

IMPLEMENTATION AND NUMERICAL TESTING OF REACTION-DIFFUSION MODEL OF BACTERIAL COLONY GROWTH

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ABSTRACT

In this paper the solution of a reaction-diffusion model of the bacterial colony growth is presented. The finite difference method with two computational schemes, explicit scheme and method of lines, is used for discretisation. Testing calculations performed with implementation of the described methods are compared with each other by evaluation of obtained result differences and time-consumption. With respect to the gained information the explicit scheme is picked out for trying to reproduce the published results of the reaction-diffusion model. Obtained solutions are briefly discussed.

Keywords: Pattern formation, reaction-diffusion model, finite difference method

1 BACILLUS SUBTILIS COLONY PATTERNS

It is known that colonies of bacterial species called *Bacillus subtilis* exhibit diverse growth patterns. The colony patterns change when two environmental conditions, the concentration of nutrient C_n and agar C_a , are varied. Fig. 1 shows morphological diagram of *Bacillus subtilis* colony patterns [2], where patterns are qualitatively classified into five types.

If concentration of nutrient is low and agar concentration is high (see Fig.1, region A) the colony patterns show dendritic growth with branch structures. If nutrient concentration is increased with fixed higher agar concentration, each branch becomes thicker and the colony has a roughly round shape with rough envelope (see Fig.1, region B). If agar concentration is decreased with fixed lower nutrient concentration, the colony shows dense-branching pattern with smooth envelope (see Fig.1, region E). If nutrient concentration is high and agar concentration is low (see Fig.1, region D), the colony is homogeneously spreading and developing disk-like pattern. In the last region C, bacteria actively move and suddenly stop while performing cell-division, then repeating the cycle so we can observe the concentric ring pattern [1].

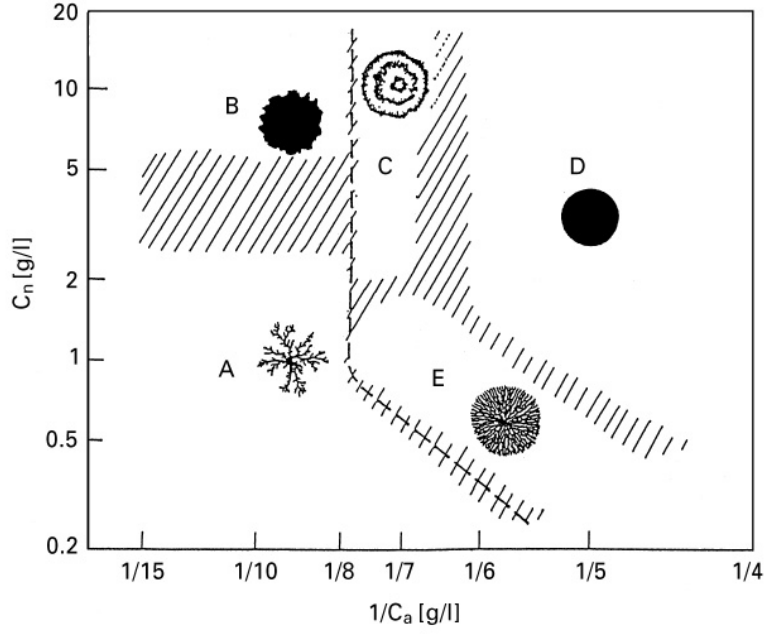


Figure 1: Morfological diagram of *Bacillus subtilis* colony patterns [2]

2 MATHEMATICAL MODEL OF BACTERIA COLONY GROWTH

There are two types of *Bacillus subtilis* bacteria species investigated, one is the active bacteria which move, grow and perform cell-division. The other ones are inactive bacteria which do nothing at all. Let $A(t, x, y)$ be a density of the active bacteria and $I(t, x, y)$ be a density of the inactive bacteria at position (x, y) and time t . Concentration of nutrient be denoted as $N(t, x, y)$. Now we can write the reaction-diffusion model for A, I and N [1].

$$\begin{aligned}
 \frac{\partial A}{\partial t} &= \nabla(d_A \nabla A) + v g(N)A - a(A, N, I)A + b(A, N, I)I \\
 \frac{\partial N}{\partial t} &= d_N \Delta N - g(N)A \\
 \frac{\partial I}{\partial t} &= a(A, N, I)A - b(A, N, I)I,
 \end{aligned} \tag{1}$$

where d_A is the motility of active bacteria and d_N is the diffusion rate of nutrients. $v g(N)$ is the growth rate with a positive constant v , $a(A, N, I)$ and $b(A, N, I)$ are conversion rates between active bacteria and inactive ones.

If the agar concentration C_a is low, the substrate is soft then bacteria can move and it can be described by a normal diffusion. But, if agar concentration is higher, bacteria can hardly move but they perform cell-division and the colony can expand by a sort of “population pressure” of bacteria. This situation can be described in terms of nonlinear diffusion $d_A = d_A(B)$ with total density of bacteria $B = A + I$. Nonlinear diffusion is monotonously

increasing with B and satisfying $d_A(0) = 0$. As a form of d_A , we take

$$d_A(B) = \begin{cases} d_0 & \text{for soft agar} \\ d_1 B & \text{for hard agar,} \end{cases} \quad (2)$$

where d_0 and d_1 are suitable positive constants. Because nutrients diffuse in the agar, we take d_N to be a positive constant. The growth rate $g(N)$ is monotonously increasing with nutrients concentration N . For simplicity we specify $g(N) = \alpha N$ as the Malthusian growth rate with suitable positive constant α .

By the observation that once active bacteria become inactive ones, they never become active again unless food is added, we specify $b(A, N, I) = 0$. When the nutrients concentration becomes lower, the activity of cells becomes weaker. That's why, we take $a(A, N)$ as a monotonously decreasing with N . Unfortunately the dependency of the active bacteria $a(A, N)$ on A is still unclear, but some observations show that $a(A, N)$ is also monotonously decreasing with A [1].

By using suitable dimensionless methods, we can rewrite (1) as the following reaction-diffusion system of equations, where u and w are dimensionless population density of active respectively inactive bacteria, v is the dimensionless concentration of nutrients.

$$\begin{aligned} \frac{\partial u}{\partial t} &= \nabla(d(b)\nabla u) + uv - \frac{u}{(1 + \frac{u}{a_1})(1 + \frac{v}{a_2})} \\ \frac{\partial v}{\partial t} &= \Delta v - uv \\ \frac{\partial w}{\partial t} &= \frac{u}{(1 + \frac{u}{a_1})(1 + \frac{v}{a_2})}, \end{aligned} \quad (3)$$

where $b = u + v$, $d(b)$ is the ratio of the diffusion rates d_A and d_N , a_1 and a_2 are suitable positive constants.

We consider (3) in a two-dimensional bounded region Ω . The initial conditions are

$$\begin{aligned} u(0, x, y) &= u_0(x, y) \geq 0 \\ v(0, x, y) &= v_0 > 0, \quad t > 0, (x, y) \in \Omega \\ w(0, x, y) &\equiv 0. \end{aligned} \quad (4)$$

We take $u_0(x, y)$ to be delta-like function in the center of Ω and v_0 to be a positive constant in Ω . The boundary conditions on the boundary $\partial\Omega$ are

$$\frac{\partial u}{\partial n} = 0 = \frac{\partial v}{\partial n}, \quad t > 0, (x, y) \in \partial\Omega, \quad (5)$$

where n is the outward normal vector on $\partial\Omega$.

3 NUMERICAL SOLUTION OF REACTION-DIFFUSION MODEL

We use the finite difference method (FDM) for spatial discretisation of the problem (3)-(5). FDM is a method for solving partial differential equations which is based on Taylor

$\sum(u_1 - u_2)^2$	V_1 vs. V_2	V_2 vs. V_3	V_3 vs. V_4	V_4 vs. V_5
ML	2,6974	0,3847	0,0206	0,0010
ES	2,9460	0,4023	0,0208	0,0010
$\max u_1 - u_2 $	V_1 vs. V_2	V_2 vs. V_3	V_3 vs. V_4	V_4 vs. V_5
ML	0,8908	0,4555	0,1096	0,0227
ES	0,9131	0,4651	0,1103	0,0227

Table 1: Values of $\sum(u_1 - u_2)^2$ and $\max |u_1 - u_2|$ for various space discretisations

expansions and direct application of the derivatives definition. The basic idea of FDM is to express derivatives from developed Taylor expansions. E.g. for given function $u(x)$, it can be simply shown that approximation of derivative $\frac{\partial u}{\partial x} \equiv u_x$ is

$$u_x(x) = \frac{u(x+\Delta x) - u(x)}{\Delta x} + O(\Delta x) = \frac{u(x) - u(x-\Delta x)}{\Delta x} + O(\Delta x) = \frac{u(x+\Delta x) - u(x-\Delta x)}{2\Delta x} + O(\Delta x^2).$$

By using similar techniques we can obtain formulas for higher-order derivatives. FDM is usually applied on uniform mesh with high degree of mesh regularity, i.e. mesh must be set up in a structured way, whereby the mesh points in an n -dimensional space are located at the intersections of n family of rectilinear or curved lines. These curves appear as a form of numerical coordinate lines and each point must lie on one and only one line of each family [3].

If we replace all the spatial derivatives by their approximations and the temporal derivative by the forward formula, i.e. $u_t(t) \approx \frac{u(t+\Delta t) - u(t)}{\Delta t}$, we obtain the *explicit scheme* (ES). *Method of lines* (ML) is a semi-discrete schema in which spatial derivatives are replaced only by particular difference formulas but the temporal derivatives are still continuous. We obtain an ordinary differential equation (ODE) or a system of ODE's which can be solved by using of standard methods. In our computation we use the fourth-order Runge-Kutta method.

First of all we performed several calculation of the system of equation (3)-(5). We used "stable" parameters (Fig.1, region D) which have been published in [1], both methods and various fine-meshed space ($V_1 : \Delta x = 1 \Delta t = 0, 2$; $V_2 : \Delta x = 0, 5 \Delta t = 0, 05$; $V_3 : \Delta x = 0, 25 \Delta t = 0, 01$; $V_4 : \Delta x = 0, 125 \Delta t = 0, 002$; $V_5 : \Delta x = 0, 0625 \Delta t = 0, 0005$). We evaluated mutual difference of the obtained results, time-consumption of the particular calculations and finally we picked out the best scheme. Criterion of the solution distance is the norm in space $L_2(t_0, t_1; \Omega)$ which is approximated by $\sum(u_1 - u_2)^2$:

$$\int_{t_0}^{t_1} \int_{\Omega} (u_1 - u_2)^2 \approx \sum(u_1 - u_2)^2.$$

u_1 and u_2 are results of given scheme for two particular discretisations in the same mesh point and time. We also evaluated "maximum error" $\max |u_1 - u_2|$ and "relative error" $\max \frac{|u_1 - u_2|}{u_1 + u_2}$ to observe error spreading in the last time step.

We pick out the explicit scheme for reproducing the published results by reason that all the error values of both schemata are almost identical (see Tab.1) but using of method of lines is significantly more time-consuming than using of explicit scheme.

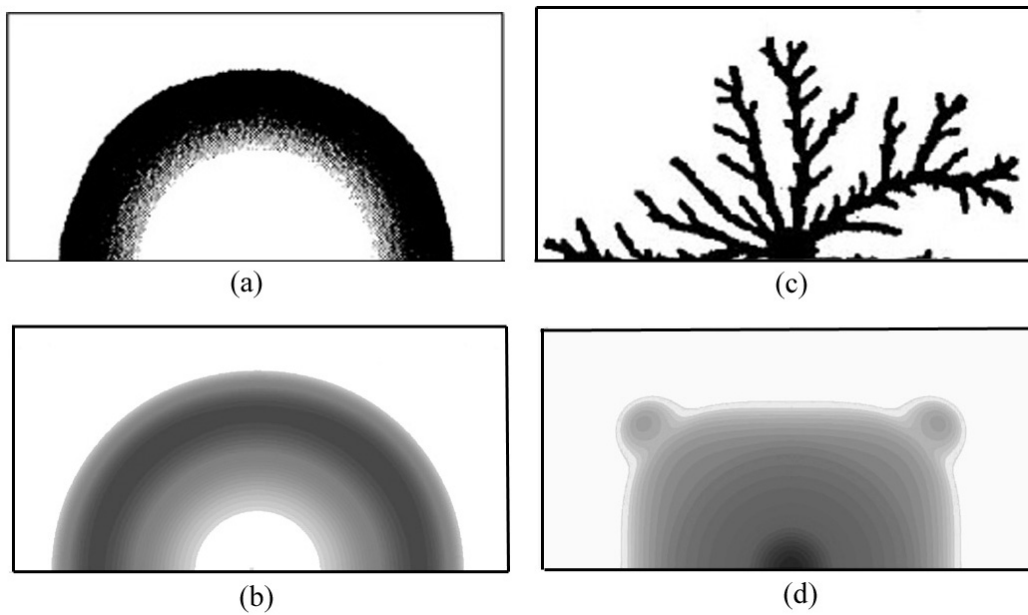


Figure 2: Comparison of our calculated results (b, d) with published ones (a, c) [1]. (a, b) show disk-like patterns and (c, d) show dendritic branch patterns.

4 CONCLUSION

During numerical solution of reaction-diffusion system of equations (3)-(5) we find out that we are unable to reproduce all the results published in [1]. We obtain only the symmetric results namely homogeneously spreading and developing disk-like pattern of bacterial colony and symmetric version of dendritic growth (see Fig.2). The reason is simple, the model (3) contains symmetric equations and the initial conditions are also symmetric so that we should gain just the symmetric solutions. To obtain a nonsymmetric solution like dendritic branching pattern we propose to introduce a small noise function into the model or to apply a method using unstructured meshes. Now we are working on implementation of the finite volume scheme which uses such an unstructured mesh.

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