CHEMOTACTIC CELLULAR MIGRATION: SMOOTH AND DISCONTINUOUS TRAVELLING WAVE SOLUTIONS

K. A. LANDMAN, G. J. PETTET, AND D. F. NEWGREEN

Abstract. A simple model of chemotactic cell migration gives rise to travelling wave solutions. By varying the cellular growth rate and chemoattractant production rate, travelling waves with both smooth and discontinuous fronts are found using phase plane analysis. The phase plane exhibits a curve of singularities whose position relative to the equilibrium points in the phase plane determines the nature of the heteroclinic orbits, where they exist. Smooth solutions have trajectories connecting the steady states lying to one side of the singular curve. Travelling shock waves arise by connecting trajectories passing through a special point in the singular curve and recrossing the singular curve, by way of a discontinuity. Hyperbolic partial differential equation theory gives the necessary shock condition. Conditions on the parameter values determine when the solutions are smooth travelling waves versus discontinuous travelling wave solutions. These conditions provide bounds on the travelling wave speeds, corresponding to bounds on the chemotactic velocity or bounds on cellular growth rate. This analysis gives rise to the possibility of representing sharp fronts to waves of invading cells through a simple chemotactic term, without introducing a nonlinear diffusion term. This is more appropriate when cell populations are sufficiently dense.

Key words. migration, chemotaxis, travelling wave, phase plane, shock

AMS subject classifications. 34A34, 35L40, 35L67, 92C17

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1. Introduction. The active migration of cells is a significant feature of numerous biological phenomena ranging from wound healing, scar tissue formation, and tumor invasion to embryo implantation and organogenesis.

Despite having been the focus of much research, a comprehensive understanding of the processes of receptor activation, cell-cell signalling, and intracellular organization associated with cell migration in various contexts eludes us. In part this is due to the numerous and complicated mechanisms that are involved and, perhaps more importantly, to the cooperative or antagonistic interactions between such processes.

Mathematical modelling of biological phenomena provides a timely and efficient theoretical tool for considering the interaction of various cell migration mechanisms, and the emergent behavior that arises from these interactions. To date, much of the mathematical modelling of cell migration has been predicated on the phenomena of diffusion, chemotaxis, and haptotaxis, either singly or in combination. Such models typically support travelling wave solutions, which are taken to represent the invading fronts of populations of migrating cells. An exemplar of such a model based on the process of diffusion is Fisher’s equation on a one-dimensional spatial domain [15]. Chemotaxis-based models employ a gradient of a diffusible signaling chemical to determine the velocity of cell migration [1], [14], [18], whilst haptotaxis-based models...
employ a gradient of extracellular matrix or ligand density [17] to this end.

The extensive literature developed over the last few decades concerning the theoretical modelling of chemotaxis is testament to the perceived importance of the role it plays in cell migration. Many of these mathematical models can identify their origins in the work of Keller and Segel [9] describing the motion of bacteria as a chemotactic response. Significant contributions to this body of knowledge include those by Tranquillo [22], Tranquillo and Alt [23], Hillen [8], and Othmer and Stevens [16], while others may be identified in a recent review by Ford and Cummings [6].

The analysis of such models can lead to an understanding of the relative contributions by the mechanisms modelled to the speed of the invading front of cells, and, by implication, potential strategies for effecting changes to the speed of the invading front can be hypothesized and investigated.

Typically, invasive phenomena in the context of migrating populations of cells are characterized by a well-defined boundary. This feature is difficult to reproduce when using a diffusive flux to represent the migration process. Mathematical models involving a linear diffusive flux give rise to smooth-fronted solutions, with the solution being nonzero everywhere (albeit small). A nonlinear diffusive flux, where the diffusivity is density dependent (and equal to zero when the density is zero), gives rise to solutions with distinct interfaces beyond which the density equals zero. Such models have been explored in describing population pressures and moisture infiltration [5], [7], [15], [20], [24], [25]. Even though such solutions have compact support, they are smooth when the density is positive and do not exhibit shocks. Solutions with shocks are not realizable with a diffusive mechanism.

For a limited number of specific and very simple models based on chemotaxis, recent research by Pettet, McElwain, and Norbury [19] and others [17], [12] has shown the potential for chemotaxis-based models to exhibit travelling wave solutions with shock fronts. Such sharp-fronted solutions may be viewed as being more indicative of invading cell populations with a well-defined front or margin than those described above.

In this article we consider a simple model of chemotactic cell migration, where there is no contribution to the cell velocity from a diffusion-like term. We explore this theoretical model of cell migration numerically and analytically to show that, for various parameter regimes, smooth-fronted or shock-fronted travelling wave solutions can be supported.

A coupled system of partial differential equations for cell density and chemoattractant concentration is considered. We introduce a travelling wave coordinate system with an unknown wave speed to convert the system into a coupled system of ordinary differential equations. This is explored using phase plane analysis, giving rise to a rich variety of possible solutions. Consideration of the original system as a hyperbolic system allows shock conditions to be specified uniquely. Some asymptotic analysis for large wave speed is also examined.

2. Chemotactic cell migration in a fixed spatial domain of one dimension. We begin by describing a simple system of equations designed to describe the chemotactic migration of cells in a fixed domain. We use a coordinate $x$ fixed in space (i.e., a Eulerian system). The cell density per unit length and the chemoattractant concentration are denoted by $n(x, t)$ and $g(x, t)$, respectively. The usual conservation-of-mass argument for a generic chemotaxis problem gives

$$\frac{\partial n}{\partial t} = -\chi \frac{\partial}{\partial x} \left( n \frac{\partial g}{\partial x} \right) + f(n, g),$$

(2.1)
Fig. 2.1. Chemotactic cell migration at different wave speeds. Numerical solutions of equations (2.1)–(2.4) on [0, 1] with the inclusion of Fickian diffusion ($D_n \frac{\partial^2 n}{\partial x^2}$) in (2.1). Here $D_n = 0.00001$, $\lambda_1 = 2$, $k_1 = 1$, $\lambda_2 = 0.25$, $\lambda_3 = 1$, $k_2 = 1$ and $\chi = 0.0001, 0.001, 0.002$ and 0.003. Initial conditions are $n(x, 0) = e^{-500x^2}$ and $g(x, 0) = 1$ with zero flux boundary conditions at $x = 0, 1$. (a) Advancing front (moving left to right) of migrating cells at dimensioned time $t = 17.5$. (b) Retreating front (moving left to right) of chemoattractant at dimensioned time $t = 17.5$.

\[
\frac{\partial g}{\partial t} = h(n, g),
\]

where the chemotactic factor $\chi$ is assumed to be a constant and $f$ and $h$ represent the kinetic terms. This type of model system, where only chemotaxis contributes to the cell migration, has been studied by several authors [2], [19], [11]. For this reason we have excluded diffusivity from the model equations (2.1)–(2.2).

Our problem concerns cells $n$, which proliferate by mitosis and may die or differentiate into another cell type. These two effects can be incorporated into a logistic-type term for $f$. The chemoattractant $g$ is produced uniformly throughout the domain and has a maximum value. Furthermore, the cells consume the chemoattractant, which creates a gradient of $g$ and produces a migration velocity. These effects are reflected in our choice of $f$ and $h$ as

\[
f = \lambda_1 n(k_1 - n),
\]

\[
h = \lambda_2 g(k_2 - g) - \lambda_3 ng.
\]

Numerical solutions to such a system on a finite domain exhibit travelling wave solutions, as illustrated in Figure 2.1. Here we have included a small amount of diffusion in $n$ in order to stabilize the system, allowing the use of the Numerical Algorithms Group (NAG) parabolic partial differential equations package DO3PCF. In Landman, Pettet, and Newgreen [10] we explicitly introduce two migration mechanisms, namely, chemotaxis and diffusion. We look at the effect of decreasing diffusivity, when the diffusion coefficient is small in comparison to the chemotactic sensitivity coefficient, and show that the solutions look almost identical as the diffusion coefficient is reduced by several orders of magnitude. Since our interest is in systems of invasion, for which chemotaxis is the dominant cell migration mechanism, the arguments considered in [10] allow us to neglect any effect attributable to the small diffusivity introduced for these numerical results.

We observe that the front of $n$ steepens as the chemoattractant coefficient $\chi$ increases. If the parameter is pushed too far, the solution appears to develop a numerical instability which may be interpreted as the evolution of a jump discontinuity. These numerical simulations initiate questions about the nature of such solutions and whether or not smooth and discontinuous travelling wave solutions can be determined analytically.
An appropriate dimensionalization is carried out with the following transformation, where we introduce a length scale $L$ and scaled parameters $a$ and $b$ as shown:

\begin{align}
(2.5) & \quad n = k_1 n^*, \quad g = k_2 g^*, \quad t = T^*, \quad x = Lx^*, \\
(2.6) & \quad T = \frac{1}{\lambda_3 k_1}, \quad L^2 = \frac{\lambda k_2}{\lambda_3 k_1}, \quad a = \frac{\lambda_1}{\lambda_3}, \quad b = \frac{\lambda_2 k_2}{\lambda_3 k_1}.
\end{align}

Omitting the asterisk notation, the dimensionless system is

\begin{align}
(2.7) & \quad \frac{\partial n}{\partial t} = - \frac{\partial}{\partial x} \left( n \frac{\partial g}{\partial x} \right) + an(1 - n), \\
(2.8) & \quad \frac{\partial g}{\partial t} = bg(1 - g) - ng.
\end{align}

There are many scalings we could have chosen. This scaling focuses on the two most important terms in the problem, namely, chemotactic migration and the interaction terms between $n$ and $g$.

Now, making the travelling wave coordinate transformation $z = x - ct$, we obtain

\begin{align}
(2.9) & \quad \frac{d n}{d z} = \frac{1}{c} \frac{d}{d z} \left( n \frac{d g}{d z} \right) - \frac{an}{c} (1 - n), \\
(2.10) & \quad \frac{d g}{d z} = - \frac{1}{c} \left[ bg(1 - g) - ng \right],
\end{align}

which, after appropriate substitutions from (2.10) into (2.9), may be written as

\begin{align}
(2.11) & \quad \left[ 1 + \frac{g}{c^2} (b(1 - g) - 2n) \right] \frac{d n}{d z} = \frac{ng}{c^2} \left[ b(1 - 2g) - n \right] \left[ b(1 - g) - n \right] - \frac{an}{c} (1 - n), \\
(2.12) & \quad \frac{d g}{d z} = - \frac{1}{c} \left[ bg(1 - g) - ng \right].
\end{align}

We will be considering (2.11)–(2.12) in the phase plane, and we will plot trajectories in the $(g, n)$ plane. For $b > 0$, the steady states of the system are $(g, n) = (0,0), (1,0), (0,1)$ and $(1 - \frac{1}{b}, 1)$. Since we are interested only in solutions where $n$ and $g$ are nonnegative, the last state exists only for $b > 1$. When $b = 0$, the steady state $(0, 0)$ is replaced by a continuum of steady states $(g, 0)$. In this paper, we concentrate on the case $b > 0$ and briefly comment on the degenerate case $b = 0$ in section 5.3.

We seek travelling wave solutions connecting $(0,1)$ or $(1 - \frac{1}{b}, 1)$ and $(1,0)$. Linearization about the steady states yields the nature of these states. This information, together with the eigenvalues and eigenvectors, is listed in Table 1.

3. Phase plane analysis. We will investigate the positive quadrant of the $(g, n)$ phase plane: this is made interesting by the position of the curve, where the function premultiplying $\frac{d g}{d z}$ in (2.11) is identically equal to zero. Pettet, McElwain, and Norbury [19] defined such a curve as a “wall-of-singularities.” Here the wall-of-singularities can be written as

\begin{align}
(3.1) & \quad n = \frac{1}{2} \left( \frac{c^2}{g} + b(1 - g) \right).
\end{align}

This wall is asymptotic to the $n$-axis, cutting the positive $g$-axis at

$$g = \frac{1}{2} \left( 1 + \sqrt{1 + \frac{4c^2}{b}} \right),$$
Table 1

<table>
<thead>
<tr>
<th>$(g, n)$</th>
<th>Type</th>
<th>Eigenvalues</th>
<th>Corresponding eigenvectors $(g, n)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(0, 0)$</td>
<td>Stable node</td>
<td>$-\frac{a}{c}, -\frac{b}{c}$</td>
<td>$(0, 1), (1, 0)$</td>
</tr>
<tr>
<td>$(1, 0)$</td>
<td>Saddle</td>
<td>$-\frac{a}{c}, -\frac{b}{c}$</td>
<td>$(1, -a - b), (1, 0)$</td>
</tr>
<tr>
<td>$(0, 1)$</td>
<td>$b &lt; 1$ Unstable node $b &gt; 1$ Saddle</td>
<td>$\pm \frac{1-b}{c}, \pm \frac{1-b}{c}$</td>
<td>$(0, 1), \left(1, -\frac{(k-1)^2}{c^2(a+b-1)}\right)$</td>
</tr>
<tr>
<td>$(1 - \frac{1}{b}, 1)$ for $b &gt; 1$</td>
<td>Unstable node $c^2 &gt; 1 - \frac{1}{b}$ Saddle</td>
<td>$\pm \frac{1-b}{c}, \pm \frac{1-b}{c}$</td>
<td>Complicated form</td>
</tr>
</tbody>
</table>

to the right of the steady state $(1, 0)$. Hence all the steady states are to the left of the wall when $0 < b < 1$. If $b > 1$, the new steady state $(1 - \frac{1}{b}, 1)$ is below (above) the wall if $c^2 > 1 - \frac{1}{b}$ ($c^2 < 1 - \frac{1}{b}$). From Table 1, we can see that the nature of this steady state changes according to the same inequality. The wall gets closer to the origin as $c$ decreases.

Pettet, McElwain, and Norbury [19] showed that solutions approaching a wall-of-singularities could not cross the wall unless it passed through special points called gates or holes in the wall. These points are defined by both the function premultiplying $\frac{dn}{dz}$ and the right-hand side in (2.11) being equal to zero simultaneously. Thus, travelling wave solutions joining two steady states (one unstable and the other stable) on the same side of the wall-of-singularities could under some circumstance be shown not to exist when the wall-of-singularities interfered with the trajectory emanating from the unstable steady state.

Pettet, McElwain, and Norbury concerned themselves only with smooth-fronted travelling waves. They presumed that any trajectory exiting the unstable steady state of interest that passed through a hole in the wall could then not recross the wall in order to connect with the stable steady state. However, Marchant, Norbury, and Perumpanani [12] showed that for a very simple system of equations (in the class of (2.1)–(2.2)) a trajectory in the phase plane could indeed follow such a path, recrossing the wall by way of a jump discontinuity.

In the system we describe here, there is always a hole at the intersection of the wall with the $g$-axis. However, it is necessary for the holes to lie within the positive $(g, n)$ quadrant if any trajectory passing through the hole is to remain in that quadrant. Depending on the parameter values, for our system there can be no, one, or two holes contained within the positive quadrant.

The interaction of the trajectories and the wall-of-singularities is extremely interesting. We start by giving some examples.

Consider first the case $0 < b < 1$. We seek a trajectory connecting the unstable node $(0, 1)$ to the saddle $(1, 0)$. By considering the vector field associated with (2.11) and (2.12), it can be shown that such a trajectory certainly exists if the wall is sufficiently far from the axes. For example, we fix the wall position (fix $b$ and $c$) and vary $a$, the effective cellular growth rate or mitotic index of $n$, as illustrated in Figure 3.1. For sufficiently small values of $a$ there is a unique trajectory to the left of the
Fig. 3.1. Phase plane for \((g, n)\) for increasing values of cellular growth rate \(a\). Here \(b = 0.25, c = 1\). The wall is indicated with a dark line; the holes in the wall and the steady states are marked with a \(\bullet\). (a) \(a = 0.5\), no holes. (b) \(a = 1.0\), two holes (both with \(g > 0\)). (c) \(a = 2.0\), one hole. (d) \(a = 4.0\), one hole.

wall, connecting the two states (shown here with \(a = 0.5\) and 1); this gives a smooth travelling wave. However, for large enough values of \(a\), no such trajectory can be found below the wall, as shown here with \(a = 2\) and 4. In fact, there appears to be a trajectory from \((0, 1)\) travelling towards the hole in the wall.

Alternatively, we can consider the effect of fixing the two rates \(a\) and \(b\) and decreasing the wave speed \(c\). This translates the wall closer to the axes, as shown in Figure 3.2. When \(c = 1.5\), there is a trajectory lying below the wall joining the steady states. However, for \(c = 1\) and 0.5, no such trajectory exists, but again there is one trajectory from \((0, 1)\) heading towards the hole in the wall.

Since trajectories cannot cross each other, or cross the wall at any point other than a hole in the wall, we must determine how it is possible for a trajectory passing through a hole to recross the wall and connect to the other steady state. Marchant [11] investigated this scenario for his system, and his arguments apply equally to our system of equations. No smooth connection between the two states can be made; however, there is the possibility for the solution to be nonsmooth, by containing a jump discontinuity.

It is appropriate to apply Marchant’s approach here to our system. We do this now, and then return to the phase plane analysis in section 5.
Fig. 3.2. Phase plane for \((g, n)\) for decreasing values of wave speed \(c\). Here \(a = 2.0, b = 0.25\). Wall, holes, and steady states marked as indicated previously. Each example has one hole in the positive quadrant. (a) \(c = 1.5\). (b) \(c = 1.0\). (c) \(c = 0.5\).

4. Hyperbolic PDE theory: Shocks and discontinuities. Introducing a third variable \(u = \frac{\partial g}{\partial x}\), consider the scaled generic chemotaxis problem (2.7) and (2.8) as a hyperbolic system, namely,

\[
\begin{align*}
\frac{\partial n}{\partial t} &= -\frac{\partial}{\partial x}(nu) + f(n, g) = -u \frac{\partial n}{\partial x} - n \frac{\partial u}{\partial x} + f(n, g), \\
\frac{\partial u}{\partial t} &= h_n \frac{\partial n}{\partial x} + h_g \frac{\partial g}{\partial x}, \\
\frac{\partial g}{\partial t} &= h(n, g),
\end{align*}
\]

which in matrix form becomes

\[
\frac{\partial}{\partial t} \begin{bmatrix} n \\ u \\ g \end{bmatrix} + \begin{bmatrix} u & n & 0 \\ -h_n & 0 & -h_g \\ 0 & 0 & 0 \end{bmatrix} \frac{\partial}{\partial x} \begin{bmatrix} n \\ u \\ g \end{bmatrix} = \begin{bmatrix} f \\ 0 \\ h \end{bmatrix}.
\]

The characteristic slopes are determined from the eigenvalues of the \(3 \times 3\) matrix in (4.4). These are solutions of

\[
\lambda [(u - \lambda)(\lambda) - nh_n] = 0.
\]

There are three distinct solutions for \(h_n < 0\) and \(n > 0\). This confirms that the
system is strictly hyperbolic [21] with

$$\lambda_1 = \frac{1}{2} \left[ u - \sqrt{u^2 - 4nh_n} \right] \leq \lambda_2 = 0 \leq \lambda_3 = \frac{1}{2} \left[ u + \sqrt{u^2 - 4nh_n} \right].$$  

(4.6)

The characteristics have gradient $dx/dt = \lambda_i$, which is never infinite, so the line $t = 0$ is nowhere tangent to a characteristic. Hence if initial data for $n, u, g$ is given along the line $t = 0$, the resulting Cauchy problem is well posed. By considering the matrix of right eigenvectors, which correspond to each $\lambda_i$, the $\lambda_2$ field is always linearly degenerate, and the $\lambda_1$ and $\lambda_3$ fields are genuinely nonlinear characteristic fields for $(n, u, g)$ in the positive quadrant.

A shock (i.e., a curve separating intersecting characteristics defining a discontinuity in at least one of the variables on either side of the curve) may exist in either of the two genuinely nonlinear fields. We are looking for a shock that propagates with the travelling wave speed $c$, since all the information on a travelling wave moves with this speed. Following Marchant [11], [12], the Lax entropy condition ensures that the shocks are physically relevant [4]; hence, since the wave speed $c > 0$, only the $\lambda_3$ field is relevant.

### 4.1. Shock conditions.

We write the system (4.4) in conservation form,

$$\frac{\partial P}{\partial t} + \frac{\partial Q}{\partial x} = S,$$  

(4.7)

where

$$P = \begin{bmatrix} n \\ u \\ g \end{bmatrix}, \quad Q = \begin{bmatrix} nu \\ -h \\ 0 \end{bmatrix}, \quad S = \begin{bmatrix} f \\ 0 \\ h \end{bmatrix}.$$  

(4.8)

The Rankine–Hugoniot jump condition [4] defining the shock moving with velocity $c$ in the third field is

$$[P] c = [Q],$$  

(4.9)

where $[q]$ denotes the jump in the quantity $q$. For our system this gives

$$[n] c = [nu],$$  

(4.10)

$$[u] c = [-h],$$  

(4.11)

$$[g] c = 0.$$  

(4.12)

Since $u = \frac{\partial g}{\partial x} = -\frac{1}{c} h$, the second equation always holds, while the third equation says that there is no discontinuity in $g$. Using the definition of $u$ and our particular choice of (dimensionless) kinetic term $h = bg(1 - g) - ng$, the first equation gives

$$[n] c = [nu] = \left[ -\frac{1}{c} nh \right]$$  

(4.13)

$$= -\frac{1}{c} bgn(1 - g) - n^2 g$$  

$$= -\frac{1}{c} bgn(1 - g) + \frac{1}{c} g[n^2].$$

This simplifies to

$$(c^2 + bg(1 - g)) [n] = g [n^2].$$  

(4.14)
Using the definition \[ |n| = n_L - n_R, \] where \( n_L \) and \( n_R \) are the values of \( n \) on either side of the shock, (4.14) and (4.12) reduce to

\[
(4.15) \quad n_L + n_R = \frac{1}{g} \left( c^2 + bg(1 - g) \right), \quad g_L = g_R.
\]

Recall that the wall-of-singularities satisfies (3.1). Hence, the geometric center of the jump \( \frac{1}{2}(n_L + n_R) \) lies exactly on the wall-of-singularities, and therefore any jump takes the trajectory to the other side of the wall. Of course, a jump is only allowable if \( n_R > 0 \). Note that the Lax entropy condition [4] for the \( \lambda_3 \) field is satisfied only if \( n_L > n_R \).

4.2. **Power series.** The trajectories needed to construct a travelling shock wave can be determined by power series solutions. Equations (2.11) and (2.12) can be written in the form

\[
(4.16) \quad \frac{dn}{dg} = -\frac{ng}{[1 + \frac{g}{2}(b(1 - g) - 2n)][bg(1 - g) - ng]}.
\]

Solutions \( n(g) \) can be found by expanding in powers about special points. Such points are steady-state solutions to the system and holes in the wall. Let \((g_s, n_s)\) be such a point, and then write

\[
(4.17) \quad g = g_s + f,
\]

\[
(4.18) \quad n(g) = n_s + \alpha_1 f + \alpha_2 f^2 + \alpha_3 f^3 + \cdots.
\]

The coefficients \( \alpha_i \) are determined sequentially by substituting into (4.16) and then matching powers of \( f \). The resulting power series has a radius of convergence defined by the analyticity of the right-hand side of (4.16). This term is not analytic along the wall, and the lines \( g = 0 \) and \( n = bg(1 - g) \). Below we will be generating a power series about a hole in the wall and around \((1,0)\).

5. Phase plane revisited.

5.1. **Production rate of \( g \) satisfies \( 0 < b < 1 \).** We now show how to construct a travelling shock wave to the example in Figure 3.1(c), where there is one hole in the wall in the positive quadrant. This is illustrated in Figure 5.1(a). We first determine the power series about this hole and find that there are two possible values of \( \alpha_1 \). Each of these values provides unique values of the other \( \alpha_i \); hence we obtain two trajectories through the hole in the wall. One of these passes through the \( n \)-axis at \( n = 1 \), and this is the one of interest. Points on this curve, to the right of the hole, are possible values of \( n_L \). We next determine the power series through \((1,0)\) and determine its intersection with the wall (the limit of its convergence). To the right of this, we determine the curve which lies below the wall, which marks the outer envelope of the possible points for \( n_R \), such that the midpoint of the shock lies on the wall. There is a unique value of \( g \) that satisfies the jump conditions (4.15). Hence we obtain two trajectories, one allowing passage through the hole, and, by recrossing the wall with a jump discontinuity, the other connecting to the steady state on the \( g \)-axis. The corresponding \( n(z) \) and \( g(z) \) are shown in Figure 5.1(b) (where we have arbitrarily placed the shock at \( z = 0 \)).

This example illustrates two interesting facts about the solutions for \( n \). For wave speed sufficiently large, a unique smooth travelling solution exists between the steady states \((0,1)\) and \((1,0)\). Furthermore, there exists a sufficiently large cellular growth
rate such that smooth solutions no longer exist and a travelling wave with a shock exists. Alternatively, for fixed $a$ and $b$, there is a minimum wave speed such that smooth travelling wave solutions exist for $c > c_{\text{crit}}$. We have also found that if $c$ is decreased further, travelling shock wave solutions exist for $c_{\text{min}} < c < c_{\text{crit}}$. The $c_{\text{min}}$ is the value which determines the trajectory which jumps directly to the steady state $(1,0)$. For $0 < c < c_{\text{min}}$, no smooth or nonsmooth trajectories exist, since to the right of the hole the distance between the wall and the trajectory through the hole is greater than the distance between the wall and the $g$-axis.

5.2. Production rate of $g$ satisfies $b > 1$. We now turn to increasing $b$. Within the range $0 < b < 1$, the qualitative behavior of the phase plane is the same as outlined here with $b = 0.25$. It remains qualitatively similar when $b = 1$, although now all trajectories (except the one along the $n$-axis) leave the point $(0, 1)$ horizontally. In Figure 5.2(a) there is a smooth trajectory corresponding to a travelling wave, and in Figure 5.2(b) there will be a trajectory with a jump corresponding to a travelling shock wave. However, as $b$ increases through unity, the steady state $(0, 1)$ changes from an unstable node to a saddle. The only outgoing trajectory emanating from this point is along the $n$-axis; hence there is no trajectory joining this point to $(1, 0)$. However, at the same time a new steady state moves into the positive quadrant, namely $(1 - \frac{1}{b}, 1)$, which is an unstable node if it lies below the wall (i.e., if $c^2 > 1 - \frac{1}{b}$), and is a saddle if it lies above the wall (i.e., if $c^2 < 1 - \frac{1}{b}$). We wish to determine whether a trajectory joining $(1 - \frac{1}{b}, 1)$ and $(1, 0)$ exists and whether it corresponds to smooth travelling wave solutions.

5.2.1. Sufficiently large wave speed: $c^2 > 1 - \frac{1}{b}$. In this case, both steady states are below the wall. Figure 5.3(a) shows that there is a trajectory connecting these two states. Again, when $a$ is increased as illustrated in Figure 5.3(b), these two states can be connected by a trajectory passing through a hole in the wall, allowing a jump discontinuity in $n$ with the wall lying at the midpoint of the jump. Hence again there is a transition from smooth travelling solutions to travelling solutions with a discontinuity.
Fig. 5.2. Phase plane for \((g, n)\) for increasing values of cellular growth rate \(a\). Here \(b = 1.0, c = 1.0\). Wall, holes, and steady states marked as indicated previously. (a) \(a = 0.5\), no holes. (b) \(a = 3.0\), one hole.

Fig. 5.3. Phase plane for \((g, n)\) for sufficiently large wave speed and increasing values of cellular growth rate \(a\). Here \(b = 1.5, c = 1.0\), and so \(c^2 > 1 - \frac{1}{b}\). Wall, holes, and steady states marked as indicated previously. (a) \(a = 0.5\), no holes. (b) \(a = 3.0\), one hole.

### 5.2.2. Sufficiently small wave speed: \(c^2 < 1 - \frac{1}{b}\).

In this case, both steady states are separated by the wall. The only possible way to connect them would be with a trajectory passing through a hole in the wall. In the two examples shown in Figure 5.4 (and in others we have tried), there appears to be no connection between these states. To understand the phase plane figures, it is useful to use a coordinate transformation similar to that employed by Pettet, McElwain, and Norbury [19], namely,

\[
\frac{d}{dZ} = \left[1 + \frac{g}{c^2}(b(1 - g) - 2n)\right] \frac{d}{dz}
\]

when \(1 + \frac{g}{c^2}(b(1 - g) - 2n) \neq 0\). Now the holes in the wall become new steady states, and the wall becomes a \(g\)-nullcline. Figure 5.5 gives the transformed phase plane corresponding to the examples in Figure 5.4. In Figure 5.5(a), the hole becomes a stable spiral, and the one on the \(g\)-axis is a stable node. It appears that there is a limit cycle in this example. Since there is no physical or biological interpretation of \(Z\), unlike \(z = x - ct\), it is not fruitful to pursue the limit cycle analysis here. In
5.3. Production rate of $g$ satisfies $b = 0$. In this case, the chemoattractant has no production term. Since this degenerate case is similar to other recent work [11], [12], [17], we just summarize the results. When $b = 0$, the steady state $(0, 0)$ is replaced by a continuum of steady states $(\bar{g}, 0)$. Smooth travelling waves exist between $(0, 1)$ and $(\bar{g}, 0)$ for $\bar{g} < \bar{g}_{\text{crit}}$, as shown in Figure 5.6. Using the power series method about the hole, we find that there are two values of $\alpha_1$, resulting in two trajectories through the hole in the wall. One of these passes through the $n$-axis at $n = 1$, and the other passes through the $g$-axis at $g = \bar{g}$, thus defining $\bar{g}_{\text{crit}}$. For $\bar{g}_{\text{crit}} < \bar{g} < \bar{g}_{\text{max}}$, the connecting trajectory passes through a hole in the wall and has a jump in it, satisfying the jump condition. The maximum value $\bar{g}_{\text{max}}$ is defined as the value of $g$ when the trajectory through the hole jumps directly to a point on the $g$-axis, that is, $n_R = 0$. 

Figure 5.5(b), one hole becomes an unstable spiral and the other a stable node, while the one on the $g$-axis is a saddle.
6. Asymptotic analysis for large wave speed $c$. We have demonstrated that there is a minimum wave speed for a smooth travelling wave to exist. The phase plane analysis does not actually allow for a calculation of the actual solution. It can be found numerically on a finite domain, but the numerical solution will always tend to the minimum wave speed (see Figure 2.1). Here we investigate the analytic form of the solution for large wave speed $c$, following Canosa [3]. We introduce a new space variable as $z = c\xi$ and $\epsilon = \frac{1}{2c}$ into (2.11)–(2.12) and obtain

\[ (1 + \epsilon g(b(1 - g) - 2n)) \frac{dn}{d\xi} = \epsilon ng[b(1 - 2g) - n] [b(1 - g) - n] - an(1 - n), \]  
\[ \frac{dg}{d\xi} = -(bg(1 - g) - ng). \]

For small $\epsilon$ we look for an asymptotic expansion of the solution in terms of $\epsilon$ as

\[ n = n_0 + \epsilon n_1 + \epsilon^2 n_2 + \cdots, \]
\[ g = g_0 + \epsilon g_1 + \epsilon^2 g_2 + \cdots. \]

Here we investigate the lowest order terms $n_0$ and $g_0$ of the solution. These satisfy

\[ \frac{dn_0}{d\xi} = -an_0(1 - n_0), \]
\[ \frac{dg_0}{d\xi} = -bg_0(1 - g_0) + n_0g_0. \]

The $n_0$ equation is decoupled and can be solved as

\[ n_0 = (1 + e^{a\xi})^{-1}, \]

where the integration constant has been chosen without any loss of generality so that $n_0(0) = \frac{1}{2}$. Equation (6.6) can be solved analytically, but it is in terms of hypergeometric functions, which is not very helpful. For $b = 0$, the solution is simply

\[ g_0 = (1 + e^{-a\xi})^{-1/a}, \]

so that $n_0 = 1 - g_0^a$. We see in Figure 6.1 that the numerical solution for $g_0$ when $0 < b < 1$ differs only slightly from the solution when $b = 0$, and all solutions for
Fig. 6.1. The lowest order solution profiles for \( n \) and \( g \) versus \( \xi = z/c \) for large wave speed \( c \). Here \( a = 1.0 \). The \( g \) curves depend on its production rate \( b \); here \( b = 0, 0.5, 1.0, \) and \( 1.5 \).

\( g_0 \) tend to zero as \( \xi \to -\infty \). For \( b > 1 \), \( g_0 \) tends to \( 1 - \frac{1}{b} \). Increasing the cellular growth rate \( a \) steepens the gradient of the front for \( n_0 \), as expected from our previous analysis. In particular, the slope \(-\partial n/\partial \xi(0) = a\), and so it increases linearly with \( a \) and is independent of \( b \) to lowest order.

7. Conclusions. In this article we have considered a simple mathematical model of cell migration, where the dominant mechanism driving the migration is the phenomenon of chemotaxis. Such models have been explored in a number of contexts, generally with the view to seeking travelling wave solutions that may in some way characterize the front of invasion.

We have explored the possibility of the existence of both smooth-fronted and shock-fronted travelling wave solutions to a general model of chemotactic cell migration. Not surprisingly the mathematical model supports a rich variety of solutions exhibiting a family of identifiable characteristic behaviors such as shock-fronted travelling wave solutions with lower wave speeds than the smooth-fronted waves.

We have shown that for the model of chemotactic migration considered, for fixed \( a \) and \( 0 < b < 1 \), there is a minimum wave speed such that smooth travelling wave solutions exist between the steady states \((0,1)\) and \((1,0)\) for \( c > c_{\text{crit}} \). We have also found that if \( c \) is decreased further, travelling shock wave solutions exist for \( c_{\text{min}} < c < c_{\text{crit}} \). The \( c_{\text{min}} \) is the value which gives the trajectory that jumps directly to the steady state \((1,0)\). For \( 0 < c < c_{\text{min}} \), no smooth or nonsmooth trajectories exist, since to the right of the hole in the wall, the distance between the wall and the trajectory through the hole is greater than the distance between the wall and the \( g \)-axis. A similar argument holds for the case of a sufficiently large wave speed \( c \), such that for fixed \( b \) and \( c \) it is possible to increase the cellular growth rate \( a \) through a critical value so that there is a transition from the existence of a smooth-fronted to a sharp-fronted travelling wave.

When \( b > 1 \), similar critical wave speeds can be found defining smooth and discontinuous travelling wave solutions between the steady states \((1 - \frac{1}{b}, 1)\) and \((1,0)\), but only if the steady states are both on the same side of the wall. If the wall separates these two steady states, then no travelling wave solutions appear to exist.

The wave speeds described above are dimensionless. In terms of dimensioned variables they correspond to \( \frac{v}{L} = \frac{v}{\sqrt{\chi \lambda_3 \kappa_1 \kappa_2}} \), using (2.5)–(2.6) and where \( v \) is dimensioned wave speed. Hence, converting bounds on \( c \) to bounds on \( \chi \), smooth travelling wave solutions exist for \( 0 < \chi < \chi_{\text{crit}} \), and travelling shock solutions exist for \( \chi_{\text{crit}} < \chi < \chi_{\text{max}} \). For \( \chi > \chi_{\text{max}} \), no smooth or nonsmooth trajectories exist.
These results have been obtained by considering a phase plane analysis for a coupled system of equations (2.11)–(2.12), along with power series solutions around some special points. It should be noted that, near the wall, this system is a singularly perturbed system, since then the coefficient multiplying the derivative in (2.11) is small and vanishes identically on the wall. Hence at the wall the system reduces to a differential-algebraic system. The dynamics near the wall could be decomposed into fast and slow times. Solutions consist of outer segments away from the wall and inner segments near the wall; matching occurs at holes in the wall. Such an approach could be used to establish our results theoretically. This is beyond the scope of this current paper, which is concerned with establishing the possibility of both smooth-fronted and shock-fronted travelling wave solutions to a general model of chemotactic cell migration.

Typically, migrating cell populations in invasive phenomena are characterized by a well-defined boundary. A nonlinear diffusive flux can capture this feature, but does not allow for shock solutions. Of particular interest here, though, is the possibility of representing sharp fronts to waves of invading cells by the simple chemotactic term, without the need for nonlinear diffusion. As presented here, the chemotactic cell migration model (2.1)–(2.2) supports jump discontinuities when $c_{\text{min}} < c < c_{\text{crit}}$. However, solutions with compact support exist only for $c = c_{\text{min}}$, whereas for $c_{\text{min}} < c < c_{\text{crit}}$ there is a smooth leading segment of the front ahead of the discontinuity. We anticipate that the minimum invasion speed solution (with $c_{\text{min}}$) will evolve as the stable solution, using a hyperbolic numerical solver, as indicated by Marchant and Norbury [13]. Furthermore, the numerical solutions in Figure 2.1 suggest that this may be the case, since as $\chi$ increases, corresponding to $c$ decreasing, the leading edge contracts. We are presently tackling these issues.

When cell population numbers are sufficiently dense to imply frequent and significant cell-cell interactions, the suitability of a diffusive flux term comes into question. In such circumstances, mathematical models of cell migration in which a chemotactic flux dominates over the diffusive flux are more appropriate. Being essentially hyperbolic in nature, these models have the potential to support shock-fronted solutions, which may be seen as a new paradigm for the representation of cell migration.

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REFERENCES

CHEMOTACTIC CELLULAR MIGRATION