing the available experimental data and predicting the behavior of corresponding systems.

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О.М. Васильєв, А.О. Слободянюк

ФУНКЦІЯ ЧУТЛИВОСТІ ХЕМОТАКСИСУ ДЛЯ СИСТЕМИ ЗІ СФЕРИЧНОЮ ГЕОМЕТРІЄЮ

У статті розв'язується задача визначення функції чутливості хемотаксису для системи, що має геометрію сфери. Функція чутливості хемотаксису використовується як характеристика неоднорідності розподілу бактерій в системі, де є атрактант. За наявності атрактанту бактерії розподіляються в системі відповідно до розподілу атрактанту. При цьому важливу роль відіграє геометрія системи, межові умови, режим підведення атрактанту та регулювання кількості бактерій в системі. Нами розглядається система, в якій бактерії розподілені по поверхні сфери. Концентрація атрактанту в системі регулюється шляхом фіксації концентрації атрактанту на полюсах сфери з використанням тонкого капіляру. Кількість бактерій в системі вважається фіксованою. Для такої системи отримується аналітичний вираз для функції чутливості хемотаксису. Отримані результати можуть бути корисними при поясненні поведінки бактерій в реальних системах зі складною геометрією та при обробленні експериментальних даних.

Ключові слова: хемотаксис, бактерія, атрактант, концентрація, розподіл.