

## Nonlinear Aspects of Chemotaxis\*

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*Received 7 November 1980; revised 17 March 1981.*

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### ABSTRACT

A simplified Keller-Segel model for the chemotactic movements of cellular slime mold is reconsidered. In particular, we ask for the circumstances under which the cell distribution can autonomously develop a  $\delta$ -function singularity. By the use of suitable differential inequalities, we show that this cannot happen in the case of one-dimensional aggregation. For three or more dimensions, we produce time developments which do become singular, while in the important special case of two-dimensional motion, we advance arguments that the possibility of chemotactic collapse requires a threshold number of cells in the system.

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### 1. INTRODUCTION

Chemotaxis, the directed movement of an organism in response to ambient chemical gradients, is a prominent feature in the organization of many biological populations. This paper is devoted to a nonlinear problem arising in mathematical models of chemotaxis. Our motivation comes from studies of the aggregation of the cellular slime molds, and specifically from the continuum aggregation model formulated by Keller and Segel [3]. For the relevant biological background we refer to Bonner [1]. A similar and more elaborate class of models has been discussed by Segel and Stoeckly [5].

In the Keller-Segel model, a large number of identical biological subunits, which we here will call cells, move about in space in response to one or more chemicals. The version of the model to be considered in this paper [3, p. 399] is described by the two continuum equations

$$\frac{\partial a}{\partial t} + \nabla \cdot [\chi(a, b) \nabla b - \mu(a, b) \nabla a] = 0, \quad (1.1)$$

$$\frac{\partial b}{\partial t} - af(b) + g(b) - \nu_0 \nabla^2 b = 0, \quad (1.2)$$

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\*Supported in part by the National Science Foundation under grant MCS-79-02766.

where  $a(x, t)$  is the number density of cells and  $b(x, t)$  is the concentration of a single chemical attractant, at a point  $x$  in  $R_n$  at time  $t$ . By (1.1), the flux of cells  $\mathbf{F}$  defined by

$$\mathbf{F} = \chi \nabla b - \mu \nabla a \quad (1.3)$$

involves both chemotaxis and diffusion,  $\chi$  being a coefficient determining the intensity of the chemotactic flux in response to the chemical gradient. By (1.2), the attractant is produced in proportion to cell density and is degraded by fast reactions with subsidiary chemicals; the attractant also diffuses with coefficient  $\nu_0$ . We take all functions appearing in (1.1), (1.2) to be nonnegative, this being an important property to be exploited in our analysis. Since we shall be dealing with an initial boundary value problem for  $a, b$ , the condition of nonnegativity implies restrictions on the possible forms of  $\chi$  and  $g$ .

The mechanism proposed by Keller and Segel for the initiation of cell aggregation can be described as an instability of the spatially homogeneous equilibria of (1.1), (1.2). In this paper our concern is the nonlinear development of solutions following the onset of the aggregation instability. Little is known about the evolution of  $a, b$  for the general system (1.1), (1.2), since there appear to be no interesting forms which are exactly solvable. Some nonlinear analysis was carried out by Nanjundiah [4], whose surprising results stimulated the present study. Nanjundiah suggests that aggregation proceeds to the formation of  $\delta$ -functions in cell density, a phenomenon we refer to here as "chemotactic collapse." At first this result would seem to contradict the diffusive nature of the model, but the fact that chemotaxis has some features of "negative diffusion" [cf. (1.3)] suggests the possibility of singular behavior.

The arguments advanced by Nanjundiah are actually independent of the dimension of the space in which aggregation occurs. We shall show here that in fact singular behavior and chemotactic collapse is not possible in one dimension (Section 2). In higher than two dimensions, we present (in Section 3) results supporting Nanjundiah's contention that collapse can occur, and extend this result in Section 4 to two dimensions, at least provided that an appropriate measure of total cell number is sufficiently large. (We assume that the total cell number is fixed.)

We are interested here in functions in (1.1), (1.2) satisfying the following inequalities:

$$\begin{aligned} \chi(a, b) &\leq \chi_0 a, & \mu(a, b) &\geq \mu_0, \\ f(b) &\leq f_0, & g(b) &\geq g_0 b, \end{aligned} \quad (1.4)$$

where the subscript zero denotes a positive constant. In fact we shall restrict

attention in this paper to the “minimal system”

$$\frac{\partial a}{\partial t} + \chi_0 \nabla \cdot (a \nabla b) - \mu_0 \nabla^2 a = 0, \quad (1.5)$$

$$\frac{\partial b}{\partial t} - f_0 a + g_0 b - \nu_0 \nabla^2 b = 0, \quad (1.6)$$

which has often been taken as a prototype of (1.1), (1.2). We conjecture that the one-dimensional theory of Section 2 carries over to (1.4), while the subsequent calculations of chemotactic collapse provide examples of this behavior within the class (1.4).

Intuitively, the possibility of collapse can be understood as follows: since cell number is conserved, the magnitude of  $a$  in an aggregate in  $R^n$  will be  $O(\delta^{-n})$ , where  $\delta$  is an aggregate dimension that decreases to 0 under collapse. The degradation  $b$  in (1.6) can of course be dropped in comparison with diffusion  $\nabla^2 b$  under these conditions. If we further choose  $b \sim \delta^{1-(n/2)}$  and  $t \sim \delta^{1+(n/2)}$ , so that  $\partial/\partial t \sim \delta^{-1-(n/2)}$  and  $\nabla \sim \delta^{-1}$ , Equations (1.5) and (1.6) take the form

$$\begin{aligned} \delta^{-(1+3n/2)}(\delta^0, \delta^0, \delta^{n/2-1}) &= 0, \\ \delta^{-n}(\delta^0, \delta^0, \delta^{n/2-1}) &= 0, \end{aligned} \quad (1.7)$$

where the  $\delta$ -dependence of the various terms has been indicated. In other words, if  $n=1$ , diffusion dominates at small  $\delta$ , precluding a collapse. If  $n>2$ , diffusion can be neglected and collapse is enforced. At  $n=2$ , dynamics remains balanced for arbitrarily small  $\delta$ , to this order, so that collapse depends upon higher-order corrections, which turn out to be logarithmic.

## 2. THE ONE-DIMENSIONAL PROBLEM.

### A. THE IMPOSSIBILITY OF $\delta$ -FUNCTION AGGREGATES

We take the domain to be the full line  $R$ , and suppose that initially

$$\begin{aligned} a(x, 0) = a_0(x) \geq 0, \quad b(x, 0) = b_0(x) \geq 0, \\ \lim_{|x| \rightarrow \infty} a_0(x), a'_0(x), b_0(x), b'_0(x) = 0. \end{aligned} \quad (2.1)$$

The diffusion equations, now

$$\frac{\partial a}{\partial t} + \chi_0(ab')' - \mu_0 a'' = 0, \quad (2.2)$$

$$\frac{\partial b}{\partial t} - f_0 a + g_0 b - \nu_0 b'' = 0, \quad (2.3)$$

maintain both positivity and asymptotic conditions in time. Our aim is to show that no solution of (2.1), (2.2), (2.3) can cause the cell density  $a(x, t)$  to evolve into a stationary set of  $\delta$ -functions. In fact, we shall prove the stronger result that the second moment

$$Q_a(t) = \int a^2 dx \quad (2.4)$$

remains bounded.

A first estimate of the development of (2.2) and (2.3) is supplied by conservation laws. Integrating (2.2) over  $R$  yields

$$\frac{d}{dt} m_a(t) = 0, \quad (2.5)$$

where  $m_a(t) = \int a dx$ , so that  $m_a(t)$  maintains its value  $m_a(0) \equiv m_a$ . For  $b$ , we have similarly

$$\frac{d}{dt} \int b dx = \dot{m}_b(t) \leq f_0 m_a - g_0 m_b(t),$$

so that

$$m_b(t) \leq \frac{f_0 m_a}{g_0} + \left( m_b - \frac{f_0 m_a}{g_0} \right) e^{-g_0 t}. \quad (2.6)$$

In particular, if  $m_a$  and  $m_b$  are initially bounded, they remain so.

To refine these estimates of the developing structures—which are not peculiar to one-dimensional space—we next show that

$$N_b(t) = \int (b')^2 dx \quad (2.7)$$

can be bounded from above by a constant  $K$ . Going over to the Fourier transform

$$b(x, t) = \frac{1}{2\pi} \int \tilde{b}(k, t) e^{-ikx} dk, \quad (2.8)$$

Equation (2.3) takes the form

$$\frac{\partial \tilde{b}}{\partial t} + (g_0 + k^2) \tilde{b} = f_0 \tilde{a},$$

with the solution

$$\tilde{b}(k, t) = \tilde{b}(k, 0) e^{-(g_0 + k^2)t} + f_0 \int_0^t \tilde{a}(k, t') \exp\{-(g_0 + k^2)(t - t')\} dt'.$$

Since  $a(x, t) \geq 0$ , then  $\tilde{a}(k, t) \leq \int |a(x, t)| dx = m_a$ , and we therefore have

$$\begin{aligned} |\tilde{b}(k, t)| &\leq |\tilde{b}(k, 0)| \exp(-(g_0 + k^2)t) + f_0 m_a \frac{1 - \exp(-(g_0 + k^2)t)}{g_0 + k^2} \\ &\leq |\tilde{b}(k, 0)| + \frac{f_0 m_a}{g_0 + k^2}. \end{aligned} \quad (2.9)$$

It follows at once from (2.9) that if  $N_b(0)$  is bounded, then

$$N_b(t) = \frac{1}{2\pi} \int k^2 |\tilde{b}(k, t)|^2 dk \leq K^2, \quad t \geq 0, \quad (2.10)$$

for suitable  $K$ . Equation (2.10), it may be noted, will hold only for spatial dimension  $n < \frac{3}{2}$ .

The growth of  $a$  can now be assessed via the differential inequality

$$\frac{1}{2} \dot{Q}_a \leq \chi_0 \int a |a'| |b'| dx - \mu_0 \int (a')^2 dx, \quad (2.11)$$

obtained by integrating a times (2.2) and using (2.1) at arbitrary time. If

$$M_a(t) \equiv \max_R a(x, t) \quad (2.12)$$

and Schwartz's inequality is used for  $\int |a'| |b'| dx$ , we rewrite (2.11) by virtue of (2.10) as

$$\frac{1}{2} \dot{Q}_a \leq \chi_0 k M_a^{1/2} N_a^{1/2} - \mu_0 N_a. \quad (2.13)$$

One more general differential inequality of Sobolev type is then required, namely

$$N_a m_a \geq \frac{16}{9} M_a^3. \quad (2.14)$$

This is a consequence of positivity (and differentiability) together with Schwartz's inequality. Since  $a \geq 0$ , we set  $a(x) = g(x)^2$ , and observe that  $\int a'(x)^2 dx \int a(x) dx = 4 \int g(x)^2 g'(x)^2 dx \int g(x)^2 dx \geq 4 [\int g(x)^2 |g'(x)| dx]^2$ . For an unordered pair  $(\alpha, \beta)$  of adjacent maxima and minima,

$\int_a^\beta g(x)^2 |g'(x)| dx = \frac{1}{3} |g(\alpha)^3 - g(\beta)^3| = \frac{1}{3} |a(\alpha)^{3/2} - a(\beta)^{3/2}|$ , whence

$$\int a'(x)^2 dx \int a(x) dx \geq \frac{4}{9} [\text{Var } a(x)^{3/2}]^2, \quad (2.15)$$

where  $\text{Var } f(x)$  denotes the total variation of  $f(x)$ . But since  $a(x) \rightarrow 0$  as  $|x| \rightarrow \infty$ , then certainly  $\text{Var } a^{3/2} \geq 2M_a^{3/2}$ , which establishes (2.14)—again a strictly one-dimensional result. Equation (2.14) is a prototype for a large number of differential inequalities which can be similarly established.

In order to apply (2.14) to (2.11), we shall find a  $\bar{Q}$  such that

$$\dot{Q}_a < 0 \quad \text{whenever} \quad Q_a > \bar{Q}. \quad (2.16)$$

Now if  $Q_a > \bar{Q}$ , then since  $Q_a \leq M_a m_a$ , (2.14) implies

$$N_a > \frac{16}{9} \frac{M_a^3}{m_a} \geq \frac{16}{9} \frac{Q_a^3}{m_a^4} > \frac{16}{9} \frac{\bar{Q}^3}{m_a^4}.$$

On the other hand, direct substitution of (2.14) into (2.13) yields

$$\frac{1}{2} \dot{Q}_a < \chi_0 K \left( \frac{9}{16} m_a \right)^{1/3} N_a^{5/6} - \mu_0 N_a,$$

so that  $\dot{Q}_a < 0$  if  $N_a > K^6 (\chi_0 / \mu_0)^6 m_a^2 (\frac{3}{4})^4$ . We conclude that (2.16) holds if we choose

$$\bar{Q} = \left( \frac{3}{4} \frac{K m_a \chi_0}{\mu_0} \right)^2. \quad (2.17)$$

Thus if  $Q_a(0) > \bar{Q}$ ,  $Q_a(t)$  will decrease at least until  $Q_a(t) \leq \bar{Q}$ , while if  $Q_a(0) < \bar{Q}$ , it will remain so. The boundedness of  $Q_a$  in particular precludes the development of  $\delta$ -function distributions, in conformity with the analysis of (1.7).

#### B. ASYMPTOTIC FORM OF STATIONARY SOLUTIONS

The above results suggest that in one dimension, nontrivial aggregated states will exist for parameter values associated with chemotactic instability. To verify this, we now consider stationary solutions of the minimal system (2.2), (2.3) when the cell density in the aggregate is large. Since our standard of comparison will be the uniform system,  $m_a$  will be finite only when the system is bounded:

$$x \in I \equiv [0, L], \quad (2.18)$$

and we correspondingly choose zero-flux (reflecting) boundary conditions

$$a'(x) = b'(x) = 0 \quad \text{at } x = 0, L. \quad (2.19)$$

The analysis of Section 2.A goes through with minor modifications in this case.

In a stationary aggregate, the cell flux (1.3) in one dimension is constant, and hence vanishes by (2.19). For the special form (2.2), we can solve for  $a$ ,

$$a = a_0 e^{\lambda b}, \quad \lambda \equiv \chi_0 / \mu_0, \quad (2.20)$$

where  $a_0$  is a constant, and thereupon eliminate  $a$  from Equation (2.3):

$$b'' + \frac{f_0}{\nu_0} a_0 e^{\lambda b} - \frac{g_0}{\nu_0} b = 0. \quad (2.21)$$

We seek solutions corresponding to aggregation toward the left endpoint of the interval  $I$ , in the limit as  $b(0) \rightarrow \infty$ . It is convenient to introduce new dimensionless variables and parameters

$$\begin{aligned} \beta(\xi) &= \lambda [b(0) - b(x)], \\ \xi &= \gamma x, \quad \gamma = B_0 \sqrt{g_0 / \nu_0}, \quad B_0 = \lambda b(0), \end{aligned} \quad (2.22)$$

$$k = \frac{\lambda f_0 a_0}{g_0} \frac{e^{B_0}}{B_0^2},$$

in terms of which

$$\beta_{\xi\xi} - k e^{-\beta} + \frac{1}{B_0} - \frac{\beta}{B_0^2} = 0. \quad (2.23)$$

Multiplying by  $\beta_\xi$  and integrating, using  $\beta_\xi = 0$  at  $\beta = 0$ , we get

$$\begin{aligned} \frac{1}{2} (\beta_\xi)^2 + V(\beta) &= k \\ V(\beta) &= k e^{-\beta} + \frac{1}{2} - \frac{1}{2} \left( 1 - \frac{\beta}{B_0} \right)^2, \end{aligned} \quad (2.24)$$

leading to a “trajectory”—the dashed line in Figure 1, truncating when  $\beta_\xi = 0$  again at  $V(\beta_{\max}) = k$ .

For large  $B_0$ ,  $k = V(\beta_{\max}) \leq \frac{1}{2}$ . Indeed,  $k = O(1)$ , as we shall soon see. Now in the region  $\beta = O(1)$ , the “potential”  $V(\beta)$  reduces to  $k e^{-\beta}$ , yielding an

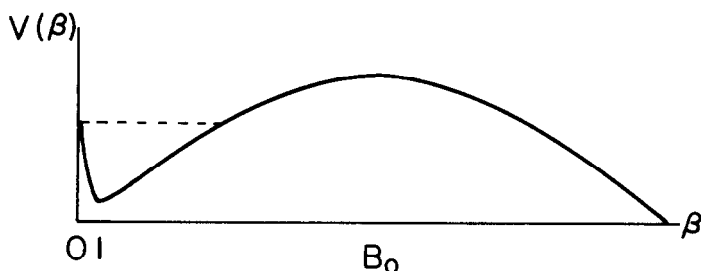


FIG. 1. Trajectory in  $\beta$ -space for solution of Equation (2.24) with boundary conditions (2.19).

“inner” solution to (2.24) of

$$\beta(\xi) = 2 \ln \cosh(\sqrt{k/2} \xi). \quad (2.25)$$

It follows that the cell density, proportional to  $e^\beta$ , decays exponentially as  $\xi \rightarrow \infty$ . For the corresponding “outer” solution  $\beta = O(B_0)$ ,  $V(\beta)$  reduces to  $\frac{1}{2} - \frac{1}{2}(1 - \beta/B_0)^2$ . With the boundary condition  $\beta_\xi(\gamma L) = 0$ , we solve (2.24) to yield

$$\beta(\xi) = B_0 - B_0 \sqrt{1 - 2k} \cosh \frac{1}{B_0} (\gamma L - \xi). \quad (2.26)$$

The relation between  $B_0$  and  $k$  at given  $L$  is then determined by the matching condition that  $\beta/B_0 = 0$  at  $\xi/B_0 = 0$ , which requires

$$\begin{aligned} k &= \frac{1}{2} \tanh^2 \bar{L}, \\ \bar{L} &= \frac{\gamma}{B_0} L = \sqrt{g_0/\nu_0} L. \end{aligned} \quad (2.27)$$

The value of  $B_0$  achieved is of course determined by the cell population. In our asymptotic limit, only the inner solution contributes, so that  $m_a = \int_0^\infty a_0 e^{B_0} \operatorname{sech}^2(\sqrt{k/2} \xi) dx = \sqrt{2/k} a_0 e^{B_0} / \gamma = 2\sqrt{\nu_0/g_0} (e^{B_0}/B_0) \coth \bar{L} a_0$ . Solving (2.21) and (2.27) for  $a_0$  [ $= \frac{1}{2}(g_0/\lambda f_0) B_0^2 e^{-B_0} \tanh^2 \bar{L}$ ], we then have

$$\frac{\lambda f_0}{\sqrt{\nu_0 g_0}} m_a = B_0 \tanh \bar{L}.$$

### C. BIFURCATION STRUCTURE

We complete our discussion of the one-dimensional case by studying the bifurcation of stationary solutions of (2.2), (2.3) from the homogeneous



solution  $a = bg_0/f_0 = \text{const.}$  Since  $m_a$  is a constant of the dynamics, we can identify the bifurcating state by the parameter

$$\theta = \frac{\lambda f_0}{\sqrt{\nu_0 g_0}} m_a, \quad (2.28)$$

and we choose to characterize the state by the peak attractant intensity  $B_0$ . As we have just seen, the relation

$$\theta = B_0 \tanh \bar{L} \quad (2.29)$$

holds for large  $B_0$ : the bifurcating curves are asymptotically straight lines with slope  $\coth \bar{L}$ . On the other hand, for sufficiently small uniform  $a$ , with  $\theta = (\lambda f_0 / \sqrt{\nu_0 g_0}) La = (\lambda f_0 / g_0) \bar{L} a$ , we shall have  $B_0 = \lambda b = \lambda (f_0 / g_0) a$ , or

$$\theta = B_0 \bar{L}, \quad \text{small } B_0. \quad (2.30)$$

Equation (2.30) and the continuation of (2.29) will meet at some  $B_{\text{crit}}(\bar{L})$ .  $B_{\text{crit}}$  can be found by asking for the lowest  $\bar{L}$  attainable from (2.24) at a given  $B_0$ . Figure 1 shows that  $\bar{L}$ , the duration of the trajectory, can be increased arbitrarily by raising  $k$  so that the trajectory approaches tangency with  $V(\beta)$ , or by allowing more than one cycle in the pattern. For minimum  $\bar{L}$ ,  $k$  must be decreased until the minimum of  $V(\beta)$  is pushed to  $\beta = 0$ , i.e. with  $k = 1/B_0$ . But then  $\bar{L} = (1/B_0)\pi/[V''(\beta)]^{1/2} = \pi/(B_0 - 1)^{1/2}$ , so that in terms of the fundamental wave number on the interval

$$\kappa = \pi/\bar{L},$$

we have

$$\begin{aligned} B_{\text{crit}} &= 1 + \kappa^2, \\ \theta_{\text{crit}} &= 2\pi \left( \kappa + \frac{1}{\kappa} \right). \end{aligned} \quad (2.31)$$

We have explored numerically the solution to (2.24) for the parameter range joining (2.29) and (2.30), and find the behavior shown in Figure 2. In the usual classification of nonlinear stability theory, the instability is said to be supercritical or subcritical according as curve A or B of Figure 2 applies. The stability of the branches shown in the figure may be decided by recalling that the system evolves along lines  $\theta = \text{const.}$  so that stable and unstable stationary solutions alternate as  $B_0$  increases. Stability is therefore decided by linear stability at  $B_0$ , and indeed a standard analysis shows that the uniform solution is stable for  $B_0 < B_{\text{crit}}$ , unstable for  $B_0 > B_{\text{crit}}$ .

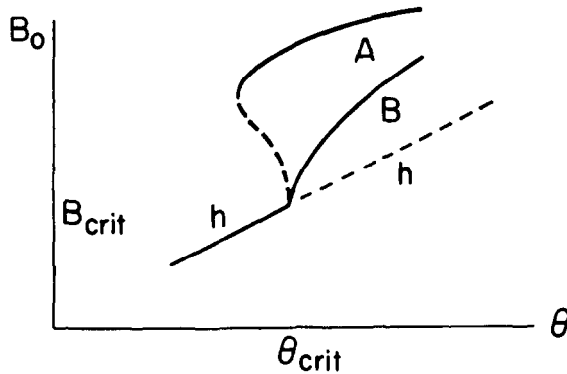


FIG. 2. Qualitative form of bifurcation curves for one-dimensional chemotaxis to a single aggregate, as measured by the maximum value of  $b$ . Curve A results for subcritical bifurcation,  $\kappa^2 < \frac{1}{2}$ ; curve B for supercritical bifurcation,  $\kappa^2 > \frac{1}{2}$ . Unstable branches are dashed. The homogeneous solution is labeled  $h$ .

Whether case A or B prevails depends upon the number of maxima as well as the length of the interval. Consider then the bifurcation curve near  $B_0 = B_{crit}$  corresponding to a single aggregate, and carry out the Fourier expansion

$$\begin{aligned} B = & b_0 + \epsilon b_1 \cos \kappa s + \epsilon^2 (b_{02} + b_{22} \cos 2\kappa s) \\ & + \epsilon^3 b_{33} \cos 3\kappa s + \epsilon^4 (b_{04} + b_{24} \cos 2\kappa s + b_{44} \cos 4\kappa s) \\ & + \epsilon^5 (b_{35} \cos 3\kappa s + b_{55} \cos 5\kappa s) + O(\epsilon^6), \end{aligned} \quad (2.32)$$

where  $s = \sqrt{g_0/\nu_0} x$ ,  $B = \lambda b$ . We correspondingly set

$$\Lambda \equiv \frac{\lambda f_0 a_0}{g_0} = \Lambda_0 + \epsilon^2 \Lambda_2 + \epsilon^4 \Lambda^4 + O(\epsilon^6) \quad (2.33)$$

and solve (2.21) recursively, finding in sequence

$$\Lambda_0 e^{b_0} = b_0, \quad (2.34a)$$

$$-\kappa^2 b_1 + \Lambda_0 e^{b_0} b_1 - b_1 = 0, \quad (2.34b)$$

$$-4\kappa^2 b_{22} + \Lambda_0 e^{b_0} b_{22} - b_{22} + \frac{\Lambda_0}{4} e^{b_0} = 0, \quad (2.34c)$$

$$\Lambda_0 e^{b_0} b_{02} - b_{02} + \frac{1}{4} \Lambda_0 e^{b_0} + \Lambda_2 e^{b_0} = 0, \quad (2.34d)$$

$$\frac{1}{2} \Lambda_0 e^{b_0} b_{22} + \Lambda_2 e^{b_0} + \frac{1}{8} \Lambda_0 e^{b_0} + \Lambda_0 e^{b_0} b_{02} = 0. \quad (2.34e)$$

$\vdots$

From (a) and (b) we have  $b_0 = 1 + \kappa^2$ , duplicating (2.31); from (c),  $b_{22} = b_0/12\kappa^2$ , and then from (d) and (e),

$$b_{02} = \frac{(1 + \kappa^2)(2\kappa^2 - 1)}{24\kappa^2}. \quad (2.35)$$

It readily follows that, to leading order, since

$$\theta - \theta_{\text{crit}} = \frac{\pi}{\kappa} b_{02} (B_0 - B_{\text{crit}})^2 \quad (2.36)$$

(where  $B_{\text{crit}} = b_0$ ,  $\theta_{\text{crit}} = b_0 \bar{L}$ ), then we have

$$\text{instability is } \left\{ \begin{array}{l} \text{supercritical} \\ \text{subcritical} \end{array} \right\} \quad \text{for } \left\{ \begin{array}{l} \kappa^2 > \frac{1}{2}, \\ \kappa^2 < \frac{1}{2} \end{array} \right\} \quad (2.37)$$

In Table 1, we have numerically verified this analysis by following the evolution in time, from initial conditions to final converged solutions, for a number of cases with both subcritical and supercritical values of  $\bar{L}$ .

It can be shown that chemotactic instabilities are in fact locally subcritical for sufficiently large interval for the class of problems defined by (1.1)–(1.4) [2], consistent with the small- $\kappa$  case of (2.37). The long-wavelength analysis used to establish this general result is also applicable to higher dimensions.

TABLE 1

Numerical Examples from Converged Solutions of the  
Initial-Value Problem for Bifurcation<sup>a</sup>

(a) $\bar{L}^2 = 2.25\pi^2$		(b) $\bar{L}^2 = 1.75\pi^2$	
$\theta - \theta_{\text{crit}}$	$B_0/B_0^h$	$\theta - \theta_{\text{crit}}$	$B_0/B_0^h$
0.626	3.26	1.258	3.30
0.273	3.21	0.926	3.18
-0.0212	3.16	0.308	2.79
-0.0630	3.10	0.213	2.69
-0.105	3.04	0.071	2.59
-0.147	2.96	-0.356	1
-0.482	1	-0.499	1
-0.524	1	-0.546	1

<sup>a</sup>As in Figure 2, using (1.5), (1.6) in one dimension with  $\mu_0 = \nu_0 = f_0 = \chi_0 = 1$ . The changeover from subcritical to supercritical occurs when  $\bar{L}^2 = 2\pi^2$ ;  $\theta_{\text{crit}} = 6.807$  and  $6.531$  in cases (a) and (b) respectively.  $B_0^h$  is the value for homogeneous solutions.

### 3. SYMMETRIC COLLAPSE IN $n > 2$ DIMENSIONS

In this section, we confirm the possibility of collapse in  $n > 2$  dimensions, as suggested by (1.7). We restrict attention to spherically symmetric collapse, and to the simple system (1.5), (1.6).

According to (1.7), a spatial scale of  $\delta$  implies a temporal scale of  $\delta^{(n+2)/2}$ . Assuming that the collapse occurs at a finite time  $t_0$ , this suggests introducing the scaled variable

$$\mathbf{R} = (t_0 - t)^{-2/(n+2)} \mathbf{r}, \quad (3.1)$$

and with amplitudes dictated by the discussion of (1.7), making the similarity *Ansatz*

$$\begin{aligned} a(\mathbf{r}, t) &= (t_0 - t)^{-2n/(n+2)} A(\mathbf{R}) \\ b(\mathbf{r}, t) &= (t_0 - t)^{-(n-2)/(n+2)} B(\mathbf{R}). \end{aligned} \quad (3.2)$$

Since

$$\frac{\partial}{\partial t} \mathbf{R} = \frac{2}{n+2} \frac{1}{t_0 - t} \mathbf{R}, \quad \frac{\partial}{\partial r_\alpha} R_\alpha = (t_0 - t)^{-2/(n-2)},$$

substituting into (1.5), (1.6) yields

$$\begin{aligned} \left( \frac{2n}{n+2} + \frac{2}{n+2} \mathbf{R} \cdot \nabla_{\mathbf{R}} \right) A(\mathbf{R}) + \chi_0 \nabla_{\mathbf{R}} \cdot (A \nabla_{\mathbf{R}} B) \\ = (t_0 - t)^{(n-2)/(n+2)} \mu_0 \nabla_{\mathbf{R}}^2 A(\mathbf{R}) \end{aligned}$$

and

$$\begin{aligned} \left( \frac{n-2}{n+2} + \frac{2}{n+2} \mathbf{R} \cdot \nabla_{\mathbf{R}} \right) B(\mathbf{R}) - f_0 A(\mathbf{R}) \\ = (t_0 - t)^{(n-2)/(n+2)} \nu_0 \nabla_{\mathbf{R}}^2 B(\mathbf{R}) - (t_0 - t)^{(n-2)/(n+2)} g_0 B(\mathbf{R}). \end{aligned}$$

As  $t \rightarrow t_0$ , these become consistent with time-independent fields satisfying

$$\frac{2}{\chi_0(n+2)} \nabla_{\mathbf{R}} \cdot (\mathbf{R} A) + \nabla \cdot (A \nabla_{\mathbf{R}} B) = 0, \quad (3.3)$$

$$(n-2+2\mathbf{R} \cdot \nabla_{\mathbf{R}}) B = (n+2) f_0 A. \quad (3.4)$$

According to (3.3),  $\nabla \cdot \{A[\nabla B + 2\mathbf{R}/\chi_0(n+2)]\} = 0$ . If  $A$  and  $B$  are nonsingular functions of the magnitude  $R$  alone, this implies that  $A[\nabla B +$

$2\mathbf{R}/\chi_0(n+2)] = 0$ . Hence

$$\begin{aligned} \text{either } B &= K - \frac{R^2}{\chi_0(n+2)} \\ \text{or } A &= 0 \end{aligned} \quad (3.5)$$

Substituting into (3.4), we have respectively

$$\begin{aligned} \text{either } A &= \frac{1}{(n+2)f_0\chi_0} [(n-2)\chi_0 K - R^2] \\ \text{or } B &= K' R^{-(n-2)/2}. \end{aligned} \quad (3.6)$$

Clearly,  $A$  reaches its lower limit of 0 before  $B$  does. Hence writing  $K = R_0^2/\chi_0(n-2)$  and evaluating  $K'$  by continuity, we have the aggregation profile

$$\left. \begin{aligned} A &= \frac{1}{(n+2)f_0\chi_0} (R_0^2 - R^2) \\ B &= \frac{1}{(n+2)\chi_0} \left( \frac{n+2}{n-2} R_0^2 - R^2 \right) \end{aligned} \right\} \quad R \leq R_0, \quad (3.7)$$

$$\left. \begin{aligned} A &= 0 \\ B &= \frac{4}{(n^2-4)\chi_0} \left( \frac{R_0}{R} \right)^{(n-2)/2} \end{aligned} \right\} \quad R \geq R_0. \quad (3.8)$$

At fixed  $\mathbf{r}$ , and hence very large  $\mathbf{R}$ ,  $a(\mathbf{r}, t)$  behaves like a point source of strength

$$\int a(\mathbf{r}, t) d\mathbf{r}^n = \int A(\mathbf{R}) d\mathbf{R}^n = \frac{2S_n}{(n+2)^2 f_0 \chi_0} R_0^2,$$

where  $S_n$  is the surface of a unit  $n$ -sphere. Hence  $R_0$  is determined by

$$R_0 = (n+2) \left( \frac{f_0 \chi_0 n_a}{2S_n} \right)^{1/2}, \quad (3.9)$$

and  $b$  has a time-independent asymptotic form given by the asymptotic solution of  $g_0 b - \nu_0 \nabla^2 b = f_0 m_a \delta(\mathbf{r})$ , or

$$b(\mathbf{r}) = \frac{f_0 m_a}{(n-2)S_n} \frac{1}{r^{n-2}} \exp \left\{ - \left( \frac{g_0}{\nu_0} \right)^{1/2} r \right\}, \quad (3.10)$$

which joins (3.8) at

$$R_1(t) = \left( \frac{n+2}{4} \frac{f_0 \chi_0 m_a}{S_n} \right)^{2/(n-2)} \frac{1}{R_0(t_0 - t)^{4/(n+2)}}, \quad (3.11)$$

i.e., increasingly far down the tail of the condensation.

#### 4. SYMMETRIC COLLAPSE IN TWO DIMENSIONS

##### A. ASYMPTOTIC FORM OF STATIONARY SOLUTIONS

We turn now to the possibility of collapse in two dimensions, restricting attention to rotationally symmetric aggregation in a disc of radius  $L$ , and again to the simple system (1.5), (1.6).

Consider first the form taken by a stationary aggregate when chemotaxis is sufficiently strong that the size of the aggregate is small compared to  $L$ . In this case, we expect the term  $g_0 b$  in (1.6) to be negligible in comparison with the diffusion term, and this can be verified *a posteriori*. We proceed then as in Section 2.B, substituting  $a = a_0 e^{\lambda b}$ , and setting

$$\beta(r) = B_0 - \lambda b(x), \quad r = \sqrt{g_0/\nu_0} x, \quad \Lambda = \lambda f_0 a_0 / g_0 \quad (4.1)$$

to obtain

$$\frac{1}{r} \frac{d}{dr} r \frac{d\beta}{dr} = \Lambda e^{B_0} e^{-\beta} + \beta - B_0. \quad (4.2)$$

Again assume that  $B_0$  is large; if we set

$$k = \Lambda e^{B_0/2}, \quad \rho = r e^{B_0/4}, \quad (4.3)$$

the inner solution as  $B_0 \rightarrow \infty$  then satisfies

$$\frac{1}{\rho} \frac{d}{d\rho} \left( \rho \frac{d\beta}{d\rho} \right) = k e^{-\beta}, \quad \beta(0) = \beta'(0) = 0. \quad (4.4)$$

Using the independent variable  $\ln \rho$ , this is straightforward to solve, resulting in

$$\beta = 2 \ln \left( \frac{k}{8} \rho^2 + 1 \right). \quad (4.5)$$

It follows now that

$$a = \Lambda e^{B_0} \frac{g_0}{\lambda f_0} \left( \frac{k}{8} \rho^2 + 1 \right)^{-2}, \quad (4.6)$$

so that if we define the chemotactic strength parameter by

$$\theta = \frac{\lambda}{2\pi} \frac{f_0}{\nu_0} m_a, \quad (4.7)$$

then on applying (4.2) and (4.6),

$$\theta = k \int_0^\infty \frac{\rho \, d\rho}{\left(\frac{1}{8}k^2\rho^2 + 1\right)^2} = 4. \quad (4.8)$$

Consequently, in the limit  $B_0 \rightarrow \infty$ , dense stationary aggregates carry the unique value  $\theta = 4$ . However, we surmise that if  $\theta > 4$  none of the finite- $B_0$  stationary solutions will be stable. This follows from the observation that standard linear stability analysis of the uniform solution in the disc of radius  $\bar{L} = \sqrt{g_0/\nu_0} L$  in the variable  $r$  produces a crossover from stability to instability via a single radial condensation at

$$\begin{aligned} B_{\text{crit}} &= 1 + \left( \frac{3.832}{\bar{L}} \right)^2, \\ \theta_{\text{crit}} &= 7.3 \dots, \end{aligned} \quad (4.9)$$

where 3.832 is the first positive zero of  $J_1(r)$  (and larger  $B_{\text{crit}}, \theta_{\text{crit}}$  for annular condensation as well). The apparent uniqueness of the solution to (4.2) thus suggests a bifurcation diagram as in Figure 3. According to this diagram, chemotactic collapse can result from a sufficiently large perturbation when  $\theta > 4$ , culminating in a singular solution, but cannot occur for  $\theta < 4$ .

This striking result applies here under the condition of rotational symmetry, but to the extent that a dense aggregate is rotationally symmetric, the

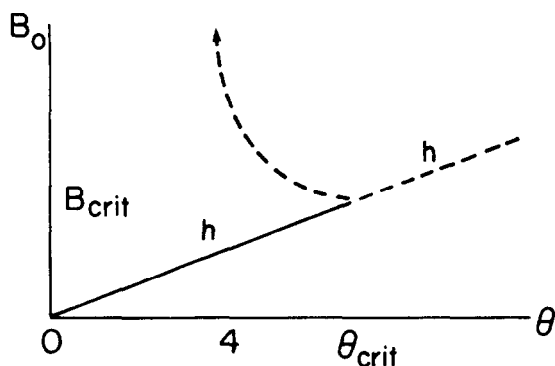


FIG. 3. Conjectured bifurcation diagram for two-dimensional aggregation.  $h$  signifies homogeneous solution, and dashed curves are unstable.

estimate should apply to any two-dimensional domain. With symmetry imposed, we show in Figure 4 numerical results for the time evolution of the distribution from two values of  $\theta$  on either side of the limiting value of 4. For no initial values have we been able to achieve collapse with  $\theta < 4$ , whereas collapse has always been found for suitable initial conditions when  $\theta > 4$ .

#### B. TIME-DEPENDENT COLLAPSE

In order to study the development of a collapsing symmetric aggregate, we shall suppose that diffusion of  $b$  predominates over diffusion of  $a$ , or that  $\nu_0 \gg \mu_0$ . In that case, both the time derivative and the term  $g_0 b$  in (1.6) are negligible. We then solve (1.6) as

$$r \frac{\partial b}{\partial r} = -\frac{1}{\nu_0} \int_0^r r a \, dr \equiv -\frac{A(r)}{f_0 \lambda} \quad (4.10)$$

and substitute into (1.5). Setting  $\sigma = r^2$ ,  $\tau = \mu_0 t$ , and appending initial and boundary conditions, we obtain on integration

$$\frac{\partial A}{\partial \tau} - 2A \frac{\partial A}{\partial \sigma} - 4\sigma \frac{\partial^2 A}{\partial \sigma^2} = 0, \quad (4.11a)$$

$$A(L^2, \tau) = \theta, \quad \frac{\partial A}{\partial \sigma}(L^2, \tau) = 0, \quad A(\sigma, 0) = A_0(\sigma), \quad (4.11b)$$

to which we add the definition

$$\alpha(\tau) \equiv A(0, \tau). \quad (4.11c)$$

Here,  $\alpha(\tau)$  is the cell number concentrated at the origin, nonvanishing only for a  $\delta$ -function singularity. Initially,  $\alpha(\tau) = 0$ , and this value is then retained until collapse occurs. Collapse may in principle involve at first only part of the cell population,  $\alpha(\tau)$  thus increasing to its terminal value of  $\theta$  as the collapsed aggregate attracts the remaining cells. The alternative form of (4.11a)

$$\frac{\partial A}{\partial \tau} - \frac{\partial}{\partial \sigma} \left( A^2 - 4A + 4\sigma \frac{\partial A}{\partial \sigma} \right) = 0 \quad (4.12)$$

suggests that as collapse is approached, we have

$$\int_0^\epsilon \frac{\partial A}{\partial \tau} d\sigma \simeq (A^2 - 4A)_{\sigma=\epsilon}. \quad (4.13)$$



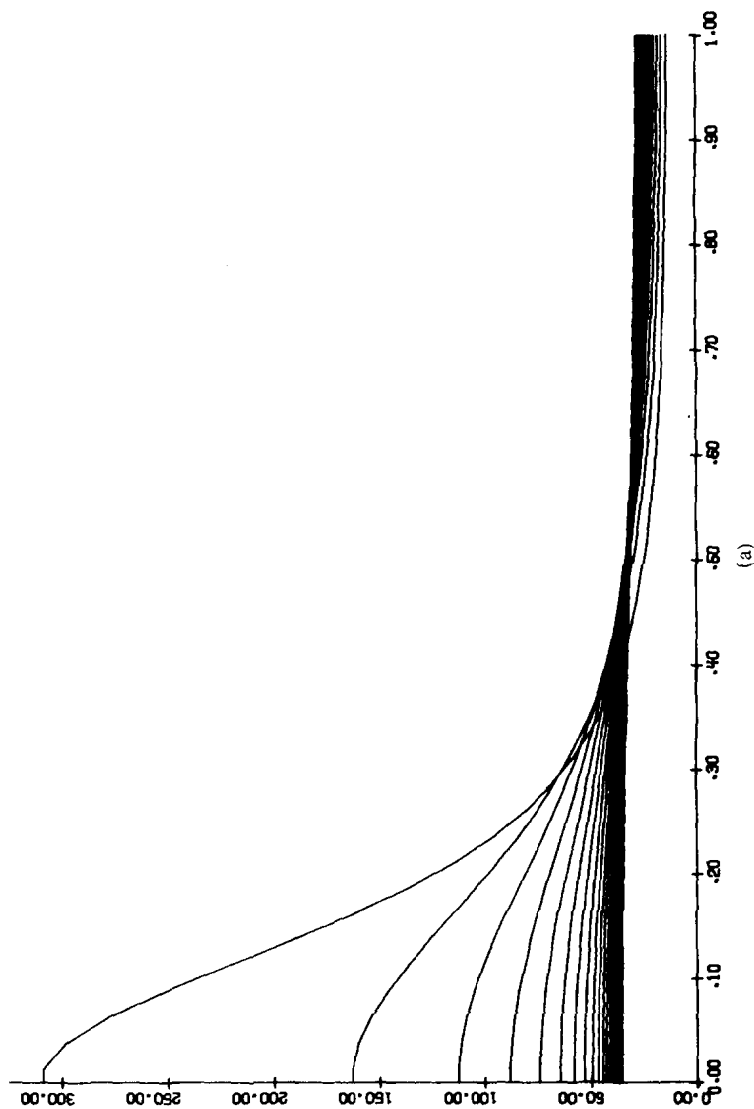


Fig. 4 Symmetric chemotaxis in a disc of radius  $L$  based on Equations (1.5), (1.6) with  $\chi_0 = f_0 = 1$ ,  $g_0 L^2 = 4$ ,  $\mu_0 = 1.6$ ,  $\mu_0 = 0.8$ . (a)  $L^2 a(r/L)$  versus  $r/L$  during chemotactic collapse. The initial values are  $L^2 a = 30[L^2/(L^2 + r^2) + 1 - \ln 2]$ ,  $b = 7.5$ , and  $\theta = 11.72$ . (b)  $b$  versus  $r/L$  for run (a) above. (c) Decay to homogeneity when  $\theta = 2.34$ , the other parameters as in (a). The initial values are  $L^2 a = 6[1 + 10L^2/(L^2 + r^2) - 10 \ln 2]$ ,  $b = 1.5$ .

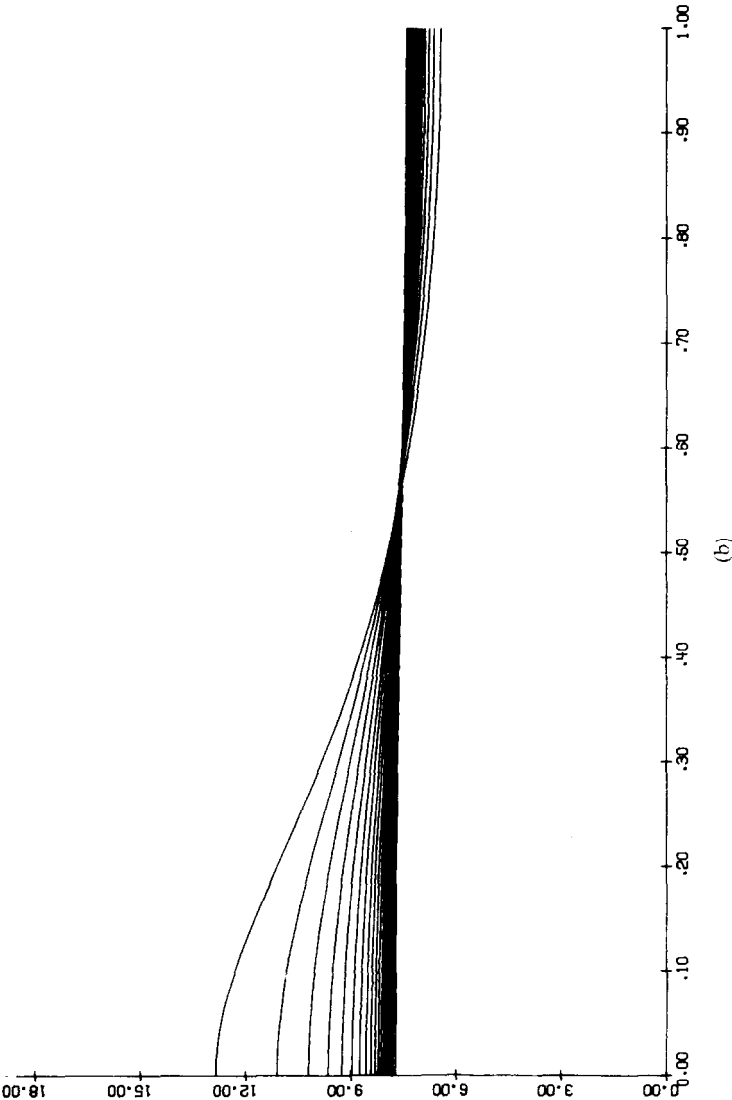


Fig. 4. continued.

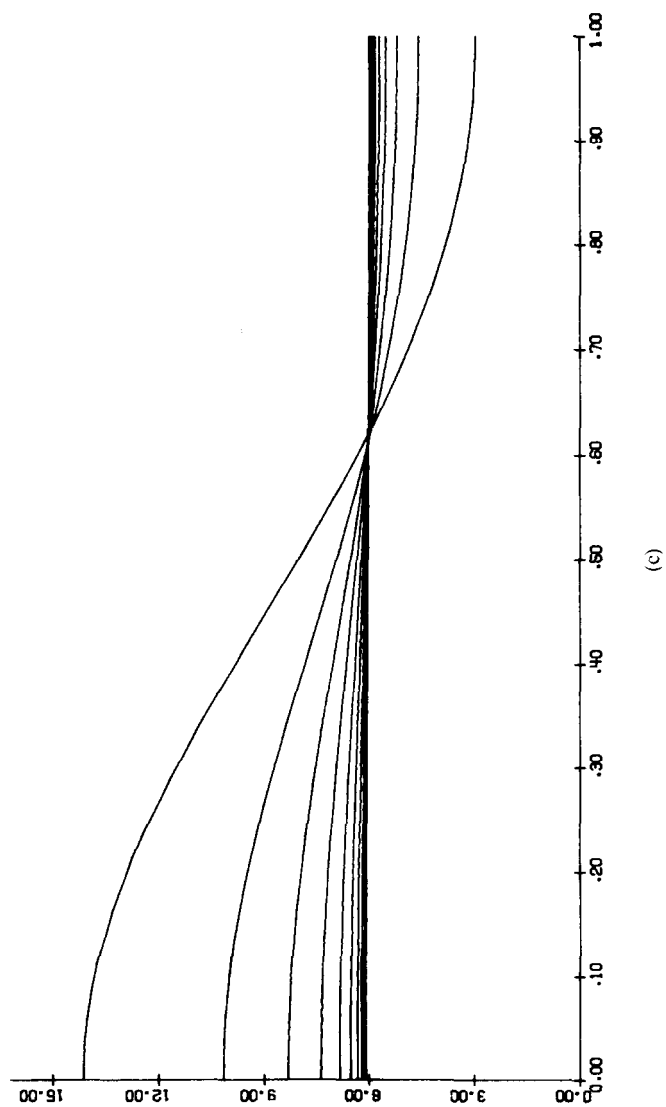


Fig. 4. continued.

Since the value of  $A$  at position  $\sigma$  measures the number of cells to the left of this point, we expect  $A$  to be increasing in time near the left midpoint, and therefore  $A^2 - 4A > 0$  at  $\sigma = \varepsilon$ . This suggests that there is a time  $\tau_{\text{crit}}$  such that  $\alpha = 0$  for  $\tau < \tau_{\text{crit}}$  and  $\alpha(\tau) \geq 4$  for  $\tau > \tau_{\text{crit}}$ . This minimum size of collapsed aggregates is consistent with the conjecture of the previous section.

It is possible to place an upper bound on  $\tau_{\text{crit}}$  as follows: since  $a$  is nonnegative, then  $A$  is monotone increasing in  $\sigma$ , and the positive quantity

$$Q(\tau) = \int_0^{L^2} (\theta - A) d\sigma \quad (4.14)$$

provides a measure of the uncollapsed population. Consider now a time interval where  $\alpha(\tau) = 0$ . Then from (4.11) we have

$$\begin{aligned} \frac{dQ}{d\tau} &= -\theta(\theta - 4) - 4 \left[ \sigma \frac{\partial A}{\partial \sigma} \right]_{\sigma=0}^{\sigma=L^2} \\ &= -\theta(\theta - 4), \end{aligned} \quad (4.15)$$

and consequently

$$\tau_{\text{crit}} \leq \frac{Q(0)}{\theta(\theta - 4)}. \quad (4.16)$$

Note that the stationary solutions of (4.11) are

$$A_k(\sigma) = \frac{4k\sigma}{8 + k\sigma}, \quad (4.17)$$

where  $k$  is arbitrary, this being another form of (4.6). The assumptions leading to (4.11a) imply  $k \gg 1$  if (4.17) is to be a valid approximate solution to the full system. Consequently, the collapse time should actually be somewhat longer than could be predicted on the basis of (4.11a), since some aggregation must take place before (4.11a) becomes the relevant approximate equation.

## 5. CONCLUSION

The biological phenomenon of chemotactic collapse is well documented, and the conditions under which a uniform cell population becomes unstable in model systems are well known. The interesting suggestion has been made that the collapse may in fact lead to a  $\delta$ -function singularity, to within the excluded volume of the cells. It turns out that this is far from the whole story, in that the possibility of collapse depends crucially upon the dimensionality of the system space. In particular, for the special model we have investigated, collapse cannot occur in a one-dimensional space; may or may not in two

dimensions, depending upon the cell population; and must, we surmise, in three or more dimensions under a perturbation of sufficiently high symmetry. We thus have another instance of the critical role of dimensionality in determining the qualitative character of nonlinearly driven systems.

## REFERENCES

- 1 J. Bonner, *Morphogenesis*, Atheneum, 1963, Chapter 5.
- 2 S. Childress and J. K. Percus, *Mathematical Models in Developmental Biology*, C.I.M.S. Lecture Notes, 1978.
- 3 E. F. Keller and L. A. Segel, Initiation of slime mold aggregation viewed as an instability, *J. Theoret. Biol.* 26: 399 (1970); 30:225 (1971).
- 4 V. Nanjundiah, Chemotaxis, signal relaying, and aggregation morphology, *J. Theoret. Biol.* 42:63 (1973).
- 5 L. A. Segel and B. Stoeckly, Instability of a layer of chemostatic cells, attractant and degrading enzymes, *J. Theoret. Biol.* 37:561 (1972).