Asymptotic Analysis of Traveling Cell Solutions of a Cell Motility Model

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Abstract

This paper uses formal asymptotic analysis to study the properties of traveling cell solutions of a one-dimensional cell motility model proposed by Mogilner and Verzi (2003). In an earlier paper (Choi, Lee and Lui, 2004), it was proved that Mogilner-Verzi's model admits traveling cell solutions that have a constant length and move with a constant speed. In this paper, we derive asymptotic formulas for the length and speed of the traveling cell. In addition, under the assumption that the length density of bundled filaments is large compared to the magnitudes of the other parameters in the model, we show that the traveling cell is linearly asymptotically stable.

1 Introduction

The movement of cells along surfaces is an important biological process that has been studied by the biologists for decades. Proper understanding of cell movement has many important applications such as in the study of metastasis of cancer cells, wound healing by skin cells, and locomotion of white blood cells responsible for proper functioning of the immune system. For the past thirty years, many mathematical models have been developed to describe certain aspects of cell movement such as protrusion at the front (Mogilner and Oster, 1996) or cell-substratum adhesions (Dembo et al., 1981; DiMilla et al., 1991). More recently, several mathematical models that describe the movement of an entire cell have been developed (Bottino and Fauci, 1998; Bottino et al., 2002; Gracheva and Othmer, 2004; Mogilner et al., 2001; Mogilner and Verzi, 2003; Rubinstein, Jacobson and Mogilner, to appear). One such model is by Mogilner and Verzi (2003) which describes the crawling movement of a nematode sperm cell on a surface. Nematode sperm cell is MSP (major sperm protein) based and lacks motor protein and hence their movement is easier to model than actin-based cells. Using

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mass balance, Mogilner and Verzi proposed the following system of equations for their model:

$$\begin{cases} \dfrac{\partial b}{\partial t} & = & -\dfrac{\partial}{\partial x}(bv) - \gamma_b b \,, \\[2mm] \dfrac{\partial p}{\partial t} & = & -\dfrac{\partial}{\partial x}(pv) + \gamma_b b - \gamma_p p \,, \\[2mm] \dfrac{\partial c}{\partial t} & = & -\dfrac{\partial}{\partial x}(cv) \,. \end{cases} \tag{1.1}$$

In the above system, b, p denote the length densities of the bundled filaments and free filaments inside the cell, respectively, c is the density of the cytoskeletal nodes, v is the velocity of the cell, $\gamma_b = \gamma_b(y)$ is the rate of unbundling of the bundled filaments, $\gamma_p = \gamma_p(y)$ is the rate of disassembly of the free filaments, and y is the distance between x and the rear of the cell. See Mogilner and Verzi (2003) for a detail description of the model.

System (1.1) is assumed to hold between $r(t)$ and $f(t)$, which are the rear and front ends of the cell at time t, respectively. Hence, $y = x - r(t)$ in (1.1). Mogilner and Verzi (2003) assumed that

$$v(x,t) = \frac{1}{\xi}\frac{\partial \sigma}{\partial x} \tag{1.2}$$

where σ is the stress in the cell and $\xi = \xi(y)$ is the effective drag coefficient between the cell and the substratum. In their paper, they assume that σ is of the form

$$\sigma = Kb\left(\frac{1}{c} - \rho\right) + \kappa\frac{p}{c} \tag{1.3}$$

where K and κ are the effective spring constants for the bundled and free filaments, respectively, ρ is the rest length of the bundled filaments and the free filaments are assumed to have natural length 0. Formula (1.3) is based on Hooke's law and represents the sum of the forces created by the bundled and free filaments which are mounted between two cytoskeletal nodes whose average distance apart is $1/c$.

The boundary conditions for (1.1) are as follow. There is no stress at the front and rear so that $\sigma = 0$ on $r(t)$ and $f(t)$. Also, at the front, there is no free filament ($p = 0$) and the amount of bundled filaments is known ($b = b_0$). From (1.3), $c = 1/\rho$ at the front. Therefore, the boundary conditions at the front are:

$$\sigma = 0\,, \quad b = b_0\,, \quad p = 0\,, \quad \text{and} \quad c = \frac{1}{\rho}\,. \tag{1.4}$$

The boundary condition at the back is simply $\sigma = 0$.

The front and rear ends of the cell constitute the moving boundaries and need to be solved together with (1.1). Mogilner and Verzi (2003) assumed that the front and back movements are governed by the equations

$$\begin{cases} \dfrac{df}{dt} & = & V_p \left.\right|_{f(t)} + v \left.\right|_{f(t)} \,, \\[2mm] \dfrac{dr}{dt} & = & V_d + v \left.\right|_{r(t)} \end{cases} \tag{1.5}$$

where

$$V_p = V_0 \left[0.5 + \frac{1}{\pi} \arctan(\eta(y - L)) \right] \frac{L}{f(t) - r(t)} \tag{1.6}$$

is the rate of MSP polymerization at the front and $V_d > 0$ is the prescribed rate of disassembly of the free filaments at the rear. The exact form of V_p in (1.6) is not important. What is important is the fact that V_p is inversely proportional to the size of the cell so that polymerization is more rapid for smaller cells. We assume that initially the cell is of size ℓ_0 and, without loss of generality, we may assume that it lies on the interval $[0, \ell_0]$ so that $r(0) = 0$ and $f(0) = \ell_0$. Choi, Groulx and Lui (2004) proved that if $\gamma_p = 0$ in (1.1), $K = \kappa$ in (1.3) and the initial data satisfy some compatibility conditions which we shall not detail here, then there exists $\tau > 0$ such that the Mogilner-Verzi model admits a unique solution for $0 \leq t < \tau$. Suppose further that the initial data satisfy the condition $\sigma + \rho K b = \rho K b_0$, then it can be shown by the method of characteristics that this relation also holds inside the cell for all $t > 0$. From (1.3), $\xi v = -\rho K b_x$. System (1.1) and the boundary conditions (1.4), $\sigma(r, t) = 0$ may be reduced to the following problem on b:

$$\begin{cases} b_t &= \rho K \left(\frac{b\, b_x}{\xi} \right)_x - \gamma_b b \,, \\ b(r, t) &= b_0, \quad b(f, t) = b_0 \,. \end{cases} \tag{1.7}$$

Global existence of this moving boundary problem has been proved by Choi, Groulx and Lui (2004).

Remark: The above condition on the initial data may not always be necessary. Let $w = K(b + p)/c$. From system (1.1), w satisfies the hyperbolic equation $w_t + v w_x = 0$. Let Γ be the characteristic of the above hyperbolic equation starting from the point $(t, x) = (0, \ell_0)$. Suppose Γ intersects the rear $r(t)$ at some time $T > 0$. Then since $w = \rho K b_0$ on the front and w is constant along characteristics, $w = \rho K b_0$ in the region inside the cell above Γ. Hence, the assumption on the initial data is unnecessary if Γ intersects the rear and if we consider the solution for $t \geq T$.

For the rest of this paper, we shall focus on the simpler model (1.7). Using asymptotic analysis, we derive simple and explicit formulas for the speed and length of the traveling cell solution. Under the assumption that b_0 is large, we also show that the traveling cell solution is linearly asymptotically stable.

2   Traveling Cell Solutions

Traveling cell solutions are special solutions of the form $b(x, t) = \tilde{b}(x - kt)$. Biologically, this means that the cell maintains a constant shape and moves with a constant velocity k. Substituting this form of solution into (1.7), we have

$$\rho K \left[\frac{\tilde{b}\, \tilde{b}'}{\xi} \right]' + k\tilde{b}' - \gamma_b \tilde{b} = 0 \tag{2.1}$$

where $' = d/dy$. If the cell is of length ℓ and moves with a velocity k, then the back of the cell is located at $r(t) = kt$ and the front is located at $f(t) = kt + \ell$ so that

$$\tilde{b}(0) = b_0, \quad \tilde{b}(\ell) = b_0 \,. \tag{2.2}$$

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System (1.5) becomes

$$
\begin{cases}
k = V_p(\ell) - \rho K \dfrac{\tilde{b}_x(\ell)}{\xi(\ell)} \,, \\[3mm]
k = V_d - \rho K \dfrac{\tilde{b}_x(0)}{\xi(0)} \,.
\end{cases}
\tag{2.3}
$$

The existence of traveling cell solution is to find constants k, ℓ, and function $\tilde{b}$ defined on $[0, \ell]$ such that equations (2.1), (2.2) and (2.3) are satisfied. It was shown in Choi, Lee and Lui (2004) that under the hypotheses

(HA) There exists $\ell^* > 0$ such that
    (a) $V_p(\ell^*) = V_d$,
    (b) $V_p : (0, \ell^*] \to (0, \infty)$ is a C^1 function,
    (c) $V_p(\ell) \to \infty$ as $\ell \to 0^+$,
    (d) $V_p(\ell) > V_d$ for all $\ell \in (0, \ell^*)$ and
    (e) $V_p'(\ell^*) < 0$,

and

(HB) There exist positive constants $\gamma_0, \gamma_1, \xi_0, \xi_1$ such that
    (a) $\xi, \gamma_b \in C^1[0, \ell^*]$,
    (b) $\gamma_0 \le \gamma_b(y) \le \gamma_1$,
    (c) $\xi_0 \le \xi(y) \le \xi_1$,

there exists a traveling cell solution with speed $\overline{k}$ and length $\overline{\ell}$. Furthermore, if V_p is decreasing on $(0, \ell^*)$ and ξ and γ_b are constants, then the traveling cell solution is unique. These results are special cases of more general theorems proved in Choi, Lee and Lui (2004) where $K \ne \kappa$ was allowed and only the assumption $\gamma_p = 0$ was made. In Choi and Lui (2004), traveling cell solution was shown to exist assuming that γ_b and γ_p are constants but γ_p is not necessarily zero.

The following is the graph of the traveling cell solution $\tilde{b}$ obtained from solving equations (2.1), (2.2) and (2.3) using the dimensional parameter values given in Table II of Molginer and Verzi (2003). In particular, $b_0 = 500\,\mu m/\mu m$, $K = \kappa = 1\,pN/\mu m$, $V_0 = 3.2\,\mu m/s$, $\rho = 1\,\mu m$, $V_d = 1.25\,\mu m/s$, and $\gamma_b = 0.175/s$. The drag coefficient was assumed to be of the form

$$
\xi(y) = \alpha_\xi + \frac{2\beta_\xi}{\pi} arctan(\eta(y - L_c))
\tag{2.4}
$$

where $L_c = 11\,\mu m$ is the length of the cell body, $\alpha_\xi = 70\,pN \cdot s/\mu m^2$, $\beta_\xi = 50\,pN \cdot s/\mu m^2$ and $\eta = 1/\mu m$. We found that $\overline{k} \approx 1.31959\,\mu m/s$ and $\overline{\ell} \approx 0.78806\,\mu m$. Also, ℓ^*, defined in (HA), is approximately .8831. Note that b_0 is much larger in value than the other parameters. If we let $b_0 \downarrow 0$, then a boundary layer begins to develop near $x = 0$. Figure 2 shows the graph of $\tilde{b}$ when $b_0 = 1$ with the same set of parameter values except for b_0. We found that $\overline{k} \approx 1.38019\,\mu m/s$ and $\overline{\ell} \approx 0.79168\,\mu m$. These values do not seem to vary a lot with b_0.

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Figure 1. Graph of length density of bundled polymer b with b_0 = 500.

Figure 2. Graph of length density of bundled polymer b with b_0 = 1.
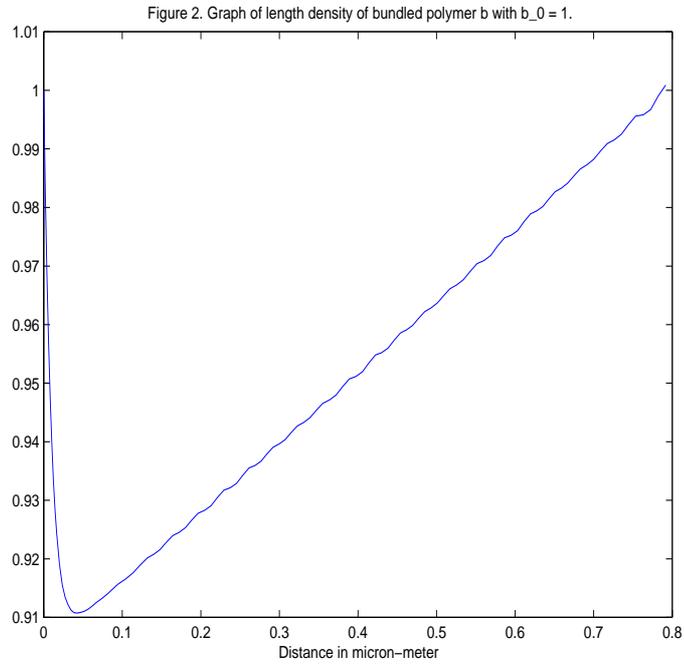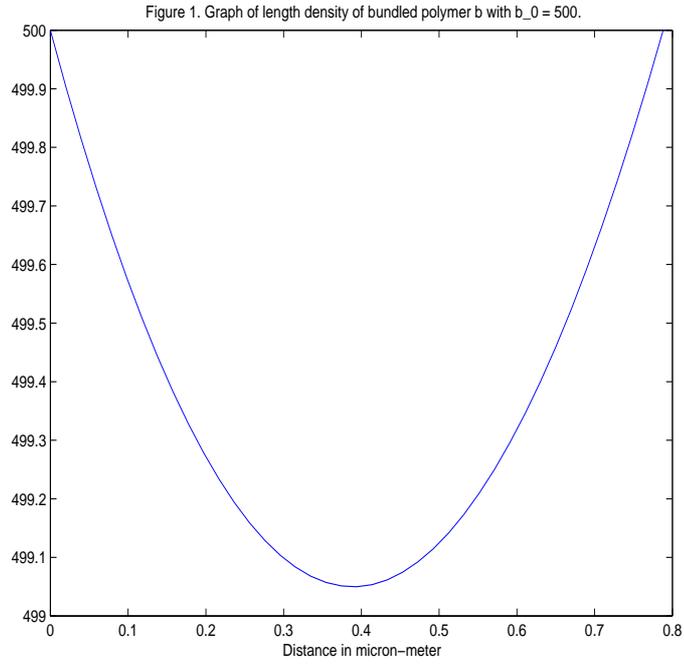
3   Asymptotic Analysis for Large b_0

In this section, we shall derive formulas for $\overline{k}$ and $\overline{\ell}$ assuming that b_0 is large compared to the magnitudes of the other parameters in the model. We first scale the domain $[0, \overline{\ell}]$ to $[0, 1]$ by

defining $\overline{x} = y/\overline{\ell}$ and letting $\tilde{b}(\overline{x}) = b(\overline{\ell}\overline{x})$. Then (2.1) becomes

$$
\begin{cases}
\dfrac{1}{\overline{\ell}^2}\left(\dfrac{\tilde{b}\,\tilde{b}'}{\xi}\right)' + \dfrac{\overline{k}}{K\rho\overline{\ell}}\,\tilde{b}' - \dfrac{\gamma_b}{K\rho}\,\tilde{b} = 0 \,, \\[2ex]
\tilde{b}(0) = b_0, \quad \tilde{b}(1) = b_0 \,.
\end{cases}
\tag{3.1}
$$

If we examine figure 1, we see that b is roughly a constant. Therefore, we assume that $b_0 = 1/\epsilon$ where $0 < \epsilon << 1$, and that $\tilde{b}$ has the formal asymptotic expansion

$$
\tilde{b}(x) = \dfrac{1}{\epsilon} + g(x) + \epsilon g_1(x) + \dots
\tag{3.2}
$$

where we have replaced $\overline{x}$ by x for simplicity in notation. Substituting this into (3.1) and comparing the $1/\epsilon$ terms, we have

$$
\dfrac{1}{\overline{\ell}^2}\left\{\dfrac{g'(x)}{\xi(\overline{\ell}x)}\right\}' - \dfrac{\gamma_b}{K\rho} = 0 \,.
$$

Strictly speaking we should also employ the expansions $\overline{\ell} = \overline{\ell}_0 + \epsilon\overline{\ell}_1 + \dots$ and $\overline{k} = \overline{k}_0 + \epsilon\overline{k}_1 + \dots$ in the above calculation. The $\overline{\ell}$ in the above equation is in fact $\overline{\ell}_0$. However this will complicate our notation and since we are interested only in the leading order effect, we shall use $\overline{\ell}$ for both $\overline{\ell}$ and its leading order expansion $\overline{\ell}_0$. A similar remark applies for $\overline{k}$.

Since $g(0) = g(1) = 0$, integrating the above equation, we have

$$
g(x) = \dfrac{\overline{\ell}^2}{K\rho}\int_0^x \xi(\overline{\ell}\tau)\,d\tau \int_0^\tau \gamma_b(\overline{\ell}t)dt - C_1 \int_0^x \xi(\overline{\ell}t)\,dt
$$

where

$$
C_1 = \dfrac{\overline{\ell}^2 \displaystyle\int_0^1 \xi(\overline{\ell}\tau)d\tau \int_0^\tau \gamma_b(\overline{\ell}t)dt}{K\rho \displaystyle\int_0^1 \xi(\overline{\ell}t)\,dt} \,.
$$

System (2.3) becomes

$$
\begin{cases}
\overline{k} = V_p(\overline{\ell}) - \dfrac{K\rho\tilde{b}_x(1)}{\overline{\ell}\,\xi(\overline{\ell})} \,, \\[2ex]
\overline{k} = V_d - \dfrac{K\rho\tilde{b}_x(0)}{\overline{\ell}\,\xi(0)} \,.
\end{cases}
\tag{3.3}
$$

From (3.2), we have

$$
\begin{cases}
\tilde{b}_x(0) = -C_1\xi(0) \,, \\[2ex]
\tilde{b}_x(1) = \left(\dfrac{\overline{\ell}^2}{K\rho}\int_0^1 \gamma_b(\overline{\ell}t)dt - C_1\right)\xi(\overline{\ell}) \,.
\end{cases}
\tag{3.4}
$$

Substituting these back into (3.3) and eliminating $\bar{k}$, we obtain, to leading order, our basic equation

$$\bar{\ell} \int_0^1 \gamma_b(\bar{\ell}t)dt - V_p(\bar{\ell}) + V_d = 0 \,. \tag{3.5}$$

From hypotheses (HA), the left side of (3.5) approaches $-\infty$ as $\bar{\ell} \downarrow 0$ and is positive at ℓ^*. Therefore, (3.5) has a solution $\bar{\ell} \in (0, \ell^*)$. Furthermore, if V_p is decreasing, this solution is unique (?). If we use the parameter values given near the end of last section and find the root of the above equation, we obtain $\bar{\ell} = 0.78803$ which is almost identical to $\bar{\ell} = 0.78806$ obtained from using shooting argument to find the traveling cell solution.

Once $\bar{\ell}$ is determined, the wave speed $\bar{k}$ may be obtained from either of the equations in (3.3). It is clear from the formula for C_1 that $\tilde{b}_x(0) < 0$ and $\tilde{b}_x(1) > 0$ so that $V_d < \bar{k} < V_p(\bar{\ell})$, which has already been proved in Choi, Lee and Lui (2004). Explicitly, to leading order,

$$\bar{k} = V_d + \frac{\bar{\ell} \int_0^1 \xi(\bar{\ell}\tau)d\tau \int_0^\tau \gamma_b(\bar{\ell}t)dt}{\int_0^1 \xi(\bar{\ell}t)\,dt} \,. \tag{3.6}$$

We have the following conclusions. Equation (3.5) says that to leading order the cell length is that value for which the rate of polymerization at the front is equal to the sum of the rate of disassembly of the free filaments at the rear and the total depolymerization of the bundled filaments throughout the cell. This length is independent of ρ, K and the drag coefficient ξ. While the traveling cell speed is also independent ρ and K, it is clear from (3.6) that $\bar{k}$ is independent of ξ only when the drag coefficient is a constant. Interchanging the order of integration, we can write (3.6) as

$$\bar{k} = V_d + \frac{\bar{\ell} \int_0^1 \gamma_b(\bar{\ell}t)dt \int_t^1 \xi(\bar{\ell}\tau)d\tau}{\int_0^1 \xi(\bar{\ell}t)\,dt} \,. \tag{3.7}$$

If $\xi(x) = \xi_0\delta(x)$ where $\delta(x)$ is the dirac delta function concentrated at the origin and ξ_0 is a positive constant, i.e. friction is concentrated at the rear, then (3.7) gives $\bar{k} = V_d$. On the other hand, when there is no friction except at the front, i.e. $\xi = \xi_0\delta(x - \bar{\ell})$, it can readily be checked using (3.7) and (3.5) that $\bar{k} = V_p(\bar{\ell})$. Such results reconcile with our intuition.

When γ_b is a constant, (3.6) becomes

$$\bar{k} = V_d + \gamma_b \frac{\int_0^{\bar{\ell}} x\xi(x)\,dx}{\int_0^{\bar{\ell}} \xi(x)\,dx} = V_d + \gamma_b\ell_c \,, \tag{3.8}$$

where ℓ_c is the center of mass for the function ξ on the interval $[0, \bar{\ell}]$. Therefore, greater frictional force at the front produces a faster moving cell.

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4 Asymptotic Analysis for Small b_0

In case b_0 is very small, figure 2 suggests that a boundary layer is formed near the rear of the cell. In this section we derive formulas for $\overline{k}$ and $\overline{\ell}$ for small b_0 using inner and outer expansion techniques.

Consider equations (2.1), (2.2) and (2.3) in §2. A boundary layer develops near the rear as $b_0 \downarrow 0$ since the convection velocity $\overline{k}$ is in the negative $x-$direction and its magnitude is large compared to the diffusion coefficient $\rho K b / \xi$. Let us first consider the outer expansion. Assume that b has the formal asymptotic expansion

$$b = \epsilon u(x) + \epsilon^2 u_1(x) + ... \quad \text{for } x \text{ bounded away from zero.} \tag{4.1}$$

Substituting (4.1) into (2.1) and comparing coefficients of the $O(\epsilon)$ terms, we have

$$\overline{k}u' - \gamma_b u = 0 \tag{4.2}$$

with boundary condition $u(\overline{\ell}) = 1$. This gives the outer solution

$$u(x) = \exp\left(-\frac{1}{\overline{k}} \int_x^{\overline{\ell}} \gamma_b(t)\, dt\right) . \tag{4.3}$$

Inside the boundary layer, we let $X = x/\epsilon$ and assume that the inner solution of b has an expansion of the form

$$b = \epsilon U(X) + \epsilon^2 U_1(X) + ... \quad \text{for } x \text{ close to } 0 \tag{4.4}$$

where $U(X) = U(x/\epsilon) = u(x)$. Substituting this into (2.1) and comparing the coefficients of the $O(\epsilon)$ terms, we have

$$\frac{\rho K}{\xi(0)}(UU')' + \overline{k}U' = 0 . \tag{4.5}$$

where $' = d/dX$. Integrating, we have

$$\frac{\rho K}{\xi(0)}U' = \frac{C_1}{U} - \overline{k} \tag{4.6}$$

where C_1 is a constant to be determined. Since $b(0) = b_0 = \epsilon$, (4.4) implies that $U(0) = 1$. It is also clear from (4.6) that $U > 0$. Integrating (4.6), we have

$$\frac{\xi(0)}{\rho K}X + C_2 = -\frac{U}{\overline{k}} - \frac{C_1}{\overline{k}^2} \log|\overline{k}U - C_1| . \tag{4.7}$$

Since $U(0) = 1$, we have

$$C_2 = -\frac{1}{\overline{k}} - \frac{C_1}{\overline{k}^2} \log|\overline{k} - C_1| . \tag{4.8}$$

For the inner and outer expansion to match, we need $\lim_{X \to \infty} U(X) = \lim_{x \to 0} u(x)$, i.e.,

$$\lim_{X \to \infty} U(X) = \exp\left(-\frac{1}{\overline{k}} \int_0^{\overline{\ell}} \gamma_b(t)\, dt\right) .$$

From (4.7), U approaches the constant $C_1/\overline{k}$ as $X \to \infty$ which implies that

$$C_1 = \overline{k} \exp\left(-\frac{1}{\overline{k}} \int_0^{\overline{\ell}} \gamma_b(t)\, dt\right) . \tag{4.9}$$

Thus $C_1 < \overline{k}$ and U is a decreasing function of X on the interval $[0, \infty)$ according to (4.6). Since the outer solution $u(x)$ is increasing on $(0,1)$, we have

$$\min_{0 \le x \le \overline{\ell}} b = b_0 \exp\left(-\frac{1}{\overline{k}} \int_0^{\overline{\ell}} \gamma_b(t)\, dt\right) . \tag{4.10}$$

Moreover $b_x(0) < 0$ and $b_x(1) > 0$ so that (2.3) implies that $V_d < \overline{k} < V_p(\overline{\ell})$.

Having determined C_1 and C_2, the asymptotic solution is completely known provided that $\overline{k}$ and $\overline{\ell}$ can be computed. Since $b_x(\overline{\ell}) = \epsilon u_x(\overline{\ell})$, which is $O(\epsilon)$, (2.3a) gives $\overline{k} = V_p(\overline{\ell})$ to leading order. From (4.6), $b_x(0) = U_X(0) = (C_1 - \overline{k})\xi(0)/\rho K$ and (2.3b) implies that $\overline{k} = V_d - (C_1 - \overline{k})$. Thus, the traveling speed $\overline{k}$ and cell length $\overline{\ell}$ may be calculated from

$$\begin{cases} \overline{k} = V_p(\overline{\ell}) , \\[2mm] V_d = \overline{k} \exp\left(-\frac{1}{\overline{k}} \int_0^{\overline{\ell}} \gamma_b(t)\, dt\right) \end{cases} \tag{4.11}$$

if $b_0 << 1$. It is clear that both $\overline{k}$ and $\overline{\ell}$ are independent of ρ, K and the function ξ. Eliminating $\overline{k}$ from the above equations, $\overline{\ell}$ satisfies the equation

$$V_p(\overline{\ell}) \exp\left(-\frac{1}{V_p(\overline{\ell})} \int_0^{\overline{\ell}} \gamma_b(t)\, dt\right) - V_d = 0 . \tag{4.12}$$

Let the left side of (4.12) be denoted by $h(\overline{\ell})$. Then (HA)(c) implies that $\lim_{\overline{\ell}\downarrow 0} h(\overline{\ell}) > 0$. On the other hand, (HA)(a) implies that $h(\ell^*) < 0$. Hence, equation (4.12) has a root $\overline{\ell} \in (0, \ell^*)$. If V_p is a decreasing function, it can be easily checked that $h' < 0$ and hence this root is unique. Once we have found $\overline{\ell}$, we can compute $\overline{k}$ from either of the equations (4.11). As an example, consider the data set given near the end of §2 with $b_0 = 1$. Using Matlab to solve equation (4.12), we obtain $\overline{\ell} \approx 0.79177 \mu m$ and $\overline{k} \approx 1.38184\, \mu m/s$. We recall from section 2 that $\overline{\ell} \approx 0.79168\, \mu m$ and $\overline{k} \approx 1.38019\, \mu m/s$ from the traveling cell solution. From (4.10), the minimum of b is approximately $0.9046\, \mu m/\mu m$ which is roughly what figure 2 shows.

5 Linearized Stability

As mentioned in §1, global existence of the moving boundary problem (1.7) and (1.5) has been proved by Choi, Groulx and Lui (2004). In this section, we shall present a formal argument that the traveling cell solution is linearly asymptotically stable if $b_0 >> 1$. We shall assume that ξ is a positive constant for otherwise the algebra will become very involved. To prove linearized stability, one must first straighten out the moving boundaries, derive the linearized system and then show that

the eigenvalues of the linearized system have negative real parts. The derivation of the linearized system is very technical and we only document the results here.

Let $\xi = \xi_0 > 0$ and let $u = b - \tilde{b}$, $\zeta_1 = \ell - \bar{\ell}$ where $\tilde{b}$ is the traveling cell solution described in §2. Then the linearized system is

$$\begin{cases} u_t & = & Lu - p(x)\zeta_1 - E_1 u \\ \\ \zeta_1' & = & \left[V_p'(\bar{\ell}) + \dfrac{V_p(\bar{\ell}) - V_d}{\bar{\ell}} \right] \zeta_1 + E_2 u \end{cases} \tag{5.1}$$

where

$$\begin{cases} Lu & = & \dfrac{\rho K}{\bar{\ell}^2 \xi_0} \left(\tilde{b} u \right)_{xx} + \dfrac{\bar{k}}{\bar{\ell}} u_x - \gamma_b\, u \\ \\ p(x) & = & \dfrac{2}{\bar{\ell}} (\gamma_b \tilde{b}) - \dfrac{V_d \tilde{b}_x}{\bar{\ell}^2} - \dfrac{x \tilde{b}_x}{\bar{\ell}} A_{\bar{\ell}} \\ \\ A_{\bar{\ell}} & = & \left[V_p'(\bar{\ell}) + \dfrac{V_p(\bar{\ell}) - V_d}{\bar{\ell}} \right] \\ \\ E_1 u & = & \dfrac{\rho K \tilde{b}_x}{\bar{\ell}^2 \xi_0} \left[x u_x(1) + (1 - x) u_x(0) \right] \quad \text{and} \\ \\ E_2 u & = & \dfrac{\rho K}{\xi_0} \left(\dfrac{u_x(0, t) - u_x(1, t)}{\bar{\ell}} \right) . \end{cases} \tag{5.2}$$

Let $u(x, t) = \phi(x) e^{\lambda t}$ and $\zeta_1(t) = c e^{\lambda t}$, then (5.1) becomes

$$\begin{cases} L\phi - p(x)c - E_1\phi & = & \lambda\,\phi \\ \\ A_{\bar{\ell}} c + E_2 \phi & = & \lambda\, c \end{cases} \tag{5.3}$$

We now show that under the assumption (3.2), the leading order of any eigenvalue λ of (5.3) is real and negative. We can actually derive a formula for the leading order term that agrees well with the numerical solutions of (5.3).

Let

$$\tilde{b} = \frac{1}{\epsilon} + g + \epsilon g_1 + \dots$$

$$\lambda = \frac{1}{\epsilon} \lambda_{-1} + \lambda_0 + \epsilon \lambda_1 + \dots$$

$$\phi = \frac{1}{\epsilon} \phi_{-1} + \phi_0 + \epsilon \phi_1 + \dots .$$

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There are three cases to consider:

Case 1: $c = 0$.

System (5.3) becomes

$$\begin{cases} \dfrac{\rho K}{\overline{\ell}^2 \xi_0}(\tilde{b}\phi)_{xx} + \dfrac{\overline{k}}{\overline{\ell}}\phi_x - \gamma_b\phi - \dfrac{\rho K\tilde{b}_x}{\overline{\ell}^2 \xi_0}[x\phi_x(1) + (1-x)\phi_x(0)] &= \lambda\phi \\[4mm] E_2\phi &= 0\,. \end{cases}$$

Looking at the $1/\epsilon^2$ term, we have

$$\frac{\rho K}{\overline{\ell}^2 \xi_0}(\phi_{-1})_{xx} = \lambda_{-1}\phi_{-1}\,.$$

Together with the boundary conditions $\phi(0) = \phi(1) = 0$, this gives $\lambda_{-1} = -\rho K n^2 \pi^2/\xi_0\overline{\ell}^2$ and $\phi_{-1}(x) = A_n \sin(n\pi x)$ for some $A_n \neq 0, n = 1, 2, 3, \ldots$. The condition $E_2\phi_{-1} = 0$ reduces to $n\pi A_n [1 - (-1)^n] = 0$ which can only be satisfied if n is even.

Case 2: $c \neq 0$, $\lambda_{-1} \neq 0$

We can divide the two equations in (5.3) by c and let $\psi = \phi/c$. System (5.3) becomes

$$\begin{cases} \dfrac{\rho K}{\overline{\ell}^2 \xi_0}(\tilde{b}\psi)_{xx} + \dfrac{\overline{k}}{\overline{\ell}}\psi_x - \gamma_b\psi - \dfrac{\rho K\tilde{b}_x}{\overline{\ell}^2 \xi_0}[x\psi_x(1) + (1-x)\psi_x(0)] - p(x) &= \lambda\psi \\[4mm] E_2\psi + A_{\overline{\ell}} &= \lambda\,. \end{cases}$$

Comparing the $1/\epsilon^2$ term in the first equation and $1/\epsilon$ term in the second equation, we have

$$\begin{cases} \dfrac{\rho K}{\overline{\ell}^2 \xi_0}(\psi_{-1})_{xx} &= \lambda_{-1}\psi_{-1} \\[4mm] E_2\psi_{-1} &= \lambda_{-1}\,. \end{cases}$$

Proceeding as before, we have $\lambda_{-1} = -\rho K n^2 \pi^2/\xi_0\overline{\ell}^2$ and $\psi_{-1} = A_n \sin(n\pi x)$ for some $A_n, n = 1, 2, 3, \ldots$. The second equation above becomes

$$A_n \frac{\rho K}{\xi_0}\frac{n\pi}{\overline{\ell}}[1 - (-1)^n] = -\frac{\rho K n^2 \pi^2}{\xi_0\overline{\ell}^2}$$

which can be satisfied only if n is odd. The magnitude of A_n is fixed in this case since we have already normalized the eigenfunction (ϕ, c) so that $c = 1$.

Case 3: $c \neq 0$, $\lambda_{-1} = 0$.

For this case $\psi_{-1} = 0$ so that we have

$$
\begin{cases}
\dfrac{\rho K}{\bar{\ell}^2 \xi_0}(\psi_0)_{xx} - \dfrac{2\gamma_b}{\bar{\ell}} &= 0 \\[3mm]
E_2\psi_0 + A_{\bar{\ell}} &= \lambda_0 \,,
\end{cases}
$$

where $\gamma_b = \gamma_b(\bar{\ell}x)$. With boundary conditions $\psi_0(0) = \psi_0(1) = 0$, the first equation yields

$$
\psi_0(x) = \frac{2\xi_0\bar{\ell}}{\rho K}\int_0^x (x-t)\gamma_b(\bar{\ell}t)\,dt - \frac{2\xi_0\bar{\ell}x}{\rho K}\int_0^1 (1-t)\gamma_b(\bar{\ell}t)\,dt \,.
$$

The second equation then gives $\lambda_0 = -2\int_0^1 \gamma_b(\bar{\ell}t)\,dt + A_{\bar{\ell}}$. Since $\bar{\ell}$ satisfies (3.5), we have $\lambda_0 = V_p'(\bar{\ell}) - \int_0^1 \gamma_b(\bar{\ell}t)\,dt$.

Summary: Let $b_0 = 1/\epsilon$. Then, to leading order, the eigenvalues of (5.3) are

$$
\begin{cases}
\lambda &= -\dfrac{\rho K b_0 n^2 \pi^2}{\xi_0 \bar{\ell}^2}\,, \quad n = 1, 2, 3, \ldots \\[4mm]
\lambda &= V_p'(\bar{\ell}) - \displaystyle\int_0^1 \gamma_b(\bar{\ell}t)\,dt \,.
\end{cases}
\tag{5.4}
$$

A necessary and sufficient condition for the traveling cell solution to be linearly asymptotically stable is

$$
V_p'(\bar{\ell}) < \int_0^1 \gamma_b(\bar{\ell}t)\,dt \,.
\tag{5.5}
$$

In particular, if V_p is a decreasing function of ℓ, then (5.5) always holds and the traveling cell solution is linearly asymptotically stable.

Table 1 compares the relative errors between the 12 largest eigenvalues obtained from numerically solving equation (5.3) and using the above formula. The numerical calculation was done by discretizing the interval $[0, 1]$ into 1000 equal parts and calling the Matlab function *eig* to find the eigenvalues of the resulting matrix. The traveling cell solution $\tilde{b}$ was obtained by a shooting argument using the set of dimensional parameter values found in Table 2 of the paper Molginer and Verzi (2003). Note that the largest eigenvalue, given by (5.4b) is significantly larger than the rest of the eigenvalues. Relative errors are calculated using the formula $|(a - b)/b| \times 100$ where b is the value obtained from (5.4). The numerical calculations are inaccurate for large eigenvalues but the largest 100 eigenvalues all have relative error less than 1%.

6 Summary and Discussion

Many cells possess the ability to crawl over surfaces and it is well known that cell movement is important for the proper functioning of many physiological processes. Although recently many mathematical models have been developed to model the movement of a single cell (see the references given in §1), very few of these models have been rigorously analyzed. This paper is an attempt to

Table 1: Comparison of 12 largest eigenvalues

Using (5.4)	Solving (5.3) numerically	Relative Error
-41807.697120	-41749.583857	0.139001
-34551.815801	-34504.205390	0.137794
-27986.970799	-27948.659114	0.136891
-22113.162113	-22082.983561	0.136473
-16930.389743	-16907.269524	0.136560
-12438.653688	-12421.525704	0.137700
-8637.953950	-8625.854456	0.140074
-5528.290528	-5520.212489	0.146122
-3109.663422	-3104.763214	0.157580
-1382.072632	-1379.315927	0.199462
-345.518158	-344.655110	0.249784
-1.800790	-1.803155	0.131375

study one of these models using formal asymptotic analysis. The model we chose to analyze was proposed by Mogilner and Verzi in 2003 to describe the movement of a nematode sperm cell, *Ascaris suum*. Most animal cells are actin based. One of the main differences between a nematode sperm cell and an actin based cell is that the former lacks motor protein (myosin) which is responsible for the contraction at the rear of an actin based cell. Molginer and Verzi (2003) models the contraction at the rear by the disassembly and unbundling of the free filaments which releases energy, causes contraction at the rear, and thus pulls the cell body forward. Although most animal cells are actin-based, a mathematically consistent model describing the crawling motion of an actin-based cell is, to the best of our knowledge, still forthcoming. Mathematically consistent here means that the model should at least be shown to have a solution locally in time.

Molginer and Verzi's model is mathematically consistent and gives rise to a moving boundary problem. It was shown by Choi, Lee and Lui (2004) that under some assumptions, traveling cell solutions exist for this model. A traveling cell has a cell length and a velocity, and it is important to know how these two quantities depend on the parameters of the model. Using formal asymptotic analysis, we derived formulas for the cell length and velocity of the traveling cell when the length density of the bundled filaments (b_0) at the front is very large and very small. The two curves shown in Figure 1 are produced by the same set of data as in Molginer and Verzi (2003) using these formulas. The upper curve is produced by formulas (4.12) and (4.11a) while the lower curve is produced by formulas (3.5) and (3.8) with the rate of unbundling (γ_b) ranging between $0.1/s$ and $2.0/s$. Note that the curves are relatively close to each other considering the fact that b_0 is near zero in one case and near infinity in the other.
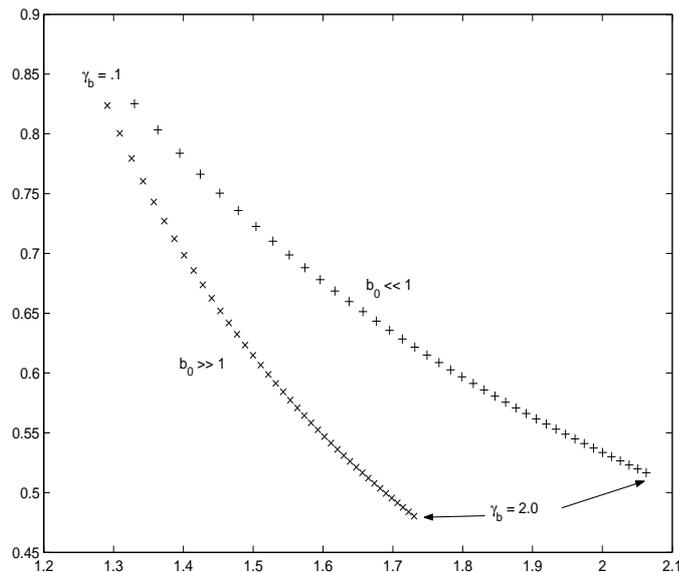
Fig. 1. Graphs of $\bar{\ell}$ versus $\bar{k}$ for small and large b_0 with varying γ_b.

After establishing a traveling cell solution exists, one would like to know if such a solution is stable. Proving the stability of traveling wave solution is mathematically very challenging and there is a large amount of literature devoted to it. The starting point of the proof is usually to study the spectrum of the linear operator obtained by linearizing the evolution equation or system about the traveling wave. For our model, we are able to derive asymptotic formulas for the eigenvalues of the linearized operator for b_0 very large. These eigenvalues are all real and agree well with those obtained by numerical simulation. Since the traveling cell solution develops a boundary layer as $b_0 \downarrow 0$, we are unable to compute the eigenvalues when b_0 is near zero. However, we conjecture that all the eigenvalues of (5.3) are real and so far we are able to prove that any *real* eigenvalue of (5.3) must be negative so that our conjecture would imply that the traveling cell solution is linearly asymptotically stable. The conjecture is difficult to prove since (5.3) is a non-selfadjoint, nonlocal system.

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