Chemotactic Aggregation of an Ensemble of Identical Living Organisms in One Dimension

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Abstract

Simple living organisms ("cells") are known to move both by diffusion and by chemotaxis. The latter denotes directed movement towards regions of higher concentration of a chemical substance secreted by the cells. We perform a mathematical analysis of this phenomenon, using the Keller-Segal model.

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1 Introduction

The Keller-Segel model [1] of cell aggregation is studied using different mathematical techniques. A constant number of cells is supposed to be located on a line segment. The cells secrete at a constant rate a chemical attractant, which diffuses and decays. The cells move by diffusion as well as towards regions of higher attractant concentration.

One of the questions concerning this model is: Given an arbitrary initial distribution of the cells, will they aggregate in clusters or other spatially inhomogeneous patterns? [3, 4, 5]

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We will examine stationary inhomogeneous distributions of the cells as well as the time evolution toward such distributions.

2 Continuum Model

We denote the cell density by $\nu(x,t)$ and the attractant density by $\alpha(x,t)$, the cell and the attractant diffusion constants by D_ν and D_α, the attractant generation and decay rates by h_ν and h_α. The chemotactic constant is denoted by χ. The model is described by the equations

$$\frac{\partial \nu}{\partial t} = \nabla(D_\nu \nabla \nu - \nu\chi\nabla\alpha) \tag{1}$$

and

$$\frac{\partial \alpha}{\partial t} = h_\nu \nu - h_\alpha \alpha + \nabla(D_\alpha \nabla \alpha) \tag{2}$$

with the boundary conditions

$$\nabla\alpha|_{x=0} = \nabla\alpha|_{x=L} = 0, \tag{3}$$

and

$$\nabla\nu|_{x=0} = \nabla\nu|_{x=L} = 0. \tag{4}$$

Equation (1) expresses the fact that diffusion and chemotactic movement compete in determining the local rate of change of the cell concentration. The three terms of the right-hand side of Eq. (2) represent attractant generation, decay and diffusion, respectively. The boundary conditions are so chosen that neither cells nor attractant will leave the line segment of length L.

A first result for the steady state of the system (i.e. $\frac{\partial \nu}{\partial t} = 0$, $\frac{\partial \alpha}{\partial t} = 0$) is

$$A = \frac{h_\nu}{h_\alpha} M \tag{5}$$

where A and M are the total masses of attractant and cells, respectively. It is convenient to introduce dimensionless quantities

$$\begin{aligned} &\xi = \sqrt{\frac{h_\alpha}{D_\alpha}}x, \qquad \tau = h_\alpha t, \qquad D = \frac{D_\nu}{D_\alpha}, \\ &n(\xi,\tau) = \frac{\chi h_\nu}{D_\nu h_\alpha}\nu(x,t), \qquad \alpha(\xi,\tau) = \frac{\chi}{D_\nu}\alpha(x,t), \end{aligned} \tag{6}$$

which reduces Eqs. (1) and (2) to

$$\frac{1}{D}\frac{\partial n}{\partial \tau} = n'' - n'a' - na'' \tag{7}$$

and

$$\frac{\partial a}{\partial \tau} = a'' - a + n, \tag{8}$$

where the prime denotes differentiation with respect to ξ.

The boundary conditions are

$$a'(0) = a'(l) = 0, \quad n'(0) = n'(l) = 0, \quad l = \sqrt{\frac{h_\alpha}{h_\nu}} L. \tag{9}$$

3 The Steady State

In the steady state, Eqs. (7-9) yield

$$n(\xi) = n(0) \mathrm{e}^{a(\xi) - a(0)} \tag{10}$$

and

$$a'(\xi)^2 = 2n(0) \left[1 - \mathrm{e}^{a(\xi) - a(0)} \right] - a(0)^2 + a(\xi)^2 \equiv \psi(a; a(0), n(0)). \tag{11}$$

The behavior of the solution $a(\xi)$ can be analyzed by studying the function $\psi(a)$ for different pairs of values $(a(0), n(0))$ (to be published). It is more realistic to assume that the total cell mass is given, and not the boundary values $n(0)$, $a(0)$. For this case it is convenient to use the equation

$$a - a'' - \frac{1}{2} a^2 + \frac{1}{2} a'^2 + c = 0 \tag{12}$$

and the relation

$$n = a - a''. \tag{13}$$

If the solution it assumed to deviate little from the uniform distribution $n(\xi) = \text{constant}$, it can be expressed in terms of Jacobian elliptic functions or trigonometric functions []. For the former it is found that

$$a(\xi) = a_0 + A \, \mathrm{sn}^2(\xi | m). \tag{14}$$

The parameters a_0, A and m are determined by the total cell mass and the length of the interval over which this mass is distributed. Since this distribution (14) is periodic, several solutions are possible whose periods are fractions of the interval length.

Using the approximation Eq. (14) to find the appropriate starting value $a(0)$ and the constant c from the knowledge of the total cell mass, Eq. (12) can be easily integrated numerically.

Figure 1 shows one of the clustered steady states of cell density distribution. The curve shows the results of both the elliptic function approximation and the numerical integration, which are conincident within the accuracy of the graphical representation.

It is found, although not detailed in this report, that, for certain combinations of the total cell mass and interval length l, there are no density distributions which deviate only slightly from the uniform distribution: large deviations develop. We study these bifurcation phenomena and find that the usual analysis based on a trigonometric development [3, 5] may not adequately describe the bifurcation point.

To clarify the situation, a stochastic method was adopted to study the time-dependent behavior of the system.

4 Stochastic Time Evolution of the Cell Density

The system is discretized by choosing N equidistant points ξ_i in the interval $[0, l]$ at times τ_k ($i = 0, 1, 2, \ldots, l/N$; $k = 0, 1, 2, \ldots$). It is assumed that at τ_0 the cells are randomly distributed over all points ξ_i with uniform distribution and that the attractant density is zero. Thereafter, attractant density varies according to Eq. (8), except that, because $n(\tau, \xi)$ and $a(\tau, \xi)$ are only defined in discrete points of the time and the coordinate axis, derivatives are replaced by their usual discrete counterparts.

The stochastic aspect of the process enters through the assumption made concerning the chemotactic movement of the cells: at every time point τ_k and point ξ_i, each cell (except those at $\xi = 0$ and $\xi = l$) has a certain probability p_+ of moving to ξ_{i+1} and a probability p_- of moving to ξ_{i-1}. These probabilities are chosen as

$$p_s = \left[1 + \exp\left(\frac{1}{\alpha_0}\left|\frac{\partial a}{\partial \xi}\right|\right)\right]^{-1} \tag{15}$$

$$p_\Sigma = 1 - p_s \tag{16}$$

where $s = \text{sign}(\frac{\partial a}{\partial \xi})$ takes on the values "+" if $\frac{\partial a}{\partial \xi} \geq 0$ and "−" if $\frac{\partial a}{\partial \xi} < 0$ and p_Σ is its complement, that is, p_Σ="−" ifp_s ="+" and *vice-versa*. This choice implements chemotatic attraction by creating a cell current in the direction of enhanced attractant density.

After iteration over a large number of time steps both homogeneous and clustered quasi-stationary cell distributions are obtained, depending on the parameters of the case. Figure 2 shows one of the clustered quasi-stationary states obtained with $N = 100$ and 10^5 time steps.

5 Conclusion

The results for the one-dimensional continuum Keller-Segel model, obtained both analytically and numerically, show clustering of cells in the stationary state. This clustering only occurs if the total cell mass is sufficiently large and the interval sufficiently small. A precise bifurcation analysis of strong vs. weak clustering is yet outstanding. A discretized stochastic time-dependent treatment of the problem bears out these conclusions.

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Figure 1: Attractant density $a(\xi)$ (broken line) and cell density $n(\xi)$ (solid line) along the line segment 0-10 calculated by the elliptic function approximation as well as by numerical integration for a total cell mass of 26.95 (in reduced units).

Figure 2: Results of the stochastic time evolution model for a certain choice of parameters. At $t = 0$, the cell density is uniformly distributed along the line segment [0,100] and the attractant density is zero. The attractant density $a(\tau, \xi)$ is shown at different times (solid lines). The clustering increases with time. The cell density is shown as a broken line at the end of the process.